NUCLEIC ACIDS

Nucleic acids form genetic material of all living organisms. The term nucleic acid comes from the fact that they are found mainly in the nucleus. They are made up of units called ***nucleotides***. These are arranged to form extremely long molecules called ***polynucleotide***.

Structure of nucleotides.

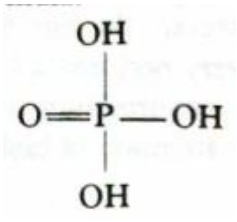
Individual nucleotides comprise of three parts: (a) ***Phosphoric acid*** (phosphate H_3PO_4). This has the same structure in all nucleotides. (b) ***Pentose sugar***, two types occur, (i) ***Ribose*** ($C_5H_{10}O_5$) and (ii) ***deoxyribose*** ($C_5H_{10}O_4$). (c) ***Organic base***. There are five different bases which are divided into two groups, (i) ***Purines***: These are double rings comprising a six – sided and a five - sided ring. Two examples are ***Adenine*** and ***Guanine***. (ii) ***Pyrimidine***: these are single rings each with six sides. Examples, ***cytosine***, ***Thymine*** and ***uracil***.

The three components are combined by ***condensation*** reactions (a water molecule is lost) which involves formation of; (i) **Nucleoside** when pentose sugar joins to an organic base. (ii) ***Nucleotide***, when nucleoside joins to a phosphate group. (iii) By similar condensation reaction between the sugar and phosphate groups of two nucleotides, a ***dinucleotide*** is formed by ***phosphodiester*** bonds. (iv) Continued condensation reaction leads to formation of ***polynucleotide***.

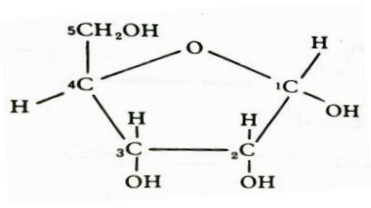
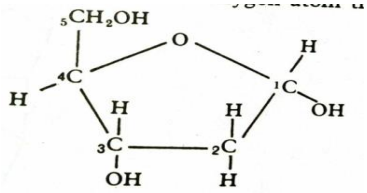
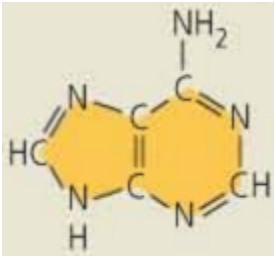
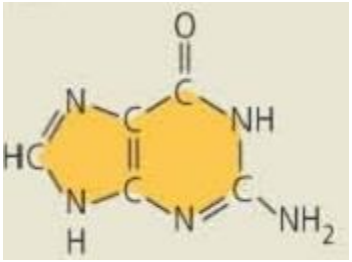
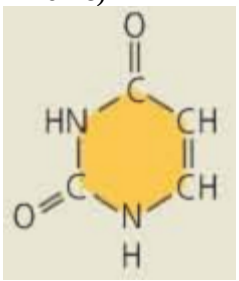
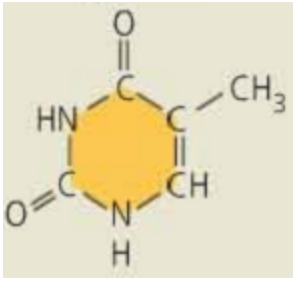
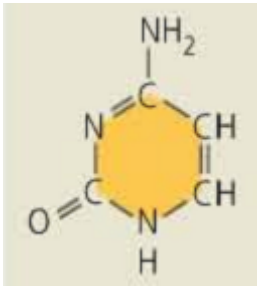
The main function of nucleotides is the formation of nucleic acids, RNA and DNA which play vital role in protein synthesis and heredity. In addition they form part of other metabolically important molecules.
Biologically important molecules containing nucleotides and their functions.

Molecule	***Abbreviation***	***Function***
Deoxyribonucleic acid	DNA	Contain genetic information of cells.
Ribonucleic acid	RNA	All three types play a vital role in protein synthesis
Adenosine monophosphate Adenosine diphosphate Adenosine triphosphate	AMP ADP ATP	Coenzymes important in making energy available to cells for metabolic activities, osmotic work, muscular contractions, etc.
Nicotinamide adenine dinucleotide Flavin adenine dinucleotide	NAD FAD	Electron(Hydrogen) carriers , important in respiration in transferring hydrogen atoms from the Krebs cycle along the respiratory chain
Nicotinamide adenine dinucleotide phosphate	NADP	Electron (Hydrogen) carrier, important in photosynthesis for accepting electrons from the chlorophyll molecule and making them available for photolysis of water.
Coenzyme A	CoA	Coenzyme important in respiration in combining with pyruvate to form acetyl coenzyme A and transferring the acetyl group into the Krebs cycle.

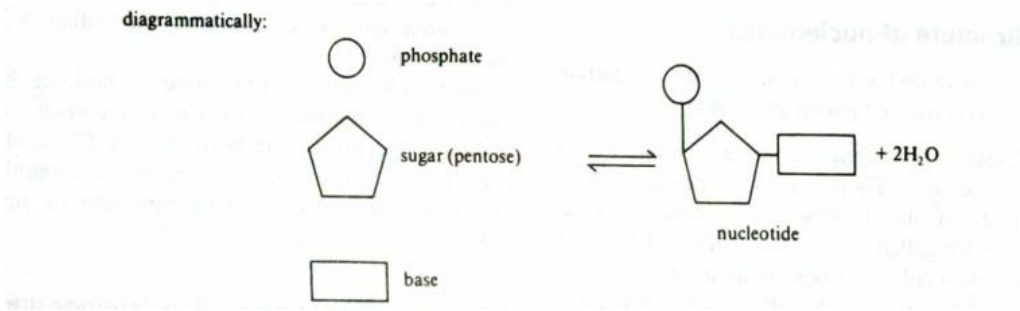
Structure of molecules in a nucleotide

Name of molecule	***Chemical structure***
Phosphate	

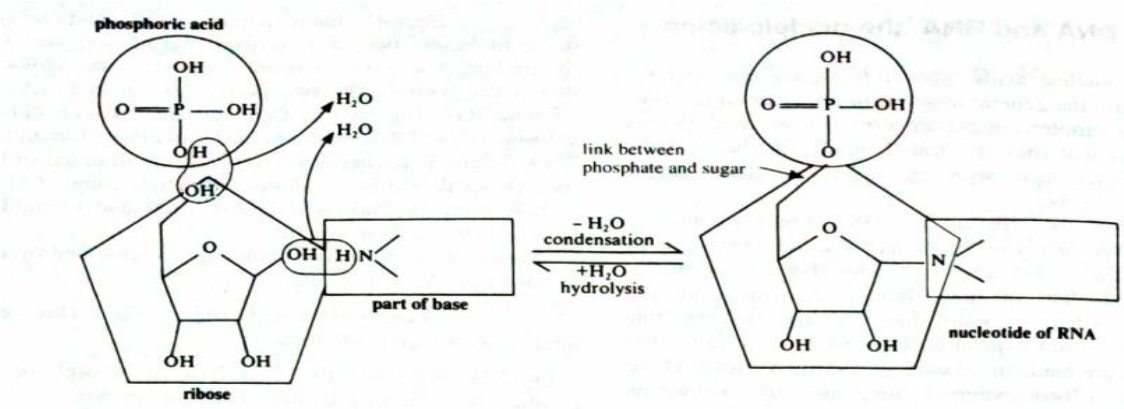
BY: SEMMANDA CHARLES ZZIWA, 0705 950374, semmandazziwa@gmail.com @SCZ Salongo 2016

Ribose 	**Deoxyribose** 
Adenine (a purine) 	**Guanine** (a purine) 
Uracil (a pyrimidine) 	**Thymine** (a pyrimidine) 
Cytosine (a pyrimidine) 	

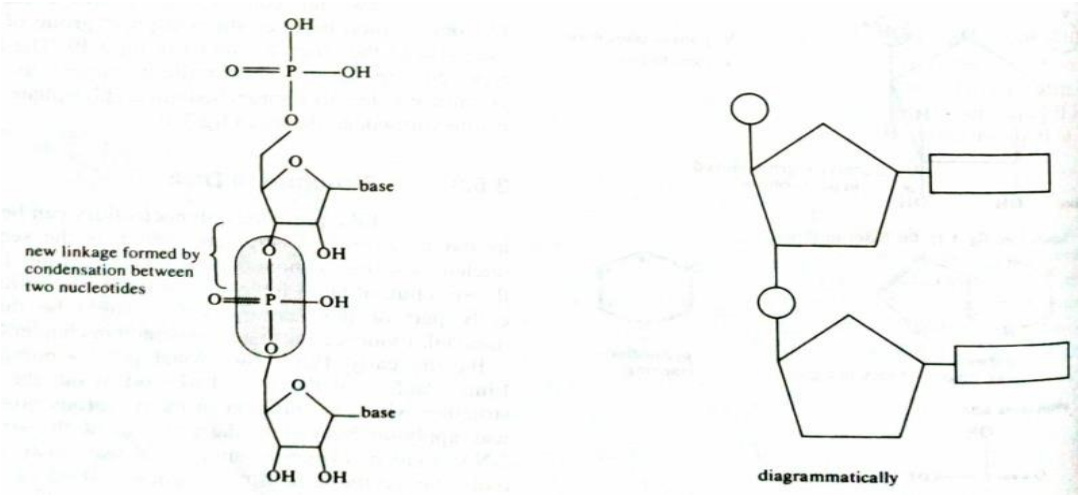
Formation of a nucleotide



BY: SEMMANDA CHARLES ZZIWA, 0705 950374, semmandazziwa@gmail.com



Structure of a dinucleotide

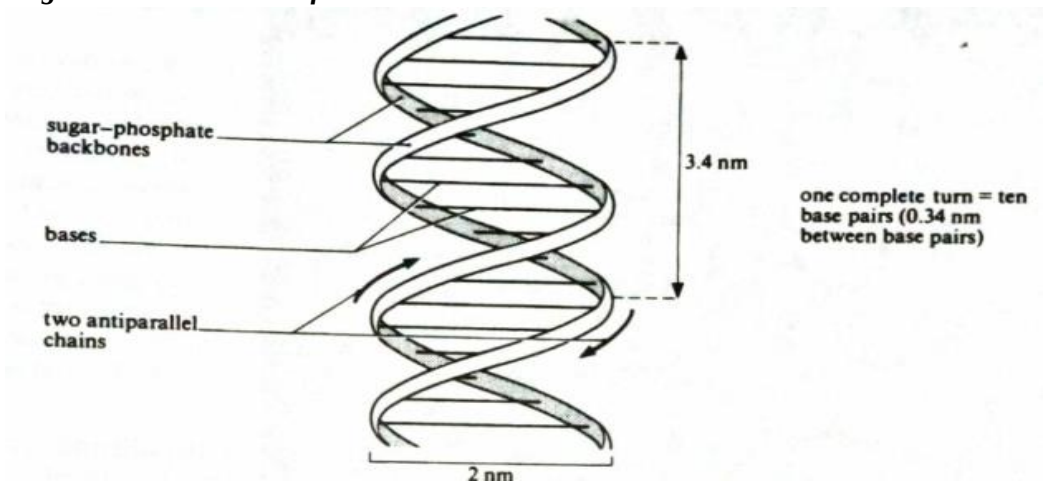


Deoxyribonucleic acid (DNA)

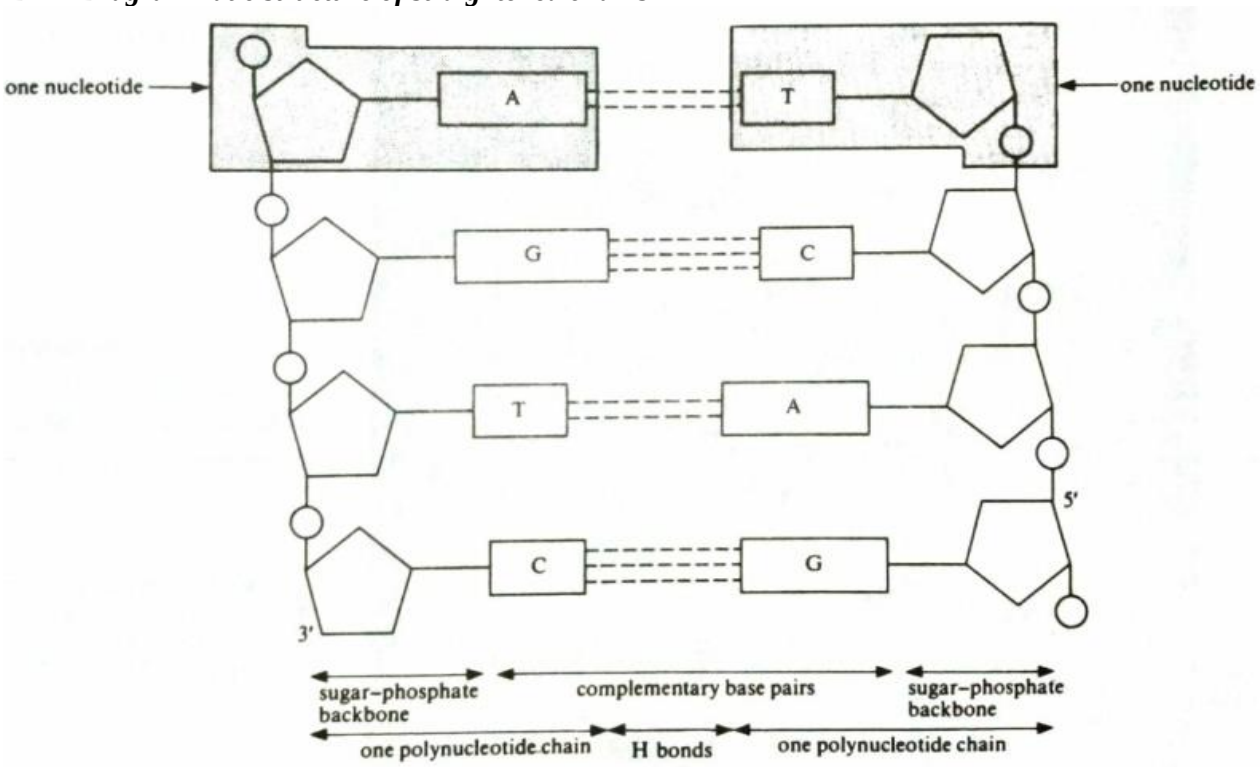
DNA is a double – stranded polynucleotide where the pentose sugar is always deoxyribose and organic bases are adenine, guanine, cytosine and thymine but never uracil. Each of these polynucleotide chains is extremely long and may contain many million nucleotide units. The available facts about DNA include: (i) It is very long, thin molecule made up of nucleotide. (ii) It contains four organic bases: adenine, Guanine, cytosine, and thymine. (iii) The amount of guanine is usually equal to that of cytosine. (iv) The amount of Adenine is usually equal to that of thymine. (v) It is probably in form of helix whose shape is maintained by hydrogen bonding.

According to ***Watson and Crick*** (1953), DNA consists of two polynucleotide chains, each chain forms a right handed helical spiral and the two chains coil around each other to form a ***double helix***. The chains run in opposite directions, that is are ***antiparallel.*** Each chain has a sugar phosphate backbone with bases which project at right angles and hydrogen bond with the bases of the opposite chain across a double helix. The width between the two backbones is constant and equal to the width of a base pair. The pairings are always cytosine with guanine and adenine with thymine. There is no restriction in sequence of bases in one chain, but because of rules of base pairing, the sequence in one chain determines that in another, the two chains are thus said to be ***complementary***.

Diagrammatic structure of DNA



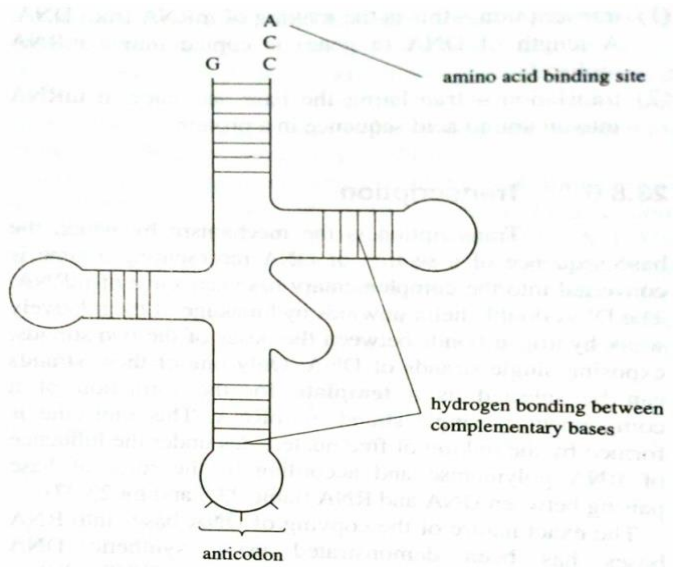
DNA Diagrammatic structure of straightened chains



Ribonucleic acid (RNA)

RNA is a single – stranded polynucleotide where the pentose sugar is always ribose and the organic bases are Adenine, guanine, cytosine and uracil. There are three types of RNA found in cells, all of which are involved in protein synthesis.

Ribosomal RNA (rRNA): is a large complex molecule made up of both double and single helices. Although it is manufactured by DNA of the nucleus, it is found in cytoplasm where it makes up more than half the mass of the ribosomes. It comprises more than half the mass of total RNA of a cell and its base sequence is similar in all organisms.

Transfer RNA (tRNA)	***Structure of tRNA***
Is a ***small*** molecule comprising a single strand. Again it is manufactured by nuclear DNA, Makes up ***10% to 15%*** of cells RNA and all types are fundamentally similar. It's one end of chain end in ***cytosine – cytosine – adenine sequence***. It is at this point that an amino acid attaches itself. There are at least 20 types of tRNA each carrying a different amino acid. At an intermediate point point along the chain is an important sequence of three bases, called the ***anticodon***. These lineup alongside the appropriate codon on the mRNA during protein synthesis.	

Messenger RNA (mRNA): Is a ***long single*** stranded molecule, of up to thousands of nucleotides, which is formed into a helix. Manufactured in the nucleus, it is a mirror copy of part of one strand of DNA helix. There is hence a variety of types. It enters the cytoplasm where it associates with the ribosomes and acts as a ***template for protein synthesis***. It makes up less than 5% of the total cellular RNA. It is easily and quickly broken down, sometimes existing for only a matter of minutes.

Differences between DNA and RNA

RNA	***DNA***
Single polynucleotide chain	Double polynucleotide chain
Smaller molecular mass	Larger molecular mass
May have single or double helix	Always a double helix
Pentose sugar is ribose	Pentose sugar is deoxyribose
Organic bases present are Adenine,guanine,cytosine and uracil	Organic bases present are adenine, guanine, cytosine and thymine
Ratio of Adenine and uracil to cytosine and guanine varies	Ratio of adenine and thymine to cytosine and guanine is one.
Manufactured in nucleus but found throughout cell	Found almost entirely in the nucleus
Amount varies from cell to cell and within cell according to metabolic activity.	Amount is constant for all cells of a species except gametes and spores.
Chemically less stable	Chemically very stable
May be temporarily existing for short periods only	Permanent
Three basic forms: messenger, transfer and ribosomal RNA	Only one basic form, but with almost infinite variety with in that form.

DNA Replication

This is a process by which a DNA molecule make exact copies of its self from existing ones.

Biologists at the time proposed three alternative hypotheses about how the old and new strands might interact during replication:

1. **Semiconservative replication:** If the old, ***parental*** strands of DNA separated, each could then be used as a template for the synthesis of a new, **daughter** strand. This hypothesis is called semiconservative replication ***because*** each new daughter DNA molecule would consist of one old strand and one new strand.

2. **Conservative replication:** If the bases temporarily turned outward so that complementary strands no longer faced each other, they could serve as a template for the synthesis of an entirely new double helix all at once. This hypothesis, ***called*** conservative replication, ***because*** would result in an intact parental molecule and a daughter DNA molecule consisting entirely of newly synthesized strands.

3. **Dispersive replication:** If the parental double helix were cut wherever one strand crossed over another and DNA was synthesized in short sections by extending each of the cut parental strands to the next strand crossover, then there would be a mix of new and old segments along each replicated molecule. This possibility is called dispersive replication ***because*** stretches of old DNA would be interspersed with new DNA down the length of each daughter strand

It starts with unwinding / untwisting and unzipping of the DNA double helix by breaking hydrogen bonds between bases forming a Y- shaped ***Replication fork,*** controlled by enzyme ***Helicase***. DNA does not become tightly coiled ahead of the replication fork, ***because*** the twisting induced by helicase is relaxed by proteins called ***topoisomerases.*** A ***topoisomerase*** is an enzyme that cuts DNA, allows it to unwind, and rejoins it ahead of the advancing replication fork. ***RNA primase*** enzyme lays down an ***RNA primer*** at the 3' end of the DNA strand to guide the action of ***DNA polymerase***. DNA polymerase (1) works only in the 5′ to 3′ direction and (2) requires both a 3′ end to extend from and a single-stranded template. ***DNA polymerase*** then binds to a single stranded DNA that results and and starts to move along the strand. Each time it meets the next base on DNA, free nucleotides approach the DNA strand, and the one with correct complimentary base hydrogen – bonds to the base in DNA. The enzyme's product is called the ***leading strand***, or continuous strand, ***because*** it leads into the replication fork and is synthesized continuously. The strand of DNA that extends in the direction away from the replication fork is called the ***lagging strand,*** or discontinuous strand, ***because*** it lags behind the synthesis occurring at the fork. As the replication fork moves, it exposes gaps of single-stranded template DNA. ***Okazaki fragments*** are portions of the lagging strand. ***DNA ligase*** closes the gaps between the new DNA strands. The two new daughter molecules coil up to form a double helix.

Proteins Required for DNA Synthesis

NAME	***FUNCTION***
Opening the helix	
Helicase	Catalyzes the breaking of hydrogen bonds between base pairs to open the double helix
Topoisomerase	Breaks and rejoins the DNA double helix to relieve twisting forces caused by the opening of the helix
Leading strand synthesis	
Primase	Catalyzes the synthesis of the RNA primer
DNA polymerase III	Extends the leading strand
Lagging strand synthesis	
Primase	Catalyzes the synthesis of the RNA primer on an Okazaki fragment
DNA polymerase III	Extends an Okazaki fragment
DNA polymerase I	Removes the RNA primer and replaces it with DNA

DNA ligase	Catalyzes the joining of Okazaki fragments into a continuous strand

Illustration of DNA replication

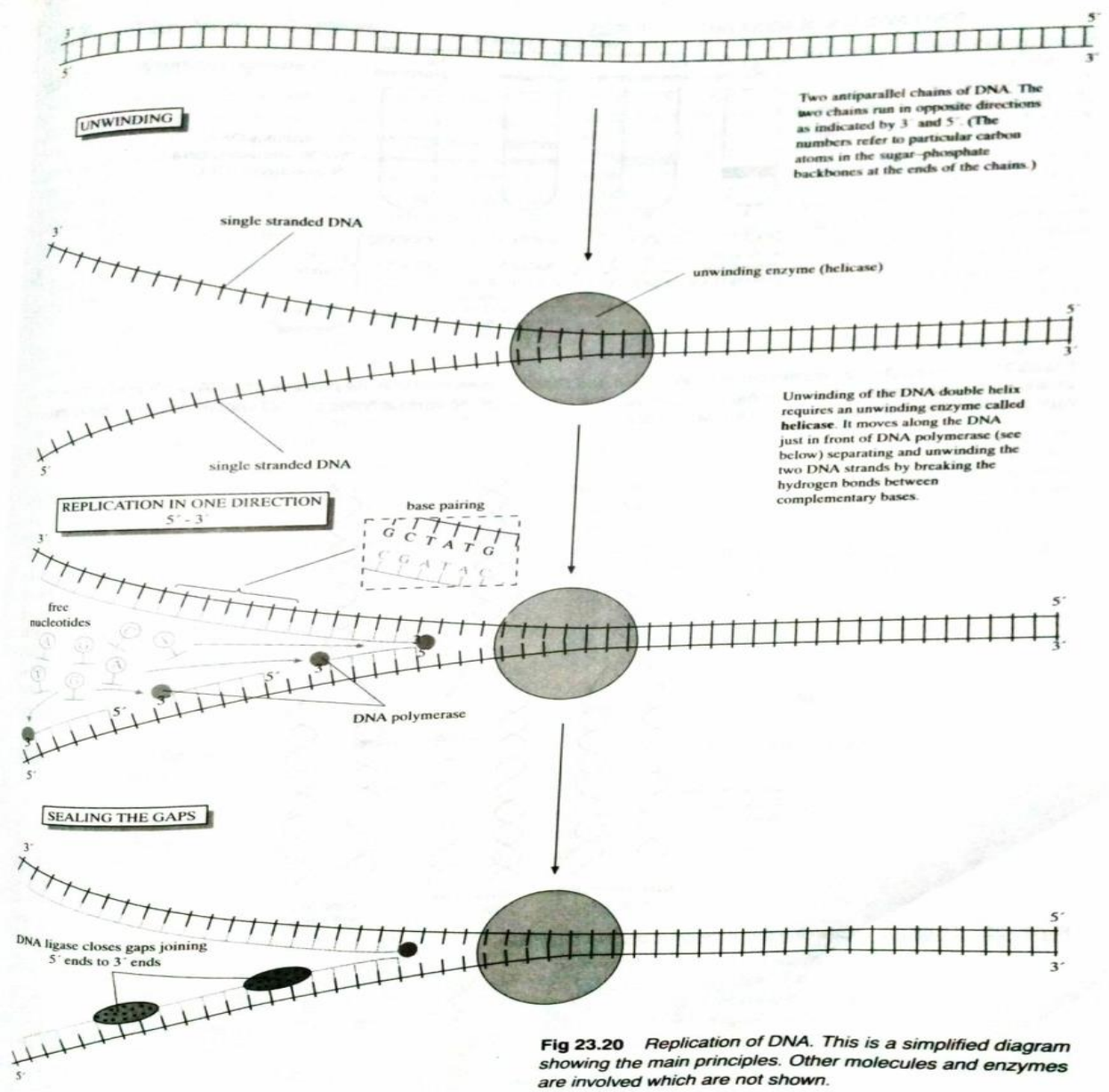


Fig 23.20 *Replication of DNA. This is a simplified diagram showing the main principles. Other molecules and enzymes are involved which are not shown.*

CHECK UP

By now you should be able to: **(i)** describe the structure of nucleotides. **(ii)** Describe the structure of DNA and RNA. **(iii)** Distinguish DNA and RNA. **(iv)** Explain the Watson Crick hypothesis of the nature of DNA. **(v)** Explain the process of DNA replication.

Sample questions.

1. What does it mean to say that strands in a double helix are antiparallel? A. Their primary sequences consist of a sequence of complementary bases. B. They each have a sugar–phosphate backbone. C. They each have a 5′S3′ directionality. D. They have opposite directionality, or polarity.

2. Which of the following is not a property of DNA polymerase? A. It adds dNTPs only in the 5′S3′ direction. B. It requires a primer to work. C. It is associated with a sliding clamp only on the leading strand. D. Its exonuclease activity is involved in proofreading.

3. The enzyme that removes twists in DNA ahead of the replication fork is _____.

4. What is the function of primase? A. synthesis of the short section of double-stranded DNA required by DNA polymerase B. synthesis of a short RNA, complementary to single-stranded DNA. C. closing the gap at the 3′ end of DNA after excision repair. D. removing primers and synthesizing a short section of DNA to replace them

5. How are Okazaki fragments synthesized? A. using the leading strand template, and synthesizing 5′S3′ B. using the leading strand template, and synthesizing 3′S5′ C. using the lagging strand template, and synthesizing 5′S3′ D. using the lagging strand template, and synthesizing 3′S5′

6. An enzyme that uses an internal RNA template to synthesize DNA is _____.

7. Researchers design experiments so that only one thing is different between the treatments that are being compared. In the Hershey– Chase experiment, what was this single difference?

8. What is the relationship between defective DNA repair and cancer?

9. Why is the synthesis of the lagging strand of DNA discontinuous? How is it possible for the synthesis of the leading strand to be continuous?

10. Explain how telomerase prevents linear chromosomes from shortening during replication.

11. Predict what would occur in a bacterial mutant that lost the ability to chemically mark the template strand of DNA. A. The mutation rate would. B. The ability of DNA polymerase to discriminate between correct and incorrect base pairs would decrease. C. The energy differences between correct and incorrect base pairs would decrease. D. The energy differences between correct and incorrect base pairs would increase.

12. What aspect of DNA structure makes it possible for the enzymes of nucleotide excision repair to recognize many different types of DNA damage? A. the polarity of each DNA strand B. the antiparallel orientation of strands in the double helix. C. the energy differences between correct and incorrect base pairs. D. the regularity of DNA's overall structure.

THE CENTRAL DOGMA OF MOLECULAR BIOLOGY

The central dogma summarizes the flow of information in cells. It simply states that ***DNA codes for RNA, which codes for proteins***: The sequence of bases in DNA specifies the sequence of bases in an RNA molecule, which specifies the sequence of amino acids in a protein. In this way, genes ultimately code for proteins.

Biologists use specialized vocabulary to summarize the sequence of events captured in the central dogma. (1). DNA is ***transcribed*** to RNA by RNA polymerase. ***Transcription i***s the process of copying hereditary

BY: SEMMANDA CHARLES ZZIWA, 0705 950374, semmandazziwa@gmail.com @SCZ Salongo 2016

information in DNA to RNA. (2). Messenger RNA is ***translated*** to proteins in ribosomes**.** ***Translation*** is the process of using the information in nucleic acids to synthesize proteins. Translation is also referred to simply as ***protein synthesis.*** The following equation summarizes the relationship between transcription and translation as well as the relationships between DNA, RNA, and proteins: DNA (information storage) **by** Transcription to mRNA (information carrier) **by** Translation **to** Proteins (active cell machinery) **Therefore**; an organism's **genotype** is determined by the sequence of bases in its DNA, while its **phenotype** is a product of the proteins it produces.

Exceptions to the Central Dogma: (i) many genes code for RNA molecules that do not function as mRNAs—they are not translated into proteins. (ii) In some cases, information flows from RNA back to DNA

The Genetic code

The rules that specify the relationship between a sequence of nucleotides in DNA or RNA and the sequence of amino acids in a protein.

Features of a genetic code. (a) The code is a **triplet**: Meaning:; three bases in DNA code for one amino acid in a protein. The complimentary triplets in mRNA are referred to as **codons**. Each codon is thus three bases long. (b) The code is **degenerate**: Some amino acids are coded for by several codons, number of amino acids is less than number of codons. (c) The code is **punctuated**; three codons act as full stops in determining the end of code message e.g. UAA, sometimes called nonsense codons do not code for amino acids. Some act as signals for initiation of polypeptide chains e.g. AUG for methionine. (d) The code is **universal**: Common to all living organisms containing same 20 amino acids and same 5 bases. (e) The code is **redundant**. All amino acids except methionine and tryptophan are coded by more than one codon. (f) The code is unambiguous. A single codon never codes for more than one amino acid. (h) The code **is non-overlapping**. Once the ribosome locks onto the first codon, it then reads each separate codon one after another. (i) The code is **conservative**. When several codons specify the same amino acid, the first two bases in those codons are almost always identical.

The Genetic code table

Ala = alanine
Arg = arginine
Asn = asparagine
Asp = aspartic acid
Cys = cysteine
Gln = glutamine
Glu = glutamic acid
Gly = glycine
His = histidine
Ile = isoleucine
Leu = leucine
Lys = lysine
Met = methionine
Phe = phenylalanine
Pro = proline
Ser = serine
Thr = threonine
Try = tryptophan
Tyr = tyrosine
Val = valine

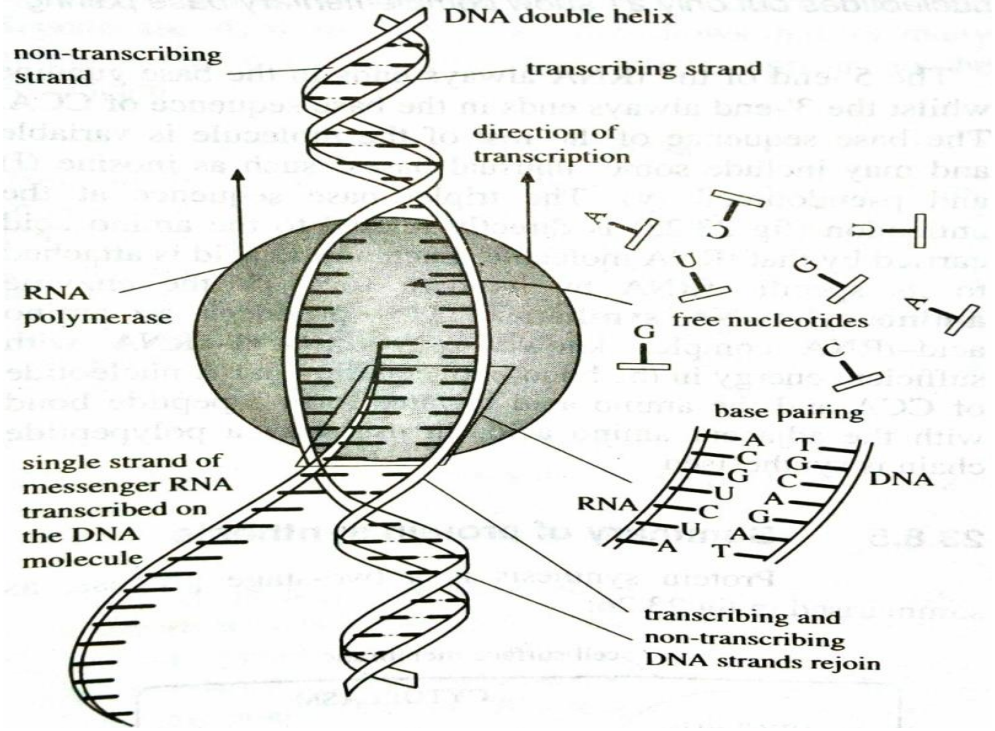
first base	second base: U		C		A		G		third base
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Cys	C
	UUA	Leu	UCA	Ser	UAA	Nonsense	UGA	Nonsense	A
	UUG	Leu	UCG	Ser	UAG	Nonsense	UGG	Try	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC	Leu	CCC	Pro	CAC	His	CGC	Arg	C
	CUA	Leu	CCA	Pro	CAA	Gln	CGA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

BY: SEMMANDA CHARLES ZZIWA, 0705 950374, semmandazziwa@gmail.com @SCZ Salongo 2016

Transcription:

Transcription is the mechanism by which the base sequence of section of DNA is converted into a complimentary base sequence of mRNA. Transcription involves: (i) Using a group of proteins called **transcription factors**, **RNA polymerase** binds to the DNA strand at the **promoter**, these binding sites were named promoters, ***because*** they are sections of DNA that promote the start of transcription. (ii) RNA polymerase causes the DNA double helix to unwind by breaking relatively weak hydrogen bonds between the bases of the two strands, exposing single strands of DNA. (iii) Only one strand is selected as a **template** for formation of a complimentary mRNA. The other strand is called **non template strand** (antisense strand). (iv) mRNA is formed by linking of free nucleotides under the influence of RNA polymerase and according to rules of base pairing. As transcription proceeds, the **introns** (non coding sections) are removed from the growing RNA strand by a process known as **splicing**. (v) When **polyadenylation signal** or **poly (A)** signal is transcribed, the RNA is cut by an enzyme downstream of the poly (A) signal as the polymerase continues to transcribe the DNA template. Eventually RNA polymerase falls off the DNA template and terminates transcription. The newly synthesized mRNA is edited by addition of the cap and tail, leave the nucleus via nuclear pores to ribosomes in cytoplasm for translation.

Diagram showing the mechanism of transcription



Translation:

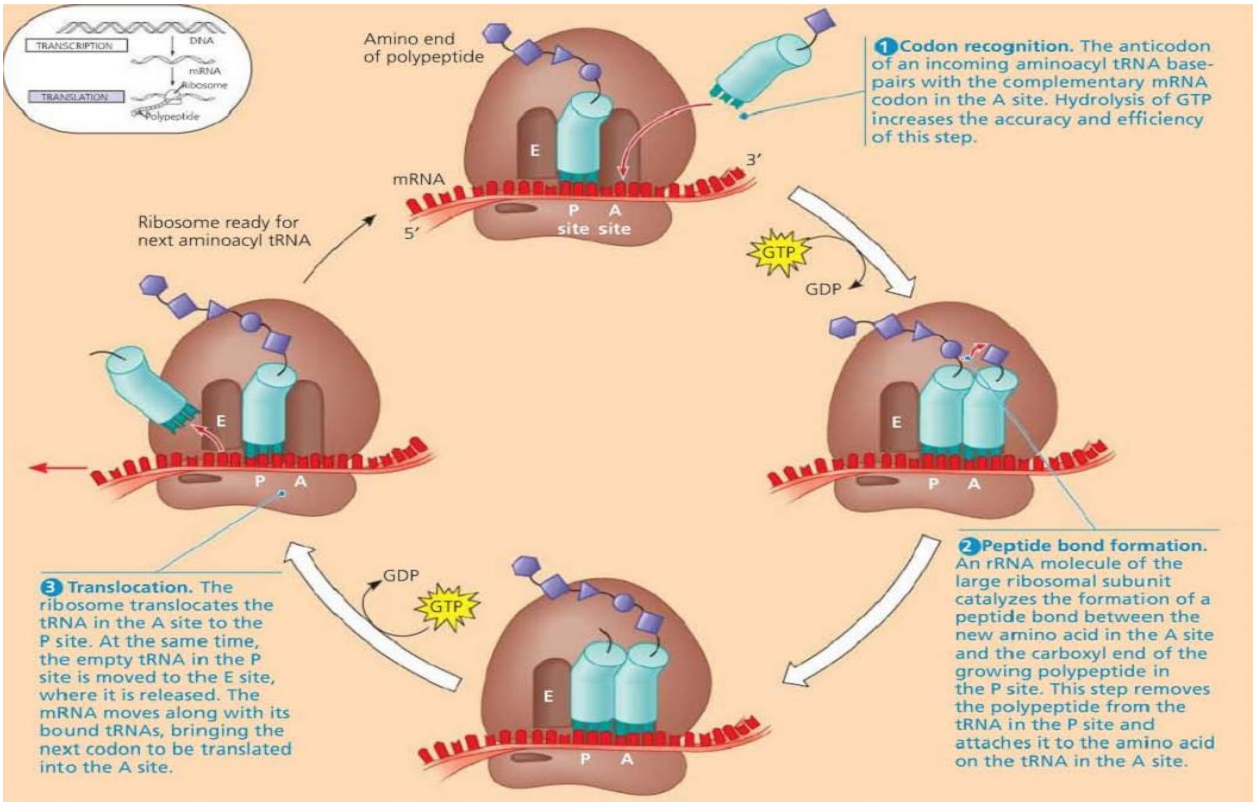
Translation is the mechanism by which sequence of bases in a mRNA molecule is converted into a sequence of amino acids in a polypeptide chain. Occurs on ribosomes, by forming a **polysome** / polyribosome (several ribosomes attached to a molecule of mRNA like beads on string)

This involves: (a) Initiation (b) Elongation and (c) Termination.

(a) **Initiation**: Involves: (i) The mRNA binds to a small ribosomal subunit, (ii) the initiator aminoacyl tRNA bearing methionine binds to the start codon (UAG) on mRNA. (iii) The large ribosomal subunit binds, completing the complex.

(b) **Elongation**: Involves: (i) Arrival of aminoacyl tRNA whose anti codon compliments to condon on mRNA and fits in the **A – site** of the ribosome while the initiator aminoacyl tRNA bearing methionine fits in the **p – site** of ribosome. (2) **peptide-bond** formation, between methionine and the amino acid carried by the second tRNA. (3) **Translocation**, Methionine specific tRNA leaves the p – site while the ribosome moves so that the second tRNA occupies the p – site allowing the third codon on mRNA to occupy A – site. Third tRNA whose anticodon compliments the third codon on mRNA fits the A – site of the ribosome , formation of peptide bond between second and third amino acid. The second tRNA leaves the p – site while the ribosome moves so that the third tRNA occupies the p – site allowing the fourth codon on mRNA to occupy A – site. Fourth tRNA whose anticodon compliments the fourth codon on mRNA fits the A – site of the ribosome , formation of peptide bond between third and fourth amino acid. The third tRNA leaves the p – site while the ribosome moves so that the fourth tRNA occupies the p – site allowing the fifth codon on mRNA to occupy A – site.

(c) **Termination**: When the translocating ribosome reaches one of the stop codons (UAA, UAG, and UGA) a protein called a **release factor** recognizes the stop codon and fills the A site, because they have the size and shape of a tRNA coming into the ribosome. However, release factors do not carry an amino acid. When a release factor occupies the A site, the protein's active site catalyzes the hydrolysis of the bond that links the tRNA in the P site to the polypeptide chain. This reaction frees the polypeptide.



BY: SEMMANDA CHARLES ZZIWA, 0705 950374, semmandazziwa@gmail.com @SCZ Salongo 2016

Proteins are not fully formed and functional when termination occurs. Most proteins go through an extensive series of processing steps, collectively called **post-translational modification**, before they are completely functional. These steps require a wide array of molecules and events and take place in many different locations throughout the cell. For example, in ***rough endoplasmic reticulum*** and the ***Golgi apparatus***, small chemical groups may be added to proteins often sugar or lipid groups that are critical for normal functioning.

CHECK UP

By now you should be able to; **(i)** Describe formation of mRNA. **(ii)** Describe the process of protein synthesis**. (iii)** State role of DNA and RNA in protein synthesis. (iv) Describe the structure of genetic code.

Try this

1. How did the A site of the ribosome get its name? A. It is where amino acids are joined to tRNAs, producing aminoacyl tRNAs. B.It is where the amino group on the growing polypeptide chain is available for peptide-bond formation. C. It is the site occupied by incoming aminoacyl tRNAs. D.It is surrounded by α-helices of ribosomal proteins.

2. Where is the start codon located? A. at the very start (5′ end) of the mRNA B.at the downstream end of the 3′ untranslated region (UTR) C. at the downstream end of the 5′ untranslated region (UTR) D.at the upstream end of the 3′ untranslated region (UTR)

3. Where is an amino acid attached to a tRNA?

4. Explain the relationship between eukaryotic promoter sequences, basal transcription factors, and RNA polymerase.

5. Describe the sequence of events that occurs during translation as a protein elongates by one amino acid and the ribosome moves down the mRNA. Your answer should specify what is happening in the ribosome's A site, P site, and E site.