NUCLEIC ACIDS

Examples: **1.** Deoxyribonucleic acid (**DNA**) **2.** Ribonucleic acid (**RNA**)

GENERAL STRUCTURE OF NUCLEIC ACIDS – *(Describe the structure of nucleic acids /a nucleic acid)*

Nucleic acids are **polymers** made of subunits called **nucleotides.**

A **nucleotide** is made up of three molecules:

(i) Phosphate group

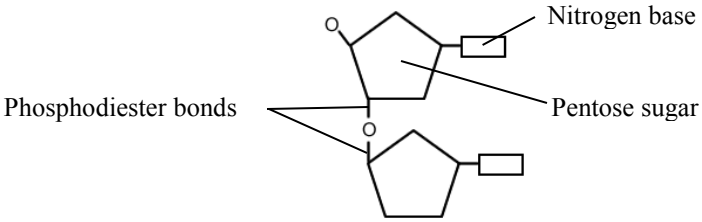
(ii) Pentose sugar – either Deoxyribose (in DNA) or Ribose (in RNA)

(iii) Nitrogen base – any purine (Adenine, Guanine) or pyrimidine (Cytosine and either Thymine in DNA or Uracil in RNA)

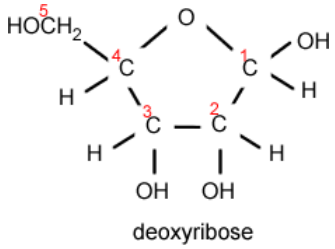
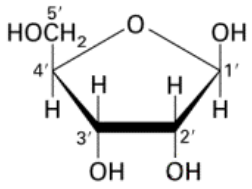
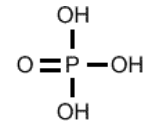
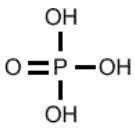
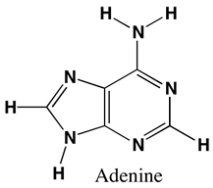
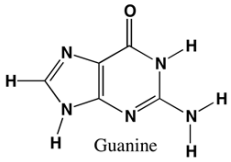
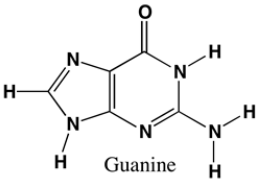
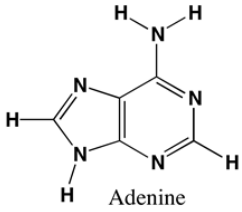
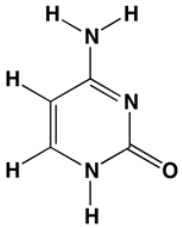
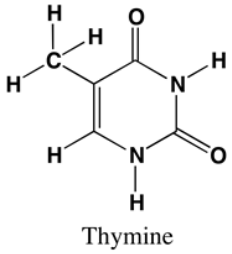
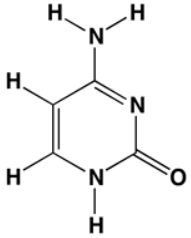
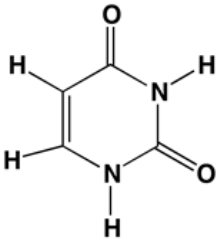
Nucleoside forms when a pentose sugar joins an organic base by **condensation reaction** (a **water molecule** is lost).

Nucleotide forms when a **nucleoside** (pentose sugar + organic base) joins a phosphate by loss of **second water molecule.**

The **sugar-phosphate-sugar backbone** is formed when the 3' carbon on one sugar joins to the 5' carbon on the next sugar by **phosphodiester bonds** repeatedly to form a **polynucleotide** (long chain of nucleotides) with organic bases protruding sideways from sugars.



COMPONENTS OF NUCLEOTIDES

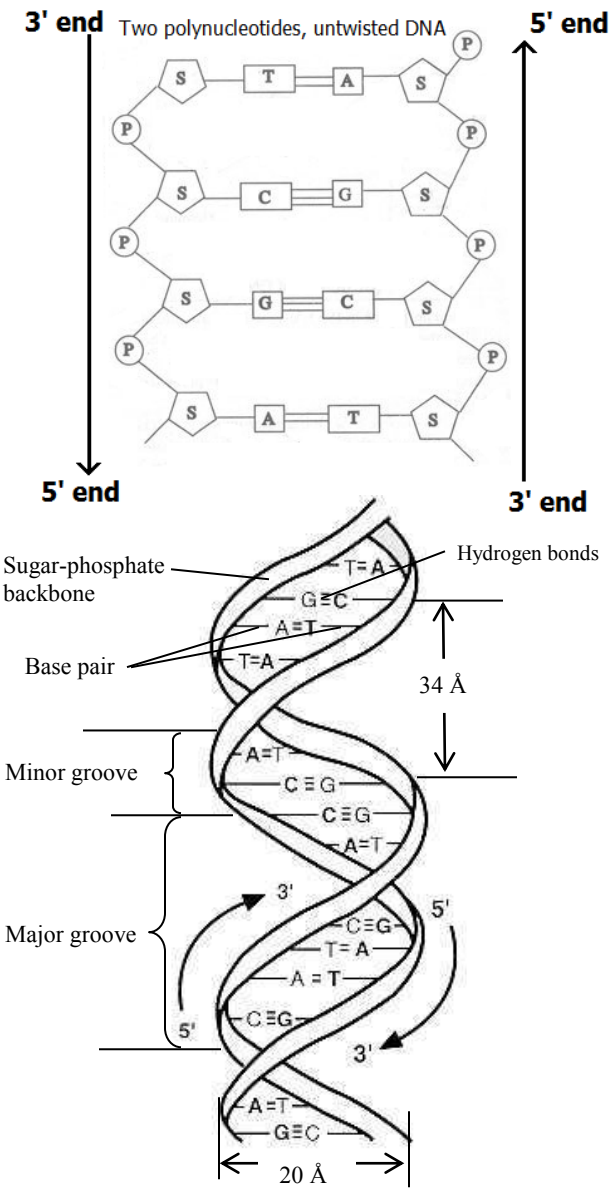
MOLECULE	DNA	RNA
Pentose sugar	 deoxyribose	 **Ribose**
Phosphoric acid	 Phosphoric acid	 Phosphoric acid
Purines (Double ringed organic bases)	 Adenine  Guanine	 Guanine  Adenine
Pyrimidines (Single ringed organic bases)	 Cytosine  Thymine	 Cytosine  Uracil

DNA STRUCTURE ACCORDING TO WATSON AND CRICK

- DNA is a very large polymer of **nucleotides**.
- A DNA **nucleotide** is made up of three molecules:

(i) Phosphate group
(ii) Deoxyribose sugar
(iii) Nitrogen base - either adenine **(A)**, guanine **(G)**, thymine **(T)** or cytosine **(C)**.

- The polynucleotide stands are antiparallel (face in opposite directions) i.e. one runs from 3' to 5' direction while another runs from 5' to 3' direction.
- Untwisted DNA is ladder-like, in which the sugar-phosphate backbones represent the handrails while the nitrogen base pairs represent the rungs.
- Twisted DNA forms a double helix of major and minor grooves.
- The sugar-phosphate-sugar backbone is held by covalent **phosphodiester bonds,** while the nitrogen bases from the two strands form **weak hydrogen bonds** by complimentary base pairing i.e. A with T, C with G.



ADAPTATIONS OF DNA

(i) Sugar-phosphate backbone is held together by strong covalent phosphodiester bonds to provide stability.
(ii) The two sugar-phosphate backbones are antiparallel which enables purine and pyrimidine nitrogen bases to project towards each other for complimentary pairing.
(iii) Sugar-phosphate backbones are two / it is double stranded to provide stability.
(iv) The two sugar-phosphate backbones form a double helix to protect bases/hydrogen bonds.
(v) Long/large molecule for storage of much information.
(vi) Double helical structure makes the molecule compact to fit in the nucleus.
(vii) Base sequence allows information to be stored.
(viii) Double stranded for replication to occur semi-conservatively/ strands can act as templates.
(ix) There is complementary base pairing / A-T and G-C for accurate replication/identical copies can be made;
(x) Weak hydrogen bonds enable unzipping/separation of strands to occur readily.
(xi) There are many hydrogen bonds which increase stability of DNA molecule.

THEORIES OF DNA REPLICATION

DNA replication is the process by which the parent DNA molecule makes another copy of itself.

1. Fragmentation hypothesis (Dispersive hypothesis)

The parent DNA molecule breaks into segments and new nucleotides fill in the gaps precisely.

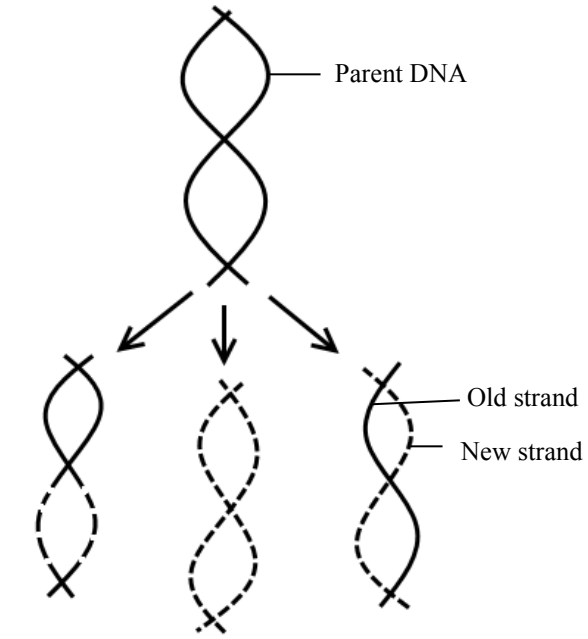
2. Conservative hypothesis

The complete parent DNA molecule acts as a template for the new daughter molecule, which is assembled from new nucleotides. The parent molecule is unchanged.

3. Semi-conservative hypothesis

The parent DNA molecule separates into its two component strands, each of which acts as a template for the formation of a new complementary strand. The two daughter molecules therefore contain half the parent DNA and half new DNA.
The semi conservative hypothesis was shown to be the true mechanism by the work of Meselsohn and Stahl (1958) in their experiment on bacterium *E.coli* using radioactive ^{15}N.

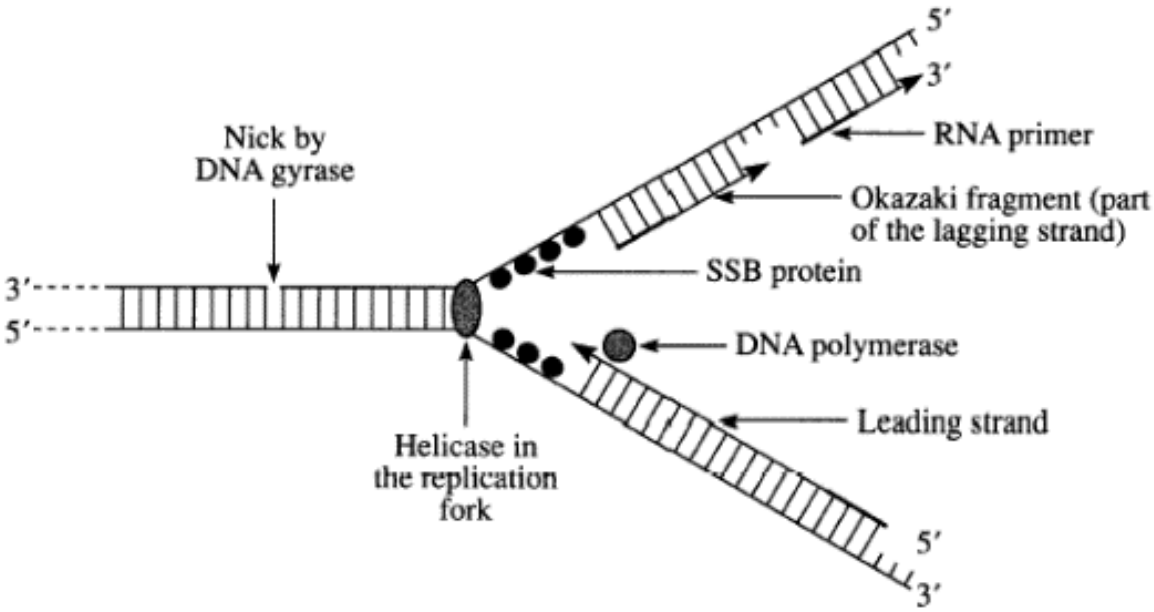
Illustration of three possible theories of DNA replication



DESCRIPTION OF DNA REPLICATION

- DNA replication is the process by which parent DNA molecule makes another copy of itself, **semi conservatively** (1 new, 1 old strand together).
- It occurs during the **synthesis** phase of interphase.
- **DNA Helicase** enzyme untwists and unzips DNA by breaking the hydrogen bonds to expose the bases, creating the Y-shaped **replication fork**, the two opened strands of DNA behind it (DNA is replicated a bit at a time and the whole molecule is never completely uncoiled).
- **RNA primase** enzyme lays down an RNA primer at the **3' end** of the old DNA strand to guide the action of **DNA polymerase**.
- **DNA polymerase** enzyme removes the RNA primer from the new strand then moves along the exposed base sequences, attaching free DNA nucleotides of complementary bases to create a new DNA strand as it goes.
- **DNA ligase** joins adjacent Okazaki fragments on the lagging strand (new strand laid down in the opposite direction of the replication fork) and any sections of new DNA on the leading strand (new strand laid down in the direction of the replication fork) that need to be joined.
- **DNA polymerase** reads the exposed code from **3' to 5'** end and therefore assembles the new strand from **5' to 3'end**
- Several molecules of **DNA polymerase** act simultaneously at multiple sites, each assembling a separate section of the new strand of DNA.
- These new DNA segments are then joined together by the enzyme **DNA ligase**.
- The two new daughter molecules then coil up again to reform the double helix structure.

Illustration of DNA replication

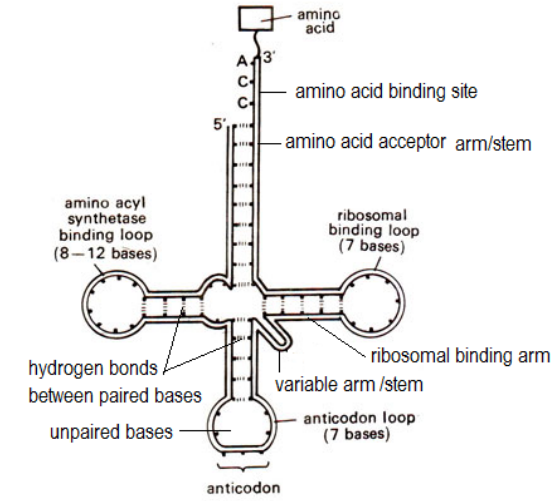


GENERAL STRUCTURE OF RNA

- RNA molecules are small/short, single stranded (rRNA and mRNA) or double stranded (tRNA) polymer of **nucleotides**.
- RNA **nucleotide** is made up of three molecules: **(i)** Phosphate group **(ii)** Ribose sugar **(iii)** Nitrogen base - either adenine **(A)**, guanine **(G)**, cytosine **(C)** or uracil **(U)**
- The sugar-phosphate-sugar backbone is held by covalent **phosphodiester bonds.**
- RNA occurs in three types whose sizes, shapes, amounts/abundance and roles vary:

1. Ribosomal RNA (rRNA)	**2. Messenger RNA** (mRNA)
Forms 80% of the total RNA in a cell. rRNA in different species vary in size e.g. in humans 18S rRNA has 1868 nucleotides while 28S rRNA has 5025. Permanently combined with protein to form catalytic component of ribosomes. Manufactured in nucleolus. rRNA is a site of protein synthesis in cells.	Forms 3-5% of the total RNA in a cell. Single stranded polynucleotide chains with 5' to 3' polarity Average size of eukaryotic mRNAs is 1500 to 2000 nucleotides Manufactured in the nucleus mRNA carries coded information from DNA to ribosomes in the cytoplasm

3. Transfer RNA (tRNA)
Forms about 15% of the total cell RNA.
Primary structure in all tRNAs has sequences of 73 to 93 nucleotides.
3' end *always terminates* with the sequence CCA, where amino acid attaches while the 5' end terminates in base G.
Secondary structure forms a clover leaf shape with 4 hydrogen bonded base-paired *stems*
Cloverleaf contains three non-base-paired *loops*:
(i) Amino acyl synthetase binding loop
(ii) Anticodon
(iii) Ribosomal binding loop.
Tertiary structure is a compact "*L*" shape whereby the anticodon stem and acceptor stem form a double helix.
Anticodon is a single stranded loop at the bottom.
tRNA carries amino acids in the cytoplasm to ribosomes.
Adaptations of tRNA: (1) Active sites (*anticodon* and *amino acid*) are maximally separated to avoid interference (2) Small size for mobility readily.



COMPARISON OF DNA AND RNA

Similarities

Both: **(1)** are polymers of nucleotides **(2)** carry genetic information **(3)** have same purine bases adenine and guanine plus pyrimidine bases cytosine **(4)** originate from the nucleus **(5)** occur in the cytoplasm

Differences

Aspect	**Deoxyribonucleic Acid (DNA)**	**Ribonucleic Acid (RNA)**
Function	(i) It's the blueprint of biological guidelines in organisms (ii) Stores genetic information for a long time and transmits it.	(i) Helps carry out DNA's blueprint guidelines. (ii) Transfers genetic code needed for the creation of proteins from the nucleus to the ribosome.
Structure	(iii) Double-stranded. (iv) Hydrogen bonds occur between complementary nitrogen bases of opposite strands (A-T, C-G) (v) Spirally twisted to produce a regular helix (vi) Occurs in form of chromatin or chromosomes	(iii) Single-stranded. (iv) Base pairing through hydrogen bonds occurs in the coiled parts (v) The strand may fold at places to form a secondary helix (vi) Occurs in ribosomes or forms association with ribosomes

Base Pairing	(vii) Adenine links to thymine (A-T) (viii) Purine and pyrimidine bases are in equal number	(vii) Adenine links to uracil (A-U) (viii) No proportionality between numbers of purine and pyrimidine bases.
Location	(ix) Much of DNA is in the nucleus of a cell, little in mitochondria and chloroplasts.	(ix) Much of RNA is in the cytoplasm, little in the nucleus.
Stability	(x) Deoxyribose sugar in DNA is less reactive because of C-H bonds. (xi) Stable in alkaline conditions. (xii) Long lived	(x) Ribose sugar is more reactive because of C-OH (hydroxyl) bonds. (xi) Not stable in alkaline conditions. (xii) Some RNA are very short lived while others have somewhat longer life.
Propagation	(xiii) DNA is self-replicating.	(xiii) RNA is synthesized from DNA when needed.
Unique Features	(xiv) DNA is protected in the nucleus, as it is tightly packed.	(xiv) RNA strands are continually made, broken down and reused.
Size	(xv) Very large/long (has over a million nucleotides) (xvi) Quantity is fixed in a cell	(xv) Much shorter (Depending on the type, RNA contains 70 – 12,000 nucleotides). (xvi) Quantity is variable
Types	(xvii) Only two types: intra nuclear and extra nuclear DNA	(xviii) Three different types: mRNA, tRNA and rRNA

THE CENTRAL DOGMA OF MOLECULAR BIOLOGY
It states that **DNA makes RNA makes proteins**

PROTEIN SYNTHESIS
Protein synthesis is the process by which individual cells construct proteins.
Protein synthesis occurs in separate but interrelated steps as follows:

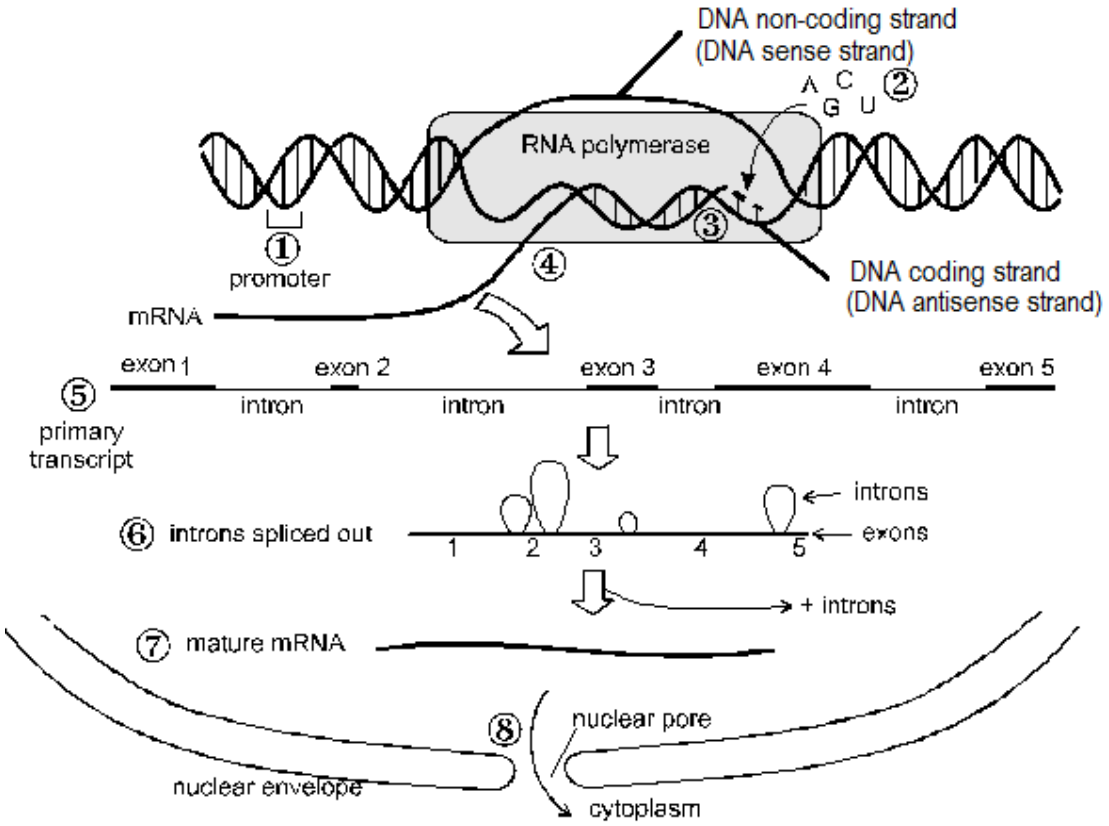
1. TRANSCRIPTION
Transcription is the process whereby the DNA code of a gene is copied to make messenger RNA (m-RNA).
Importance of transcription
(i) DNA is too large to fit through the nuclear pores, yet mRNA being small can readily exit the nucleus.
(ii) DNA contains many codes that aren't always needed at a given time, so m-RNA only carries that code needed to make specific proteins out of the nucleus to the ribosome.

- **Transcription** is performed by an enzyme called **RNA polymerase** and a number of accessory proteins called **transcription factors** which together form the **transcription initiation complex**.

- Transcription is **initiated** when **RNA polymerase enzyme**:

(i) Binds to the DNA strand at a **promoter.** The promoter is the beginning code of DNA on the gene where the RNA polymerase begins reading the DNA code, and is always the 3 letter triplet TAC.
(ii) Untwists then unzips the two strands of DNA.
(iii) Reads the antisense strand of DNA from 3' to 5' (***antisense*** - side containing the code to make a polypeptide).
(iv) Matches new nucleotides with their complements on the DNA strand (G with C, A with U) in the 5' to 3' direction.
(v) Binds these new RNA nucleotides together to form a complimentary copy of the DNA strand (mRNA)

- The sense strand of DNA is the side of DNA that does not contain a code to make a polypeptide. It is not read by the RNA polymerase.
- Elongation occurs when the new m-RNA strand is lengthened in the 5'-3' direction.
- Transcription stops when the terminator code is section of DNA is reached. Its code is complementary to the stop codons of m-RNA.
- The newly created m-RNA of eukaryotic cells is edited by removal of non-coding sections, called **introns** since they remain in the nucleus.
- The finished m-RNA (with **exons only)** containing the code needed to make the polypeptide leaves via nuclear pores to the ribosome in the cytoplasm for translation.



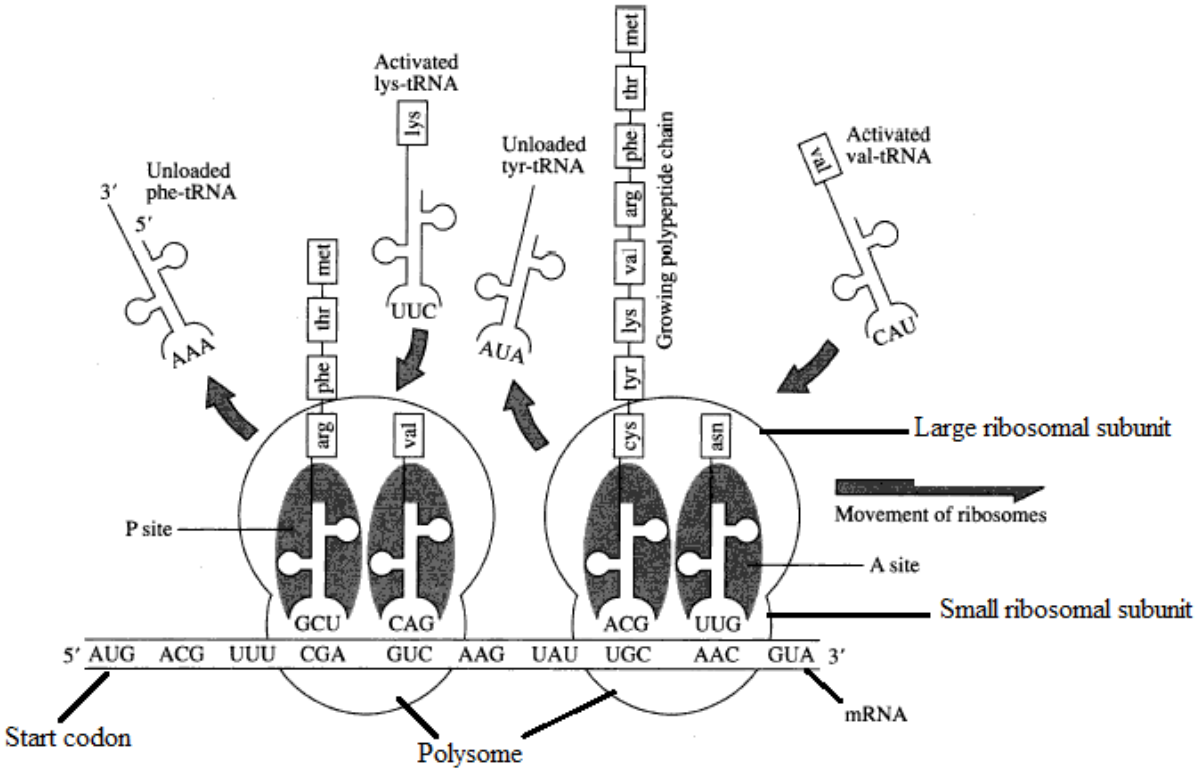
2. TRANSLATION

Translation involves three main steps: (1) Initiation (2) Elongation (3) Termination

Initiation occurs when the small ribosomal subunit binds at 5' end of mRNA molecule where there is the start codon AUG. tRNA molecule carrying the amino acid methionine binds to the ribosomal small sub-unit corresponding to the start codon (AUG) on mRNA.
The large ribosomal subunit binds on the small sub-unit to complete the initiation complex.
The large ribosomal subunit has two amino acid binding sites: **peptidyl site (P-site)** and **amino acyl site (A-site)**.

Elongation occurs when the first tRNA with anti-codon UAC (carrying the amino acid methionine) fits into the P-site of the ribosome while the second tRNA, whose anti-codon compliments the codon on mRNA fits into the A-site of the ribosome.
A peptide bond forms between the methionine and the amino acid carried by the second tRNA.
The methionine-specific tRNA leaves the P-site while the ribosome shifts so that the second tRNA now occupies the P-site, allowing the third codon on mRNA to occupy the A-site.
A third tRNA (carrying the third amino acid), whose anti-codon compliments the codon on mRNA fits into the A-site of the ribosome, enabling the formation of a second peptide bond between the second and third amino acids.
The second tRNA leaves the P-site while the ribosome shifts down one codon so that the third tRNA now occupies the P-site, allowing the fourth codon on mRNA to occupy the A-site.

Termination occurs when all the codons on mRNA are read. The ribosome reaches one or more stop codons on mRNA (UAA, UAG, UGA). The ribosome detaches from the mRNA and splits into its small and large sub-units, while the new protein floats away
Note:
1. Several ribosomes can attach to a molecule of mRNA (to form **polysomes/polyribosomes**) one after another so that several proteins of the same type can be made from one mRNA at the same time.
2. Newly synthesised proteins are packaged and sent to Golgi complex for modification/processing. This is called p**ost-translation processing of the protein**



TYPICAL EXAMINATION QUESTIONS

Compare the processes of DNA replication and transcription

Similarities

Both: **(1)** involve unwinding the helix **(2)** involve separating the two strands **(3)** involve breaking hydrogen bonds between bases **(4)** involve complementary base pairing **(5)** involve C pairing with G **(6)** work in a 5` to 3` direction **(7)** involve linking/ polymerization of nucleotides **(8)** DNA or RNA polymerase require a start signal

Differences

DNA replication	**Transcription**
Involves DNA nucleotides, where the pentose sugar is deoxyribose, and the base adenine pairs with thymine	Involves RNA nucleotides where the pentose sugar is ribose, and the base adenine pairs with uracil
Both strands are copied	Only one strand copied not both
Ligase enzyme / no Okazaki fragments are involved	No ligase enzyme / no Okazaki fragments
Has multiple starting points	Has only one starting point
replication gives two DNA molecules	whilst transcription gives mRNA

Compare DNA transcription with translation

Both: **(1)** Occur in 5' to 3' direction **(2)** Require ATP

Differences

(i) DNA is transcribed while mRNA is translated
(ii) Transcription produces RNA while translation produces polypeptides/ protein
(iii) RNA polymerase for transcription while ribosomes for translation/ ribosomes in translation only
(iv) Transcription occurs in the nucleus (of eukaryotes) while translation occurs in the cytoplasm/ at ER
(v) tRNA is needed for translation but not transcription

Explain briefly the advantages and disadvantages of the universality of the genetic code to humans.

(i) Genetic material can be transferred between species/ between humans
(ii) One species could use a useful gene from another species
(iii) Bacteria/ yeasts can be genetically engineered to make a useful product
(1) Viruses can invade cells and take over their genetic apparatus e.g. HIV
(2) Viruses cause disease

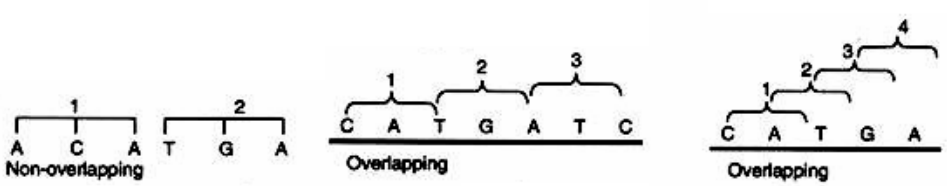
GENETIC CODE

The genetic code is the set of rules by which information encoded in genetic material (DNA or RNA sequences) is translated into proteins (amino acid sequences) by living cells.

THE GENETIC CODE CHART / TABLE

BASE		SECOND BASE U	SECOND BASE C	SECOND BASE A	SECOND BASE G		BASE
FIRST BASE	U	UUU: Phenylalanine UUC: Phenylalanine UUA: Leucine UUG: Leucine	UCU: Serine UCC: Serine UCA: Serine UCG: Serine	UAU: Tyrosine UAC: Tyrosine UAA: Stop UAG: Stop	UGU: Cysteine UGC: Cysteine UGA: Stop UGG: Tryptophan	U C A G	THIRD BASE
	C	CUU Leucine CUC: Leucine CUA: Leucine CUG: Leucine	CCU: Proline CCC: Proline CCA: Proline CCG: Proline	CAU: Histidine CAC: Histidine CAA: Glutamine CAG: Glutamine	CGU: Arginine CGC: Arginine CGA: Arginine CGG: Arginine	U C A G	
	A	AUU: Isoleucine AUC: Isoleucine AUA: soleucine AUG: Methionine	ACU: Threonine ACC: Threonine ACA: Threonine ACG: Threonine	AAU: Asparagine AAC: Asparagine AAA: Lysine AAG: Lysine	AGU: Serine AGC: Serine AGA: Arginine AGG: Arginine	U C A G	
	G	GUU: Valine GUC: Valine GUA: Valine GUG: Valine	GCU: Alanine GCC: Alanine GCA: Alanine GCG: Alanine	GAU: Aspartic acid GAC: Aspartic acid GAA: Glutamic acid GAG: Glutamic acid	GGU: Glycine GGC: Glycine GGA: Glycine GGG: Glycine	U C A G	

MOST IMPORTANT PROPERTIES OF GENETIC CODE

Property	Explanation
1. The code is a triplet codon	The nucleotides of mRNA are arranged as a linear sequence of codons, each codon consisting of three successive nitrogenous bases, i.e., the code is a triplet codon.
2. The code is non-overlapping	In translating mRNA molecules the codons do not overlap but are "read" sequentially. 
3. The code is commaless	This means that no codon is reserved for punctuations. After one amino acid is coded, the second amino acid will be automatically, coded by the next three letters and that no letters are wasted as the punctuation marks.
4. The code is non-ambiguous	A particular codon will always code for the same amino acid. The same codon shall never code for two different amino acids.
5. The code has polarity	The code is always read in a fixed direction, i.e., in the 5'→3′ direction.
6. The code is degenerate	More than one codon may specify the same amino acid; For example, except for tryptophan and methionine, which have a single codon each, all other 18 amino acids have more than one codon. **Biological advantages of degeneracy** **(i)** It permits essentially the same complement of enzymes and other proteins to be specified by microorganisms varying widely in their DNA base composition. **(ii)** It provides a mechanism of minimising mutational lethality. E.g. Substitution of the third base-**U** in **GUU (**for valine**)** with **C/A/G** does not change the amino acid coded for.
7. Some codes are start codons	In most organisms, **AUG** codon is the start or initiation codon, i.e., the polypeptide chain starts either with methionine (eukaryotes) or N-formylmethionine (prokaryotes).
8. Some codes are stop codons	Three codons **UAG, UAA** and **UGA** are the chain stop or termination codons. They do not code for any of the amino acids. These codons are also called **nonsense codons**, since they do not specify any amino acid.
9. The code is universal	Same genetic code is found valid for all organisms ranging from bacteria to man.