Chromosomes: Structure and Functions

Chromosomes are composed of a DNA molecule and proteins. During normal cell function, if the DNA were organized into chromosomes, they would look like single-stranded structures. However, during the early stages of cell division when chromosomes become visible, they're made up of two strands, or two DNA molecules, joined together at a constricted area called the *centromere***.** The reason there are two strands is simple: The DNA molecules have *replicated,* and one strand is an exact copy of the other.

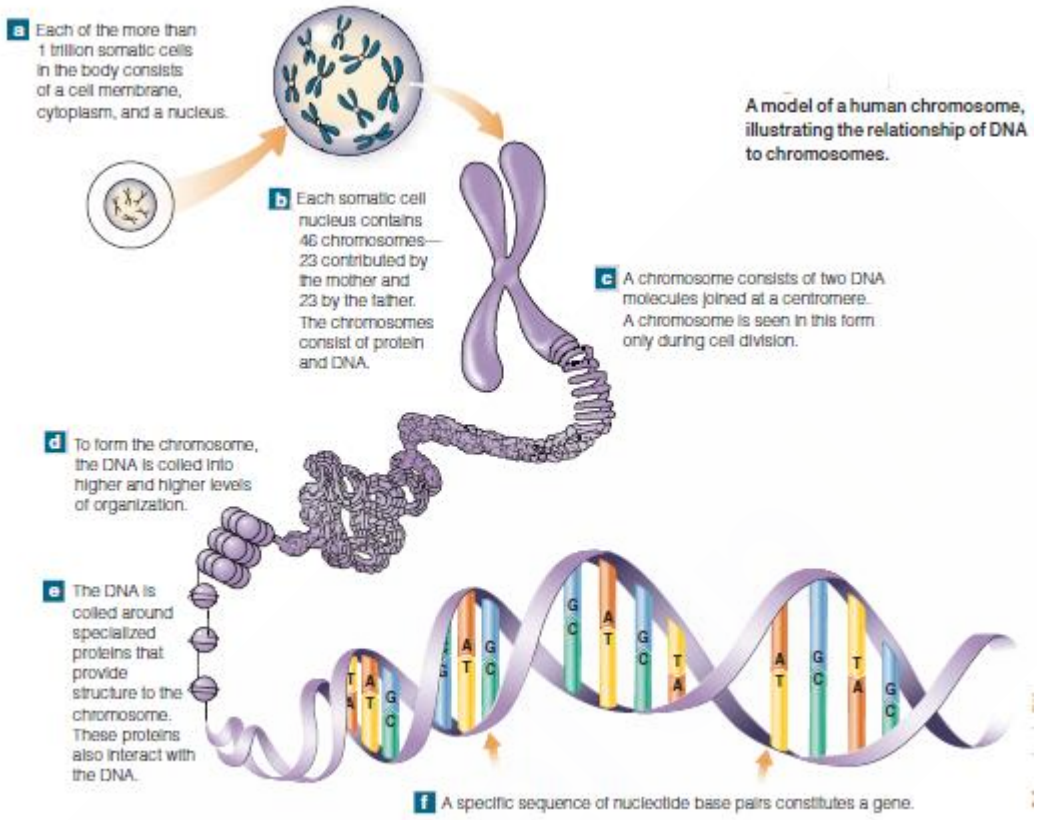
There are two basic types of chromosomes: **autosomes and sex or allosomal chromosomes**. Autosomes carry genetic information that governs all physical characteristics except primary sex determination. In mammals, the two sex chromosomes are the X and Y chromosomes, and the Y chromosome is directly involved in determining maleness. Although the X chromosome is called a "sex chromosome," it actually functions more like an autosome because it's not involved in primary sex determination, and it influences many other traits. Among mammals, all genetically normal females have two X chromosomes (XX), and they're female only because they don't have a Y chromosome. (Female is the default setting.) All genetically normal males have one X and one Y chromosome (XY). In other classes of animals, such as birds or insects, primary sex determination is governed by various other chromosomal mechanisms and factors.

Chromosomes occur in pairs, so all normal human somatic cells have 22 pairs of autosomes and one pair of sex chromosomes (23 pairs in all). Abnormal numbers of autosomes, with few exceptions, are fatal—usually soon after conception. Although abnormal numbers of sex chromosomes aren't usually fatal, they may result in sterility and frequently have other consequences as well. So, to function normally, it's essential for a human cell to possess both members of each chromosomal pair, or a total of 46 chromosomes.
Offspring inherit one member of each chromosomal pair from the father and one member from the mother. Members of chromosomal pairs are alike in size and position of the centromere, and they carry genetic information governing the same traits. But this doesn't mean that partner chromosomes are genetically identical; it just means they influence the same traits.

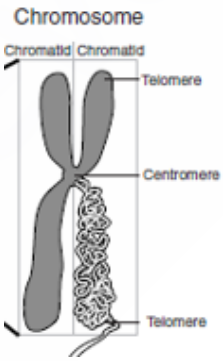
Until 1956, it was thought that the number of chromosomes in man was 48, when it was established that it is 46. Each human cell, except for the gametes, i.e. ovum (egg) and the sperm cells, contains 23 pairs of chromosomes (22 pairs of autosomes and one pair of sex chromosome). Women possess two identical chromosomes called the X chromosomes while men possess one X chromosome and one Y chromosome. The ovum and sperm cells each contain 23 chromosomes (22 autosomes and one X or Y chromosome). The behaviour of chromosomes at somatic cell division in mitosis provides a mechanism that ensures the daughter cells to retain its own complete genetic component. Similarly, their behaviour in the reproductive cells during gametes formation in meiosis enables each mature ovum and sperm to contain a unique single set of parental genes.

Generally, the chromosomes remain unchanged but under certain natural or artificial adverse circumstances certain structural changes may occur in the chromosomes which alter the positions of gene or loss of some genes or changes in chromosomal number. Any alteration in the number of chromosomes or changes in gross structure of chromosome that disrupts this genetic balance generally produces developmental abnormalities with profound phenotypic effects in the form of physical effects and sometimes accompanied by mental imbalances. These structural and numerical alterations which affect the phenotype of the organisms in various degrees are collectively called chromosomal aberrations or anomalies or abnormalities. These accumulated sets of abnormalities so produced are called syndrome. If several specific abnormal traits present in the same individual are transmitted to his offspring as a unit, as theysss often are, it can usually be assumed that they depend jointly on a single gene. In medicine such group of characters is called a syndrome. A well-known example of a syndrome is Marfan's syndrome, or Arachnodactyly (spider-fingeredness), so called

because of the excessive length of the bones of fingers and toes. Though abnormal chromosomes account for at least 50 per cent of spontaneous abortions, only 0.65 per cent of newborns have abnormal chromosomes as most embryos and foetuses with abnormal chromosomes stop developing before birth.



A model of a human chromosome, illustrating the relationship of DNA to chromosomes.



The Groups of Chromosomes

The groups span from A to G (seven classes) in the alphabetical order based on the overall morphology.

Group A (chromosomes 1-3) Large chromosomes with approximately median centromeres.

Group B (chromosomes 4-5) Large chromosomes with sub median centromeres.

Group C (chromosomes 6-12 and the X chromosome) Medium sized chromosomes with sub median centromeres.

Group D (chromosomes 13-15) Medium sized acrocentric chromosomes. Chromosome 13 has a prominent satellite on the short arm. Chromosome 14 has a small satellite on the short arm.

Group E (chromosomes 16-18) Rather short chromosomes with approximately median (in chromosome 16) or sub median centromeres.

Group F (chromosomes 19 and 20) Short chromosomes with approximately median centromeres.

Group G (chromosomes 21, 22 and the Y chromosome) Very short acrocentric chromosomes.

Heterochromatin and Euchromatin

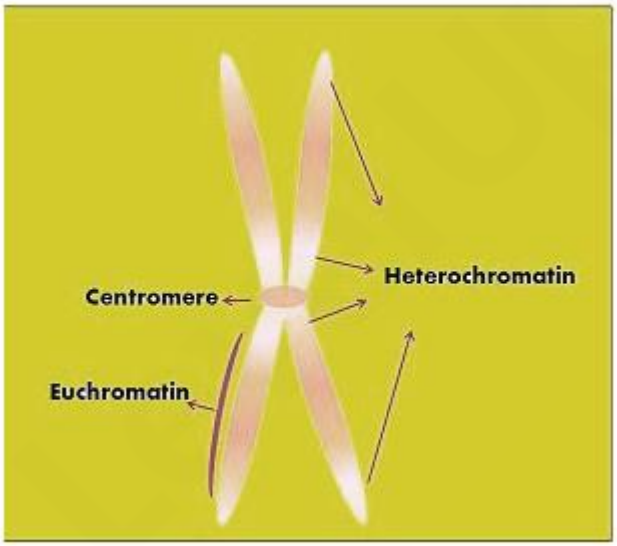
The area of the chromosomes which are **intensely stained** with DNA specific strains and are relatively condensed is known as **heterochromatin**. They are the **tightly packed** form of DNA in the nucleus.

The organization of heterochromatin is so highly compact in the way that these are inaccessible to the protein which is engaged in gene expression. Even the chromosomal crossing over is not possible due to the above reason. Resulting them to be transcriptionally as well as genetically inactive.

Heterochromatin is of two types: Facultative heterochromatin and constitutive heterochromatin. The genes which get silenced through the process of **Histone methylation or siRNA** through **RNAi** are called as **facultative heterochromatin**. Hence they contain inactive genes and is not a permanent character of every nucleus of the cells.

While the **repetitive and structurally functional genes** like telomeres or centromeres are called as **Constitutive heterochromatin**. These are the continuing nature of the cell's nucleus and contains no gene in the genome. This structure is retainable during the interphase of the cell.

The **main function** of the heterochromatin is to protect the DNA from the endonuclease damage; it is due to its compact nature. It also prevents the DNA regions to get accessed to proteins during gene expression.



Definition of Euchromatin

That part of chromosomes, which are **rich in gene** concentrations and are loosely packed form of chromatin is called as **euchromatin**. They are active during transcription. Euchromatin covers the maximum part of the dynamic genome to the inner of the nucleus and is said that euchromatin contains about **90% of the entire human genome**.

To allow the transcription, some parts of the genome containing active genes are loosely packed. The wrapping of DNA is so loose that DNA can become readily available. The structure of euchromatin resembles the nucleosomes, which consist of histones proteins having around 147 base pairs of DNA wrapped around them.

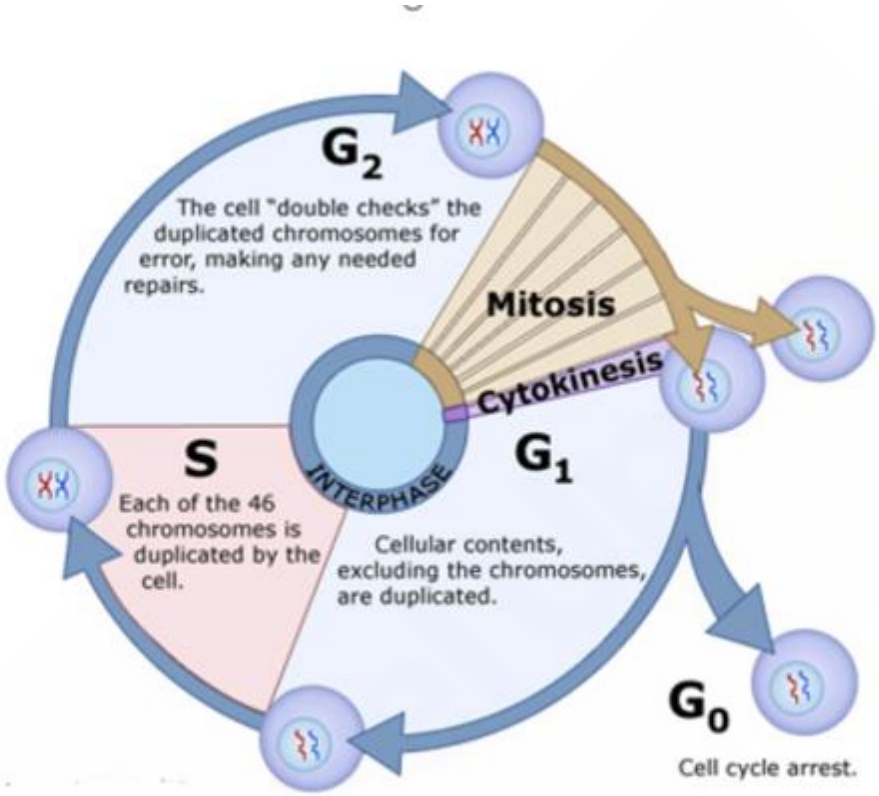
Euchromatin actively participates in transcription from DNA to RNA. The **gene regulating mechanism** is the process of transforming euchromatin into heterochromatin or vice versa. The active genes present in euchromatin gets transcribed to make mRNA whereby further encoding the functional proteins is the **main function** of euchromatin. Hence they are considered as genetically and transcriptionally active. **Housekeeping** genes are one of the forms of euchromatin.

CELL DIVISION IN HUMANS

The Cell Cycle

Living organisms are characterized by two important features, growth and reproduction. Each cell grows to a definite size and then it undergoes self-reproduction to give daughter cells.

There are two phases/periods in the life of a cell. They are N (inter phase or period of non-division) and M (phase or period of division). The longest phase in cell cycle is the inter phase (89 hours). The cycle shows 4 distinct phases.

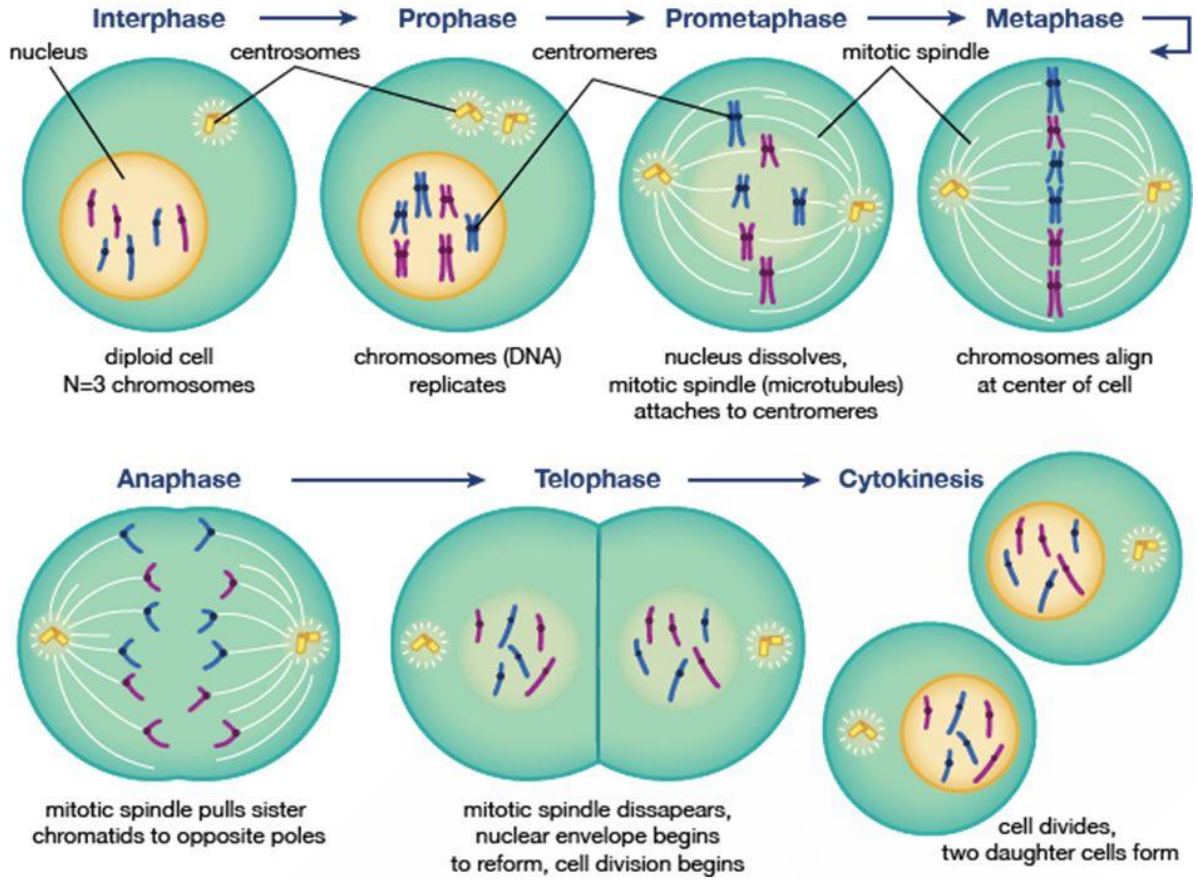


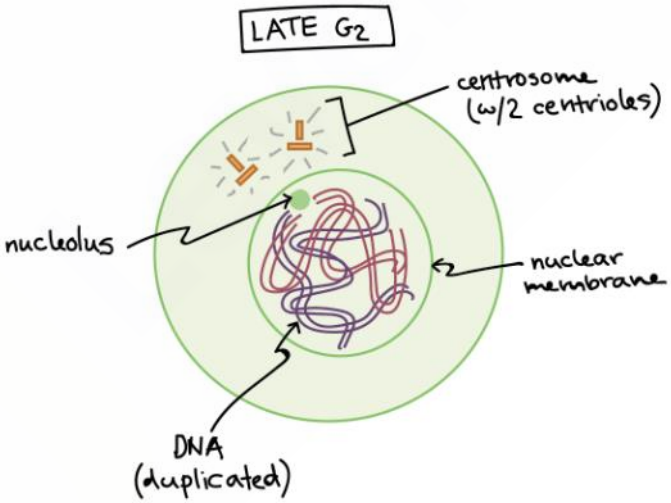
MITOSIS

Mitosis is essentially somatic cell division and was first discovered by Fleming in 1879. It is defined as that cell division which gives rise to two identical daughter cells, each with nucleus containing the same amount of DNA and same genes as the parent cell. Mitosis is necessary for growth and reproduction of all living organisms.

Phases of mitosis

Mitosis consists of four basic phases: prophase, metaphase, anaphase, and telophase. Some textbooks list five, breaking prophase into an early phase (called prophase) and a late phase (called prometaphase). These phases occur in strict sequential order, and cytokinesis - the process of dividing the cell contents to make two new cells - starts in anaphase or telophase.





Let's start by looking at a cell right before it begins mitosis. This cell is in interphase (late G2 phase) and has already copied its DNA, so the chromosomes in the nucleus each consist of two connected copies, called **sister chromatids**. You can't see the chromosomes very clearly at this point, because they are still in their long, stringy, decondensed form.

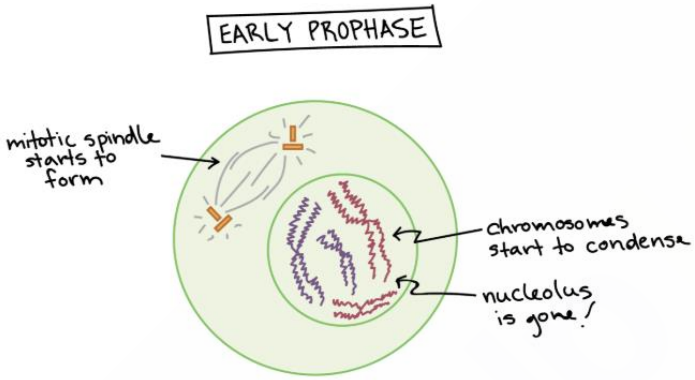
This animal cell has also made a copy of its **centrosome**, an organelle that will play a key role in orchestrating mitosis, so there are two centrosomes. (Plant cells generally don't have centrosomes with centrioles, but have a different type of **microtubule organizing center** that plays a similar role.)

Early Prophase:

In early prophase, the cell starts to break down some structures and build others up, setting the stage for division of the chromosomes. The chromosomes start to condense (making them easier to pull apart later on).

The mitotic spindle begins to form. The spindle is a structure made of microtubules, strong fibers that are part of the cell's "skeleton." Its job is to organize the chromosomes and move them around during mitosis. The spindle grows between the centrosomes as they move apart.

The nucleolus (or nucleoli, plural), a part of the nucleus where ribosomes are made, disappears. This is a sign that the nucleus is getting ready to break down.



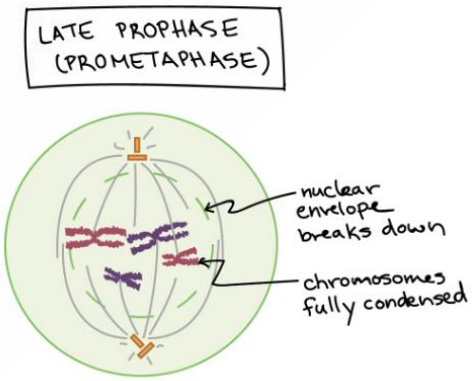
Late Prophase (ProMeta phase)

In late prophase (sometimes also called prometaphase), the mitotic spindle begins to capture and organize the chromosomes.

The chromosomes finish condensing, so they are very compact.

The nuclear envelope breaks down, releasing the chromosomes.

The mitotic spindle grows more, and some of the microtubules start to "capture" chromosomes.

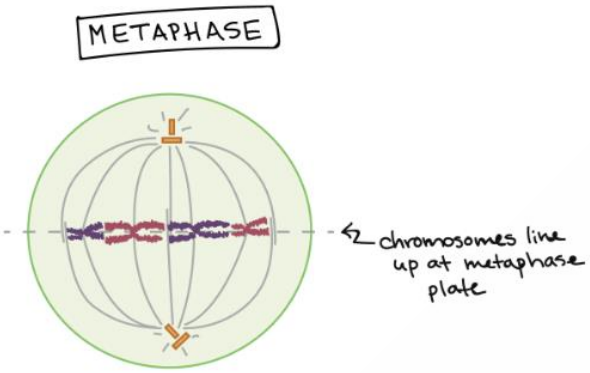


Metaphase

In metaphase, the spindle has captured all the chromosomes and lined them up at the middle of the cell, ready to divide.

All the chromosomes align at the metaphase plate (not a physical structure, just a term for the plane where the chromosomes line up).

At this stage, the two kinetochores of each chromosome should be attached to microtubules from opposite spindle poles.



Before proceeding to anaphase, the cell will check to make sure that all the chromosomes are at the metaphase plate with their kinetochores correctly attached to microtubules. This is called the **spindle checkpoint** and helps ensure that the sister chromatids will split evenly between the two daughter cells when they separate in the next step. If a chromosome is not properly aligned or attached, the cell will halt division until the problem is fixed.

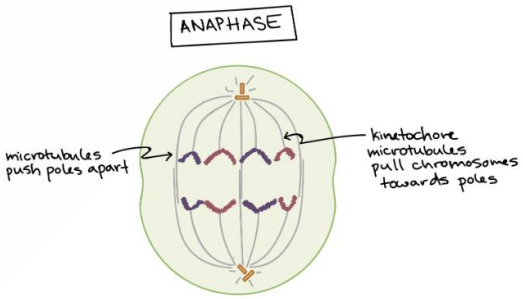
Anaphase

In anaphase, the sister chromatids separate from each other and are pulled towards opposite ends of the cell.

The protein "glue" that holds the sister chromatids together is broken down, allowing them to separate. Each is now its own chromosome. The chromosomes of each pair are pulled towards opposite ends of the cell.

Microtubules not attached to chromosomes elongate and push apart, separating the poles and making the cell longer.

All of these processes are driven by motor proteins, molecular machines that can "walk" along microtubule tracks and carry a cargo. In mitosis, motor proteins carry chromosomes or other microtubules as they walk.

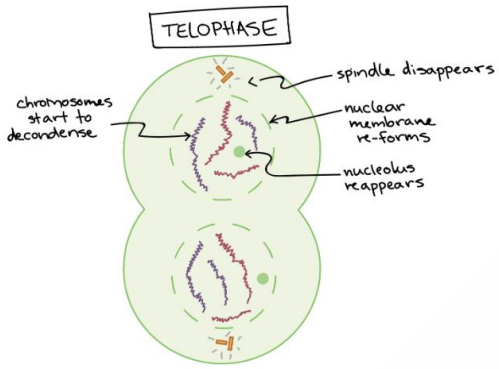


Telophase:
In telophase, the cell is nearly done dividing, and it starts to re-establish its normal structures as cytokinesis (division of the cell contents) takes place.

The mitotic spindle is broken down into its building blocks.

Two new nuclei form, one for each set of chromosomes. Nuclear membranes and nucleoli reappear.

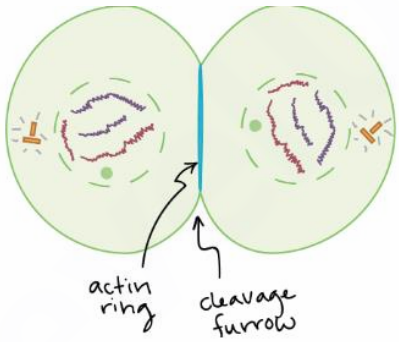
The chromosomes begin to decondense and return to their "stringy" form.



Cytokinesis

Cytokinesis, the division of the cytoplasm to form two new cells, overlaps with the final stages of mitosis. It may start in either anaphase or telophase, depending on the cell, and finishes shortly after telophase.

In animal cells, cytokinesis is contractile, pinching the cell in two like a coin purse with a drawstring. The "drawstring" is a band of filaments made of a protein called actin, and the pinch crease is known as the cleavage furrow.



MEIOSIS

Mitosis is used for almost all of your body's cell division needs. It adds new cells during development and replaces old and worn-out cells throughout your life. The goal of mitosis is to produce daughter cells that are genetically identical to their mothers, with not a single chromosome more or less.

Meiosis, on the other hand, is used for just one purpose in the human body: the production of gametes—sex cells, or sperm and eggs. Its goal is to make daughter cells with exactly half as many chromosomes as the starting cell.

To put that another way, meiosis in humans is a division process that takes us from a diploid cell—one with two sets of chromosomes—to haploid cells—ones with a single set of chromosomes. In humans, the haploid cells made in meiosis are sperm and eggs. When a sperm and an egg join in fertilization, the two haploid sets of chromosomes form a complete diploid set: a new genome.

Phases of meiosis

In many ways, meiosis is a lot like mitosis. The cell goes through similar stages and uses similar strategies to organize and separate chromosomes. In meiosis, however, the cell has a more complex

task. It still needs to separate sister chromatids (the two halves of a duplicated chromosome), as in mitosis. But it must also separate homologous chromosomes, the similar but nonidentical chromosome pairs an organism receives from its two parents.

These goals are accomplished in meiosis using a two-step division process. Homologue pairs separate during a first round of cell division, called meiosis I. Sister chromatids separate during a second round, called meiosis II.

Since cell division occurs twice during meiosis, one starting cell can produce four gametes (eggs or sperm). In each round of division, cells go through four stages: prophase, metaphase, anaphase, and telophase.

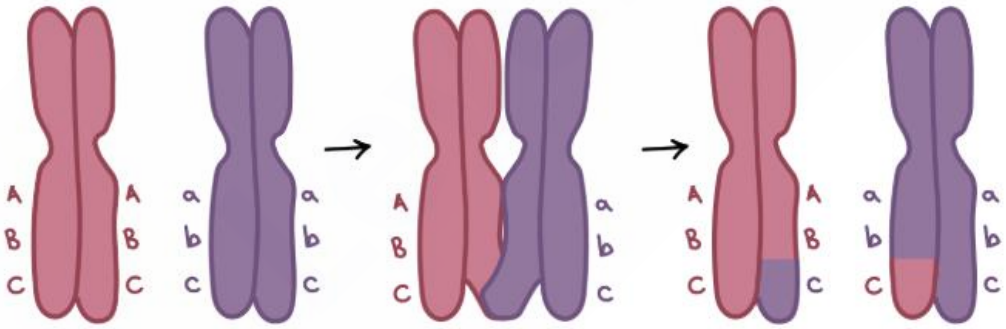
Meiosis I

Before entering meiosis, I, a cell must first go through interphase. As in mitosis, the cell grows during G1 phase, copies all of its chromosomes during S phase, and prepares for division during G2 phase.

Prophase I

During prophase I, differences from mitosis begin to appear. As in mitosis, the chromosomes begin to condense, but in meiosis I, they also pair up. Each chromosome carefully aligns with its homologue partner so that the two match up at corresponding positions along their full length.

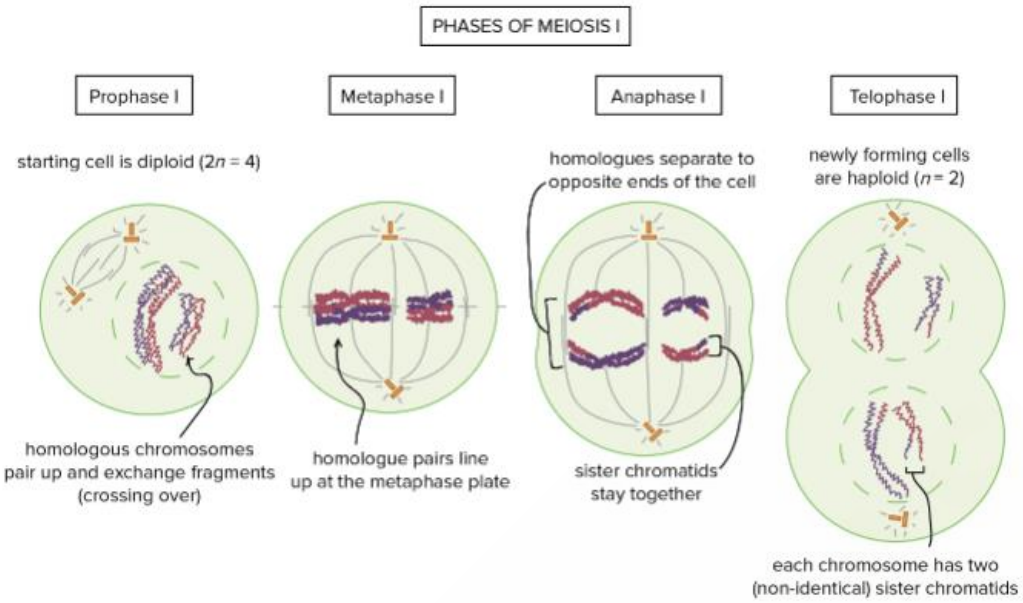
For instance, in the image below, the letters A, B, and C represent genes found at particular spots on the chromosome, with capital and lowercase letters for different forms, or alleles, of each gene. The DNA is broken at the same spot on each homologue—here, between genes B and C—and reconnected in a criss-cross pattern so that the homologues exchange part of their DNA.



This process, in which homologous chromosomes trade parts, is called crossing over. It's helped along by a protein structure called the synaptonemal complex that holds the homologues together. The chromosomes would actually be positioned one on top of the other.

Metaphase I

After crossing over, the spindle begins to capture chromosomes and move them towards the center of the cell (metaphase plate). This may seem familiar from mitosis, but there is a twist. Each chromosome attaches to microtubules from just one pole of the spindle, and the two homologues of a pair bind to microtubules from opposite poles. So, during metaphase I, homologue pairs—not individual chromosomes—line up at the metaphase plate for separation.



Anaphase I

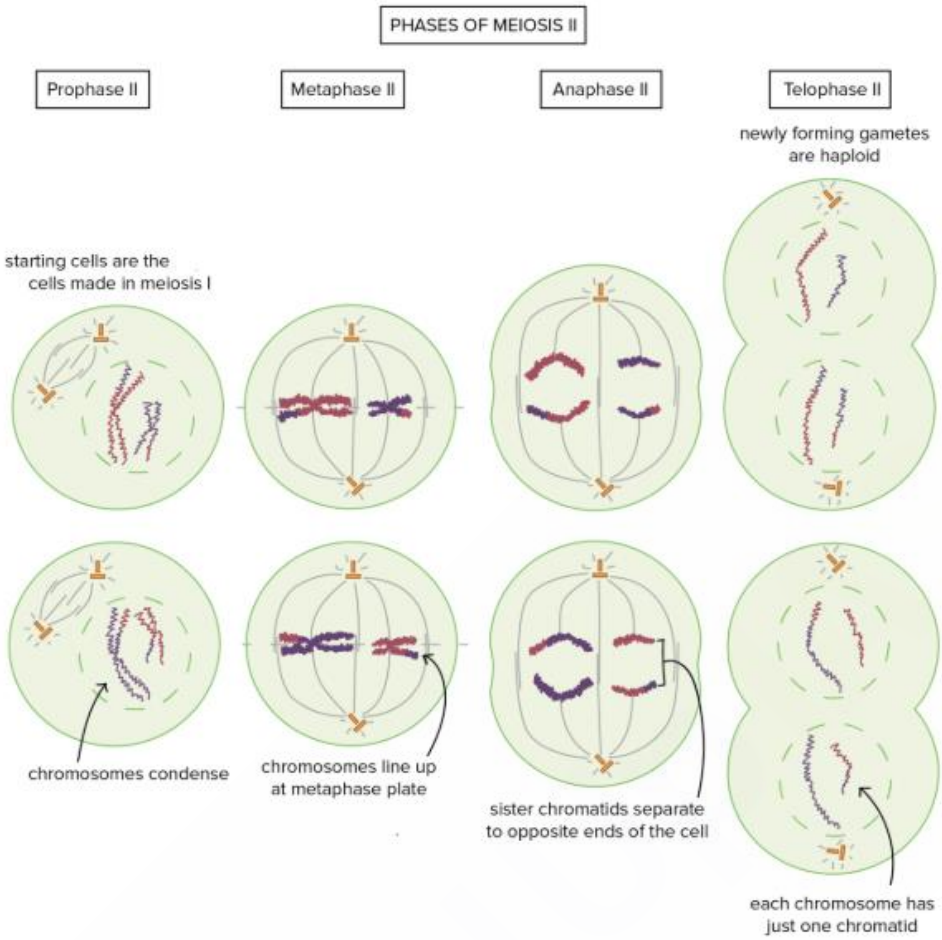
In anaphase I, the homologues are pulled apart and move apart to opposite ends of the cell. The sister chromatids of each chromosome, however, remain attached to one another and don't come apart.

Telophase I

Finally, in telophase I, the chromosomes arrive at opposite poles of the cell. In some organisms, the nuclear membrane re-forms and the chromosomes decondense, although in others, this step is skipped—since cells will soon go through another round of division, meiosis II. Cytokinesis usually occurs at the same time as telophase I, forming two daughter cells.

Meiosis II

Cells move from meiosis I to meiosis II without copying their DNA. Meiosis II is a shorter and simpler process than meiosis I.



Prophase II

During prophase II, chromosomes condense and the nuclear envelope breaks down, if needed. The centrosomes move apart, the spindle forms between them, and the spindle microtubules begin to capture chromosomes.

Metaphase II

The two sister chromatids of each chromosome are captured by microtubules from opposite spindle poles. In metaphase II, the chromosomes line up individually along the metaphase plate.

Anaphase II

In anaphase II, the sister chromatids separate and are pulled towards opposite poles of the cell**.**

Telophase II

In telophase II, nuclear membranes form around each set of chromosomes, and the chromosomes decondense. Cytokinesis splits the chromosome sets into new cells, forming the final products of meiosis: four haploid cells in which each chromosome has just one chromatid. In humans, the products of meiosis are sperm or egg cells.

GENES

Gene is a sequence of DNA bases that specifies the order of amino acids in an entire protein, a portion of a protein, or any functional product, such as RNA. A gene may be composed of thousands of DNA bases. The term gene was introduced by **Johanssen in 1909**. Prior to him Mendel had used the word

factor for a specific, distinct, particulate unit of inheritance that takes part in expression of a trait. **Johanssen has defined gene as an elementary unit of inheritance which can be assigned to a particular trait.**

A gene is:

(i) A unit of genetic material which is able to replicate,

(ii) It is a unit of recombination, i.e., capable of undergoing crossing over,

(iii) A unit of genetic material which can undergo mutation,

(iv) A unit of heredity connected with somatic structure or function that leads to a phenotypic expression.

A **locus** is the specific physical location of a gene or other DNA sequence on a chromosome, like a genetic street address. The plural of locus is "loci".

An **allele** is one of two or more versions of a gene. An individual inherits two alleles for each gene, one from each parent. If the two alleles are the same, the individual is homozygous for that gene. If the alleles are different, the individual is heterozygous.

When the human genome was sequenced in 2001, scientists determined that humans have only about 25,000 genes (International Human Genome Sequencing Consortium, 2001; Venter et al., 2001). This number has now been revised to approximately 21,000 (Pennisi, 2012). Yet we produce as many as 90,000 proteins! Furthermore, protein-coding genes (also called *coding sequences*), the DNA segments that are transcribed into proteins, make up only about 2 to 3 percent of the entire human genome! The rest is composed of noncoding DNA, or what used to be called “junk DNA” (see A Closer Look: Noncoding DNA—Not Junk After All below). Thus gene action is much more complicated than previously believed and it’s impossible for every protein to be coded for by a specific gene.

Geneticists have also learned that only some parts of genes, called exons, are actually transcribed into mRNA and thus code for specific amino acids. In fact, most of the nucleotide sequences in genes are not expressed during protein synthesis. (By *expressed* we mean that the DNA sequence is actually making a product.) Many sequences, called introns, are initially transcribed into mRNA and then clipped. Therefore, introns aren’t translated into amino acid sequences. Moreover, the intron segments that are snipped out of a gene aren’t always the same ones. This means that the exons can be combined in different ways to make segments that code for more than one protein. That’s how 21,000 coding sequences can make 90,000 proteins. Genes can also overlap one another, and there can be genes within genes. But they’re still a part of the DNA molecule, and it’s the combination of introns and exons, interspersed along a DNA strand, that makes up the unit we call a gene.

There are two types of genes. Structural genes and regulatory genes. **In the context of structural genes, it is a type of gene that encodes for any type of RNA (except siRNA and miRNA) and protein that are not regulatory proteins. Regulatory genes are a set of genes that involves the controlling of expression of structural genes.** This is the **key difference** between structural and regulatory genes. **Structural genes** are responsible for body structures, such as hair, blood, and other tissues. **Regulatory genes** turn other genes on and off, an essential activity in growth and development. If the genes that determine bones, for example, did not turn off at a certain point, bones would continue to grow well beyond what would be acceptable for a normal life.

Chickens have the genes for tooth development, but they do not develop teeth because those genes are permanently turned off. Humans have a gene for complete body hair coverage, but that gene is not turned on completely. The human genes for sexual maturity turn on during puberty, somewhat

earlier in girls than in boys. Finally, regulatory genes can lead to either lactose intolerance or lactose persistence in humans. In this instance, the gene that produces lactase—the enzyme for the digestion of milk—is turned off for most human populations around the world following weaning, usually by about age four. However, most humans of northern European and East African descent have inherited a different regulatory gene, which creates lactose persistence. A person who lacks this gene and eats dairy products experiences great gastro intestinal discomfort.

Noncoding DNA—Not Junk After All

In all fields of inquiry, important discoveries always raise new questions that eventually lead to further revelations. There's probably no statement that could be more appropriately applied to the field of genetics. For example, in 1977, geneticists recognized that during protein synthesis, the initially formed mRNA molecule contains many more nucleotides than are represented in the subsequently produced protein. This finding led to the discovery of *introns*, portions of genes that don't code for proteins. In the 1980s, geneticists learned that only about 2 percent of human DNA is contained within exons, the segments that actually provide the code for protein synthesis. We also know that a human gene can specify the production of as many as three different proteins by using different combinations of the exons interspersed within it (Pennisi, 2005).

As discussed earlier, with only 2 percent of the human genome directing protein synthesis, humans have more nonprotein coding DNA than any other species so far studied. Invertebrates and some vertebrates have only small amounts of noncoding sequences, and yet they're fully functional organisms. So just what does all this noncoding DNA (originally called "junk DNA") do in humans? Apparently much of it codes for different forms of RNA that act to regulate gene function, but it does not directly participate in protein synthesis (Pennisi, 2012; the ENCODE Project Consortium, 2012).

Almost half of all human DNA consists of noncoding segments that are repeated over and over and over. Depending on their length, these segments have been referred to as tandem repeats, satellites, or microsatellites, but now they're frequently lumped together and called copy number variants (CNVs). Microsatellites have an extremely high mutation rate and can gain or lose repeated segments and then return to their former length. But this tendency to mutate means that the number of repeats in a given microsatellite varies between individuals. And this tremendous variation has been the basis for DNA fingerprinting, a technique commonly used to provide evidence in criminal cases. Actually, anthropologists are now using microsatellite variation for all kinds of research, from tracing migrations of populations to paternity testing in nonhuman primates.

Some of the variations in microsatellite composition are associated with various disorders, so we can't help wondering why these variations exist. One answer is that some microsatellites influence the activities of protein coding DNA sequences. Also, by losing or adding material, they can alter the sequences of bases in genes, thus becoming a source of mutation in functional genes. And these mutations are a source of genetic variation.

Lastly, there are transposable elements (TEs), the so-called *jumping genes*. These are DNA sequences that can make thousands of copies of themselves, which are then scattered throughout the genome. One family of TEs, called Alu, is found only in primates. About 5 percent of the human genome is made up of Alu sequences, and although most of these are shared with other primates, about 7,000 are unique to humans (Chimpanzee Sequencing and Analysis Consortium, 2005).

TEs mainly code for proteins that enable them to move about, and because they can land right in the middle of coding sequences (exons), TEs cause mutations. Some of these mutations are harmful, and TEs have been associated with numerous disease conditions, including some forms of cancer (Deragon and Capy, 2000). But at the same time, TEs essentially create new exons, thereby generating variations on which natural selection can act. Moreover, they also regulate the activities of many genes, including those involved in development. So rather than being junk, TEs are increasingly being recognized as serving extremely important functions in the evolutionary process, including the introduction of genetic changes that have led to the origin of new lineages.

Structural Genes

A structural gene is a type of gene that codes for a particular protein or RNA. These genes codes for all proteins expect regulatory proteins. Structural gene products contain structural proteins and enzymes. In a typical aspect, these structural genes contain corresponding DNA sequences to a specific sequence of amino acid that results in a protein. Structural genes ensure the produced proteins do not involve in any form of gene regulation.

Regulatory Genes

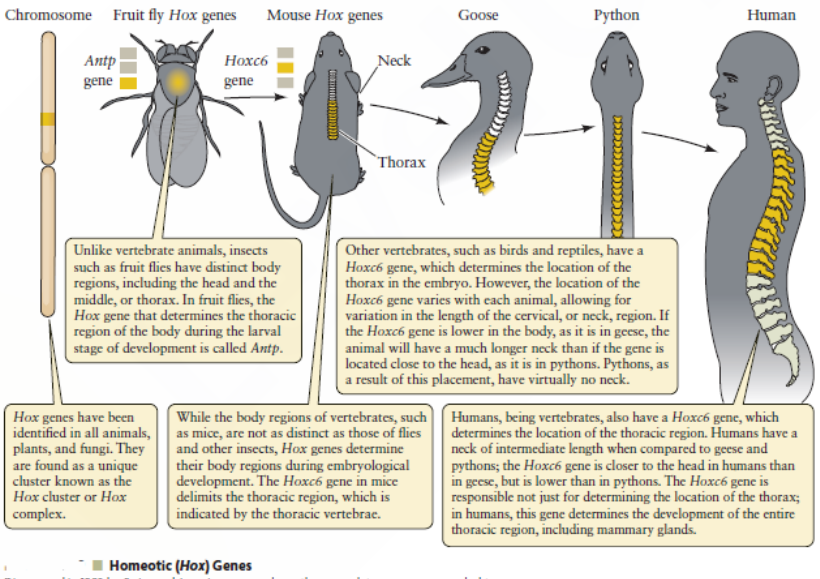
Some genes act solely to control the expression of other genes. Basically these regulatory genes make various kinds of RNA, proteins, and other molecules that switch other DNA segments (genes) on or off. Also, many regulatory genes diminish or enhance the expression of other genes. They play a fundamental role in embryological development, cellular function, and evolution. In fact, without them, life as we know it could not exist. The study of regulatory genes and their role in evolution is still in its infancy; but as information about them continues to accumulate, we will eventually be able to answer many of the questions we still have about the evolution of species.

DNA deactivation during embryonic development is one good example of how regulatory genes work. As you know, all somatic cells contain the same genetic information; but in any given cell, only a

fraction of the DNA is actually involved in protein synthesis. For example, like the cells of the stomach lining, bone cells have DNA that codes for the production of digestive enzymes. But bone cells don't produce digestive enzymes. Instead, they make collagen, the main organic component of bone. This is because cells become specialized during embryonic development to perform only certain functions, and most of their DNA is permanently switched off by regulatory genes.

In other words, they become specific types of cells, such as bone cells. There are thousands of kinds of regulatory genes and one crucially important group is referred to **as homeobox genes**. The best known homeobox genes are **the *Hox* genes**, which direct the early segmentation of embryonic tissues. They also determine the identity of individual segments, by specifying what they will become, such as part of the head or thorax. *Hox* genes interact with other genes to determine the characteristics of developing body segments and structures but not their actual development. For example, they determine where, in a developing embryo, limb buds will appear; and they establish the number and overall pattern of the different types of vertebrae, the bones that make up the spine.

All homeobox genes are highly conserved, meaning that they've been maintained throughout much of evolutionary history. They're present in all invertebrates (such as worms and insects) and vertebrates, and they don't vary greatly from species to species. This type of conservation means not only that these genes are vitally important but also that they evolved from genes that were present in some of the earliest forms of life. Moreover, changes in the behaviour of homeobox genes are responsible for various physical differences between closely related species or different breeds of domesticated animals. For these reasons, homeobox genes, and the many other kinds of regulatory genes, are now a critical area of research in evolutionary and developmental biology.



Homeotic (*Hox*) Genes

Discovered in 1983 by Swiss and American researchers, these regulatory genes are coded to produce proteins that turn on many other genes, in particular those that determine the regions of the body during embryological development. Without these genes, or if there are mutations in these genes, body development may be altered. For example, a mutation in the *Hox* genes of a fruit fly can cause a leg instead of an antenna to grow from the head.

Structural vs Regulatory Genes	
Structural gene is a type of gene that encodes for any type of RNA (except siRNA and miRNA) and protein that are not regulatory proteins.	Regulatory genes are a set of genes that involve the controlling of expression of the structural genes.
Structure	
Structural genes are complex structures.	Regulatory genes are simpler structures.
Function	
Structural genes are encoded for structural proteins and enzymes.	Regulatory genes regulate the transcription of structural genes.

Mutations

DNA mutations happen when there are changes in the nucleotide sequence that makes up the strand of DNA. This can be caused by random mistakes in DNA replication or even an environmental influence like UV rays or chemicals. The changes at the nucleotide level then influence the transcription and translation from gene to protein expression. Changing even just one nitrogen base in a sequence can change the amino acid that is expressed by that DNA codon which can lead to a completely different protein being expressed. These mutations range from being non-harmful all the way up to causing death.

Types of Mutations:

Mutations in the structure of genes can be classified as **Small-scale Mutations** and **Large Scale Mutations**.

i) Small Scale Mutations

Small-scale mutations are types of gene mutations, such as those affecting a small gene in one or a few nucleotides.

Small scale mutations are of 2 types:

a) Point Mutations

b) Frameshift Mutations

a) Point Mutations

It occurs as a **result of replacement** of one nucleotide by other in specific nucleotide sequence of gene. Point mutation brings little phenotypic change as compared to frameshift mutation.

Missense mutations: This point mutation results in the replacement of one nucleotide by another. In some cases, this change causes a change in the amino acid encoded, which may or may not have an impact on the function of the protein produced by the gene in the case of a gene encoding, or the affinity for a transcription factor, in the case of a promoter region of the DNA. We speak of mutation **transition when there is a substitution of a purine base to another base purine** (or pyrimidine base to another pyrimidine base). In contrast, a mutation **transversion is a mutation caused by the replacement of a purine by a pyrimidine base** (or pyrimidine base by a purine base).

Nonsense mutation: Change of a nucleotide causes the replacement of a codon specifying an amino acid by a stop codon. This results in the production of a truncated protein.

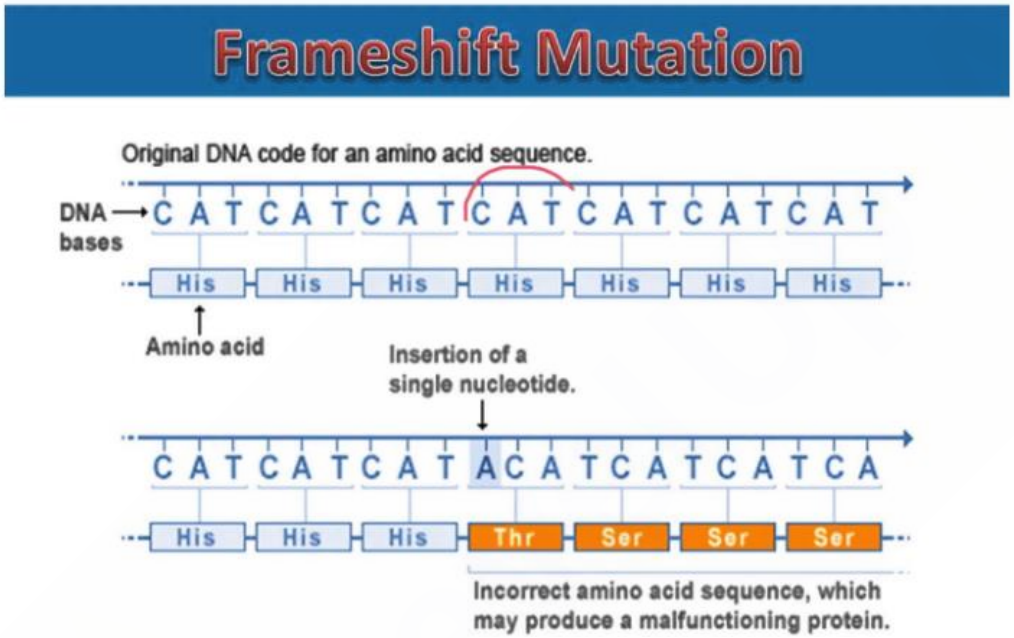
Silent mutations: These are mutations that do not alter the sequence of a protein because of the redundancy of the genetic code (the new triplet codes for the same amino acid as the original triplet), or because it affects an area not coding DNA or an intron.

b) Frameshift Mutations

It occurs as a result **of addition or deletion of nucleotide in the sequence of DNA**. Addition or deletion of nucleotide causes shift of the reading frame of mRNA.

Insertions add one or more extra nucleotides into the DNA. They are usually caused by transposable elements, or errors during replication of repeating elements (e.g., AT repeats). Insertions in the coding region of a gene may alter splicing of the mRNA (splice site mutation), or cause a shift in the reading frame (frameshift mutation), both of which can significantly alter the gene product

Deletions mean removing one or more nucleotides from the DNA. Like insertions, these mutations can alter the reading frame of the gene. In general, they are irreversible: Though exactly the same sequence might, in theory, be restored by an insertion, transposable elements able to revert a very short deletion (say 1–2 bases) in any location either are highly unlikely to exist or do not exist at all.



Large Scale Mutations

This concerns a large number of nucleotides in the DNA such that the mutation is observable when making a karyotype: duplication, translocation, inversion, deletion, insertion. It can be a loss or gain of chromosomes: Trisomy, monosomy, aneuploidy.

Causes of Gene Mutation

Gene mutations are most commonly caused as a result of two types of occurrences. Environmental factors such as chemicals, radiation, and ultraviolet light from the sun can cause mutations. These mutagens alter DNA by changing nucleotide bases and can even change the shape of DNA. These changes result in errors in DNA replication and transcription.

Other mutations are caused by errors made during mitosis and meiosis. Common errors that occur during cell division can result in point mutations and frameshift mutations. Mutations during cell division can lead to replication errors which can result in the deletion of genes, translocation of portions of chromosomes, missing chromosomes, and extra copies of chromosomes.

Mutagenesis and Mutagens

Mutagenesis is the process of inducing mutation by a number of physical, chemical or biological agents. The agents that causes mutation are called as **mutagens.** Mutation induced by mutagens is

called induced mutation. Sometime mutation occurs spontaneously due to error during DNA replication. However, mutagens increase the chances of mutation.

There are three types of mutagens.

- Physical mutagens
- Chemical mutagens
- Biological mutagens

Physical mutagens:

i) Physical mutagens are X-rays and UV light.

ii) X-rays, gamma rays, cosmic rays are ionizing radiation which ionizes water of the cell to release hydroxyl free radical (OH). The hydroxyl radical is a powerful oxidizing agent. Hydroxyl radical oxidises the phosphodiester bond of DNA. Higher dose of X-rays can even cause death of an organism.

iii) UV light is a non-ionizing radiation. It causes the formation of thymine dimer (Pyrimedine dimer). If two thymine occur together in one strand of DNA, UV light causes fusion to form thymine dimer. Nitrogenous bases absorb UV lights and the absorption is maximum at 260 nm. At the site of thymine dimer confirmation of DNA is changed, so rate of error during DNA replication is high.

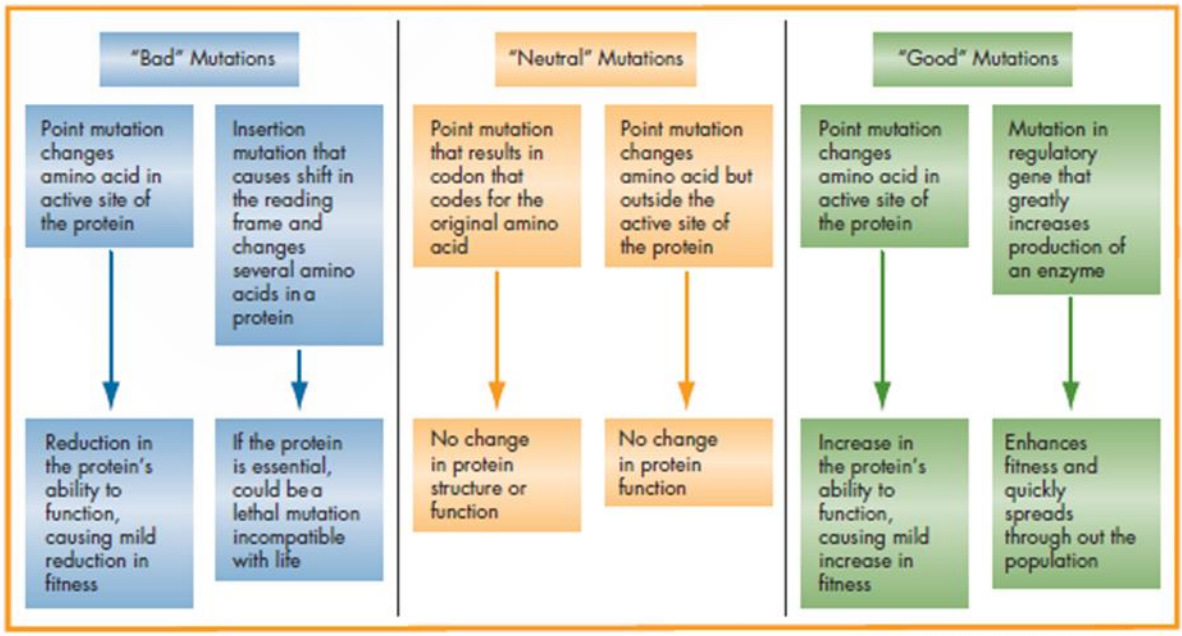
Chemical mutagens:

Three types of chemical mutagens are found.

i) Intercalating agent: The chemical intercalate or slip in between two base pair in Double stranded DNA helix and hence alter the morphology of DNA at that position. Chances of error during replication is higher at this position causing mutation. Examples; Acridine orange, ethidium bromide, proflavin

ii) Base analogue: These chemical are morphologically similar to that of normal nitrogen bases. So during replication these molecules are incorporated instead of normal nitrogen bases and hence causes mutation. Example; 2-aminopurine is analogue to Adenine, 5-bromourcail is analogue to thymine

iii) Reacting chemicals: These chemical mutagens react directly with the nitrogenous bases of DNA and chemically modify the DNA causing mutation. Example; Nitrous acid react with nitrogenous bases and remove amino group from purine and pyrimidine.



"Bad," "neutral," and "good" mutations.