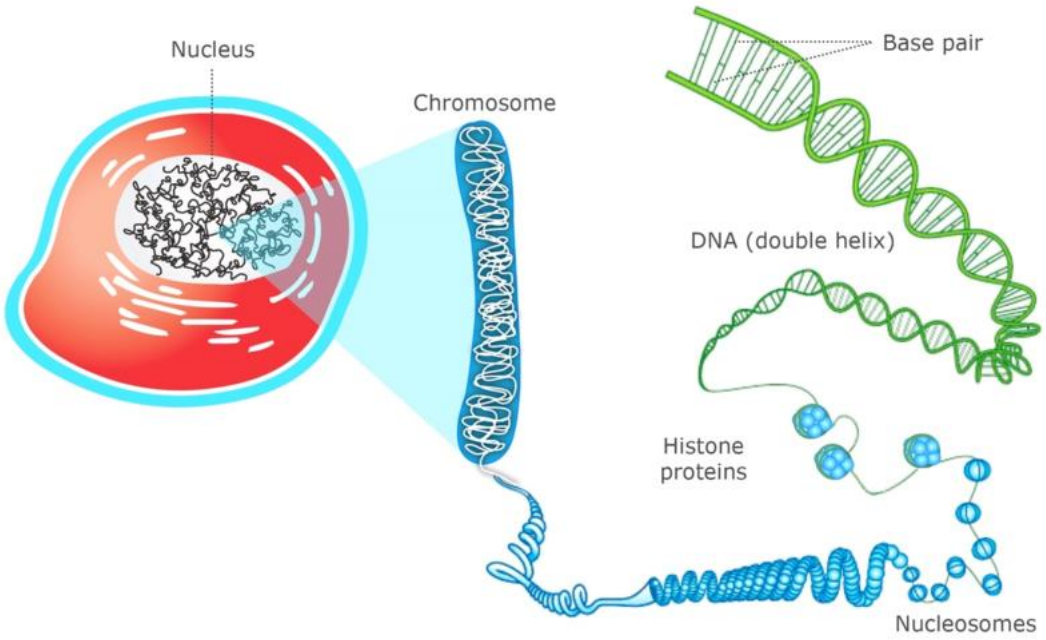
Chapter II. Segregation and the chromosomal theory of inheritance



Dr Karima DJOUADI
University Mohamed Khider –Biskra-
Faculty of life and nature sciences
Departement of agricultural sciences
E-amail : karima.djouadi@uni-biskra.dz

Outlines of the Chapter II

- Structure and physical properties of nucleic acids
- Chromosomes as carriers of genetic information.
- Cell division and mixing of genetic information.
- Inter- and interachromosomal mixing.
- Chromosomal mutations

Learning objectives of the chapter II

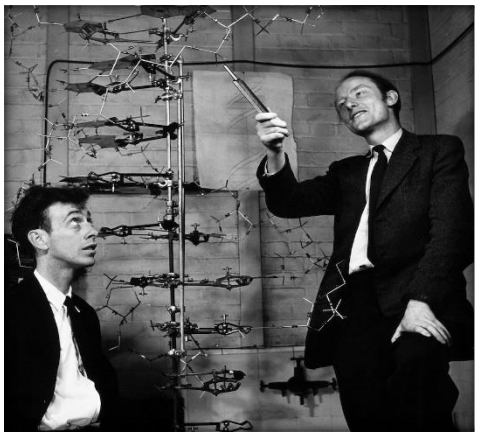
Grasp the molecular composition and physical characteristics of DNA and its role in genetic information storage.

Understand chromosome organization and formation, as well as the processes of cell division and their role in genetic mixing.

Describe the role of meiosis in gamete formation and its connection to inheritance.

Learn about chromosomal mutations, **identify**ing their types, causes, and **classify**ing them in studied examples.

Introduction



The chemical DNA was first discovered in 1869, but its role in genetic inheritance was not demonstrated until 1943. In 1953 James Watson and Francis Crick, aided by the work of biophysicists Rosalind Franklin and Maurice Wilkins, determined that the structure of DNA is a double-helix polymer, a spiral consisting of two DNA strands wound around each other. The breakthrough led to significant advances in scientists' understanding of DNA replication and hereditary control of cellular activities.

1. Structure and physical properties of nucleic acids

1.1.1. Definition: Nucleic acids are the genetic material of the cell and are composed of recurring monomeric units called nucleotides.

- **DNA** (deoxyribonucleic acid) is a more stable double stranded form that stores the genetic blueprint for cells.
- **RNA** (ribonucleic acid) is a more versatile single stranded form that transfers the genetic information for decoding.

1.1.2. The chemical nature of nucleic acids: The macromolecules of **DNA** and **RNA** are composed polynucleotide chains, each made up of numerous nucleotides. The nucleotide is considered the basic unit. A nucleotide results from the condensation of a **pentose sugar**, with a **nitrogenous base**, forming a nucleoside. The esterification of the sugar in a nucleoside by a **phosphoric acid** produces a nucleotide.

- ✓ **Nucleoside**: a structural subunit of nucleic acids, consisting of a sugar molecule linked to a nitrogen-containing organic ring compound. In the most important nucleosides, the sugar is either ribose or deoxyribose, and the nitrogen-containing compound is either a pyrimidine (cytosine, thymine, and uracil) or a purine (adenine or guanine).
- ✓ **Nucleotide**: it is a nitrogen-containing unit (base) linked to a pentose sugar and a phosphate group. Phosphate groups are attached to the sugar by ester linkages, with the most common site of esterification in natural compounds being via the hydroxyl at the C5′ position on the sugar (carbon atoms of ribose sugar are numbered 1′ to 5′ to allow their distinction from the C contained in the Nitrogenous base). Typically, one, two or three phosphates are joined, producing mono-, di- and triphosphates, respectively

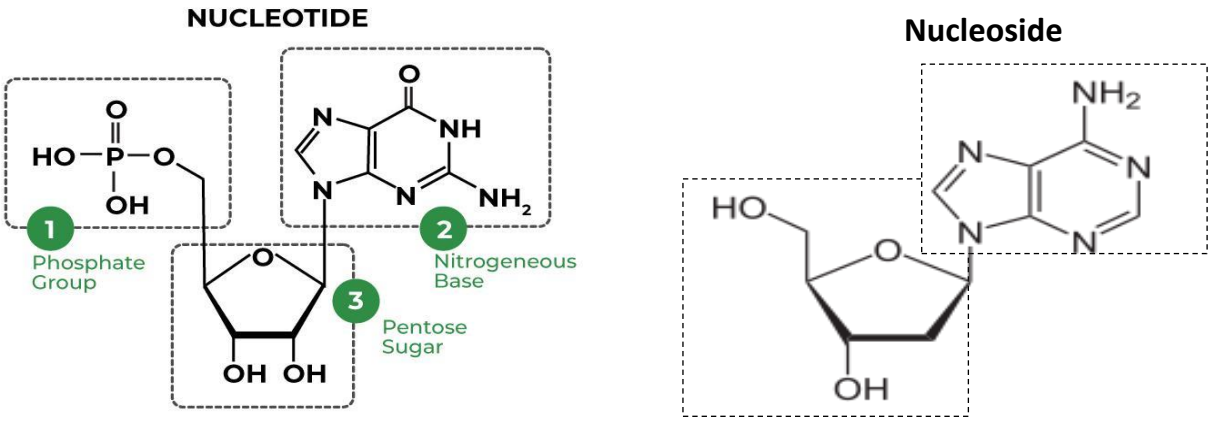


Fig. 1. The chemical structure of nucleotide (on the left side) and nucleoside (on the right side).

✓ **Nitrogenous bases:** There are 2 types :

- **Pyrimidine** is an organic compound known as an aromatic heterocyclic compound. Heterocyclic compounds are stable, ring-shaped compounds in which not all atoms in the ring are carbon. There are three main types of pyrimidines, however only one of them exists in both DNA and RNA: Cytosine. The other two are Uracil, which is RNA exclusive, and Thymine, which is DNA exclusive.
- The **purine** nucleus is made up of two heterocyclic rings, one of 6 atoms and the other of 5 atoms, with two carbons in common in the middle. In relation to these common carbons, the nitrogens occupy symmetrical positions. The purine bases are Adenine and Guanine.

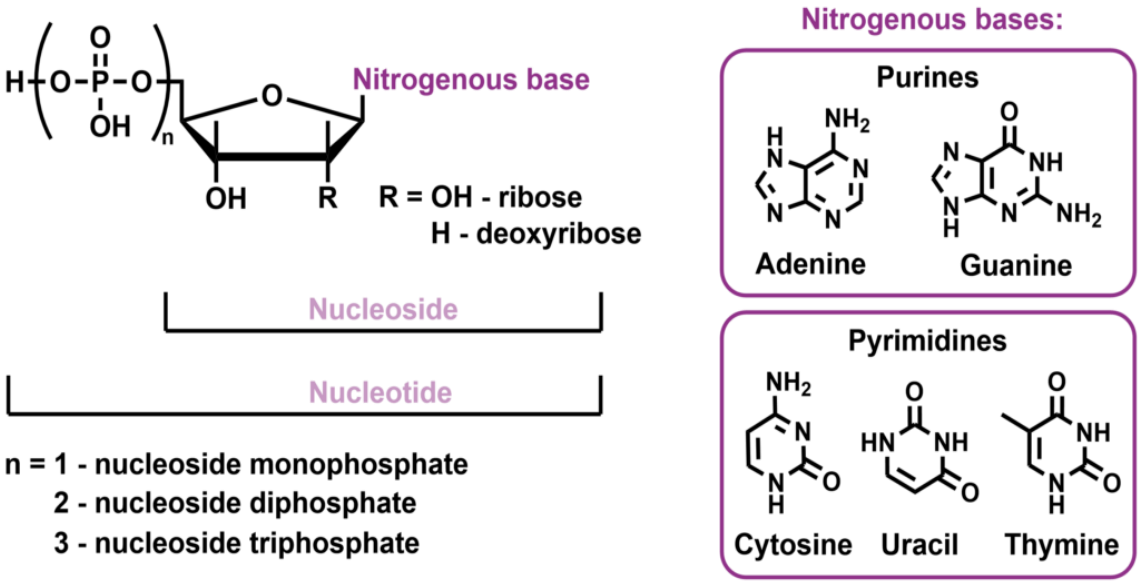


Fig.2. The basic structures of nucleosides, nucleotides and nitrogenous bases.

1.1.3. DNA physical structure properties

- **Double helix structure:** A DNA molecule is composed of two strands that wind around each other, forming a helical structure similar to a twisted ladder.
- **Antiparallel Strands:** Each strand consists of a long chain of nucleotides, with a **5' phosphate** group at one end and a **3' hydroxyl group** at the other, creating an oriented sequence. The two strands are antiparallel, meaning they run in opposite directions. The distance between the planes of each base is 3.4A°. There are 10 pairs of bases per turn of the helix, so its pitch is 34A°.

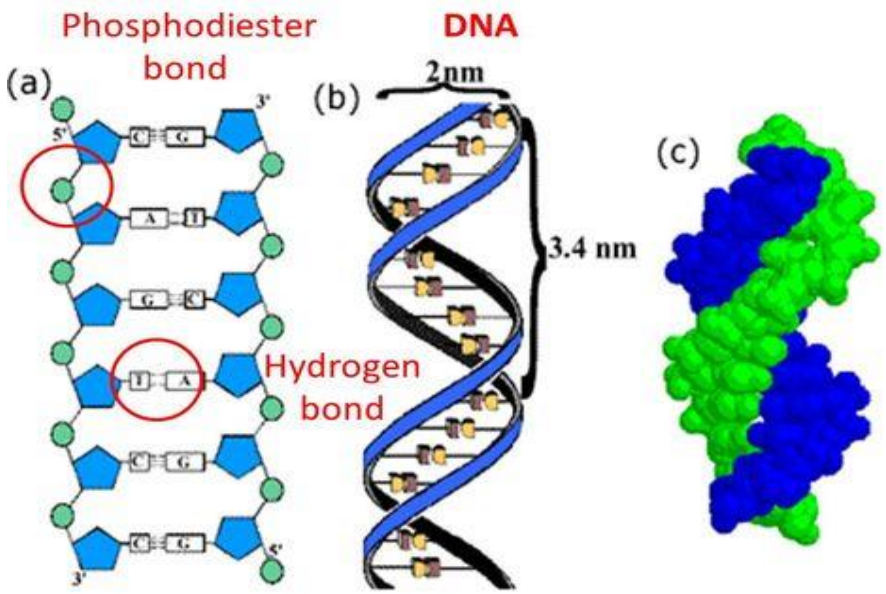


Fig.3. DNA double helix structure.

- **Stability**: the double helix stability is primarily due to hydrogen bonds between complementary bases on each strand, with adenine specifically pairing with thymine and cytosine pairing with guanine (Fig. 3 and 4) and hydrophobic interactions between stacked bases.
- **Phosphate-Sugar Backbone:** Nucleotides are linked together by covalent bonds between phosphate of one nucleotide and sugar of next. The monomers that are linked through phosphodiester bonds become the **phosphate-sugar backbone** of nucleic acids.

Some properties of DNA:

- The number of purines is always equal to the number of pyrimidines (Pur = Pyr), i.e, **A + G = T + C**.
- The amount of A is always equal to that of T, and the amount of C is always equal to that of G (A = T and G = C) Chargaff's rule (1940). However, the proportions of A + T and G + C are not equal and can vary from 25% to 75%.

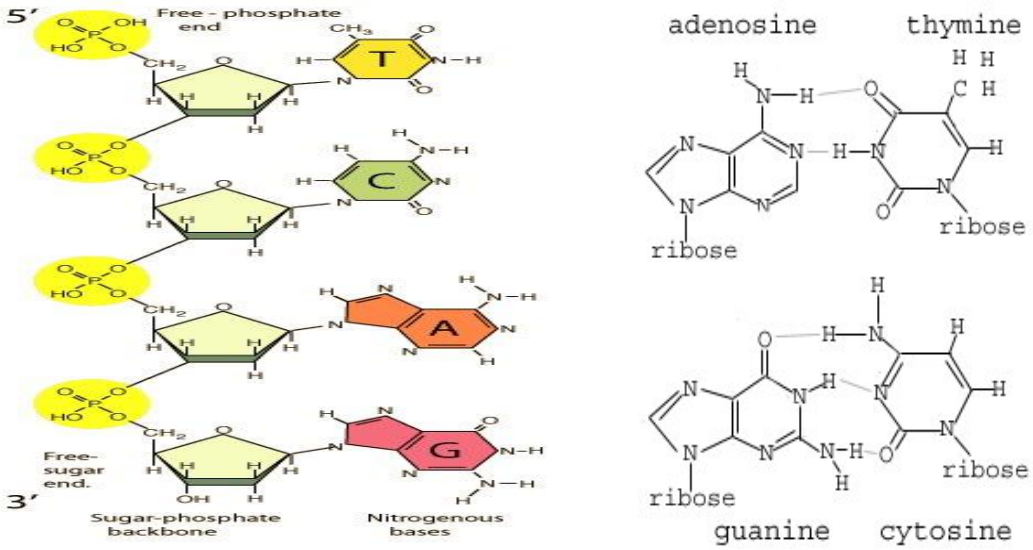


Fig.4. Sugar-phosphate backbone between nucleotides (on the left) and Hydrogen bonds between Guanine: Cytosine Base Pair and Adenine: Thymine Base Pair (on the right).

Activity: Given the following sequence of a DNA strand and based on what you learned about DNA structure, predict the sequence and orientation of the complementary DNA strand.

5′-G-A-C-C-G-T-A-A-T-C-G-C-3′

1.2.Key differences between DNA and RNA:

DNA and RNA are both polymers of nucleotides, however differ in a few key structural aspects:

- Number of strands present
- Composition of nitrogenous base
- Type of pentose sugar.

	DNA	RNA
Pentose sugar	Deoxyribose	Ribose
Base Composition	Adenine (A) Guanine (G) Cytosine (C) **Thymine (T)**	Adenine (A) Guanine (G) Cytosine (C) **Uracil (U)**
Number of strands	Double stranded (forms a double helix)	Single stranded

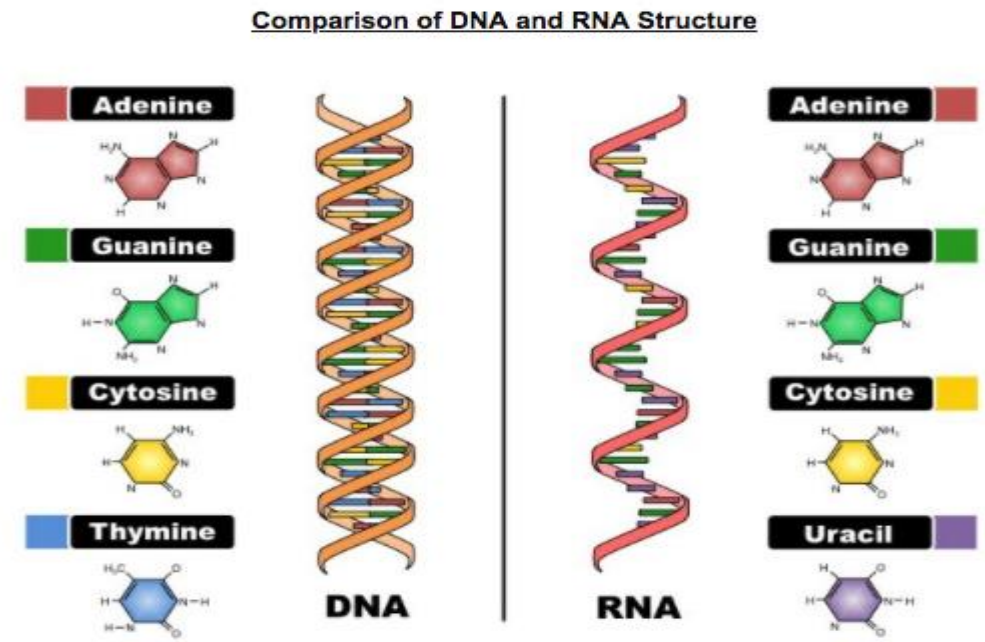
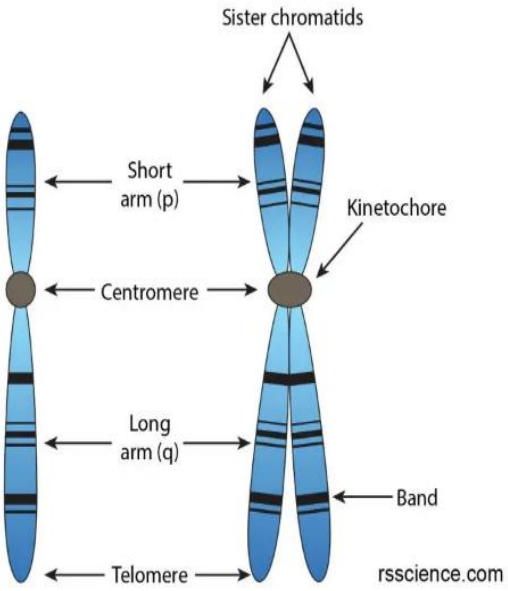


Fig.5. key differences between DNA and RNA molecules.

2. Chromosomes.

2.1.Chromosome structure:

It is the condensed form of chromatin (DNA associated with proteins), which is visible during mitosis. Each chromosome has a short arm, the **p-arm**, and a long arm, **the q- arm**. The end of the chromosome is called the "**telomere**" and contains repetitive DNA sequences associated with different proteins.



As the DNA replicates during mitosis, the chromosome will initially contain two identical DNA strands. These genetically identical strands are called **sister chromatids** and are held together by a central region called the **centromere**. When these chromatids separate during mitosis, they become independent chromosomes, each made of a single DNA strand.

- ✓ **Chromatin :** Chromatin is made up of nucleosomes (**Figure 6**) which represent the association of chromosomal DNA with histone proteins.
- ✓ **Nucleosome** : is the ordered coiling of chromosomal DNA around a histone protein. Nucleosome formation results in a DNA fiber that is about 10 nm and a packaging ratio of about 7. The higher order chromatin structure results when the 10 nm fiber is coiled into a

solenoid. The result of nucleosome coiling is a chromatin fiber of 30 nm that is observed by electron microscopy.

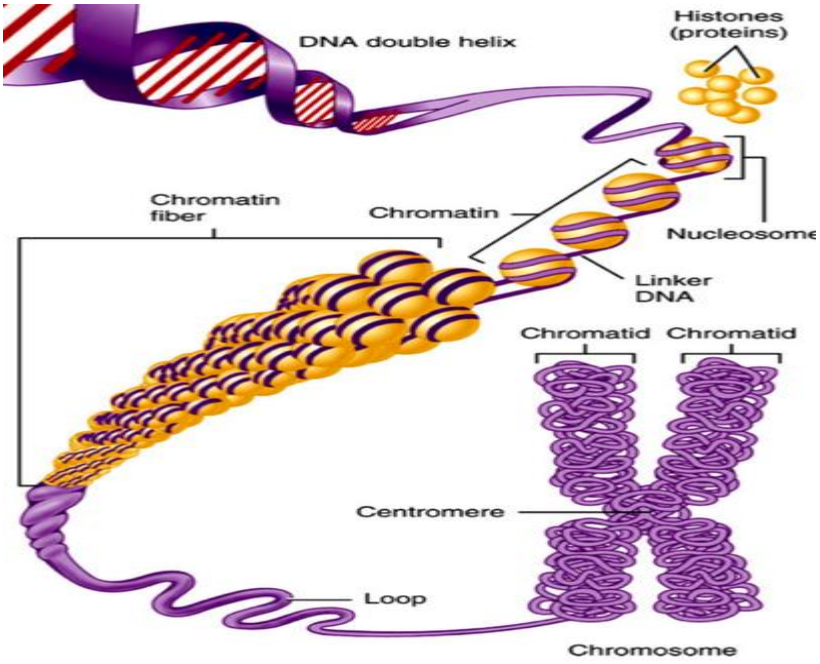


Fig.6. levels of DNA chromatin condensation in the metaphasic chromosome

2.2.Types of chromosomes

✓ Depending on the position of the centromere in the chromosome, a distinction is made between :

a. Metacentric chromosome: a chromosome whose centromere is in the middle of the chromosome, giving rise to arms of equal length.

b. Submetacentric chromosome: a chromosome in which the centromere is located in such a way that one arm is slightly shorter than the other.

c. Acrocentric chromosome: a chromosome in which the centromere is closest to one of the telomeres, resulting in a very short arm (p) and a long arm (q).

d. Telocentric chromosome: a chromosome in which the centromere occupies the terminal position so that has just one arm. This type of chromosome does not exist in human cells.

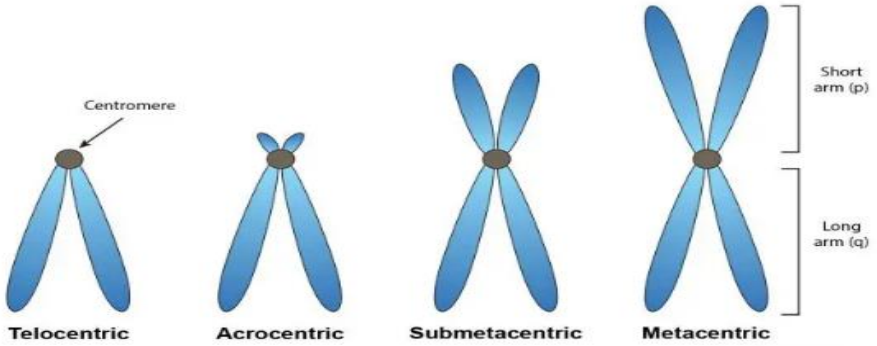
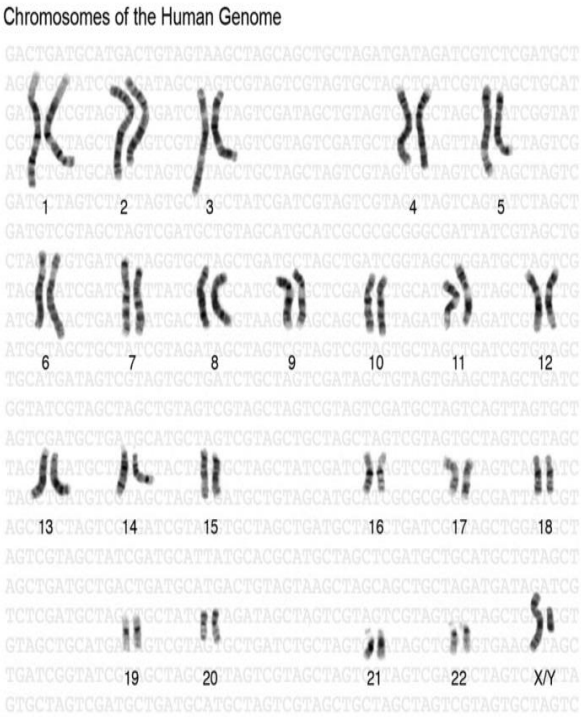


Fig.6. Types of chromosomes

✓ Depending on the type of information, we can find autosomes and sex chromosomes:

a. **Autosomes**: are the chromosomes that contain genes for our general body characteristics, such as eye colour, hair colour, and height. In humans, there are 22 pairs of autosomes, making up 44 of the 46 total chromosomes. Each pair of autosomes in a cell has the same structure and carries the same genes, one from each parent.

b. **Sex chromosomes**: are the chromosomes that determine the sex of an individual. In humans, there is one pair of sex chromosomes, making up the remaining two of the 46 total chromosomes. The two types of sex chromosomes are X and Y. Females have two X chromosomes (XX), while males have one X and one Y chromosome (XY).



3. Cell division and mixing of genetic information

Cell division involve a cell cycle consisting of two major phases; **Interphase**, when the cell is not dividing, and the **mitotic** (M) phase, when the cell is dividing.

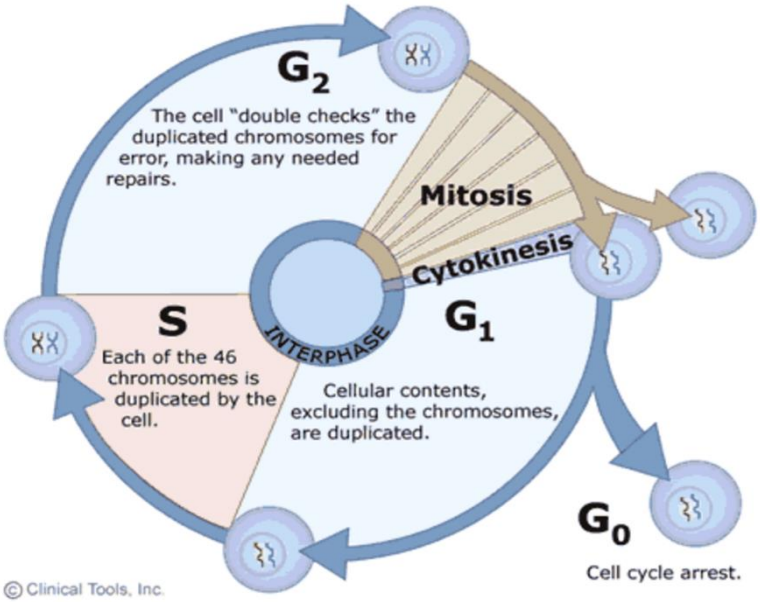


Fig.8. stages of the cell cycle.

3.1. Interphase: During interphase, the cell prepares for division by replicating its DNA and producing additional organelles and cytosolic components. It consists of three stages: **G1** phase, where the cell grows and replicates most organelles; **S** phase, where DNA replication

occurs, doubling the chromosomes; and **G2** phase, where the cell continues to grow, synthesizes proteins, and completes centrosome replication, preparing for mitosis.

3.2.Somatic cell division (Mitosis): The period of the cell cycle in which the cell and contents divide to create two genetically identical daughter cells. This phase is comprised of two distinct stages: **Mitosis (Nuclear division),** and **Cytokinesis (Cytoplasmic division),**

3.2.1. Mitosis: is an organized procession of activity in the cell that allows the replicated chromosomes to be properly divided into two identical cells. Mitosis is a continuous process involving five distinct stages; prophase, prometaphase, metaphase, anaphase and telophase explained in the table below.

3.2.2. Cytokinesis: refers to the division of the cytoplasm and organelles into two identical cells.

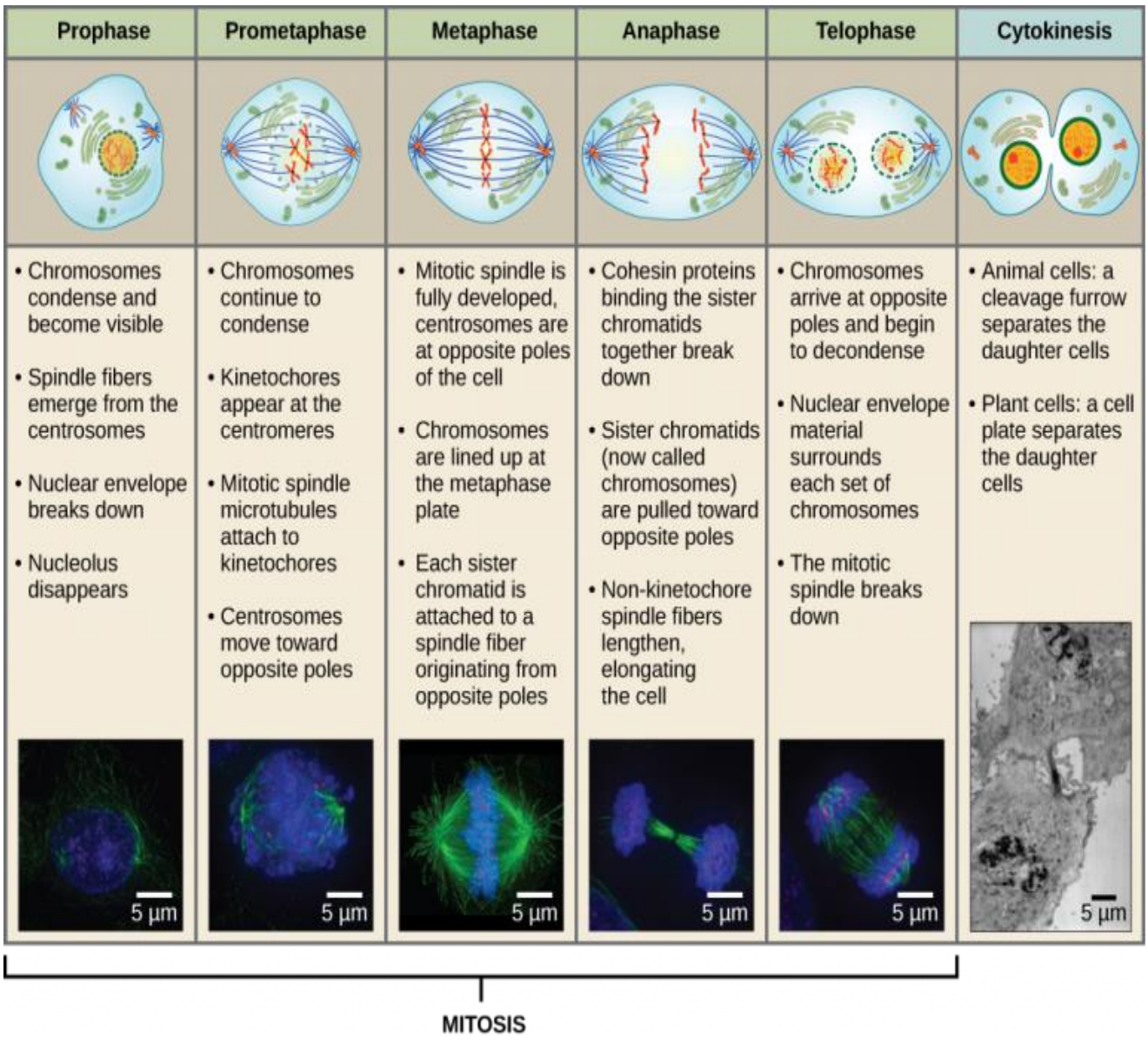


Fig.9. events occurring during mitosis stages.

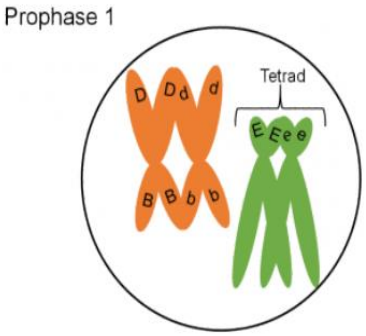
3.3.Meiosis (Gamete formation)

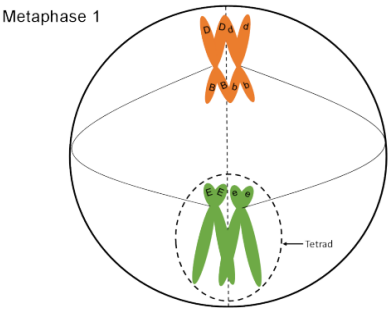
The objective of meiosis is to produce four cells from a single somatic cell. Each of the four resulting cells has half the number of chromosomes, making them **haploid**, while the original somatic cell is **diploid**. In humans, the four **gametes** will each contain 23 chromosomes, meaning the 46 chromosomes in the somatic cell must replicate during interphase, just as they do before mitosis.

Meiosis occurs in specialized cells called **germline cells**. Since meiosis involves two rounds of division, the stages are designated with either a "I" (for the first division) or a "II" (for the second division). Meiosis I reduces the number of chromosome sets from two to one. The genetic information is also mixed during this division to create unique recombinant chromosomes. Meiosis II, in which the second round of meiotic division takes place in a way that is similar to mitosis, includes prophase II, prometaphase II, and so on. Meiosis is preceded by an interphase, consisting of the G1, S, and G2 phases, which are similar to those that occur before mitosis.

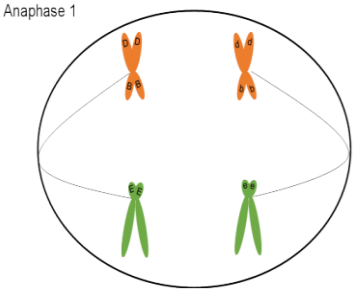
3.3.1. Meiosis I:

- **Prophase I**: This stage initiates meiosis and is similar to prophase of mitosis, the difference is the formation of **tetrads** or **bivalents**, which consist of four chromatids (two sister chromatids of the two homologous chromosomes). Homologous chromosomes pair closely in a process called **synapsis**. During which, **crossing over** occurs, allowing homologous chromosomes to exchange genetic material, leading to the **recombination** of genes that are on the same chromosome.



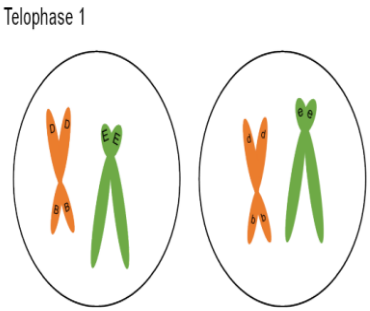


- **Metaphase I**: starts when the tetrads are at the center of the cell. The tetrads have stayed together which insures that during the first division, each cell will get one chromosome from each homologous pair.



- **Anaphase I**: The chromosomes that make up each tetrad separate during anaphase I. However, the sister chromatids will stay connected at the centromere.

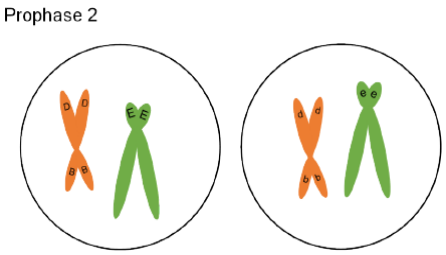
- **Telophase l:** The cell divides into two cells. The bundle of chromosomes may have a nuclear envelope develop around them. The germline cells in some organisms such as human females go through the first four stages of meiosis prior to birth. The germline cells remain at telophase I for some time.



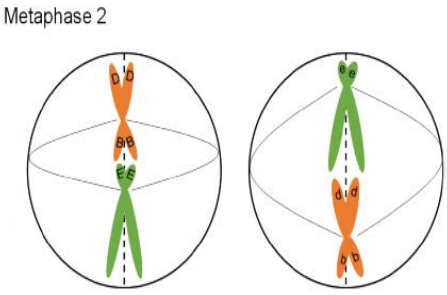
3.3.2. Meiosis II:

The second round of division occurs when the gamete is needed for reproduction. In other situations, telophase I is an abbreviated stage, and the second round of division proceeds immediately.

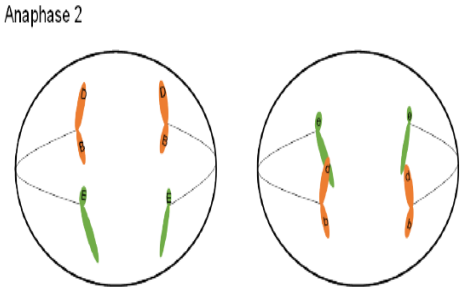
- **Prophase II**: If the chromosomes became dispersed in telophase I, they will condense again at prophase II. The spindle apparatus moves the chromosomes to the middle of the cell.

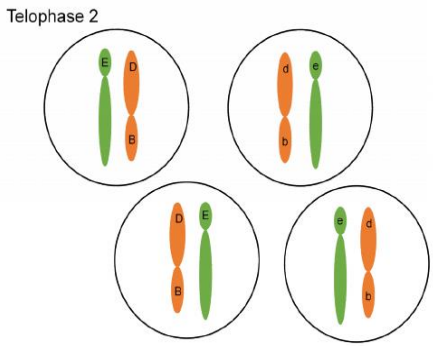


- **Metaphase II**: In metaphase II the chromosomes are aligned at the center of the cell. This time there are not homologous chromosomes to be paired with. This metaphase looks similar to metaphase of mitosis but there is a key difference.



- **Anaphase II**: During anaphase II, the chromatids are pulled apart by the spindle fibers. Now they are classified as chromosomes, not chromatids. The chromosomes move apart to opposite ends of the cell.





- **Telophase II**: In the final stage of meiosis, telophase II, the nucleus forms around the bundle of chromosomes. The cell divides. Now four cells exist that originated from one germline cell. Each cell is a gamete with half the number of chromosomes and genes as a somatic cell.

3.4.Keys differences between Mitosis and meiosis:

Mitosis	Meiosis
Chromosome number stays the same	Chromosome number is halved
One division occurs to make two cells. Four stages of this division.	Two divisions occur to make four cells. Eight stages in these divisions.
Similar or homologous chromosomes do not pair.	Homologous chromosomes pair during prophase l. Pairing is called synapsis.
Crossover exchanges between homologous chromosomes is rare.	Synapsis allows crossing over between homologous chromosomes.
Two cells made are genetically identical.	Four cells made are genetically different.

4. Inter- and interachromosomal mixing.

4.1.Interachromosomal mixing (Crossing over)

During synapsis in anaphase I of meiosis, homologous chromosomes align tightly, and the genes on non-sister chromatids are precisely matched. This alignment allows for the exchange of chromosome segments between non-sister chromatids, a process called **crossing over**, the result is an exchange of genetic material between homologous chromosomes. The chromosomes that have a mixture of maternal and paternal sequence are called **recombinant** and the chromosomes that are completely paternal or maternal are called **non-recombinant**. After the exchange, the sites where this occurs are visible as **chiasmata** (singular: chiasma, a point where two homologous chromatids remain connected after crossing over).

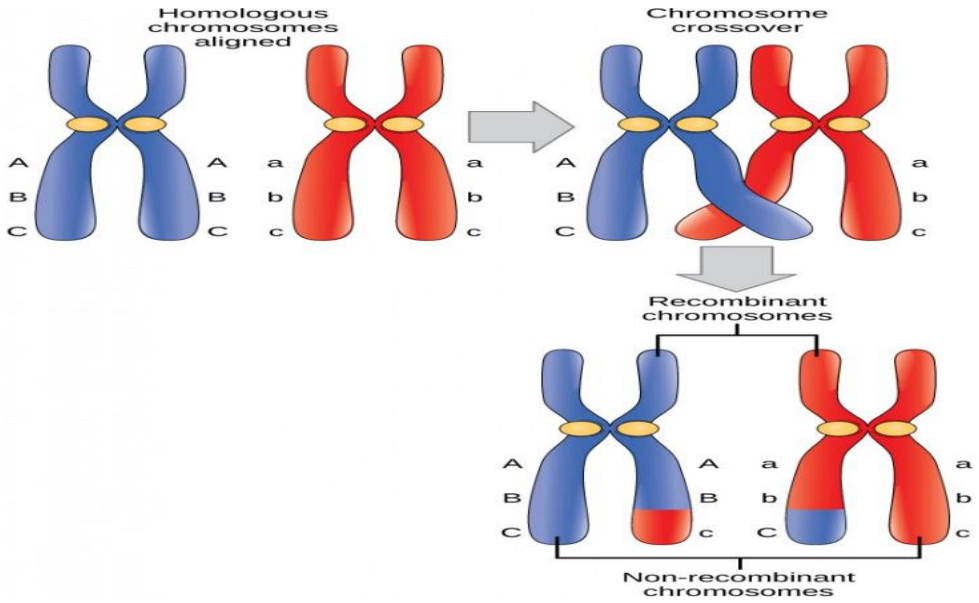


Fig.10. Crossing over between non-sister chromatids of homologous chromosomes.

4.2.Inter-chromosomal mixing of genetic information (Independent assortment of homologous chromosomes during Meiosis)

During metaphase I of meiosis, homologous chromosomes line up randomly in the center of the cell. This randomness, called **independent assortment**, means that each chromosome pair can face either pole of the cell. As a result, the chromosomes inherited from the mother and father are shuffled and separated into different gametes. This process creates a mix of parental genes, leading to genetic variation in the offspring. With 23 chromosome pairs in humans, independent assortment can produce $2^n=2^{23}$ which means over 8 million different combinations, making each gamete genetically unique.

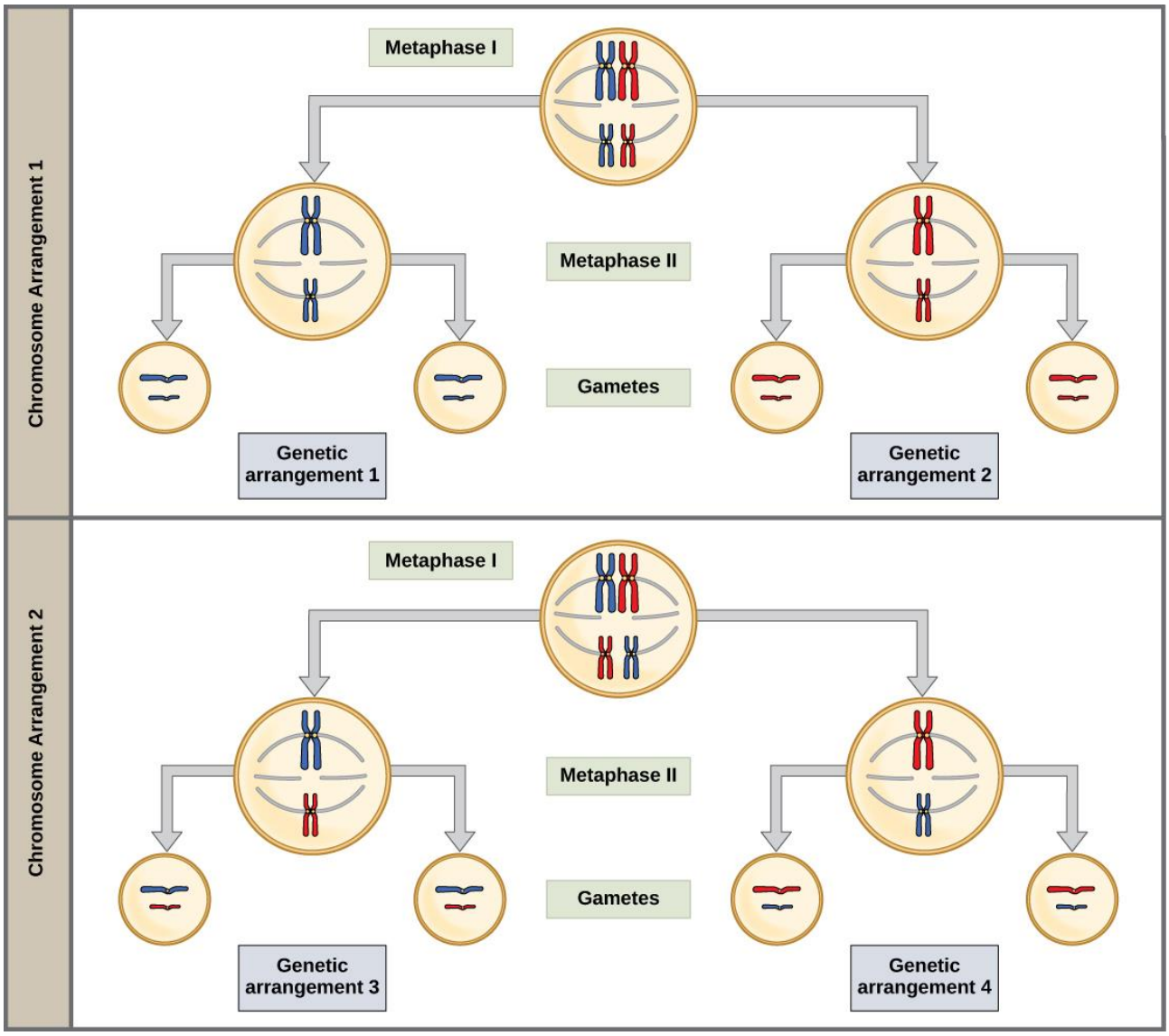


Fig.11. independent assortment at metaphase I for a cell with n = 2 (the number of possible gametes produced is 2^2=4).

5. Chromosomal mutation

5.1.Definition: A chromosome mutation refers to a heritable change in the structure of a chromosome, such as translocations or deletions that can cause alterations in the genetic material. These mutations can lead to various genetic disorders or changes in the chromosome number.

Note: The nature of a mutation can be described by genotype or phenotype. However, only mutations affecting the coding regions of genes can impact the function of the encoded proteins.

5.2.Mutagens :

- **Errors during DNA replication**: Mistakes made when DNA is copied can lead to mutations.
- **Exposure to Radiation**: Ionizing radiation can break DNA strands, leading to structural changes in chromosomes.
- **Chemical Agents**: Certain chemicals can interact with DNA and cause mutations, including some found in the environment.
- **Viral Infections**: Viruses can insert their genetic material into host chromosomes, causing changes.

5.3.Types of mutation:

All mutations fall into two basic categories:

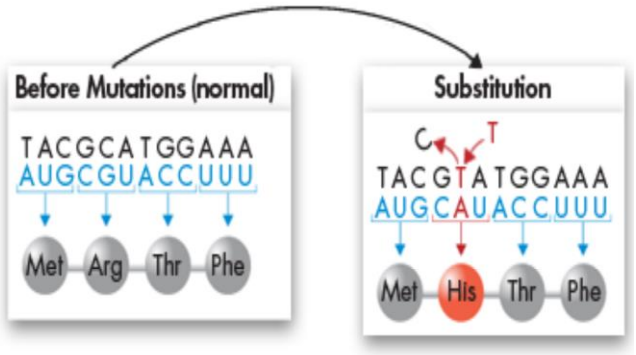
- Those that produce changes in a single gene are known as gene mutations.
- Those that produce changes in whole chromosomes are known as chromosomal mutations.

5.3.1. Gene mutation:

Mutations that involve changes in one or a few nucleotides are known as point mutations because they occur at a single point in the DNA sequence. They generally occur during replication. If a gene in one cell is altered, the alteration can be passed on to every cell that develops from the original one. Point mutations include substitutions, insertions, and deletions.

a. Substitution

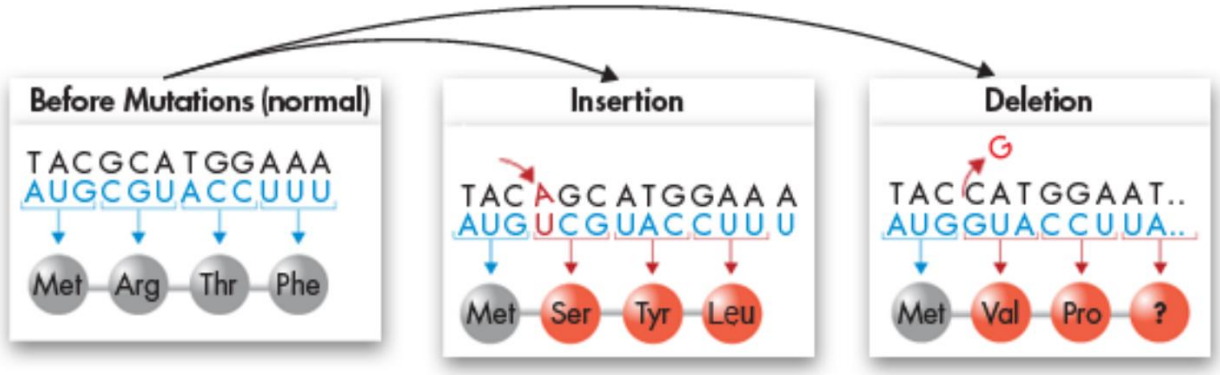
In a substitution, one base is changed to a different base. Substitutions usually affect no more than a single amino acid, and sometimes they have no effect at all.



In this example, the base cytosine is replaced by the base thymine, resulting in a change in the mRNA codon from CGU (arginine) to CAU (histidine). However, a change in the last base of the codon, from CGU to CGA for example, would still specify the amino acid arginine.

b. Insertions and Deletions

Insertions and deletions, also known as frameshift mutations, occur when a single base is added or removed from the DNA sequence. These mutations shift the "reading frame" of the genetic code, altering every codon following the mutation. As a result, frameshift mutations can change all subsequent amino acids, potentially rendering the protein nonfunctional.

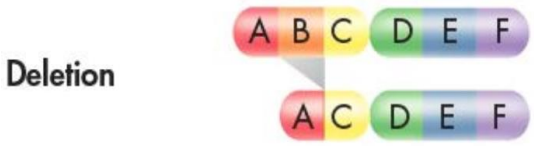


5.3.2. Chromosomal Mutations

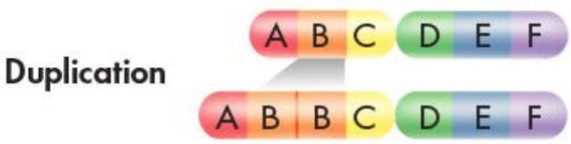
Chromosomal mutations involve changes in the number or structure of chromosomes.

a. Structural mutations: There are four types of chromosomal mutations: deletion, duplication, inversion, and translocation

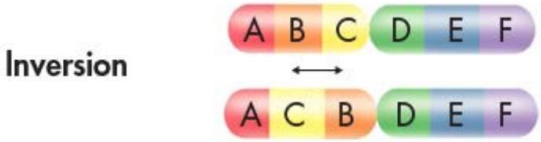
- **Deletion** involves the loss of all or part of a chromosome.



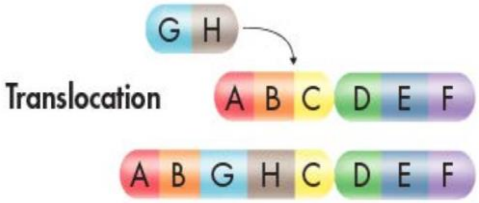
- **Duplication** produces an extra copy of all or part of a chromosome.



- **Inversion** reverses the direction of parts of a chromosome.



- **Translocation** occurs when part of one chromosome breaks off and attaches to another.



b. Mutations inducing a change in chromosomes number

- **Aneuploidy (genome mutation):** This occurs when there is a change in the number of chromosomes that affects only a part of the complete set. In other words, instead of having the usual number of chromosomes, one or a few individual chromosomes are either missing or present in extra copies, but the rest of the chromosome set remains unchanged.
- **Euploidy:** This happens when the entire set of chromosomes is either added or lost. In euploidy, the number of chromosomes changes by complete sets, not just individual chromosomes. When the number of chromosomes increases by whole sets, it is called polyploidy, which means having multiple complete sets of chromosomes (for example, triploidy, where the cell has three sets of chromosomes instead of two).