B.Sc 1st Semester(Zoology Major)
Salbari College, Baksa(BTR)
Cell Cycle and Cell division

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Introduction :

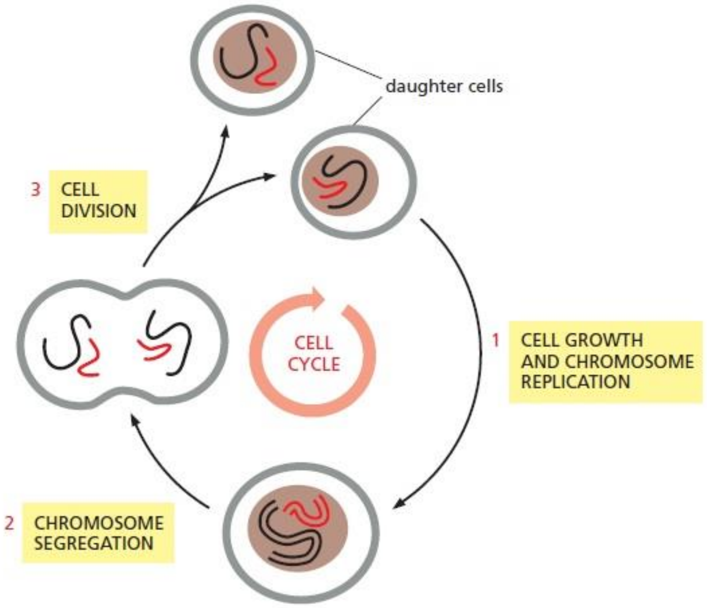
The only way to make a new cell is to duplicate a cell that already exists. This simple fact, first established in the middle of the nineteenth century, carries with it a profound message for the continuity of life. All living organisms, from the unicellular bacterium to the multicellular mammal, are products of repeated rounds of cell growth and division extending back in time to the beginnings of life on Earth over three billion years ago.

A cell reproduces by performing an orderly sequence of events in which it duplicates its contents and then divides in two. This cycle of duplication and division, known as the *cell cycle*, is the essential mechanism by which all living things reproduce. In unicellular species, such as bacteria and yeasts, each cell division produces a complete new organism. In multicellular species, long and complex sequences of cell divisions are required to produce a functioning organism. Even in the adult body, cell division is usually needed to replace cells that die. In fact, each of us must manufacture many millions of cells every second simply to survive: if all cell division were stopped—by exposure to a very large dose of x-rays, for example—we would die within a few days.

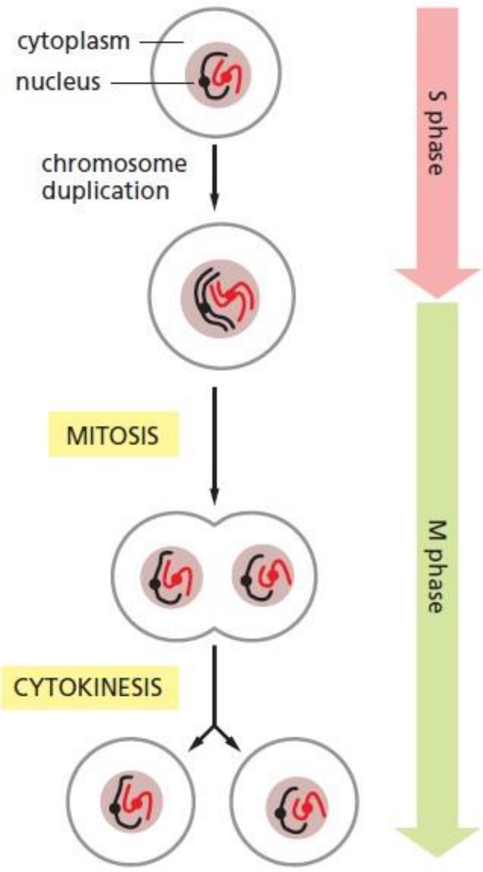
The details of the cell cycle vary from organism to organism and at different times in an organism's life. Certain characteristics, however, are universal. At a minimum, the cell must accomplish its most fundamental task: **the passing on of its genetic information to the next generation of cells**. To produce two genetically identical daughter cells, the DNA in each chromosome must first be faithfully replicated to produce two complete copies. The replicated chromosomes must then be accurately distributed (*segregated*) to the two daughter cells, so that each receives a copy of the entire genome. In addition to duplicating their genome, most cells also duplicate their other organelles and macromolecules; otherwise, daughter cells would get smaller with each division. To maintain their size, dividing cells must coordinate their growth (that is, their increase in cell mass) with their division.

Overview of Cell cycle :

The most basic function of the cell cycle is to duplicate the vast amount of DNA in the chromosomes and then segregate the copies into two genetically identical daughter cells. These processes define the two major phases of the cell cycle. **Chromosome duplication occurs during *S phase*** (S for DNA *s*ynthesis), which requires 10–12 hours and occupies about half of the cell-cycle time in a typical mammalian cell. After S phase, **chromosome segregation and cell division occur in *M phase*** (M for *m*itosis), which requires much less time (less than an hour in a mammalian cell). M phase comprises two major events: **nuclear division, or *mitosis***, during which the copied chromosomes are distributed into a pair of daughter nuclei; and **cytoplasmic division, or *cytokinesis***, when the cell itself divides in two.



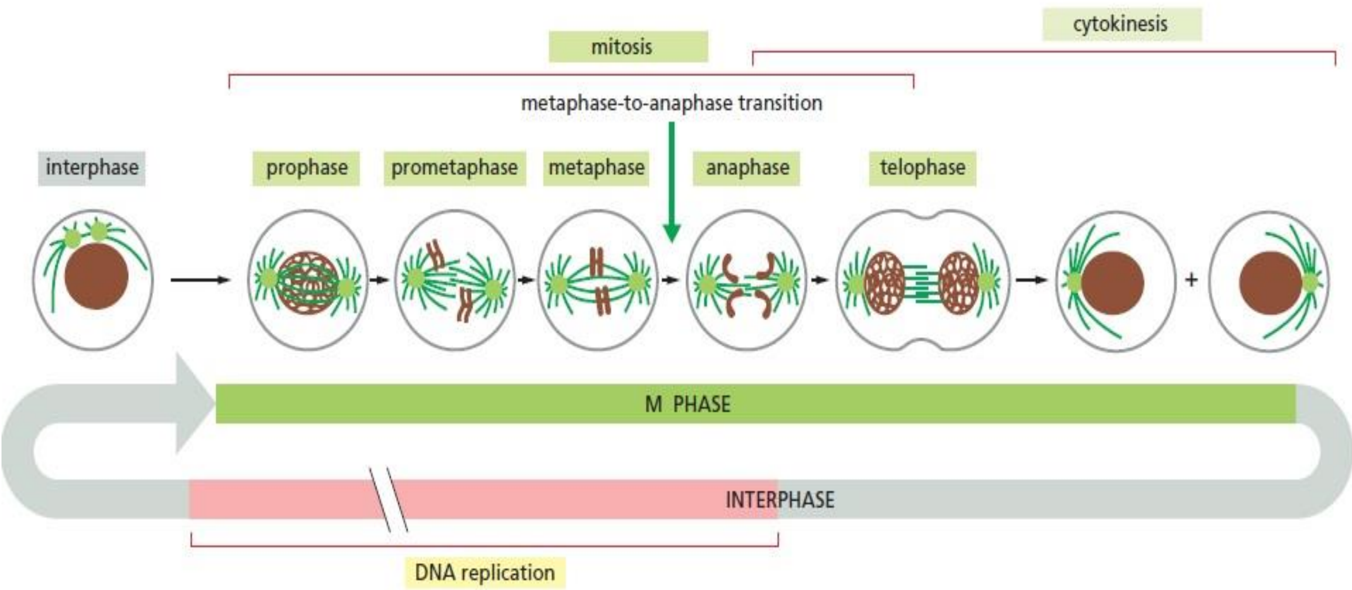
The cell cycle : The division of a hypothetical eukaryotic cell with two chromosomes (one *red*, and one *black*) is shown to illustrate how two genetically identical daughter cells are produced in each cycle. Each of the daughter cells will often continue to divide by going through additional cell cycles.



The major events of the cell cycle: The major chromosomal events of the cell cycle occur in S phase, when the chromosomes are duplicated, and M phase, when the duplicated chromosomes are segregated into a pair of daughter nuclei (in mitosis), after which the cell itself divides into two (cytokinesis).

The Eukayotic Cell Cycle usually consists of four phases :

Most cells require much more time to grow and double their mass of proteins and organelles than they require to duplicate their chromosomes and divide. Partly to allow time for growth, most cell cycles have ***gap phases*—a G1** phase between M phase and S phase and a **G2 phase** between S phase and mitosis. Thus, the eukaryotic cell cycle is traditionally divided into four sequential phases: **G1, S, G2, and M**. **G1, S, and G2 together are called interphase**. In a typical human cell proliferating in culture, interphase might occupy 23 hours of a 24-hour cycle, with 1 hour for M phase. Cell growth occurs throughout the cell cycle, except during mitosis. The two gap phases are more than simple time delays to allow cell growth. They also provide time for the cell to monitor the internal and external environment to ensure that conditions are suitable and preparations are complete before the cell commits itself to the major events of S phase and mitosis. The G1 phase is especially important in this respect. Its length can vary greatly depending on external conditions and extracellular signals from other cells. If extracellular conditions are unfavorable, for example, cells delay progress through G1 and may even enter a specialized resting state known as G_0 (G zero), in which they can remain for days, weeks, or even years before resuming proliferation. Indeed, many cells remain permanently in G_0 until they or the organism dies.



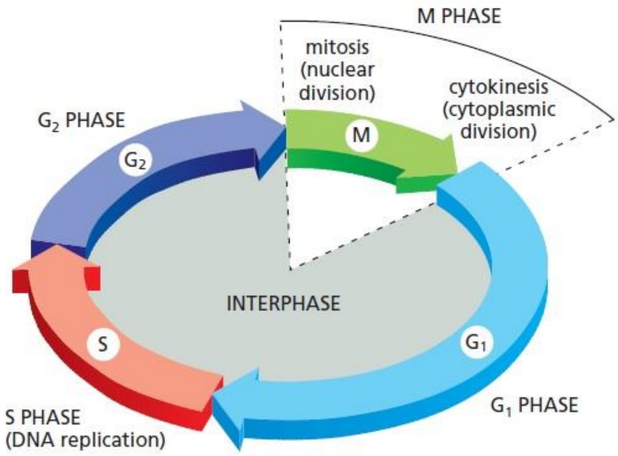
General Events of Interphase :

The interphase is characterized by the following features :
The nuclear envelop remains intact .The chromosomes occur in the form of diffused, long, coiled and indistinctly visible chromatin fibres. The DNA amount becomes double. Due to accumulation of ribosomal RNA and ribosomal proteins in the nucleolus, its size greatly increases. In animal cells , a daughter pair of centrioles originates near the already existing centriole and , thus , an interphase cell has two pairs of centrioles.

G1 Phase : After the M phase of previous cell cycle, the daughter cells begin G1 of interphase of new cell cycle. G1 is a resting phase. It is called first gap phase, since no DNA synthesis takes place during this stage; currently, G1 is also called first growth phase, since it involves synthesis of RNA. proteins and membranes which leads to the growth of nucleus and cytoplasm of each daughter cell towards their mature size.

S Phase : During the S phase or synthetic phase of interphase, replication of DNA and synthesis of histone proteins occur. New histones are required in massive amounts immediately at the beginning of the S period of DNA synthesis to provide the new DNA with nucleosomes. Thus, at the end of S phase, each chromosome has two DNA molecules and a duplicate set of genes.

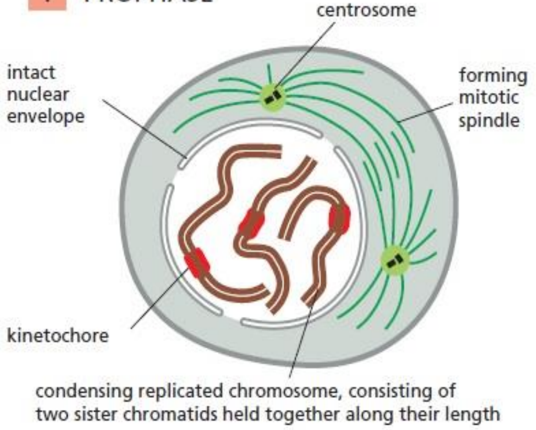
G2 Phase : This is a second gap or growth phase or resting phase of interphase. During G_2 phase, synthesis of RNA and proteins continues which is required for cell growth. It may occupy 10 to 20 per cent time of cell cycle. As the G2 phase draws to a close, the cell enters the M phase.



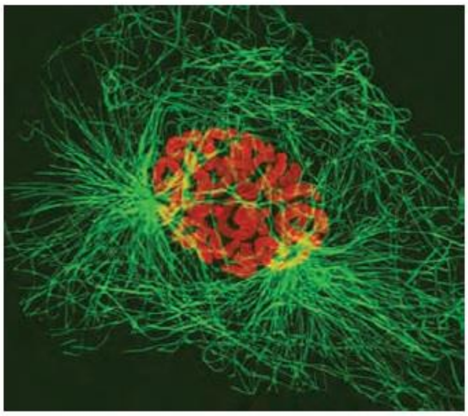
Mitosis:

Following the completion of S phase and transition through G2, the cell undergoes the dramatic upheaval of M phase. This begins with mitosis, during which the sister chromatids are separated and distributed (*segregated*) to a pair of identical daughter nuclei, each with its own copy of the genome. Mitosis is also called **equational cell division** because the chromosome number is maintained after each round of mitotic division. The mitosis occurs in the somatic cells and is meant for the multiplication of cell number during embryogenesis and blastogenesis of plants and animals . Fundamentally, it remains related with the growth of an individual from zygote to adult stage. Mitosis is traditionally divided into five stages—***prophase*, *prometaphase*, *metaphase*, *anaphase*, and *telophase***—defined primarily on the basis of chromosome behavior as seen in a microscope. As mitosis is completed, the second major event of M phase—**cytokinesis**— divides the cell into two halves, each with an identical nucleus.

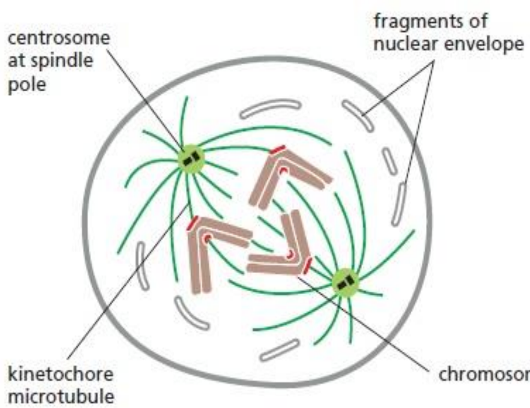
1 PROPHASE



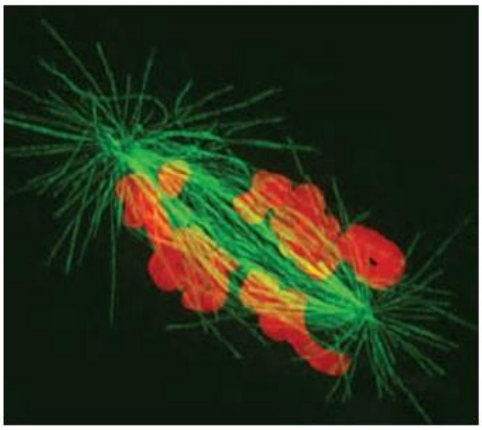
At prophase, the replicated chromosomes, each consisting of two closely associated sister chromatids, condense. Outside the nucleus, the mitotic spindle assembles between the two centrosomes, which have replicated and moved apart. For simplicity, only three chromosomes are shown. In diploid cells, there would be two copies of each chromosome present. In the fluorescence micrograph, chromosomes are stained *orange* and microtubules are *green*.



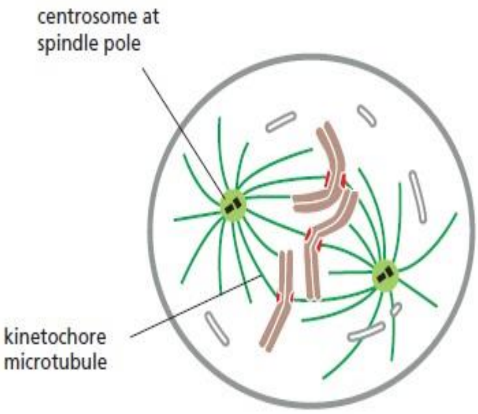
2 PROMETAPHASE



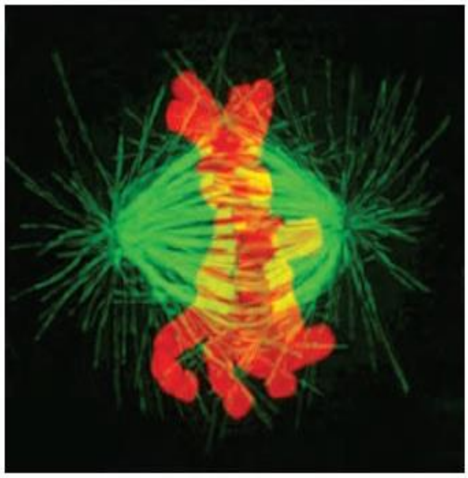
Prometaphase starts abruptly with the breakdown of the nuclear envelope. Chromosomes can now attach to spindle microtubules via their kinetochores and undergo active movement.



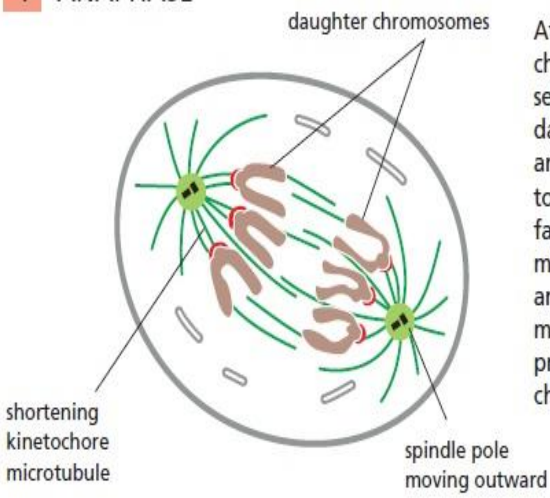
3 METAPHASE



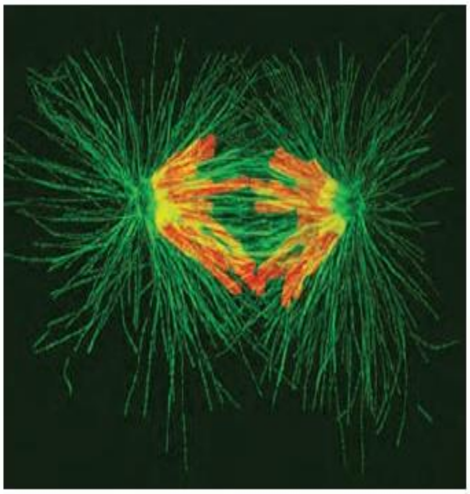
At metaphase, the chromosomes are aligned at the equator of the spindle, midway between the spindle poles. The kinetochore microtubules attach sister chromatids to opposite poles of the spindle.



4 ANAPHASE



At anaphase, the sister chromatids synchronously separate to form two daughter chromosomes, and each is pulled slowly toward the spindle pole it faces. The kinetochore microtubules get shorter, and the spindle poles also move apart; both processes contribute to chromosome segregation.



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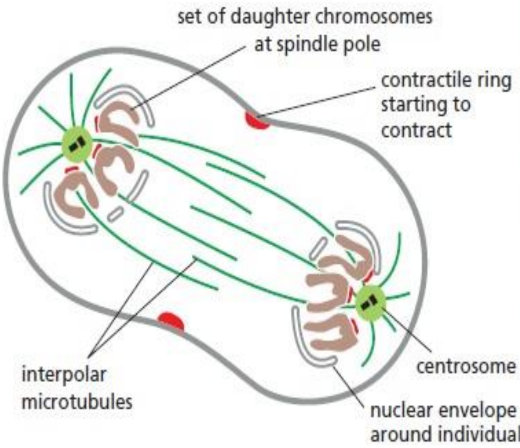
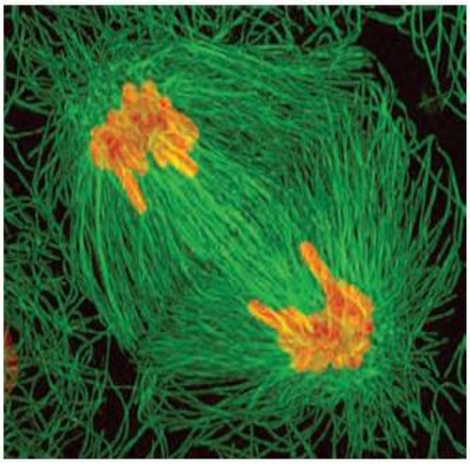
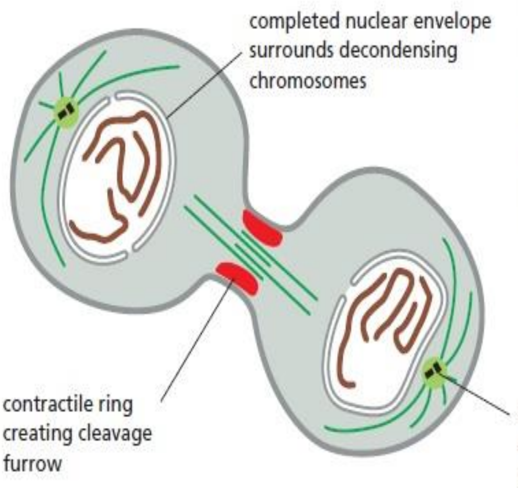
5 TELOPHASE



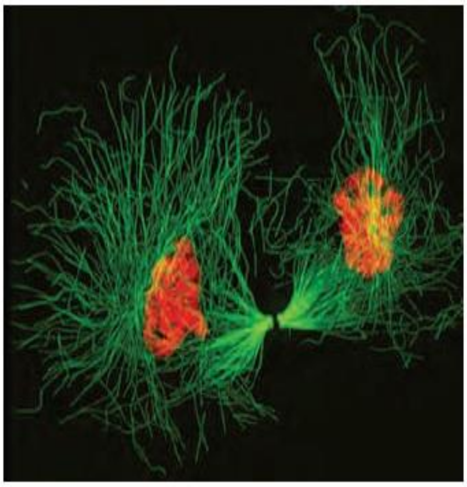
During telophase, the two sets of daughter chromosomes arrive at the poles of the spindle and decondense. A new nuclear envelope reassembles around each set, completing the formation of two nuclei and marking the end of mitosis. The division of the cytoplasm begins with contraction of the contractile ring.



6 CYTOKINESIS



During cytokinesis, the cytoplasm is divided in two by a contractile ring of actin and myosin filaments, which pinches the cell in two to create two daughters, each with one nucleus.



(Micrographs courtesy of Julie Canman and Ted Salmon.)

Meiosis :

Most eukaryotic organisms reproduce sexually: the genomes of two parents mix to generate offspring that are genetically distinct from either parent. The cells of these organisms are generally *diploid*: that is, they contain two slightly different copies, or *homologs*, of each chromosome, one from each parent. Sexual reproduction depends on a specialized nuclear division process called ***meiosis***, which produces *haploid* cells carrying only a single copy of each chromosome. Hence, meiosis is also called **reductional cell division** because chromosome number gets halved after completion of a meiotic division. In many organisms, the haploid cells differentiate into specialized reproductive cells called ***gametes*—eggs and sperm** in most species. In these species, the reproductive cycle ends when a sperm and egg fuse to form a diploid *zygote*, which has the potential to form a new individual. Without meiosis, the chromosome number would double with each generation, and sexual reproduction would not be possible.

Meiotic division consists of two successive division of the cell. The first division is accompanied wit the reduction in the number of chromosomes while the second division involves separation of chromatids of chromosomes. Thus, meiosis is a complex process and comprises of two successive divisions, meiosis I and meiosis II. Interphase occurs prior to meiosis. It is similar to interphase of mitosis except that S phase is prolonged.

Meiosis I (FirstMeiotic or Heterotypic division)

Meiosis I is a heterotypic and is also called reductional division as the chromosome number is halved. The first meiotic division can be divided into ***Prophase I , Metaphase I ,Anaphase I and Telophase I.***

Prophase I : This stage of meiotic division is the longest in duration . The main events existing during Prophase I are :

i) Intimate pairing between homologous chromosomes.
ii) Condensation of chromosomes.
iii) Crossing over between homologous chromosomes.
iv) Movement of homologous chromosomes away from each other so that chiasma become observable.
v) Movement of chromosomes during chromosome pairing and chiasma terminalisation.

Based on the above events , prophase I is divided into five sub stages : ***Leptotene, Zygotene , Pachytene , Diplotene and Diakinesis.***

Leptotene : During Leptotene , following main events take place :

i) There is a marked increase in the nuclear volume .
ii) There is chromosome condensation so that they become visible as fine threads.
iii) There is RNA synthesis as a result of which the volume of nucleolus increases appreciably.
iv) Proteins needed for chromosome condensation are synthesized.

Zygotene : This stage begins with the initiation of pairing between homologous chromosomes and it ends when the pairing is completed . The main events occurring in this stage can be summarised as follows :

i) Pairing between homologous chromosomes.
ii) Synthesis of a specific nuclear protein.
iii) Development of the synaptonemal complex. Though the function of synaptonemal complex is uncertain but it is believed to be essential for crossing over.
iv) Progressive condensation of chromosomes.
v) Pairing between homologous chromosome is extremely precise so that only the homologous segments of the two chromosomes pair with each other. Pairing between homologous chromosomes is often known as synapsis.

Pachytene : Pachytene begins when synapsis comes to an end and it ends when homologous chromosomes begin to move away from each other. The main events that exist during this stage are as follows :

i) There is a further condensation of chromosomes so that chromosomes pairs become shorter and thicker.
ii) The nucleus is distinct and quite large.
iii) Crossing over between homologous chromosome take place during this stage. Crossing over is a important event because it is the crossing over because of which the genetic variation occurs.

Diplotene:

The main events taking place in this stage are:

i) Homologous chromosomes of each bivalent begin to move away from each other which marks the begining of this stage.
ii) The two homologues of each bivalent appears to be attached with each other at one or more points , these attachments are called as chiasma.
iii) As diplotene progresses , chiasma slowly move towards the end of chromosome. This movement is called as chiasma terminalization.
iv) There is further condensation chromosomes of so that they become progressively shorter and thicker.

Diakinesis:

The end of the chiasma terminalization marks the begining of this stage . The main events of diakinesis are as follows :

i) Chiasma terminalization is completed just before this stage so that the two homologous chromosomes of each bivalent are now attached at or close to one or both the telomeres only.
ii) Choromerosomes become shorter and thicker due to further condensation.
iii) Towards the end of diakinesis, bivalents move away from each other and spread towards the periphery of cells.
iv) Nucleolus and nuclear envelop disappear.
v) The spindle apparatus is organised. The bivalents now migrate to the equatorial plate of cells such marks the end of diakinesis.

Metaphase I :

Just prior to the beginning of metaphase ,

i) Nucleolus diasppears.
ii) Nuclear envelope disintegrates.
iii) spindle apparatus is organised.
iv) All the bivalents within a cell migrate to equatorial plate.

During Metaphase, following events take place :

i) Bivalents are arranged at the metaphase plate.
ii) Centromeres of the two homologues of each bivalent lie on the either side of the equatorial plate.
iii) Metaphase stage terminates as soon as the homologous chromosomes begin to seperate from each other and to migrate to the opposite poles of the cell.

Anaphase I:

i) Seperation of the two homologous chromosomes of each bivalent marks the begining of anaphase stage.
ii) One chromosome from each bivalent begins to migrate to one pole ,while the other migrates to the opposite pole.
iii) At the end of Anaphase I , one chromosome from each of the bivalents gather about one pole , while the second chromosome from the bivalent move to the other pole.

Telophase I:

During Meiotic Telophase I :

i) The chromosomes uncoil only partially , while a complete uncoiling takes place during mitotic telophase.
ii) Nuclear envelop becomes organised around the two groups of chromosomes.
iii) Nucleolus also reappears.

Meiosis II (Second Meiotic Division) :

Meiosis II is equational (mitotic) in character. It differs from mitosis in that DNA does not duplicate but centromeres do so. The two haploid cells formed as the result of heterotypic division divide mitotically into two cells each. Meiosis II consists of four phases , ***Prophase II, Metaphase II, Anaphase II and Telophase II.***

Prophase II :

This stage is quite similar to that of mitosis . There is further condensation of chromosomes so that they become thicker and shorter. At the end of this stages , nucleolus and nuclear envelop disappear and spindle apparatus is organised. Following this phase , the chromosome migrate to the equatorial plate .

Metaphase II :

This stage begins when the chromosome become arranged on the equatorial plate. During this stage :

i) Nucleolus and nuclear envelop are absent .
ii) Spindle apparatus is present .
iii) Centromeres of all the chromosomes are arranged in a single plane at the equatorial plate.
iv) Chromosomes become more condensed, thicker and shorter.

Anaphase II :

In this phase centromeres of chromosomes observably divide longitudinally and the two sister chromatids of each chromosome begin to separate and move away to the opposite poles . This stage comes to an end when sister chromatids of chromosomes reach the opposite poles.

Telophase II :

Telophase II begins when sister chromatids of chromosomes reach the opposite poles. During this stage, the chromatids uncoil so that they assume the appearance of a loose ball of thread. The nuclear envelop is reorganised from the elements of Endoplasmic Reticulum and nucleolus reappears.

Cytokinesis :

By the end of Telophase II, the cytoplasm of each of the two cells divide into two parts . As a result , one parent cell produces four haploid daughter cells after the completion of two meiotic division. The four haploid cells produced by meiotic division of a single cell can differentiate into gametes or spores.

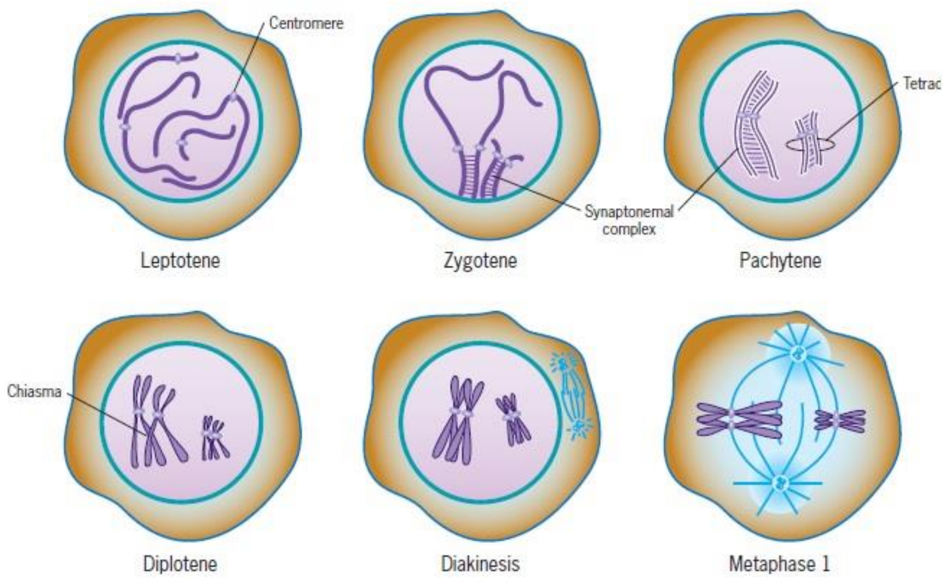


Figure : Stages of Prophase I

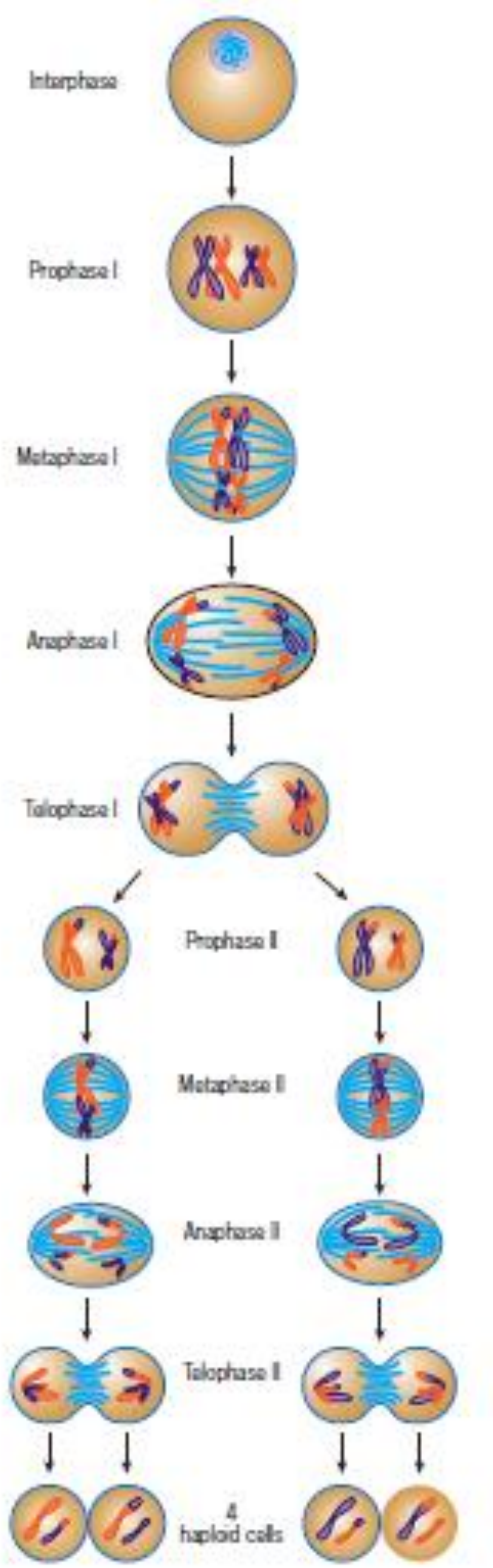


Figure : Stages of Meiosis