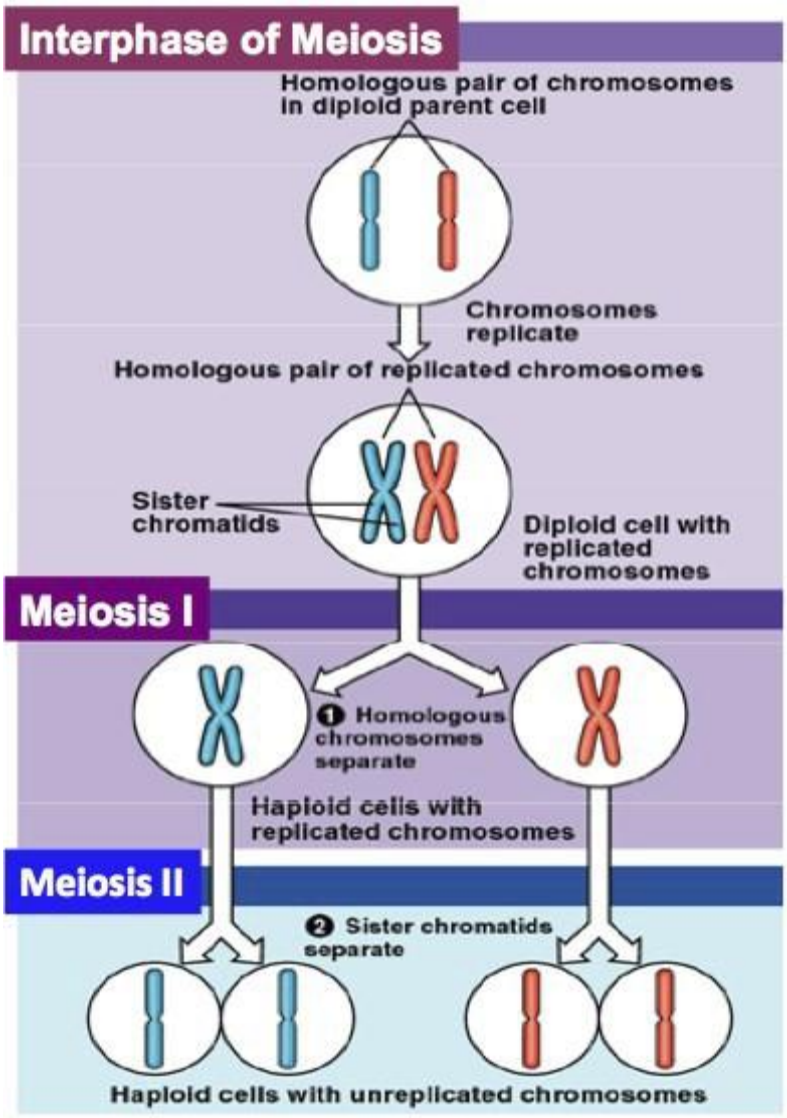
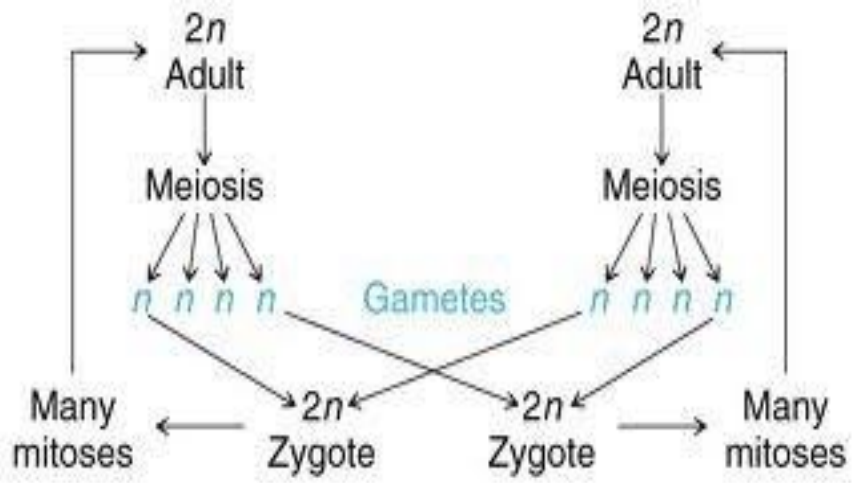
MEIOSIS AND SEXUAL REPRODUCTION

Meiosis is a special type of cell division necessary for sexual reproduction, in eukaryotes, such as animals, plants and fungi, to produce gametes (figure below). The process includes: 1) number of sets of chromosomes in the cell undergoing meiosis is reduced to half the original number, typically from two sets (diploid) to one set (haploid).
2) the chromosome is reduced from double to single structure.



In many organisms, including all animals and land plants (but not some other groups such as fungi), gametes are called sperm in males and egg cells (or ova) in females. Since meiosis has halved the number of sets of chromosomes, when two gametes fuse during fertilization, the number of

sets of chromosomes in the resulting zygotes restored to the original number.



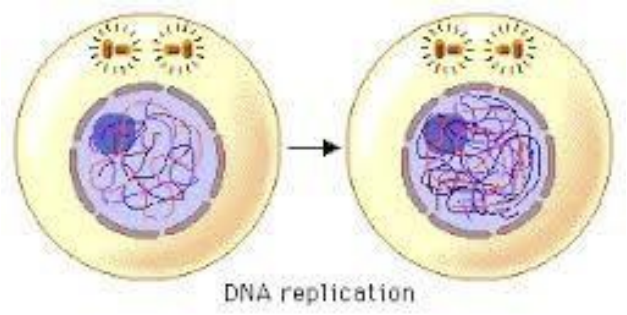
Meiosis is divided into two stages, meiosis I and meiosis II which are further divided into Karyokinesis I (prophase I, metaphase I, anaphase I, telophase I) and Cytokinesis I then Karyokinesis II (prophase II, metaphase II, anaphase II, telophase II) and Cytokinesis II, respectively, dividing the cells once at each stage.

The first stage (Meiosis I) begins with a diploid cell that has two copies of each type of chromosome, one from each the mother and father (homologous chromosomes). All homologous chromosomes pair up and may exchange genetic material with each other in a process called crossover. Each pair then separates as two haploid cells are formed, each with one chromosome from every homologous pair.

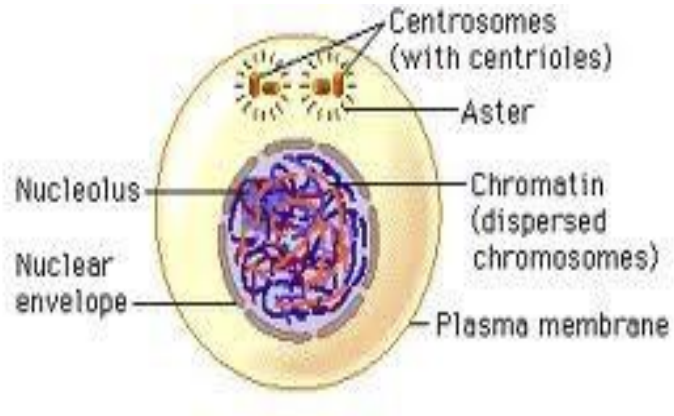
In the second stage (Meiosis II), each chromosome splits into two, with each half, called a sister chromatid, being separated into two new cells, which are still haploid. This occurs in both of the haploid cells formed in meiosis I. Therefore from each original cell, four genetically distinct (genetically different) haploid cells are produced. These cells can mature into gametes.

Meiosis I (reduction division)

Because meiosis is a "one-way" process, it cannot be said to engage in a cell cycle as mitosis does. However, the preparatory steps that leads up to meiosis are identical in pattern and name to the interphase of the mitotic cell cycle i.e. interphase is not a part of meiosis. So, just before meiosis I there is Interphase I where there is DNA replication, organelle synthesis and an increase in energy stores.

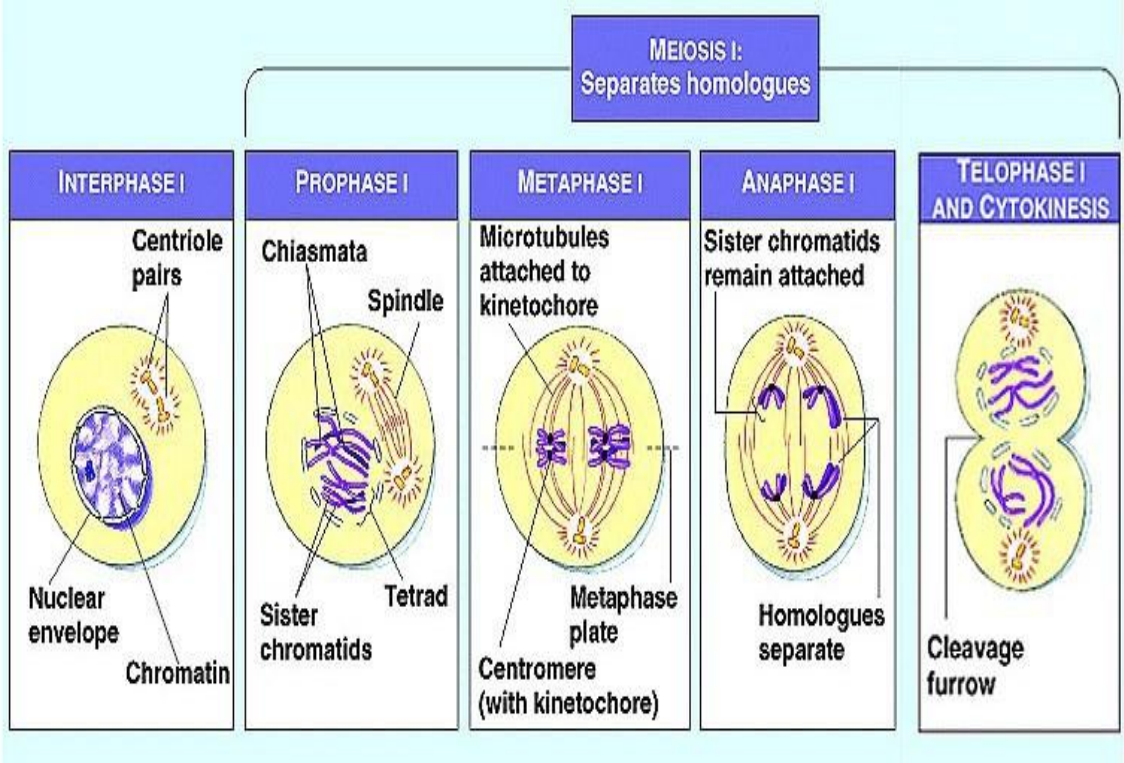


Interphase I

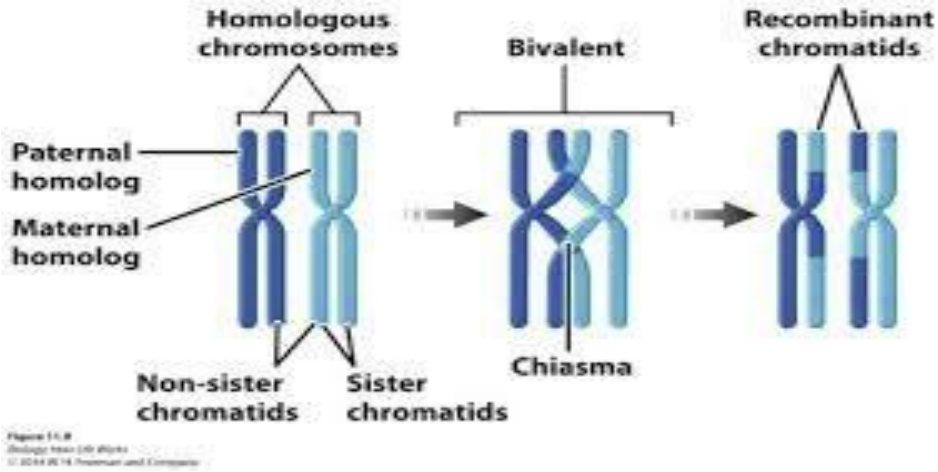


In Meiosis I, the number of sets of chromosomes in the cell undergoing meiosis I is reduced to half the original number, typically from diploid to haploid (reduction division or separates homologues), but the chromosome structure remains double.

Meiosis I is divided into Karyokinesis I (prophase I, metaphase I, anaphase I, telophase I) and Cytokinesis I (figure below).

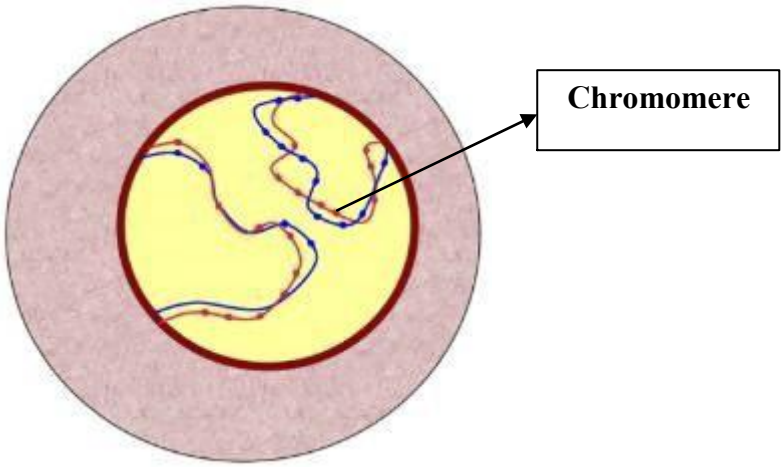


Prophase I: It is the longest phase of meiosis. During prophase I, DNA is exchanged between homologous chromosomes in a process called homologous recombination. This often results in chromosomal crossover. The new combinations of DNA created during crossover are a significant source of genetic variation, and may result in beneficial new combinations of alleles. The process of pairing the homologous chromosomes is called **synapsis.** The paired and replicated chromosomes (synapsed structure) are called **bivalents or tetrads**, which have two chromosomes (2 dyads) with four chromatids, with one chromosome coming from each parent (figure below). At this stage, non-sister chromatids may cross-over at points called **chiasmata** (singular chiasma). Both nuclear envelope and nucleoli start to disappear by the end of prophase I, while 2 pairs of centrioles would have moved to opposite poles of the cell forming the spindles, which in turn control the chromosome movement during the next phases.

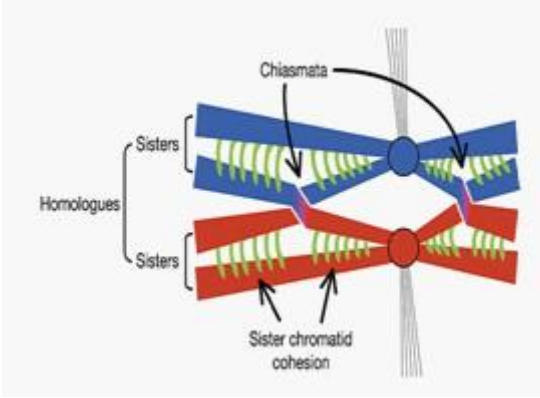


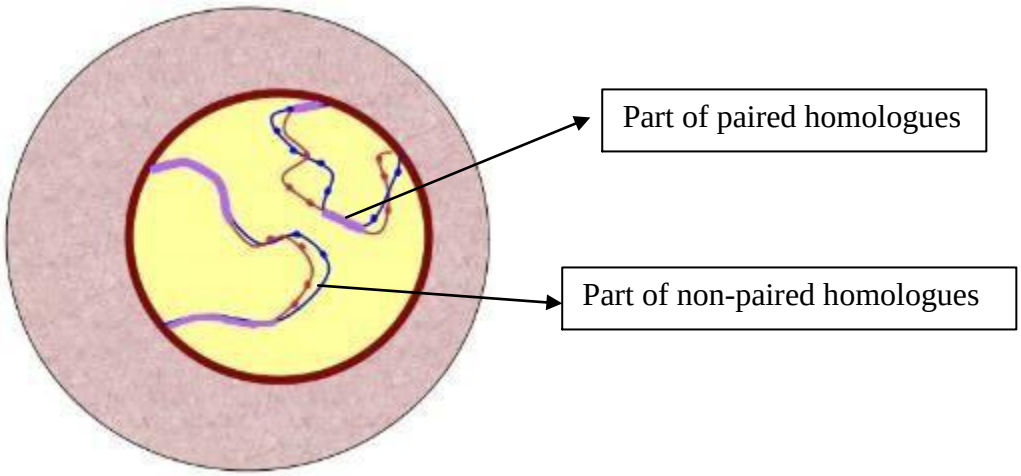
Prophase I is subdivided into the following 5 substages (figure below):

Leptotene (leptonema)**:** The first stage of prophase I that means "thin threads". This stage is of very short duration in which the individual chromosomes (each consisting of two sister chromatids, **Dyad**) change from the diffuse state they exist in during the cell's period of growth and condense (supercoil) into visible strands within the nucleus but they are not yet fully condensed. Along each chromosome some localized condensations are present and resemble beads on a string known as **chromomeres**. The chromosomes, while they have this threadlike form, are called *chromatonemata* (sing. chromonema; *-nema* is Greek for *thread*). The chromosomes appear single because the sister chromatids are still so tightly bound to each other that they cannot be separately seen. Sister chromatids of each dyad are held together along their length by cohesin and at centromeres region, they are held together by both cohesin and Shugoshin proteins. During this stage both telomeres of each chromosome are turned toward, and probably attached to, the same region of the nuclear envelope. The chromosomes are 2n and double in structure.

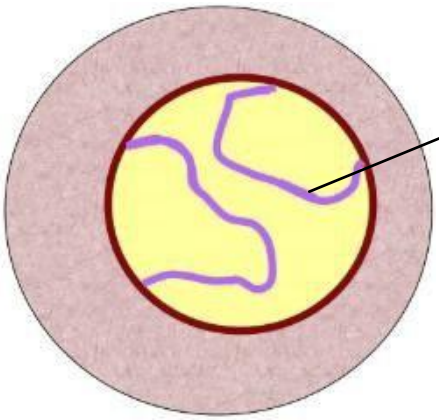


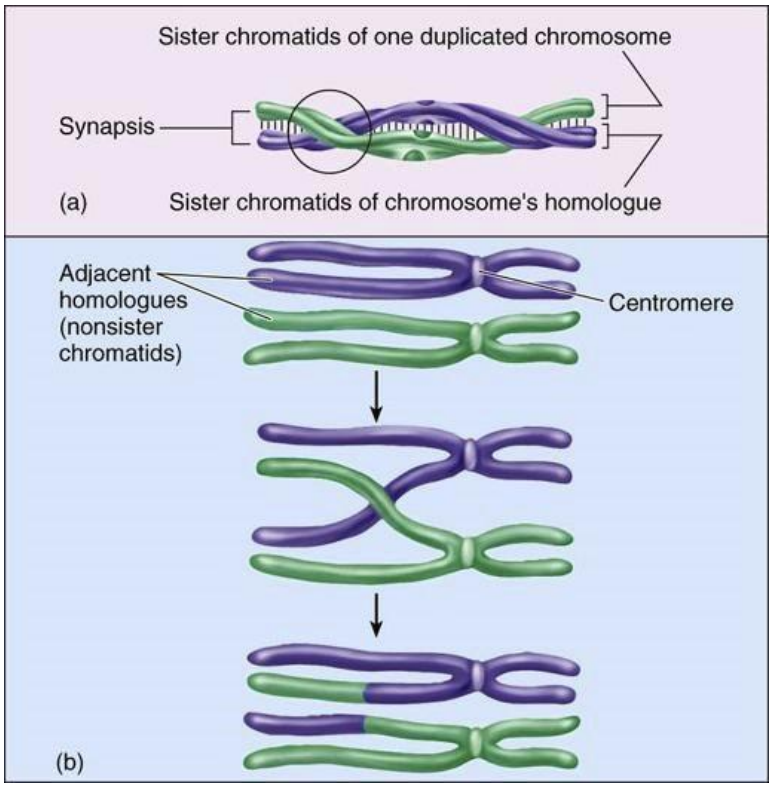
Zygotene (zygonema)**:** This stage means "paired threads", in which the chromosomes continue to shorten and thicken and approximately line up with each other into homologous chromosome pairs. This is called the bouquet or ladder-like stage because of the way the telomeres cluster at one end by synaptonemal proteins. At this stage, the synapsis (pairing/coming together) of homologous chromosomes take place so, the fused homologs look like a single chromosome under the light microscope, but they are actually double. **Synapsis** is the process of fusion that occurs between homologs by *synaptonemal complex* and begins at various points along the chromosome and extends outward in a zipper-like fashion until it completes the entire lengths in the next step. Individuals of a pair are equal in length and in position of the centromere thus pairing is highly specific and exact. The paired chromosomes are called bivalent or tetrad chromosomes. Sister chromatids of each dyad still held together along their length by cohesin and at centromeres region, they also held together by both cohesin and Shugoshin proteins (figure below).





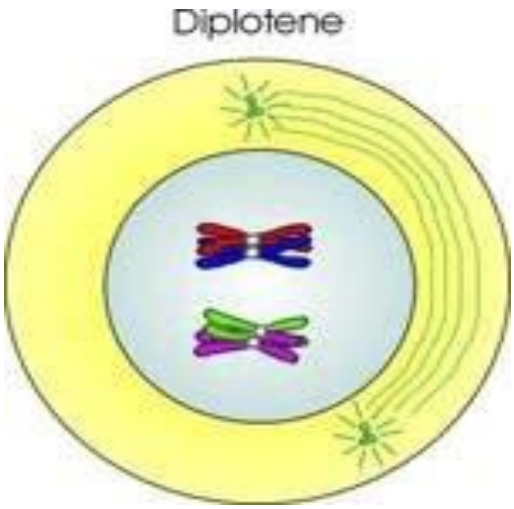
Pachytene (pachynema): it means "thick threads". At this stage, chromosomes become thicker and synapsis is completed chromosomal crossover occurs. Non-sister chromatids of homologous chromosomes may twist and start to exchange segments over regions of homology. Sex chromosomes, however, are not wholly identical, and only exchange information over a small region of homology. At the sites where exchange happens, **chiasmata form**. The exchange of information between the non-sister chromatids results in a recombination of information (mixed info) in a certain part, while the rest is the information it had before. The chromosomes are n bivalent.



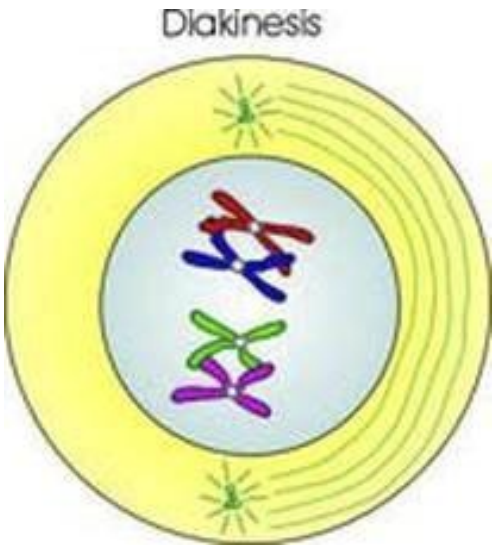


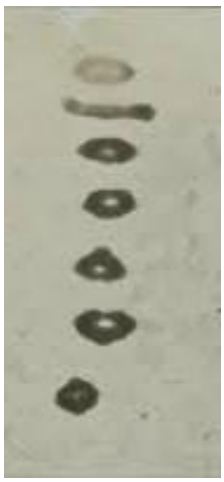
Diplotene (diplonema)**:** It means "two threads". During this stage, the crossover appears clearly due to the degradation of the synaptonemal complex (disassembly) that separate a little the homologous chromosomes from one another leading them to uncoil a bit (desynapsis). However, the homologous chromosomes of each bivalent remain tightly bound at chiasmata, the regions where crossover occurred. Chiasmata appear to "peristalse" to the tips of the chromatids, where they remain attached in a process known as **terminalization**. The chiasmata

remain on the chromosomes until they are separated in anaphase I. The chromosomes still n bivalent.



Diakinesis: It means "moving through". Chromosomes condense further during this stage. This is the first point in meiosis where the four parts of the tetrads are actually visible. Sites of crossover entangle together, effectively overlapping, making chiasmata more visible. The **terminalization** of the tetrads continues to get either ring or rod bivalents when it is completed or intermediate chiasmata may be formed due to incomplete terminalization in same/other chromosomes. The chromosomes still n bivalent. Other than this observation, the rest of the stage closely resembles late prophase of mitosis; the nucleoli disappear, the nuclear membrane disintegrates into vesicles, and the meiotic spindle begins to form and attach to kinetochores. Both nuclear envelope and nucleoli start to disappear, while the spindles begin to form from the centrosomes to control chromosome movement during meiosis I.

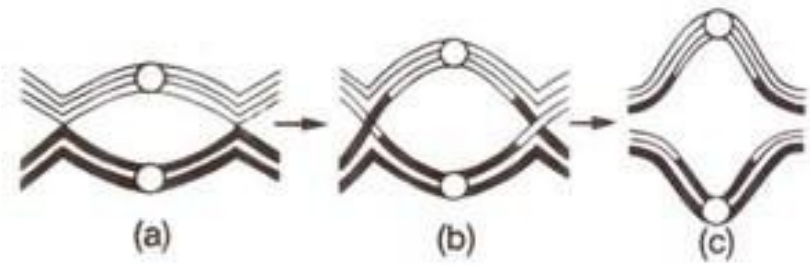




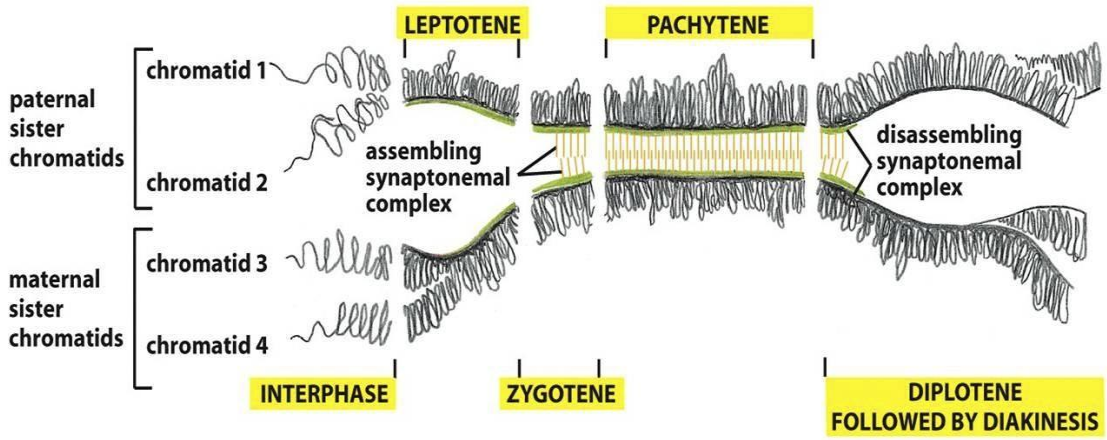
ring or rod bivalents

Terminalization of Chiasma:

The movement of chiasma to the ends of paired, non-sister chromatids. This movement starts in the diplotene and may continue until diaknesis or even metaphase I. As chiasma terminalization reaches completion, the total number of chiasma among the paired chromosomes decreases, and those that remain become concentrated near to, or at the ends of, each bivalent.



Assembling and disassembling of Synaptonemal Complex in Prophase I:



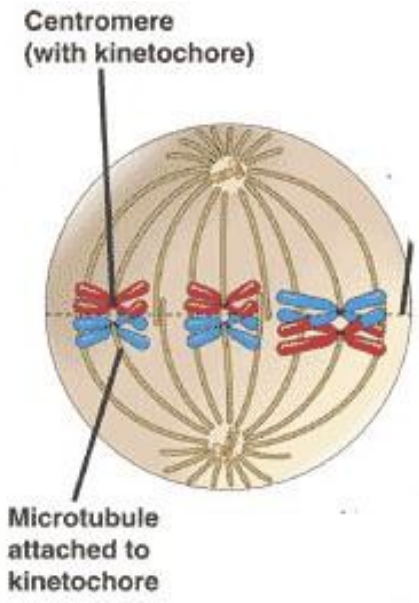
The **synaptonemal complex** (SCs) is a tripartite protein structure consisting of two parallel lateral elements, numerous transverse elements and a central element formed in the interface where two homologs unite. Three specific components of the synaptonemal complex have been characterized: SC protein-1 (SYCP1), SC protein-2 (SYCP2), and SC protein-3 (SYCP3).

It works as zipper which assembled between homologous chromosomes during the prophase of the first meiotic division. Their assembly and disassembly correlate with the successive chromatin rearrangements of meiotic prophase, namely the condensation, pairing, recombination and disjunction of homologous chromosomes.

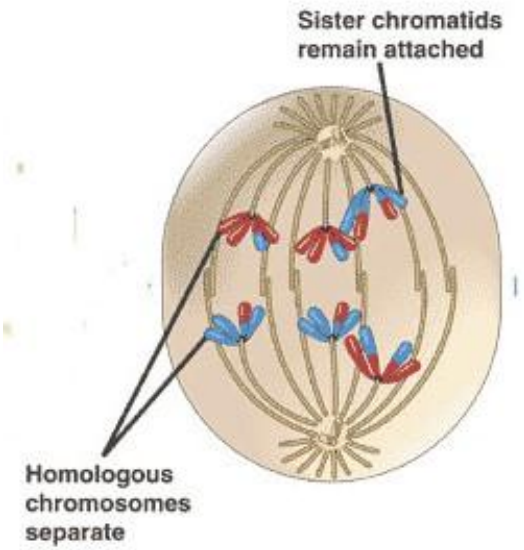
This "tripartite structure" is seen during the pachytene stage of the first meiotic prophase, both in males and in females during gametogenesis. Previous to the pachytene stage, during leptonema, the lateral elements begin to form and they initiate and complete their pairing during the zygotene stage. After pachynema ends, the SC usually becomes disassembled and can no longer be identified.

It is currently thought that the SC functions primarily as a scaffold to allow interacting chromatids to complete their crossover activities by mediating chromosome pairing, synapsis, and recombination.
SCs are now considered to be structures that control both the number and distribution of reciprocal exchanges between homologous chromosomes (crossovers) and convert crossovers into functional chiasmata.

Metaphase I: Homologous pairs move together along the metaphase plate: As kinetochore microtubules from both centrioles (of centromeres) attach to their respective kinetochores, the homologous chromosomes align along an equatorial plane that bisects the spindle fibers, due to continuous counterbalancing forces exerted on the bivalents by the microtubules emanating from the two kinetochores of homologous chromosomes. The physical basis of the independent assortment of chromosomes is the random orientation of each bivalent along the metaphase plate, with respect to the orientation of the other bivalents along the same equatorial line. Complete disappearance of nuclear membrane and nucleolus. The chromosomes still n bivalent.



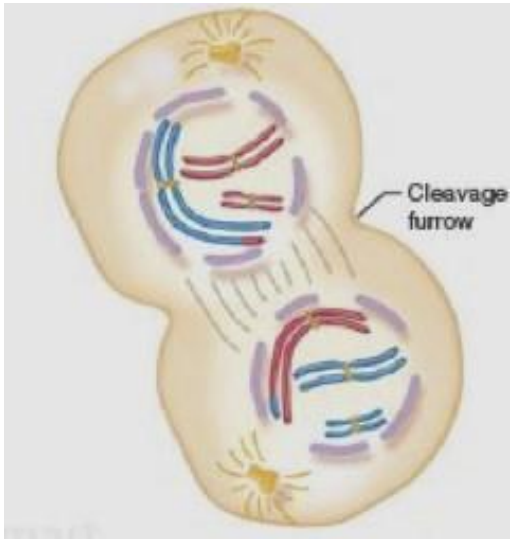
Anaphase I: Cohesin protein is degraded between sister chromatids, except at the centromere where they still connected (presence of both cohesin and shugoshin complex). Microtubules of spindle shorten leading to breaking of chiasmata, so spindle fibers separate the 2 dyads, carrying them to opposite poles. Each pole receives n number double in structure (reduction in number). The cell elongates in preparation for division down the center.



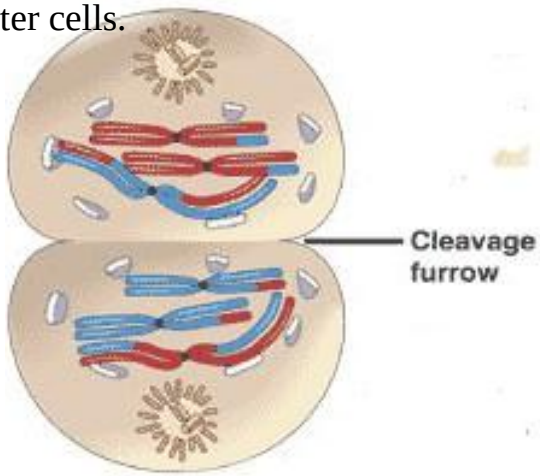
NOTE:

If crossover had not occurred in the first meiotic prophase, each dyad at each pole would consist of either paternal or maternal chromatids. However, the exchanges produced by crossover create mosaic (mix) chromatids from both paternal and maternal origin.

Telophase I: The first meiotic division effectively ends when the chromosomes arrive at the poles. Each daughter cell now has half the number of the tetrad but each chromosome consists of a pair of chromatids (dyad). The microtubules that make up the spindle network disappear, and a new nuclear membrane surrounds each haploid set. The chromosomes uncoil back into chromatin. Sister chromatids remain attached as dyads during telophase I.

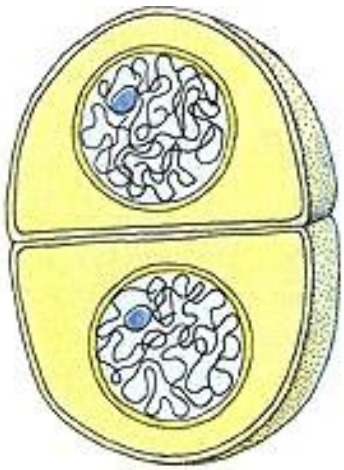


Cytokinesis I: the pinching of the cell membrane in animal cells or the formation of the cell wall in plant cells (using phragmoplasts, explained previously in mitosis) may or may not occur for completing the creation of two daughter cells. Like Mitosis, the cytoplasm and organelles are usually shared approximately equally between the daughter cells.



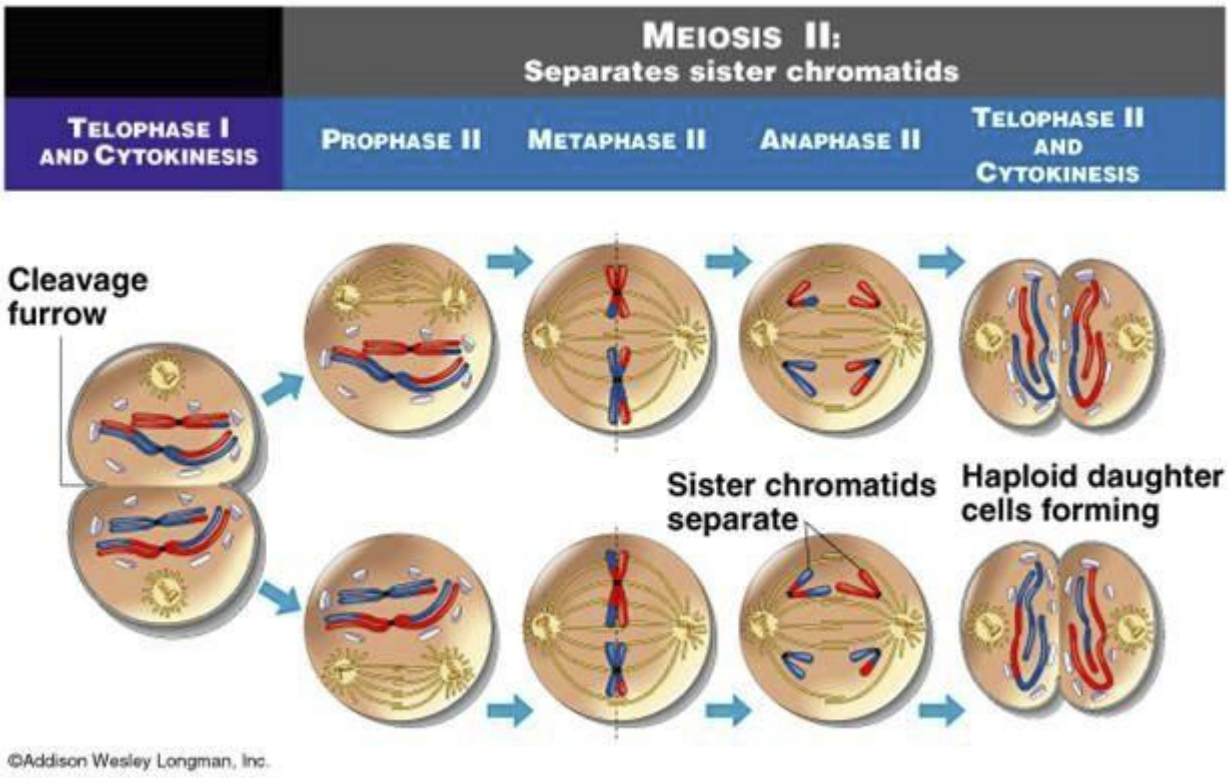
NOTE:

Cells may enter a period of rest known as **interkinesis or interphase II** where no DNA replication occurs. Like Mitosis, the genetic material in the nucleus is in form of chromatin, which appears only as dark granules because they are uncoiled into long, thin strands. Both nucleolus and nuclear membranes are present and clearly visible.

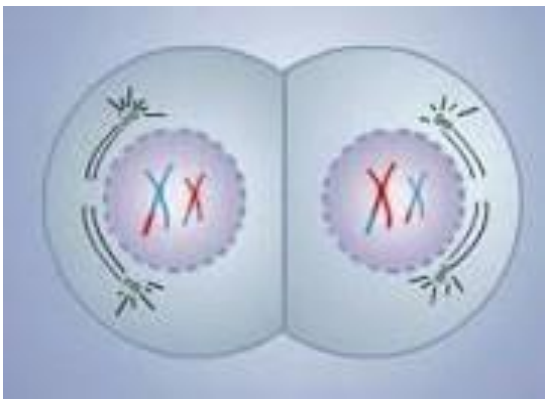


Meiosis II (similar to mitosis, reduction in structure)

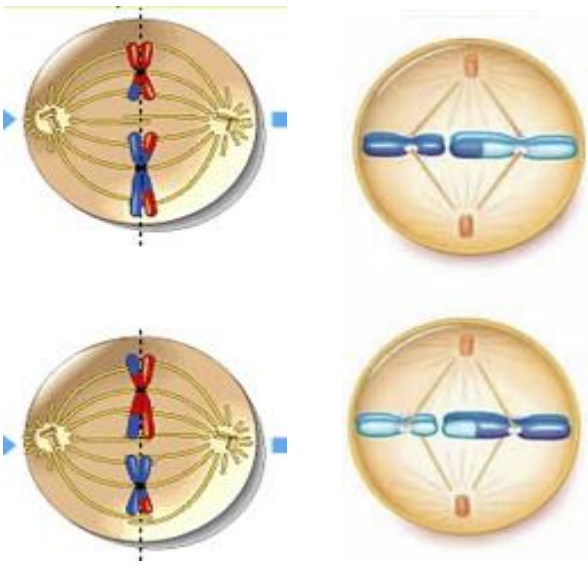
In this process, the two haploid cells (n dyads) produce 4 haploid (n monads) genetically different known as gametes. This division is physically the same as Mitosis, but the genetics of the cells are different. Meiosis II consists of Karyokinesis II (prophase II, metaphase II, anaphase II, telophase II) and Cytokinesis II (figure below).



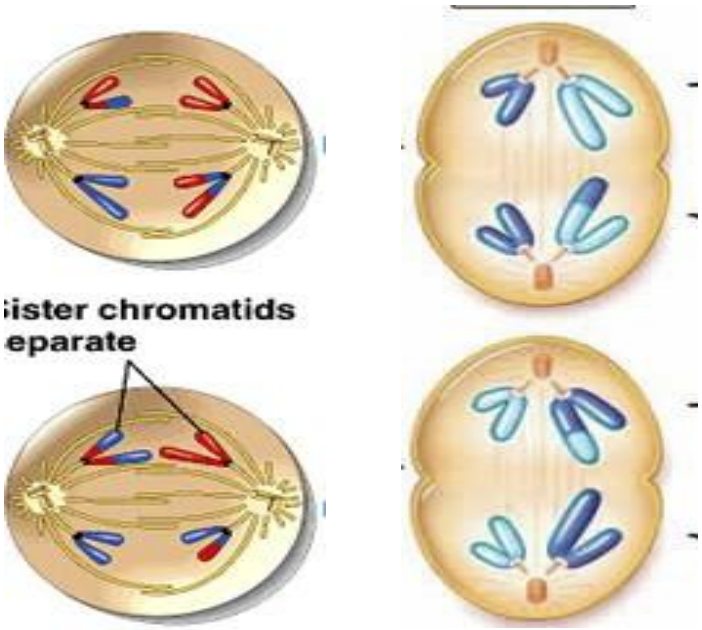
Prophase II: we see the disappearance of the nucleoli and the nuclear envelope again as well as the shortening and thickening of the chromatids which appear as dyads. Centrioles move to the polar regions and arrange spindle fibers for the second meiotic division.



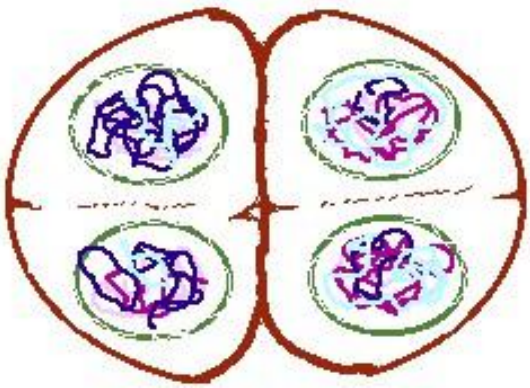
Metaphase II: The kinetochores of the dyads attach to spindle fibers formed from the centrosomes (centrioles) at each pole (i.e. directed towards the opposite poles). The chromatids of the dyads (non-homologous chromosomes) are joined by their centromeres with cohesin and shugoshin complex and aligned along the equator. In case of ♀ mother cells: the new equatorial metaphase plate is parallel to the spindle of metaphase I. In case of ♁ mother cells: the new equatorial metaphase plate is perpendicular (rotated by 90 degrees) to the previous plate of metaphase I.



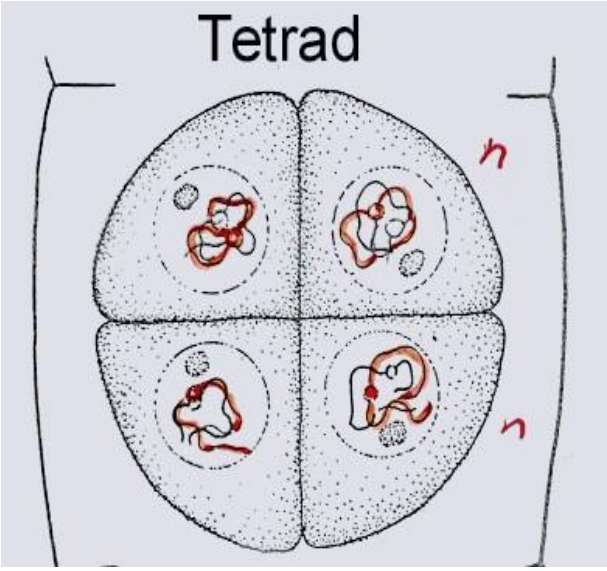
This is followed by **<u>Anaphase II</u> (reduction in structure)**, where the centromeres are cleaved by degrading cohesin and shugoshin complex, allowing microtubules attached to the kinetochores to pull the sister chromatids apart. The sister chromatids by convention are now called chromosomes (monads) as they move toward opposing poles (n single structure to each direction).



The Karypkinesis II process ends with **<u>Telophase II</u>**, which is similar to telophase I, and is marked by uncoiling and lengthening of the chromosomes and the disappearance of the spindle. Nuclear envelopes and nucleolus are reformed. Now we have 4 new haploid nuclei with monad chromosomes in one cell.



Cytokinesis II: Meiosis is now complete and ends up with four new cells by cleavage of the cell membrane in animal cells or the formation of the cell wall in plant cells (same as Cytokinesis I) producing a total of four cells, each with a haploid set of chromosomes which are single structure.



Gametogenesis:

It is the process by which the produced 4 haploid cells undergo some differentiation and developmental events to produce gametes (haploid sex cells, germ cells). It includes the formation of ♂ gametes (spermatogenesis in animals and microsporogenesis in plants) or the formation of ♀ gametes (oogenesis in animals and megasporogensis in plants) i.e. all the sex cells whether are in plants or animals undergo meiosis.

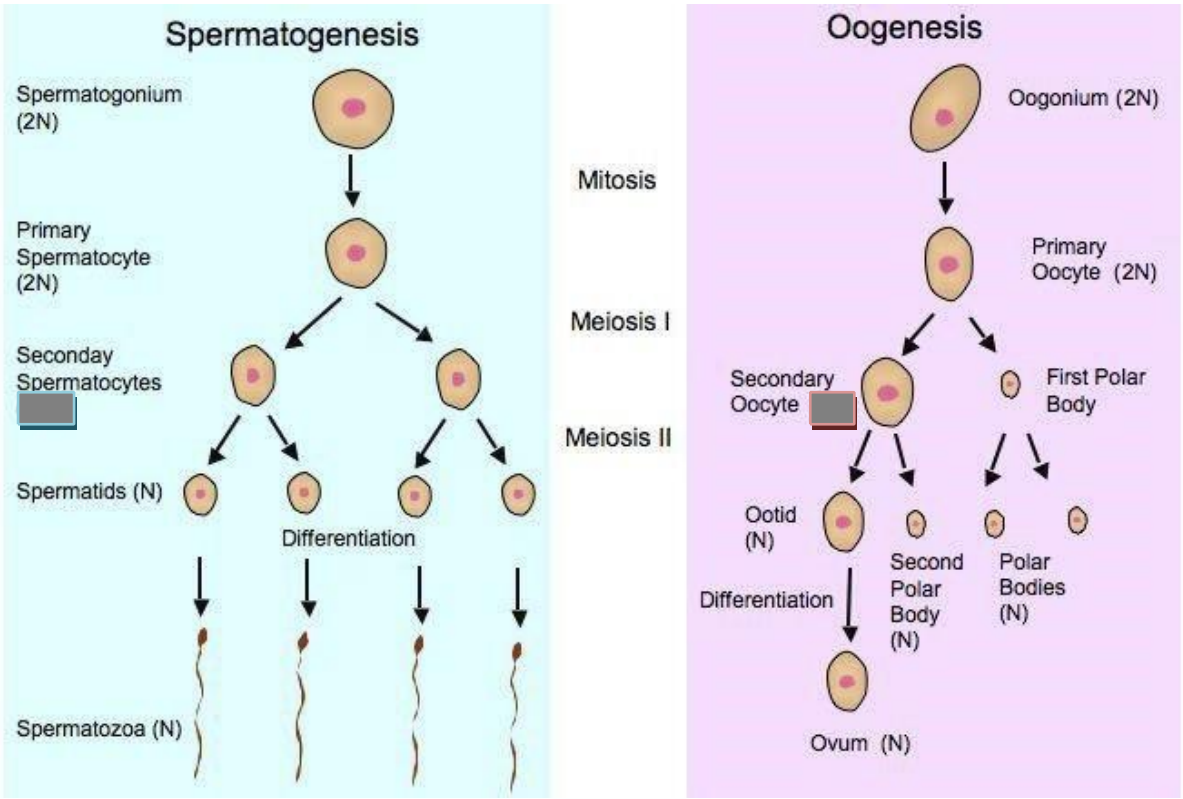
In Animal or Human: (read only)

The formation of sperm cells, or **spermatogenesis**, begins with a germ cell called spermatogonium (2n) that suffers mitosis and gives birth to the spermatocyte I (2n). The spermatocyte I undergoes meiosis I and generates two spermatocyte II (n) that then undergo meiosis II and produce four spermatids (n). Each spermatid undergoes a maturation

process called spermatogenesis and four sperm cells appear (figure below).

The formation of egg cells begins with a germ cell called oogonium (2n) that undergoes mitosis and gives birth to the oocyte I (2n). The oocyte I undergoes meiosis I that however is interrupted at prophase. After puberty during each menstrual cycle, an oocyte I finishes the meiosis I and generate one oocyte II (n) and the first polar body (n) i.e. uneven division. The first polar body is very small and almost lacks cytoplasm; it disintegrates after a period of time or stays attached to the oocyte II. With fecundation the oocyte II then undergoes meiosis II and produces the mature egg cell (n) and the second polar body (n) i.e. another uneven division. The second polar body is a very small cell that almost lacks cytoplasm and disintegrates or stays adnexal to the egg cell. The entire cytoplasmic content of the oocyte II passes to the egg cell. This process is known as **Oogenesis** and one mature egg appears (figure below).

The polar bodies are the byproducts of the primary and secondary oocyte at each point of meiotic division in oogenesis. The polar body allows for the oocyte to get rid of chromosomes while at the same time taking the least amount of resources (cytoplasm) from the oocyte. Each meiotic division serves as a means of moving the oocyte toward its need haploid number of chromosomes for fertilization. So the polar bodies function as a means of cellular structure conservation. They help ensure that the oocyte remains nutrient/resource rich while at the same time helping the oocyte reach its haploid number.

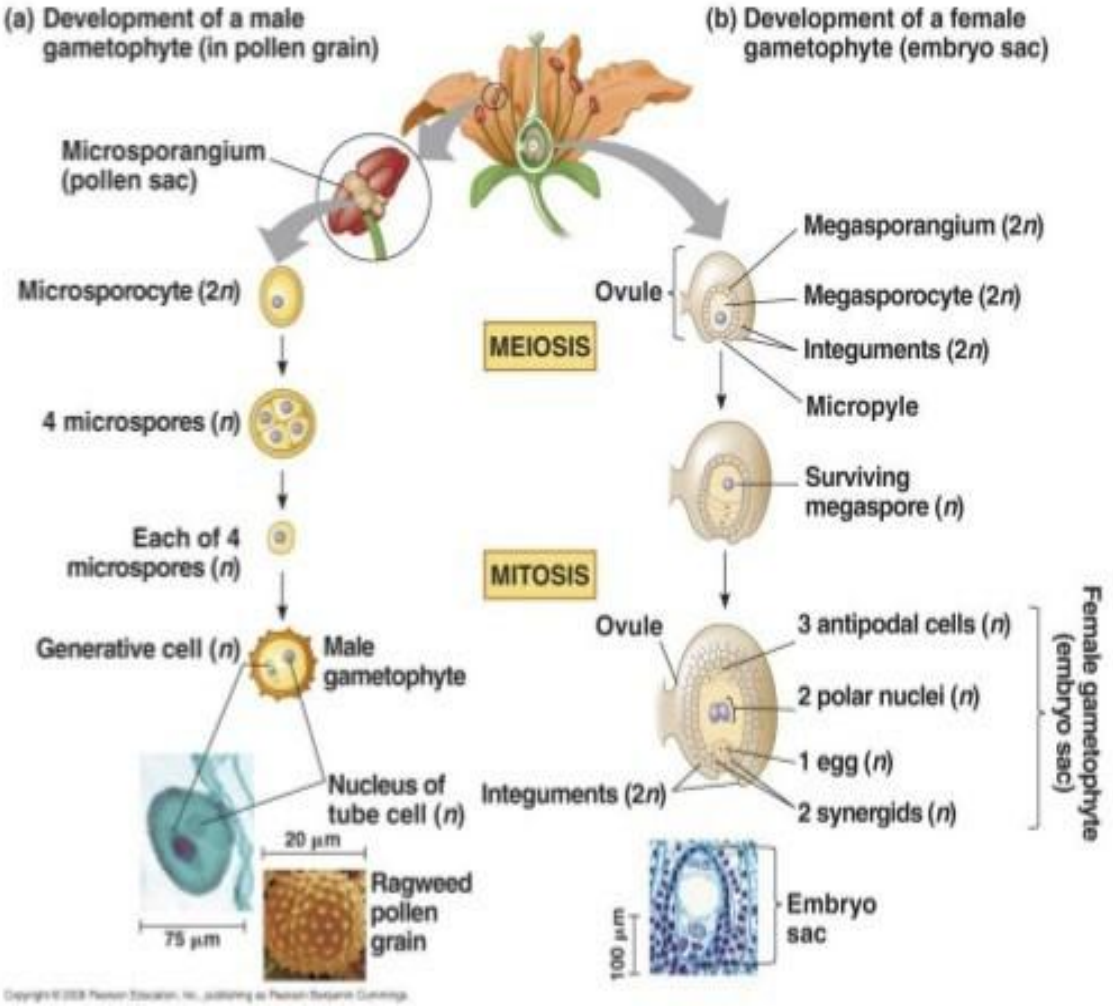


In Flowering Plants: (read only)

The microspore mother cell present in anther tissue undergoes a meiotic division (Meiosis I and II) to form 4 haploid functional microspores. This is **microsporogenesis**. From microspore the pollen grains are developed. The pollen grain contains two cells. One - **tube cell and generative cell**. Generative cell undergoes a division to form **two sperm nuclei.**

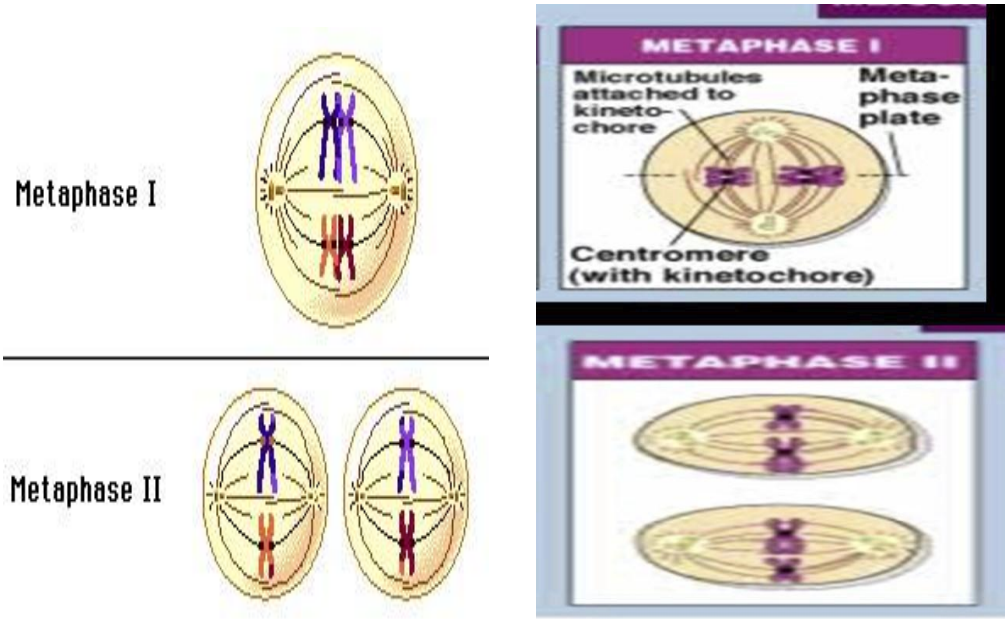
The meristematic tissue of the ovary wall called Ovule primordia. Within the nucellus of the ovule, one cell known as Archesporial cell (2n) develops larger than the surrounding cells, having a large nucleus and denser cytoplasm called know Megaspore mother cell (MMC). MMC undergoes a meiotic division (Meiosis I and II), giving rise to **four megaspores** (n). Among the four cells, **one megaspore** survives to give rise to an **embryo sac**, whereas other three aborts. Development of functional megaspore from MMC is called **megasporogenesis**. The nucleus within the functional magaspore undergoes three successive

divisions to form eight nuclei, which are arranged as three antipodal cells at one end, two central polar nuclei**,** one egg cell with two synergids at the other end. Development of eight celled embryo sac from the functional magaspore is called as **magagametogenesis**.



NOTE: (read only)

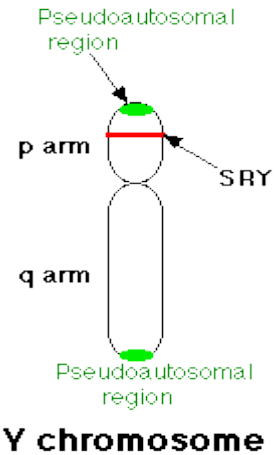
The spindle fibers direction in metaphase I and II can show if the cell will be a ♂ or ♀ gamete: if the spindle fibers are parallel, the cell will be a ♀ gametes, while if the spindle fibers are perpendicular, the cell will be a ♂ gametes.



NOTE: (read only)

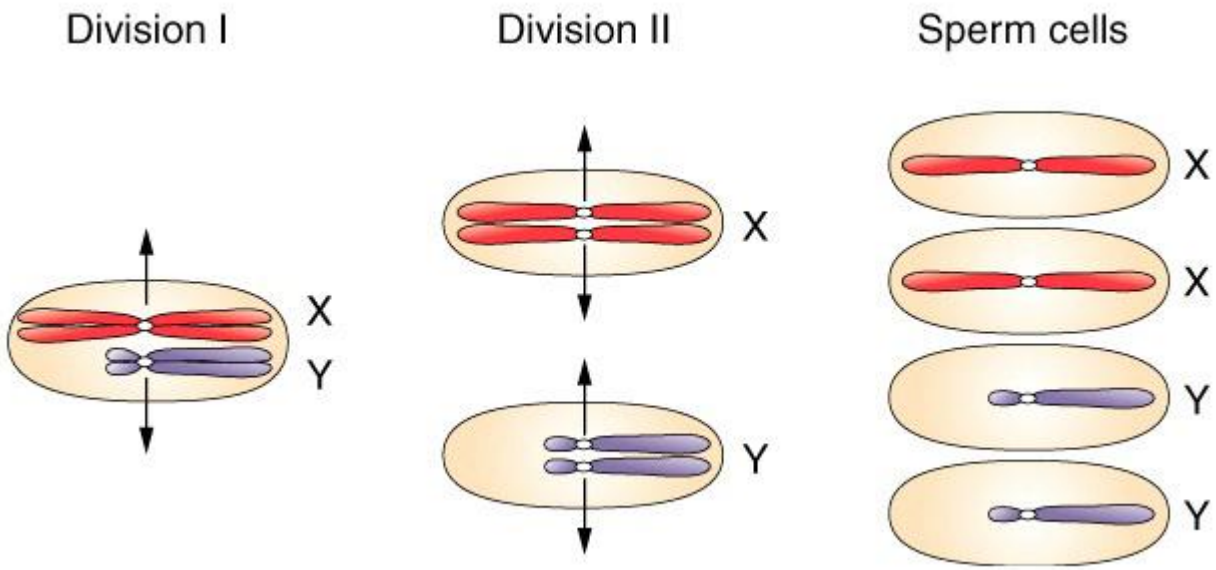
In making sperm by meiosis, the X and Y chromosomes must separate in anaphase just as homologous autosomes do. This occurs without a problem because, like homologous autosomes, the X and Y chromosome synapse during prophase of meiosis I. There is a small region of homology shared by the X and Y chromosome and synapsis occurs at that region.

The below image shows synapsis of the X and Y chromosomes of a mouse during prophase I of meiosis I. Crossing over occurs in two regions of pairing, called the **pseudoautosomal regions**. These are located at opposite ends of the chromosome.



The **pseudoautosomal regions** get their name because any genes located within them (so far only 9 have been found) are inherited just like any autosomal genes.

Males have two copies of these genes: one in the pseudoautosomal region of their Y, the other in the corresponding portion of their X chromosome. So males can inherit an allele originally present on the X chromosome of their father and females can inherit an allele originally present on the Y chromosome of their father.



The human Y chromosome is normally unable to recombine with the X chromosome, except for small pieces of pseudoautosomal regions at the telomeres (which comprise about 5% of the chromosome's length). These regions are relics of ancient homology between the X and Y chromosomes. The bulk of the Y chromosome, which does not recombine, is called the "NRY", or non-recombining region of the Y chromosome.

Genes outside the pseudoautosomal regions

Subsequently, the Y chromosome now has and mostly contains genetic junk rather than genes. In general, the human Y chromosome is extremely gene poor (few active genes), it is one of the largest gene deserts in the human genome, however there are several notable genes coded on the Y chromosome:

- NRY, with corresponding gene on X chromosome
- AMELY/AMELX (amelogenin)
- RPS4Y1/RPS4Y2/RPS4X (Ribosomal protein S4)
- NRY, other
- AZF1 (azoospermia factor 1)
- BPY2 (basic protein on the Y chromosome)
- DAZ1 (deleted in azoospermia)
- DAZ2
- PRKY (protein kinase, Y-linked)
- RBMY1A1
- SRY (sex-determining region)
- TSPY (testis-specific protein)
- USP9Y
- UTY (ubiquitously transcribed TPR gene on Y chromosome)
- ZFY (zinc finger protein)

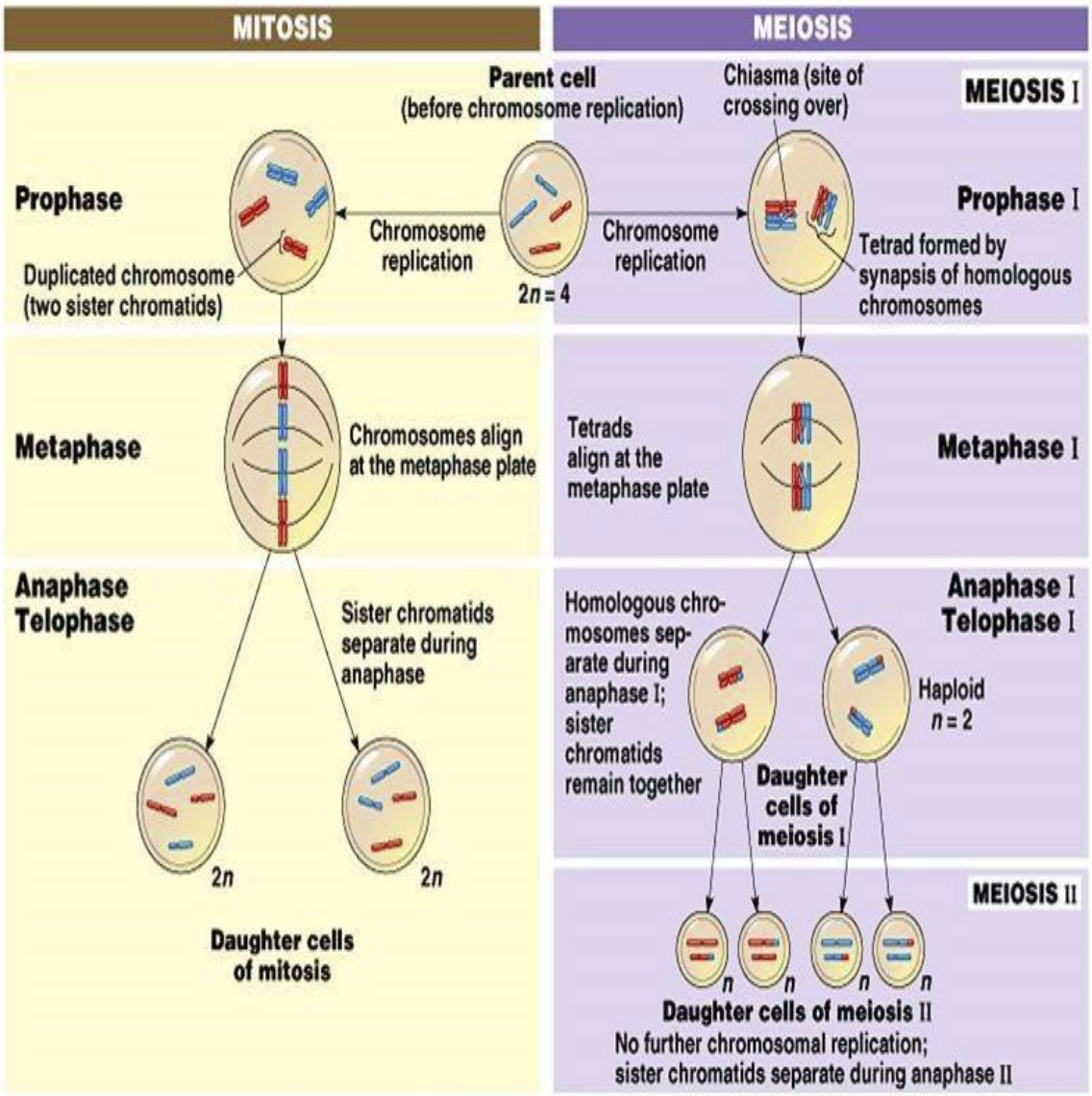
The Y chromosome is only one-third the size of the X. Although the Y has a partner in X, only the tips of these chromosomes are able to recombine via cloning. Thus, most of the Y chromosome is inherited from father to son in a pattern resembling asexual, not sexual, reproduction.

This prevents mutant Y chromosome genes from being eliminated from male genetic lines except by inactivation or deletion. The Y chromosome has about one tenth the genetic variations that occur on all other chromosomes.

In male, the Y chromosome therefore tends to accumulate changes and deletions faster than the X. Degradation doesn't occur in X chromosomes because during female meiosis, the X has the other X as a full partner in recombination.

Differences between Mitosis and Meiosis:

	Mitosis	**Meiosis**
Number of divisions	1	2
Number of produced cells	2 (daughter cells)	4 (gametes)
Genetically identical?	Yes	No
Chromosome #	Same as parent	Half of parent
Where	Somatic cells	Germ cells
Synapsis and crossover	Absent	Present
Centromere in Anaphase	Divided at anaphase	Not divided at anaphase I but at Anaphase II
When	Throughout life	At sexual maturity
Role	Growth, development, regeneration and repair	Sexual reproduction



IMPORTANCE OF MEIOSIS:

- Meiosis generates genetic diversity through:
  1. the exchange of genetic material (crossover) between homologous chromosomes during Prophase I-Meiosis I.
  2. the random alignment of chromosomes in Meiosis I and Meiosis II.
- Meiosis maintains the chromosome number in sexually reproducing organisms.

Animations: on my scholar

For more reading: (in Botany and Microbiology Department Library)

1. The world of the cell:international edition, 6th edition, 2006, Becker, Kleinsmith and Hardin (eds.).
2. Biology, 8th edition, 2008, Losos, Mason and Singer (eds.)
3. Concepts of Genetics, William S. Klug, Michael R. Cummings, Charlotte A. Spencer and Michael A. Palladino, 10th edition, 2012, Pearson Education Inc. (also present online)