Unit 2. CELL CYCLE. CELL DIVISION. MITOSIS. MEIOSIS

The continuity of life is based on the reproduction of cells, or ***cell division.*** Cell division plays several important roles in life:

1. Reproduction
2. Growth and development
3. Tissue renewal

The cell division process is an integral part of the ***cell cycle***, the life of a cell from the time it is first formed from a dividing parent cell until its own division into two daughter cells.

Phases of the Cell Cycle (fig. 1):

1. Interphase
2. Mitosis (M phase, nuclear division)
3. Cytokinesis (cytoplasmic division)

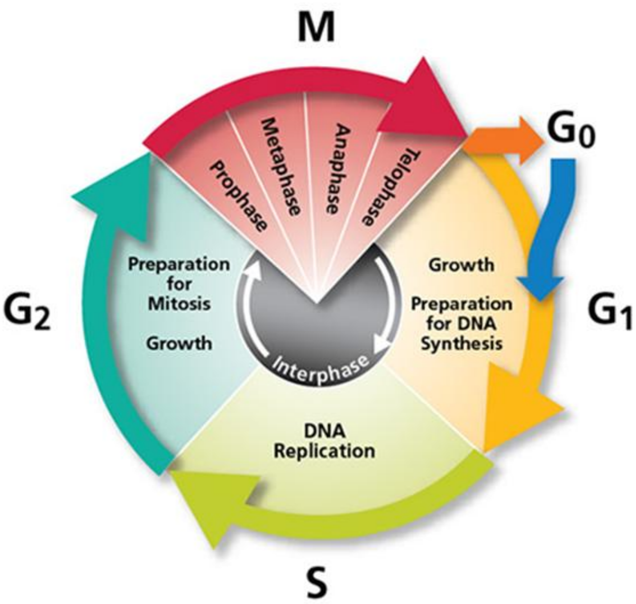


Fig. 1. Phases of the Cell Cycle

Interphase

Interphase ("resting stage) accounts for about 90% of the cycle. During interphase, a cell that is about to divide grows and copies its chromosomes in preparation for cell division. Interphase generally lasts at least 12 to 24 hours in mammalian tissue. Interphase can be divided into subphases: gap 1 **(G_1),** synthesis **(S),** and gap 2 **(G_2)** (tabl.1).

Table 1

Subphases of Interphase

G_1 ("Gap One")	The period of molecular synthesis where a newly formed cell turns on a variety of genes on its DNA to make proteins, which in turn churn the metabolism of the cell, produce and breakdown carbohydrates, lipids, etc., and transform energy from food into ATP. The cell grows and enlarges.
***S** ("synthesis")*	During this phase the chromatin (DNA and proteins) becomes synthetically active. Using elaborate teams of enzymes, the DNA molecules of each chromosome are copied by semiconservative DNA synthesis.
G_2 ("Gap Two")	The cells prepare for division. Many different proteins are synthesized, especially those that will act as spindle fibers. Stocks of energy are accumulated and many organelles, such as mitochondria, also grow and divide, increasing in number. Towards the end of G2, the cell gets ready for the M phase.

Mitosis (M phase)

The primary purpose of mitosis is to distribute the replicated chromosomes, dividing one cell nucleus into two nuclei, so that each daughter cell receives the same complement of chromosomes.

Mitosis is conventionally broken down into five stages: prophase, prometaphase, metaphase, anaphase and telophase.

Prophase (fig. 2)

- ✓ The chromatin fibers condense (each duplicated chromosome appears as two identical sister chromatids joined at their centromeres.
- ✓ The nucleoli begin to disappear.
- ✓ The mitotic spindle begins to form.
- ✓ The centrosomes move apart toward opposite poles.

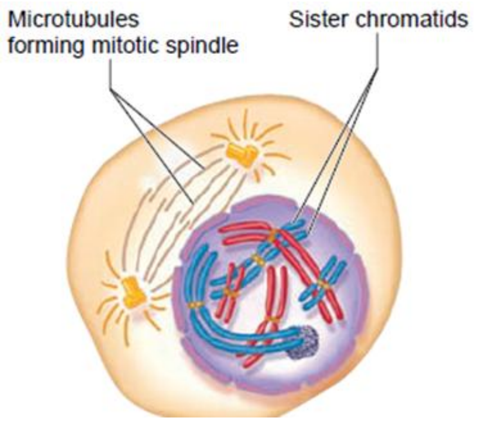


Fig. 2. Prophase

Prometaphase (fig. 3)

- ✓ Nuclear envelope breaks down.
- ✓ Microtubules from the centrosomes invade the nucleus.
- ✓ Sister chromatids attach to microtubules from opposite centrosomes.

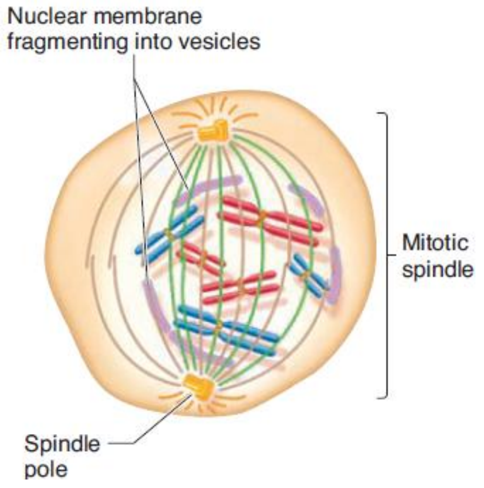


Fig. 3. Prometaphase

Metaphase (fig.4)

- ✓ The centrosomes are at opposite poles of the cell.
- ✓ The chromosomes align on the *metaphase plate*
- ✓ Each pair of chromatids is attached to both poles by kinetochore microtubules.

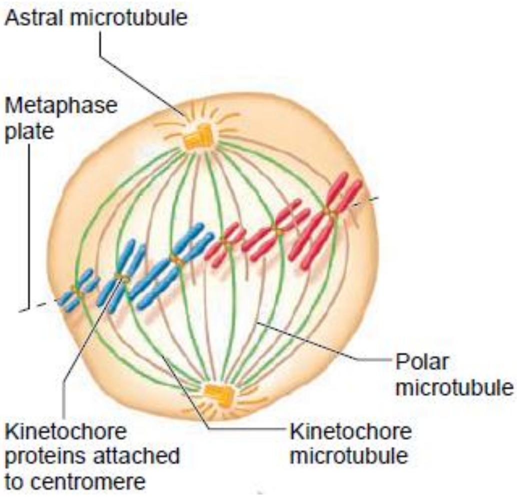


Fig. 4. Metaphase

Anaphase (fig.5)

The two liberated daughter chromosomes begin moving toward opposite ends of the cell as their kinetochore microtubules shorten.

By the end of anaphase, the two ends of the cell have equivalent and complete collections of chromosomes.

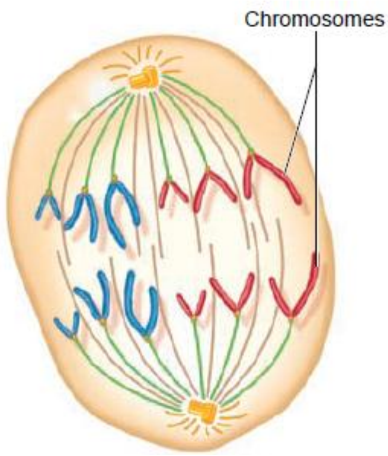


Fig. 5. Anaphase

Telophase (fig.6)

- ✓ Nuclear membranes and nucleoli re-form.
- ✓ Spindle fibers disappear.
- ✓ Chromosomes uncoil and become a tangle of chromatin.

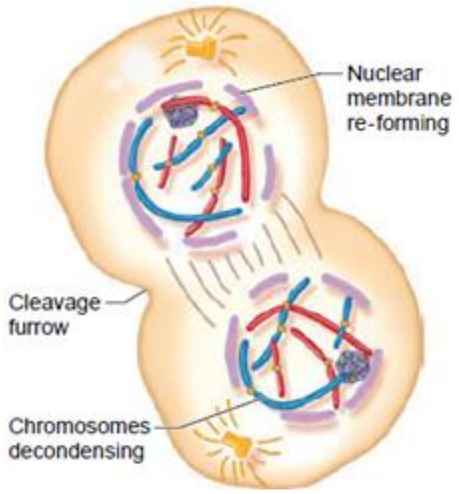


Fig. 6. Telophase

Cytokinesis

The division of the cytoplasm is usually well under way by late telophase, so the two daughter cells appear shortly after the end of mitosis. In animal cells, cytokinesis involves the formation of a cleavage furrow, which pinches the cell in two (fig.7 (a)). In plant cells, cytokinesis is accomplished by the formation of a membranous cell plate between the daughter cells; eventually, walls composed of cellulose are built on either side of the cell plate (fig.7 (b)).

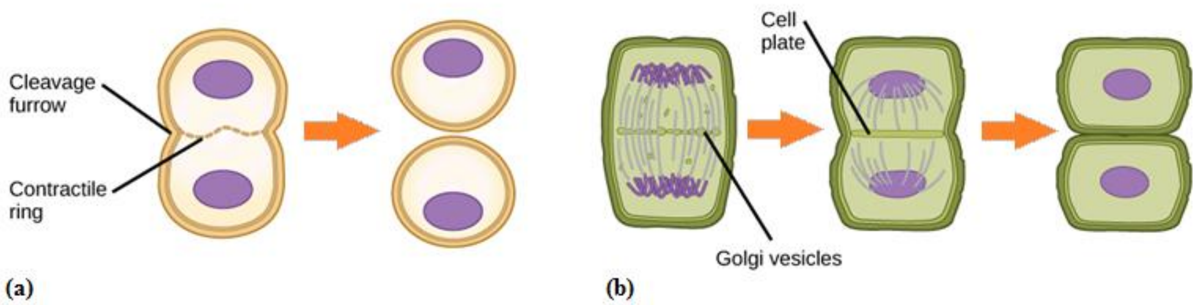


Fig. 7. Cytokinesis: (a) animal cell, (b) plant cell

<u>The outcomes of and biological significance of Mitosis</u>

Mitosis always produces two cells that are genetically identical to each other and the original cell.

Cellular Organization of the Genetic Material

In eukaryotes, genetic material is housed (mostly) in the nucleus and tightly packaged into linear chromosomes. Chromosomes are made up of a DNA-protein complex called chromatin. During most of a cell's life cycle, DNA exists as a mass of loose strands. While the DNA is spread throughout the nucleus, the cell performs the functions needed for survival. During this time, the DNA is duplicated, or copied. Before division, the chromosomes compact by means chromatin packaging. There are up to six levels of chromatin packaging to fit into the nucleus of one cell:

1. Nucleosome (10 nm chromatin fibers)
2. Solenoid (30 nm chromatic fibers)
3. Radial Loop Domains (300 nm chromatin fibers)
4. Interphase Chromosome (700 nm)
5. Metaphase Chromosome (1400 nm)

Structure of metaphase chromosome

During cell division (at metaphase) chromosome has X-shaped structure called a *metaphase chromosome*. It consists of two sister chromatides. *Centromere* divides a chromosome in two arms (short arm – *p*, long arm – *q*) (fig.8).

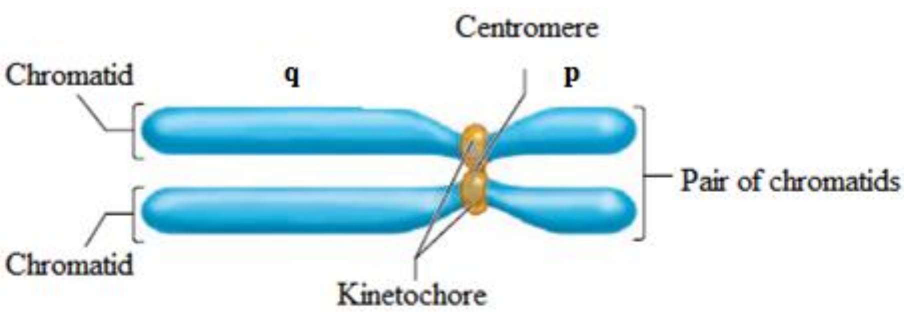


Fig. 8. Structure of metaphase chromosome

The *kinetochore* is a group of proteins that are bound to the centromere. Fibers of mitotic spindle attaches to this during mitosis.

Depending on the position of the centromere, chromosomes are classified as *metacentric, submetacentric, acrocentric,* or *telocentric* (tabl. 2).

Table 2

Centromere locations and the chromosome designations

Centromere location	***Designation***	***Metaphase shape***
Middle	Metacentric	
Between middle and end	Submetacentric	
Closer to end	Acrocentric	
At end	Telocentric	

Chromatin packing also offers an additional mechanism for controlling gene expression. Specifically, cells can control access to their DNA by modifying the structure of their chromatin. Highly compacted chromatin ***heterochromatin*** is not accessible to the enzymes involved in DNA transcription, replication, or repair**.** The less condensed regions, ***euchromatin***, are associated with genes being actively transcribed (fig.9).

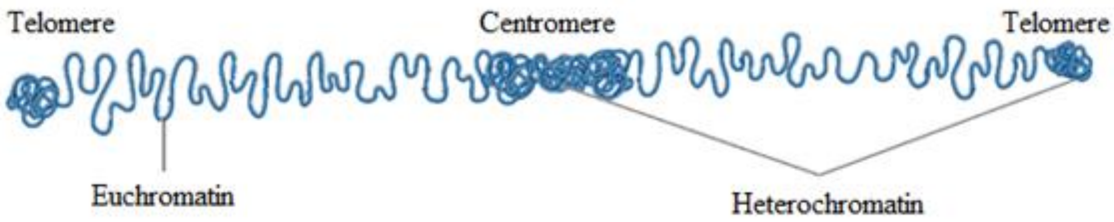


Fig. 9. Euchromatin and Heterochromatin

Within each species of organism, the number of chromosomes is constant. For example, humans have 46 chromosomes.

All somatic cells contain an identical number of chromosomes. This represents the *diploid number* (2n) of chromosome. With the exception of sex chromosomes, each chromosome exists in pair, called pare of ***homologous chromosomes***. It means for each chromosome exhibiting a specific length and centromere placement, another exists with identical features.

In comparison with somatic cells, germ cells (gametes) are typically ***haploid*** (1n), which means they contain half the number of chromosomes as diploid cells (For example, a diploid human cell contains 46 chromosomes, but a sperm or egg contains only 23 chromosomes). During the process known as ***meiosis*** (from the Greek meaning less), haploid cells are produced from a cell that was originally diploid.

Meiosis

The process of meiosis bears striking similarities to mitosis. Like mitosis, meiosis begins after a cell has progressed through the G1, S, and G2 phases of the cell cycle. However, meiosis involves two successive divisions rather than one (as in mitosis). Prior to meiosis, the chromosomes are replicated in S phase to produce pairs of sister chromatids. This single replication event is then followed by two sequential cell divisions called meiosis I and II. As in mitosis, each of these is subdivided into prophase, prometaphase, metaphase, anaphase, and telophase.

Prophase of meiosis I

This stage is further subdivided into stages known as *leptotene*, *zygotene*, *pachytene*, *diplotene,* and *diakinesis*.

Leptotene. The replicated threadlike chromosomes begin to condense.

Zygotene. A recognition process known as ***synapsis***, in which the homologous chromosomes recognize each other and begin to align themselves.

Pachytene. The homologs have become completely aligned. The associated chromatids are known as ***bivalents***. Each bivalent contains two pairs of sister chromatids (a total of four chromatids). In most eukaryotic species, a ***synaptonemal complex*** is formed between the homologous chromosomes. Prior to the pachytene stage, when synapsis is complete, an event known as ***crossing over*** usually occurs. Crossing over involves a physical exchange of chromosome pieces. The connection that results from crossing over is called a ***chiasma*** (plural: ***chiasmata***), because it physically resembles the Greek letter chi, χ .

Diplotene. The synaptonemal complex has largely disappeared. The bivalent pulls apart. A bivalent is also called a ***tetrad*** (from the prefix "tetra-," meaning four) because it is composed of four chromatids.

Diakinesis. The synaptonemal complex completely disappears.

Figure 27 emphasizes some of the important events that occur during prophase of meiosis I.

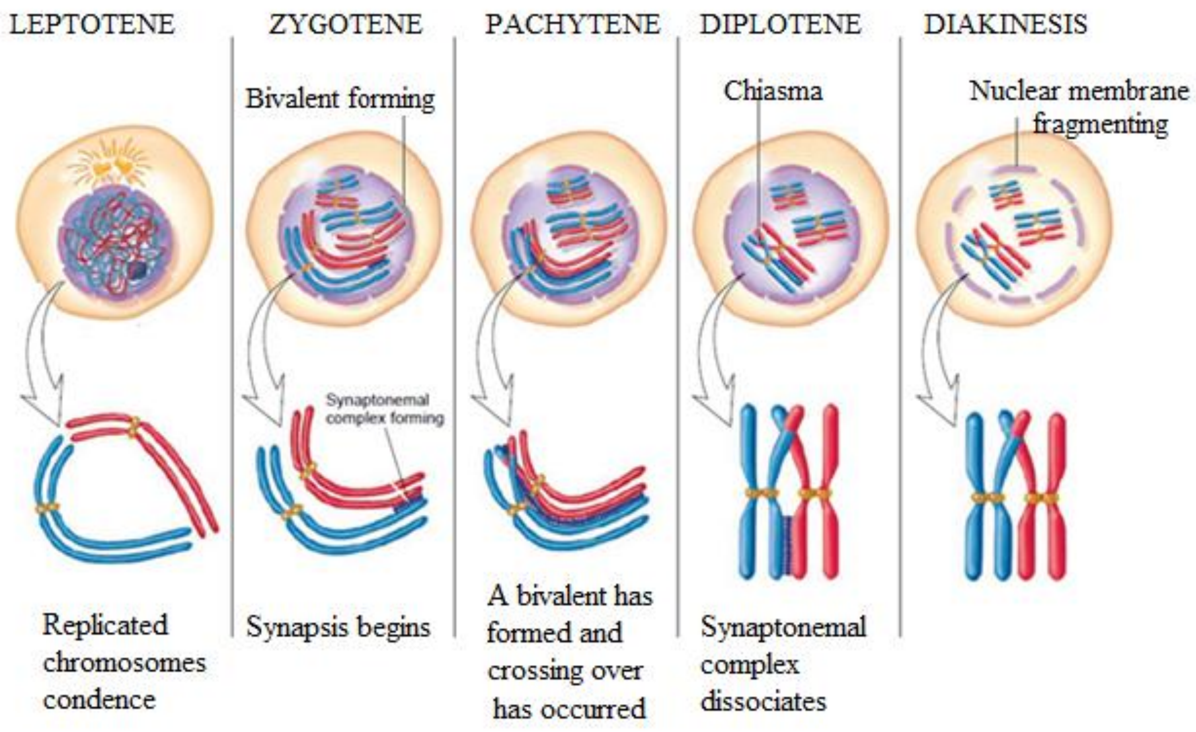


Fig. 10. Prophase of meiosis I[1]

Prometaphase I

The spindle apparatus is complete, and the chromatids are attached via kinetochore microtubules.

Metaphase I

The bivalents are organized along the metaphase plate. The paired chromosomes orient toward opposite poles of the spindle.

Anaphase I

The two pairs of sister chromatids within a bivalent separate from each other. However, the connection that holds sister chromatids together does not break. Instead, each joined pair of chromatids migrates to one pole, and the homologous pair of chromatids moves to the opposite pole.

Telophase I

The sister chromatids have reached their respective poles, and decondensation occurs (in many, but not all, species). The nuclear membrane may re-form to produce two separate nuclei.

The meiosis I is a ***reduction*** division. The original diploid cell had its chromosomes in homologous pairs, but the two cells produced at the end of meiosis I are considered to be haploid; they do not have pairs of homologous chromosomes.

The meiosis II is a ***equational*** division.

Prophase II

The chromosomes condense and become attached to a new spindle apparatus.

Metaphase II

The chromosomes move to positions in the equatorial plane of the cell.

Anaphase II

The centromeres of chromosomes split to allow the constituent sister chromatids to move to opposite poles (a phenomenon is called chromatid disjunction).

Telophase II

The separated chromatids — now called chromosomes — gather at the poles and daughter nuclei form around them. Each daughter nucleus contains a haploid set of chromosomes.

Figure 28 emphasizes the events that occur during meiosis II.

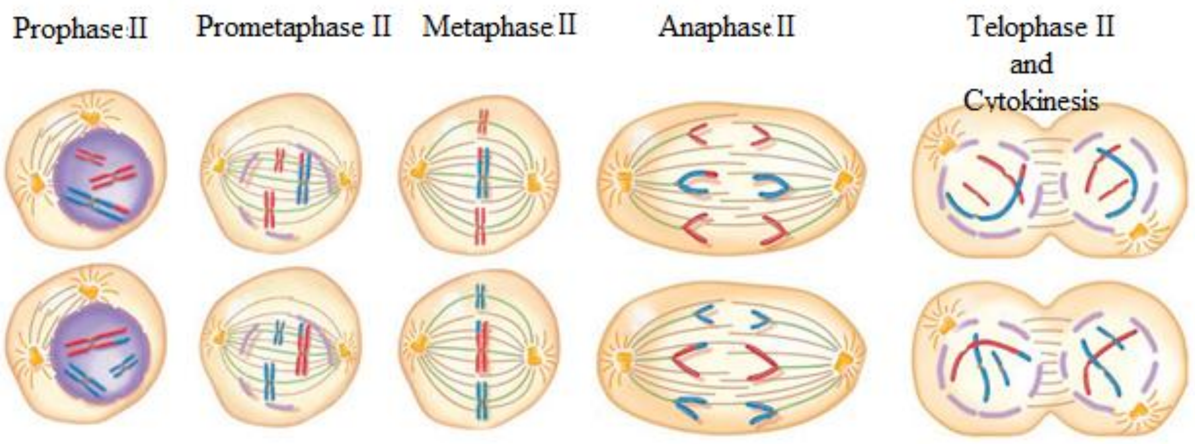


Fig. 11. The events of meiosis II[2]

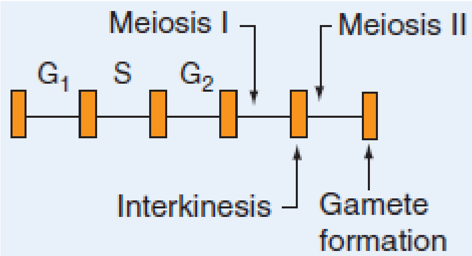
<u>The outcomes and biological significance of Meiosis:</u>

- ✓ To ensure the production of haploid cells (gametes).
- ✓ To maintain diploid number of chromosome in each generation.
- ✓ Through the shuffling of chromosomes (independent assortment) and chromosomal recombination (by means of crossing over), new sets of chromosomes with a mix of paternal and maternal chromosomes are created, generating diversity in gametes.

The sorting events that occur during meiosis II are similar to those that occur during mitosis, but never the less both processes have much more differeces (tabl.5)

Table 3

A Comparison of Mitosis and Meiosis

Mitosis	Meiosis
Occurs in somatic cells. Diploid cells can undergo mitosis. One round of division.	Occurs in germ cells as part of the sexual cycle.Two rounds of division, meiosis I and meiosis II. Only diploid cells undergo meiosis
Mitosis is preceded by S phase (chromosome duplication).	Chromosomes duplicate prior to meiosis I but not before meiosis II. 
Homologous chromosomes do not pair.	During prophase of meiosis I, homologous chromosomes pair (synapse) along their length.
Genetic exchange between homologous chromosomes is very rare.	Crossing-over occurs between homologous chromosomes during prophase of meiosis I.
Sister chromatids attach to spindle fibers from opposite poles during metaphase.	Homologous chromosomes (not sister chromatids) attach to spindle fibers from opposite poles during metaphase I.
The centromere splits at the beginning of anaphase.	The centromere does not split during meiosis I. Sister chromatids attach to spindle fibers from opposite poles during metaphase II. The centromere splits at the beginning of anaphase II.
Mitosis produces two new daughter cells, identical to each other and the original cell. Mitosis is thus genetically conservative.	Meiosis produces four haploid cells, one (egg) or all (sperm) of which can become gametes. None of these is identical to each other or to the original cell, because meiosis results in combinatorial change.