BIO 201 INTRODUCTION TO GENETICS

Dr. Segun I. OYEDEJI

Federal University Oye-Ekiti

Department of Animal & Environmental Biology

2018 Lecture Guide

1

REFERENCE TEXTBOOKS

1) Bruce Alberts, Alexander Johnson, Julian Lewis, David Morgan, Martin Raff, Keith Roberts, and Peter Walter (2015). Molecular biology of the cell (Sixth Edition). Published by Garland Science, Taylor & Francis Group, New York, USA.

2) Bruce Alberts, Dennis Bray, Karen Hopkin, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, and Peter Walter (2015). Essential Cell Biology (Fourth Edition). Published by Garland Science, Taylor & Francis Group, New York, USA.

2

THE SCIENCE OF GENETICS

Genetics may be defined as the scientific study of heredity. i.e how traits are inherited.

Geneticists are interested in understanding how genes are passed from generation to generation.

Geneticists are also interested in variation.

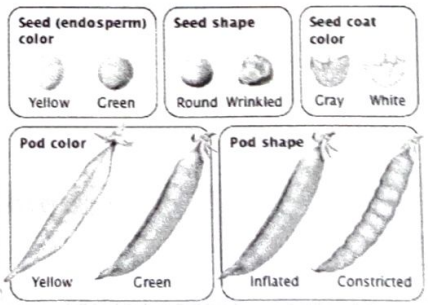
Traits are controlled by factors known as genes (located on chromosomes), and are transmitted through gametes from generation to generation.

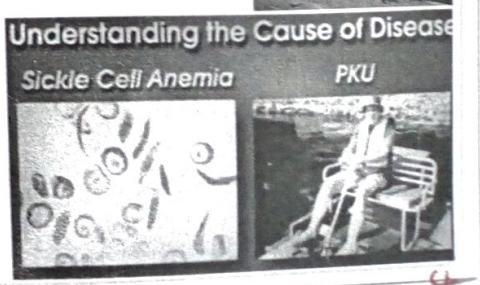
3

THE SCIENCE OF GENETICS

The following pictures illustrate the great differences in our species in terms of height, weight and skin colour (diverse human and plant species).

But there are other differences that are invisible to the eyes such as who has sickle cell anaemia, or high risk of heart disease, or cancer, or diabetics, or hypertension etc.





4

DIVISIONS OF GENETICS

Traditionally, the study of genetics has been divided into three major sub-disciplines: classical (transmission/Mendelian) genetics, molecular genetics, and population genetics.

Classical (transmission) genetics: A discipline that describes how physical characteristics (traits) are passed from one generation to another.

It focuses on how an individual organism inherits its genetic makeup and how it passes its genes to the next generation.

DIVISIONS OF GENETICS

Molecular genetics: A discipline that studies the chemical and physical nature of the genetic material (DNA), how genetic information is encoded, replicated, and expressed.

It includes the cellular processes of replication, transcription, translation and gene regulation- the processes that control the expression of genetic information.

The focus of molecular genetics is:
DNA - RNA - PROTEIN

DIVISIONS OF GENETICS

Population genetics explores the genetic composition of groups of individuals of the same species (populations) and how that composition changes over time and space.

Population genetics explore genetic changes that are relevant to the process of evolution. The focus of population genetics is the group of genes found in a population.

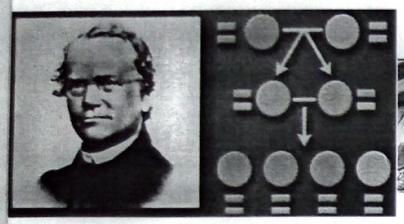
DIVISIONS OF GENETICS

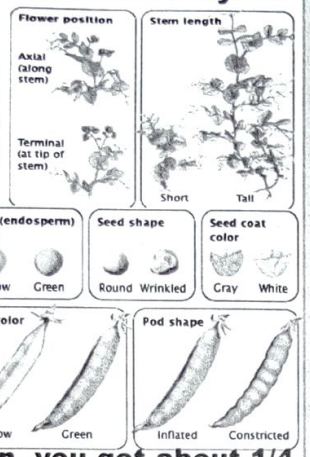
It may be convenient or traditional to divide the study of genetics into these three groups, but we should also recognize that the fields overlap, and that each major sub-division *can be further divided* into a number of more specialized fields, such as chromosomal genetics, biochemical genetics, quantitative genetics, plant genetics, microbial genetics, animal genetics, human genetics, fungal genetics, or field-related e.g. clinical genetics, immuno-genetics, behavioural genetics, developmental genetics, and each of these organisms can be studied at the level of transmission, molecular, and population genetics.

MENDELS EXPERIMENTS

The modern approach to genetics can be traced to the mid-nineteenth century with Gregor Mendel's careful analyses of inheritance in peas.

The idea of taking two pure-breeding strains, in this case, green pea and yellow pea, crossing them together & observing & counting in the next generation and the next generation, how many of each colour you get.



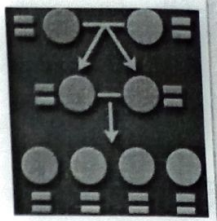


He observed that in the second generation, you get about 1/4 of yellow peas. Mendel's incredible clarity really organized the ideas of genetics for us.

9

LAWS OF INHERITANCE

1. **The characteristics of a diploid organism are determined by alleles which occur in pairs. Of a pair of such alleles, only one can be carried in a single gamete.**

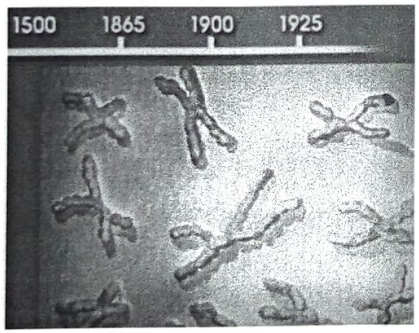


2. **Each of a pair of alleles for a particular gene can combine randomly with either of another pair of alleles for a different gene.**

10

20th Century

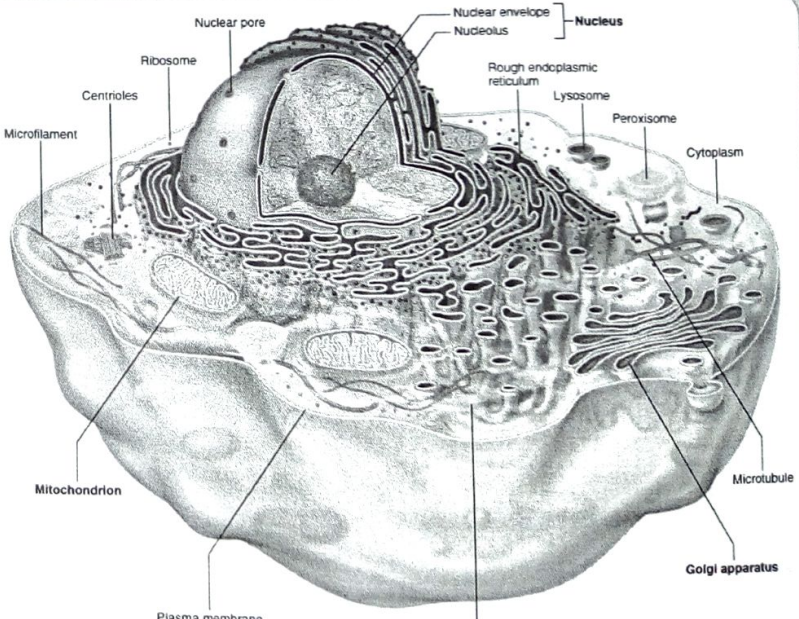
The first quarter of the 20th century was devoted to figuring out the fact that heredity resided in cellular structures called chromosomes.
(Walter Sutton and Theodore Boveri, 1902)



CHROMOSOMAL THEORY OF HEREDITY

Chromosomes carry the genetic information (the DNA), and their behaviour during meiosis provides the physical basis for the segregation and independent assortment of genes.

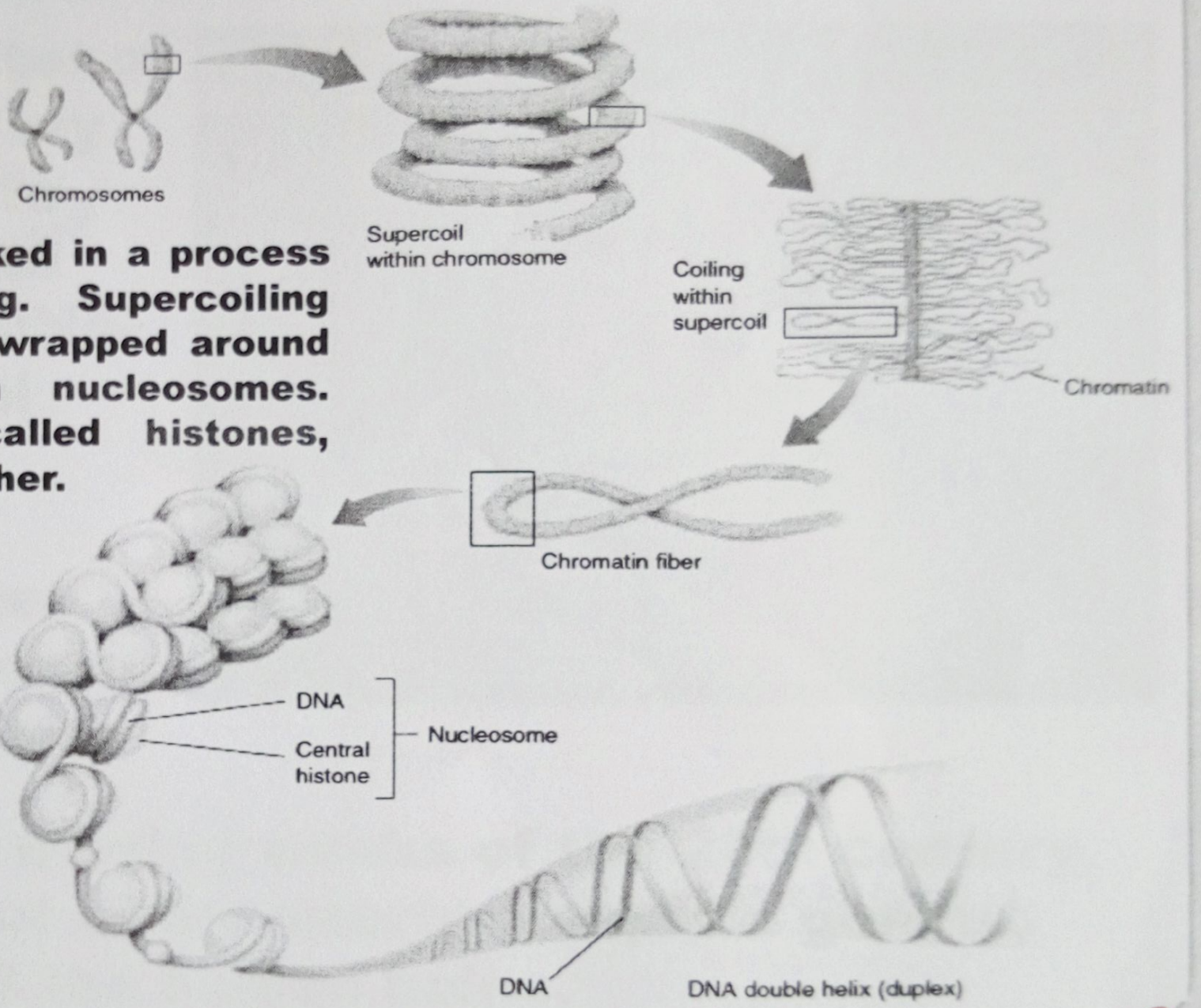
11



Typical structure of animal cell

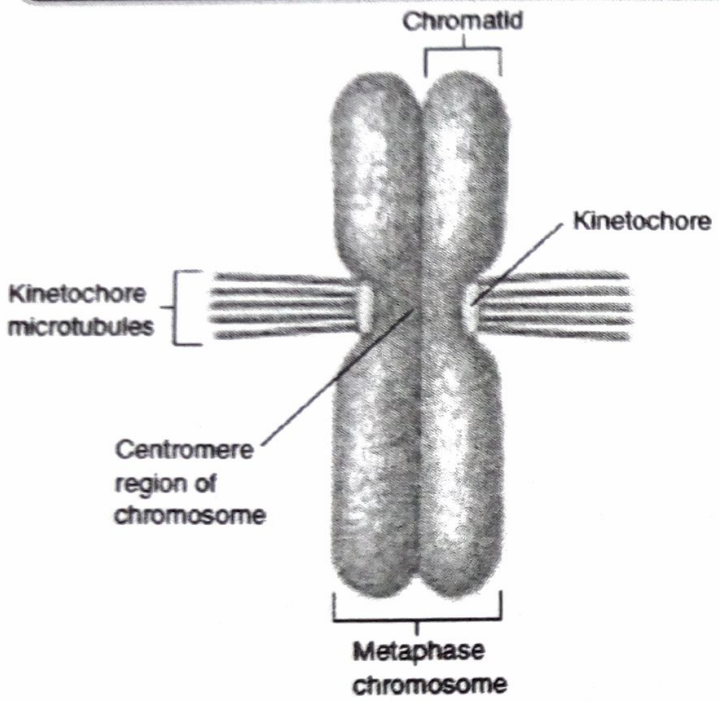
12

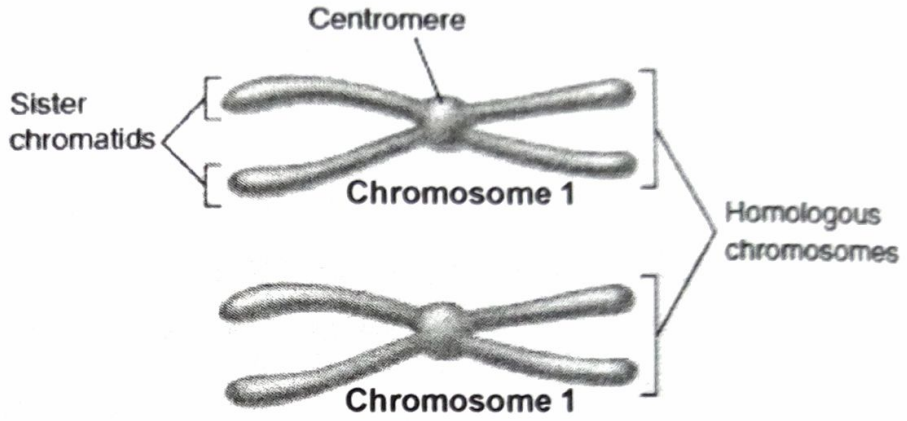
The Chromosome



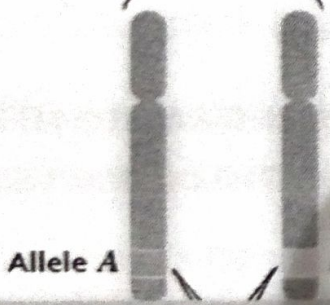
DNA is tightly packed in a process called supercoiling. Supercoiling allows DNA to be wrapped around proteins to form nucleosomes. Other proteins, called histones, hold the coils together.

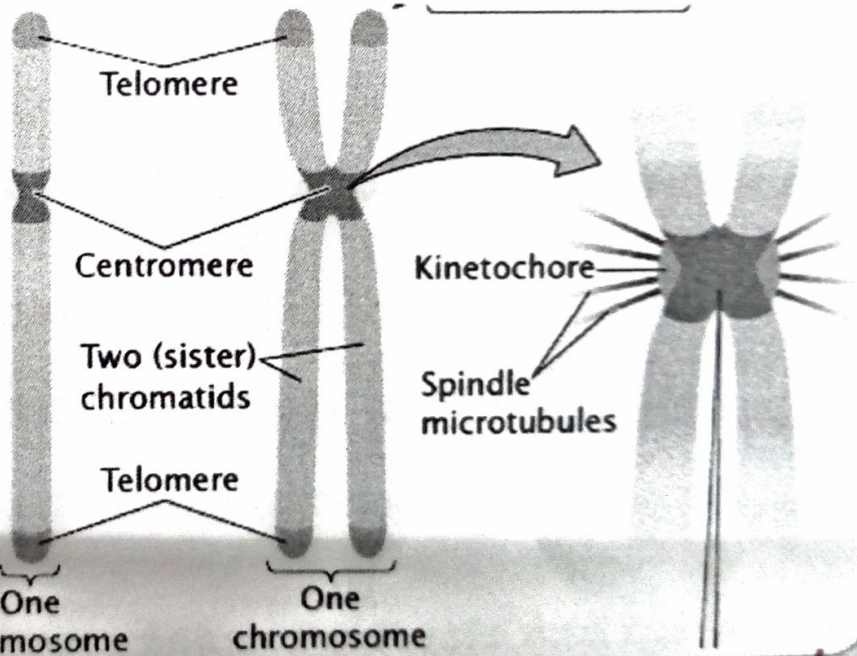
The Chromosome





A *diploid* organism has two sets of chromosomes organized as *homologous* pairs.





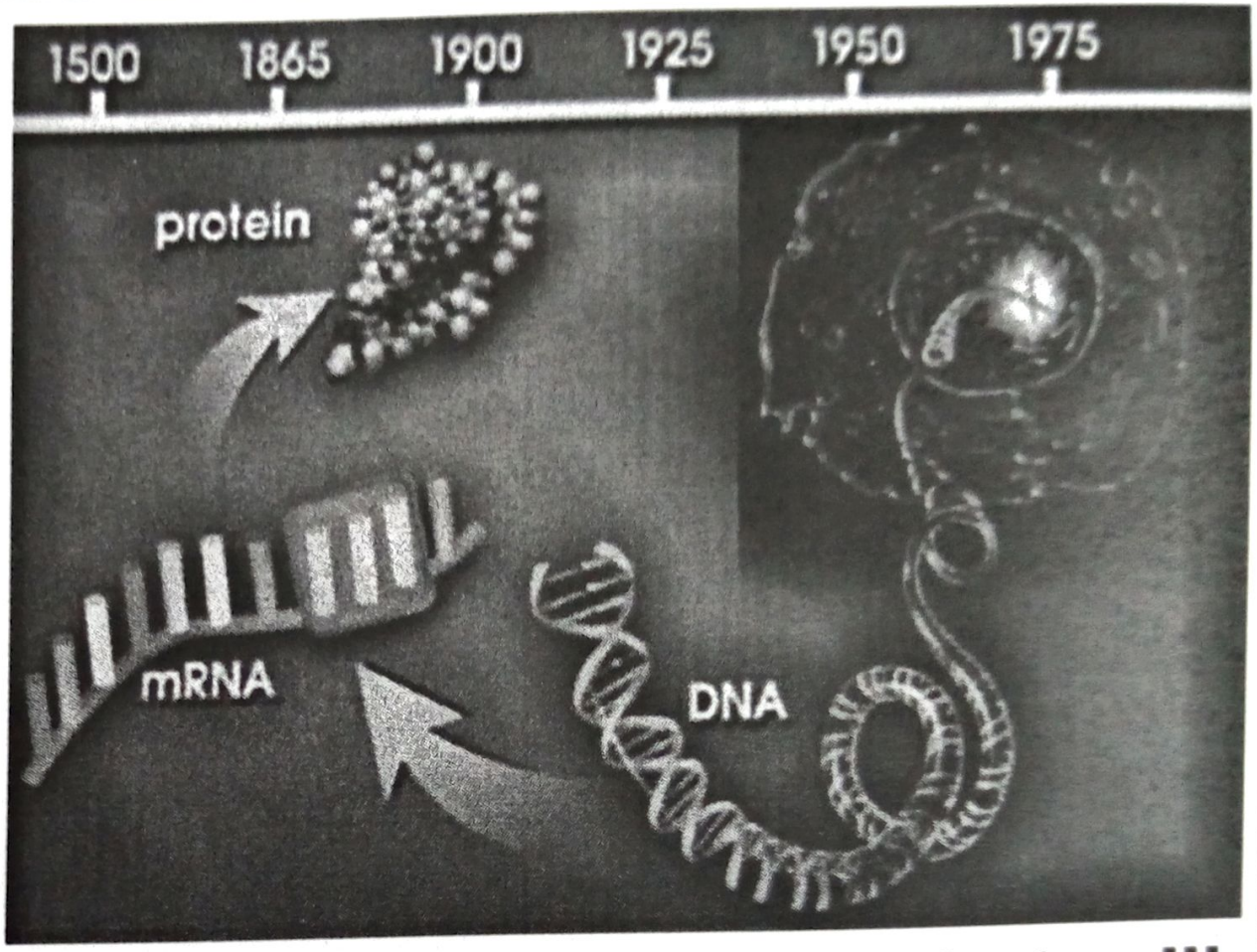
20th Century

The second quarter of the 20th century was pretty much devoted to finding out the molecular basis of the cellular structure (chromosome), and that the DNA molecule was the physical molecular basis of the information in the chromosomes, and that it has a double helical structure.

By mid-century, James Watson and Francis Crick worked out the double-helical nature of DNA (1953).

20th Century

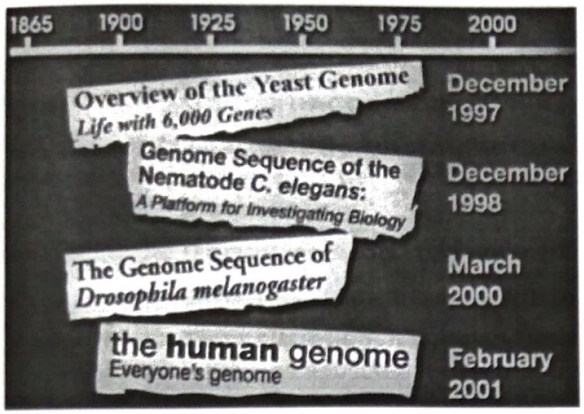
The third quarter of the 20th century was devoted to figuring out how the information was written (DNA-RNA-Protein),



Also, finding the laboratory techniques that will allow us to read out that information- through recombinant DNA technology, gene cloning and sequencing.

20th Century

The last quarter of the 20th century was devoted to reading out the sequence of DNA- first individual genes, then collection of genes, and then entire genomes of small organisms.



Finally, in the closing weeks of the 20th century, the reading out of the nearly complete genetic information of the human being.

CONCEPTS & DEFINITIONS

A gene is the fundamental unit of heredity.

Genes come in multiple forms called alleles.

Genes encode phenotypes.

The genetic information that an individual organism possesses is its genotype while the trait (physical characteristics) is its phenotype.

Genes are located on chromosomes

Chromosomes are made up of DNA and associated proteins.

The cells of each species have a characteristic number of chromosomes. for example, bacterial cells normally possess a single chromosome; human cells possess 46 chromosomes; pigeon cells possess 80 chromosomes.

Cells can be categorized into Somatic cells and gametes

Chromosomes can be categorized into Autosomes and sex chromosomes

Chromosomes separate through the processes of mitosis and meiosis.

Genetic information is transferred from DNA to RNA to protein.

CONCEPTS & DEFINITIONS

Allele is an alternative form of a given gene pair; tall and dwarf (Tt) are the alleles for the height of a pea plant.

Dominant allele: the allele that expresses its phenotype at the expense of an alternate allele.

Recessive allele: an allele whose expression is suppressed in the presence of a dominant allele.

More than two alleles can exist in a population but only two can be found in an individual.

Homozygote: organism which has only one type of allelic pair; for example *DD* is homozygous dominant and *dd* is homozygous recessive. Pure lines are homozygous for the gene of interest.

Heterozygote: organism with two different alleles; for example the *Dd* / *Tt* heterozygote.

Codominant alleles: the heterozygotes express both homozygous phenotypes e.g. A and B alleles of the ABO Blood group system.

THE GENETIC MATERIAL

Life is characterized by tremendous diversity, but the coding instructions of all living organisms are written in the same genetic language- that of nucleic acids (DNA or RNA).

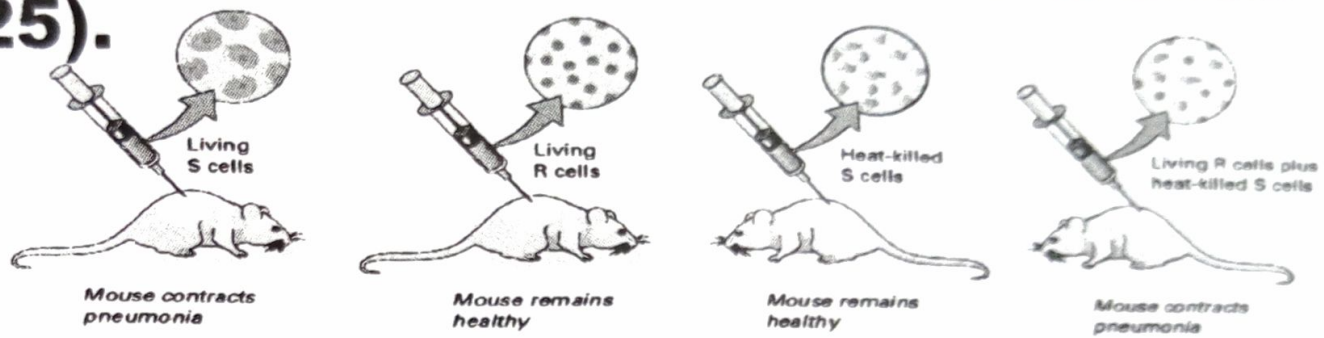
In all cellular organisms, the genetic material is DNA.

Several lines of indirect evidence suggested that DNA harbours the genetic information of living organisms. For example, most of the DNA of cells is located in the chromosomes, whereas RNA and proteins are abundant in the cytoplasm. However, these are not sufficient to prove that DNA is the genetic material. By 1887, researchers had concluded that the physical basis of heredity lies in the nucleus.

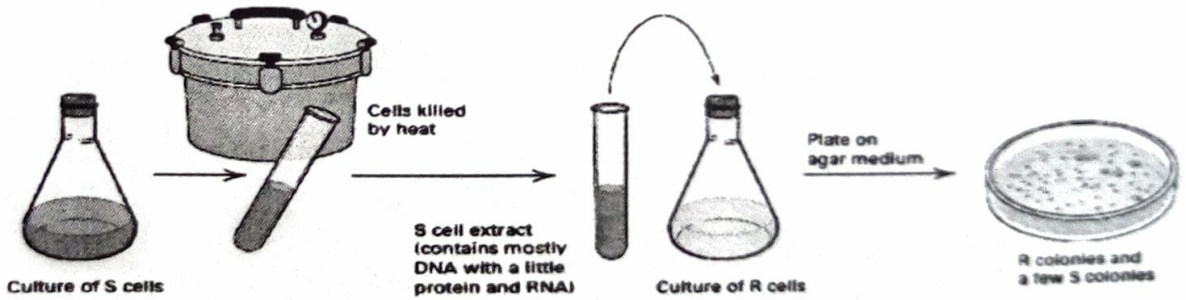
Several line of investigations were conducted in the 2nd quarter of the 20th Century which showed that DNA was truly the genetic material.

THE GENETIC MATERIAL

Sir Frederick Griffith demonstrated transformation in bacterial (1925).



Colin MacLeod, and Maclyn McCarty- demonstrated that the transformation material is DNA (1944).



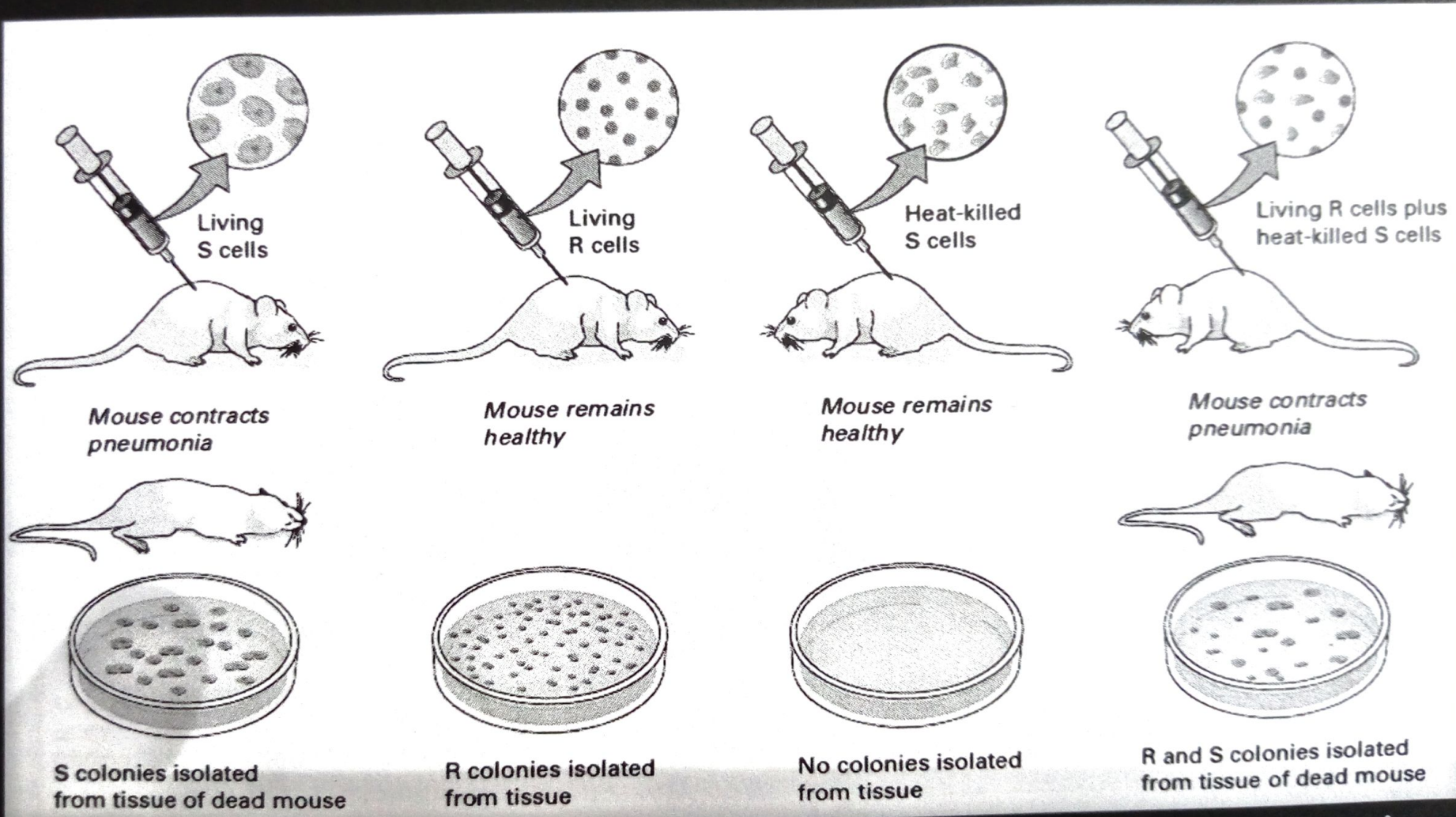
Alfred Hershey and Martha Chase provided convincing evidence that DNA is the genetic material (1952).

THE GENETIC MATERIAL

The first clue that DNA was the carrier of hereditary information came with the demonstration that DNA was responsible for a phenomenon called *transformation. The phenomenon* was first observed in 1928 by Sir Frederick Griffith, an English physician whose special interest was the bacterium that causes pneumonia, *Streptococcus pneumonia.*

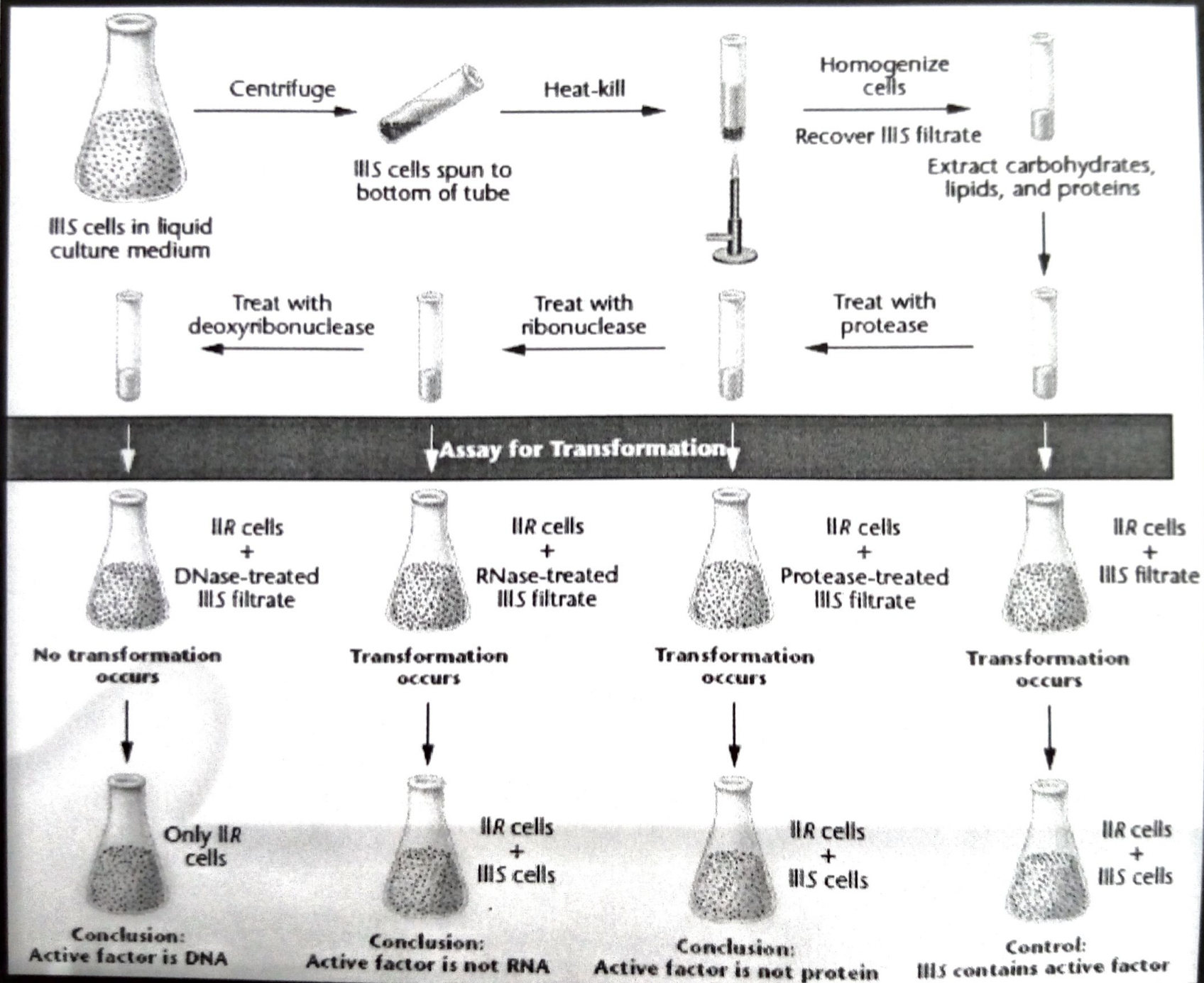
***Griffith had* succeeded in isolating several strains of *S. Pneumonia* (type I, II, III, and so forth). In the virulent (disease-causing) forms of a strain, each bacterium is surrounded by a polysaccharide coat, which makes the bacterial colony appear smooth when grown on an agar plate; these forms are referred to as S, for smooth. Griffith found that these virulent forms occasionally mutated to non-virulent forms, which lack a polysaccharide coat and produce a rough appearing colony on an agar plate; these forms are referred to as R, for rough.**

Griffith's transformation experiment



The Griffith's experiment demonstrating bacterial transformation. A mouse remains healthy if injected with either the nonvirulent R strain of *S. pneumoniae or heat-killed cell fragments* of the usually virulent S strain. R cells in the presence of heat-killed S cells are transformed into the virulent S strain, causing pneumonia in the mouse.

The Avery, MacLeod, and McCarty Experiment



A diagram of the Avery–MacLeod–McCarty experiment that demonstrated that DNA is the active material in bacterial transformation.

(A) The transforming activity is not destroyed by either protease or RNase.

(B) The transforming activity is not destroyed by either protease or RNase.

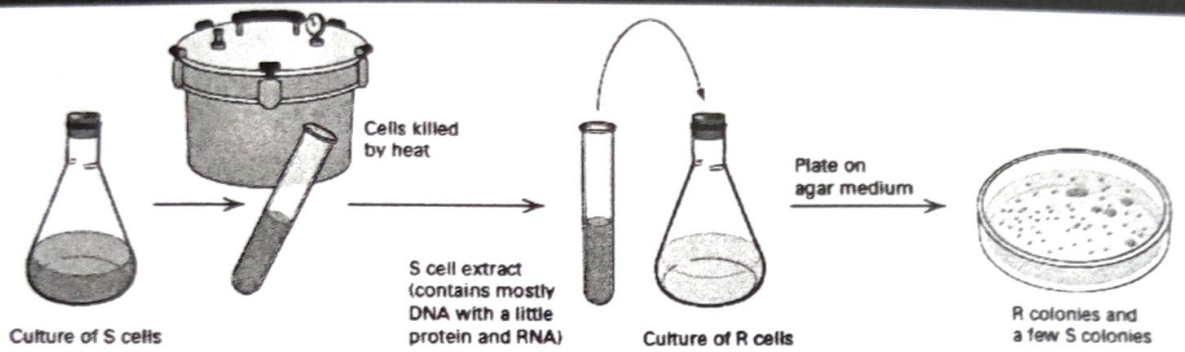
(C) The transforming activity was destroyed by DNase and so probably consists of DNA.

Conclusion: The evidence presented supports the belief that a nucleic acid of the deoxyribose type is the fundamental unit of the transforming principle of Pneumococcus Type IIIS

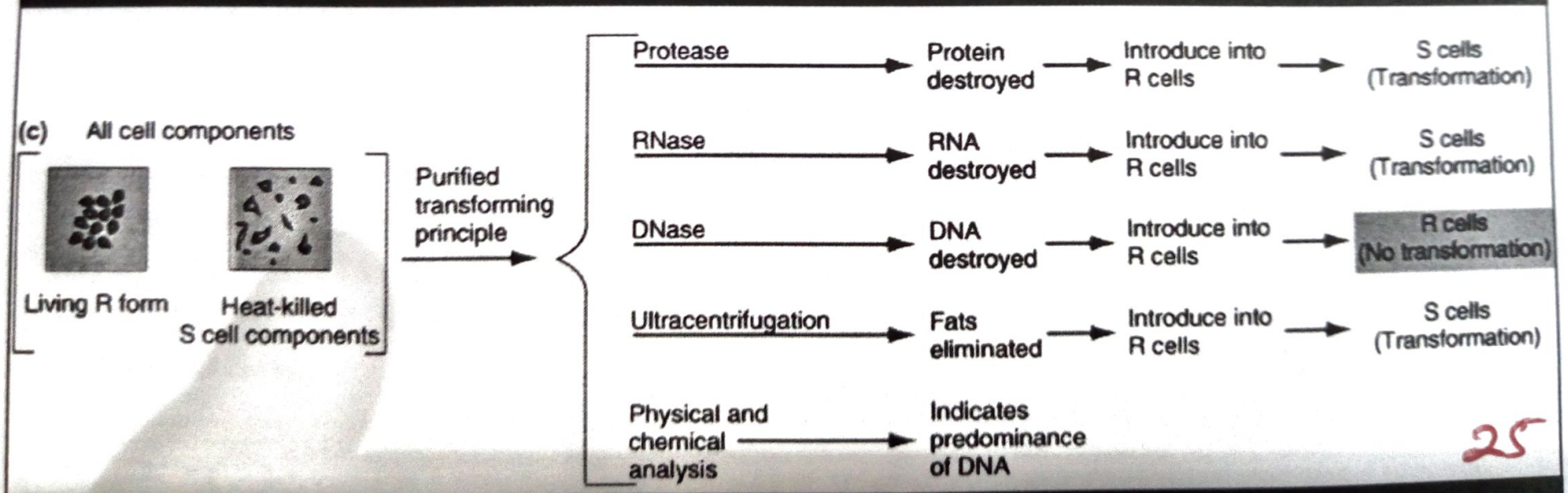
The Avery, MacLeod, and McCarty Experiment

Experiment

Question: What is the chemical nature of the transforming substance?



The transforming activity in S cells is not destroyed by heat.



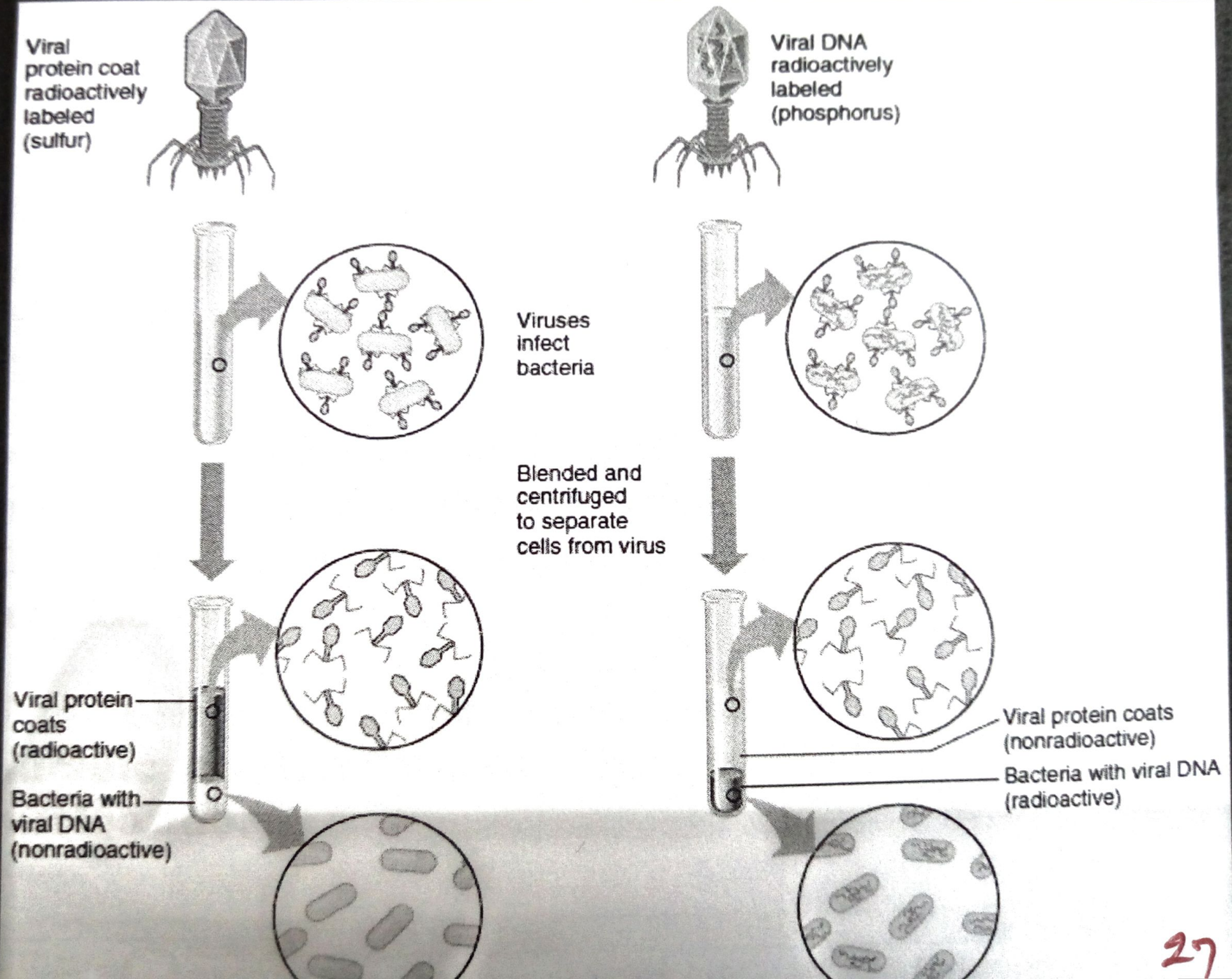
25

The Hershey–Chase Experiment

Hershey and Chase experiments

- 1952 – Alfred Hershey and Martha Chase provide convincing evidence that DNA is genetic material
- Performed experiment using T2 bacteriophage and bacteria
- Radioactive labels ^{32}P for DNA and ^{35}S for protein

The Hershey–Chase Experiment

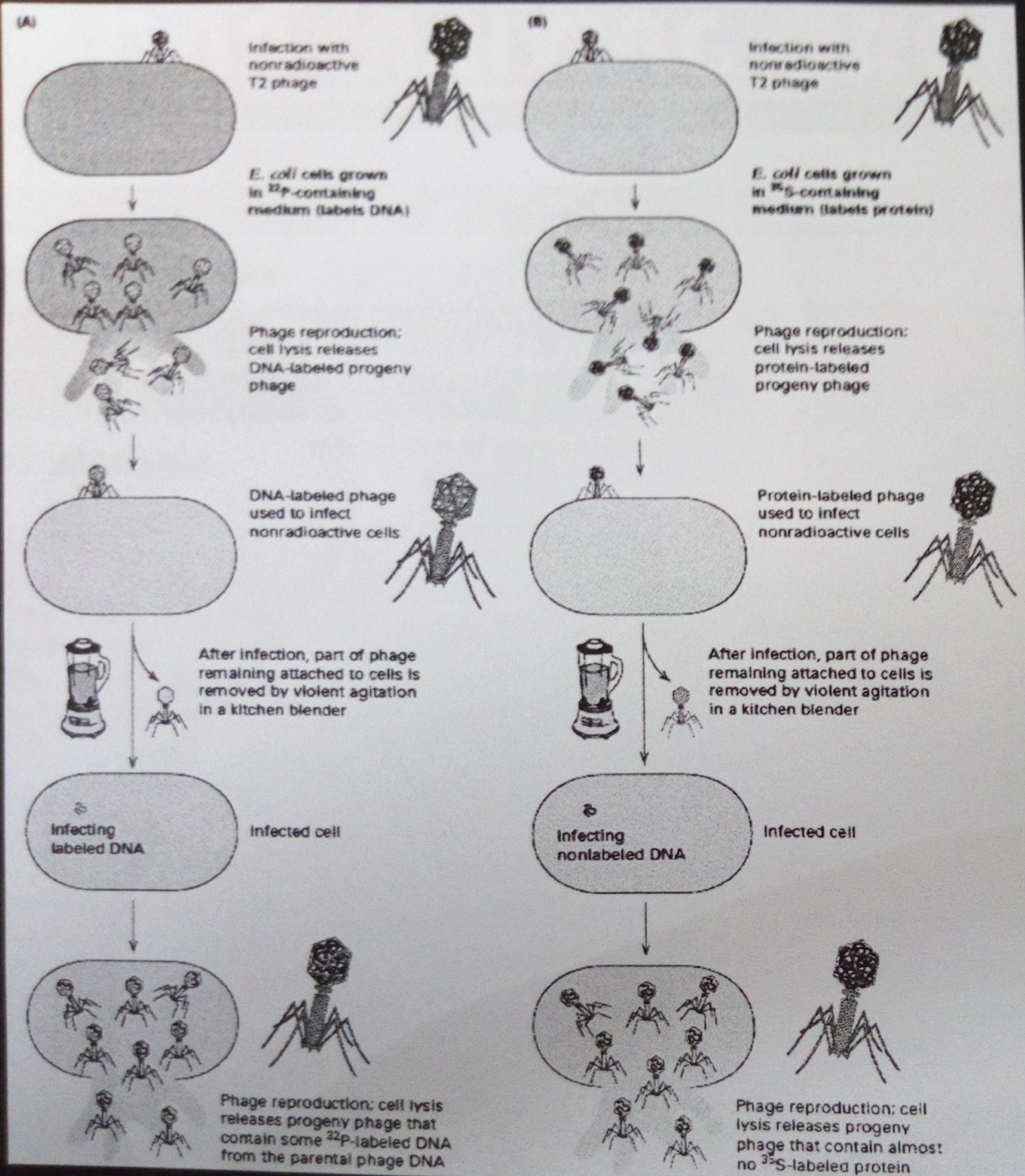


The Hershey–Chase Experiment

The Hershey–Chase ("blender") experiment demonstrating that DNA, not protein, is responsible for directing the reproduction of phage T_2 in infected *E. coli* cells.

(A) Radioactive DNA is transmitted to progeny phage in substantial amounts. ^{32}P

(B) Radioactive protein is transmitted to progeny phage in negligible amounts. ^{35}S



TEST OF KNOWLEDGE

I. Why did Hershey and Chase choose 32P and 35S for use in their experiment?

II. Could they have used radioactive isotopes of carbon (C) and oxygen (O) instead? Why or why not?

REFERENCE TEXTBOOK

1) Bruce Alberts, Alexander Johnson, Julian Lewis, David Morgan, Martin Raff, Keith Roberts, and Peter Walter (2015). Molecular biology of the cell (Sixth Edition). Published by Garland Science, Taylor & Francis Group, New York, USA.

2) Bruce Alberts, Dennis Bray, Karen Hopkin, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, and Peter Walter (2015). Essential Cell Biology (Fourth Edition). Published by Garland Science, Taylor & Francis Group, New York, USA.

DNA STRUCTURE & FUNCTION

Dr. Segun I. OYEDEJI

Federal University Oye-Ekiti

Department of Animal & Environmental Biology

2018 Lecture Guide

GENETIC MATERIAL & NUCLEIC ACIDS

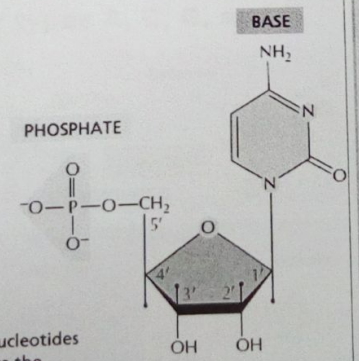
We have established from three experiments discussed in the previous class that DNA is the Genetic Material.

However, genetic information may be carried in DNA or RNA. DNA and RNA are referred to as Nucleic acids.

The basic building block of nucleic acids (DNA or RNA) is nucleotide.

NUCLEOTIDES

A nucleotide consists of a nitrogen-containing base, a five-carbon sugar, and one or more phosphate groups.



Nucleotides are the subunits of the nucleic acids.

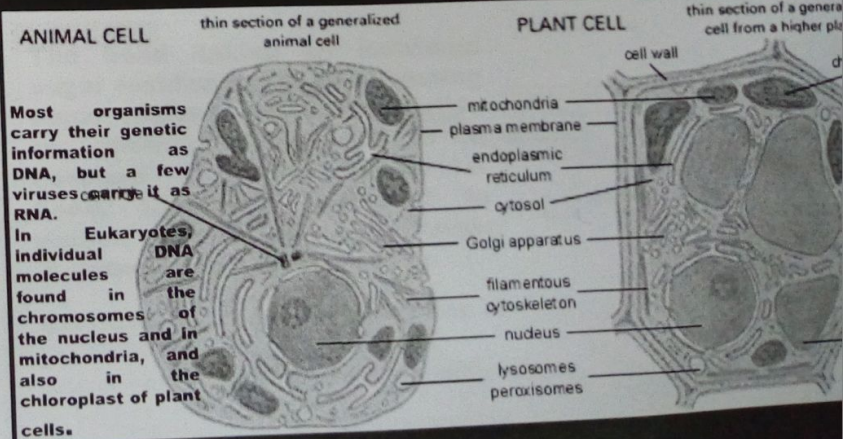
DNA IN LIVING ORGANISMS

Three-domain system

Bacteria	Archaea	← Eukarya

Six-kingdom system

Bacteria	Archaea	Protista	Plantae	Fungi	Animalia



Most organisms carry their genetic information as DNA, but a few viruses carry it as RNA.

In Eukaryotes, individual DNA molecules are found in the chromosomes of the nucleus and in mitochondria, and also in the chloroplast of plant cells.

FUNCTIONS OF THE GENETIC MATERIAL

The genetic material must be able to perform three essential functions:

The Genotypic function (Storage & Replication) The genetic material must store genetic information and accurately transmit that information from parents to offspring, from one generation to another.

The Phenotypic function (Gene expression) The genetic material must control the development of the phenotype of the organism – it must dictate the growth of the organism from the single-celled zygote to the mature adult.

The Evolutionary function (Mutation)

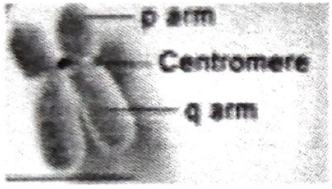
The genetic material must undergo changes to produce variations that allow organisms to adapt to modifications in the environment so that evolution can occur.

INFORMATION MACROMOLECULE

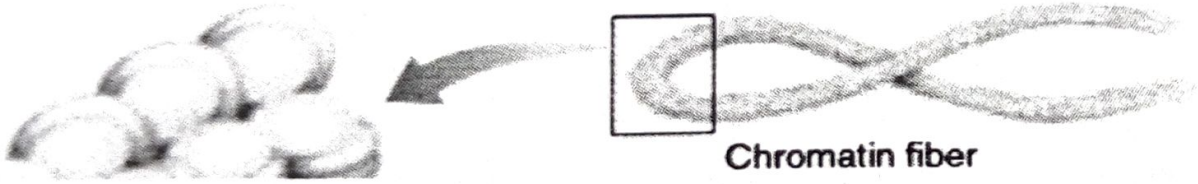
DNA resides in the nucleus of Eukaryotic organisms in structures known as Chromosomes.

Chromosomes consists of DNA coiled many times around proteins called histones that stabilize their structure.

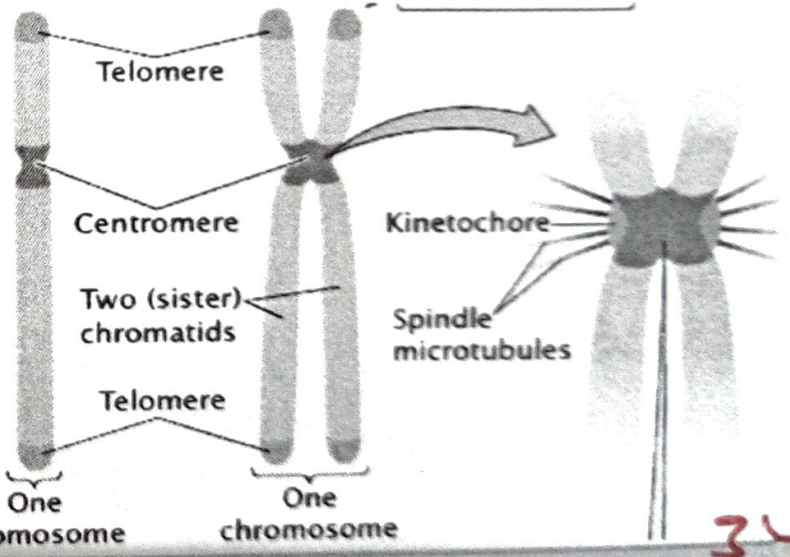
Chromosomes have centromeres, which are points at which they constrict and divides the chromosomes into two sections or arms.



The short arm is labeled the "p arm", the long "q arm". Centromere location gives the chromosome its characteristic shape.



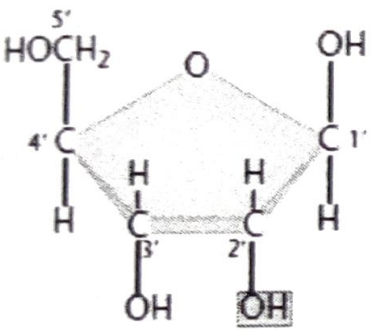
Chromatin is the general structure of any chromosome, and the basic units are nucleosome (DNA + Histone proteins)



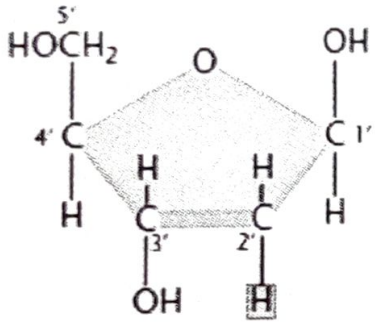
COMPOSITION OF NUCLEIC ACIDS

Nucleic acids (DNA or RNA) are polymers consisting of repeating units of nucleotides. Each nucleotide consists of a five-carbon sugar, a phosphate, and a heterocyclic nitrogenous base.

The nitrogenous bases in DNA are of four types A, C, G, and T.



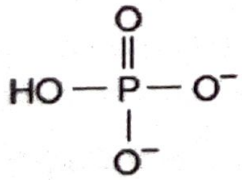
Ribose



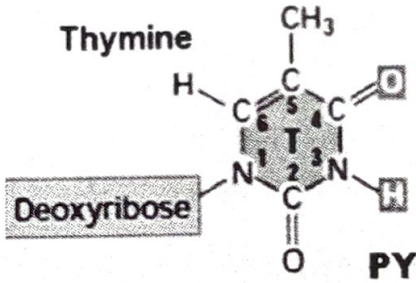
2-Deoxyribose

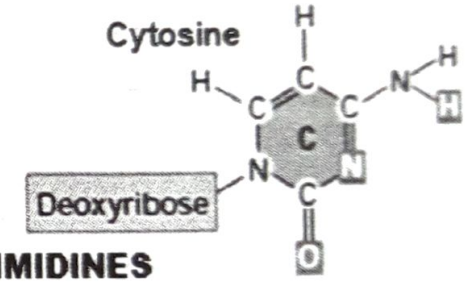
5-carbon sugar (Pentose)

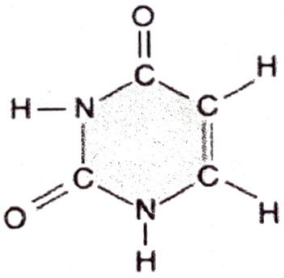
The five-carbon sugar in DNA is 2-deoxyribose; in RNA, it is ribose.



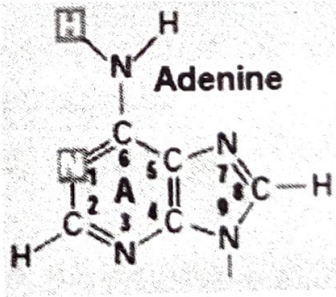
Phosphate

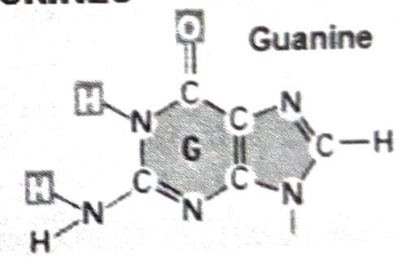






Uracil
(RNA only)





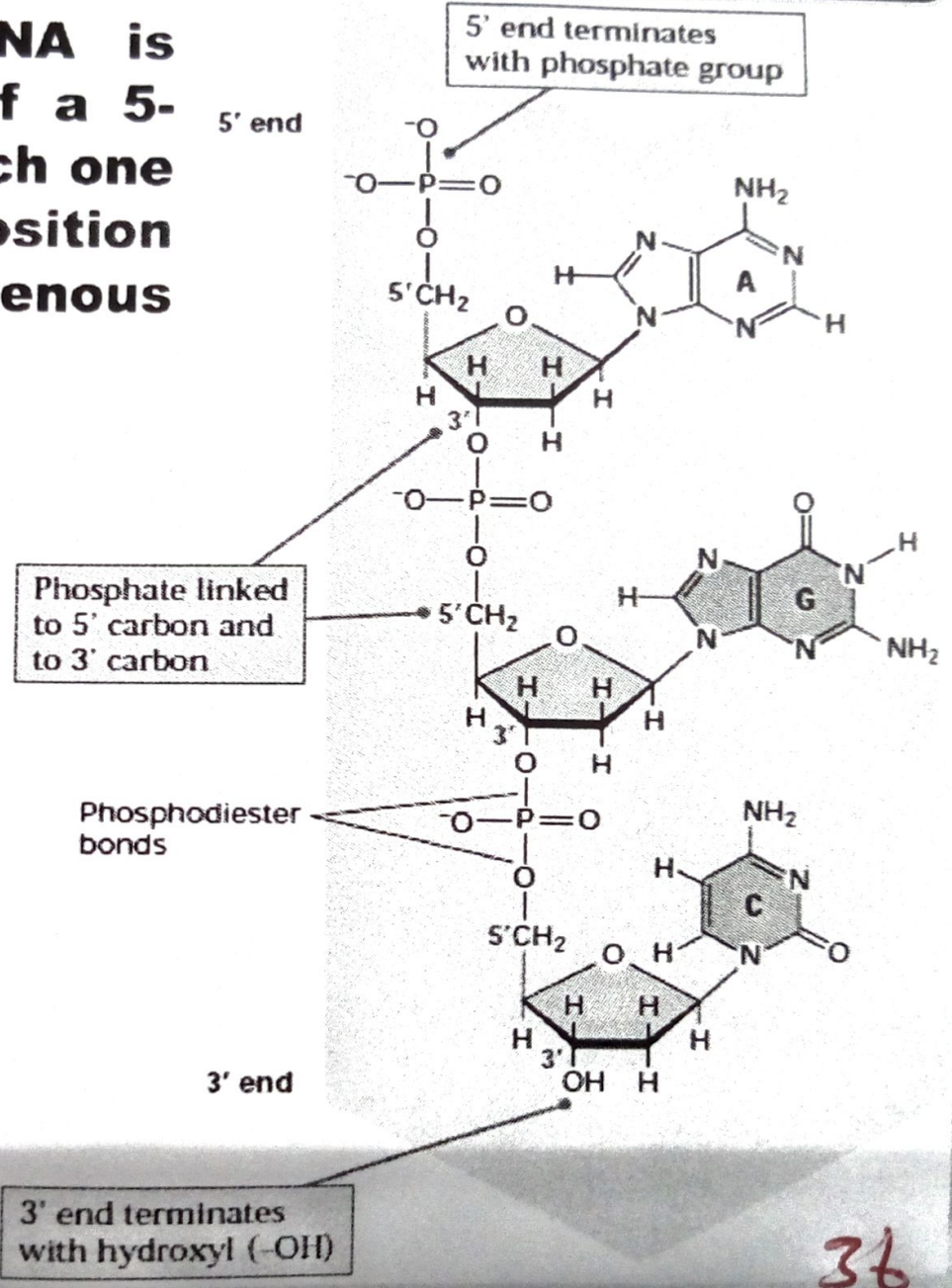
35

DNA STRUCTURE

The basic building block of DNA is nucleotide. Nucleotide consists of a 5-carbon sugar (deoxyribose) to which one phosphate is attached at the 5' position of the sugar ring and one nitrogenous base is attached at the 1' site.

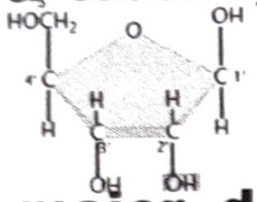
The bond linking an individual sugar residue to the neighbouring sugar residues (OR a nucleotide to another nucleotide) is a covalent 3',5' -phosphodiester bond. Covalently attached to carbon atom 1' of each sugar residue is a nitrogenous base.

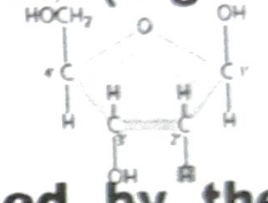
Because of the phosphate group in the DNA molecule, DNA is negatively charged hence, soluble in water.



DNA STRUCTURE- NUCLEOSIDES & NUCLEOTIDES

A molecule which consists of one of the four nitrogenous bases linked to a pentose sugar is known as a nucleoside. If the sugar is deoxyribose, the nucleoside is a deoxyribonucleoside (e.g in DNA); If the sugar is a ribose, the nucleoside is ribonucleoside (e.g in RNA).



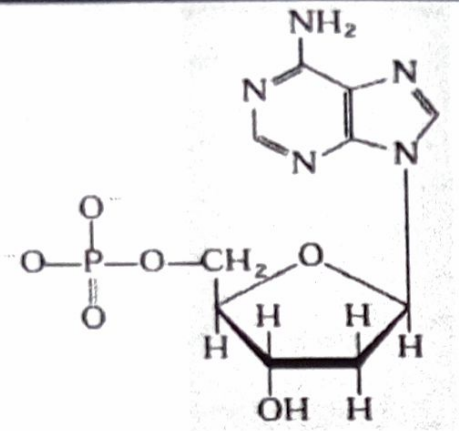


There are four major deoxyribonucleosides distinguished by the attached base: deoxyadenosine, deoxyguanosine, deoxythymidine, and deoxycytidine.

If the nucleoside has one or more attached phosphate groups (generally at the 5' position, but alternatively at the 3' position), the molecule is a nucleotide. Examples include: deoxyadenosine monophosphate (dAMP), deoxyguanosine diphosphate (dGDP), deoxythymidine monophosphate (dTMP) and deoxycytidine triphosphate (dCTP). The nucleotides employed in energy metabolism, such as adenosine triphosphate (ATP), are ribose-containing molecules.

Nucleotides are covalently linked to one another to form a linear polymer, or strand with a backbone composed of alternating sugar and phosphate groups joined by 3'-5'- phosphodiester bonds.

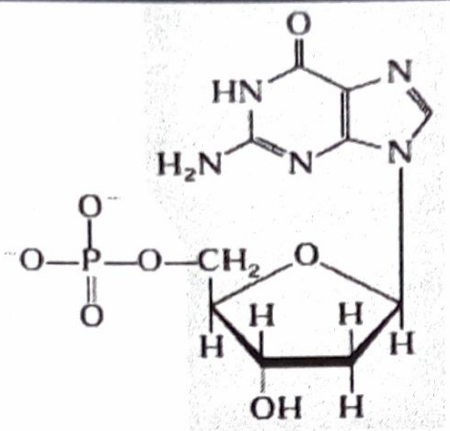
STRUCTURE OF NUCLEIC ACIDS



Nucleotide: Deoxyadenylate (deoxyadenosine 5′-monophosphate)

Symbols: A, dA, dAMP

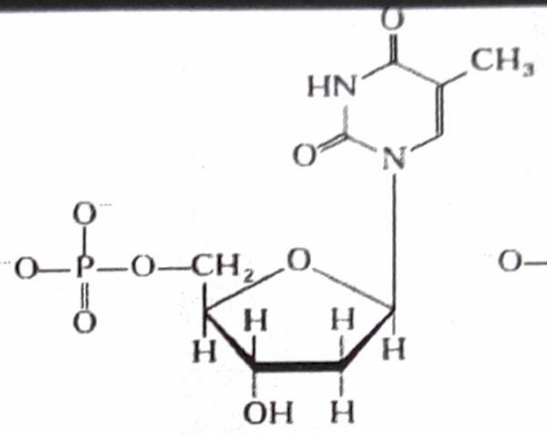
Nucleoside: Deoxyadenosine



Deoxyguanylate (deoxyguanosine 5′-monophosphate)

G, dG, dGMP

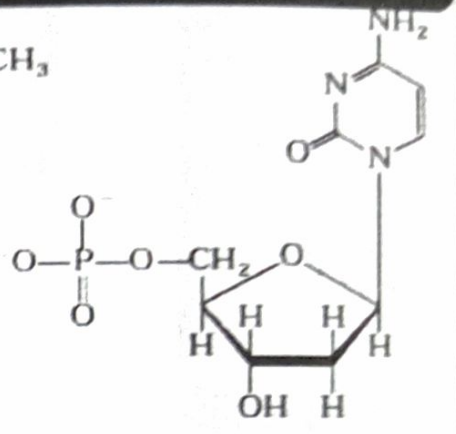
Deoxyguanosine



Deoxythymidylate (deoxythymidine 5′-monophosphate)

T, dT, dTMP

Deoxythymidine

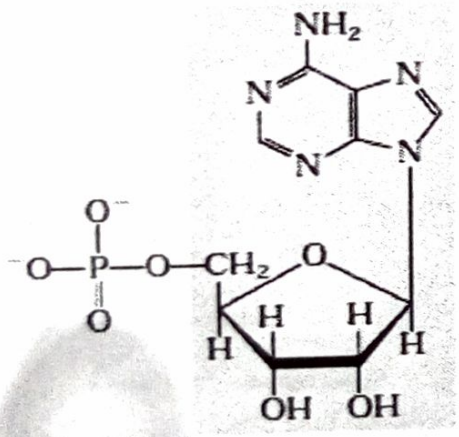


Deoxycytidylate (deoxycytidine 5′-monophosphate)

C, dC, dCMP

Deoxycytidine

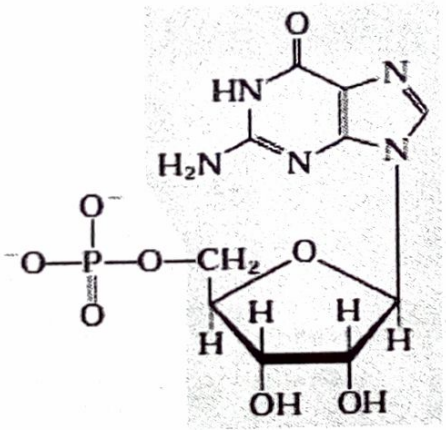
(a) Deoxyribonucleotides



Nucleotide: Adenylate (adenosine 5′-monophosphate)

Symbols: A, AMP

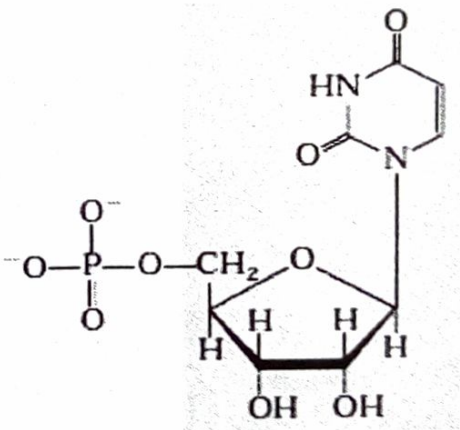
Nucleoside: Adenosine



Guanylate (guanosine 5′-monophosphate)

G, GMP

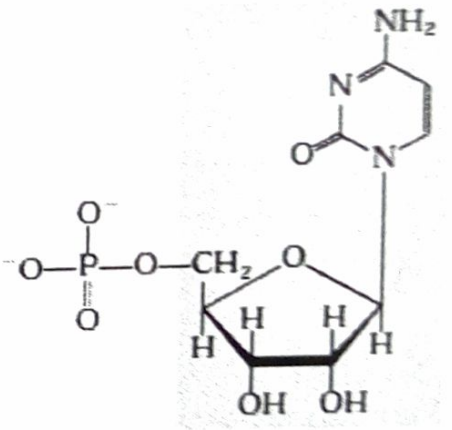
Guanosine



Uridylate (uridine 5′-monophosphate)

U, UMP

Uridine



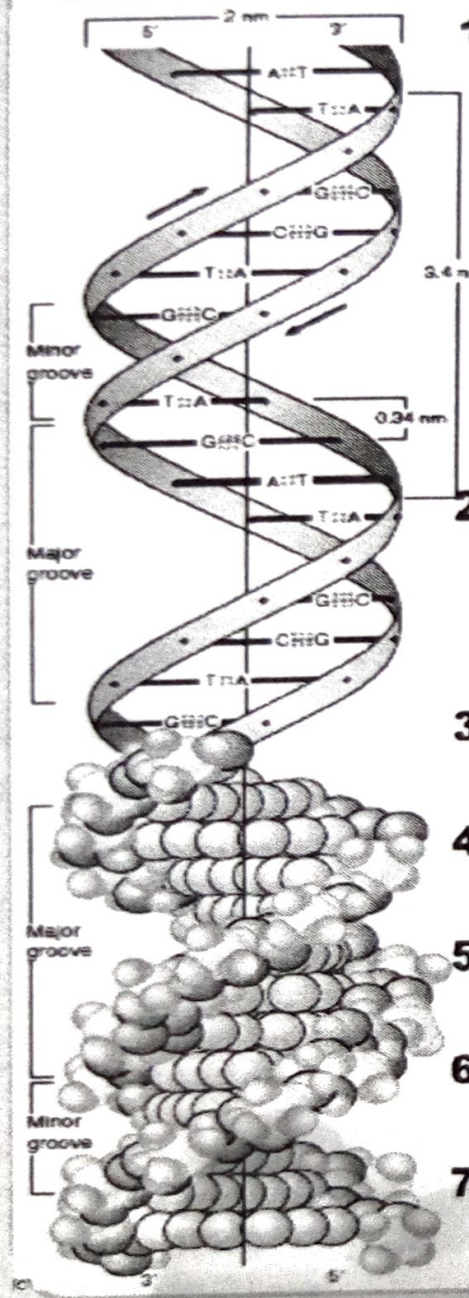
Cytidylate (cytidine 5′-monophosphate)

C, CMP

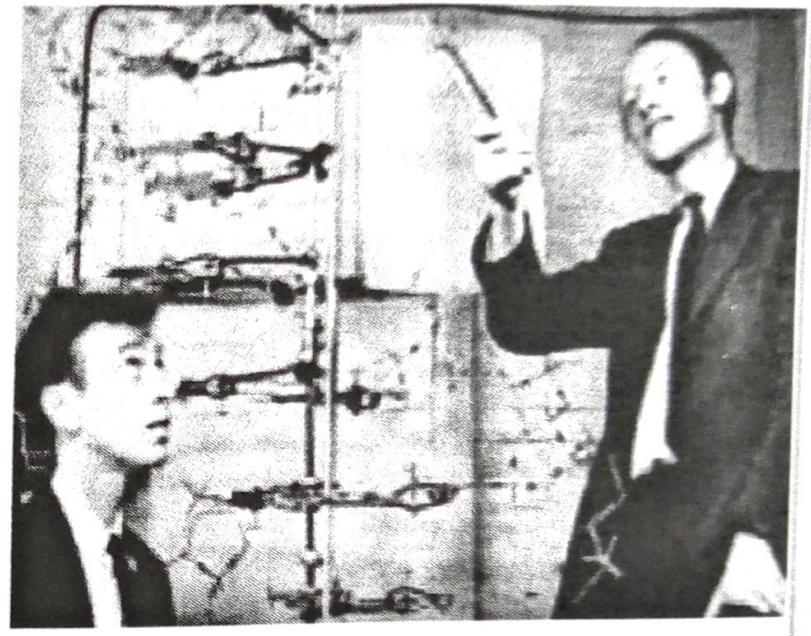
Cytidine

(b) Ribonucleotides

DNA STRUCTURE & COMPOSITION



1) **DNA has the structure of a double helix, consisting of two anti-parallel polynucleotide chains, held together by hydrogen bonds between complementary bases- adenines and thymines, and between guanines and cytosines.**



2) **Adenine always pair with thymine (A-T), while cytosine will always pair with guanine (G-C).**

3) **The proportion of adenine in DNA always equals that of thymine, and the proportion of guanine always equals that of cytosine.**

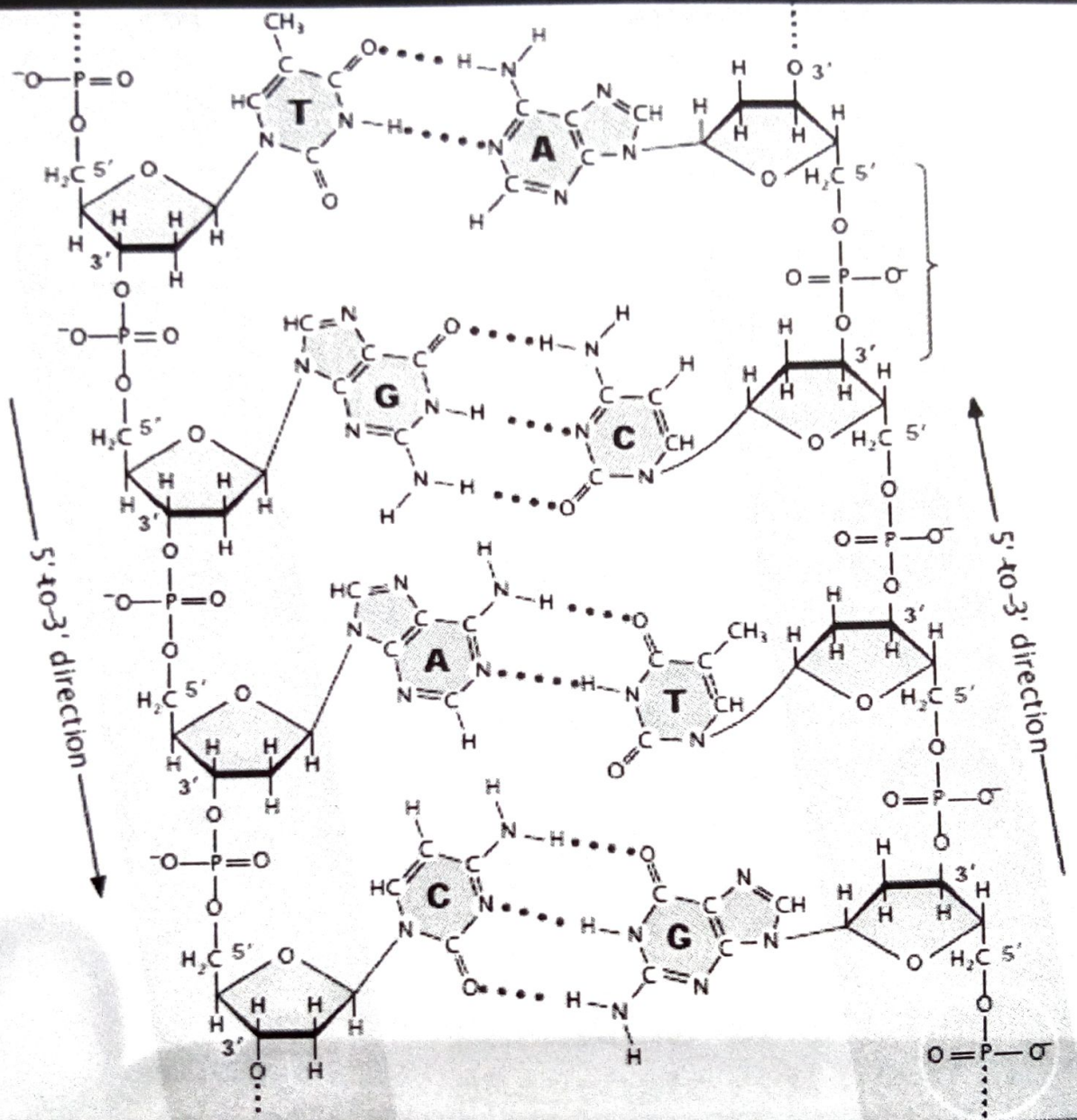
4) **Furthermore, the proportion of purines (A and G) and pyrimidines (C and T) is always equal.**

5) **The base composition of DNA generally varies from one species to another.**

6) **DNA specimens isolated from different tissues of the same species have the same base composition.**

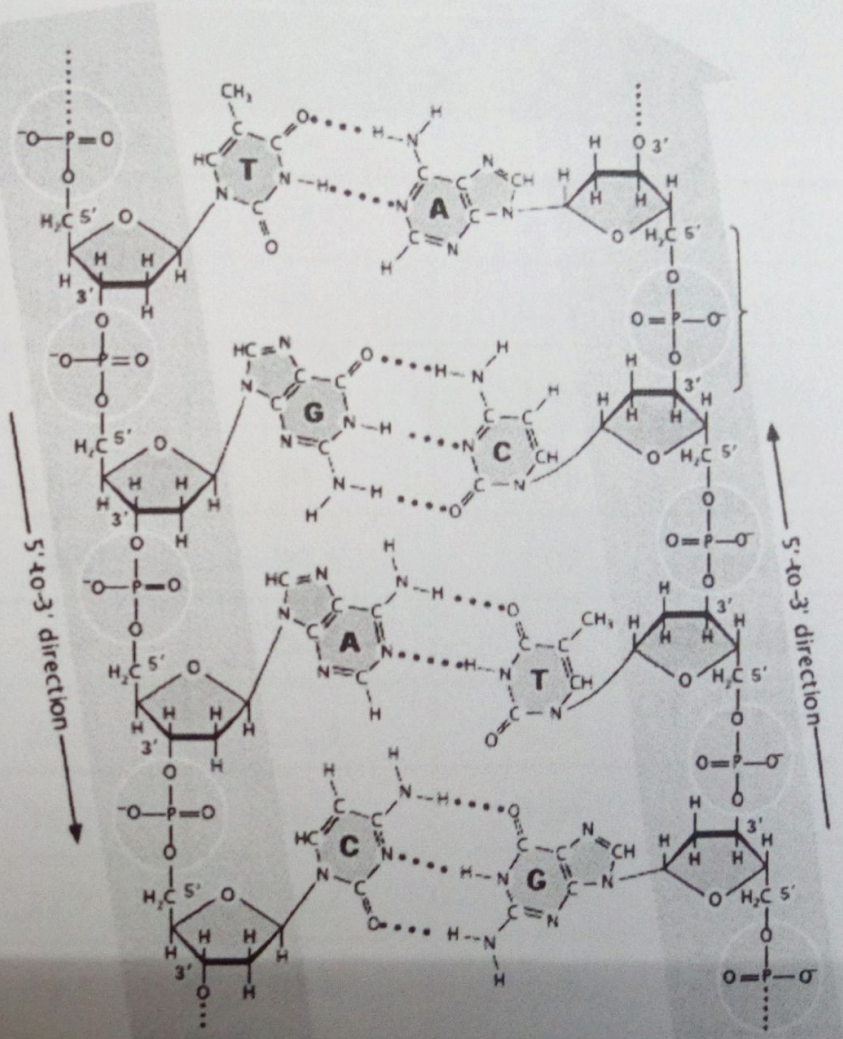
7) **The base composition of DNA in a given species does not change with an organism's age, nutritional state, or changing environment.**

DNA STRUCTURE

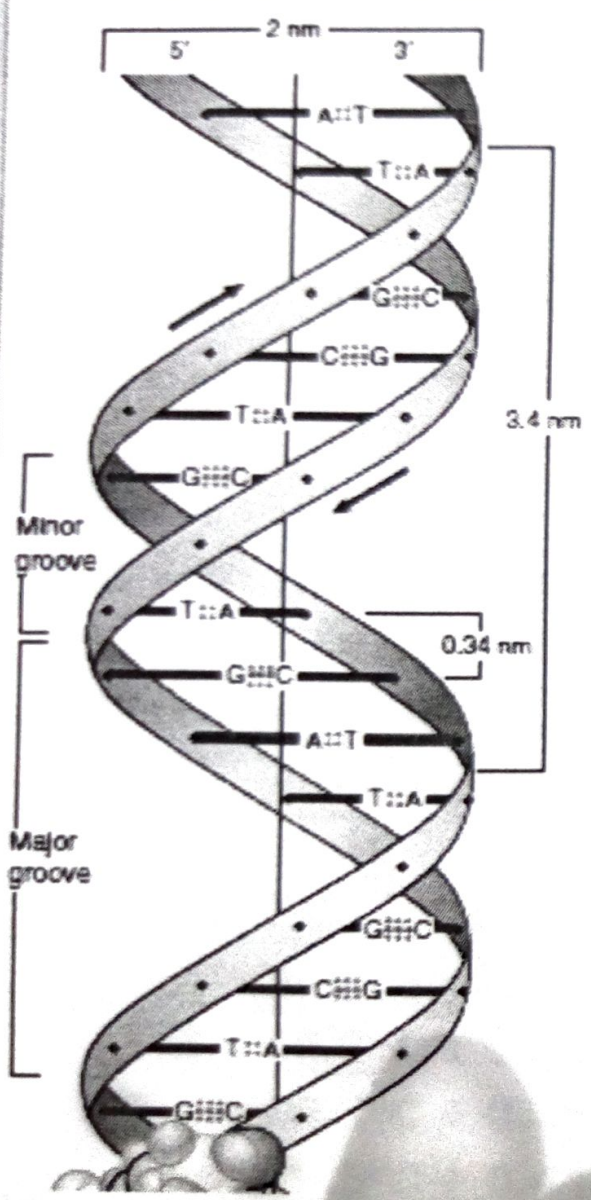


DNA STRUCTURE

Nitrogenous bases form hydrogen bonds with each other across the width of the helix. Adenine (A) on one strand always pairs with thymine (T) on the opposite strand. Likewise, guanine (G) always pairs with cytosine (C). The term *complementary* is sometimes used to describe these pairings. For example, A is complementary to T, and C is complementary to G. Therefore, the order of nucleotides on one strand of the DNA helix predicts the order of nucleotides on the other strand. Thus, if one strand of the DNA molecule is composed of nucleotides AACGATCCG, we know that the order of nucleotides on the other strand is TTGCTAGGC.

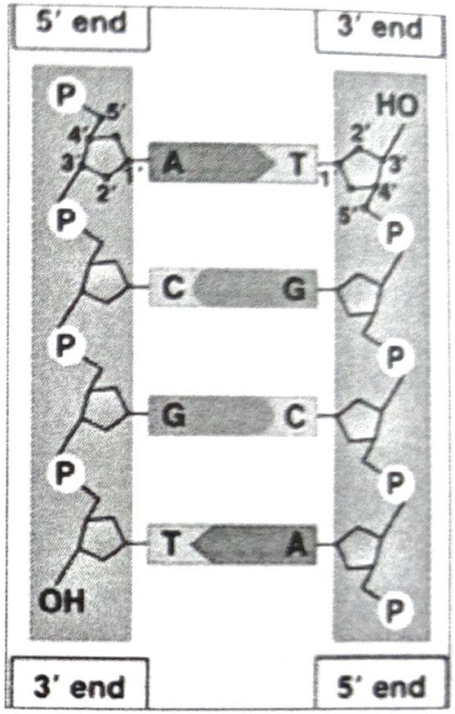


DNA STRUCTURE



The DNA double helix is ~ 2 nanometers in diameter. It also consists of a major groove and a minor groove. One turn (pitch) of a double helix = 10 base pairs = ~ 3.4nm (distance occupied by a single turn of the helix).

Thus, the base pairs in DNA are stacked about 0.34nm apart, with 10 base pairs per turn (360) of the double helix.



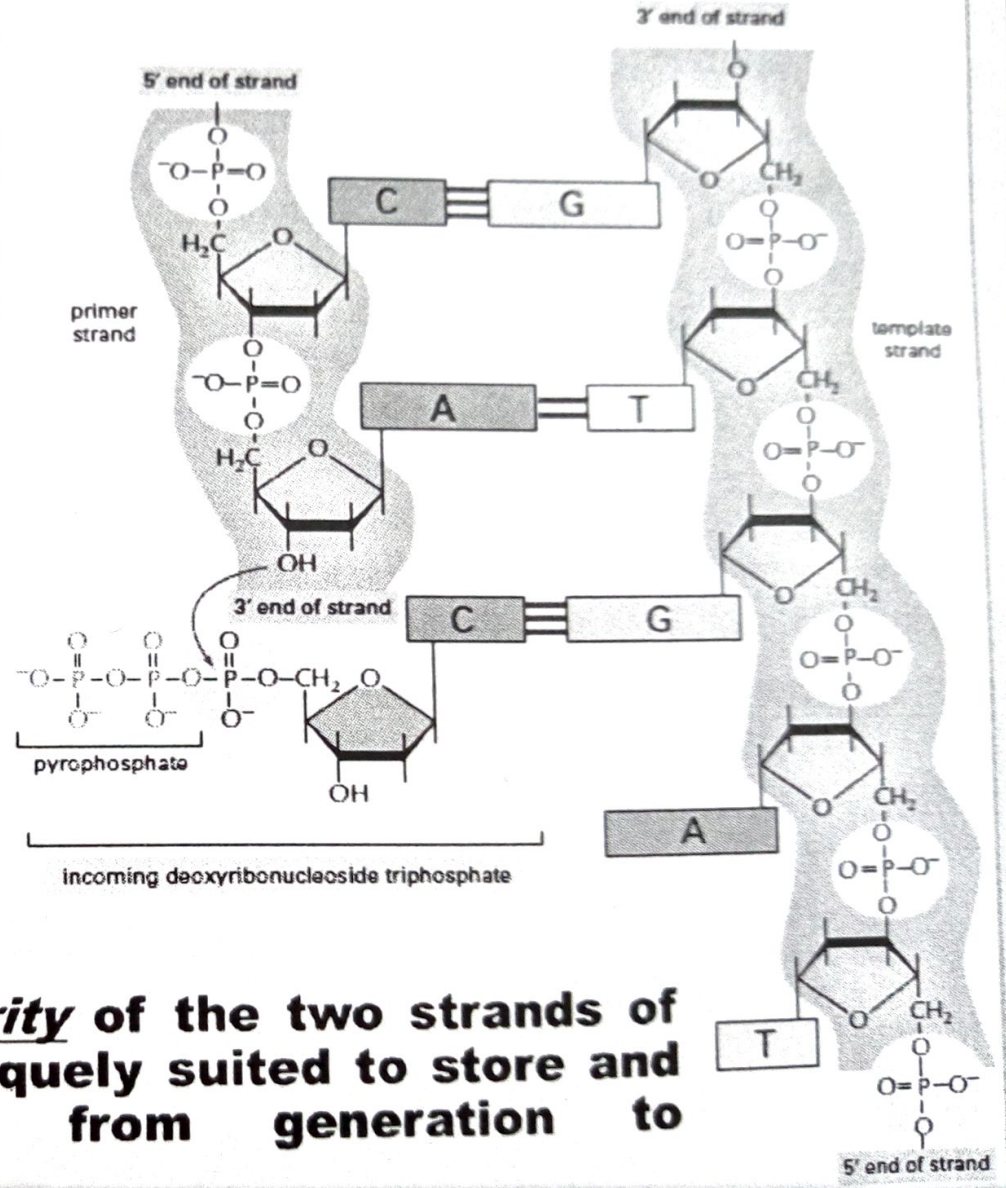
DNA is antiparallel

42

DNA STRUCTURE

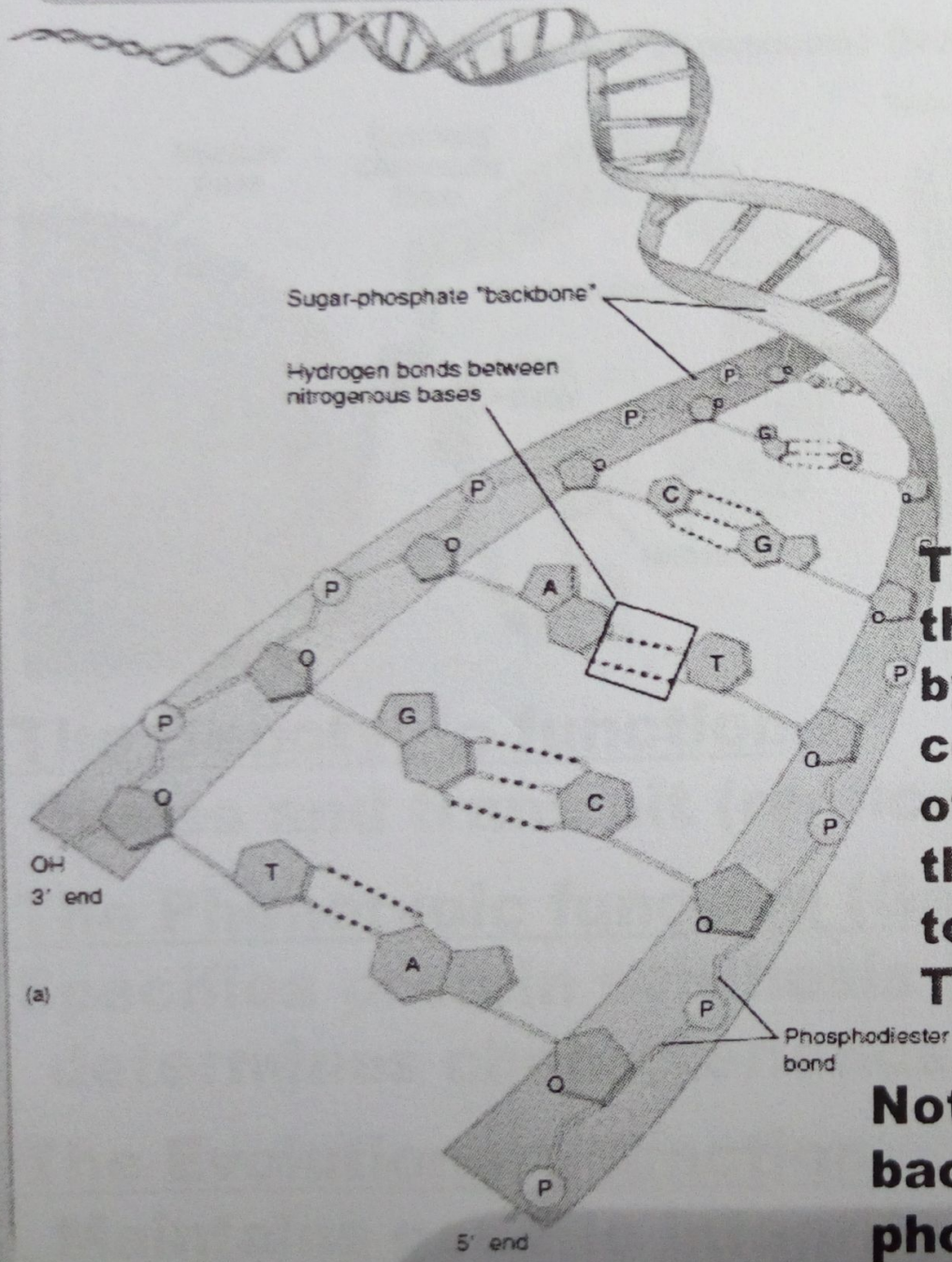
The two strands of a DNA duplex are said to be antiparallel because they always associate in such a way that the 5'-3' direction of one DNA strand is the opposite to that of its partner.

The two strands of a DNA double helix are said to be complementary or exhibit complementarity as the sequence of bases of one DNA strand can readily be inferred if the DNA sequence of its complementary strand is already known.



This property, the *complementarity* of the two strands of the double helix, makes DNA uniquely suited to store and transmit genetic information from generation to generation.

DNA STRUCTURE AND BASE PAIRING



Chargaff's rules:

1. The proportion of A always equals that of T, and the proportion of G always equals that of C:
A = T, and G = C.

2. It follows that there is always an equal proportion of purines (A and G) and pyrimidines (C and T).

The base composition of DNA can therefore be specified unambiguously by quoting its %GC (=%G + %C) composition. For example, if a source of DNA is quoted as being 42%GC, the base composition can be inferred to be: G=21%; C=21%; A= 29%; T=29%.

Note that DNA consist of linear backbone of alternating sugar and phosphate residues.

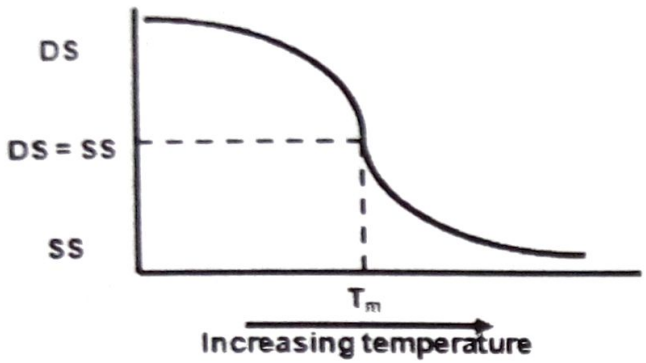
Chargaff's Data on Nucleotide Base Composition in the DNA of Various Organisms

	Percentage of Base in DNA				Ratios	
Organism	*A*	*T*	*G*	*C*	*A:T*	*G:C*
Staphylococcus aermentarns	12.8	12.9	36.9	37.5	0.99	0.99
Escherichia coli	26.0	23.9	24.9	25.2	1.09	0.99
Yeast	31.3	32.9	18.7	17.1	0.95	1.09
*Caenorhabditis elegans**	31.2	29.1	19.3	20.5	1.07	0.96
*Arabadopsis thaliana**	29.1	29.7	20.5	20.7	0.98	0.99
Drosophila melanogaster	27.3	27.6	22.5	22.5	0.99	1.00
Honeybee	34.4	33.0	16.2	16.4	1.04	0.99
Mus musculus (mouse)	29.2	29.4	21.7	19.7	0.99	1.10
Human (liver)	30.7	31.2	19.3	18.8	0.98	1.03

*Data for *C. elegans* and *A. thaliana* is based on that for close relative organisms.

Note that even though the level of any one nucleotide is different in different organisms, the amount of A always approximately equals the amount of T, and the level of G is always similar to that of C. Moreover, as you can calculate for yourself, the total amount of purines (A plus G) nearly always equals the total amount of pyrimidines (C plus T).

DNA CHEMISTRY/ BIOPHYSICS



The maximum absorbance of DNA is at 260 nm.

The melting temperature of DNA is the temperature at which the double stranded DNA "melts" forming two single strands, *OR* The temperature at which 50% of a nucleic acid is hybridized to its complementary strand.

The Tm is the temperature when 50% of the double strands unwound. GC pairs have three hydrogen bonds and AT have two. A high GC% leads to high Tm.

The relationship between the melting temperature (T_m) and GC content can be expressed in its much simplified form by the formula T_m= 69.3°C + 0.41(%GC)°C

GC content has a direct effect on Tm. The following examples, demonstrate the point.

Tm = 69.3°C + 0.41(45)°C = 87.75°C

Tm = 69.3°C + 0.41(40)°C = 85.7°C

Tm = 69.3°C + 0.41(60)°C = 93.9°C

DNA REPLICATION

Dr. Segun I. OYEDEJI

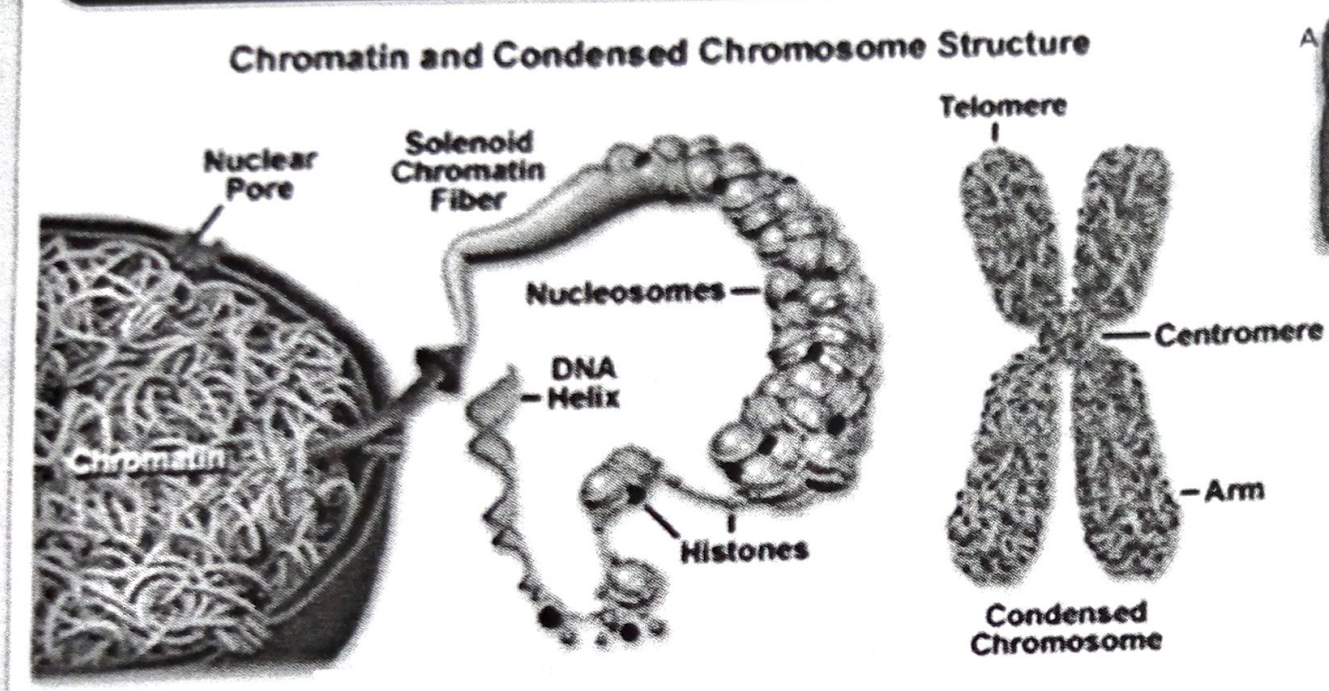
Federal University Oye-Ekiti

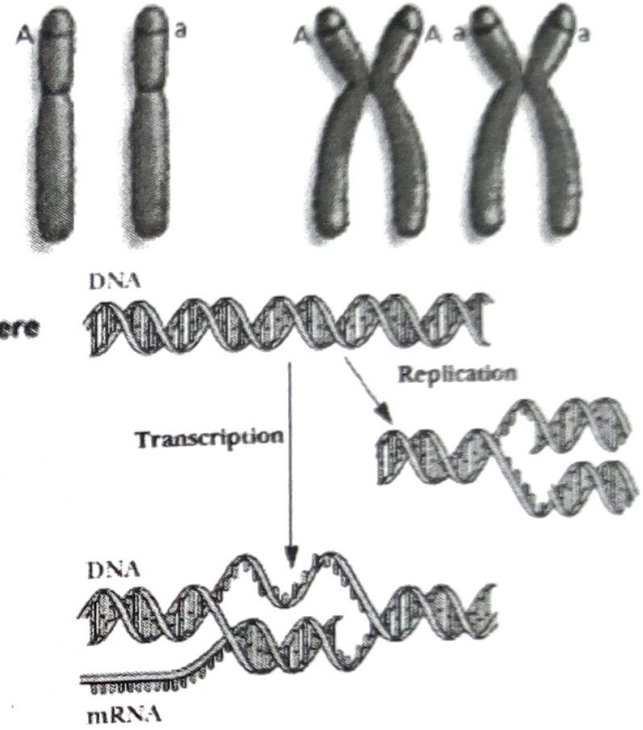
Department of Animal & Environmental Biology

2018 Lecture Guide

47

CELL: DNA FUNCTIONS





The Genotypic function

Stores and transmit (replicate) genetic information

The Phenotypic function (Gene expression)

Specifies protein synthesis (Transcription & Translation), determines characteristics/traits, controls growth

The Evolutionary function

Maintains genetic integrity, allows for adaptation

48

DNA REPLICATION

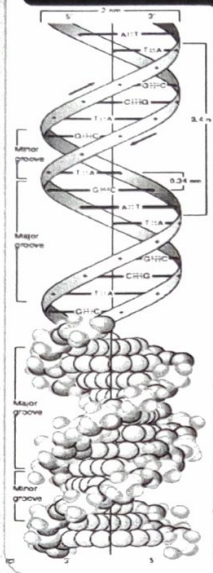
The ability of cells to maintain a high degree of order in a chaotic universe depends upon the accurate duplication of vast quantities of genetic information carried in chemical form as DNA.

This process is called *DNA replication*.

All organisms must duplicate their DNA with extraordinary accuracy before each cell division, so DNA replication must occur before a cell can produce two genetically identical daughter cells.

In humans, the synthesis of a new strand of DNA occurs at the rate of about 3000 nucleotides per minute. In bacteria, about 30,000 nucleotides are added to a nascent DNA chain per minute. This implies that the cellular machinery responsible for DNA replication must work very fast, but even more importantly, it must work with great precision.

DNA REPLICATION- Structural basis



DNA has the structure of a double helix, consisting of two polynucleotide chains, held together by hydrogen bonds between complementary bases- adenines and thymines, and between guanines and cytosines

The physical structure of DNA proposed by Watson and Crick has great explanatory power.

The fact that adenine can pair only with thymine and that cytosine can pair only with guanine suggest a simple way in which the DNA molecule could be copied, or replicated: The original strands could serve as templates on which to build the new strands.

DNA REPLICATION

The ability of each strand of a DNA molecule to act as a template for producing a complementary strand enables a cell to copy or replicate its gene before passing them on to its descendants.

PROCESS OF DNA REPLICATION

1. The hydrogen bonds connecting the two strands are broken.

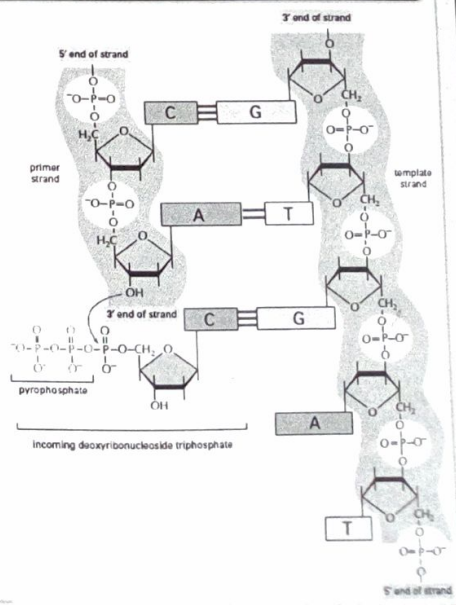
2. Breaking the hydrogen bonds would cause the two strands to unwind and separate.

3. Each strand could then be used as a template for the construction of a new strand of DNA. We now know that the main enzyme involved in the replication of DNA is called DNA polymerase.

4. When this process is completed, there would be two copies of the DNA molecule, each composed of one "old" strand of DNA (from the parent DNA molecule), and one newly synthesized strand of DNA.

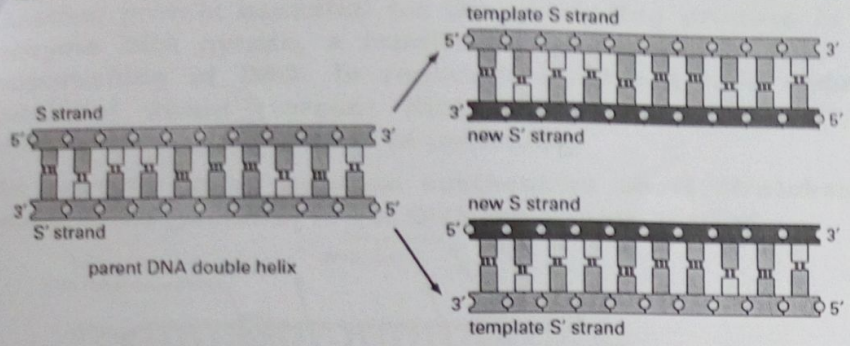
DNA STRUCTURE

If the two complementary strands of a double helix is separated, by breaking the hydrogen bonds of each base pair, each parental strand could direct the synthesis of a new complementary strand.



DNA replication is semi-conservative because each daughter DNA double helix is composed of one of the original (parent) strands plus one newly synthesized strand.

DNA REPLICATION



During DNA replication inside a cell, each of the two old DNA strands serves as a template for the formation of a new strand. Because each of the two daughters of a dividing cell inherits a new DNA double helix containing one old and one new strand, the DNA double helix is said to be replicated "semi-conservatively" by DNA polymerase.

53

REQUIREMENTS OF DNA REPLICATION

Although the process of replication includes many components, they can be combined into three major groups:

1. A template consisting of single-stranded DNA;

2. Raw materials (substrates) to be assembled into a new nucleotide strand (dNTPs); and

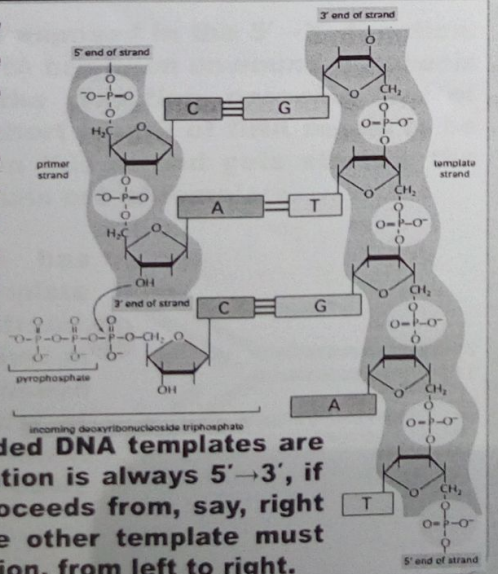
3. Enzymes and other proteins that "read" the template and assemble the substrates into a DNA molecule.

The positions at which the DNA is first opened are called origins of replication. They are marked by a particular sequence of nucleotides which attract initiator proteins.

54

DNA REPLICATION

In DNA synthesis, new nucleotides are joined one at a time to the 3′ end of the newly synthesized strand. DNA polymerases, the enzymes that synthesize DNA, can add nucleotides only to the 3′ end of the growing strand (not the 5 end), so new DNA strands always elongate in the same 5-to-3 direction (5′→3′).



Because the two single-stranded DNA templates are antiparallel and strand elongation is always 5′→3′, if synthesis on one template proceeds from, say, right to left, then synthesis on the other template must proceed in the opposite direction, from left to right.

55

DNA REPLICATION MECHANISM

Initiator proteins bind to origin of replication or site of initiation and cause a short section of DNA to unwind. This unwinding allows helicase and other single-strand-binding proteins to attach to the polynucleotide strand.

DNA helicases break the hydrogen bonds that exist between the bases of the two nucleotide strands of a DNA molecule. The initiator proteins first separate DNA strands at the origin, providing a short stretch and then helicases unwound the double-stranded DNA.

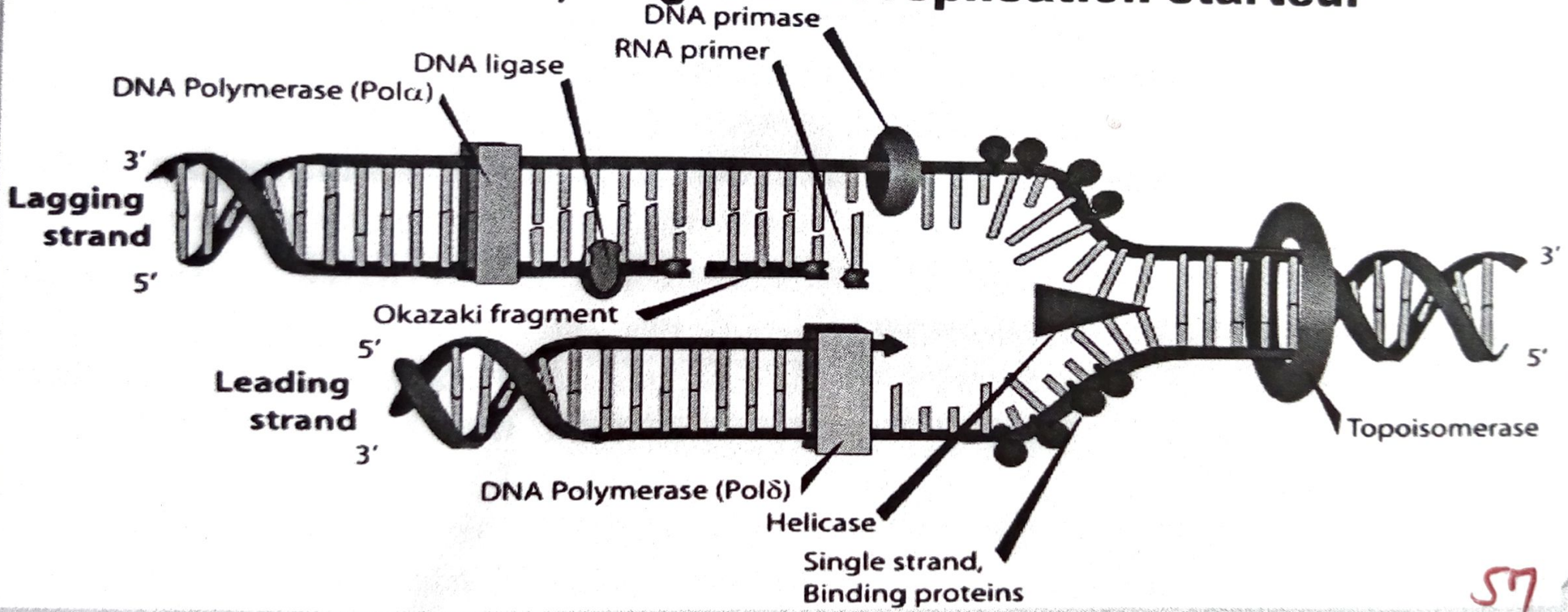
To stabilize the single-stranded DNA long enough for replication to take place, single-strand-binding (SSB) proteins attach tightly to the exposed single-stranded DNA.

56

DNA REPLICATION MECHANISM

Another protein essential for the unwinding process is the enzyme DNA gyrase, a topoisomerase which controls the supercoiling of DNA. In replication, DNA gyrase reduces torsional strain (torque) that builds up ahead of the replication fork as a result of unwinding

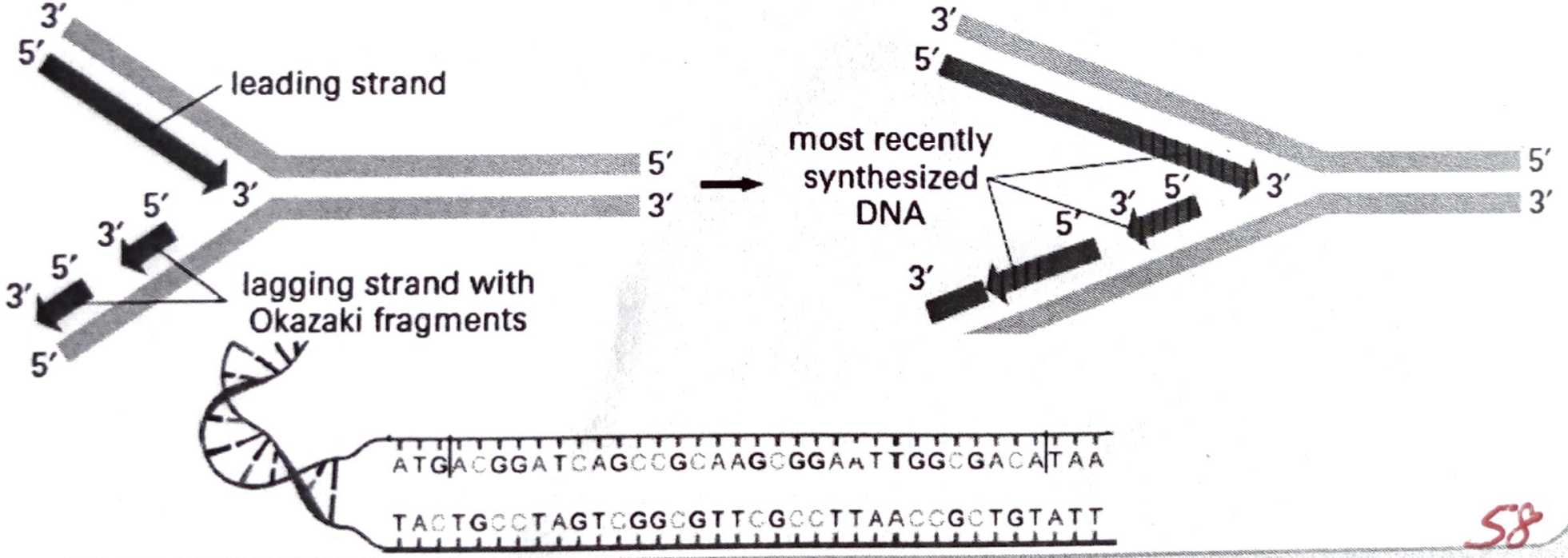
An enzyme called primase synthesizes short stretches of nucleotides (primers) to get DNA replication started.



DNA REPLICATION

As DNA unwinds during replication, the antiparallel nature of the two DNA strands means that one template is exposed in the 5′→3′ direction and the other template is exposed in the 3′→5′ direction.

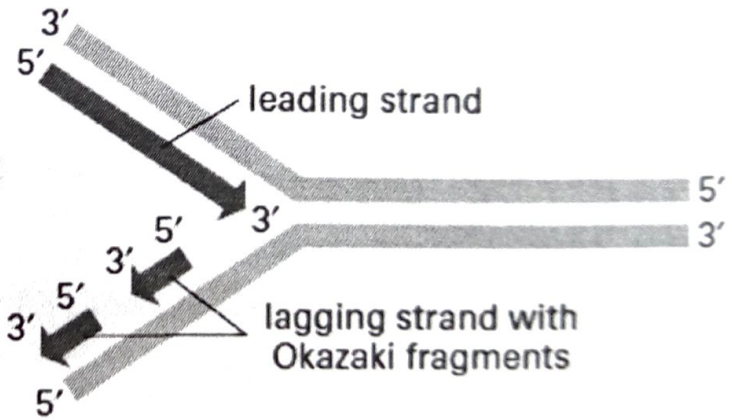
As the DNA unwinds, the template strand that is exposed in the 3′→5′ direction allows the new strand to be synthesized continuously, in the 5′→3′ direction. This new strand, which undergoes continuous replication, is called the leading strand.



DNA REPLICATION

The other template strand is exposed in the 5′→3′ direction. After a short length of the DNA has been unwound, synthesis proceed in the 5′→3′, i.e the direction *opposite that* of unwinding. Because only a short length of DNA needs to be unwound before synthesis on this strand gets started, the replication machinery soon runs out of template.

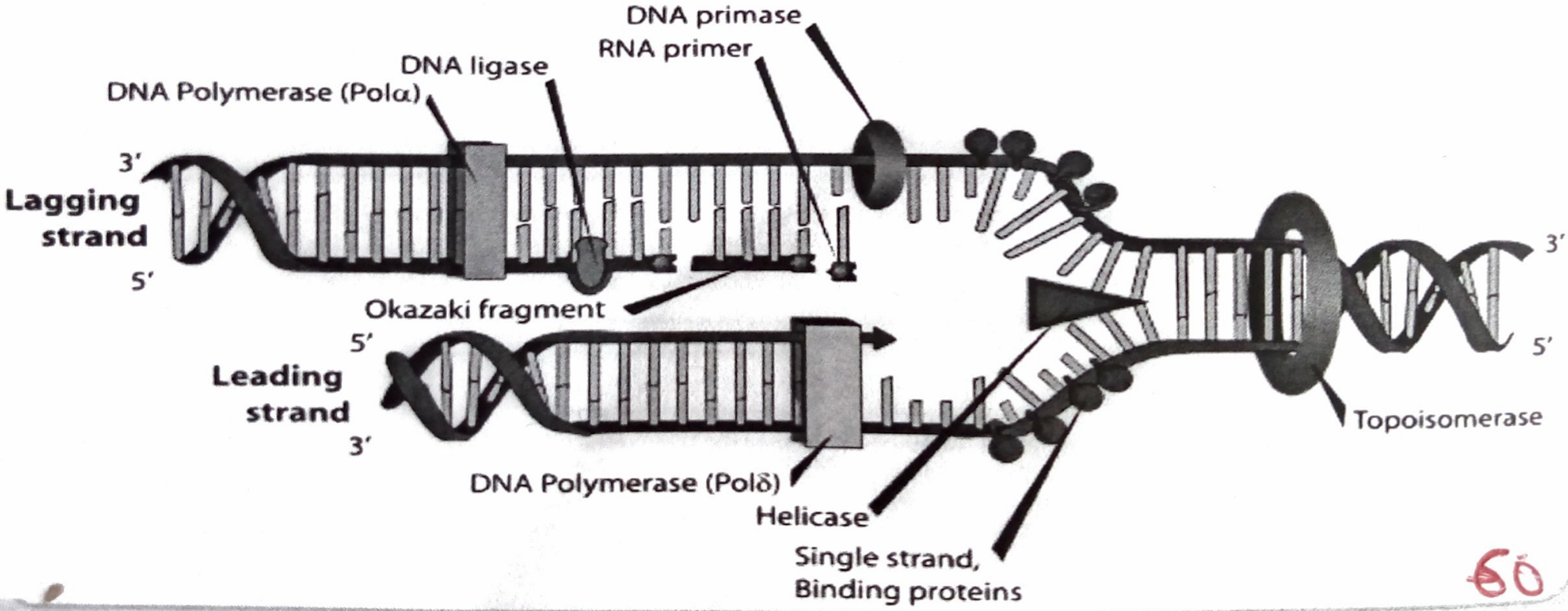
By that time, more DNA has unwound, providing new template at the 5 end of the new strand. DNA synthesis must start anew at the replication fork and proceed in the direction opposite that of the movement of the fork until it runs into the previously replicated segment of DNA.



DNA REPLICATION

This process is repeated again and again, so synthesis of this strand is in short, discontinuous bursts. The newly made strand that undergoes discontinuous replication is called the lagging strand.

The short lengths of DNA produced by discontinuous replication of the lagging strand are called Okazaki fragments, which are then linked together to create a continuous new DNA molecule.



Characteristics of DNA Polymerases in *E. coli*

DNA Polymerase	5′→3′ Polymerization	3′→5′ Exonuclease	5′→3′ Exonuclease	Function
I	Yes	Yes	Yes	Removes and replaces primers
II	Yes	Yes	No	DNA repair; restarts replication after damaged DNA halts synthesis
III	Yes	Yes	No	Elongates DNA
IV	Yes	No	No	DNA repair
V	Yes	No	No	DNA repair; translesion DNA synthesis

Two of the enzymes, DNA polymerase I and DNA polymerase III, carry out DNA synthesis associated with replication; the other three have specialized functions in DNA repair.

DNA polymerase III is a large multi-protein complex that acts as the main workhorse of replication. DNA polymerase III synthesizes nucleotide strands by adding new nucleotides to the 3 end of growing DNA molecules. Its 5′→3′ polymerase activity allows it to add new nucleotides in the 5′→3′ direction. Its 3′→5′ exonuclease activity allows it to remove nucleotides in the 3′→5′ direction, enabling it to correct errors.

However, the removal and replacement of primers appear to constitute the main function of DNA polymerase I.

GENE STRUCTURE

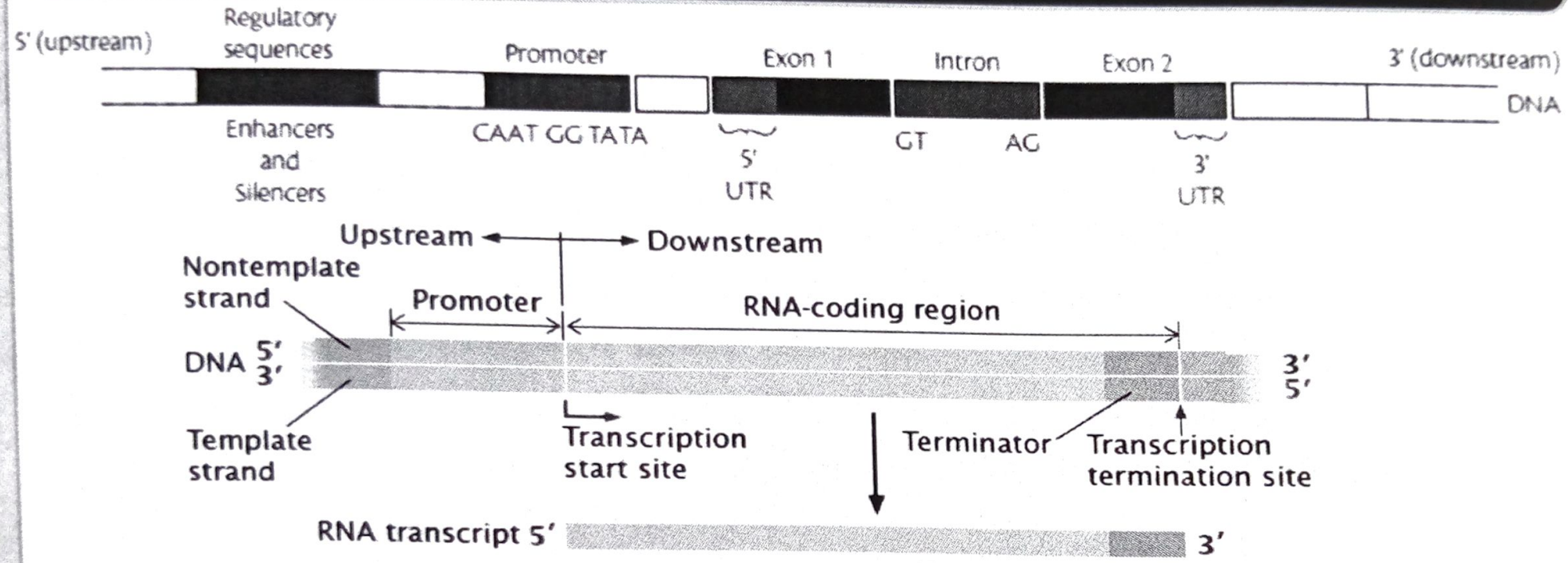
Dr. Segun I. OYEDEJI

Federal University Oye-Ekiti

Department of Animal & Environmental Biology

2018 Lecture Guide

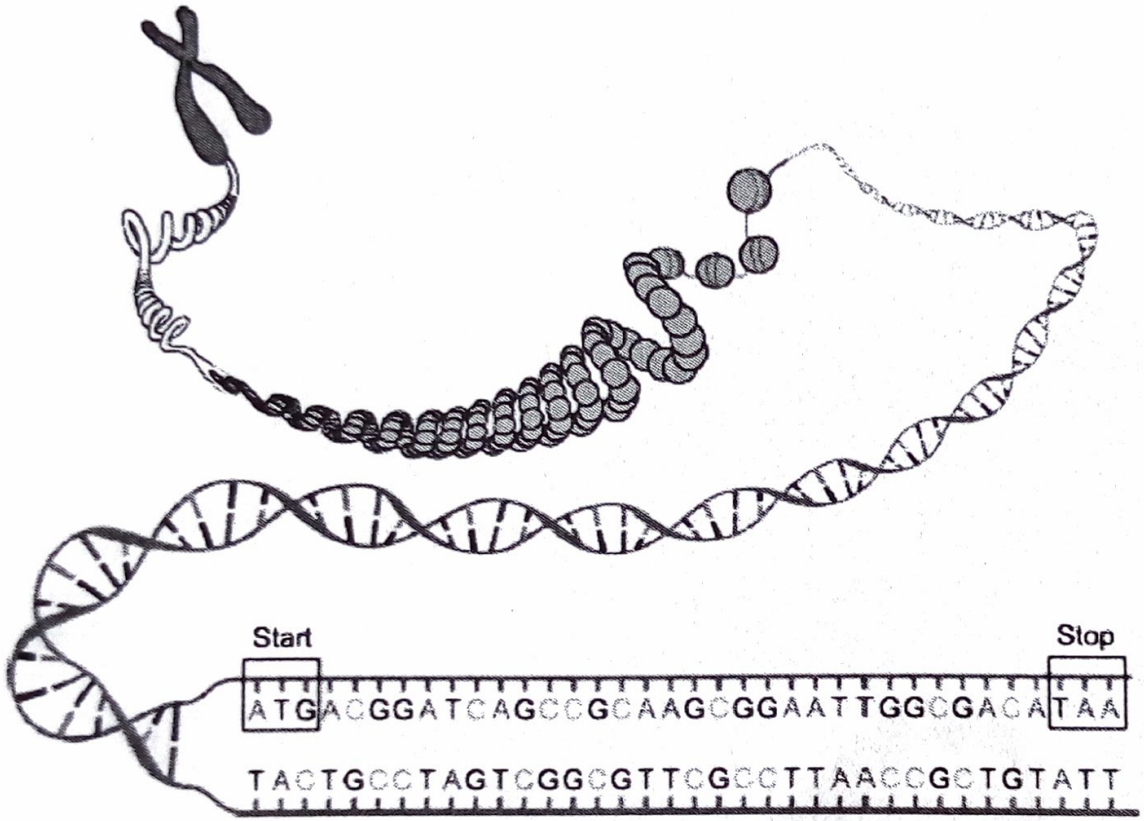
The structure of a typical Eukaryotic gene

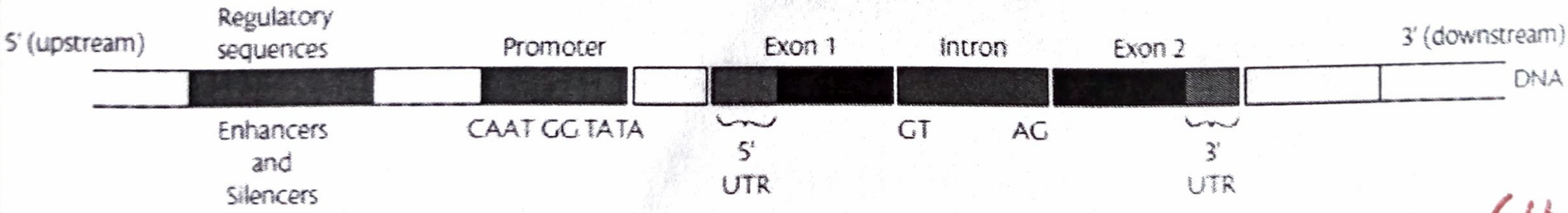


In addition to exons and introns, each gene contains a closely adjacent upstream (5′) regulatory promoter region and other regulatory sequences including enhancers, silencers, and sometimes a locus control region. The promoter region contains specific sequences such as a TATA box, a CG box, and a CAAT box, which provide binding sites for transcription factors. The enhancer and silencer sequences fulfil a similar purpose, but are located at a greater distance from the coding sequences.

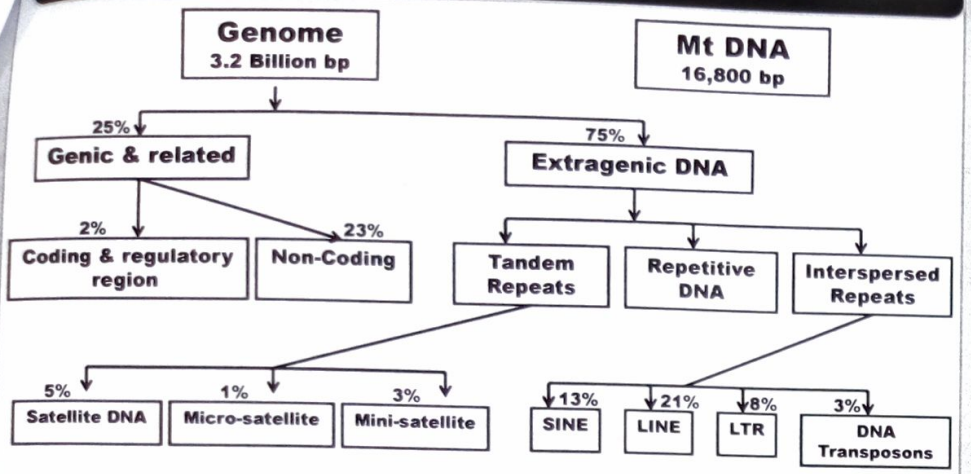
The first and last exons contain *untranslated regions,* known as the 5′ UTR and 3′ UTR respectively. The 5′ UTR marks the start of transcription and contains an initiator codon which indicates the site of the start of translation. The 3′ UTR contains a termination codon, which marks the end of translation, plus nucleotides which encode a sequence of adenosine residues known as *poly(A) tail.*

The structure of a typical Eukaryotic gene





HUMAN GENOME STRUCTURE



SINE= Short interspersed elements e.g Alu SINE

LINE= Long interspersed elements

LTR= Long terminal repeats

Cell Structure & Genome of Prokaryotes

They are microscopic organisms.

Their genome is a single, circular DNA molecule.

Their genome size is in the order of a few million base pairs [0.6–8].

Their *gene density*- the number of genes per base pairs in the genome- is approximately one gene per 1,000 base pairs.

Their genome is lean and mean, containing few useless parts (70 percent is coding for proteins).

Their genes do not overlap.

Their genes are transcribed (copied into messenger RNA) right after a control region called a *promoter.* These messenger RNA (mRNA) are collinear with the genome sequence. In other words, genes are in a single piece, not interrupted by noncoding patches (called *introns*).

Cell Structure & Genome of Eukaryotes

Their genome consists of multiple linear pieces of DNA called *chromosomes* (up to a hundred million base pairs long).

Their genome size (10–670,000 million base pairs), especially for animals and plants, is *much bigger* than in prokaryotes.

Their gene density is much lower than that for prokaryotes (one human gene per 100,000 base pairs).

Their genome is no model of efficiency, containing junk sequences (less than 5 percent of the human genome code for proteins)

Gene sequences are not collinear with the final messenger RNA (mRNA) and protein sequences. Only small bits (the *exons*) are retained in the mature mRNA that encodes the final product.

Genes often exhibit more than one mRNA (and protein) form.

Genes of higher eukaryotes (animals) may span up to millions of base pairs- the human dystrophin gene (the mutation of which causes a dreadful disease), for example, is 2.2 million base pairs long.

GENE EXPRESSION

TRANSCRIPTION & TRANSLATION

Dr. Segun I. OYEDEJI

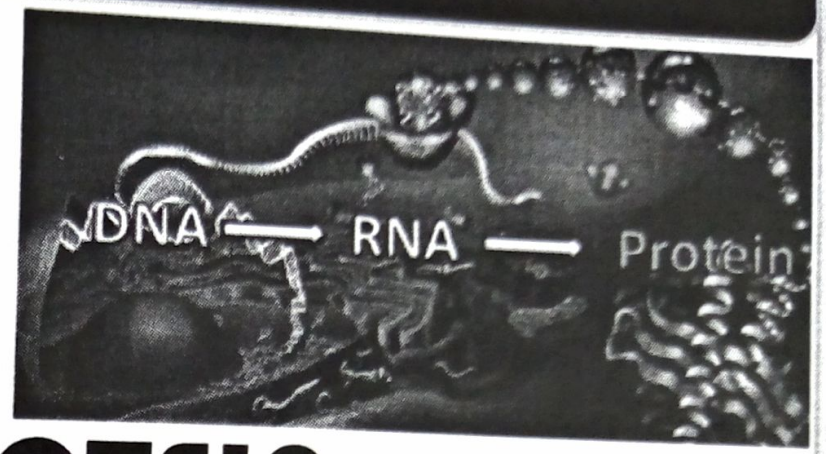
Federal University Oye-Ekiti

Department of Animal & Environmental Biology

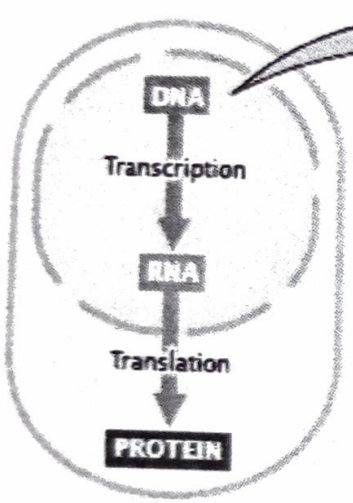
2018 Lecture Guide

CENTRAL DOGMA

The central dogma in biology is that information stored in DNA is transferred to RNA molecules during transcription and to protein during translation.



DNA → RNA → PROTEIN



DNA 5′ — 3′
DNA 3′ — 5′

Transcription

mRNA 5′ — 3′

Codons

Translation

Polypeptide chain: Arg Gly Tyr Thr Phe Ala Val Ser

Amino acids

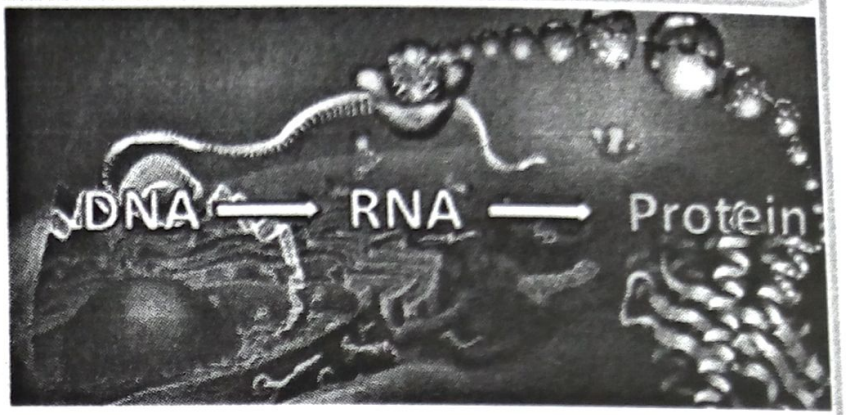
1 A continuous sequence of nucleotides in the DNA...

2 ...codes for a continuous sequence of amino acids in the protein.

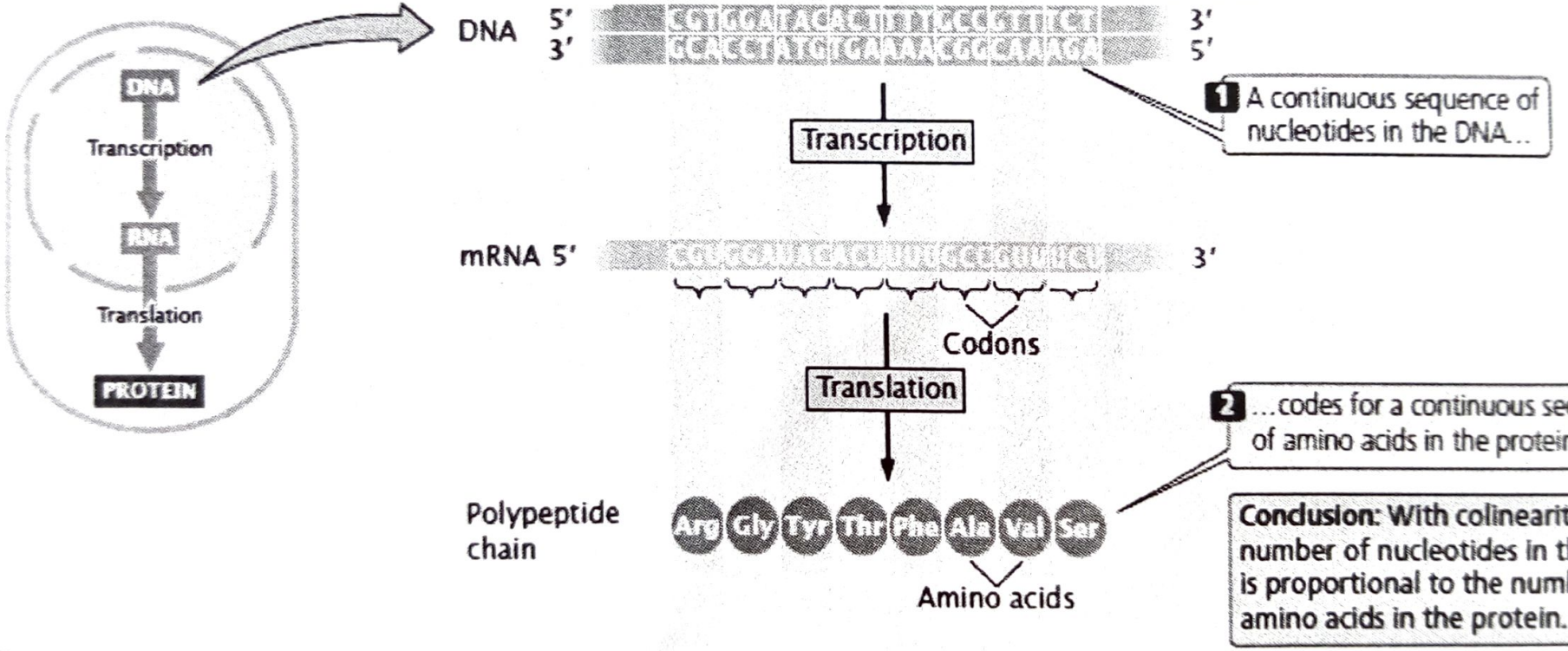
Conclusion: With colinearity, the number of nucleotides in the gene is proportional to the number of amino acids in the protein.

DNA-RNA-PROTEIN

DNA, RNA, and proteins are three major classes of biological molecules that regulate cellular functions and carry genetic information passed from parents to offspring.

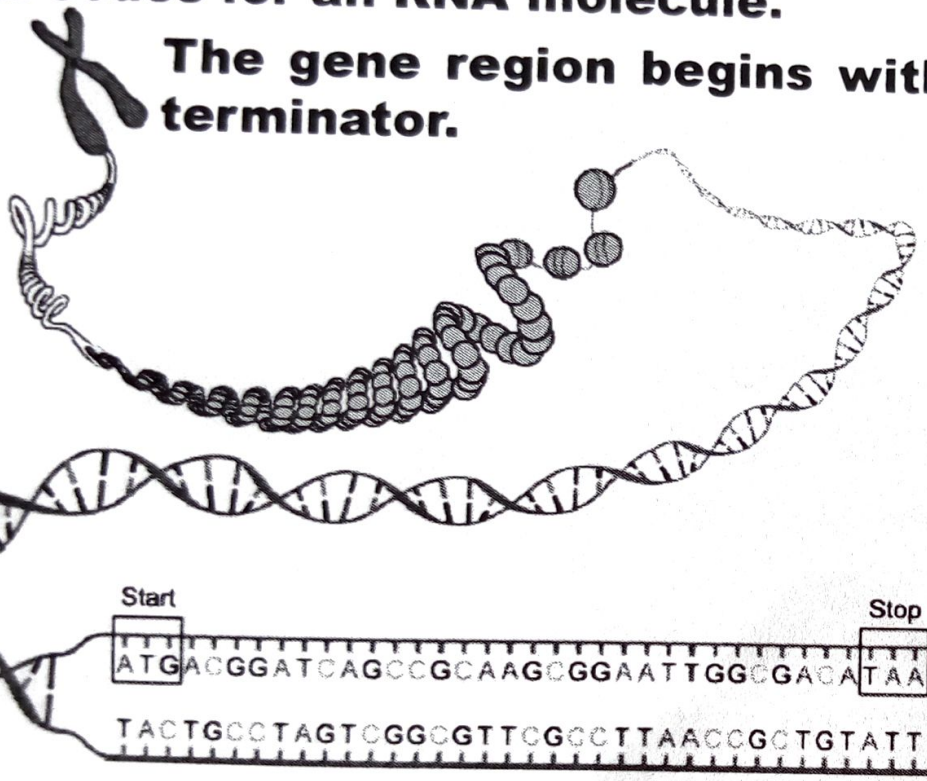


DNA → RNA → PROTEIN



Eukaryotic gene and Gene expression

DNA contains genes- sequence of nucleotides containing region that codes for an RNA molecule.

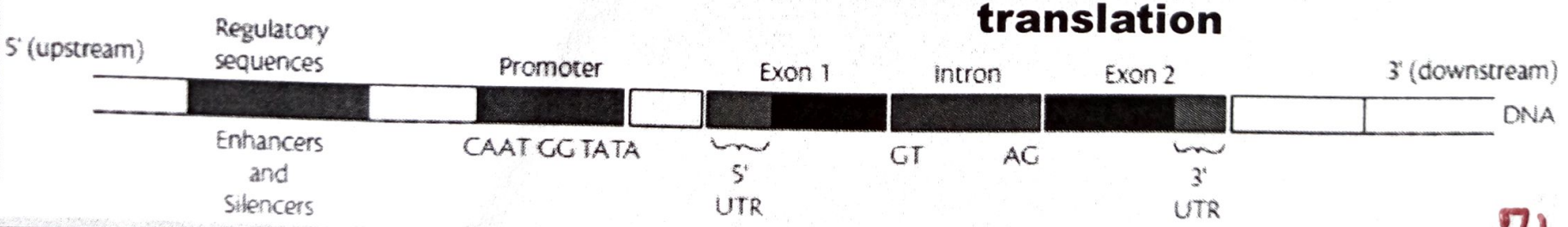


The gene region begins with a promoter and ends with a terminator.

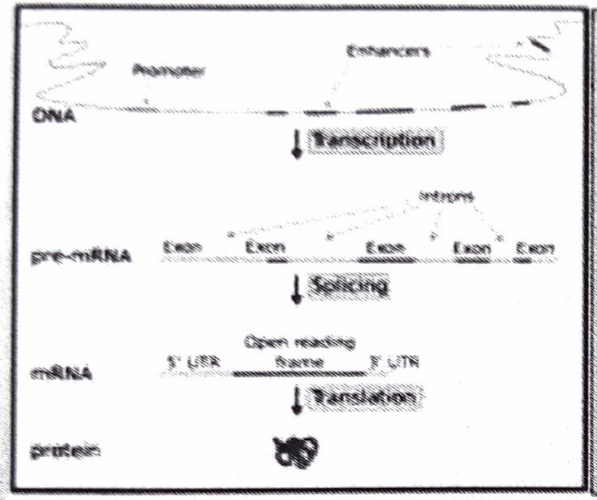
Genes also contain regulatory sequences.

For some genes, the encoded RNA is used to synthesize a protein, in a process called gene expression.

For these genes, expression can be divided into two process: transcription and translation



Eukaryotic gene and Gene expression



The initiation of transcription requires a promoter sequence.

RNA polymerase & other transcription factors bind to the promoter site.

Promoter sequences are found -30, -75 and -90 base pairs upstream from the start site of transcription.

Mutations in the promoter sequence commonly result in a dramatic decrease in gene transcription.

Transcription begins at the the initiation codon, and ends at the termination codon. Between initiation and termination sections of the DNA may be non-coding (introns) or coding (exons).

Enhancer sites are sections of DNA where transcription factors bind. Silencer sites are where negative regulators (repressors) bind.

TRANSCRIPTION AND TRANSLATION

The properties of a protein, which are responsible for its biological function are determined by its three-dimensional structure, which is in turn determined by the sequence of the amino acids of which it is composed, which is determined by the sequence of nucleotide bases in DNA.

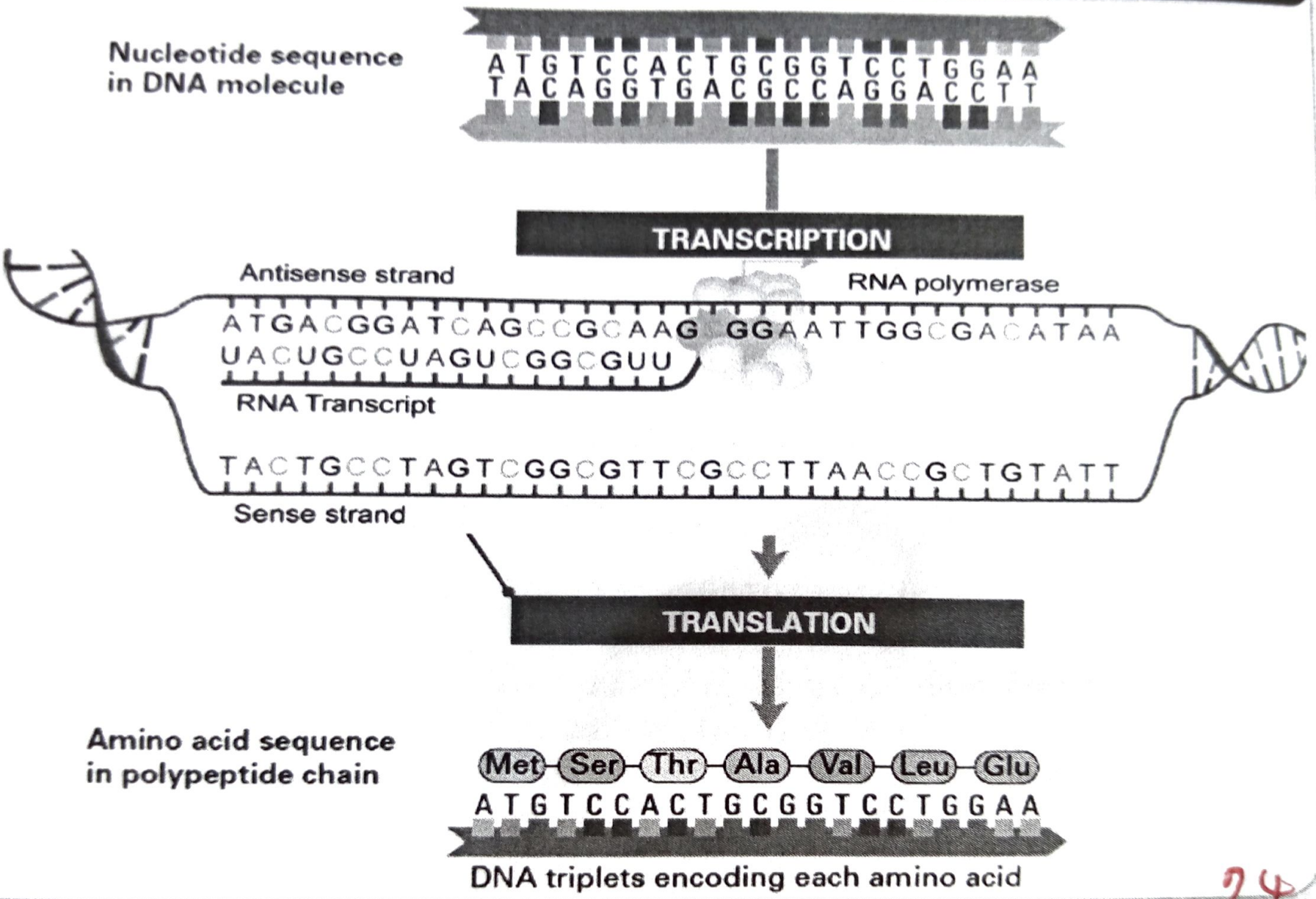
The transfer of genetic information from DNA to protein involves two steps:

1) Transcription: the transfer of the genetic information from DNA to RNA. It is the synthesis of RNA molecules, with DNA as a template.
2) Translation: the transfer of information from RNA to protein

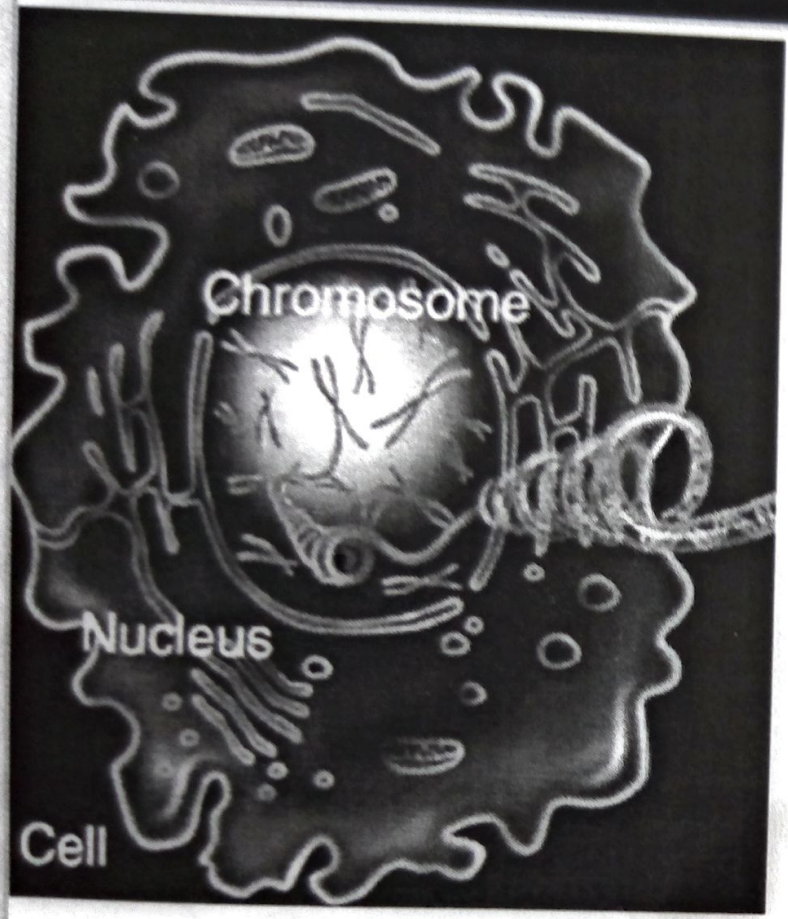
Gene expression is a sequence of several processes including: transcription of DNA sequence unto an RNA molecule, processing of the RNA transcript, transport of RNA to the cytoplasm, translation of mRNA to amino acid, generation of protein.

Transcription and Translation are the means by which cells read out, or express, their genetic instructions.

GENE EXPRESSION



TRANSCRIPTION & TRANSLATION



In Eukaryotic cells, transcription occurs in the nucleus where DNA is used as a template to make messenger RNA (mRNA).

Translation however occurs in the cytoplasm where the information contained in the mRNA is used to make a polypeptide.

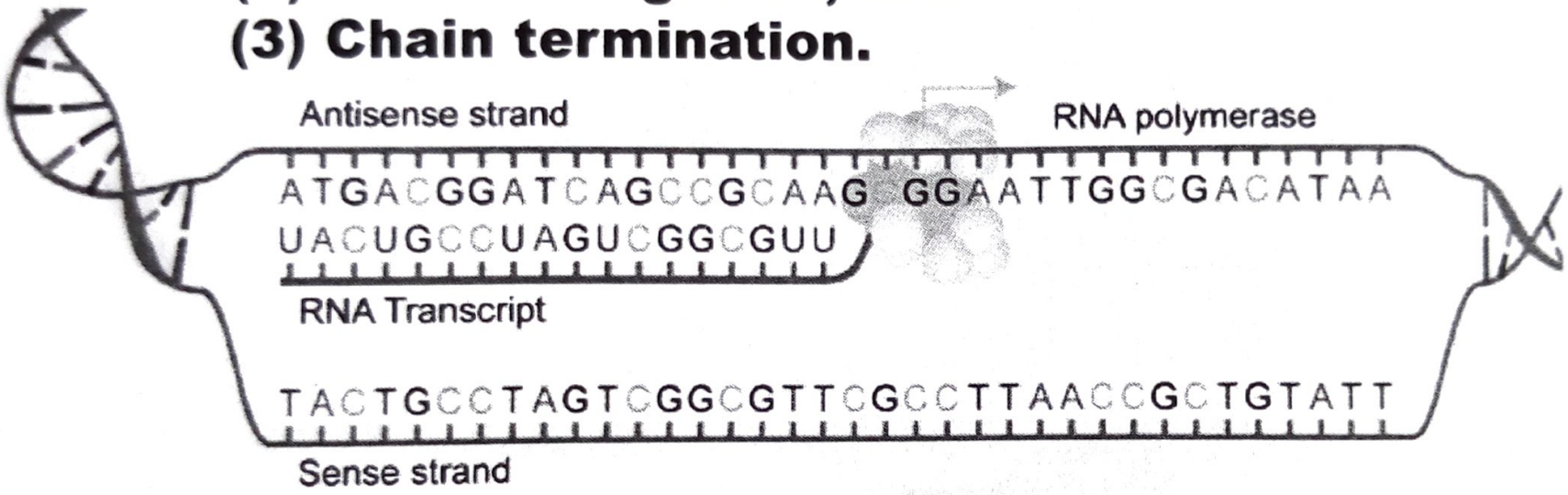
Transcription- Steps and Requirements

The process of transcription involves three steps:

(1) Chain initiation,

(2) Chain elongation, and

(3) Chain termination.



Like replication, transcription requires three major components :

1. **A template consisting of single-stranded DNA,**
2. **Raw materials (substrates), ribonucleoside triphosphosphates (rNTPs) needed to build a new a new RNA molecule; and**
3. **The transcription apparatus, consisting of the proteins necessary to catalyze the synthesis of RNA.**

TRANSCRIPTION

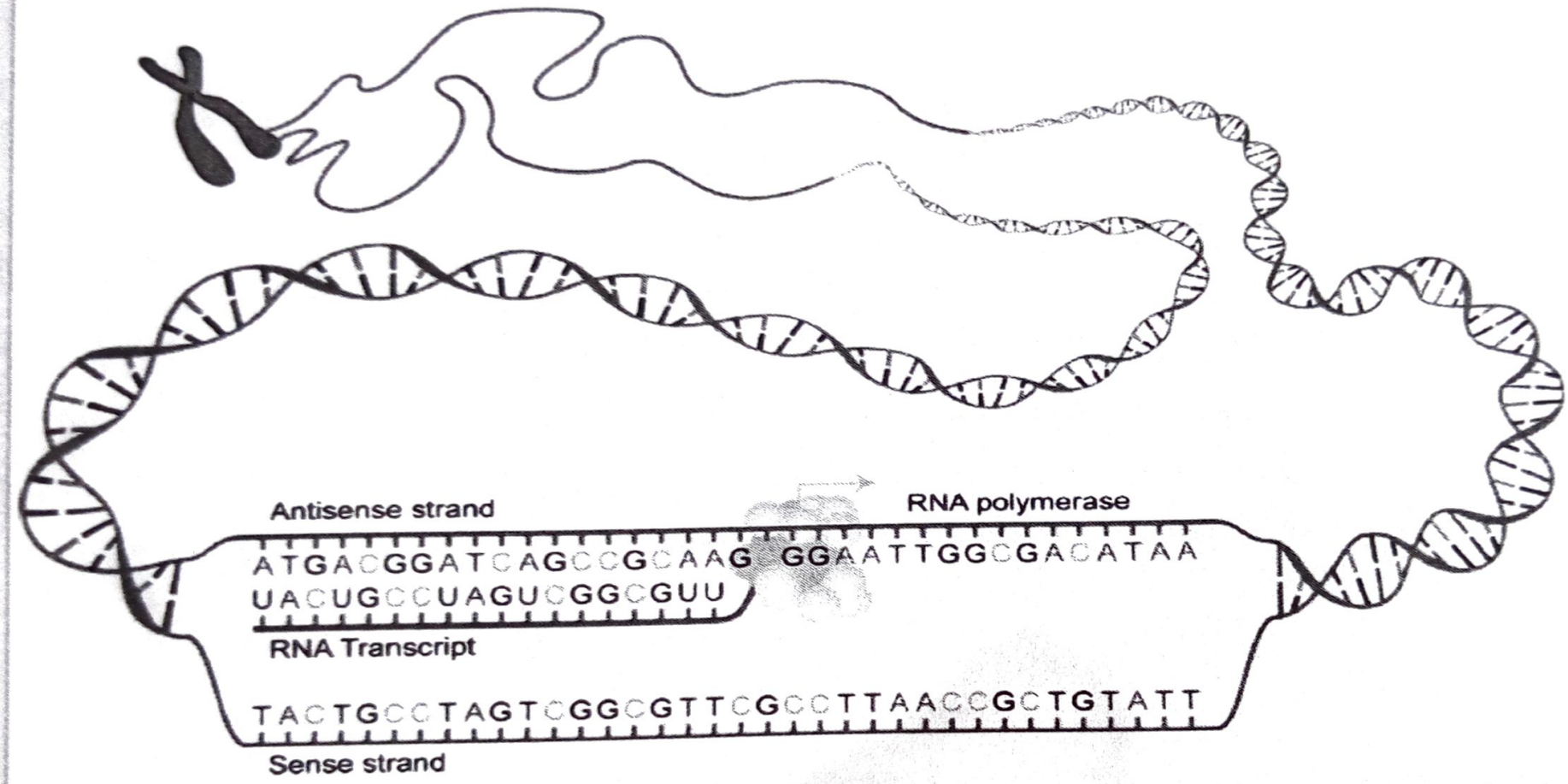
Transcription is carried out by RNA polymerase. During transcription, one strand of DNA of a gene is used as a template to synthesize a complementary strand of RNA, called the gene transcript.

RNA polymerase recognizes and bind to a specific sequence called promoter, and initiates the synthesis of mRNA from an adjacent position.

During transcription, an RNA molecule is synthesized that is complementary and antiparallel to the DNA template strand. The RNA transcript has the same polarity and base sequence as does the non template strand, with the exception that U in RNA substitutes for T in DNA.

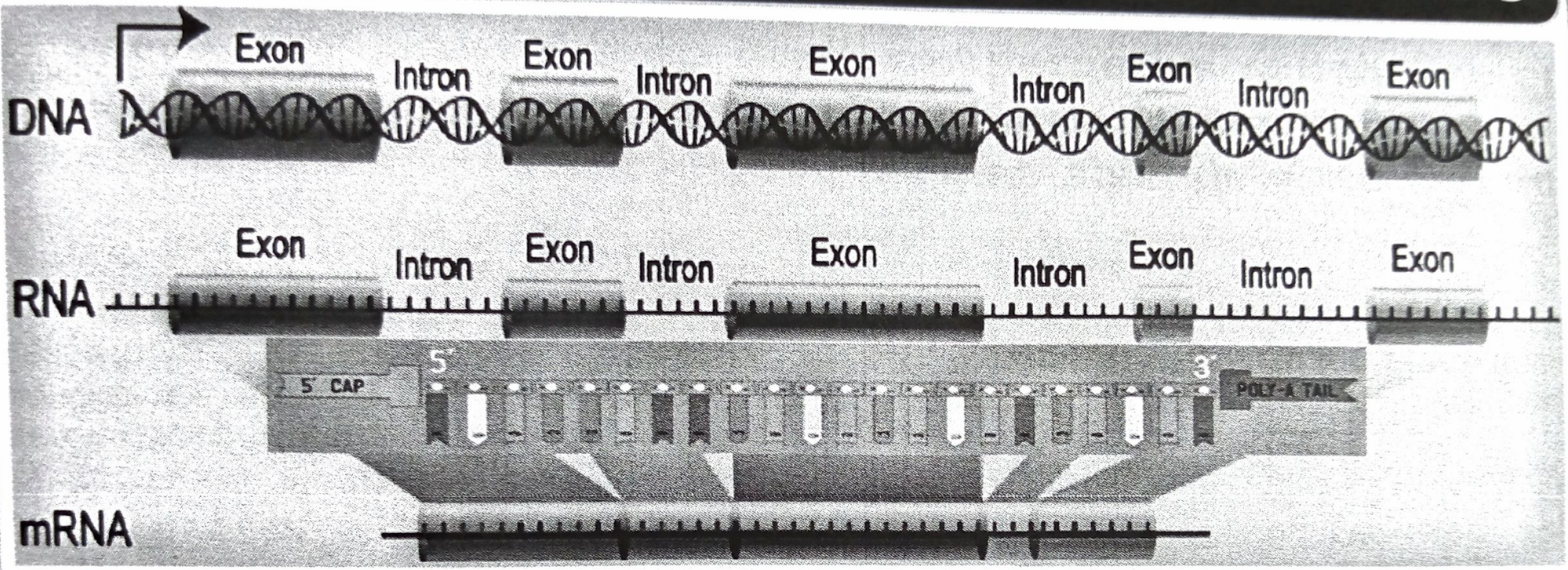
The completed mRNA moves out of the nucleus to the ribosomes, the site of translation.

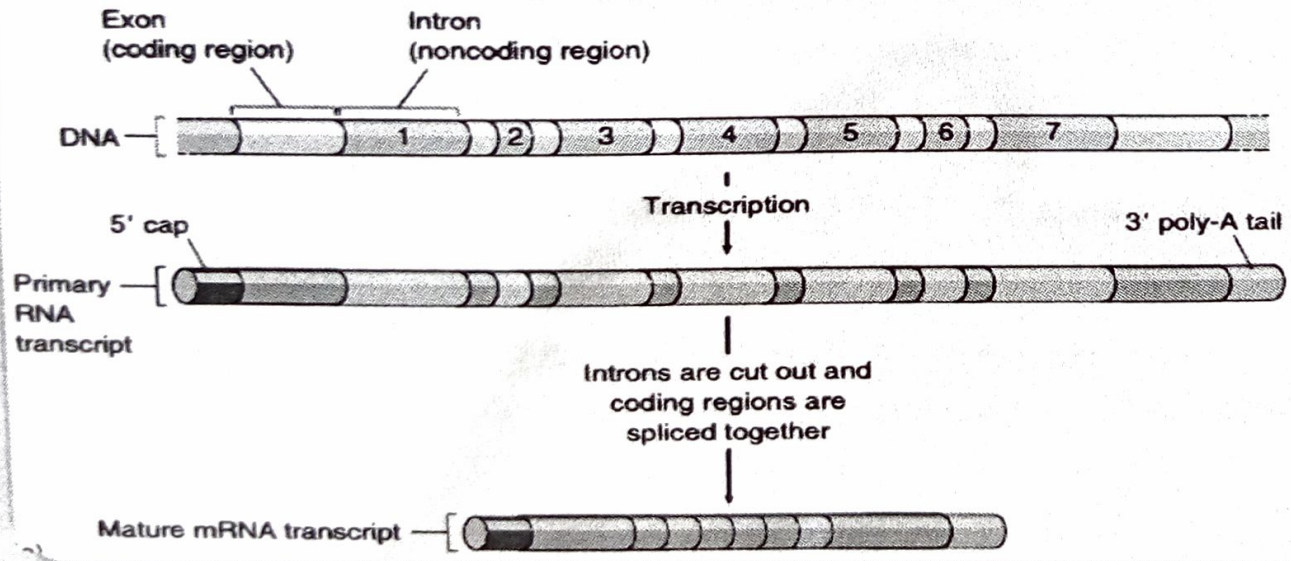
TRANSCRIPTION



The DNA strand (non template strand) that codes for the protein is called the sense strand because its sequence reads the same as that of the messenger RNA. The other strand (template strand) is called the antisense strand and serves as the template for RNA polymerase during transcription.

TRANSCRIPTION: RNA Processing/Intron Splicing

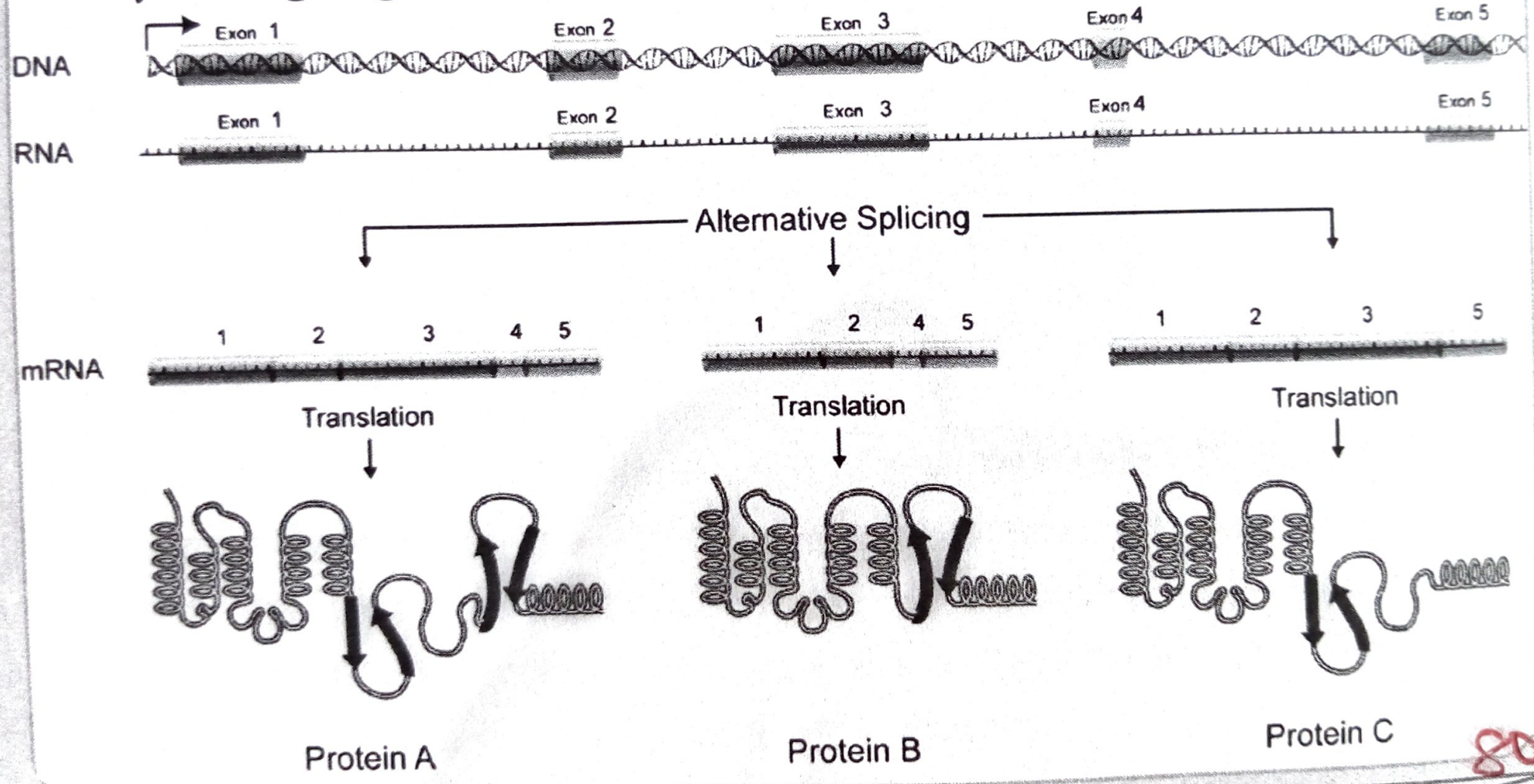




During transcription, DNA is used as a template to make mRNA.
The strand of mRNA that is made during transcription includes regions called exons that codes for polypeptides, and non-coding regions called introns.

TRANSCRIPTION: Alternative Splicing

❖**Alternative splicing refers to the process by which a given gene is spliced into more than one type of mRNA molecule. Thus, a single gene can encode a number of related protein.**



FUNCTIONS OF RNA

1. RNA brings genetic information from the DNA for protein synthesis.
2. It helps to associate ribosomes with the messenger molecule during protein synthesis.
3. It functions as carrier of amino-acids.
4. It plays a significant role in the preparation of messenger molecule.
5. It is involved in post-transcriptional editing of genetic message.
6. It is involved in the process of translation.

RNA is classified according to the function in which it is involved. For example, the RNA involved in the first function above is aptly called as messenger RNA (mRNA). The one involved in second function is called as ribosomal RNA (rRNA). The RNA involved in carriage of amino acids is called as transfer RNA (tRNA). Small nuclear RNA (snRNA) are involved in preparation of messenger RNA, while guide RNA (gRNA) is involved in post-transcriptional alteration in the genetic message (RNA editing). The RNA species involved in a given function tends to have its own structural peculiarities.

RNA POLYMERASES OF EUKARYOTES

Whereas a single RNA polymerase catalyzes all transcription in prokaryotes, three (3) different RNA polymerases are present in eukaryotes; each enzyme catalyzes the transcription of a specific class of genes. They are more complex than the prokaryotic RNA polymerase, with ten or more subunits. All the three eukaryotic RNA polymerases require the assistance of other proteins called transcription factors in order to initiate the synthesis of RNA.

RNA Polymerase II transcribes nuclear genes that encode proteins.

The key features of the 3 eukaryotic RNA polymerases are:

Enzyme	Location	Products	Sensitivity to α-Amanitin
RNA Polymerase I	Nucleolus	rRNA excluding 5SrRNA	No sensitivity (No inhibition)
RNA Polymerase II	Nucleus	Nuclear pre-mRNAs	Complete sensitivity (Inhibition)
RNA Polymerase III	Nucleus	tRNA, snRNAs, 5SrRNA	Intermediate sensitivity

The 3 RNA polymerases exhibit very different sensitivities to inhibition by α-amanitin, a metabolic poison produced by the mushroom *Amanita phalloides*.

TYPES OF RNA MOLECULES

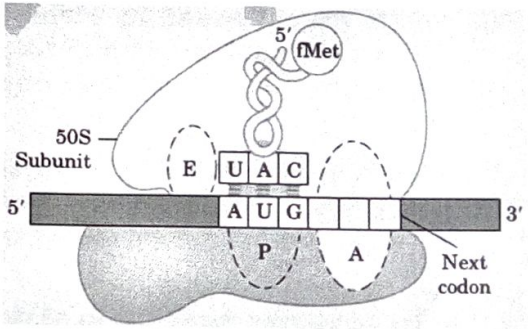
Messenger RNA (mRNA) carries the coding instructions for polypeptide chains from DNA to the ribosome. They travel to the ribosomes to direct precisely *which amino acids are assembled* into polypeptides.

Ribosomal RNA (rRNA): these are structural and catalytical components of the ribosomes, the intricate machines that translate nucleotides sequences of mRNA into amino acid sequences of polypeptides. rRNA along with ribosomal protein subunits, makes up the ribosome, the site of protein assembly. During polypeptide synthesis, rRNA provides the site where polypeptides are assembled.

Transfer RNA (tRNA): these are small RNA molecules that function as adaptors between amino acids and the codons in mRNA during translation, thereby serving as the link between the coding sequence of nucleotides in the mRNA and the amino acid sequence of a polypeptide chain. tRNA molecules both transport the amino acids to the ribosome for use in building the polypeptides and position each amino acid at the correct place on the elongating polypeptide chain.

Small nuclear RNAs (snRNAs): these are structural components of spliceosomes, the nuclear structures that excise introns from nuclear genes.

TRANSLATION



Translation is the process by which the genetic information stored in the sequence of nucleotides in an mRNA is translated into the amino acid sequences of polypeptides according to the specifications of the genetic code.

TRANSLATION

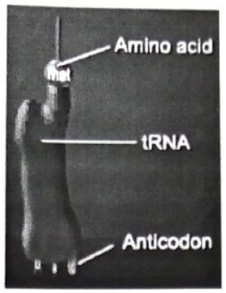
Translation begins when an rRNA molecule within the ribosome recognizes and binds to a "start" sequence (AUG) on the mRNA. The mRNA molecule is translated in non-overlapping groups of three bases called codons.

The ribosome then moves along the mRNA molecule, three nucleotides at a time. Each group of three nucleotides is a codeword that specifies which amino acid will be added to the growing polypeptide chain.

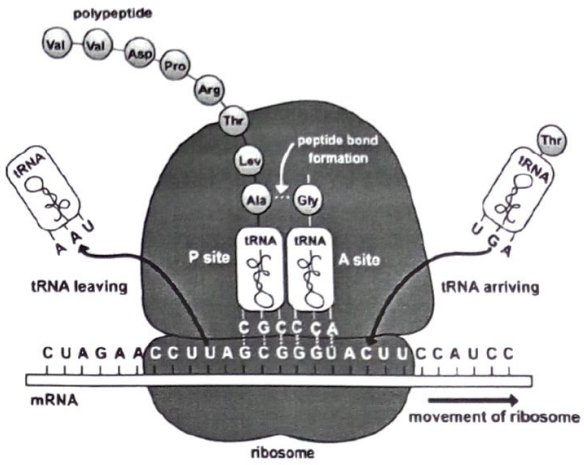
For each codon in the mRNA that specifies an amino acid, there is one tRNA molecule containing a complementary group of three adjacent bases that can pair with the codon.

The ribosome continues until it encounters a translational "stop" signal; then it disengages from the mRNA and releases the completed polypeptide.

TRANSLATION



A tRNA with charged amino acids



THE GENETIC CODE

The rules by which the nucleotide sequence of a gene, through the medium of mRNA, is translated into the amino acid sequence of a protein are known as the genetic code

The sequence of nucleotides in the mRNA molecule is read consecutively in groups of three.

Each group of three consecutive nucleotides in RNA is called a codon, and each specifies one amino acid.

THE GENETIC CODE

A codon consists of three bases which code for a specific amino acid. As there are four bases, there are 4 x 4 x 4 = 64 possible codons. These represent the genetic code (next slide).

The code is described as being *degenerate* because there are 64 codons but only 20 amino acids, so several different codons specify the same amino acid.

Translation always begins (start) at a codon for methionine (AUG), which is often then removed before the completion of synthesis of the polypeptide. This is referred to as the initiator codon, and it determines the reading frame of the mRNA.

Three combinations (UAA, UAG, UGA) specify stop codons, also known as nonsense or termination codons. These signal the end of translation.

PROPERTIES OF THE GENETIC CODE

1) The genetic code is composed of nucleotide triplets
2) The genetic code is non-overlapping and comma-free
3) The genetic code is unambiguous (1 codon, 1 AA)
4) The genetic code is degenerate or redundant
5) The genetic code contains start and stop codons
6) The genetic code is nearly universal

20 NATURALLY OCCURING AMINO ACIDS

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

THE STANDARD GENETIC CODE

Second nucleotide in codon

First nucleotide in codon (5' end)	U				C				A				G				Third nucleotide in codon (3' end)
U	UUU	Phe	F	*Phenylalanine*	UCU	Ser	S	*Serine*	UAU	Tyr	Y	*Tyrosine*	UGU	Cys	C	*Cysteine*	U
	UUC	Phe	F	*Phenylalanine*	UCC	Ser	S	*Serine*	UAC	Tyr	Y	*Tyrosine*	UGC	Cys	C	*Cysteine*	C
	UUA	Leu	L	*Leucine*	UCA	Ser	S	*Serine*	UAA		Termination		UGA		Termination		A
	UUG	Leu	L	*Leucine*	UCG	Ser	S	*Serine*	UAG		Termination		UGG	Trp	W	*Tryptophan*	G
C	CUU	Leu	L	*Leucine*	CCU	Pro	P	*Proline*	CAU	His	H	*Histidine*	CGU	Arg	R	*Arginine*	U
	CUC	Leu	L	*Leucine*	CCC	Pro	P	*Proline*	CAC	His	H	*Histidine*	CGC	Arg	R	*Arginine*	C
	CUA	Leu	L	*Leucine*	CCA	Pro	P	*Proline*	CAA	Gln	Q	*Glutamine*	CGA	Arg	R	*Arginine*	A
	CUG	Leu	L	*Leucine*	CCG	Pro	P	*Proline*	CAG	Gln	Q	*Glutamine*	CGG	Arg	R	*Arginine*	G
A	AUU	Ile	I	*Isoleucine*	ACU	Thr	T	*Threonine*	AAU	Asn	N	*Asparagine*	AGU	Ser	S	*Serine*	U
	AUC	Ile	I	*Isoleucine*	ACC	Thr	T	*Threonine*	AAC	Asn	N	*Asparagine*	AGC	Ser	S	*Serine*	C
	AUA	Ile	I	*Isoleucine*	ACA	Thr	T	*Threonine*	AAA	Lys	K	*Lysine*	AGA	Arg	R	*Arginine*	A
	AUG	Met	M	*Methionine*	ACG	Thr	T	*Threonine*	AAG	Lys	K	*Lysine*	AGG	Arg	R	*Arginine*	G
G	GUU	Val	V	*Valine*	GCU	Ala	A	*Alanine*	GAU	Asp	D	*Aspartic acid*	GGU	Gly	G	*Glycine*	U
	GUC	Val	V	*Valine*	GCC	Ala	A	*Alanine*	GAC	Asp	D	*Aspartic acid*	GGC	Gly	G	*Glycine*	C
	GUA	Val	V	*Valine*	GCA	Ala	A	*Alanine*	GAA	Glu	E	*Glutamic acid*	GGA	Gly	G	*Glycine*	A
	GUG	Val	V	*Valine*	GCG	Ala	A	*Alanine*	GAG	Glu	E	*Glutamic acid*	GGG	Gly	G	*Glycine*	G

Codon

Three-letter and single-letter abbreviations

tRNA

The tRNA is an adaptor molecule that mediate the specification of amino acids by codons in mRNAs during protein synthesis. They contain a triplet nucleotide sequence (the anticodon), which is complementary to the base-pairs with the codon sequence in mRNA during translation.

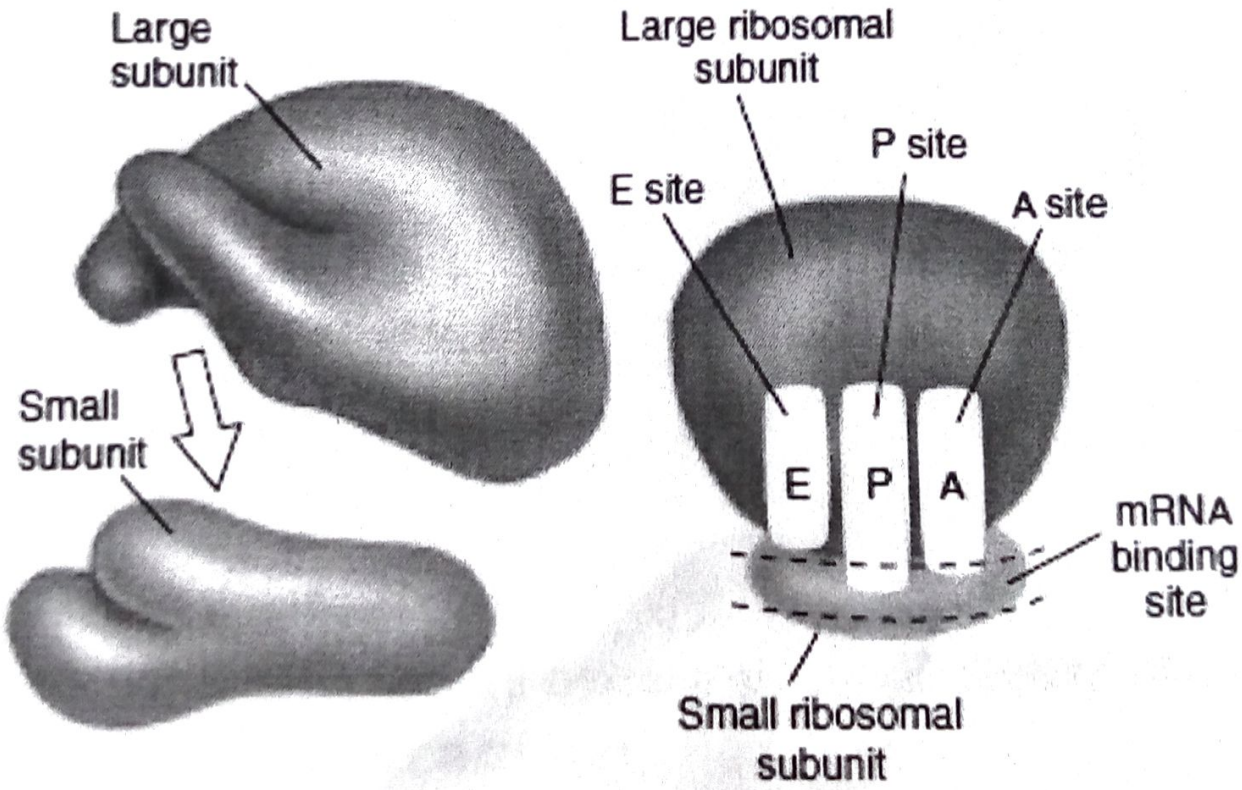
Amino acids are attached to the tRNAs by high-energy bonds between the carboxyl groups of the amino acids and the 3'-hydroxyl termini of the tRNAs. The enzyme aminoacyl-tRNA synthetase catalyze this process. Once an amino acid has been added to a tRNA, it becomes activated or charged.

There are three tRNA binding sites on each ribosome (E, P and A sites).

1) The A or aminoacyl site binds the incoming aminoacyl-tRNA which is the tRNA carrying the next amino acid to be added to the growing polypeptide chain.
2) The P or peptidyl site binds the tRNA to which the growing peptide is attached.
3) The E or exit site binds the departing uncharged tRNA.

TRANSLATION- The Ribosome

A ribosome is composed of two subunits. The smaller subunit fits into a depression on the surface of the larger one. The A, P, and E sites on the ribosome, play key roles in protein synthesis.



Peptide Chain Elongation

There are three basic steps involved in the process of elongation during polypeptide synthesis:

1) **Aminoacyl-tRNA selection:** where the charged initiator tRNA occupies the P site and the second aminoacyl-tRNA enters and becomes bound to the A site of the ribosome.
2) **Peptide bond formation:** where peptide bond formation occurs between the two amino acids, catalyzed by the enzyme peptidyl transferase, a component of the large subunit of the ribosome.
3) **Translocation:** where the ribosome moves three nucleotides (one codon) along the mRNA in the 5'-3' direction.

MUTATION

Dr. Segun I. OYEDEJI
Federal University Oye-Ekiti
Department of Animal & Environmental Biology

2018 Lecture Guide

MUTATION

Mutation may be defined as any heritable change in the genetic material of the cell. Mutations can happen at any time and in any cell. It occurs in all genes of all living organisms from viruses to humans.

Remember that the cells of a sexually reproducing animal or plant are of two types: germ cells and somatic cells. The germ cells transmit genetic information from parent to offspring; the somatic cells form the body of the organism.

Germ cells must be protected against high rates of mutation to maintain the species. However, the somatic cells of multicellular organisms must also be protected from genetic change to properly maintain the organized structure of the body.

Nucleotide changes in somatic cells can give rise to variant cells, some of which, through "local" natural selection, proliferate rapidly at the expense of the rest of the organism. In an extreme case, the result is the uncontrolled cell proliferation that we know as cancer, a disease that causes more than 20% of human deaths each year. These deaths are due largely to an accumulation of changes in the DNA sequences of somatic cells.

MUTATION

Mutations can occur in Somatic or Germinal cell

Somatic mutations are mutations that occur in somatic cells hence it will not be transmitted to the progeny.

Germinal mutations occur in the germ cells and are transmitted to the progeny.

There are two categories mutations:

1) **Gene mutations, in which the structure or sequence of a gene is altered at the molecular level.**
2) **Chromosome mutations/aberrations, in which the structure of one or more chromosomes is affected; OR there may be addition or subtraction of one or more whole chromosomes.**

GENE MUTATION

Gene mutations are alterations or changes in gene structure or sequence, and they result in different versions of a gene which are called alleles.

Alleles may be different versions of a gene that produce the same basic effect, or the effect may be very different. The effect of a mutant allele on the development of an individual varies.

Gene mutations may be point mutations involving a single base pair .

Point mutations: these are chemical changes in just one base pair of a gene.

There are three basic types of point mutations:

(1) substitutions, (2) insertions and (3) deletions.

Insertions and deletions are commonly referred to as indels.

GENE MUTATION- Substitution

HBB Sequence in Normal Adult Hemoglobin (Hb A):

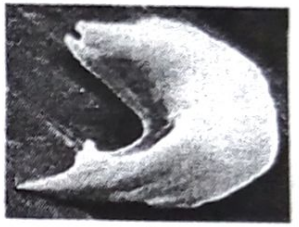
Nucleotide	CTG	ACT	CCT	GAG	GAG	AAG	TCT
Amino Acid	Leu	Thr	Pro	Glu	Glu	Lys	Ser
	3			6			9

Normal, disc-shaped red blood cells

Normal transport of oxygen

HBB Sequence in Mutant Adult Hemoglobin (Hb S):

Nucleotide	CTG	ACT	CCT	GTG	GAG	AAG	TCT
Amino Acid	Leu	Thr	Pro	Val	Glu	Lys	Ser
	3			6			9



Mutant, sickle-shaped red blood cells

Sickle-cell anemia

There are two types of substitution mutation:

1) **Transition mutation: When a purine base is substituted for the other purine, or one pyrimidine is substituted for the other pyrimidine. Transition mutations are the most common form of substitution errors.**
2) **Transversion mutation: When a purine replaces a pyrimidine (or vice versa).**

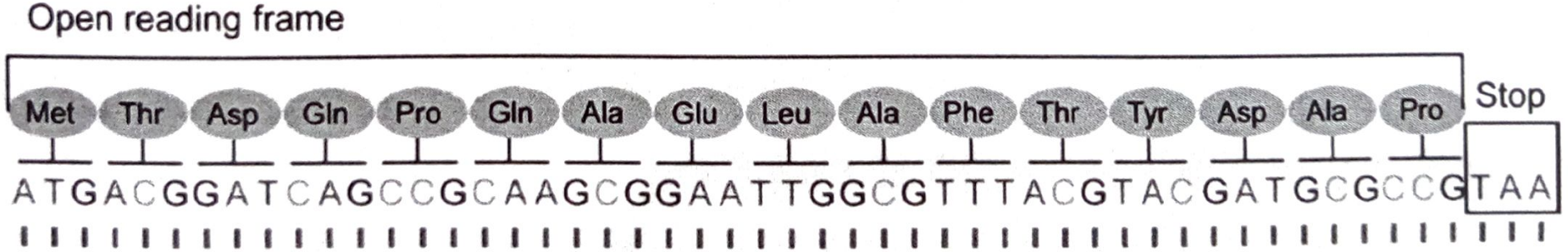
98

GENE MUTATION- Insertions & Deletions

Insertions and deletions are also referred to as FRAMESHIFT MUTATIONS. This is because a single base deletion or insertion may result in a shifted reading frame

ATG CCA GAG CAT AAC	Reading Frame 1
ATGC CAG AGC ATA AC	Reading Frame 2
ATGCC AGA GCA TAA C	Reading Frame 3

DNA strand can be read in three different reading frames. In Bioinformatics, the computer must perform six different translations for any given double-stranded DNA sequence.



THE STANDARD GENETIC CODE

First nucleotide in codon (5' end)	Second nucleotide in codon: U				Second nucleotide in codon: C				Second nucleotide in codon: A				Second nucleotide in codon: G				Third nucleotide in codon (3' end)
U	UUU	Phe	F	*Phenylalanine*	UCU	Ser	S	*Serine*	UAU	Tyr	Y	*Tyrosine*	UGU	Cys	C	*Cysteine*	U
	UUC	Phe	F	*Phenylalanine*	UCC	Ser	S	*Serine*	UAC	Tyr	Y	*Tyrosine*	UGC	Cys	C	*Cysteine*	C
	UUA	Leu	L	*Leucine*	UCA	Ser	S	*Serine*	UAA			Termination	UGA			Termination	A
	UUG	Leu	L	*Leucine*	UCG	Ser	S	*Serine*	UAG			Termination	UGG	Trp	W	*Tryptophan*	G
C	CUU	Leu	L	*Leucine*	CCU	Pro	P	*Proline*	CAU	His	H	*Histidine*	CGU	Arg	R	*Arginine*	U
	CUC	Leu	L	*Leucine*	CCC	Pro	P	*Proline*	CAC	His	H	*Histidine*	CGC	Arg	R	*Arginine*	C
	CUA	Leu	L	*Leucine*	CCA	Pro	P	*Proline*	CAA	Gln	Q	*Glutamine*	CGA	Arg	R	*Arginine*	A
	CUG	Leu	L	*Leucine*	CCG	Pro	P	*Proline*	CAG	Gln	Q	*Glutamine*	CGG	Arg	R	*Arginine*	G
A	AUU	Ile	I	*Isoleucine*	ACU	Thr	T	*Threonine*	AAU	Asn	N	*Asparagine*	AGU	Ser	S	*Serine*	U
	AUC	Ile	I	*Isoleucine*	ACC	Thr	T	*Threonine*	AAC	Asn	N	*Asparagine*	AGC	Ser	S	*Serine*	C
	AUA	Ile	I	*Isoleucine*	ACA	Thr	T	*Threonine*	AAA	Lys	K	*Lysine*	AGA	Arg	R	*Arginine*	A
	AUG	Met	M	*Methionine*	ACG	Thr	T	*Threonine*	AAG	Lys	K	*Lysine*	AGG	Arg	R	*Arginine*	G
G	GUU	Val	V	*Valine*	GCU	Ala	A	*Alanine*	GAU	Asp	D	*Aspartic acid*	GGU	Gly	G	*Glycine*	U
	GUC	Val	V	*Valine*	GCC	Ala	A	*Alanine*	GAC	Asp	D	*Aspartic acid*	GGC	Gly	G	*Glycine*	C
	GUA	Val	V	*Valine*	GCA	Ala	A	*Alanine*	GAA	Glu	E	*Glutamic acid*	GGA	Gly	G	*Glycine*	A
	GUG	Val	V	*Valine*	GCG	Ala	A	*Alanine*	GAG	Glu	E	*Glutamic acid*	GGG	Gly	G	*Glycine*	G

Codon

Three-letter and single-letter abbreviations

1 UD

GENE MUTATION EFFECT

Mutations in the coding sequence of a gene can have various effects on the polypeptide which my be classified thus:.

1) **Silent mutations: these are base substitutions that do not alter the amino acid sequence of the polypeptide, due to the degeneracy of the genetic code.**

2) **Missense mutations: these are base substitutions that alter the amino acid sequence of the polypeptide.**

Example: Sickle-cell anemia

3) **Nonsense mutations: these are base substitutions that change a normal codon to a termination codon.**

4) **Frameshift mutations: this involves the addition or deletion of nucleotides which leads to a shift in reading frame so that a completely different amino acid sequence occurs downstream from the mutation.**

GENE MUTATION

Some mutations are recessive, meaning that their effects are invisible as long as a normal allele is present e.g. cystic fibrosis or sickle cell anaemia. Often recessive mutations result in non-functional alleles. With these types of mutations, a heterozygous individual has a normal phenotype because the normal allele is substituting for its dysfunctional partner.

Some mutations may be dominant, causing a change that essentially overpowers the normal function e.g. Huntington's disease. So, their effects are seen even when a normal allele is present. A heterozygous individual will have the disease phenotype when he carries dominant disease alleles.

Other mutations are codominant. An individual who is heterozygous for codominant alleles will express both alleles.

OCCURRENCE AND CAUSES OF MUTATION

Mutations can occur spontaneously or be induced

Spontaneous mutations

Result from abnormalities in cellular/biological processes e.g DNA replication errors. Substitution of one base for another is an important mechanism of spontaneous mutation.

Induced mutations

Caused by environmental factors/agents

Agents that are known to alter DNA structure are termed mutagens. These can be chemical or physical agents such as UV light and X-rays. Most mutagens are also carcinogens.

Features of Mutation:

1) **Mutation originate at the DNA level**

2) **The effects of mutation are usually found at the protein level**

3) **Mutation can be Inherited or may occur spontaneously**

TYPES OF CHROMOSOME MUTATION

Chromosome mutations can be grouped into three basic categories:

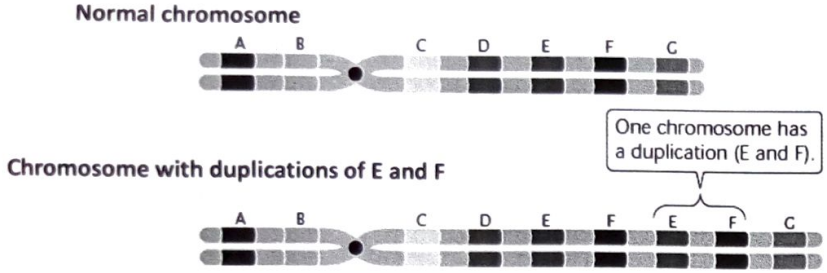
1) **Chromosome rearrangements,**
2) **Aneuploids, and**
3) **Polyploids.**

Chromosome rearrangements alter the structure of chromosomes; for example, a piece of a chromosome might be duplicated, deleted, or inverted.
In Aneuploidy, the number of chromosomes is altered: one or more individual chromosomes are added or deleted.
In Polyploidy, one or more complete sets of chromosomes are added. Some organisms (such as yeast) possess a single chromosome set (1n) for most of their life cycles and are referred to as haploid, whereas others possess two chromosome sets and are referred to as diploid (2*n*). A polyploid is any organism that has more than two sets of chromosomes (3n, 4n, 5n, or more).

CHROMOSOME REARRANGEMENT

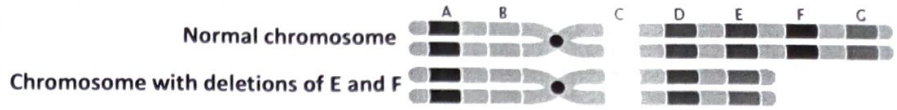
Chromosome rearrangements are mutations that change the structure of individual chromosomes. The four basic types of rearrangements are duplications, deletions, inversions, and translocations.

1) **Chromosome duplication** is a mutation in which part of the chromosome has been doubled as shown below.

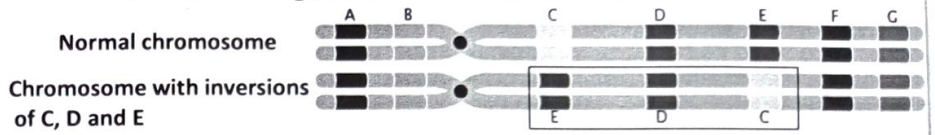


CHROMOSOME REARRANGEMENT

2) **Chromosome deletions** is a mutation in which there is a loss of a chromosome segment or deletion of part of the chromosome.



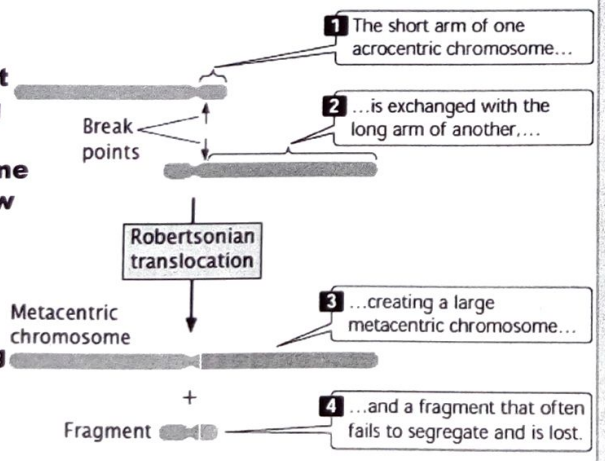
3) **Chromosome inversions** is a mutation in which a chromosome segment is inverted or turned 180 °C.



CHROMOSOME REARRANGEMENT

4) **Chromosome Translocations** is a mutation in which there is the movement of genetic material between non-homologous chromosomes or within the same chromosome.

Translocations may affect the phenotype by causing genes to move to new locations, where they come under the influence of new regulatory sequences, or by breaking genes and disrupting their function. Translocation should not be confused with crossing over, in which there is an exchange of genetic material between *homologous* chromosomes.



ANEUPLOIDY

This is an abnormal condition were one or more chromosomes of a normal set of chromosomes are missing or present in more than their usual number of copies. Aneuploidy can be sub-divided into:

1) **Nullisomy:** which is the loss of both pairs of homologous chromosomes (nullisomics) e.g the loss of both pari of chromosome 2 from both parents (i.e 2n-2).

2) **Monosomy:** the loss of a single chromosome (i.e 2n-1)

3) **Trisomy:** the gain of an extra copy of a chromosome (i.e 2n+1)

4) **Tetrasomy:** the gain of an extra pair of homologou chromosome (2n+2)

Some of these chromosomal aberrations can give rise genetic diseases which can be detected by Karyotyping.

ANEUPLOIDY

Aneuploidy can arise in several ways:

First, a chromosome may be lost in the course of mitosis or meiosis if, for example, its centromere is deleted. Loss of the centromere prevents the spindle fibers from attaching; so the chromosome fails to move to the spindle pole and does not become incorporated into a nucleus after cell division.

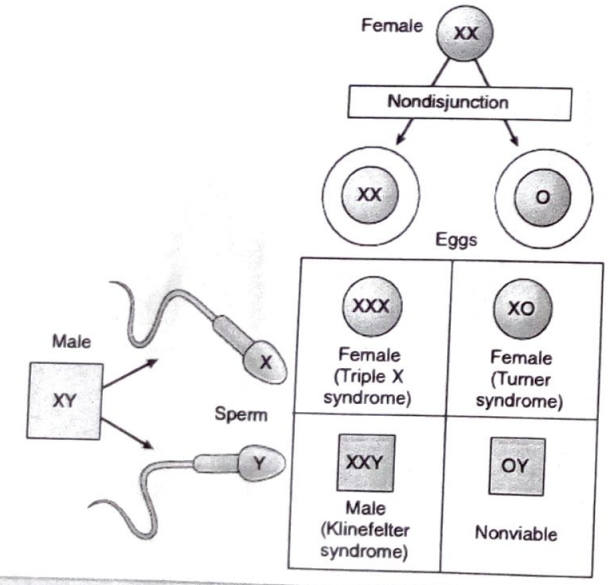
Second, the small chromosome generated by a Robertsonian translocation may be lost in mitosis or meiosis.

Third, aneuploids may arise through non-disjunction as shown in next slide. Non-disjunction is the failure of homologous chromosomes or sister chromatids to separate during meiosis or mitosis.

CHROMOSOME ABERRATIONS

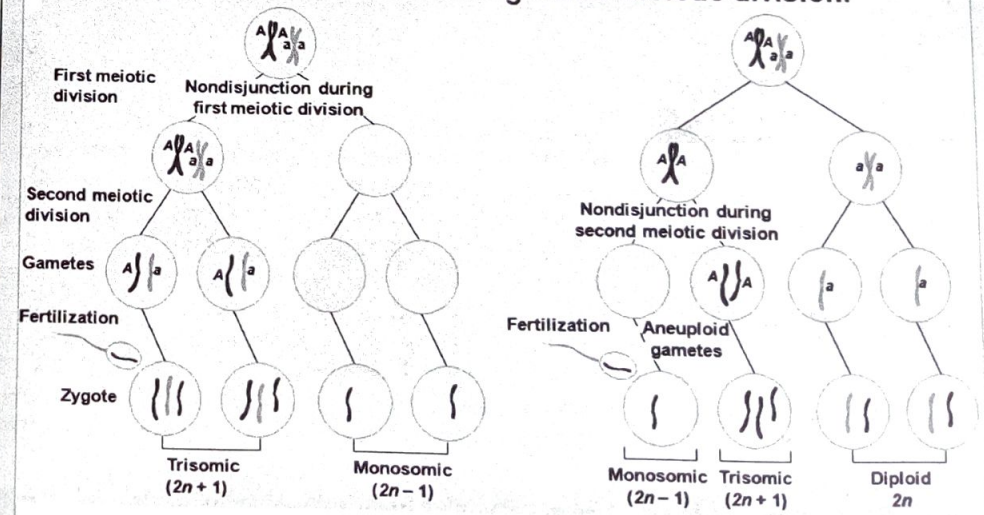
Abbreviation	What It Means
46,XY	Normal male
46,XX	Normal female
45,X	Turner syndrome (female)
47,XXY	Klinefelter syndrome (male)
47,XYY	Jacobs syndrome (male)
46,XY, del (7*q*)	A male missing part of the long arm of chromosome 7
47,XX, + 21	A female with trisomy 21 Down syndrome
46,XY, t(7;9)(*p*21.1; *q*34.1)	A male with a translocation between the short arm of chromosome 7 at band 21.1 and the long arm of chromosome 9 at band 34.1
48, XXYY	A male with an extra X and an extra Y

CHROMOSOME ABERRATIONS



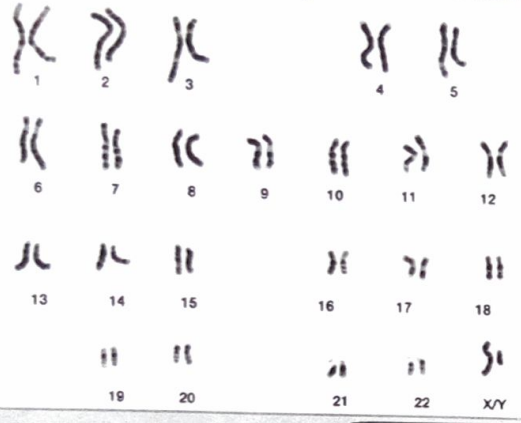
ANEUPLOIDY: NON-DISJUNCTION

Non-disjunction can occur during either meiotic division.

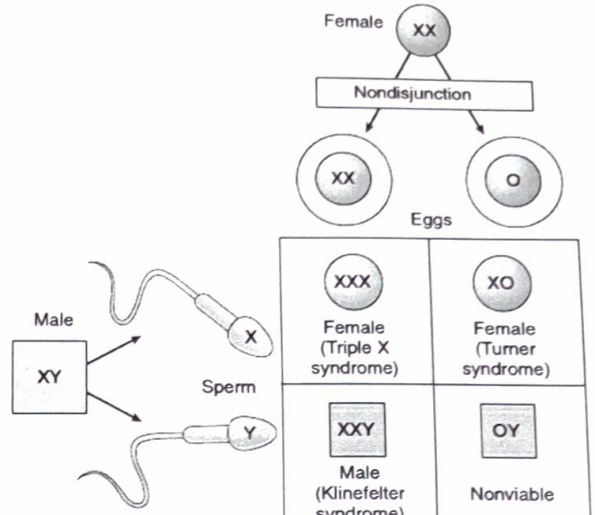


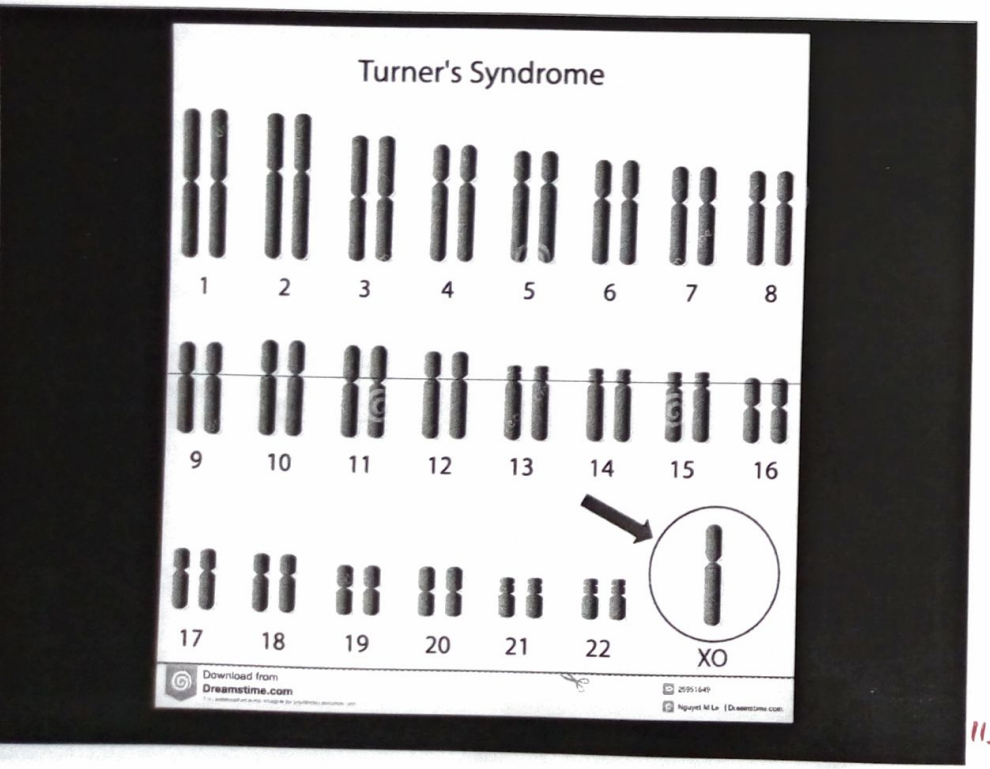
Detecting Genetic Diseases

Certain genetic diseases can be detected by karyotyping e.g. diseases resulting from chromosomal abberations such as Down syndrome, Turner syndrome, Klinefelter syndrome etc.

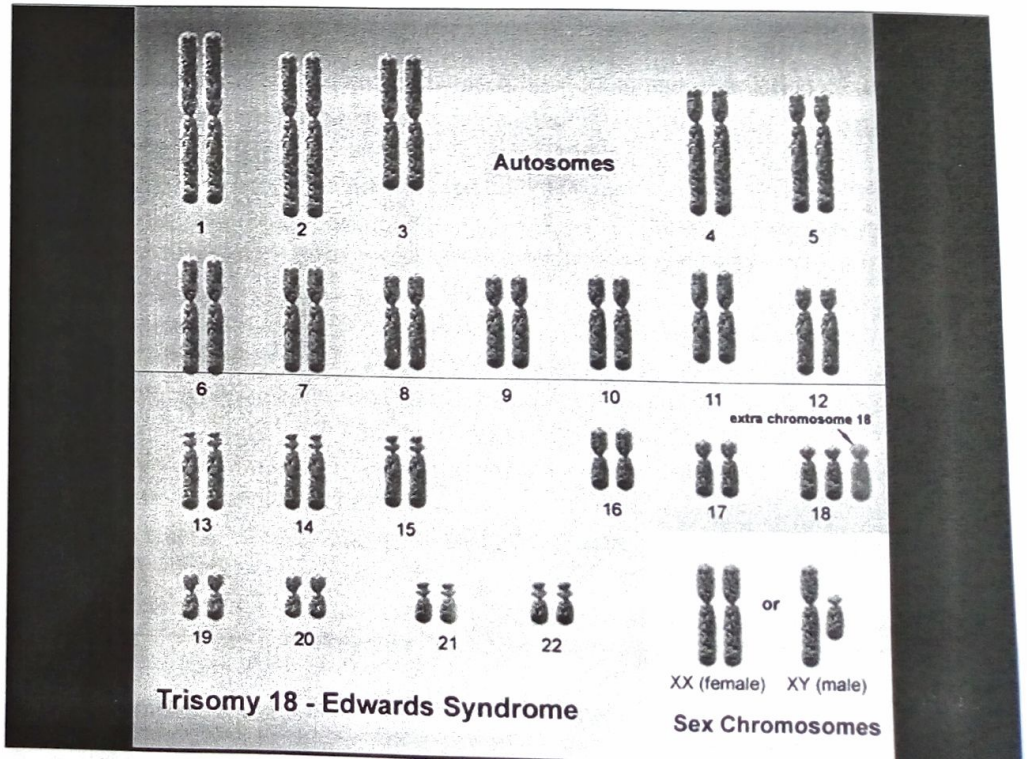


CHROMOSOME MUTATION DURING MEIOSIS





115



TEST OF KNOWLEDGE

1) Since introns are largely genetic "junk," they do not have to be removed precisely from the primary transcript during RNA splicing. Why or Why not.

2. Which of the following mutational changes would you predict to be the most deleterious to gene function? Explain your answers.

a. Insertion of a single nucleotide near the end of the coding sequence.

b. Removal of a single nucleotide near the beginning of the coding sequence.

c. Deletion of three consecutive nucleotides in the middle of the coding sequence.

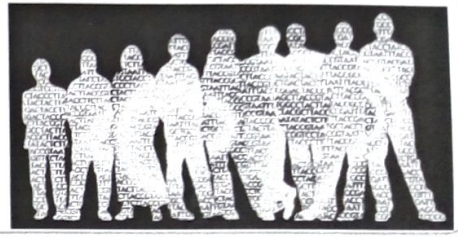
d. Substitution of one nucleotide for another in the middle of the coding sequence.

TEST OF KNOWLEDGE (05/12/2016)

1. Distinguish between gene and genome

2. Distinguish between genotype and phenotype; dominant and recessive; an autosome and a sex chromosome; DNA and RNA.

The human genome is the complete set of genetic information encoded in the sequence of building blocks of the molecule deoxyribonucleic acid (DNA), including protein-encoding genes and other DNA sequences, characteristic of an organism.



ASSIGNMENT (21/12/2015)

1. What is transformation?

2. How did the transformation experiments of Griffith differ from those of Avery and his colleagues?

3. How did Avery and his colleagues demonstrate that the transforming principle is DNA?

4. (a) Why did Hershey and Chase choose 32P and 35S for use in their experiment?
(b) Could they have used radioactive isotopes of carbon (C) and oxygen (O) instead? Why or why not?

5. Which human chromosome contains the largest DNA molecule? How large is it? How many genes does it contain?

6. When Avery and his colleagues had obtained what was concluded to be the transforming factor from the III*S virulent cells,* they treated the fraction with proteases, RNase, and DNase, followed in each case by the assay for retention or loss of transforming ability. What were the purpose and results of these experiments? What conclusions were drawn?

TEST I (23/01/2017)

1) Distinguish between gene and allele
2) Differentiate between sister chromatids and homologous chromosomes
3) What are the two basic cell types in the human body?
4) Mention the two types of chromosomes in the human body.
5) Why was Griffith's work not considered evidence for DNA as the genetic material?
6) What was the conclusion of the experiment carried out by Avery, MacLeod and McCarty?
7) What was the objective of the experiment carried out by Hershey and Chase?
8) List the three essential functions of the genetic material.
9) Itemize the differences between DNA and RNA.
10) Distinguish between purines and pyrimidines.

BIO 201 QUIZ (18/01/2016)

1) What is the full meaning of dCTP?

2) Distinguish between ATP and dAMP

3) List the 4 major types of deoxyribonucleosides

4) Distinguish between Nucleotides and Nucleosides

5) The φx *E. coli* virus stores its genetic information in single stranded DNA. When its DNA was extracted and analyzed, 21% of the bases were found to be G residues. Determine the % of bases in this DNA.

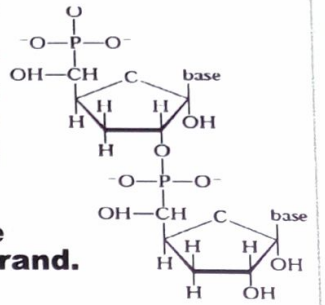
6) Indicate whether each of the following statements about the structure of DNA is true or false.

(a) A+T = G+C; (b) A=G; C=T (c) A/T = C/G
(d) T/A = C/G; (e) A+G = C+T; (f) G/C = 1

TEST OF KNOWLEDGE

7) If one strand of DNA in the Watson-Crick double helix has a base sequence of 5'-ACTGCACA-3', what is the base sequence of the complementary strand?

8) For entertainment on a Friday night, a professor of genetics proposed that one of his children make a diagram of a polynucleotide strand of DNA. Having learned about DNA in school, his 12-year-old daughter was able to draw a polynucleotide strand, but she made a few mistakes.



(a) Make a list of all the mistakes in the structure of this DNA polynucleotide strand.

(b) Draw the correct structure for the polynucleotide strand of DNA.

TEST OF KNOWLEDGE

7)Explain the Figure

A = T
C ≡ G

8) Distinguish between purines and pyrimidines

What are alleles?
Is it possible for more than two alleles of a gene to exist? Explain citing examples where necessary.

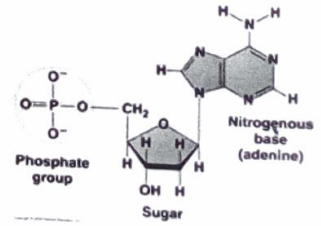
(a) What role do the following cellular components play in the storage, expression, or transmission of genetic information: (a) chromosome, (b) nucleus, (c) ribosome (d) histones (e) chromosome

TEST OF KNOWLEDGE

9) The relationship between the melting temperature (T_m) and GC content can be expressed in its much simplified form by the formula $T_m = 69.3°C + 0.41(\%GC)°C$

a)Calculate the melting temperature of *E. coli* DNA that has about 54% GC

b)Estimate the % GC of DNA from a human kidney cell where $T_m = 75°C$



TEST OF KNOWLEDGE

1) Since introns are largely genetic "junk," they do not have to be removed precisely from the primary transcript during RNA splicing. Why or Why not

2) DNA isolated from the bacterial virus M13 contains 25% A, 33% T, 22% C, and 20% G. Do these results strike you as peculiar? Why or why not? How might you explain these values?

TEST OF KNOWLEDGE

1) What differences in the chemical structures of DNA and protein allow scientists to label one or the other of these macromolecules with radioactive isotope?

2) If the G_1 stage of human chromosome contains a single molecule of DNA, how many DNA molecules would be present in the chromosomes of the nucleus of

a) a human egg
b) a human sperm
c) a human diploid somatic cell in stage G_1
d) a human diploid somatic cell in stage G_2
e) a human primary oocyte

TEST OF KNOWLEDGE

1) Write a concise note on RNA processing or editing.

2) A scientist is studying the transcription of a gene in mouse cells growing in culture. How can she determine whether the gene is transcribed by RNA polymerase I, RNA polymerase II, or RNA polymerase III?

TEST OF KNOWLEDGE

Explain the terms locus, allele, dominant, recessive, co-dominant, homozygous, heterozygous, phenotype and genotype.

What kind of chromosomal aberration is Down syndrome?

A 3-year-old child exhibited some early indication of Turner syndrome, which results from a 45,X chromosome composition.

Karyotypic analysis demonstrated two cell types: 46,XX (normal) and 45,X. Propose a mechanism for the origin of this mosaicism.

TEST OF KNOWLEDGE

1) Suppose a gene contains 10 codons:

a) how many coding nucleotides does the gene contain?

b) how many amino acids are expected to be present in its polypeptide product?

2) RNA is synthesized using DNA as a template. Is DNA ever synthesized using RNA as a template? Explain

TEST OF KNOWLEDGE

3. Which of these is not an amino acid:
a) alanine
b) glycine
c) cytosine
d) cysteine

4. Which process involves tRNA:
a) transciption
b) translation
c) DNA replication
d) gene mutation

5. The formation of RNA does not involve:
a) ribose sugar
b) thymine
c) removal of water
d) phosphate

6. Where in the cell can mRNA be found:
a) nucleus
b) cytoplasm
c) ribosome
d) all of the above
e) none of the above

GOD 1ST

FAJANA