Unit III: Cell biology and Biomolecules

Chapter 7

Cell Cycle

Learning Objectives

The learner will be able to,

- *Outline the cell cycle and different stages in cell division.*
- *Recognise the importance of mitosis in the production of genetically identical cells.*
- *Have an insight on the significant of mitosis and meiosis.*
- *Familiarize the behaviour of chromosomes in plants and animal cells during meiosis.*

DO YOU KNOW?

Neurons can be replaced!

Stem cells in the human brain - most neurons are in G_0 and do not divide. As neurons and neuroglia die or injured they are replaced by neural stem cells

One of the most important features of the living cells is their power to grow and divide. New cells are formed by the division of pre-existing cells. Cells increase in number by cell division. The parent cell divides and passes on genetic material to the daughter cells.

7.1 Nuclear Divisions

There are two types of nuclear division, as **mitosis** and **meiosis**. In mitosis, the daughter cells formed will have the same number of chromosomes as the parent cell, typically diploid (2n) state. Mitosis is the nuclear division that occurs when cells grow or when cells need to be replaced and when organism reproduces asexually.

In meiosis, the daughter cells contain half the number of chromosomes of the parent cell and is known as **haploid state (n)**.

Whichever division takes place, it is normally followed by division of the cytoplasm to form separate cells, called as **cytokinesis**.

Chapter Outline

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Edouard Van Beneden, a Belgian cytologist, embryologist and marine biologist. He was Professor of Zoology at the University of Liège. He contributed to cytogenetics by his works on the roundworm *Ascaris*. In his work he discovered how chromosomes organized meiosis (the production of gametes).

7.2 Cell Cycle

Definition: A series of events leading to the formation of new cell is known as **cell cycle**. The series of events include several phases.

History of a Cell

Table 7.1: History of Cell		
Year	**Scientist**	**Events**
1665	Robert Hooke	Coined word “Cell”
1670–74	Anthony van Leeuwenhoek	First living cells observed in microscope - Structure of bacteria
1831–33	Robert Brown	Presence of nucleus in cells of orchid roots
1839	Jan Evangelista Purkyne (J.E. Purkinje)	Coined “protoplasm”
1838–39	Schleiden & Schwann	Cell theory
1858	Rudolph Ludwig Carl Virchow	Cell theory ‘*omnis cellula e cellula*’
1873	Anton Schneider	Described chromosomes (Nuclear filaments) for the first time
1882	Walther Flemming	Coined the word mitosis; chromosome behaviour
1883	Edouard Van Beneden	Cell division in round worm
1888	Theodor Boveri	Centrosome; Chromosome Theory

7.2.1 Duration of Cell Cycle

Different kinds of cells have varied duration for cell cycle phases. Eukaryotic cell divides every 24 hours. The cell cycle is divided into mitosis and interphase. In a cell cycle 95% is spent for interphase whereas the mitosis and cytokinesis last only for an hour.

Table 7.2: Cell cycle of a proliferating human cell	
Phase	**Time duration (in hrs)**
G_1	11
S	8
G_2	4
M	1

The different phases of cell cycle are as follows (Figure 7.1).

7.2.2 Interphase

Longest part of the cell cycle, but it is of extremely variable length. At first glance the nucleus appears to be resting but this is not the case at all. The chromosomes previously visible as thread like structure, have dispersed. Now they are actively involved in protein synthesis, at least for most of the interphase.

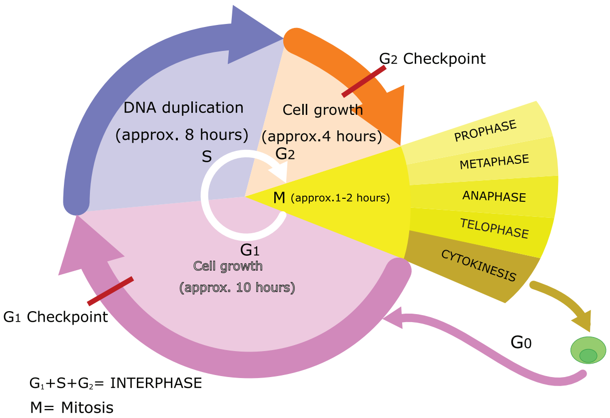

Figure 7.1: Cell cycle

C-Value is the amount in picograms of DNA contained within a haploid nucleus.

7.2.3 G_1 Phase

The first gap phase – 2C amount of DNA in cells of G_1. Cells become metabolically active and grows by producing proteins, lipids, carbohydrates and cell organelles including mitochondria and endoplasmic reticulum. Many checkpoints control the cell cycle. The check point are also called as the **restriction point.** First check point at the end of G_1, determines a cells fate whether it will continue in the cell cycle and divide or enter a stage called $\mathbf{G_0}$ a quiescent stage, probably as specified cell or die. Cells are arrested in G_1 due to:

- Nutrient deprivation
- Lack of growth factors or density dependant inhibition
- Undergo metabolic changes and enter into G_0 state.

Biochemicals inside cell activates the cell division. The proteins called **kinases** and cyclins activate genes and their proteins to perform cell division. Cyclins act as major checkpoint which operates in G_1 to determine whether or not a cell divides.

> DO YOU KNOW?
>
> **Dolly**
>
> Since the DNA of cells in G_0, do not replicate. Researchers are able to fuse the donor cells from a sheep's mammary glands into G_0 state by culturing in the nutrient free state. The G_0 donor nucleus synchronised with cytoplasm of the recipient egg, which developed into the clone Dolly.

7.2.4 G_0 Phase

Some cells exit G_1 and enters a quiescent stage called $\mathbf{G_0}$, where the cell remains metabolically active without proliferation. Cells can exist for long periods in G_0 phase. In G_0, cells cease growth with reduced rate of RNA and protein synthesis. The G_0 phase is not permanent. Mature neuron and skeletal muscle cell remain permanently in G_0. Many cells in animals remains in G_0 unless called on to proliferate by appropriate growth factors or other extracellular signals. G_0 cells are not dormant.

7.2.5 S phase – Synthesis phase – cells with intermediate amounts of DNA.

Growth of the cell continues as replication of DNA occur, protein molecules called **histones** are synthesised and attach to the DNA. The centrioles duplicate in the cytoplasm. DNA content increases from 2C to 4C.

7.2.6 G_2 – The second Gap phase – 4C amount of DNA in cells of G_2 and mitosis

Cell growth continues by protein and cell organelle synthesis, mitochondria and chloroplasts divide. DNA content remains as 4C. Tubulin is synthesised and microtubules are formed. Microtubles organise to form spindle fibre. The spindle begins to form and nuclear division follows.

One of the proteins synthesized only in the G_2 period is known as **Maturation Promoting Factor (MPF)**. It brings about condensation of interphase chromosomes into the mitotic form.

DNA damage checkpoints operates in G_1 S and G_2 phases of the cell cycle.

7.3 Cell Division

7.3.1 Amitosis (Direct Cell Division)

Amitosis is also called **direct** or **incipient cell division**. Here there is no spindle formation and chromatin material does not condense. It consist of two steps: (Figure 7.2).

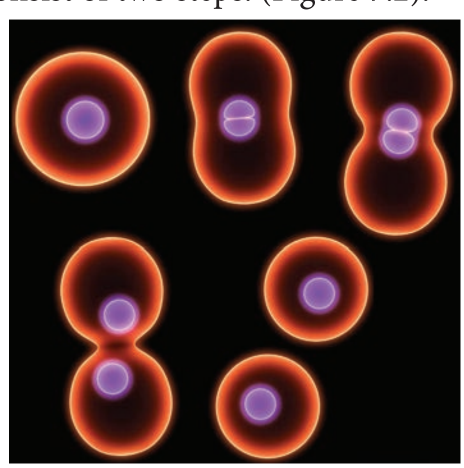

Figure 7.2: Amitosis

❖ **Karyokinesis:**

- Involves division of nucleus.
- Nucleus develops a constriction at the center and becomes dumbell shaped.
- Constriction deepens and divides the nucleus into two.

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❖ **Cytokinesis:**

- Involves division of cytoplasm.
- Plasma membrane develops a constriction along nuclear constriction.
- It deepens centripetally and finally divides the cell into two cells.

Example: Cells of mammalian cartilage, macronucleus of *Paramecium* and old degenerating cells of higher plants.

Drawbacks of Amitosis

- Causes unequal distribution of chromosomes.
- Can lead to abnormalities in metabolism and reproduction.

7.3.2 Mitosis

Mitosis occurs in shoot and root tips and other meristematic tissues of plants associated with growth. The number of chromosomes in the parent and the daughter (Progeny) cells remain the same so it is also called as **equational division**.

7.3.3 Closed and Open Mitosis

In closed mitosis, the nuclear envelope remains intact and chromosomes migrate to opposite poles of a spindle within the nucleus (Figure 7.3).

Example: Many single celled eukaryotes including yeast and slime molds.

In open mitosis, the nuclear envelope breaks down and then reforms around the 2 sets of separated chromosome.

Example: Most plants and animals

- Some animals are able to regenerate whole parts of the body.

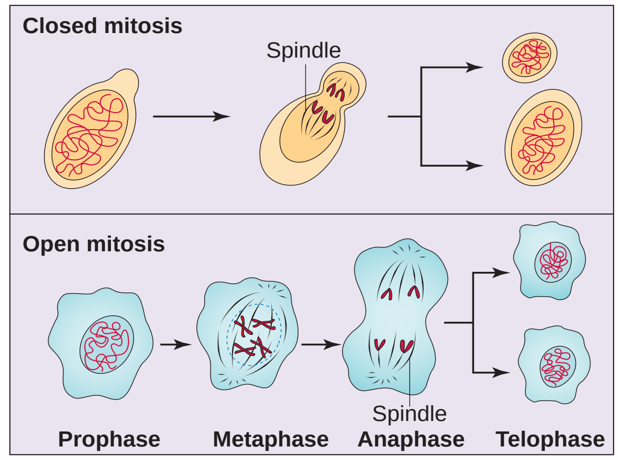


Figure 7.3: Closed and Open mitosis

Mitosis is divided into four stages prophase, metaphase, anaphase and telophase (Figure 7.6).

Prophase

Prophase is the longest phase in mitosis. Chromosomes become visible as long thin thread like structure, condenses to form compact mitotic chromosomes. In plant cells initiation of spindle fibres takes place, nucleolus disappears. Nuclear envelope breaks down. Golgi apparatus and endoplasmic reticulum disappear.

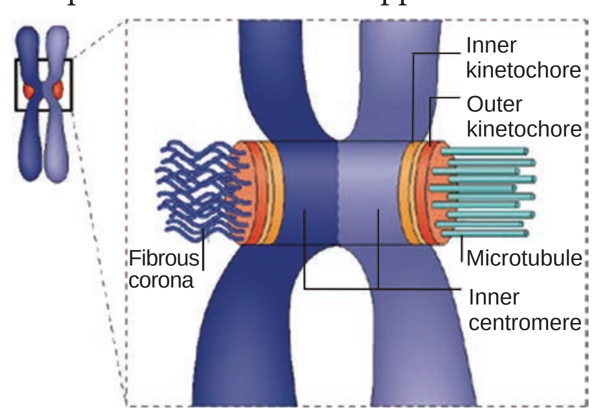


Figure 7.4: Centromere

In animal cell the centrioles extend a radial array of microtubules (Figure 7.4) and reach the poles of the cell. This arrangement of microtubules is called **an aster**. Plant cells do not form asters.

Metaphase

Chromosomes (two sister chromatids) are attached to the spindle fibres by kinetochore of the centromere. The spindle fibres are made up of tubulin. The alignment of chromosome into compact group at the equator of the cell is known as **metaphase plate**. This is the stage where the chromosomal morphology can be easily studied.

Kinetochore is a DNA–Protein complex present at the centromere where microtubules are attached. It is a trilaminar disc like plate.

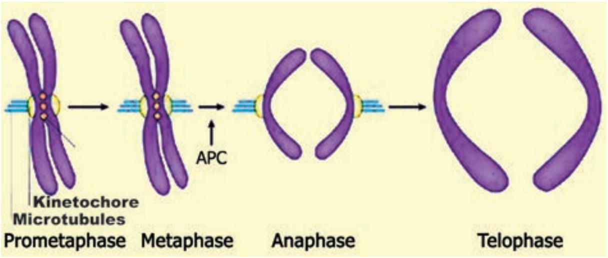


Figure 7.5: Anaphase promoting complex cyclosome

Anaphase

Each chromosome splits simultaneously and two daughter chromatids begin to migrate towards two opposite poles of a cell. Each centromere splits longitudinally into two, freeing the two sister chromatids from each other. When sister chromatids separate the actual partitioning of the replicated genome is complete.

APC (Anaphase Promoting Complex) is a cluster of proteins that induces the breaking down of cohesion proteins which leads to the separation of chromatids during mitosis (Figure 7.5). Thus it helps in the transition of metaphase to anaphase.

Telophase

Two sets of daughter chromosomes reach opposite poles of the cell and mitotic spindle disappears. Division of genetic material is completed during karyokinesis, followed by cytokinesis (division of cytoplasm). Nucleolus and nuclear membranes reforms. Nuclear membrane form around each set of **chromosomes**. Now the chromosomes decondense. In plants, phragmoplast are formed between the daughter cells. Cell plate is formed between the two daughter cells, reconstruction of cell wall takes place. Finally cells are separated by the distribution of organelles, macromolecules into two newly formed daughter cells.

7.3.4 Cytokinesis

Cytokinesis in Animal Cells

It is a contractile process. The ring consists of a bundle of microfilaments assembled from **actin** and **myosin**. This fibril generates a contractile force, that draws the ring inward forming a cleavage furrow in the cell. Thus it divides the cell into two.

> **Check your grasp!**
> What effect does mitosis have on transcription?
> During mitosis transcription stops.

Cytokinesis in Plant Cell

Division of the cytoplasm often starts during telophase. In plants, cell plate grows from centre towards lateral walls.

Phragmoplast contains microtubules, actin filaments and vesicles from golgi apparatus and ER. Microtubule of the pharagmoplast move to the equator, fuse to form a new plasma membrane and the materials which are placed

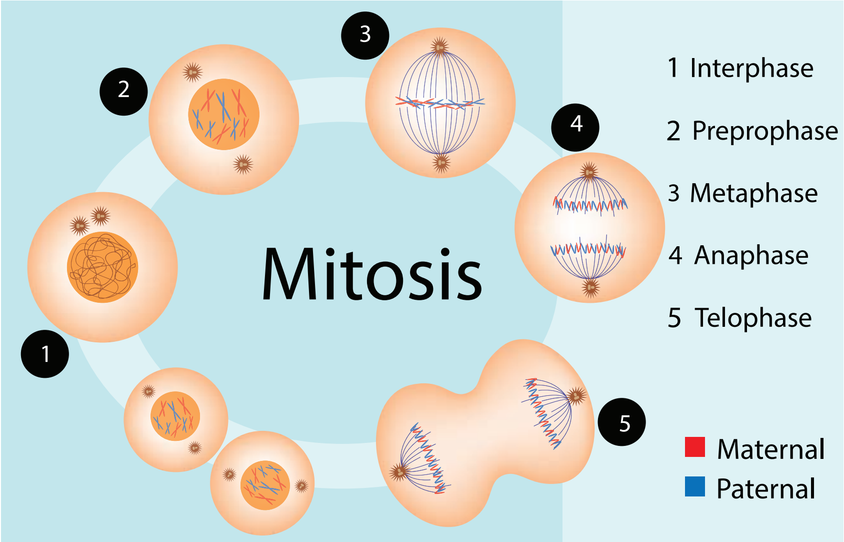
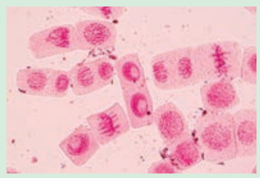


Figure 7.6: Mitosis

there becomes new cell wall. The first stage of cell wall construction is a line dividing the newly forming cells called a **cell plate**. The cell plate eventually stretches right across the cell forming the middle lamella. Cellulose builds up on each side of the middle lamella to form the cell walls of two new plant cells.

Activity

Squash preparation of onion root tip to visualize and study various stages of mitosis.



A Culture of animal cells in which the cell cycles were asynchronous was incubated with 3H-Thymidine for 10 minutes. Autoradiography showed that 50% of the cells were labelled. If the cell cycle time (generation time) was 16 hrs how long was the S period?

Length of the S period = Fraction of cells in DNA replication × generation time

Length of the S period = 0.5 × 16 hours = 8 hours

DO YOU KNOW? Skin cells and the cells lining our gut are constantly dying and are being replaced by identical cells.

7.3.5 Significance of Mitosis

Exact copy of the parent cell is produced by mitosis (genetically identical).

1. **Genetic stability** – daughter cells are genetically identical to parent cells.
2. **Growth** – as multicellular organisms grow, the number of cells making up their tissue increases. The new cells must be identical to the existing ones.
3. **Repair of tissues** - damaged cells must be replaced by identical new cells by mitosis.
4. **Asexual reproduction** – asexual reproduction results in offspring that are identical to the parent. Example Yeast and Amoeba.
5. In flowering plants, structure such as bulbs, corms, tubers, rhizomes and runners are produced by mitotic division. When they separate from the parent, they form a new individual.
   The production of large numbers of offsprings in a short period of time, is possible only by mitosis. In genetic engineering and biotechnology, tissues are grown by mitosis (i.e. in tissue culture).
6. **Regeneration** – Arms of star fish.

7.3.6 Meiosis

In Greek *meioum* means to reduce. Meiosis is unique because of synapsis, homologous recombination and reduction division. Meiosis takes place in the reproductive organs. It results in the formation of gametes with half the normal chromosome number.

Haploid sperms are made in testes; haploid eggs are made in ovaries of animals.

In flowering plants meiosis occurs during microsporogenesis in anthers and megasporogenesis in ovule. In contrast to mitosis, meiosis produces cells that are not genetically identical. So meiosis has a key role in producing new genetic types which results in genetic variation.

Stages in Meiosis

Meiosis can be studied under two divisions i.e., meiosis I and meiosis II. As with mitosis, the cell is said to be in interphase when it is not dividing.

Prophase I is the longest and most complex stage in meiosis. Pairing of homologous chromosomes (bivalents) take place.

Meiosis I-Reduction Division

Prophase I – Prophase I is of longer duration and it is divided into 5 substages – Leptotene, Zygotene, Pachytene, Diplotene and Diakinesis (Figure 7.7).

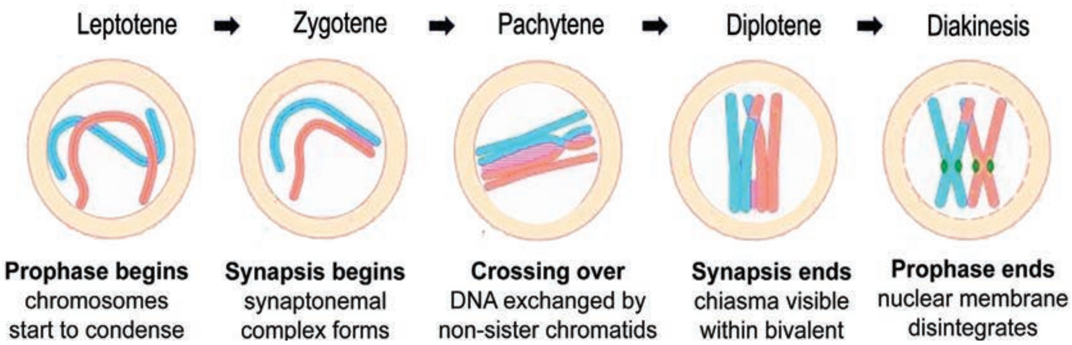


Figure 7.7: Prophase I

Leptotene – Chromosomes are visible under light microscope. Condensation of chromosomes takes place. Paired sister chromatids begin to condense.

Zygotene – Pairing of homologous chromosomes takes place and it is known as **synapsis**. Chromosome synapsis is made by the formation of synaptonemal complex. The complex formed by the homologous chromosomes are called as **bivalent (tetrads)**.

Pachytene – At this stage bivalent chromosomes are clearly visible as tetrads. Bivalent of meiosis I consists of 4 chromatids and 2 centromeres. Synapsis is completed and recombination nodules appear at a site where crossing over takes place between non-sister chromatids of homologous chromosome. Recombination of homologous chromosomes is completed by the end of the stage but the chromosomes are linked at the sites of crossing over. This is mediated by the enzyme recombinase.

Diplotene – Synaptonemal complex disassembled and dissolves. The homologous chromosomes remain attached at one or more points where crossing over has taken place. These points of attachment where 'X' shaped structures occur at the sites of crossing over is called **Chiasmata**. Chiasmata are chromatin structures at sites where recombination has been taken place. They are specialised chromosomal structures that hold the homologous chromosomes together. Sister chromatids remain closely associated whereas the homologous chromosomes tend to separate from each other but are held together by chiasmata. This substage may last for days or years depending on the sex and organism.

Diakinesis – Terminalisation of chiasmata, homologous chromosomes become short and condensed. Nucleolus and nuclear envelope disappears. Spindle fibres assemble.

Metaphase I

Spindle fibres are attached to the centromeres of the two homologous chromosomes. Bivalent (pairs of homologous chromosomes) aligned at the equator of the cell known as **metaphase plate**.

The random distribution of homologous chromosomes in a cell in Metaphase I is called **independent assortment**.

Anaphase I

Homologous chromosomes are separated from each other by shortening of spindle fibers. Each homologous chromosomes with its two chromatids and undivided centromere move towards the opposite poles of the cells. The actual reduction in the number of chromosomes takes place at this stage. Homologous chromosomes which move to the opposite poles are either paternal or maternal in origin. Sister chromatids remain attached with their centromeres.

Telophase I

Haploid set of chromosomes are present at each pole. The formation of two daughter cells, each with haploid number of chromosomes takes place. Nuclei reassembled. Nuclear envelope forms around the chromosome and the chromosomes becomes uncoiled. Nucleolus reappears.

In plants after karyokinesis, cytokinesis takes place by which two daughter cells are formed by the cell plate between 2 groups of chromosomes known as **dyad of cells (haploid)**.

The stage between the two meiotic divisions is called **interkinesis** which is short-lived.

Meiosis II – Equational division.

This division is otherwise called **mitotic meiosis** because it resembles mitosis. Since it includes all the stages of mitotic divisions.

Prophase II

The chromosome with 2 chromatids becomes short, condensed, thick and becomes visible. New spindle develops at right angles to the cell axis. Nuclear membrane and nucleolus disappear.

Metaphase II

Chromosome arranged at the equatorial plane of the spindle. Microtubules of spindle gets attached to the centromere of sister chromatids.

Anaphase II

Sister chromatids separate. The daughter chromosomes move to the opposite poles due to shortening of spindle fibres. Centromere of each chromosome split, allowing to move towards opposite poles of the cells holding the sister chromatids.

Telophase II

Four groups of chromosomes are organised into four haploid nuclei. The spindle disappears. Nuclear envelope, nucleolus reappear.

After karyokinesis, cytokinesis follows and four haploid daughter cells are formed, called **tetrads**.

7.3.7 Significance of Meiosis

- This maintains a definite constant number of chromosomes in organisms.
- Crossing over takes place and exchange of genetic material leads to variations among species. These variations are the raw materials to evolution. Meiosis leads to genetic variability by partitioning different combinations of genes into gametes through independent assortment.
- Adaptation of organisms to various environmental stress.

Table 7.3: Difference between mitosis in Plants and Animals

Plants	Animals
Centrioles are absent	Centrioles are present
Asters are not formed	Asters are formed
Cell division involves the formation of a cell plate	Cell division involves furrowing and cleavage of cytoplasm
Occurs mainly at meristem	Occurs in tissues throughout the body

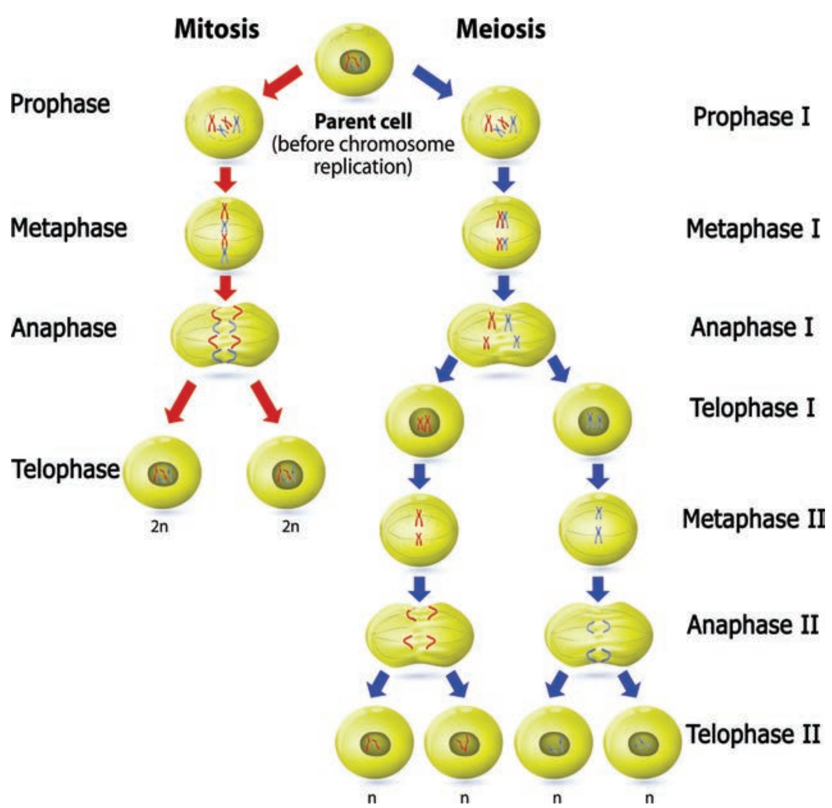
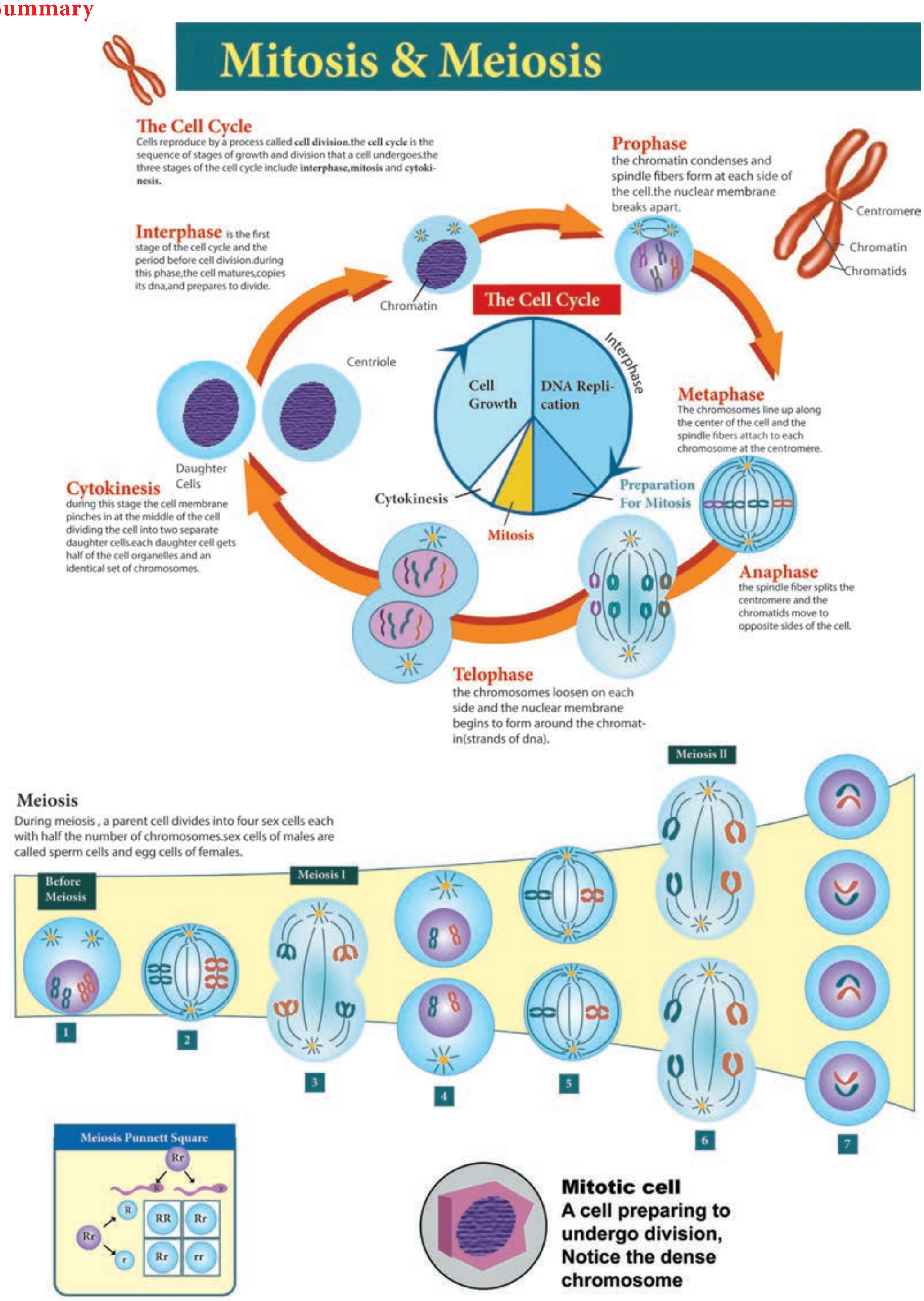


Figure 7.8: Meiosis

Table 7.4: Difference Between Mitosis and Meiosis (Figure 7.8)

Mitosis	Meiosis
One division	Two divisions
Number of chromosome remain the same	Number of chromosomes is halved
Homologous chromosomes line up separately on the metaphase plate	Homologous chromosomes line up in pairs at the metaphase plate
Homologous chromosome do not pair up	Homologous chromosome pairup to form bivalent
Chiasmata do not form and crossing over never occurs	Chiasmata form and crossingover occurs
Daughter cells are genetically identical	Daughter cells are genetically different from parent cell
Two daughter cells are formed	Four daughter cells are formed

Summary



Evaluation

1. The correct sequence in cell cycle is
   a. S-M-G1-G2
   b. S-G1-G2-M
   c. G1-S-G2-M
   d. M-G-G2-S

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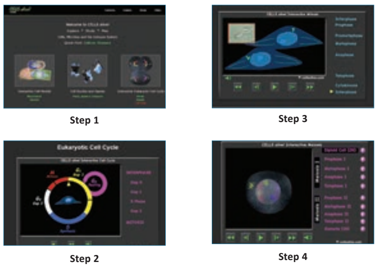
2. If mitotic division is restricted in G1 phase of the cell cycle then the condition is known as
   a. S Phase   b. G2 Phase
   c. M Phase   d. G_0 Phase
3. Anaphase promoting complex APC is a protein degradation machinery necessary for proper mitosis of animal cells. If APC is defective in human cell, which of the following is expected to occur?
   a. Chromosomes will be fragmented
   b. Chromosomes will not condense
   c. Chromosomes will not segregate
   d. Recombination of chromosomes will occur
4. In S phase of the cell cycle
   a. Amount of DNA doubles in each cell
   b. Amount of DNA remains same in each cell
   c. Chromosome number is increased
   d. Amount of DNA is reduced to half in each cell
5. Centromere is required for
   a. transcription
   b. crossing over
   c. Cytoplasmic cleavage
   d. movement of chromosome towards pole
6. Synapsis occur between
   a. mRNA and ribosomes
   b. spindle fibres and centromeres
   c. two homologous chromosomes
   d. a male and a female gamete
7. In meiosis crossing over is initiated at
   a. Diplotene   c. Leptotene
   b. Pachytene   d. Zygotene
8. Colchicine prevents the mitosis of the cells at which of the following stage
   a. Anaphase   c. Prophase
   b. Metaphase   d. interphase
9. The paring of homologous chromosomes on meiosis is known as
   a. Bivalent   c. Disjunction
   b. Synapsis   d. Synergids
10. Write any three significance of mitosis.
11. Differentiate between mitosis and meiosis.
12. Given an account of G_0 phase.
13. Differentiate cytokinesis in plant cells and animal cells.
14. Write about Pachytene and Diplotene of Prophase I.

ICT Corner

Cell Division

How do cells are multiply?



Steps

- Scan the QR code
- Click Mitosis and start the animation press play
- Select mitosis in the top of the page – play it - use forward button to slow down
- Select meiosis in the top of the page – play it - use forward button to slow down

Activity

- Select meiosis and cell cycle.
- Record your observations.

URL: https://www.cellsalive.com/

* Pictures are indicative only

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