CELL CYCLE (CELL DIVISION)

- Growth and reproduction are characteristics of cells, indeed of all living organisms.
- All cells reproduce by dividing into two, with each parental cell giving rise to two daughter cells each time they divide.
- These newly formed daughter cells can 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.
- In other words, such cycles of growth and division allow a single cell to form a structure consisting of millions of cells.
- Cell division is a very important process in all living organisms.
- Some substances stimulate cell division these are called **mitogen** - **e.g. Cytokinins, Epidermal Growth Factor or EGF, Platelet Derived Growth Factor or PDGF, Lymphokines**.
- Some substances inhibit cell division these are called mitotic poison **e.g. Cyanides, Azides, Chalones, Colchicine.**
- **Low surface volume ratio, nucleocytoplasmic ratio also stimulate cell division in the cell.**
- During the division of a cell, DNA replication and cell growth also take place.
- All these processes, i.e., cell division, DNA replication, and cell growth, hence, have to take place in a coordinated way to ensure correct division and formation of progeny cells containing intact genomes.
- The sequence of events by which a cell duplicates its genome, synthesises the other constituents of the cell and eventually divides into two daughter cells is termed cell cycle.
- 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

- It involves programmed cyclic changes in the cell that leads to duplicates its genome, change in cellular components and ultimately cell divides to form two cells and is termed as cell cycle.
- This process is genetically controlled.
- The duration between two cell cycles is generation time.
- The duration of cell cycle is vary from organism to organism and for difference cell type. For example **human cell** takes approximately **24 hours** while **yeast cell** takes about **90 minutes** to divide (one time).

Cell cycle involves two stages

(1) Interphase or I-phase or Intermitosis or Nondividing phase or Energy phase.

- It takes 95% of the duration of a cell cycle.
- It is longest phase. It is differentiated into three stages.

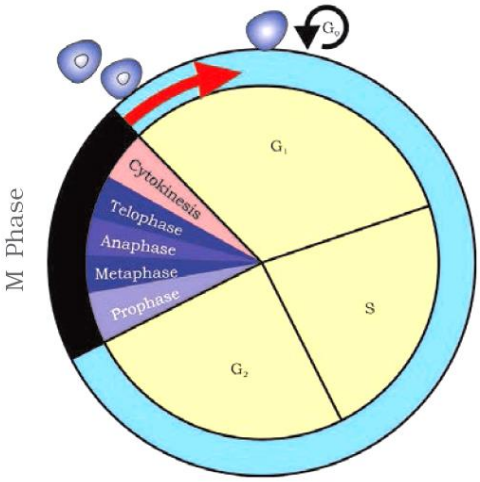
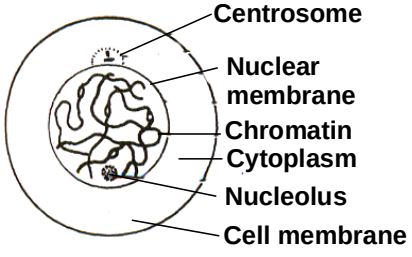


Figure: A diagrammatic view of cell cycle indicating formation of two cells from one cell

(A) G_1-phase or first gap phase or first growth phase or pre synthetic phase or post mitotic phase

- In this phase some changes occur like synthesis of RNA, proteins, enzymes for DNA synthesis, amino acids for histone formation.
- Most of the organelle duplication also occurs in this phase.
- Some time, G_1-phase arrest at the middle and cell undergoes differentiation it is called **G_0 phase** or **quiescent** stage.
- In this stage cells remain metabolically active but no longer proliferate until division required.
- The Deciding factors are energy producing substances and mitogens this point is called check point.
- Once a cell is passed from check point this stage is called **Antephase (Bullough)** now cell will divide even in unfavourable conditions.
- **Size of cell and nucleus becomes doubled in G_1 phase.**

(B) S-phase (Synthetic phase):



(i)

Figure: Interphase

- **Replication of DNA** of chromosome takes place in S-phase that is amount of DNA per cell doubles but not chromosome number. For example if amount of DNA is 2C than it will becomes 4C in this phase.
- **Histone protein synthesizes** in this phase.
- **Replication of centrioles (centrosome) takes place in cytoplasm.**

(C) G_2-phase (Second gap phase or second growth phase or postsynthetic phase or pre-mitotic

phase):

- **It is the phase of cytoplasmic growth.**
- Synthesis of RNA and proteins takes place. **Tubulin protein** is **formed**.

(2) M-Phase (Mitotic phase): It divides into two stages

(A) Karyokinesis **(B) Cytokinesis**

MITOSIS

It occurs either in diploid (animal) cells or both in diploid and haploid (plant) cells.

(A) Karyokinesis : It can be divided into four stages for sake of convinience

(I) Prophase **(II) Metaphase** **(III) Anaphase** **(IV) Telophase**

(I) Prophase: It is longest phase.

It involves three phases.

(a) Early prophase:

- Chromatin undergoes dehydration to form long thin & coiled chromosomes that are called spiralization and their ends are indistinct and this stage is called **spireme stage**.
- Centrosomes move away to each other and move towards opposite poles.

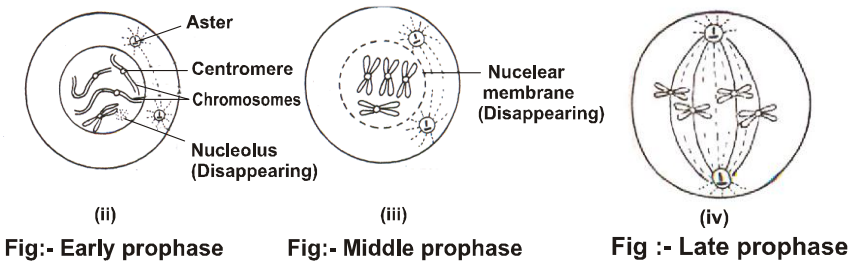
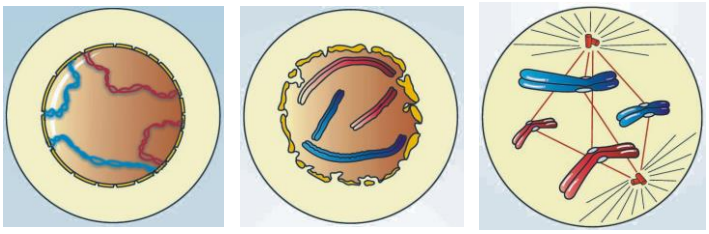


Fig:- Early prophase Fig:- Middle prophase Fig :- Late prophase



Early Prophase Late Prophase Transition to metaphase

(b) Mid prophase:

- Chromosomes are thickened and shifted in the peripheral part of nucleus.
- Formation of Astral rays starts. Nuclear membrane starts breakdown. Nucleolus reduces in size.

(c) Late prophase:

- Chromosome are comparatively thickened.
- Centrosomes are reached to the opposite poles.
- In this phase nuclear membrane is disappeared.
- Nucleolus, ER & GB are also disappeared.
- Aster is formed at each pole by a pair of centrioles and astral rays.
- Centrioles start formation of spindle fibres.

- Centrosome helps in the initiation of cell division in animal cells by forming spindle.
- **In plant cells centrosome is absent.**
- **The spindle fibre arise from tubulin protein by gelation in the cytoplasm thus in plant cell centriole and asters have no role in the formation of spindle apparatus.**
- The middle broad part of spindle apparatus is called equator.

(II) Metaphase:

- **The shape, size and structure of chromosomes can be studied in the metaphase stage.**

  Spindle fibres consists of **mostly tubulin protein, some RNA** and trace amount of actin, myosin & Lipid.
- Spindle fibres are of three types.

  (A) Continuous fibres: That connect two poles.

  (B) Discontinuous fibres: They originate from a pole and do not reach at other pole.

  (C) Chromosomal fibres: They connect chromosome and poles.
- The tightening of chromosomal fibres brings chromosomes at the equator. This process is called **congression or metakinesis**.
- The centromeres of all the chromosomes arrange in linear sequence at the equator to form **single metaphase plate (That is plane of alignment of the chromosomes at equator).**
- Kinetochore of chromosomes connect chromosomes to the spindle fibre. Each chromosomes has two distinct chromatids.
- The arms of each chromosome lie in different direction and the centromere lie on equator.

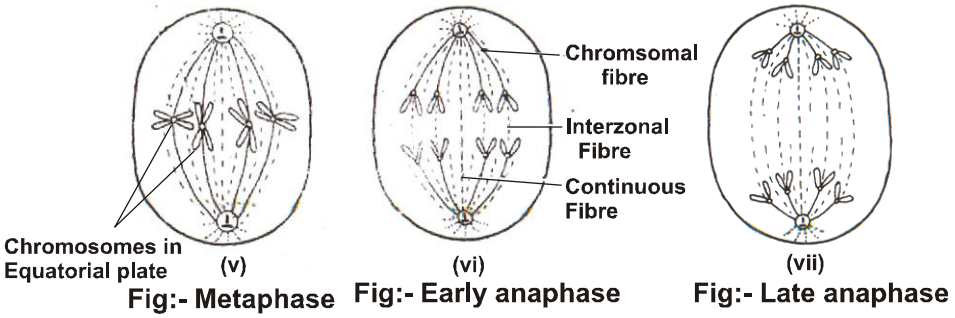
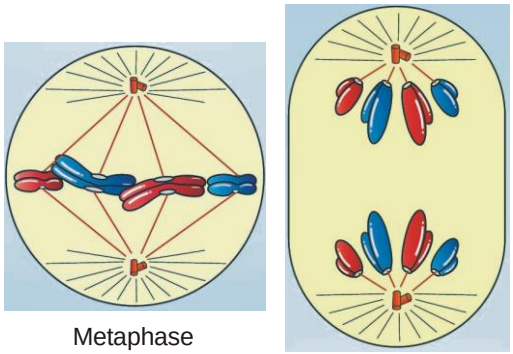


Fig:- Metaphase Fig:- Early anaphase Fig:- Late anaphase



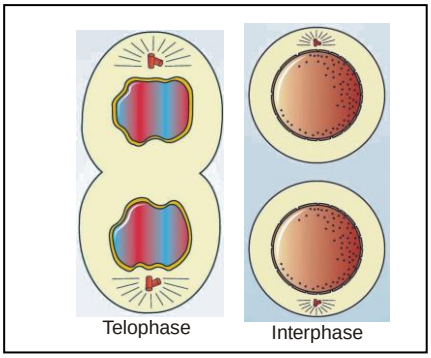
Metaphase Anaphase

(III) Anaphase:

- It causes equatorial division in each chromosome as a result the number of chromosomes becomes doubled.
- Now half chromosomes move towards one pole and remaining half chromosomes move towards opposite pole by the constriction of chromosomal fibre. It is called **Anaphasic movement**.
- The chromosomes are inter connected by **interzonal fibres**.
- At this time centromere of each chromosome lies towards poles and its arms behind it.
- The rate of anaphasic movement of each chromosome is 0·2 μm to 5μm / min. 20–25 ATP are consumed by a chromosome during anaphasic movement.
- Each chromosome has **single chromatid** & it is **V-shaped / L-shaped / J-shaped / I-shaped.**

(IV) Telophase:

- It is reversal of prophase.
- Chromosomes are reached on the opposite poles and now they become uncoiled, loose their idividuality and converted into long thin chromatin network.
- Nuclear membranes, ER, GB are reappeared. NOR forms nucleolus.
- Thus each pole has a nucleus in telophase stage.
- Spindle fibres are disappeared.



(B) Cytokinesis: It is a division of cytoplasm. It starts in late anaphase & Completed at the end of telophase.

Cytokinesis comprises two types.

(i) Cell furrow or cell cleavage method

- A viscous fibrous dense **mid body** is formed in the centre.
- Constriction of peripheral microfilaments takes place toward centre **(Centripetal)** and finally both sides meet and two daughter cells are formed **e.g. Animal cell.**

(ii) Cell plate method

- In case of plant cell, some spindle fibres exist that form **phragmoplast**.
- **Golgi vesicles and some ER vesicles** deposite in the central part of phragmoplast and their deposition proceeds towards peripheral part **(centrifugal)** and finally a cell plate is formed followed by the formation of middle lamella.
- Now primary wall deposites at each side of middle lamella and ultimately both cells get seperated to form two daugther plant cells.
- In some organisms karyokinesis is not followed by cytokinesis as a result of which multinucleate condition arises leading to the formation of syncytium **(e.g.liquid endosperm in coconut)**.

Significance of Mitosis

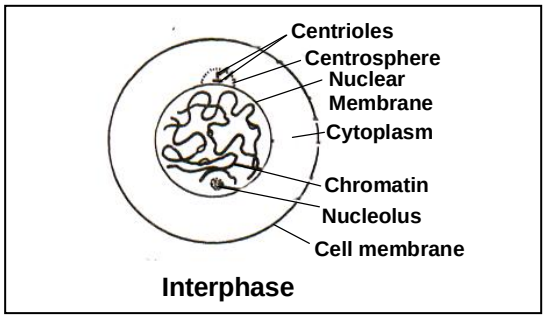
1. Mitosis results in two daughter cells which are gentically identical.
2. Growth and repair (cells of the upper layer of the epidermis, cells of the lining of the gut, and blood cells are being constantly replaced).
3. To restore nucleole-cytoplasmic ratio.

Key points of Mitosis

- Number of chromosomes remains same after mitosis.
- DNA content of daughter cells will be same as that of parent cell (G_1).
- Two cells will be formed after mitosis.
- There will be no change in ploidy of the daughter cells.
- During metaphase, the chromosomes are arranged in a single metaphasic plane.
- Sister chromatids get separated in Anaphase of mitosis.

MEIOSIS

- Always occurs in diploid cells to form haploid cells
- It is essential for sexual reproduction.
- It involves meiosis-I and meiosis-II. Interphase involves - G_1, S, G_2 phase. Out of them G_2 phase is short.
- Centrosome replicates in this stage.



Interphase

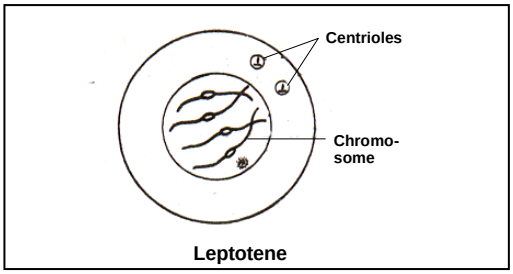
Meiosis-I: M-phase-It involves karyokinesis & cytokinesis.

Karyokinesis: It involves **prophase-I, Metaphase-I, Anaphase-I, Telophase-I.**

(A) Prophase- I: It is longest and complex phase. It can be differentiated into five stages.

(a) Laptotene:

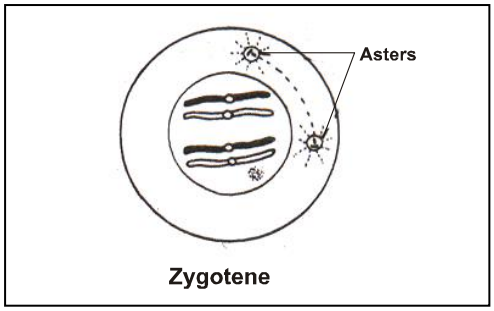
- Chromatin is condensed to form chromosomes.
- All the chromosomes converge towards a common point near centrosome and form basket like arrangement this stage is called **bouquet stage**.
- In some plants they form **synzetic knot e.g. Lilium**.
- The chromatids of chromosomes are not distinct due to nucleoprotein.



Leptotene

(b) Zygotene:

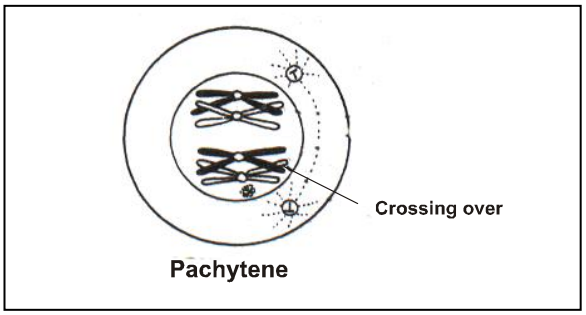
- Chromosomes are comparatively small & thick.
- Homologous chromosomes perform pairing.
- One **homolgous chromosome** is maternal and second is paternal.
- This pairing of two homolgous chromosomes is called **synapsis / Syndesis.**
- It forms **Bivalent**.



- Nucleoprotein core form a complex that is called **syneptonemal complex.**
- Syneptonemal complex consists of one central element and two lateral element.
- Each lateral element lies between two chromatids of a chromosome.
- Each central element lies between two chromosomes.

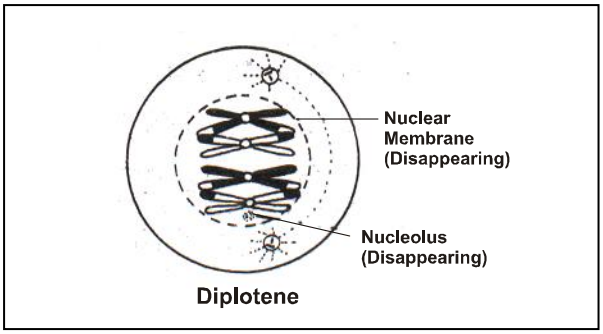
(c) Pachytene:

- In this stage **Recombination nodule** is formed between two nonsister chromatids.
- The exchange of segments of **nonsister chromatids** between two **homolgous chromosomes** of a bivalent is called **crossing over (Morgan)**.
- **Recombinase** enzyme catalyzes this process.
- Chromatids of bivalents are distinct and clearly appears as **tetrads**
- Each Bivalent has four chromatids and two centromeres.



(d) Diplotene:

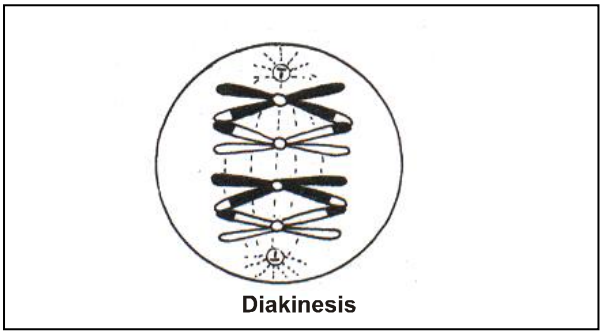
- Syneptonemal complex starts dissolving in early diplotene and two cross overed non sister chromatids start move apart. Homologous chromosomes of each bivalent start seperation.
- They are connected at certain points (at sites of cross overs) these are called **chiasmata** and the bivalents are now called tetrad.
- Chiasmata are the results of crossing over.
- In some animals (oocytes of some vertibrates) chromosomes become enlarged in size in diplotene stage they are called **Lampbrush chromosome e.g. Amphibians.**
- Nuclear membrane starts disintigration. Nucleolus decreases in size.



Diplotene

(e) Diakinesis:

- Separation of homologous chromosomes proceeds towards terminal part (terminalization) by the shifting of chiasmata towards chromsomal ends.


Diakinesis

- Centrioles are reached on opposite poles and form aster with astral rays spindle is formed that is amphiastral in animal cell and anastral in plant cell.
- This stage represents transition to metaphase.

(B) Metaphase-I:

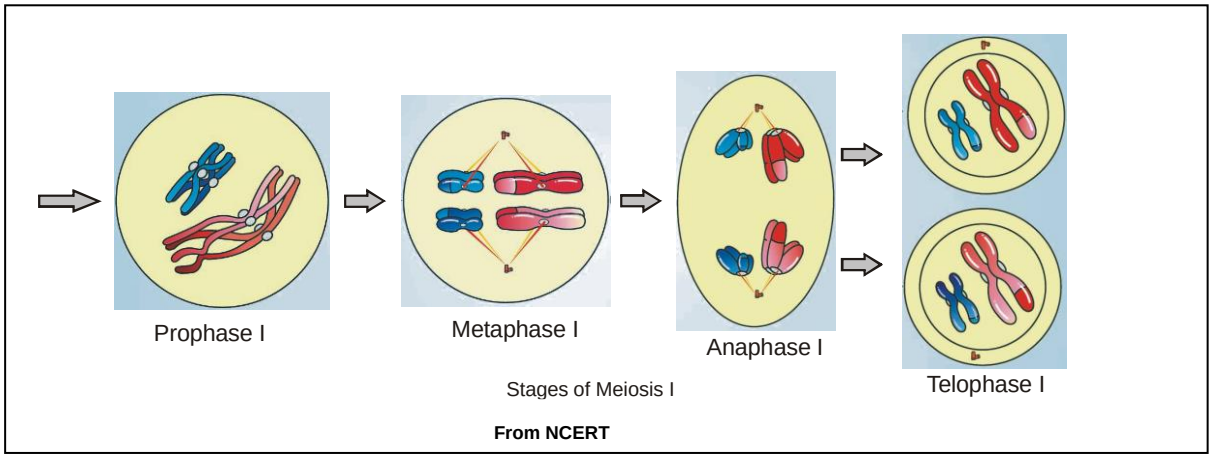
- Congression brings the bivalents on equator.
- Bivalents arrange in **two raws on equator** to form **double metaphasic plate.**
- The arms of homologous chromosomes lies parallel to the equator and their centromeres are projected outwardly towards poles.
- Each chromosome in a bivalent is connected to the spindle pole of its side by a single kinetochore microtubule (chromosomal tractile fibre) instead of two as in metaphase of mitosis.

(C) Anaphase-I:

- In this stage **reduction division** takes place & **segregation of Mendelian factors** occurs.
- The chromosome no. becomes half (2n–n).
- Maternal and paternal chromosomes of each bivalent are completely seperated it is called **disjunction**.
- They move in opposite direction towards opposite poles due to constriction of chromosomal fibres.
- It is called anaphasic movement.
- Thus bivalents are converted in univalents.
- Each univalent has divergent two chromatids.
- At the end of this phase chromosomes are reached at opposite poles.

(D) Telophase-I:

- Regrouping of Dyad chromosomes occur at each pole
- Chromosomes undergo despirilization, become thin & elongated.
- Nucleolus is rarely formed. Nuclear membrane reappears and each pole has a haploid nucleus.
- Cytokinesis may or may not occur after meiosis-I



Stages of Meiosis I

From NCERT

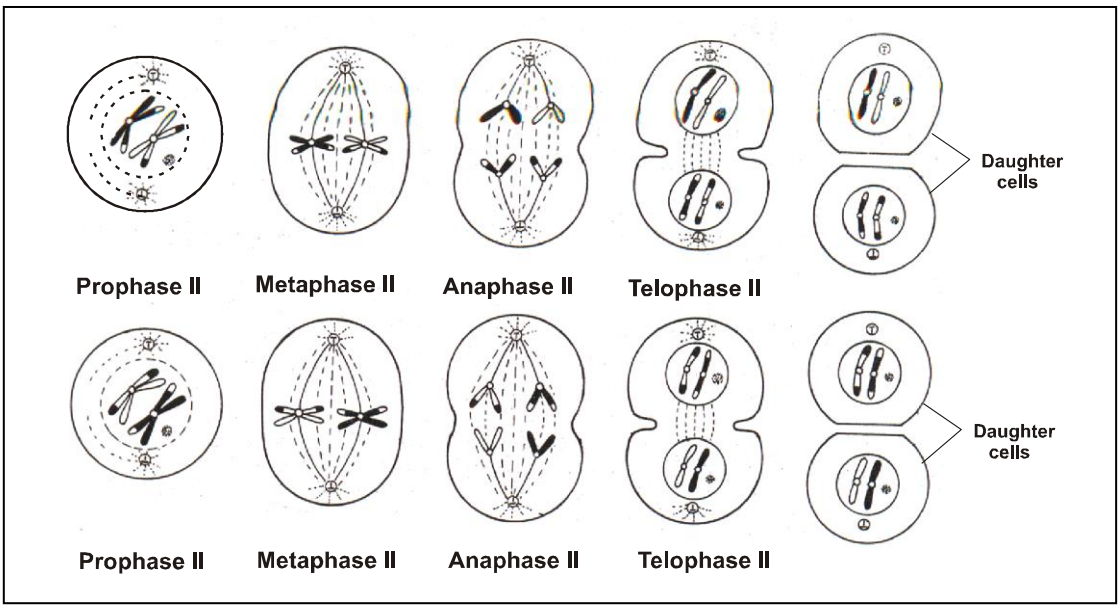
- In some plants like *Trillium* and most animals Metaphase-II directly occurs after Anaphase-I or telophase-I enters into Prophase-II.

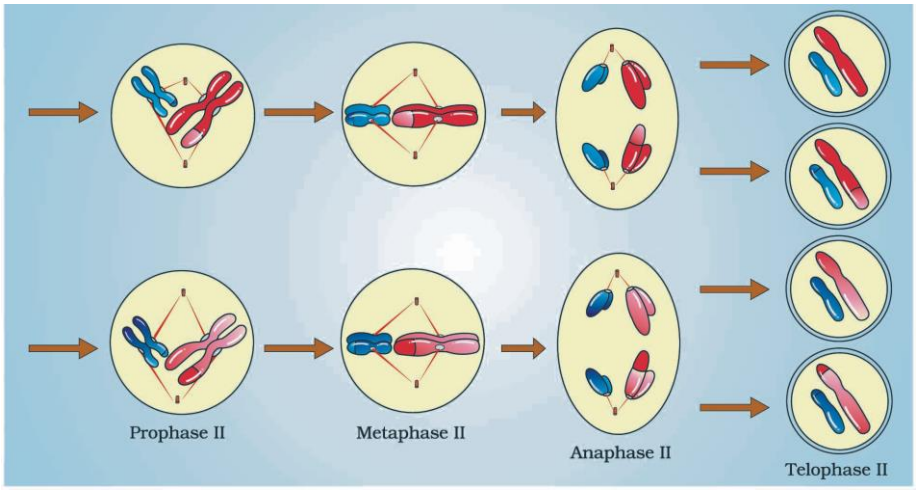
Interkinesis

- It is called intrameiotic interphase.
- In this phase some deficient substance form but synthesis of DNA does not occur.

Meiosis-II

- It is also called homotypic or homoeotypic or equational division.
- It is just like mitosis but occurs in halpoid nuclei.





Stages of Meiosis II

From NCERT

At the end of meiosis-II four haploid cells are formed that are genetically different.

Significance of meiosis:

(a) Variations: Variations are important for evolution.
  (i) Independent assortment of chromosomes
  (ii) Crossing over
  (iii) Irregular disjunction
  (iv) Gene mutation during replication & nicking for crossing over.

(b) Polyploidy: Failure of chromosomes to separate during anaphase-I leads to polyploidy.

(c) Maintenance of chromosome number

(d) Sexual reproduction

Key points of Meiosis:

Meiosis-I

1. **Prophase-I :** Devided into five stages on the basis of **chromosomal behaviour.**
   - **(a) Leptotene -** Bouquet stage
   - **(b) Zygotene -** Formation of synaptonemal complex, Synapsis or pairing of homologous chromosomes and appearance of bivalent.
   - **(c) Pachytene -** Formation of recombination nodule, activity of recombinase enzymes, crossing over between non-sister chromatids of homologous chromosomes, appearance of tetrad and persistence of synaptonemal complex.
   - **(d) Diplotene -** Dissolution of synaptonemal complex, chiasmata formation due to motion of cross overed chromatids apart.
   - **(e) Diakinesis -** Terminalisation of chiasmata, disappearance of nuclear membrane, nucleolus, ER and golgi body.
2. **Metaphase-I:** Two metaphasic planes**.**
3. **Anaphase-I:** Separation of homologous chromosomes.
4. **Telophase-I:** Completion of karyokinesis-I
5. **Cytokinesis-I:** Two cells are formed with just half number of chromosomes as that of parent cell.
   Note: Now two cells will enter into successive steps.

Interkinesis: Only deficient proteins are synthesized.

Meiosis-II

1. **Prophase-II :** Disappearance of nuclear membrane, nucleolus, ER and golgi body.
2. **Metaphase-II:** Single metaphasic plane.
3. **Anaphase-II:** Sister Chromatids move apart.
4. **Telophase-II:** Completion of karyokinesis-II.
5. **Cytokinesis-II:** In total four cells will be formed with half the chromosomes and DNA content that of parent cell (cell of G_1 phase).

Difference between Mitosis and Meiosis			
	Mitosis		**Meiosis**
1	The cells undergoing mitosis may be haploid or diploid.	**1**	The cells undergoing meiosis are always diploid.
2	It is a single division which produces two cells.	**2**	Meiosis is a double division. It gives rise to four cells.
3	Subsequent mitotic divisions are similar to earlier ones.	**3**	The two divisions of meiosis are not similar. The first one is the heterotypic or reductional while the second one is homo typic or equational like mitosis.
4	Each chromosome replicates in the interphase before every division.	**4**	The chromosomes replicate only once, prior to meiosis.
5	The number of chromosomes remains the same after mitosis.	**5**	The number of chromosomes is reduced to one half after Meiosis.
Prophase			
6	Prophase is of shorter duration.	**6**	Prophase I is of longer duration while prophase II is very brief.
7	Each chromosome has two distinct chromatids.	**7**	Chromosomes of prophase I do not show distinct chromatids.
8	No bouquet stage is recorded.	**8**	Chromosomes of animals and some plants show convergence towards one side during early prophase I. It is known as bouquet stage.
9	Pairing of chromosomes does not occur in mitosis	**9**	Pairing or synapsis of homologous chromosomes takes place during zygotene of prophase I and continues up to metaphase-I
10	A synaptonemal complex is absent.	**10**	Synapsed homologous chromosome develop a synaptonemal complex.
11	Crossing over is absent.	**11**	Crossing over or exchange of similar segments between nonsister chromatids of homologous chromosomes usually takes place during pachytene stage.
12	Chiasmata are absent.	**12**	Chiasmata or visible connections between homologous chromosomes of bivalents are observed during diplotene, diakinesis

Metaphase			
13	Centromeres produce a single metaphasic plate.	**13**	A double metaphasic plate is formed by centromeres in metaphase I but only one in metaphase II.
14	Only the centromeres lie at the equator. The limbs of chromosomes are oriented in various directions.	**14**	Limbs of the chromosomes mostly lie at the equator while the centromeres project towards the poles in metaphase I.
15	A centromere is connected with both the spindle poles.	**15**	A centromere is connected to one spindle pole in metaphase I but both in metaphase II.
16	Two chromatids of a chromosome are genetically similar.	**16**	The two chromatids of a chromosome are often genetically dissimilar due to crossing over.
Anaphase			
17	A centromere splits length-wise to form two centromeres in the beginning of anaphase.	**17**	Centromeres do not divide during anaphase I but do so in anaphase II.
18	Anaphasic chromosomes are single stranded.	**18**	Chromosomes are double stranded in anaphase I but single stranded in anaphase II.
Telophase			
19	Telophase is longer and produces interphase nuclei.	**19**	Telophase I is shorter and nuclei never enter the inter-phase.
Cytokinesis			
20	Cytokinesis follows every mitosis. It produces two cells.	**20**	Cytokinesis often does not occur after the first or reductional division. It is then simultaneous after second division to result in four new cells.

Table: Displays the various parameters changing during cell cycle (Human somatic cell with 2C DNA content for 46 chromosomes)

S.No.	Phase of Cell cycle		DNA content	No. of chromosomes[1]	No. of Chromatids[2]	No. of Centromeres[3]
1.	Interphase	G_1	2C	46	46	46
		S	Early - 2C Late - 4C	Early - 46 Late - 46	Early - 46 Late - 92	Early - 46 Late - 46
		G_2	4C	46	92	46
2.	Mitosis	Prophase	4C	46	92	46
		Metaphase	4C	46	92	46
		Anaphase	4C	92	92	92
		Telophase	4C	92	92	92
3.	Cytokinesis - Per cell		2C	46	46	46

1. In interphase, there are no chromosomes as the genetic material is present in the form of chromatin material.

2. In interphase, there are no chromatids as the genetic material is present in the form of chromatin material.

3. In interphase as genetic material is not packaged in the form of chromosomes so, as such centromeres are also not defined.

Note: In all (1, 2 and 3) we have genetic material for that many chromosomes, chromatids and centromeres which will appear later in prophase.

Table: Displays the various parameters changing during cell cycle (Human germ cell with 2C DNA content for 46 chromosomes)

S.No.	Phase of Cell cycle		DNA content	No. of chromosomes[4]	No. of Chromatids[5]	No. of Centromeres[6]
1.	Interphase	G_1	2C	46	46	46
		S	Early - 2C Late - 4C	Early - 46 Late - 46	Early - 46 Late - 92	Early - 46 Late - 46
		G_2	4C	46	92	46
2.	Meiosis-I	Prophase-I	4C	46	92	46
		Metaphase-I	4C	46	92	46
		Anaphase-I	4C	46	92	46
		Telophase-I	4C	46	92	46
3.	Cytokinesis-I Per cell		2C	23	46	23
4.	Interkinesis Per cell		2C	23	46	23
5.	Meiosis-II	Prophase-II	2C	23	46	23
		Metaphase-II	2C	23	46	23
		Anaphase-II	2C	46	46	46
		Telophase-II	2C	46	46	46
6.	Cytokinesis-II Per cell		C	23	23	23

4. In interphase, there are no chromosomes as the genetic material is present in the form of chromatin material.

5. In interphase, there are no chromatids as the genetic material is present in the form of chromatin material.

6. In interphase as genetic material is not packaged in the form of chromosomes so, as such centromeres are also not defined.

Note: In all (4, 5 and 6) we have genetic material for that many chromosomes, chromatids and centromeres which will appear later in prophase.

Resonate the Concept

(1) **Rudolf Virchow** stated that new cell develops from the division of pre-existing cell.

(2) **Strasburger** stated that new nucleus arises from pre-existing nucleus. Strasburger firstly observed mitosis in plant cell.

(3) **Van Beneden and Flemming** discovered mitosis in animal cell. The term **'Mitosis' coined by Flemming**.

(4) The term **meiosis** coined by **Farmer and moore**.

(5) **Cyclin protein: Cyclin Dependent protein Kinases (CDK) regulate the cell cycle.**

(6) **Prometaphase:** Some scientists considered prometaphase stage between prophase and metaphase. In this stage aster formation is completed. Formation of spindle fibres is also completed. Nuclear membrane and nucleolus are completely disappeared.

(7) **Eumitosis:** Formation of Extranuclear spindle and degeneration of nuclear membrane involve in it.

(8) **Premitosis:** In some **protists, fungi and algae**, formation of intranuclear spindle takes place. Nuclear membrane exists.

(9) Synapsis involves three types.

(i) Procentric: It starts from centromere and proceeds towards terminal parts.

(ii) Proterminal: It begins from terminal part.

(iii) Inter mediate type: It can begin at any point of chromosomes.

(10) Amitosis: It was discoverd by **Remak**. In this type, nucleus elongates& constricted in the middle and divide to form two daughter nuclei. Spindle formation is absent **e.g. meganucleus of Parmaecium,** cells of endosperm.

(11) Brachymeiosis: It is found in ascus bearing fungi that includes two reduction divisions and one equational division which reduce the chromosome number from tetraploid to haploid stage.

(12) Types of Meiosis:

(i) Zygotic or Initial meiosis: It occurs during zygote or zygospore germination **e.g. Ulothrix, Spirogyra and Chlamydomonas.**

(ii) Sporic or Intermediate meiosis: Meiosis occurs at the time of microspore or megaspore formation **e.g. Bryophytes, Pteridophytes, Gymnosperms and Angiosperms.**

(iii) Gametic meiosis or Terminal meiosis: It occurs at the time of gamete formation **e.g. Animals**

(13) Regulation of cell cycle

There are two key classes of regulatory molecules:

- **Cyclin -** a group of proteins that control the progression of cells through the cell cycle by activating cyclin - dependent kinase (CDK) enzymes.
- **CDKs -** A family of protein kinases that are involved in regulating transcription mRNA processing and the differentiation of cells.

The cell cycle is based on three main check points.

Phase G_1 - DNA integrity and cell size.

Phase S - DNA damage and duplication.

Phase M - Attachment of kinetochore and a spindle fibre.

The key role of checkpoint proteins is to detect DNA damage and send a signal to delay cell cycle until the damage chromosomes are repaired.