Course code: BIO205

Course Title: Introductory Molecular Biology

Content: Cell Division

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Cell division

A multicellular organism starts its life as a single cell, and it undergoes repeated division, thus, the growth and development of every living organism depends on the growth and multiplication of its cells. The cell increases in size due to growth and it is the characteristic feature of all the living organisms. After the cell attains maximum growth, it begins to divide. The vegetative growth of an organism takes place by an increase in the number of cells through cell divisions which follows the geometrical progression.

The cell division is a continuous and dynamic process, and it involves the following three stages:

1. DNA or genome replication
2. Nuclear division or **karyokinesis**
3. Cytoplasmic division or **cytokinesis**

On the basis of number of genomes present in the daughter cells in comparison to the dividing parent cell, the cell division is of two types - **mitosis** and **meiosis**.

1. **Mitosis**- The term mitosis was coined by W. Flemming in 1882. The multiplication of a body cell into two daughter cells of **equal** size and containing the same number of chromosomes as in the parent cell is called mitosis or **somatic division**.

2. **Meiosis**- The term meiosis was first coined by J. B. Farmer (1905) with J. E. Moore. Meiosis occurs only in gonads (in germ mother cells) during the formation of

gametes like sperm and ovum. Meiosis is a process by means of which double number or 2N or diploid chromosomes is reduced to its half number or N or haploid. It is also called **reduction process**.

Differences between Prokaryotic and Eukaryotic Cells

	Prokaryotic Cell	**Eukaryotic Cell Division**
1.	A prokaryotic cell is surrounded by a single membrane layer.	A eukaryotic cell is surrounded by a double membrane layer.
2.	Respiratory enzymes are present on cell membranes.	Respiratory enzymes are absent.
3.	Thylakoids occurs free in cytoplasm.	Thylakoids occurs within the chloroplast.
4.	Cytoplasm lacks organelles like centrosomes, endoplasmic reticulum, mitochondria, Golgi apparatus, microfilaments, intermediate filaments, microtubules, and micro bodies. While ribosomes are present.	All the cell organelles are present in the cell along with ribosomes.
5.	Circular DNA is present without associated proteins.	Nuclear DNA is linear and is associated with proteins, while extra nuclear DNA is present without proteins.
6.	Nucleolus absent.	Nucleolus present.
7.	Cells are haploid.	Cells are diploid.
8.	Most prokaryotes are asexual organisms.	Most eukaryotes are sexual organisms.

Prokaryotic Cell Division

Prokaryotes are much simpler in their organisation than eukaryotes. There are a great many more organelles in eukaryotes and also more chromosomes. The usual method of prokaryote cell division is termed binary fission, an example of asexual reproduction. The prokaryotic chromosome is a single, simple DNA molecule that first replicates, then attaches each copy to a different part of the cell membrane. When the cell begins to pull apart, the replicate and original chromosomes are separated. Following cell splitting (cytokinesis), there are then two cells of identical genetic composition (except for the rare chance of a spontaneous mutation).

The prokaryote chromosome is much easier to manipulate than the eukaryotic one. We thus know much more about the location of genes and their control in prokaryotes. One consequence of this asexual method of reproduction is that all organisms in a colony are genetic equals. When treating a bacterial disease, a drug that kills one bacterium (of a specific type) will also kill all other members of that clone (colony) it comes in contact with. For example, Escherichia coli, a bacterium divides by binary division.

Eukaryotic Cell Division

Due to their increased numbers of chromosomes, organelles and complexity, cell division in eukaryotes is more complicated, although the same processes of replication, segregation, and cytokinesis still occur.

Cell Cycle

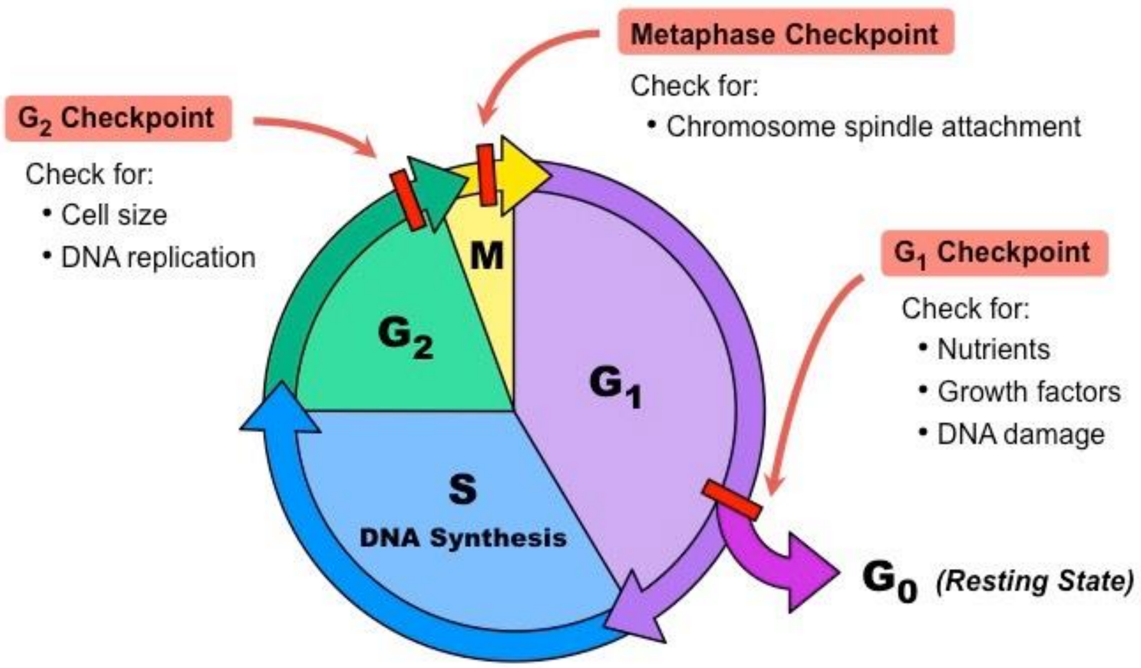
A cell starts its cycle in diploid condition. Every cell having the capacity to divide passes through a regular cycle of changes known as cell cycle.

The Cell Cycle is the sequence of growth, DNA replication, growth and cell division that all cells go through. Beginning after cytokinesis, the daughter cells are quite small and low on ATP. They acquire ATP and increase in size during the G1 phase of Interphase. Most cells are observed in Interphase, the longest part of the cell cycle.

After acquiring sufficient size and ATP, the cells then undergo DNA synthesis (replication of the original DNA molecules, making identical copies, one "new molecule" eventually destined for each new cell) which occurs during the S phase.

Phases of cell cycle

Cell cycle consists of two stages: A long un-dividing stage called **interphase** or **I-phase** and a short dividing stage called **mitotic** or **M-phase**



Cell cycle checkpoints

- Cell cycle checkpoints are mechanisms that ensure the fidelity and continued viability of mitotic division in cells.
- In a cell cycle, multiple checkpoints have been discovered, each with different specific roles:

G_1 Checkpoint

- Determine appropriate growth conditions (sufficient nutrients, cell size, presence of growth factors, etc.)
- Assess level of DNA damage (from ionising radiation or UV).

G_2 Checkpoint

- Determine state of pre-mitotic cell (suitable cell size required for successful division)
- Identify replication faults (changes to DNA sequence will distort genetic fidelity in daughter cells).

Metaphase Checkpoint (Mitosis)

- Ensure proper spindle assembly and correct attachment to centromeres (prevents non-disjunction events).

G0 Stage

- Not all cells are continually replicating – some cells may enter into a non-dividing **G_0** stage
- Some cells may either be dormant, ageing or deteriorating.
- Cells enter the G_0 phase from the G_1 phase; quiescent cells may re-enter G_1 at a later time (senescent cells do not)
- Specialised cells will often permanently enter G_0, as differentiation has prevented their capacity for further division
- Neurons are examples of cells that have been arrested in a G_0 state – these cells are *amitotic* (cannot divide).
- Some cells divide rapidly (beans, for example take 19 hours for the complete cycle.
- red blood cells must divide at a rate of 2.5 million per second).
- Others, such as nerve cells, lose their capability to divide once they reach maturity.
- Some cells, such as liver cells, retain but do not normally utilize their capacity for division.
- Liver cells will divide if part of the liver is removed. The division continues until the liver reaches its former size.
- Cancer cells are those which undergo a series of rapid divisions such that the daughter cells divide before they have reached "functional maturity".

Control of Cell Cycle

1. **Nucleo-cytoplasmic Ratio**

- The cell division starts when the ratio between the volume of the nucleus and the volume of the cytoplasm is upset.
- This was proposed by Hertwig in **1910**.
- As the cell grows, the synthesis of biomolecules (proteins, nucleic acids, lipids) and other cellular components takes place.
- During synthesis of these molecules, movements of materials through the nuclear and the cell membranes occurs.
- With the growth of the cell, its volume increases more than the surface of the nucleus and the cell, and at a critical point, the surface of the nucleus become inadequate for the exchange of materials between the nucleus and the cytoplasm required for further growth.

- The cell divides at this stage and regains the optimum and efficient nucleo-cytoplasmic ratio that allows the growth.

2. **Surface-Volume Ratio**
- With the growth of the cell size, its volume increases more than its surface area.
- It is thought that there is a critical point at which the cell division starts, and the division of the cell greatly increases the surface without increasing the volume.
- All the materials of the cell required for its maintenance and growth are drawn through its surface.
- A stage will be reached when the surface area is insufficient to supply the large volume of the cell.
- The only exemption to this theory is in case of starved cells, which may divide without doubling their size and form smaller daughter cells.

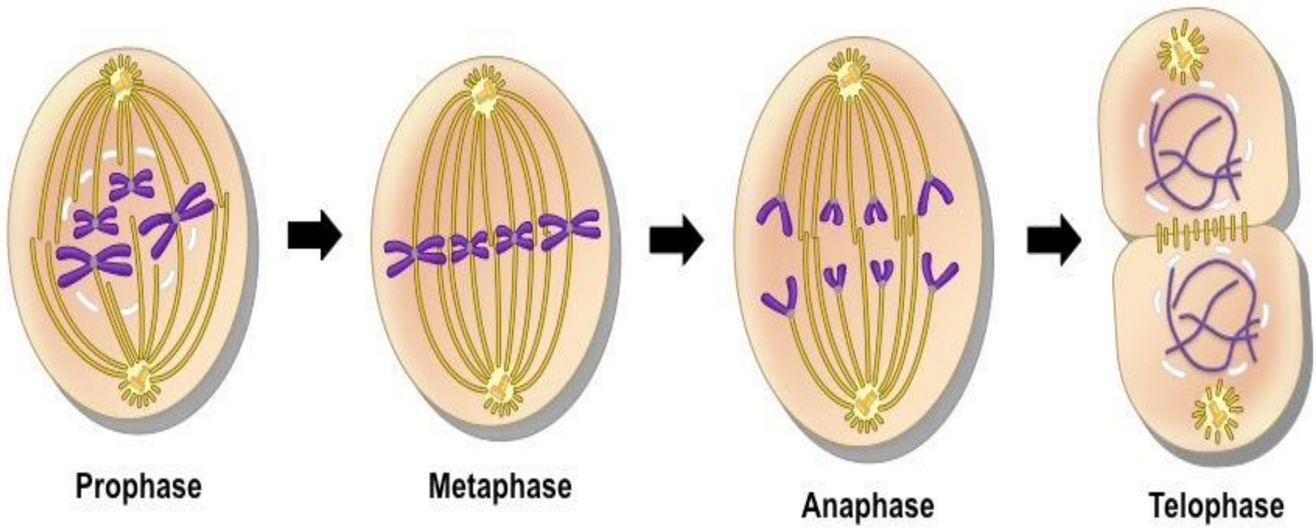
3. **Nucleolus**
- Damage to nucleolus at a certain critical time stops cell division.

4. **Cyclin**
- The concentration of the protein called cyclin appears to control mitosis as it builds up during interphase and is degraded during mitosis.

5. **Phosphorylation**
- During cell cycle, the phosphate groups are added to the histone groups as the cell enters **S phase**, increases during **M phase**, and are removed on the completion of **mitosis** before **G1 starts**.
- Phosphate groups are also added and removed to non-histone proteins during cell cycle.
- Thus, it is believed that the changes in the histones and non-histones may have a role in the control of cell cycle because these proteins have been found to regulate the activity of genes in RNA transcription during interphase.

Mitosis

- Mitosis is defined as the division of a parent cell into two identical daughter cells each with a nucleus having the same amount of DNA, the same number and kind of chromosomes, and the same hereditary instructions as the parent cell.
- Mitosis is also known as the **equational division**.
- Two main events are involved in mitosis: **Karyokinesis** or division of the nucleus and **cytokinesis** or division of cytoplasm.
- Mitosis is the most common method of cell division in eukaryotes that takes place in somatic cells of the body and hence it is also known as somatic division.
- In gonads, mitosis occurs in **undifferentiated** germ cells.
- In plants, it takes place in the cells of meristematic tissues.
- The duration of mitosis on an average is from 30 minutes to 3 hours.



Prophase:

- In an interphase cell, the chromosomes are greatly extended and spread throughout the space in the nuclear compartment.
- In the nucleus of a human cell, approximately 4 meters of DNA organized into 46 duplicated chromosomes is present.
- The prophase is long and complex that lasts for about 50 mins
- Prophase is divided into 3 sub-stages: **early prophase**, middle prophase and late prophase.
- DNA supercoils and chromosomes condense (becoming visible under microscope)

- Chromosomes are comprised of genetically identical sister **chromatids** (joined at a centromere)
- Paired centrosomes move to the opposite poles of the cell and form microtubule spindle fibres
- The nuclear membrane breaks down and the nucleus dissolves

Metaphase:

The metaphase being short and simple lasts for 2 to 10 minutes and it involves the following events:

- The spindle occupies the region of the nucleus.
- The chromosomes move to the equatorial plane of the spindle.
- Microtubule spindle fibres from both centrosomes connect to the centromere of each chromosome
- Some spindle microtubules extend to and join the chromosomes. These are called chromosomal or kinetochore microtubules.
- The chromosomes get aligned at the middle of the spindle in the form of a plate called equatorial or metaphase plate.
- During metaphase the chromosomes have fully aligned into a plate and await the separation of their chromatids.

Anaphase:

Anaphase lasts only 2 to 3 mins, and it comprises the following events:

- The sister chromatids of each chromosome slightly separate at the primary constriction so that their kinetochores stretch towards the opposite poles of the spindle.
- In all the chromosomes, separation of chromatids occurs almost simultaneously.
- The chromatids are now referred to as chromosomes because they are no longer held to their duplicates.

- After a short time, the chromatids separate completely from their former mates, and start moving to opposite poles of the spindle.

- As each chromosome is being pulled by its attached microtubules, its kinetochore leads and arms trail behind.

- As a result, the chromosomes are pulled into V, J and I shapes, depending upon the position of the kinetochore. (Metacentric, sub metacentric or telocentric respectively).

- As the chromosomes move toward their respective poles, the two poles move farther apart by elongation of spindle.

- The anaphase ends when all the chromatids reach the opposite poles.

- Each pole of the spindles receives one chromatid from every metaphase chromosome, the two groups of chromatids have the same hereditary information.

- Continued contraction of the spindle fibres causes genetically identical sister chromatids to separate.

- Once the chromatids separate, they are each considered an individual chromosome in their own right.

- The genetically identical chromosomes move to the opposite poles of the cell

Telophase

The telophase is long and complex and lasts for an hour or so. In this phase nucleus is reconstructed from each group of chromosomes. It involves the following events.

i. The chromosomes at each pole unfold and become long and slender. Finally, they become indistinguishable as were in an interphase cell.

ii. Nuclear envelope is reconstructed around each group of chromosomes gradually.

- First, the membrane vesicles associate with the individual unfolding chromosomes, partially enclosing each chromosome.

- Then they fuse to form an envelope surrounding the entire set of chromosomes at each pole.
- The lamina proteins re-associate simultaneously with the reconstruction of nuclear envelope and form a complete lamina within the nuclear envelope.

iii. Nucleolar material, composed of partially processed ribosomal subunits and processing enzymes, dispersed into the cytoplasm in the prophase return to the nucleolar organizer site and forms a small nucleolus.

- Once the two chromosome sets arrive at the poles, spindle fibres dissolve.
- Chromosomes decondense (no longer visible under light microscope).
- Nuclear membranes reform around each chromosome set.
- Cytokinesis occurs concurrently, splitting the cell into two.

CYTOKINESIS

Cytokinesis is the division of cytoplasm. It encloses the daughter nuclei formed by the karyokinesis in separate cells, thus completing the process of cell division.

- Cytokinesis is signalled at the metaphase by cytoplasmic movements that bring about equal distribution of mitochondria and other cell organelles in the two halves of the cell.

- Division occurs differently in animal cells and the plant cells.

Significance of Mitosis

i. **Maintenance of Size**: Mitosis helps maintaining the size of the cell. A cell, when full grown, divides by mitosis instead of growing further.

ii. **Growth**: A fertilized egg develops into an embryo and finally into an adult by repeated mitotic cell division.

iii. **Maintenance of Chromosome Number**: Mitosis keeps the number of chromosomes equal in all the cells of an individual. Thus, mitosis provides a complete set of genetic information to each cell, since DNA is duplicated in S phase prior to mitosis.

iv. **Repair**: Mitosis provides new cells to replace the old worn out and dying cells.

v. **Healing and Regeneration**: Mitosis produces new cells for the healing of wounds and regeneration.

vi. **Reproduction**: Mitosis brings about multiplication in the acellular organisms. In multicellular organisms also, it plays an important role in reproduction, asexual as well as sexual.

vii. **Evidence of Basic Relationship of Organisms**: Mitosis, being essentially similar in many kinds of organisms, supports the basic relationship of all living things.

MEIOSIS

- In **1887**, August Weismann predicted on theoretical grounds that the number of chromosomes must be reduced by one-half during gamete formation.

- Edouard Van Beneden demonstrated reduction division in **1887**.

- J.B. Farmer and Moore introduced the term "**meiosis**" in **1905**.

- Unlike **mitosis** which occurs in all kinds of eukaryotic cells, **meiosis** is confined to sexually reproducing organisms.

- However, special cells in the multicellular organisms switch over from mitosis to meiosis at the specific time in the life cycle.

- Meiosis produces gametes or gametic nuclei in animals, some lower plants, and various protists and fungus groups.

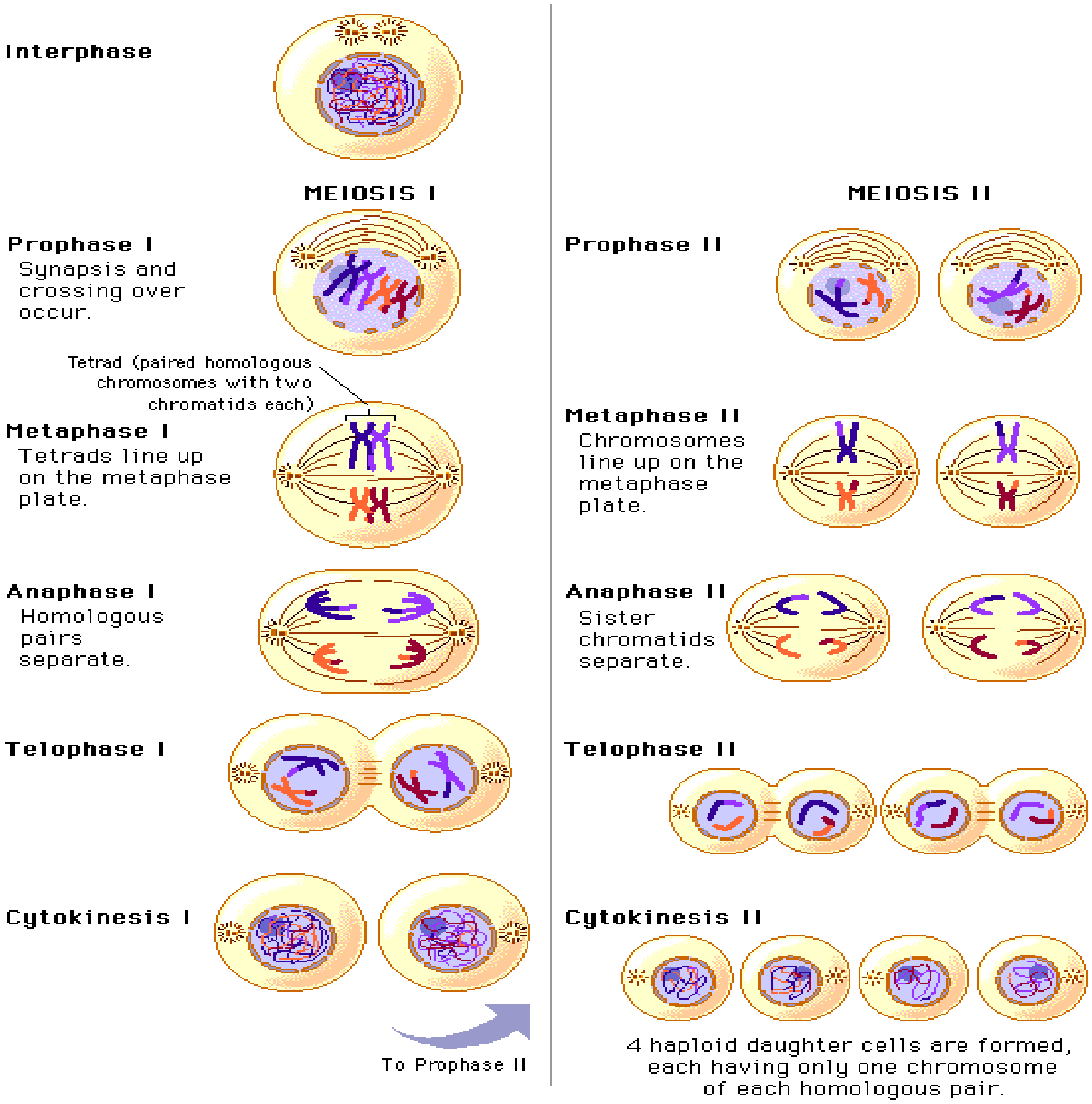
- Meiosis forms spore in higher plants. The spores give rise to gamete producing structure called gametophytes, which produces gametes by mitosis.

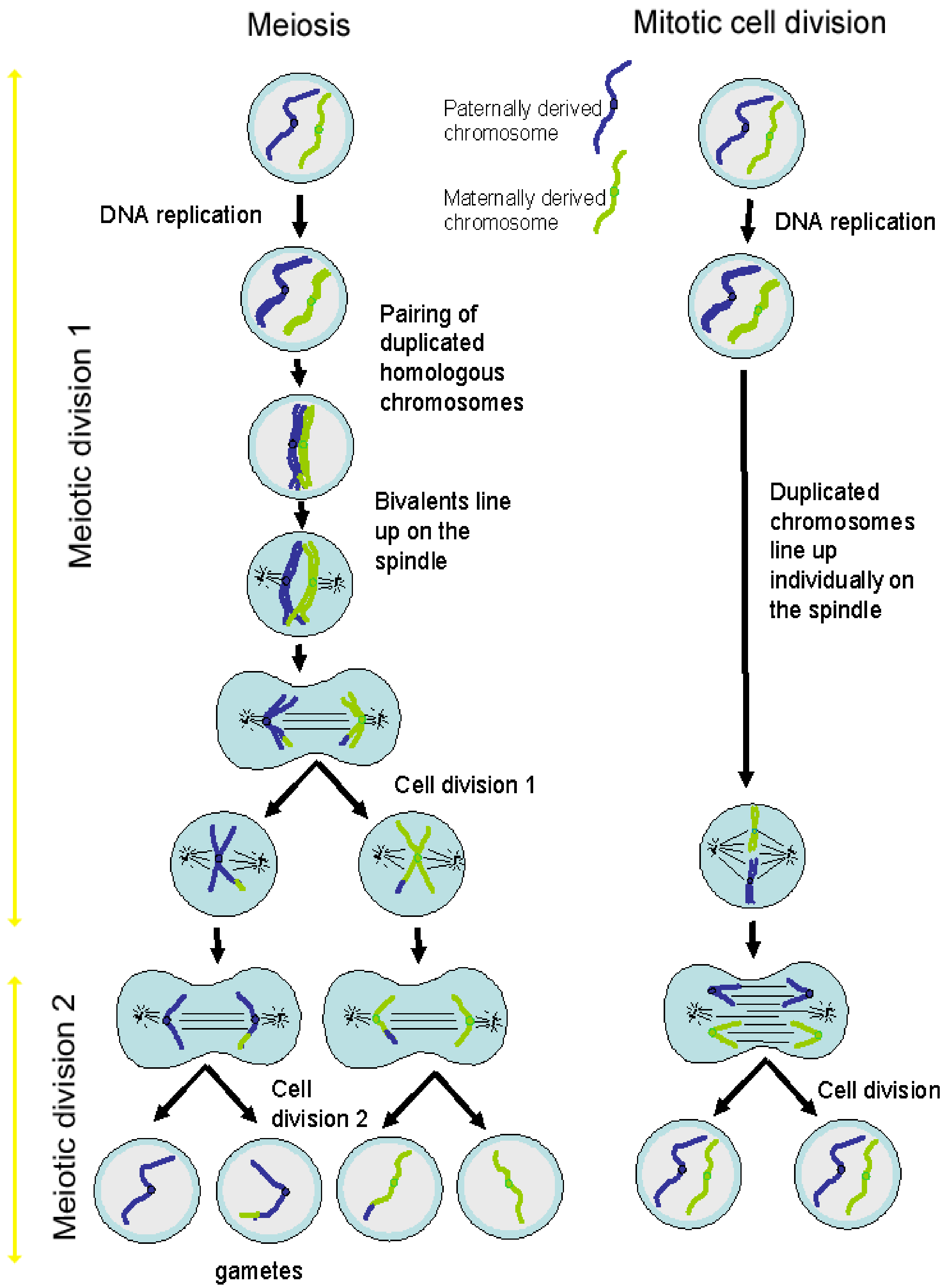
Meiosis consists of two divisions that take place in rapid succession, with the chromosomes replicating only once.

- Thus, a parent cell produces **four daughter cells**, each having half the number of chromosomes and half of the nuclear DNA amount present in the parent cell.

- Meiosis is therefore also known as reduction division.

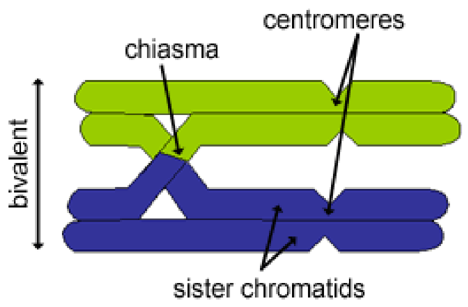
- The two divisions of meiosis are known as the first and the second meiotic divisions or meiosis-I and meiosis-II.


Interphase
MEIOSIS I
Prophase I
Synapsis and crossing over occur.
Tetrad (paired homologous chromosomes with two chromatids each)
Metaphase I
Tetrads line up on the metaphase plate.
Anaphase I
Homologous pairs separate.
Telophase I
Cytokinesis I
To Prophase II
MEIOSIS II
Prophase II
Metaphase II
Chromosomes line up on the metaphase plate.
Anaphase II
Sister chromatids separate.
Telophase II
Cytokinesis II
4 haploid daughter cells are formed, each having only one chromosome of each homologous pair.


Meiosis
Mitotic cell division
Paternally derived chromosome
Maternally derived chromosome
DNA replication
DNA replication
Pairing of duplicated homologous chromosomes
Bivalents line up on the spindle
Duplicated chromosomes line up individually on the spindle
Cell division 1
Meiotic division 1
Meiotic division 2
Cell division 2
Cell division
gametes

Meiosis versus Mitosis

In meiosis, homologous chromosomes duplicate to form sister chromatids, as in mitosis.

S/N	Meiosis	Mitosis
1.	The two pairs of homologous chromosomes (paternal and maternal) stay together on the spindle of the equator to form a bivalent (contains 4 chromatids).	Homologous chromosomes duplicate, but remain separate
2.	- In the long prophase of meiotic division 1, genetic material can 'cross over' between maternal and paternal pairs of chromosomes (non-sister chromatids). - This exhange of genetic material between maternal and paternal chromosomes is known as 'genetic recombination' - Each cross-over between two non-sister chromatids is called a chiasma (plural 'chiasmata'). - The chiasmata are also important in holding the maternal and paternal homologs together until they are separated at anaphase 1.  	Cross-overs do not occur between non-sister chromatids, as they are separate.
3.	At anaphase of meiotic division 1, the maternal and paternal chromatids are separated, such that one daughter cell inherits one mostly paternal	At mitotic anaphase, one of each pair of chromosomes goes to each daughter cell, such that each daughter cell inherits one copy

	homolog, and the other one mostly maternal homolog.	of the paternal chromosome, and one copy of the maternal chromosome.
4.	Resulting cells are **haploid**, and have a single copy of each chromosomes, and either one X or one Y chromosome (female or male gametes respectively).	The resulting cells are **diploid**.
5.	**4 haploid cells** are produced.	**2 diploid cells** are produced.