Cell division and cell cycle

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Academic year 2019-2020

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Cell cycle

Background

- Living beings produce more of their kind (procreate).
- Rudolf Virchow, a German physician, put it this way in 1855, translating which in his latin axiom “Omnis cellula e cellula,” meaning “Every cell from a cell.”
- Cell division enables unicellular organisms to reproduce and entire organimsm.
- What goes on in eukaryotes cell cycle
- Cell division involves distribution of identical genetic material, not merely the splitting of components.
- Cell division copies DNA with high fidelity.
- Functions:
    - Passing identical genetic material to cellular offspring.
    - Breakdown of cell cycle plays a role in cancer development

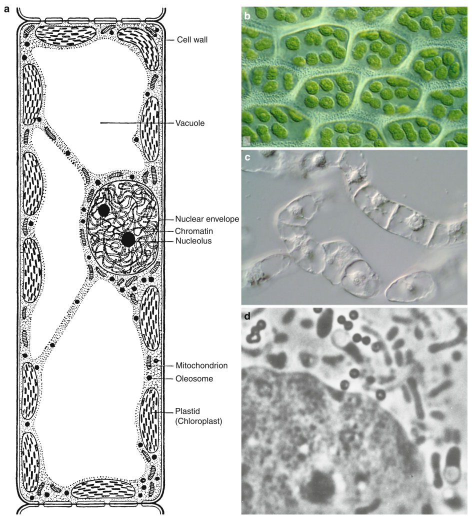


Figure 1: The plant cell under the light microscope (LM). (a) A photosynthetic parenchyma cell of a deciduous leaf. (b) Chloroplasts in the cells of a leaf (Katharina ondulata, ×300). (c) Cells in a suspension culture (tobacco; BY2) (×350): the large cells are almost filled with the central vacuole; the cell nuclei and nucleoli are in the parietal cytoplasm tube that thickens at the cell corners; numerous other cytoplasm tubes running through the cell can also be seen. (d) Nuclear region of an Allium cell, phase contrast (×3,100); chromatin and a nucleolus are in the nucleus, leucoplasts (two with pale starch-like inclusions), sausage-shaped mitochondria, and spherical oleosomes are in the cytoplasm

Organization of genetic material

- A cell's complete bulk of genetic information, DNA, is called its genome.
- Although a prokaryotic genome is often a single DNA molecule, eukaryotic genomes usually consist of a number of DNA molecules.
- Length of DNA $= \sim 250,000$ times diameter of the cell that bears it.
- When cell can divide to form genetically identical daughter cells, all of this DNA must be copied, or replicated, and then two copies must be separated so that each daughter cells ends up with a complete genome.
- DNA is packaged into **chromosomes** (*chroma* and *soma*).
- The entire complex of DNA and proteins that is the building material of chromosomes is referred to as **chromatin**.
- Most eukaryotic species have a characteristic number of chromosomes in each cell nucleus.

Structure of Chromosome

- The chromosome complement in a cell nucleus in the members of a species is called their karyotype (records all the cytologically identifiable chromosome features (size, form, number)).
- The karyotype is an important genetic, systematic, and phylogenetic characteristic.
- The number of identical chromosome sets in a cell nucleus determines the level of ploidy, *n*.
- Cell nuclei with only one set of chromosomes are haploid (*1n*; Greek *haplos*, simple) somatic (tissue) cells are predominantly diploid (*2n*) in ferns and seed plants.
- Gametic chromosome number $= 1/2$ x Somatic chromosome number
- Nuclei of extraordinary size are mostly polyploid; they contain several to many copies of the gene and chromosome complement of the species in question.
- Two compies of a chromosome are ordinarily identical in morphology, gene content and gene order; they are called **homologous chromosomes**.
- Even artificially generated polyploid cell nuclei result in enlarged cells.

- The **C value** refers to the total amount of DNA in the haploid genome, given in picograms. The C value of the bacterium Escherichia coli is 0.004, that of tobacco is 1.6, that of maize is 7.5, and that of some lily species can be over 30.
- The following chromosome features are particularly important: (Figure 6) length, position of the centromere, presence or absence of a nucleolar organizing region (NOR), and heterochromatic sections.
- Each metaphase chromosome appears to be longitudinally divided into two identical parts each of which is known as **chromatid**, a single is reffered to as sister chromatid.
- The centromere (primary constriction; Greek kentron, middle point and meros, part) is the narrowest point on the chromosome, where the chromosome bends during chromosome movements in cell division and where the microtubules of the nuclear spindle attach.

- These microtubules end in a platelike or hemispherical multilayered structure that is located on the side of the centromere and is called kinetochore.
- The part of a chromatid on either side of the centromere is referred to as an arm of the chromatid. (An uncondensed, unduplicated chromosome has a single centromere and two arms.)
- Two arms of chromosome can range for values of lengths. The **centromere index** quantifies the length ratio of the arms (short arm length divided by the total chromosome length).
- Based on the relative position of centromere on chromosomes, they can be:
  - Metacentric
  - Submetacentric
  - Acrocentric
  - Telocentric

- Centromeric region of chromosome contains satellite DNA.
- Telomeric region of chromosome is highly stable and has DNA loops.
- The chromosome region lying between secondary constriction and the nearest telomere is known as satellite. Therefore chromosomes having secondary constrictions are called satellite chromosomes.
- Nucleolus is always associated with the secondary constrictions of sat-chromosomes, thus these constrictions are sometimes also called NOR.
- In some species e.g., maize, amphibia etc, chromosomes during first prophase of meiosis (pachytene), show small bead-like structures called chroommeres.
- Homologous chromosomes always show identical pattern of chromomere distribution.

Structure of chromatin

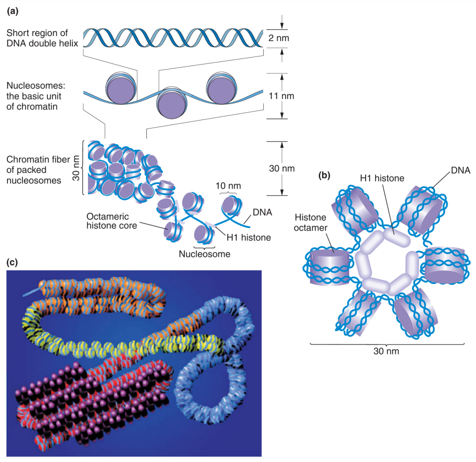


Figure 2: (a) The nucleosome in decondensed and condensed chromatin. (b) End view of the coiled chain of nucleosomes. (c) Chromatin structure varies along the length of a chromosome. The least-condensed chromatin (euchromatin) is shown in yellow, regions of intermediate condensation are in orange and blue, and heterochromatin coated with special proteins (purple) is in red.

Histones and nucleosomes

Designation	Molecular mass (kDa)	Molecule shape
H1	>24	With two positively charged processes (C-terminus and N-terminus) and a globular central domain
H2A	~18.5	Globular N-terminal domains with increasing numbers of basic amino acid residues protruding laterally
H2B	~17	
H3	15.5	
H4	11.5	

Figure 3: Overview of five basic types of histone

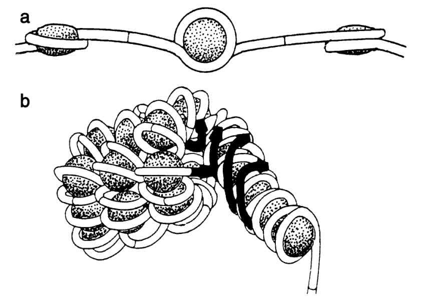
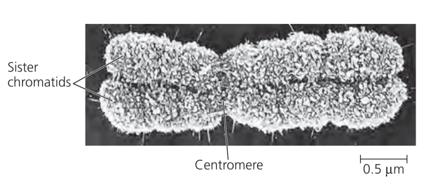


Figure 4: Nucleosomes. (a) Beaded pattern: three histone octamers (dotted) surrounded by left-handed DNA double helices bonded by DNA linkers; horizontal stripes attack sites of Micrococcus nuclease. (b) Supranucleosomal structures, mediated by H1 (black); on the right nucleofilaments, on the left chromatin fibrils (H1 not is illustrated here)

Distribution of chromosomes during eukaryotic cell division

- When a cell is not dividing, and even as it replicates its DNA in preparation for cell division, each chromosome is in the form of a long, thin chromatin fiber.
- After DNA replication, however, the chromosomes condense as a part of cell division: Each chromatin fiber becomes densely coiled and folded, making the chromosomes much shorter and so thick that we can see them with a light microscope.
- Each duplicated chromosome has two sister chromatids, which are joined copies of the original chromosome (Figure **??**).
- The two chromatids, each containing an identical DNA molecule, are initially attached all along their lengths by protein complexes called cohesins.

- Each sister chromatid has a centromere, a region containing specific DNA sequences where the chromatid is attached most closely to its sister chromatid. This attachment is mediated by protein bound to the centromeric DNA sequences and gives the condensed, duplicated chromosome a narrow “waist”.
- Later in the cell division process, the two sister chromatids of each duplicated chromosomes separate and move into two new nuclei, one forming at each end of the cell. Once they separate they are considered individual chromosomes.



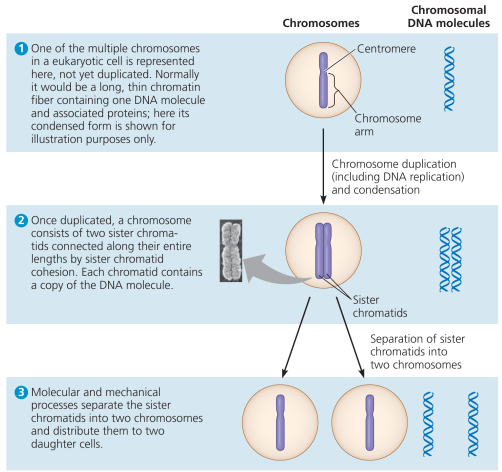


Figure 5: Overview of cell division in eukaryotic cell

Heterochromatin and euchromatin

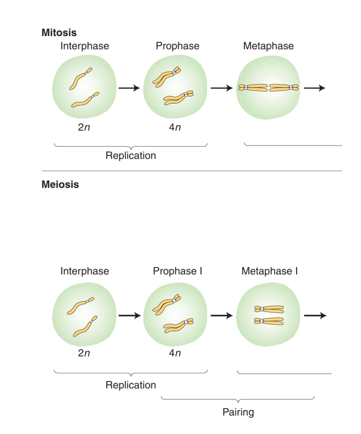
- Based on stainability of chromatin chromosomes can be Heterochromatin and Euchromatin.
- Euchromatin takes up little stain during interphase, stains only lightly during prophase, but is deeply stained during metaphase.
- Heterochromatin takes up deep stain during interphase and prophase, while during metaphase it is stained lightly.
- In general heterochromatin is found in the centromeric and telomeric regions.
- Almost all of the genes in a chromosomes are found in euchromatin region.

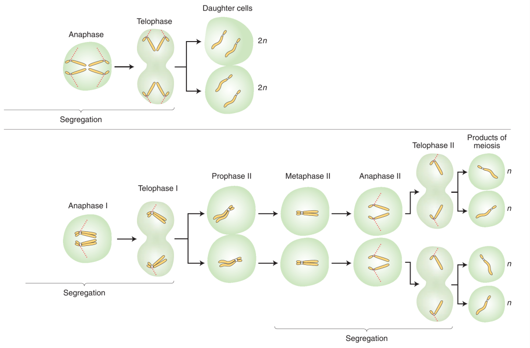
Cell division

Cell division processes

- **Mitosis** is the division of the genetic material in the nucleus, usually followed immediately by **cytokinesis**.
- Walther Flemming coined the terms *mitosis* and *chromatin*.
- Mitosis and cytokinesis produce cells that make up most of our bodies and same process continues to generate new cells to replace dead and damaged ones.
- **Meiosis** occurs in humans only in gonads (ovaries or testes) to produce eggs or sperm.
- In each division meiosis reduces the chromosome number from 46 (two sets of chromosomes) to 23 (one set), hence called the reductional division.
- Fertilization fuses gametes together and returns chromosome number to 46.

Key events in mitosis and meiosis





Mitosis

Phases of the cell cycle

- Mitotic (M) phase, including both mitosis and cytokinesis is the shortest part of the cell cycle.
- M phase alternates with **interphase** (accounts for 90% of the cycle).
- Interphase can be divided into subphases (with time lapse for a normal human cell, about **24 hours**):
  - the $\mathbf{G_1}$ phase ("first gap") $\longrightarrow$ 5-6 hours,
  - the S phase ("synthesis") $\longrightarrow$ 10-12 hours, and
  - the $\mathbf{G_2}$ phase ("second gap") $\longrightarrow$ 4-6 hours.
- During all three subphases, a cell that will eventually divide grows by producing proteins and cytoplasmic organelles such as mitochondria and endoplasmic reticulum.
- Chromosomes are duplicated only during the S phase.

Events in mitosis

- Mitotic spindle (consists of microtubules fibers and associated proteins) forms in the cytoplasm during prophase.
- Spindle formation starts at centrosomes, division of which has occured during interphase.
- An **aster**, a radial array of short microtubules extends from each centrosome.
- Each of the two sister chromatids of a duplicated chromosome has a kinetochore, a structure of proteins associated with specific sections of chromosomal DNA at each centromere.

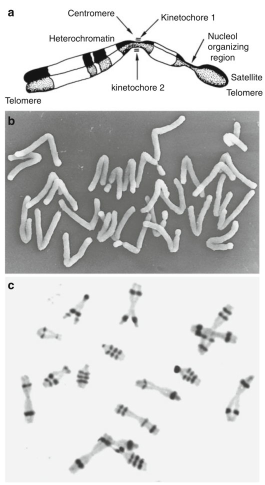


Figure 6: Chromosomes occur as compact entities during nuclear division (e.g., in metaphase and anaphase of mitosis). This entity is what was originally named 'chromosome.' (a) A satellite chromosome with the two telomeres, the centromere with the two kinetochores (insertion points of the microtubules on the spindle apparatus), heterochromatic bands (additional regions on the telomeres and in the region of the centromere), and the characteristic (for satellite chromosomes) nucleolar organizing region (NOR) and a heterochromatic satellite. The chromosome is split longitudinally into two chromatids that later become daughter chromosomes. (b) Anaphase chromosomes of barley (Hordeum vulgare) with a diploid chromosome number 2n = 28, two satellite chromosomes per complement. The four NORs and four satellites of the two complements of daughter chromosomes can be seen clearly (x1,880). (c) Chromosome complement of *Anemone blanda* (2n = 16); heterochromatic bands (except at the centromere) picked out with color (x600)

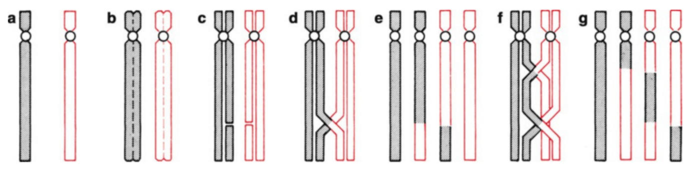
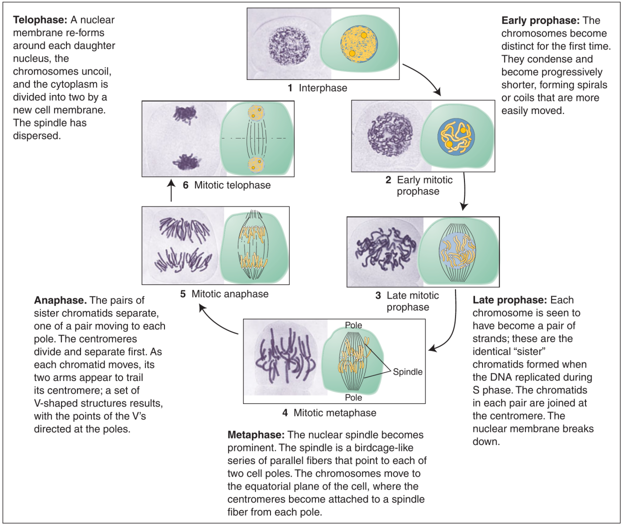


Figure 7: Chiasma genesis. (a, b) Homolog pairing. (c) Genesis of corresponding chromatid bridges and (d) cruciform healing of two homologous chromatid sections. (e) Before reduction for the neighboring ('proximal') chromosome to the centromere sections; the 'distal' sections (beyond the chiasma) after reduction. (f, g) Double crossing-over with triple-strand exchange, where the second exchange takes place between a chromatid already involved in the first exchange and a hitherto uninvolved one. Only two (always one maternal and one paternal) of four chromatids are ever involved in a crossing-over event

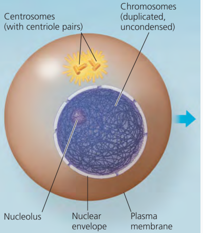
Stages of mitosis

Mitosis usually takes up only a small proportion of the cell cycle, approximately 5 to 10 percent. The remaining time is the interphase, composed of G1, S, and G2 stages. The DNA is replicated during the S phase, although the duplicated DNA does not become visible until later in mitosis. The chromosomes cannot be seen during interphase (see below), mainly because they are in an extended state and are intertwined with one another like a tangle of yarn.

The photographs below show the stages of mitosis in the nuclei of root-tip cells of the royal lily, *Lilium regale*. In each stage, a photograph is shown at the left and an interpretive drawing at the right.



G_2 of Interphase

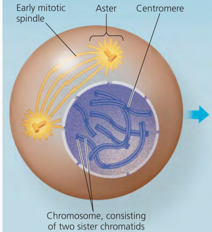


G_2 of Interphase

- A nuclear envelope encloses the nucleus.
- The nucleus contains one or more nucleoli (singular, *nucleolus*).
- Two centrosomes have formed by duplication of a single centrosome. Centrosomes are regions in animal cells that organize the microtubules of the spindle. Each centrosome contains two centrioles.
- Chromosomes, duplicated during S phase, cannot be seen individually because they have not yet condensed.

The light micrographs show dividing lung cells from a newt, which has 22 chromosomes in its somatic cells. Chromosomes appear blue, microtubules green, and intermediate filaments red. For simplicity, the drawings show only 6 chromosomes.

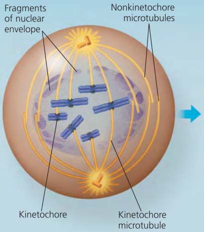
Prophase



Prophase

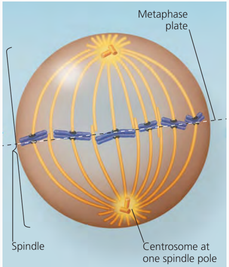
- The chromatin fibers become more tightly coiled, condensing into discrete chromosomes observable with a light microscope.
- The nucleoli disappear.
- Each duplicated chromosome appears as two identical sister chromatids joined at their centromeres and, in some species, all along their arms by cohesins (sister chromatid cohesion).
- The mitotic spindle (named for its shape) begins to form. It is composed of the centrosomes and the microtubules that extend from them. The radial arrays of shorter microtubules that extend from the centrosomes are called asters ("stars").
- The centrosomes move away from each other, propelled partly by the lengthening microtubules between them.

Prometaphase



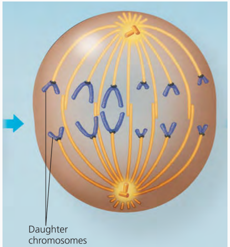
Prometaphase

- The nuclear envelope fragments.
- The microtubules extending from each centrosome can now invade the nuclear area.
- The chromosomes have become even more condensed.
- Each of the two chromatids of each chromosome now has a kinetochore, a specialized protein structure at the centromere.
- Some of the microtubules attach to the kinetochores, becoming "kinetochore microtubules," which jerk the chromosomes back and forth.
- Nonkinetochore microtubules interact with those from the opposite pole of the spindle.



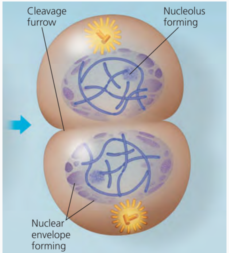
Metaphase

- The centrosomes are now at opposite poles of the cell.
- The chromosomes convene at the *metaphase plate*, a plane that is equidistant between the spindle's two poles. The chromosomes' centromeres lie at the metaphase plate.
- For each chromosome, the kinetochores of the sister chromatids are attached to kinetochore microtubules coming from opposite poles.



Anaphase

- Anaphase is the shortest stage of mitosis, often lasting only a few minutes.
- Anaphase begins when the cohesin proteins are cleaved. This allows the two sister chromatids of each pair to part suddenly. Each chromatid thus becomes a full-fledged chromosome.
- The two liberated daughter chromosomes begin moving toward opposite ends of the cell as their kinetochore microtubules shorten. Because these microtubules are attached at the centromere region, the chromosomes move centromere first (at about 1 µm/min).
- The cell elongates as the nonkinetochore microtubules lengthen.
- By the end of anaphase, the two ends of the cell have equivalent—and complete—collections of chromosomes.



Telophase

- Two daughter nuclei form in the cell. Nuclear envelopes arise from the fragments of the parent cell's nuclear envelope and other portions of the endomembrane system.
- Nucleoli reappear.
- The chromosomes become less condensed.
- Any remaining spindle microtubules are depolymerized.
- Mitosis, the division of one nucleus into two genetically identical nuclei, is now complete.

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.

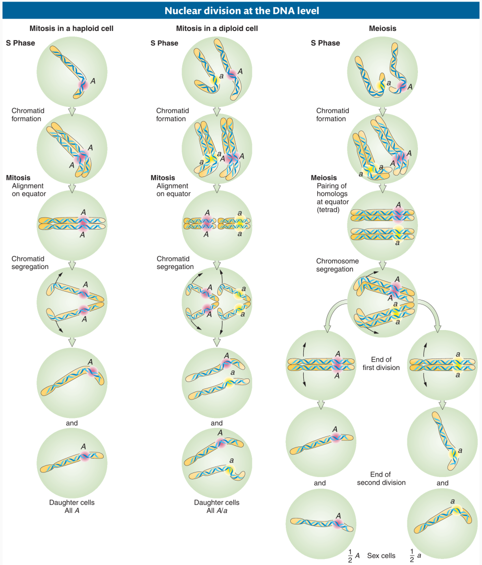
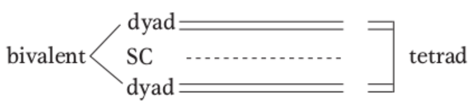


Figure 8: DNA and gene transmission in mitosis and meiosis in eukaryotes. The S phase and the main stages of mitosis and meiosis are shown. Mitotic divisions (left and middle) conserve the genotype of the original cell. At the right, the two successive meiotic divisions that take place during the sexual stage of the life cycle have the net effect of halving the number of chromosomes. The alleles A and a of one gene are used to show how genotypes are transmitted in cell division.

Meiosis

Background

- Before meiosis, chromosome replication takes place to form sister chromatids, which become visible at meiosis.
- Contrasting mitosis and meiosis:
  - Centromere appears not to divide at this stage, whereas it does in mitosis.
  - The homologous pairs of sister chromatids now unite to form a bundle of four homologous chromatids, they do not in mitosis.
- Joining of the homologous pairs is called **synapsis**, and it relies on the properties of a macromolecular assemblage called the synaptonemal complex (SC), which runs down the center of the pair.
- Replicate sister chromosomes are together called a **dyad** (from the Greek word for two). The unit comprising the pair of synapsed dyads is called a **bivalent**.
- The four chromatids that make up a bivalent are called a **tetrad** (Greek for four), to indicate that there are four homologous units in the bundle.

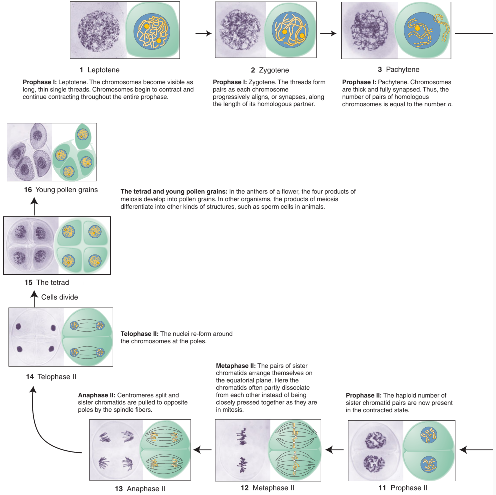


- The bivalents of all chromosomes move to the cell's equator, and, when the cell divides, one dyad moves into each new cell, pulled by spindle fibers attached to the centromeres.
- In the second cell division of meiosis, the centromeres divide and each member of a dyad (each member of a pair of chromatids) moves into a daughter cell. Hence, although the process starts with the same genomic content as that for mitosis, the two successive segregations result in four haploid cells.
- Each of the four haploid cells that constitute the four products of meiosis contains one member of a tetrad; hence, the group of four cells is sometimes called a tetrad, too.

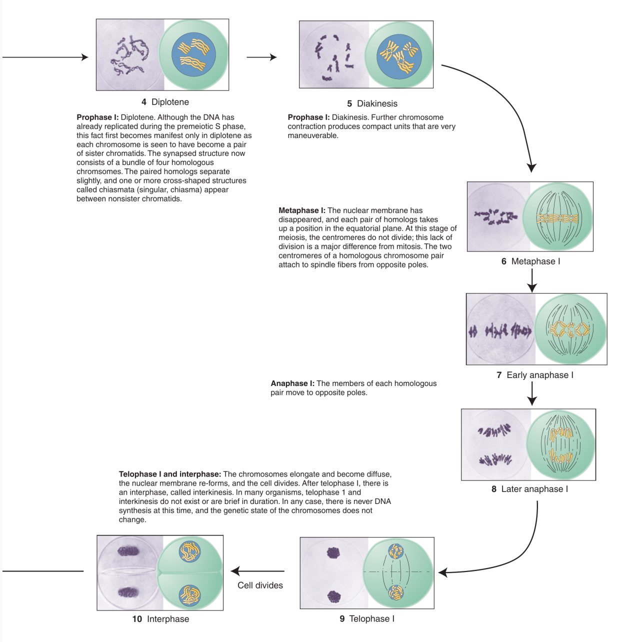
Stages of meiosis

Meiosis consists of two nuclear divisions distinguished as meiosis I and meiosis II, which take place in consecutive cell divisions. Each meiotic division is formally divided into prophase, metaphase, anaphase, and telophase. Of these stages, the most complex and lengthy is prophase I, which is divided into five stages.

The photographs below show the stages of meiosis in the nuclei of root-tip cells of the royal lily, *Lilium regale*. In each stage, a photograph is shown at the left and an interpretive drawing at the right.



The photographs show meiosis and pollen formation in *Lilium regale*. Note: For simplicity, multiple chiasmata are drawn between only two chromatids; in reality, all four chromatids can take part. [*After J. McLeish and B. Snoad, Looking at Chromosomes. Copyright 1958, St. Martin's, Macmillan.*]


4 Diplotene
Prophase I: Diplotene. Although the DNA has already replicated during the premeiotic S phase, this fact first becomes manifest only in diplotene as each chromosome is seen to have become a pair of sister chromatids. The synapsed structure now consists of a bundle of four homologous chromsomes. The paired homologs separate slightly, and one or more cross-shaped structures called chiasmata (singular, chiasma) appear between nonsister chromatids.
5 Diakinesis
Prophase I: Diakinesis. Further chromosome contraction produces compact units that are very maneuverable.
Metaphase I: The nuclear membrane has disappeared, and each pair of homologs takes up a position in the equatorial plane. At this stage of meiosis, the centromeres do not divide; this lack of division is a major difference from mitosis. The two centromeres of a homologous chromosome pair attach to spindle fibers from opposite poles.
6 Metaphase I
7 Early anaphase I
Anaphase I: The members of each homologous pair move to opposite poles.
8 Later anaphase I
Telophase I and interphase: The chromosomes elongate and become diffuse, the nuclear membrane re-forms, and the cell divides. After telophase I, there is an interphase, called interkinesis. In many organisms, telophase 1 and interkinesis do not exist or are brief in duration. In any case, there is never DNA synthesis at this time, and the genetic state of the chromosomes does not change.
Cell divides
10 Interphase
9 Telophase I

Associated events in eukaryotic cell division

Chromosome pairing in an autotetraploid

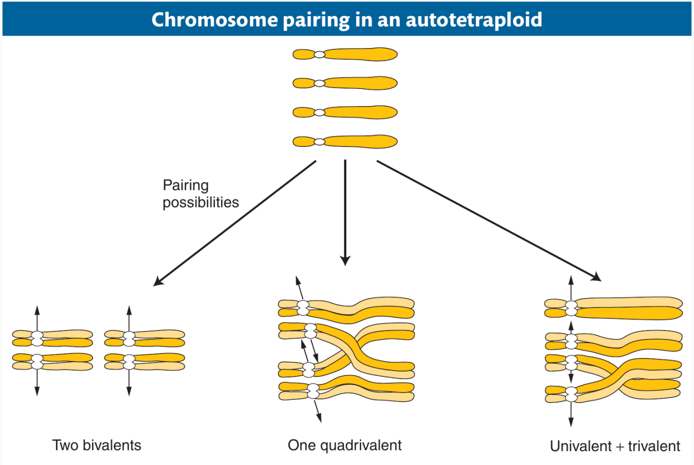


Figure 9: There are three different pairing possibilities at meiosis in tetraploids. The four homologous chromosomes may pair as two bivalents or as a quadrivalent, and each can yield functional gametes. A third possibility, a trivalent plus a univalent, yields nonfunctional gametes.

Bibliography