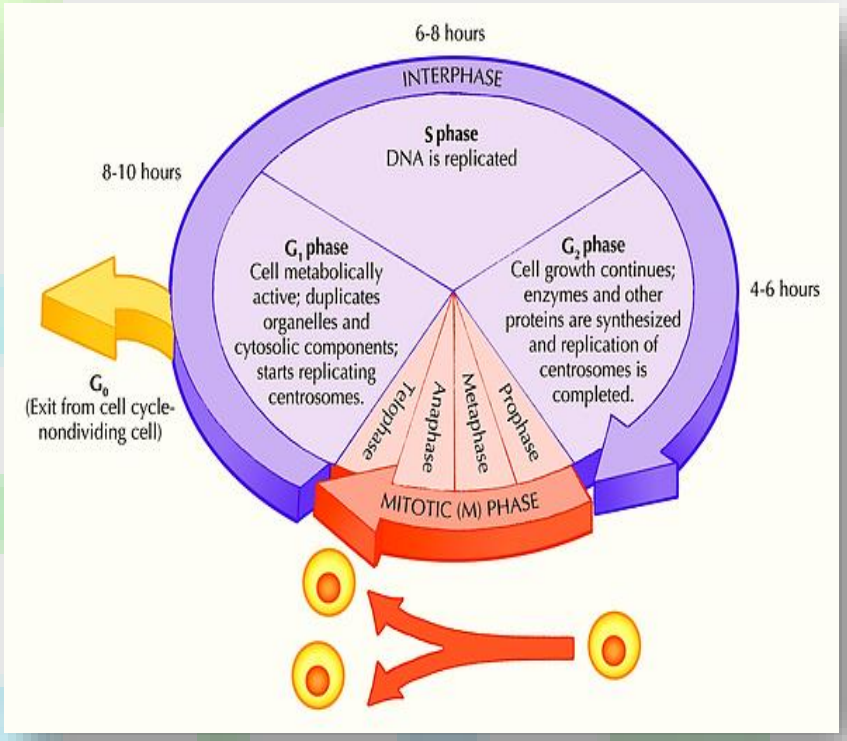
Cell Cycle and Cell Division

Lec. 6 & 7 | Cell Cycle and Cell Division (Pt.5)

INTRODUCTION

Cell Cycle and Cell Division

The ordered sequence of events that occur in a cell in preparation for cell division. The cell cycle is a four-stage process in which the cell increases in size (**gap 1, or G1, stage**), copies its DNA (synthesis, or S, stage), prepares to divide (**gap 2, or G2, stage**), and divides (**mitosis, or M, stage**). The stages G1, S, and G2 make up interphase, which accounts for the span between cell divisions. On the basis of the stimulatory and inhibitory messages a cell receives, it "decides" whether or not it should enter the cell cycle and divide.



The proteins that play a role in stimulating cell division can be classified into four groups growth factors, growth factor receptors, signal transducers, and nuclear regulatory proteins (transcription factors). For a stimulatory signal to reach the nucleus and "turn on" cell division, four main steps must occur. First, a growth factor must bind to its receptor on the cell membrane. Second, the receptor must become temporarily activated by this binding event. Third, this activation must stimulate a signal to be transmitted, or transduced, from the receptor at the cell surface to the nucleus within the cell. Finally, transcription factors within the nucleus must initiate the transcription of genes involved in cell proliferation. (Transcription is the process by which DNA is converted into RNA. Proteins are then made according to the RNA blueprint, and therefore transcription is crucial as an initial step in protein production.)

Cells use special proteins and checkpoint signaling systems to ensure that the cell cycle progresses properly. Checkpoints at the end of G1 and at the beginning of G2 are

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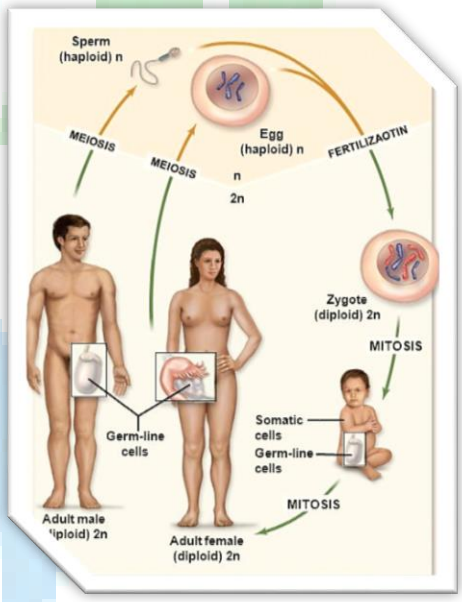
designed to assess DNA for damage before and after S phase. Likewise, a checkpoint during mitosis ensures that the cell's spindle fibers are properly aligned in metaphase before the chromosomes are separated in anaphase. If DNA damage or abnormalities in spindle formation are detected at these checkpoints, the cell is forced to undergo programmed cell death, or apoptosis. However, the cell cycle and its checkpoint systems can be sabotaged by defective proteins or genes that cause malignant transformation of the cell, which can lead to cancer. For example, mutations in a protein called p53, which normally detects abnormalities in DNA at the G1 checkpoint, can enable cancer-causing mutations to bypass this checkpoint and allow the cell to escape apoptosis.

Cell division results in genetically identical daughter cells

Cell division requires the distribution of identical genetic material DNA to two daughter cells. What is remarkable is the fidelity with which DNA is passed along, without dilution, from one generation to the next. A dividing parent cell replicates its DNA, separates the two identical copies to opposite ends of the cell, and then splits into two daughter cells, each containing an identical, complete set of DNA. A cell's genetic information, packaged as DNA, is called its genome. In prokaryotes (such as bacteria), the genome is usually a single long circular DNA molecule. In eukaryotes (such as plants and animals), the genome consists of several long linear DNA molecules packaged into **chromosomes**. DNA molecules are packaged into **chromosomes.** Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus.



- ☒ Human somatic cells (body cells) are **diploid**, and have 46 total chromosomes, made up of two sets of 23 (one from each parent).
- ☒ Human gametes (sperm or eggs) are **haploid**, and have one set of 23 chromosomes, half the number in a somatic cell.

Eukaryotic chromosomes are made of **chromatin,** a complex of a long piece of DNA wrapped around associated proteins. Each single chromosome contains one long, linear DNA molecule carrying hundreds or thousands of genes, the units that specify an organism's inherited traits. The associated proteins maintain the structure of the chromosome and help control gene activity.

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When a cell is not dividing, each **chromosome** is in the form of a long, thin **chromatin** fiber. Before cell division, chromatin condenses, coiling and folding to make a smaller package. Each duplicated chromosome consists of two **sister chromatids,** which contain identical copies of the chromosome's DNA. The condensed **sister chromatids** are initially attached by adhesive proteins at the **centromere.** Later in cell division, the **sister chromatids** are pulled apart and repackaged into two new nuclei at opposite ends of the parent cell. Once the sister chromatids separate, they are considered individual **chromatids** or chromosomes.

Three major cell cycle checkpoints are found in the G1, G2, and M phases.

- At the **G1 → S** checkpoint the cell is checked for damage to the DNA, appropriate cell size, and the presence of necessary nutrients and growth factors. If the cell passes this checkpoint is enters S phase (DNA synthesis phase).
- At the **G2 → M** checkpoint the cell is checked for damage to the DNA, complete and accurate DNA replication and appropriate cell size. If the cell passes this checkpoint it enters M phase (mitosis).
- At the **Metaphase → Anaphase** checkpoint the cell is checked for attachment of the spindle fibers to the kinetochores at centromeres of each sister chromatid and for proper alignment of the sister chromatids across the middle of the parent cell. If the cell passes this checkpoint, it will complete cytokinesis and generate two daughter cells.

Phases of Cell Cycle

A typical eukaryotic cell cycle is illustrated by human cells in culture. These cells divide once in approximately every 24 hours. However, this duration of cell cycle can vary from organism to organism and also from cell type to cell type. Yeast for example, can progress through the cell cycle in only about 90 minutes. The cell cycle is divided into two basic phases:

A. Interphase
B. M Phase (Mitosis phase)

The M Phase represents the phase when the actual cell division or mitosis occurs and the interphase represents the phase between two successive M phases. It is significant to note that in the 24 hour average duration of cell cycle of a human cell, cell division proper lasts for only about an hour. The interphase lasts more than 95% of the duration of cell cycle. The M Phase starts with the nuclear division, corresponding to the separation of daughter chromosomes (**karyokinesis**) and usually ends with division of cytoplasm (**cytokinesis**).

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The interphase, though called the **Resting Phase**, is the time during which the cell is preparing for division by undergoing both cell growth and DNA replication in an orderly manner. The interphase is divided into three further phases:

1. **G1 phase (Gap 1)**
2. **S phase (Synthesis)**
3. **G2 phase (Gap 2)**

G1 phase corresponds to the interval between mitosis and initiation of DNA replication. During G1 phase the cell is metabolically active and continuously grows but does not replicate its DNA. S or **synthesis** phase marks the period during which DNA synthesis or replication takes place.

During this time the amount of DNA per cell doubles. 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 had diploid or 2n number of chromosomes at G1, 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. During the G2 phase, proteins are synthesized in preparation for mitosis while cell growth continues.

Some cells in the adult animals do not appear to exhibit division (e.g., heart cells) and many other cells divide only occasionally, as needed to replace cells that have been lost because of injury or cell death. These cells that do not divide further exit G1 phase to enter an inactive stage called **Quiescent Stage (G0)** of the cell cycle. Cells in this stage remain metabolically active but no longer proliferate unless called on to do so depending on the requirement of the organism. In animals, mitotic cell division is only seen in the diploid somatic cells. Against this, the plants can show mitotic divisions in both haploid and diploid cells. From your recollection of examples of alternation of generations in plants identify plant species and stages at which mitosis is seen in haploid cells.

M PHASE "MITOSIS"

This is the most dramatic period of the cell cycle, involving a major reorganization of virtually all components of the cell. Since the number of chromosomes in the parent and progeny cells is the same, it is also called as equational division. Though for convenience mitosis has been divided into four stages of nuclear division, it is very essential to understand that cell division is a progressive process and very clear-cut lines cannot be drawn between various stages.

Mitosis, the formation of the two daughter nuclei, is usually followed by division of the cytoplasm, cytokinesis. These processes start with one parent cell and produce two daughter cells that are genetically identical to the original parent cell and to each other.

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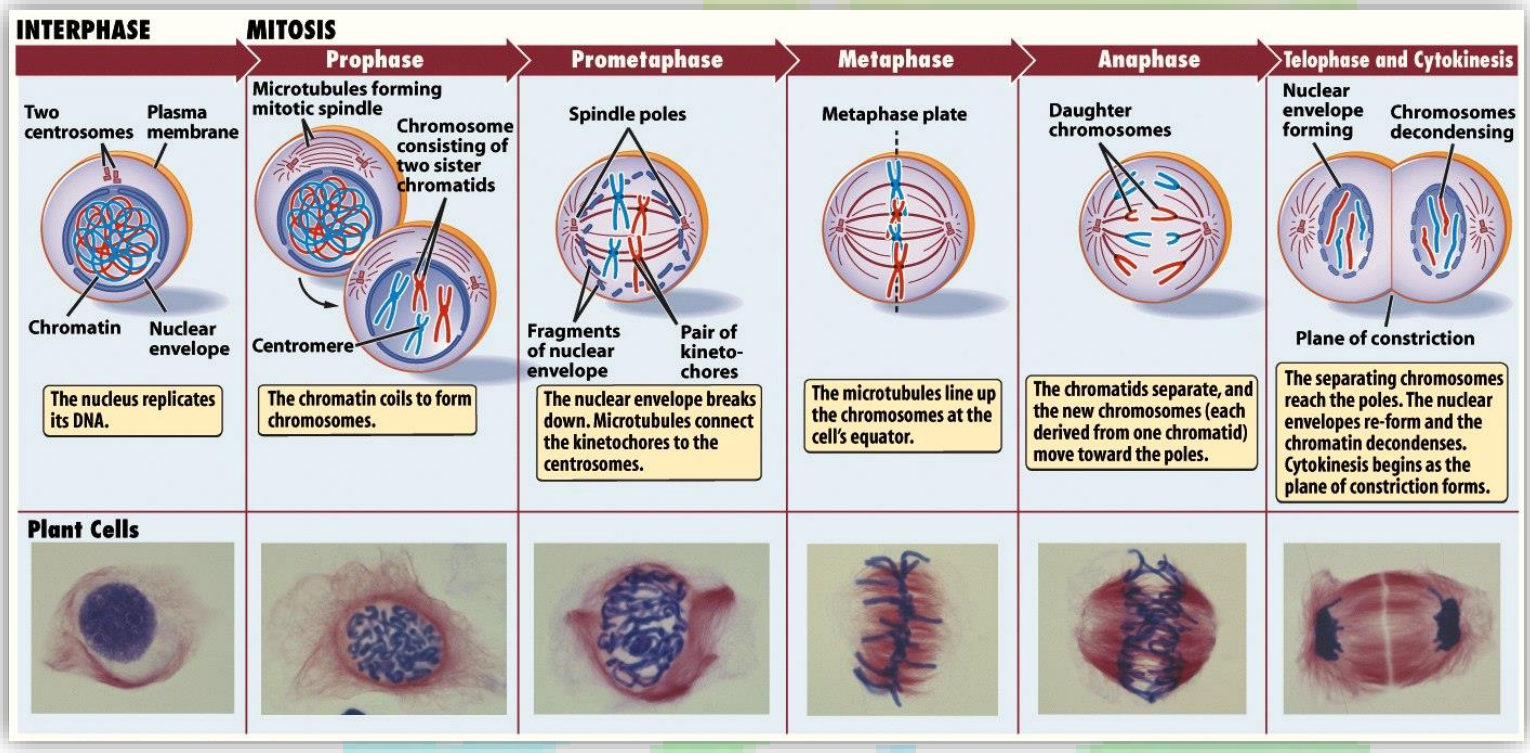
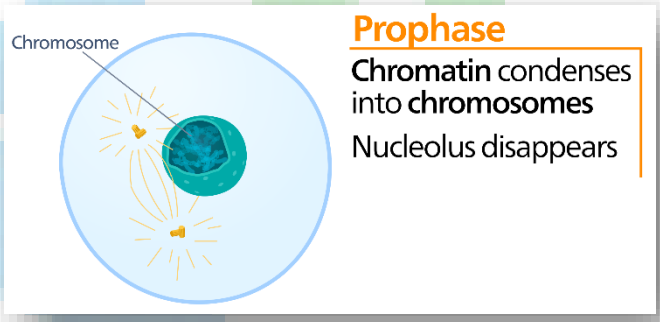


Each of us inherited 23 chromosomes from each parent: one set in an egg and one set in sperm. The fertilized egg, or zygote, underwent cycles of mitosis and cytokinesis to produce a fully developed multicellular human made up of 200 trillion somatic cells. These processes continue every day to replace dead and damaged cells. Essentially, these processes produce clones cells with identical genetic information. In contrast, gametes (eggs or sperm) are produced only in gonads (ovaries or testes) by a variation of cell division called meiosis. Meiosis yields four non identical daughter cells, each with half the chromosomes of the parent. In humans, meiosis reduces the number of chromosomes from 46 to 23. Fertilization fuses two gametes together and doubles the number of chromosomes to 46 again.



Mitosis is divided into the following four stages:

1. **Prophase**
2. **Metaphase**
3. **Anaphase**
4. **Telophase**

Prophase

Prophase which is the first stage of mitosis follows the S and G2 phases of interphase. In the S and G2 phases the new DNA molecules formed are not

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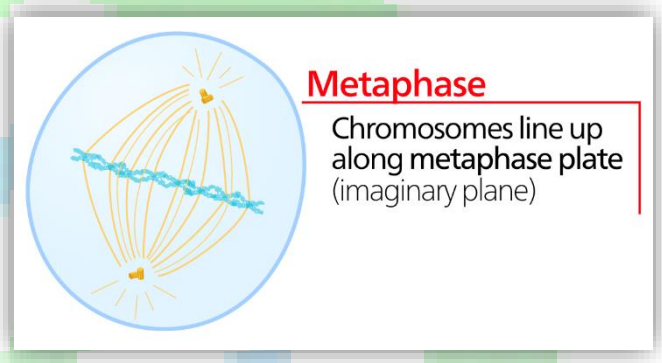
distinct but intertwined. Prophase is marked by the initiation of condensation of chromosomal material. The chromosomal material becomes untangled during the process of chromatin condensation. The centriole, which had undergone duplication during S phase of interphase, now begins to move towards opposite poles of the cell. The completion of prophase can thus be marked by the following characteristic events:

- Chromosomal material condenses to form compact mitotic chromosomes. Chromosomes are seen to be composed of two chromatids attached together at the centromere.
- Initiation of the assembly of mitotic spindle, the microtubules, the proteinaceous components of the cell cytoplasm help in the process.

Cells at the end of prophase, when viewed under the microscope, do not show Golgi complexes, endoplasmic reticulum, nucleolus and the nuclear envelope.

1. Metaphase

The complete disintegration of the nuclear envelope marks the start of the second phase of mitosis, hence the chromosomes are spread through the cytoplasm of the cell.



By this stage, condensation of chromosomes is completed and they can be observed clearly under the microscope. This then, is the stage at which morphology of chromosomes is most easily studied. At this stage, metaphase chromosome is made up of two sister chromatids, which are held together by the centromere.

Small disc-shaped structures at the surface of the centromeres are called kinetochores. These structures serve as the sites of attachment of spindle fibers (formed by the spindle fibers) to the chromosomes that are moved into position at the center of the cell.

Hence, the metaphase is characterized by all the chromosomes coming to lie at the equator with one chromatid of each chromosome connected by its kinetochore to spindle fibers from one pole and its sister chromatid connected by its kinetochore to spindle fibers from the opposite pole.

The plane of alignment of the chromosomes at metaphase is referred to as the metaphase plate. The key features of metaphase are:

- Spindle fibers attach to kinetochores of chromosomes.
- Chromosomes are moved to spindle equator and get aligned along metaphase plate through spindle fibers to both poles.

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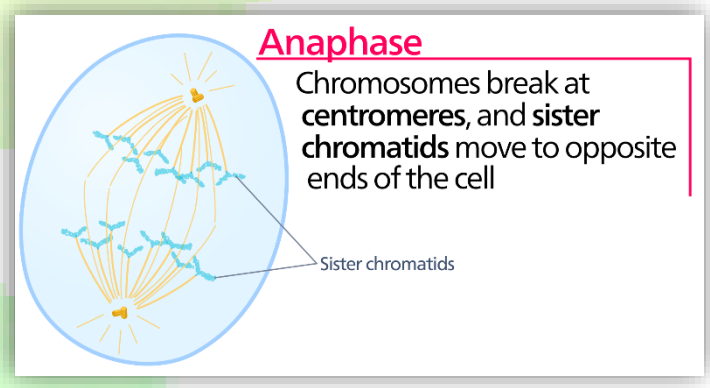
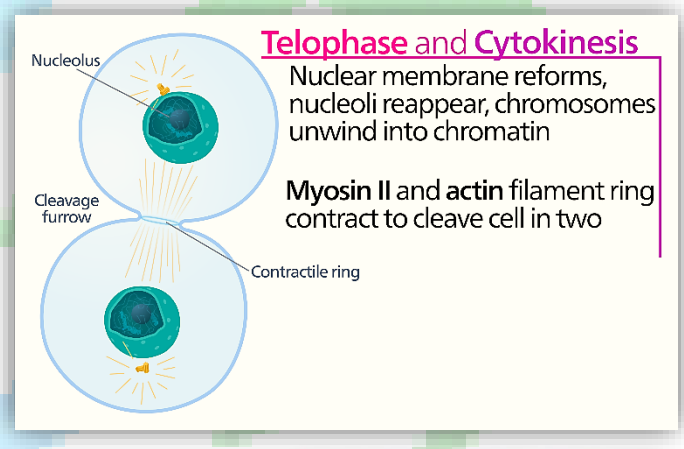
2. Anaphase



At the onset of anaphase, each chromosome arranged at the metaphase plate is split simultaneously and the two daughter chromatids, now referred to as chromosomes of the future daughter nuclei, begin their migration towards the two opposite poles. As each chromosome moves away from the equatorial plate, the centromere of each chromosome is towards the pole and hence at the leading edge, with the arms of the chromosome trailing behind. Thus, anaphase stage is characterized by the following key events:

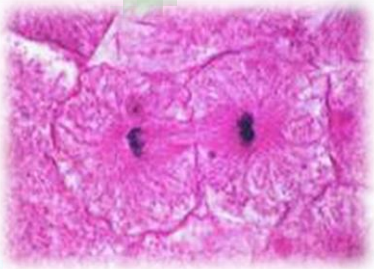
- ☒ Centromeres split and chromatids separate.
- ☒ Chromatids move to opposite poles.

3. Telophase



At the beginning of the final stage of mitosis, i.e., telophase, the chromosomes that have reached their respective poles decondense and lose their individuality. The individual chromosomes can no longer be seen and chromatin material tends to collect in a mass in the two poles. This is the stage which shows the following key events:

- ☒ Chromosomes cluster at opposite spindle poles and their identity is lost as discrete elements.
- ☒ Nuclear envelope assembles around the chromosome clusters.
- ☒ Nucleolus, Golgi complex and ER reform.



4. Cytokinesis

Mitosis accomplishes not only the segregation of duplicated chromosomes into daughter nuclei (karyokinesis), but the cell itself is divided into two daughter cells by a separate process called cytokinesis at the end of which cell division is complete.

In an animal cell, this is achieved by the appearance of a furrow in the plasma membrane. The furrow gradually deepens and ultimately joins in the center dividing the cell cytoplasm into two. Plant cells however, are enclosed by a relatively

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inextensible cell wall, therefore they undergo cytokinesis by a different mechanism. In plant cells, wall formation starts in the center of the cell and grows outward to meet the existing lateral walls.

The formation of the new cell wall begins with the formation of a simple precursor, called the cell-plate that represents the middle lamella between the walls of two adjacent cells. At the time of cytoplasmic division, organelles like mitochondria and plastids get distributed between the two daughter 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

Mitosis or the equational division is usually restricted to the diploid cells only. However, in some lower plants and in some social insects haploid cells also divide by mitosis. It is very essential to understand the significance of this division in the life of an organism. Are you aware of some examples where you have studied about haploid and diploid insects? Mitosis results in the production of diploid daughter cells with identical genetic complement usually. The growth of multicellular organisms is due to mitosis. Cell growth results in disturbing the ratio between the nucleus and the cytoplasm. It therefore becomes essential for the cell to divide to restore the nucleocytoplasmic ratio. A very significant contribution of mitosis is cell repair. The cells of the upper layer of the epidermis, cells of the lining of the gut, and blood cells are being constantly replaced. Mitotic divisions in the meristematic tissues the apical and the lateral cambium, result in a continuous growth of plants throughout their life.

MEIOSIS

The production of offspring by sexual reproduction includes the fusion of two gametes, each with a complete haploid set of chromosomes. Gametes are formed from specialized diploid cells. This specialized kind of cell division that reduces the chromosome number by half results in the production of haploid daughter cells. This kind of division is called meiosis. Meiosis ensures the production of haploid phase in the life cycle of sexually reproducing organisms whereas fertilization restores the diploid phase. We come across meiosis during gametogenesis in plants and animals. This leads to the formation of haploid gametes. The key features of meiosis are as follows:

- ☒ Meiosis involves two sequential cycles of nuclear and cell division called meiosis I and meiosis II but only a single cycle of DNA replication.

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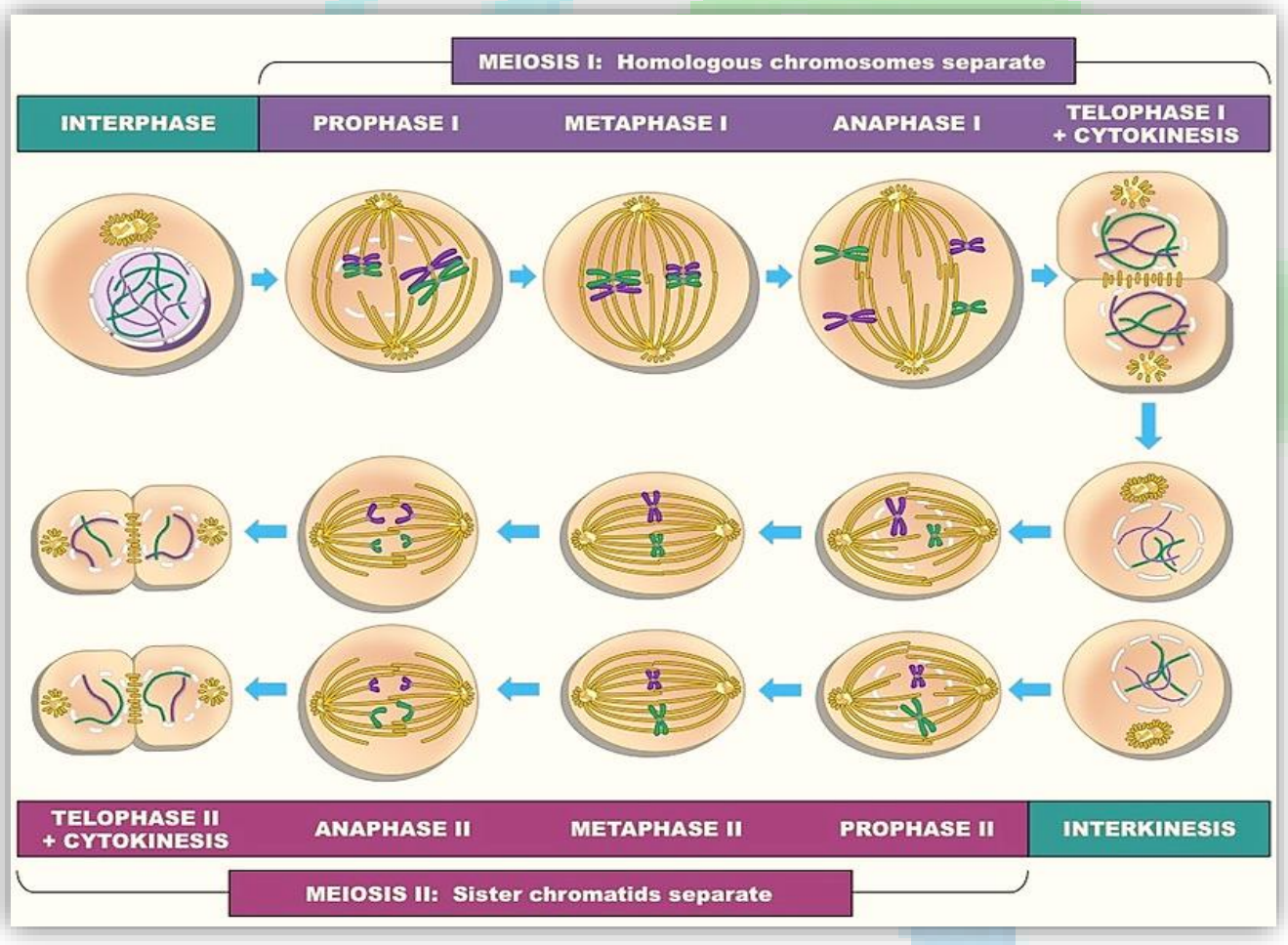
- ☒ Meiosis I is initiated after the parental chromosomes have replicated to produce identical sister chromatids at the S phase.
- ☒ Meiosis involves pairing of homologous chromosomes and recombination between them.
- ☒ Four haploid cells are formed at the end of meiosis II.

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



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Meiosis I

Prophase I:

Prophase of the first meiotic division is typically longer and more complex when compared to prophase of mitosis. It has been further subdivided into the following five phases based on chromosomal behavior, i.e., Leptotene, Zygotene, Pachytene, Diplotene and Diakinesis. During **leptotene** stage the chromosomes become gradually visible under the light microscope. The compaction of chromosomes continues throughout leptotene.

This is followed by the second stage of prophase I called **zygotene**. During this stage chromosomes start pairing together and this process of association is called synapsis. Such paired chromosomes are called homologous chromosomes. Electron micrographs of this stage indicate that chromosome synapsis is accompanied by the formation of complex structure called **synaptonemal complex.** The complex formed by a pair of synapsed homologous chromosomes is called a **bivalent** or a tetrad. However, these are more clearly visible at the next stage. The first two stages of prophase I are relatively short-lived compared to the next stage that is **pachytene**. During this stage, bivalent chromosomes now clearly appears as tetrads.

This stage is characterized by the appearance of recombination nodules, the sites at which crossing over occurs between non-sisters chromatids of the homologous chromosomes. Crossing over is the exchange of genetic material between two homologous chromosomes. Crossing over is also an enzyme-mediated process and the enzyme involved is called recombinase. Crossing over leads to recombination of genetic material on the two chromosomes.

Recombination between homologous chromosomes is completed by the end of pachytene, leaving the chromosomes linked at the sites of crossing over. The beginning of **diplotene** is recognized by the dissolution of the synaptonemal complex and the tendency of the recombined homologous chromosomes of the bivalents to separate from each other except at the sites of crossovers.

These X-shaped structures, are called **chiasmata.** In oocytes of some vertebrates, diplotene can last for months or years. The final stage of meiotic prophase I is **diakinesis.** This is marked by terminalisation of chiasmata. During this phase the chromosomes are fully condensed and the meiotic spindle is assembled to prepare the Homologous chromosomes for separation. By the end of diakinesis, the nucleolus disappears and the nuclear envelope also breaks down. Diakinesis represents transition to metaphase.

Metaphase I:

The bivalent chromosomes align on the equatorial plate. The microtubules from the opposite poles of the spindle attach to the pair of homologous chromosomes.

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Anaphase I:

The homologous chromosomes separate, while sister chromatids remain associated at their centromeres.

Telophase I:

The nuclear membrane and nucleolus reappear, cytokinesis follows and this is called as diad of cells. Although in many cases the chromosomes do undergo some dispersion, they do not reach the extremely extended state of the interphase nucleus. The stage between the two meiotic divisions is called interkinesis and is generally short lived. Interkinesis is followed by prophase II, a much simpler prophase than prophase I.

Meiosis II

Prophase II:

Meiosis II is initiated immediately after cytokinesis, usually before the chromosomes have fully elongated. In contrast to meiosis I, meiosis II resembles a normal mitosis. The nuclear membrane disappears by the end of prophase II. The chromosomes again become compact.

Metaphase II:

At this stage the chromosomes align at the equator and the microtubules from opposite poles of the spindle get attached to the kinetochores of sister chromatids.

Anaphase II:

It begins with the simultaneous splitting of the centromere of each chromosome (which was holding the sister chromatids together), allowing them to move toward opposite poles of the cell.

Telophase II:

Meiosis ends with telophase II, in which the two groups of chromosomes once again get enclosed by a nuclear envelope; cytokinesis follows resulting in the formation of tetrad of cells i.e., four haploid daughter cells.

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, even though the process, per se, paradoxically, results in reduction of chromosome number by half. It also increases the genetic variability in the population of organisms from one generation to the next. Variations are very important for the process of evolution.

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COMPARISONS OF MITOSIS AND MEIOSIS ***

MITOSIS	MEIOSIS
• Cell divides only once	• There are two cell divisions. First mitotic division and the second meiotic division.
• Takes place in somatic cells	• Takes place in germ cells.
• Duration of prophase is short (few hours)	• Prophase comparatively longer. (Takes many days).
• Prophase simple.	• Prophase complicated having five sub stages namely leptotene, zygotene, pachytene, diplotene and diakinesis.
• Synapsis does not occur.	• Synapsis of homologous chromosomes takes place during prophase.
• No exchange of segments during prophase between two chromatids of chromosomes.	• Exchange of segments during crossing over between non sisters chromatids of two homologous chromosomes.
• Each chromosome consists of two chromatids united by a centromere.	• Each bivalent has four chromatids and two centromeres.
• Chromosomes are duplicated at the beginning of prophase.	• In prophase I, chromosomes appear single although DNA replication has taken place in interphase I.
• In metaphase all the centromeres line up in the same plane.	• In metaphase I, the centromeres are lined up in two planes which are parallel to one another.
• The metaphasic plate is made up of duplicated chromosome.	• The metaphasic plate is made up of paired chromosome.
• Centromere division takes place during anaphase.	• No centromere divisions during Anaphase I, divide only during Anaphase II.
• Spindle fibers disappear completely in telophase.	• Spindle fibers do not disappear completely during telophase I.
• Reappearance of nucleoli at telophase.	• Nucleoli do not appear in telophase I.
• The chromosome number does not change at the end of mitosis.	• There is reduction in the chromosome number from diploid to haploid.
• The genetic constitution of daughter cells is absolutely identical to that of parent cells.	• The genetic constitution of daughter cells is different as compared to the parent cells. The daughter cell chromosomes contain a mixture of maternal and paternal genes.
• Mitosis is of shorter duration.	• Meiosis is of longer duration.
• It is the basis of growth and repair.	• It is basis of maintaining chromosome number in sexual reproduction, as well as for providing variation in the progeny.

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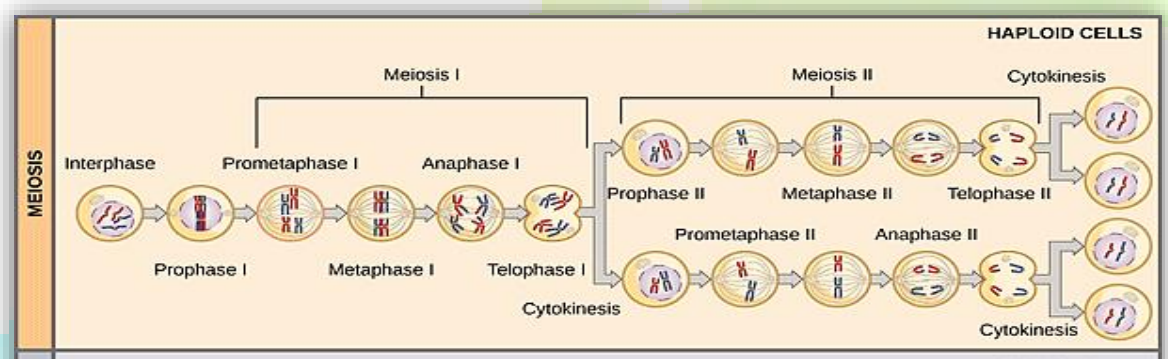

						OUTCOME
PROCESS	DNA synthesis	Synapsis of homologous chromosomes	Crossover	Homologous chromosomes line up at metaphase plate	Sister chromatids line up at metaphase plate	Number and genetic composition of daughter cells
MEIOSIS	Occurs in S phase of interphase	During prophase I	During prophase I	During metaphase I	During metaphase II	Four haploid cells at the end of meiosis II
MITOSIS	Occurs in S phase of interphase	Does not occur in mitosis	Does not occur in mitosis	Does not occur in mitosis	During metaphase	Two diploid cells at the end of mitosis