Chapter 10

Cell Cycle and Cell Division

While going through the chapter pay special attention to the following –

Terms and Definition –

(1) Synaptonemal complex	(2) Chiasmata
(3) Terminalization	(4) Brachymeiosis
(5) Bouquet stage	(6) Tetrad
(7) G_0 stage	(8) Asters
(9) Karyochorosis	(10) Recombinase enzyme
(11) Disjunction	(12) Bivalents
(13) Interkinesis	(14) Homotypic division
(15) Heterotypic division	

Differences –

(1) Cytokinesis and Karyokinesis	(2) Cytokinesis in plants and animals

- New cells arise from the pre-existing cells by process known as **cell division.**
- Cell division is an important phenomenon that occurs in all living organisms.
- In unicellular organisms, cell division directly produces two individual thus, it is a method of reproduction in these organisms.
- In multicellular organisms, life begins from a single cell **zygote** or fertilized egg, which divides & redivides to form a complete organisms.
- Each parent cell give rise to two daughter cells each time they divide. These newly formed daughter cells themselves grow and divide, giving rise to a new cell population that is formed by the growth and division of a single parental cell and its progeny.

CELL CYCLE

- Cell cycle is a genetically controlled series of changes that occur in a newly formed cell by which it duplicates its genome, synthesises other constituents, undergoes growth and divides to form two daughter cells.
- Although cell growth (in terms of cytoplasmic increase) is a continuous process, DNA synthesis occurs only during one specific stage in the cell cycle.
- The replicated chromosomes (DNA) are then distributed to daughter nuclei by a complex series of events during cell division. These events are themselves under genetic control.
- Cell cycle consists of two basic phases, states or periods. There is a long non-dividing growing **I-phase (Inter-phase)** and a short-dividing **M-phase.** Both have substages. M-phase is the period or phase of actual cell division.

Connecting Concepts

✦ The main reason for cell division is to maintain the nucleocytoplasmic ratio or karyoplasmic ratio which is ratio between nucleus and cytoplasmic mass of cell. It gets disturbed due to continuous cell growth. Further cell division is also necessary for continuity of organism or species.

Phases of Cell Cycle

> **Connecting Concepts**
>
> ✦ Time interval between two successive divisions is called ***generation time.***
>
> ✦ Nerve cells do not divide after birth and, therefore interphase last throughout the life of the individual.
>
> ✦ In G_1 phase a cell can undergo three processes. (a) in S-phase (b) enter in quiescent stage or G_0 phase. (c) Stop cell cycle and undergo differentiation. The deciding factor is availability of energy rich compounds and mitogens. The point where this decision is made is known as ***check point***. Once this check point is crossed, the cell will divide even under unfavourable conditions.
>
> ✦ Go phase: Some cells in the adult animals do not appear to exhibit division (e.g., heart cells) and many other cells divide only occasionally. These cells that do not divide further exit G_1 phase to enter an inactive stage is called **quiescent stage** (G_0) of the cell cycle. Cell in this stage remain metabolically active but no longer proliferate unless depending on the requirement of the organism.

- **Interphase :** The resting phase or stage between the two mitotic divisions is called **inter-mitotic phase** or **interphase**. During interphase, cell prepares for division by undergoing both cell growth and DNA replication in an orderly manner.
- Most of DNA, RNA and protein are made during interphase, so it is the period when metabolic activity is greatest.
- The interphase is the **longest phase** of the mitotic cycle, last more than 95% of the duration of cell cycle. It has three sub-phases: **G_1, S and G_2** which occurs in this order followed by M phase.
- Different eukaryotic cells vary in the length of time taken to complete an entire cell cycle; they also differ in the relative proportions of time allotted to each of the four stages. Thus, in continuously dividing cells, an individual cell passes through the following four phases of cell cycle.

(i) **G_1 phase:** (G stands for gap) : In this phase synthesis of substrate and enzyme necessary for DNA synthesis take place. Therefore, G_1 is marked by the transcription of rRNA, tRNA, mRNA and synthesis of different types of proteins. It corresponds to the interval between mitosis and initiation of DNA replication. During G_1 phase the cell is metabolically active and continuously grows but does not replicate its DNA.

- Time taken for completion of this phase is about **30–40%** of the total cell cycle (mitotic cycle).
- Decision of cell division occurs during this phase.

(ii) **S phase:** During S or synthesis phase, replication or duplication of chromosomal DNA and synthesis of histone proteins takes place. During this time the amount of DNA per cell doubles.

- Time taken for completion of this phase is **30–50%** of total cell cycle.
- If the initial amount of DNA is denoted as 2C then it increases to 4C. However, there is no increase in the chromosome number; if the cell has diploid or 2n number of chromosomes at G_1, even after S phase the number of chromosomes remains the same, *i.e.*, 2n. In animal cells, during the S-phase, DNA replication begins in the nucleus and the centriole duplicates in the cytoplasm.
- In contrast, in rapidly growing bacteria DNA synthesis occurs from the time a cell originates to the time it gives rise to daughter cells by division. Likewise, in simple eukaryotes such as yeast, DNA synthesis takes place throughout the interphase and ceases only during the brief period of nuclear and cell division (*i.e.*, M phase).
- Once the cell entered in S phase, it would proceed to division without any interruption.

(iii) **G_2 phase:** It is the post-DNA synthesis phase.

- Time taken for completion of this phase is **10–20%** of a total cell cycle.
- During the G_2 phase, proteins are synthesized for mitosis while cell growth continues.

(iv) **M-phase or mitotic phase or meiotic phase :** It is actual cell division phase followed by G_2 phase.

- Time taken for completion of this phase is **5–10%** of the total cell cycle and hence it is shortest of all the 4-phases.
- It is final phase of cell cycle. It consists of **karyokinesis** (division of nucleus) and **cytokinesis** (division of cell protoplasm) to form two daughter cells.

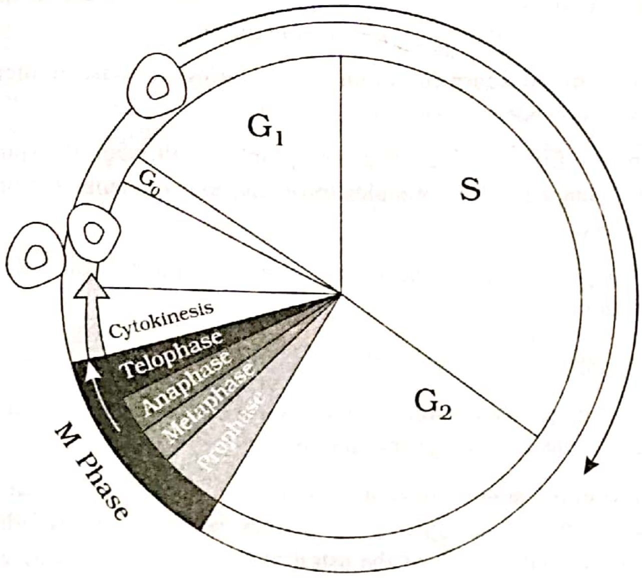

Fig. 10.1 A diagrammatic view of cell cycle

- In animals, mitotic cell division is only seen in the diploid somatic cells. While plants can show mitotic divisions in both haploid and diploid cells.

MITOSIS

- **Flemming** (1882) coined the term mitosis. However , mitosis was first observed in plants by **E. Strasburger** (1875) and in animals by **W. Flemming** (1879).
- It is also called as **equational division** as the number of chromosomes in the parent and progeny cells is the same. So mitosis increase in number of cells without any change in genetic constitution.
- It is a continuous process but for convenience it is usually divided into several stages or phases, *viz.*, prophase, metaphase, anaphase, telophase and cytokinesis.

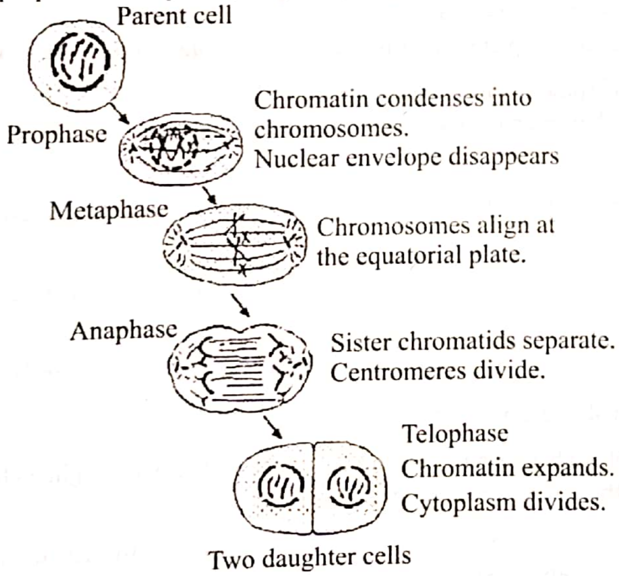

Fig. 10.2 Mitosis

Prophase

- The prophase is the first and the longest phase of the mitosis.

The prophase includes five events:

- The beginning of prophase is indicated by the onset of chromosome coiling and condensation. As a result, chromosomes become distinctly visible as thin threads inside the nucleus. At the same time, the cell becomes spheroid, more refractile, and viscous.

Connecting Concepts

- Various phases of cell cycle are controlled by proteins ***cyclins*** and **cyclin dependent kinases (CDKs or cdc kinases)** that take part in phosphorylation and dephosphorylation
- **Mitosis** is also known as ***somatic division*** because it takes place during formation of somatic or body cells. Mitosis is studied in plants in the regions of meristems, e.g. stem tip, root tip. In animals it is studied in bone marrow, skin, base of nails, etc.
- **Mitosis** is ***centric*** in animal cells and ***acentric*** (without participation of centrosome) in plants.
- The agents which stimulate cell division are called ***mitogens***, e.g., cytokinins, some steroids, platelet derived growth factor (PDGF), lymphokines.
- There are some agents which inhibit cell division. They are called ***mitotic poisons***, e.g., azides, cyanides, colchicine.
- Besides mitogens, cells are stimulated to divide in achieving a particular size, critical decrease in surface volume ratio and critical decrease in nucleocytoplasmic ratio.
- The rate of cell division is not the same in various stages of life cycle. Fertilised egg or zygote divides repeatedly to form a large number of cells, upto 6 ×10^{12} cells. Later on divisions are get slow down and restricted in certain regions like meristematic regions in plants, bone marrow and germinal tissue in animals.

Connecting Concepts

✦ Time taken by phases of cell cycle varies in different organisms and also in different tissues of same organisms, e.g., in *Vicia faba* (Broad bean or Bakla)

Phases of cell cycle	*Duration*
(i) G_1-phase	12 hrs
(ii) S-phase	6 hrs
(iii) G_2-phase	12 hrs
(iv) M-phase or mitotic phase	1 hr

✦ Therefore, cell cycle here is of 31 hrs (Interphase—30 hrs and mitotic phase—1 hr).

✦ In meiotic cell G_2 phase is either absent or very short i.e. meiotic division (M-phase) occurs just after completion of DNA-synthesis (S-phase).

✦ In **amitosis**, nucleus elongates, constricts in the middle and divides directly into two daughter nuclei. Chromatin does not condense to form chromosomes. Spindle apparatus is not formed. Nuclear division is followed by cytokinesis. It occurs through cleavage or constriction, e.g., cartilage cells, meganucleus of *Paramoecium*, cells of foetal membranes and endosperm. As amitosis does not distribute chromatin, it leads to structural and functional irregularities.

✦ A spindle fibre consists of 4–20 microtubules formed of protein tubulin.

✦ In dividing animal cells, the spindle bears asters at the two poles. Such a spindle is called ***amphiaster*** or ***centric***. In plant cells spindle is ***acentric*** or ***anastral***.

✦ In many protists, fungi and algae, the nuclear envelope does not degenerate during mitosis. Instead, spindle is formed inside the nucleus. It is called ***intranuclear mitosis*** or ***karyochorosis***.

- Each prophase chromosome is composed of two coiled identical filaments, the sister **chromatids,** which are held together by a **centromere.**
- The two pairs of **centrioles** formed by duplication during 'S' phase of interphase, separate and migrate to occupy positions on opposite sides of the nucleus.
- Initiation of spindle formation begins during prophase, although the spindle is not fully functional until metaphase. Microtubules (proteinaceous components) of cell cytoplasm help in this process.
- Cells at the end of prophase do not have Golgi complex, endoplasmic reticulum, nucleolus and the nuclear envelope.

Metaphase

- At metaphase complete disintegration of the nuclear envelope, alignment of chromosome and formation of the spindle apparatus takes place.
- The spindle apparatus is a microtubular structure that extends from pole to pole. Those cells that have centrioles typically also have **asters,** which are fibres radiating out in all directions from the poles. Each of the astral and spindle fibres is actually bundles of microtubules.
- Small disc-shaped structures at the surface of the centromere are called **kinetochores**. These are the sites of attachment of spindle fibres. During metaphase all the chromosome align to center of cell, the chromosomes become attached to some of the spindle fibres by their kinetochores.
- 97% tubulin protein (protein of microtubules) and 3% RNA are present in spindle fibres.
- Spindle microtubules are polar, their + ends are fast growing facing equator while –ve ends are slow growing face poles. Alignment of chromosome due to contraction of chromosome or kinetochore fibre is called **congression**.
- The two sister chromatids by virtue of their kinetochores and attached fibres are pulled towards opposite poles. Because they are held together at the centromere, there is pull in both directions at once, resulting in oscillatory movements that eventually align all chromosomes in one plane. This plane is called **equatorial plane** or **metaphasic plane**.
- The fibres of spindle which connect to the chromosomes are called the **chromosomal fibres**; those that extend without interruption from one pole to the other are the **continuous fibres**.
- Centromeres of all chromosomes are present over the equator, whereas its arms project in different directions.
- Morphology of chromosome can be observed and studied, clearly under the microscope in metaphase.

Anaphase

- It is phase of shortest duration.
- Mitotic anaphase begins with centromere division. The two daughter chromatids, now free from each other, move towards their respective poles.
- Because they are being pulled by their kinetochores, the chromatids would assume V- shape, L- shape, J-shape or I-shape in metacentric, submetacentric, acrocentric and telocentric chromosome respectively.
- At the same time as the chromatids move toward their poles, the poles themselves move further apart. The chromosomes move due to shortening of chromosomal fibres and the poles are pushed apart by lengthening (or stretching) of continuous or pole-to-pole fibres.
- Now, the two sister chromatids are separate structures. These are the chromosomes of future daughter nuclei.

Telophase

- In telophase, two diploid sets of daughter chromosomes gathered at opposite poles. Start to uncoil and become mass of chromatin. Their identity is lost as discrete elements.
- The nucleolus condense and reappear. The spindle fibres disperse. The nuclear envelope is assembled around the chromatin mass and endoplasmic reticulum reform again thus forming two daughter nuclei.

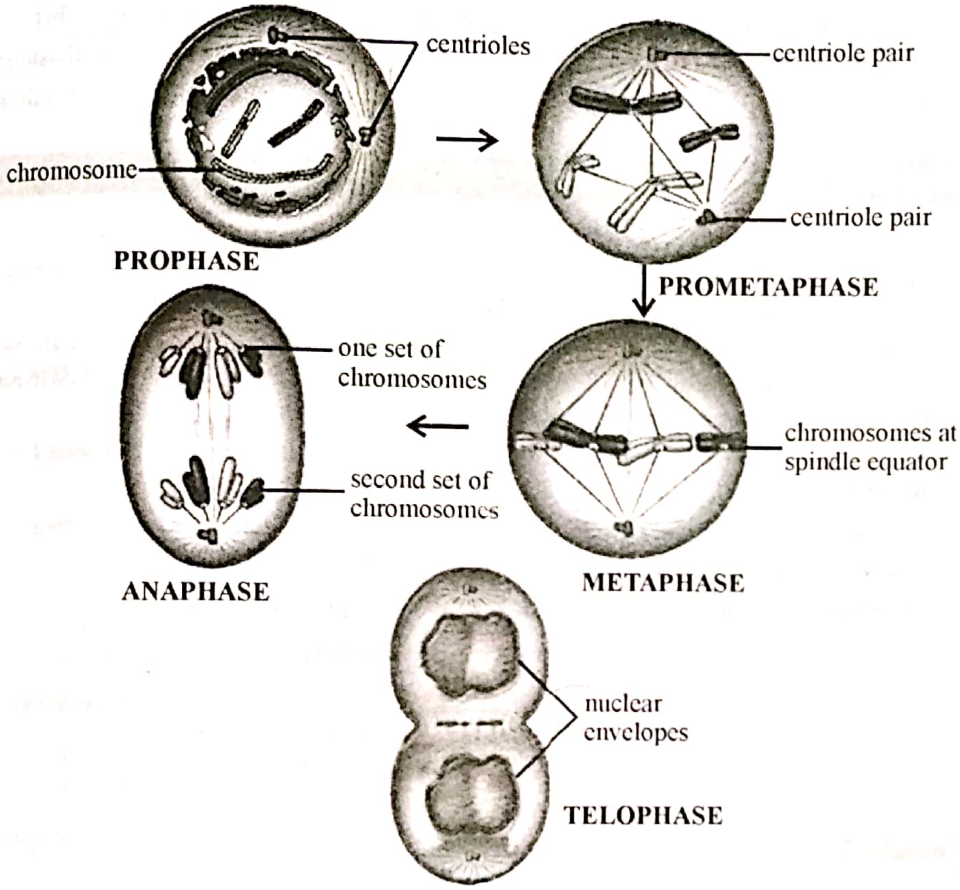

Fig. 10.3 Different stages in the mitotic division of a plant cell

Connecting Concepts

- ✦ Shape of chromosome are studied in anaphase.
- ✦ Cell complete their mitotic division in 10 minutes to several hours. Further on increasing the surrounding temperature, lesser the time taken in division.
- ✦ A deadly disease ***cancers*** is due to uncontrolled cell division. Carcinogens are cancer causing agents which are UV radiation and chemicals like benzpyrene, aflatoxin, mustard gas etc.

Cytokinesis

- **Karyokinesis** (division of nucleus into two) is followed by **cytokinesis** *i.e.*, division of cytoplasm into two daughter cells, which starts towards the middle of anaphase and is completed simultaneously by the end of telophase.
- **Plant cells :** Wall formation starts in the centre of the cell and grows outward to meet the existing lateral walls **(centrifugal).** In the equatorial region middle part of spindle persists and gets interdigitated with microtubules to form a complex structure called **phragmoplast.** The vesicle of dictyosome (Golgi complex) and the membranous elements of the ER accumulate in the region of the equator and fuse to form the **cell plate** dividing it into two equal or unequal daughter cells.
- At the time of cytoplasmic division, organelles like mitochondria, Golgi complex, lysosomes and plastids get distributed between the two daughter cells.
- **Animal cells :** A furrow appears in the cell membrane at the equator and progresses from the periphery to centre **(centripetal).** It also occurs in some lower plant.

SIGNIFICANCE OF MITOSIS

- Mitosis is necessary for the maintenance and perpetuation of life.
- It helps in the maintaining the amount of DNA and RNA in the cell.
- Mitotic divisions of vegetative or somatic cells are responsible for growth and development of organism.
- The old decaying and dead cells of body are replaced by mitosis.
- In certain organisms, mitosis is involved in asexual reproduction.
- The gonads and the seed cells depend on the mitosis for the increase in their number.
- The cleavage of egg and division of blastula during embryogenesis are mitotic divisions.
- Mitotic divisions in the apical and lateral cambium, results in a continuous growth of plants throughout their life.

MEIOSIS

- **Farmer** and **Moore** (1905) – coined the term meiosis.
- Meiosis is characterized by two successive divisions of the cytoplasm and nuclei (meiosis I and meiosis II). These haploid cells either become or give rise to gametes.
- Meiosis ensures the production of haploid phase in the life cycle of sexually reproducing organisms whereas fertilisation restores the diploid phase. Thus, meiosis is required to run the reproductive cycle of eukaryotes.
- Meiosis involves two sequential cycles of nuclear and cell division called **meiosis I** and **meiosis II** but only a single cycle of DNA replication.
- Meiosis involves pairing of homologous chromosomes and recombination between them.
- Four haploid cells are formed at the end of meiosis II.

Meiotic events can be grouped under the following phases:

Meiosis I	Meiosis II
Prophase I	Prophase II
Metaphase I	Metaphase II
Anaphase I	Anaphase II
Telophase I	Telophase II

Connecting Concepts

✦ **Brachymeiosis** is unusual meiosis occur in ascus of certain fungi (Pyronema confluens). In this type of division a reduction division followed by the two usual mitotic division occurs to restore the haploid condition in fungi in which double fertilization has produced a tetraploid primary ascus nucleus.

Meiosis I

- Meiosis starts after an interphase which is not very different from that of a mitotic interphase.
- It is the actual reduction division and known as **heterotypic division** as it converts a diploid cell into haploid cells. In meiosis I, the two chromatids of a chromosome often become different due to crossing over.
- The first stage of both meiosis I and II is prophase. The prophase of first meiotic division is very significant because most cytogenetical events such as synapsis, crossing over, *etc.*, occur during this phase.

Prophase I

The first prophase is the longest stage of the meiotic division. It includes following substages:

Leptotene

- During this stage, the chromosomes become gradually visible under the light microscope. The compaction of chromosomes continues throughout leptotene.
- The chromosomes at this stage take up a specific converge toward one side of the nucleus, where the centrosome lies (the **bouquet stage**).
- The centriole duplicates and each daughter centriole migrates towards the opposite poles of the cells. On reaching at the poles, each centriole duplicates again and thus, each pole of cell possesses two centrioles or a single diplosome.

Zygotene

- Leptotene stage is followed by zygotene. In this stage, the **pairing of homologous chromosomes** takes place. In homologous chromosome pair one chromosome comes from the mother (by ova) and one from father (by sperm) are attracted towards each other and their pairing takes place. The pairing of the homologous chromosomes is known as **synapsis** forming bivalents.

Synaptonemal Complex

- The pairing of the homologous chromosomes is very specific *i.e.* it brings alleles of homologous chromosome exactly opposite to each other.
- **Moses** in 1956 discovered **synaptonemal complex**, which is paired homologous chromosomes held together by nucleoproteins.
- This complex extends along the whole length of the paired chromosomes and is usually anchored at either end to the nuclear envelope.
- Synaptonemal pairing produces an opportunity for crossing over that occurs during pachytene and thus facilitates the genetic recombination. The paired homologous chromosome is called **bivalent**.

Pachytene

- This stage is characterised by the appearance of **recombination nodules,** the sites at which **crossing over** occurs between **non-sister chromatids** of the **homologous chromosomes.**
- **Crossing over** is the exchange of genetic material between two homologous chromosomes. It is also an enzyme-mediated process and the enzyme involved is called **recombinase**.
- Crossing over leads to **recombination** between homologous chromosomes which is completed at the end of pachytene but become linked at the site of crossing over.

Diplotene

- At diplotene further thickening and shortening of chromosome takes place. The synaptic forces between paired homologues come to an end (synaptonemal complex appears to be dissolved) and chromatid become clear and the bivalents are now called **tetrads**.
- The chromatids of the paired homologous chromosomes physically joined at one or more discrete points having X-shaped structure called **chiasmata**.
- In oocytes of some vertebrates, diplotene can last for months or years and form **lampbrush chromosomes.**
- The nucleolus is also diminished but still persists. No nuclear membrane can be seen at this stage.

Diakinesis

- The final stage of meiotic prophase I is diakinesis. At this stage the bivalent chromosomes become more condensed and evenly distributed in the nucleus.
- Ordinarily the only distinction between diplotene and diakinesis is the more contracted state of bivalents at diakinesis.
- The nucleolus detaches from the nucleolar organizer and ultimately disappears. The nuclear envelope breaks down.
- During diakinesis the chiasmata moves from the centromere towards the ends of the chromosomes and the intermediate chiasmata diminish. This type of movement of the chiasmata is known as **terminalizaton**. The chromatids still remain connected by the terminal chiasmata.

Connecting Concepts

- ✦ Number of bivalents is half the number of individual chromosomes. Bivalents are actually tetrads but the individual chromatids of the two chromosomes are not clear due to the presence of nucleoprotein core between them. Depending upon the area of initiation, synapis can be **procentric** (starting from centromeres), **proterminal** (pairing beginning from telomeric regions and proceeds inward) and **intermediate** (= random pairing starts at several points). Pairing proceeds from the starting regions towards other parts in a zipper like manner.
- ✦ In males of ***Drosophila melanogaster*** an unusual type of meiosis occurs in which synaptonemal complex (SC) formation and recombination do not occur. This type of meiosis is called **achiasmatic meiosis** and is exceptional, as nearly all eukaryotes along with ***Drosophila*** females require SC formation and recombination for successful completion of meiosis.
- ✦ Chiasmata was first seen by ***Johannsen.***
- ✦ ***Disjunction*** is the process of separation of homologous chromosome.

Check Point

1. **Give term for each of the following.**
   (a) The period between two successive mitotic divisions.
   (b) Process of cell division by which the chromosome number is halved.
   (c) Point at which two sister chromatids are held together.
   (d) Phase in the cell cycle when protein and RNA are synthesised.
   (e) Nuclear division.

Metaphase I

- At metaphase I spindle fibres attach themselves to chromosomes and chromosomes align at the **equator**.
- The centromere of each chromosome is directed towards the opposite poles. The repulsive forces between the homologous chromosomes increase greatly and the chromosomes become ready to separate.

Anaphase I

- At anaphase I, homologous chromosome pair (one chromosome is from mother and other is from father) with its two chromatids moves towards the opposite poles of the cell and separate from each other.
- This separation cause two groups of haploid chromosomes at the poles.
- Due to crossing over, the two chromatids of a chromosome do not resemble with each other in the genetical terms.
- The chromosomes with single or few terminal chiasmata usually separate more frequently than the longer chromosomes containing many chiasmata.

Telophase I

- In telophase, the nuclear membrane and nucleolus reappear. The chromosomes become uncoil.
- After the karyokinesis, cytokinesis occurs and two haploid cells are formed. This is called diad of cells. Both cells pass through a short resting phase or interphase.
- During interphase, no DNA replication occurs, so chromosomes at the second prophase are the same double-stranded structures that disappeared at the first telophase.
- The stage between the two meiotic divisions is called **interkinesis** and is generally short-lived.
- Interkinesis is followed by prophase II, which is a much simpler prophase than prophase I.

Connecting Concepts

✦ *In Trillium* both telophase I and prophase II are omitted and anaphase I directly leads to metaphase II.

Check Point

1. Name the stage of cell division
   (a) Crossing over occur between homologous chromosome.
   (b) Stage of synapsis of homologous chromo-some.
   (c) Stage of initiation of cytokinesis.
   (d) Movement of daughter chromosome towards pole.
   (e) Stage of reappearance of

Meiosis II

- The first meiotic division is followed by a second meiotic division with or without the intervening interphase. The second meiotic division is actually the mitotic division known as **homotypic division** which divides each haploid meiotic cell into two haploid cells.
- The second meiotic division includes following four stages:

Prophase II

- The nuclear membrane and the nucleolus disappear. The chromosomes with two chromatids become short, thick and compact.
- At this stage each centriole divides into two and thus, two pairs of centrioles are formed. Each pair of centrioles migrates to the opposite pole.
- The microtubules get arranged in the form of spindle at the right angle of the spindle of first meiosis.

Metaphase II

- The chromosomes get arranged on the equator of the spindle. The microtubules of the spindle are attached with the kinetochores of the chromosomes.
- The centromere divides into two and thus each chromosome produces two daughter chromosomes.

Anaphase II

- The daughter chromosomes move towards the opposite poles due to stretching of internal microtubules of the spindle.

Telophase II

- The chromatids migrate to the opposite poles and now known as chromosomes. The endoplasmic reticulum forms the nuclear envelope around the chromosomes and nucleolus reappears due to synthesis of ribosomal RNA (rRNA) and ribosomal protein. After the karyokinesis, cytokinesis follows resulting in the formation of tetrad of cells *i.e.*, four haploid daughter cells.

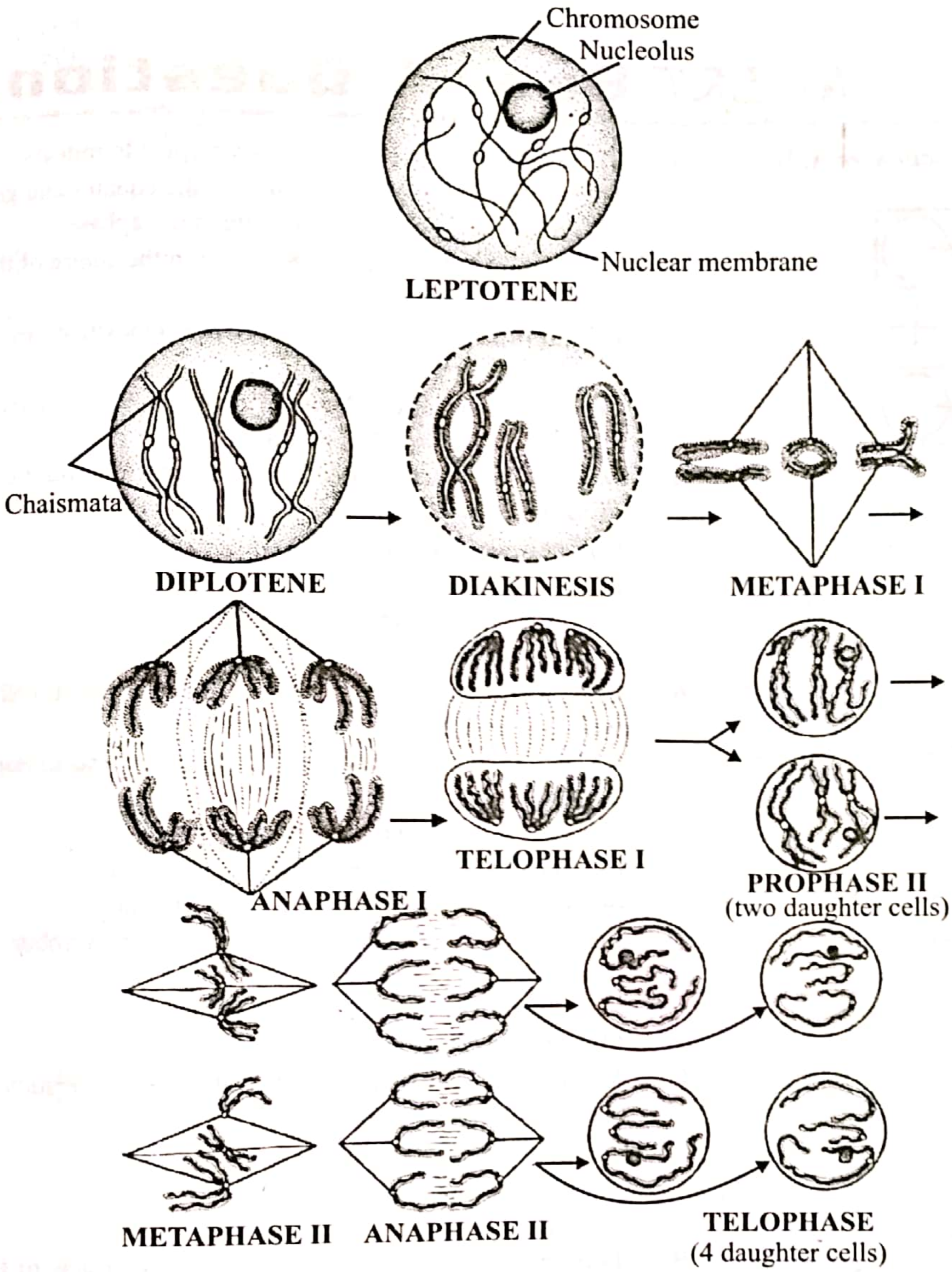

Fig. 10.4 Different stages in the meiotic division of a plant cell

SIGNIFICANCE OF MEIOSIS

- Meiosis is the mechanism by which conservation of specific chromosome number of each species is achieved across generations in sexually reproducing organisms.
- It also increases the genetic variability in the population of organisms from one generation to the next by crossing over. The variations are the raw materials of the evolutionary process.