Meiosis

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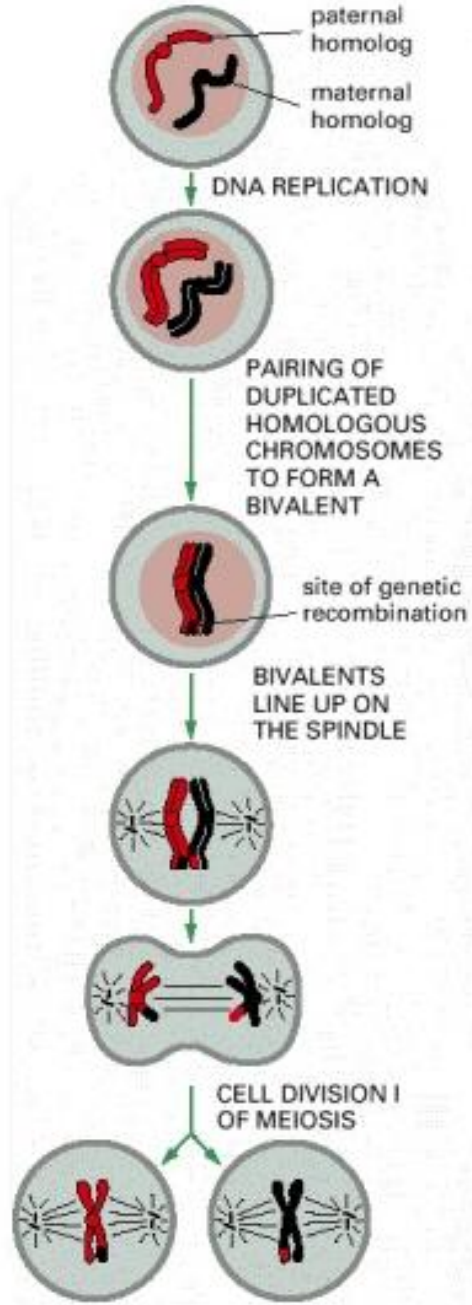
- The set of chromosomes of a typical sexually-reproducing organism consists of *autosomes,* which are common to all members of the species, and *sex chromosomes,* which are differently allocated according to the sex of the individual.
- A diploid nucleus contains two closely similar versions of each chromosome. For each of the autosomal chromosome pairs, one member was initially inherited from the male parent (a paternal chromosome) and the other was initially inherited from the female parent (a maternal chromosome).
- The two versions, which are very similar but not identical in DNA sequence, are called homologs, and in most cells they maintain a completely separate existence as independent chromosomes.
- Meiosis is the form of eukaryotic cell division that produces haploid sex cells or gametes (which contain a single copy of each chromosome) from diploid cells (which contain two copies of each chromosome).
- The process takes the form of one DNA replication followed by two successive nuclear and cellular divisions (Meiosis I and Meiosis II).
- As in mitosis, meiosis is preceded by a process of DNA replication that converts each chromosome into two sister chromatids.

Meiosis I

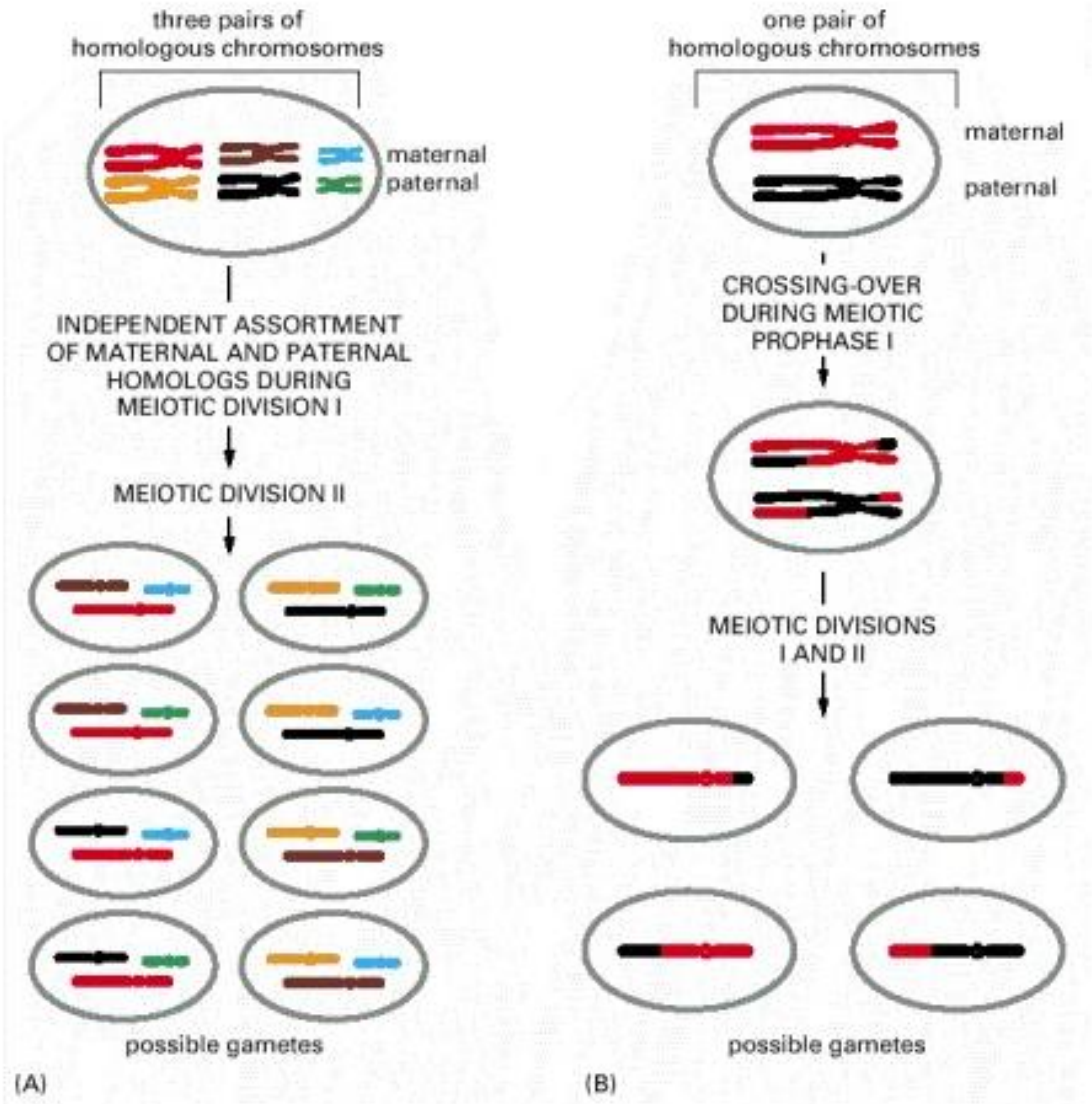
- Homologs recognize each other and become physically connected side-by-side along their entire length (Synapsis) before they line up on the spindle.
- How the maternal and the paternal copy of each chromosome recognize each other is still uncertain.
- In many organisms, the initial association (a process called **pairing**) seems to be mediated by complementary DNA base-pair interactions at numerous and widely dispersed sites along the chromosomes.
- Before the homologs pair, each chromosome in the diploid cell replicates to produce two sister chromatids, just as in a mitotic cell division.
- It is only after DNA replication has been completed that the special features of meiosis become evident.
- Each duplicated chromosome pairs with its duplicated homolog, forming a structure called a bivalent, which contains four chromatids.
- The pairing occurs during a long meiotic prophase, allows genetic recombination to occur, whereby a fragment of a maternal chromatid may be exchanged for a corresponding fragment of a homologous paternal chromatid.
- At the subsequent metaphase all of the bivalents line up on the spindle, and at anaphase the two duplicated homologs (each consisting of two sister chromatids) separate from each other and move to opposite poles of the spindle, and the cell divides.
- Meiosis I—does not produce cells with a haploid amount of DNA. Because the sister chromatids behave as a unit, each daughter cell of this division inherits two copies of one of the two homologs.
- The two copies are identical except where genetic recombination has occurred. The two daughter cells therefore contain a haploid number of chromosomes but a diploid amount of DNA.
- To produce haploid gametes, however, another cell division is required.


paternal homolog
maternal homolog
DNA REPLICATION
PAIRING OF DUPLICATED HOMOLOGOUS CHROMOSOMES TO FORM A BIVALENT
site of genetic recombination
BIVALENTS LINE UP ON THE SPINDLE
CELL DIVISION I OF MEIOSIS

Genetic Reassortment Is Enhanced by Crossing-over Between Homologous Nonsister Chromatids

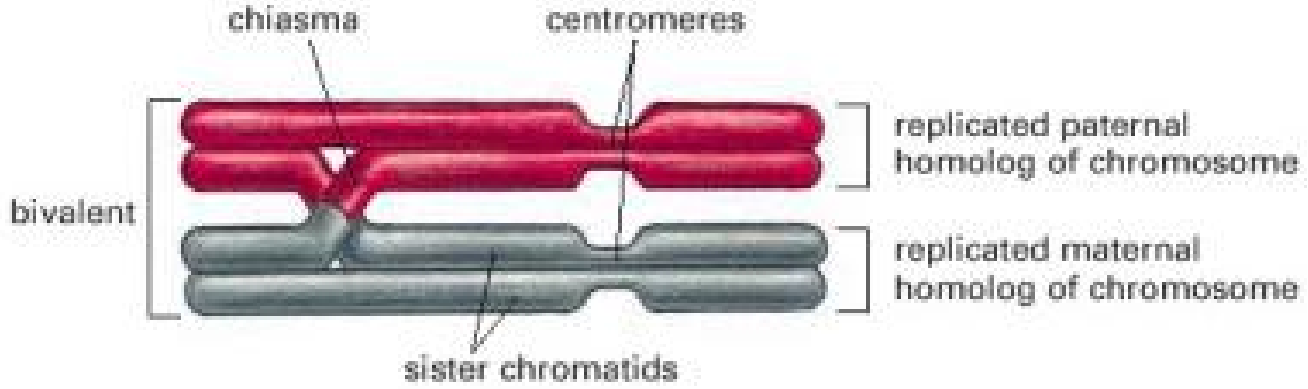
- One kind of reassortment is a consequence of the random distribution of the maternal and paternal homologs between the daughter cells at meiotic division I, as a result of which each gamete acquires a different mixture of maternal and paternal chromosomes.
- From this process alone, one individual could, in principle, produce 2^n genetically different gametes, where *n* is the haploid number of chromosomes.
- In humans, for example, each individual can produce at least $2^{23} = 8.4 \times 10^6$ genetically different gametes.
- But the actual number of variants is very much greater than this because a second type of reassortment, called chromosomal crossing-over, occurs during meiosis.
- It takes place during the long prophase of meiotic division I (prophase I), in which parts of homologous chromosomes are exchanged.
- On average, between two and three crossover events occur on each pair of human chromosomes during meiotic division I.

Two major contributions to the reassortment of genetic material that occurs in the production of gametes during meiosis



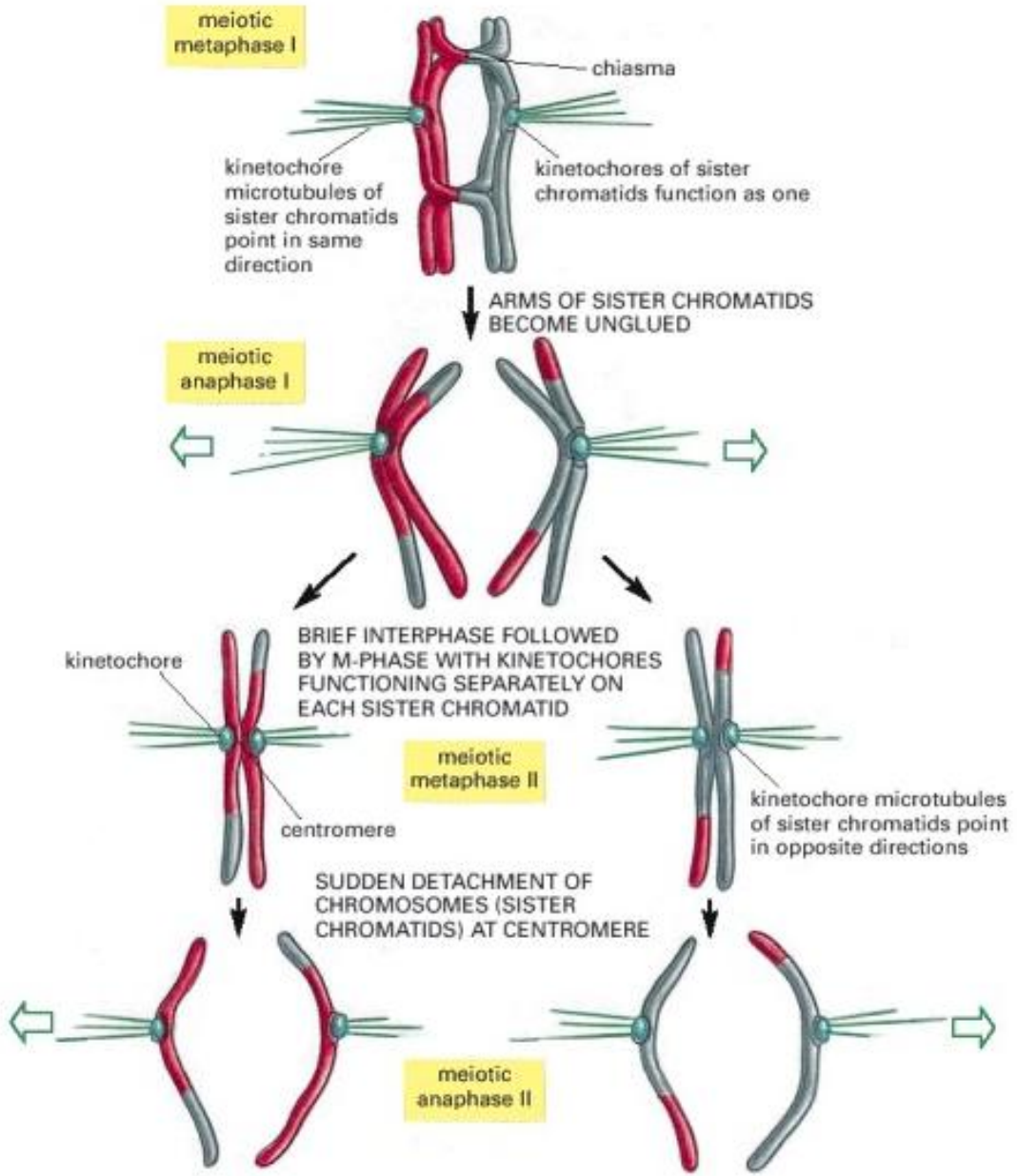
Chiasma

- During chromosomal crossing-over, the DNA double helix is broken in both a maternal chromatid and a homologous paternal chromatid, so as to exchange fragments between the two nonsister chromatids in a reciprocal fashion by a process known as **genetic recombination**.
- At this stage, the sister chromatids are tightly apposed along their entire length, and the two duplicated homologs (maternal and paternal) that form each bivalent are seen to be physically connected at specific points.
- Each connection, called a chiasma (plural **chiasmata**), corresponds to a crossover between two nonsister chromatids.



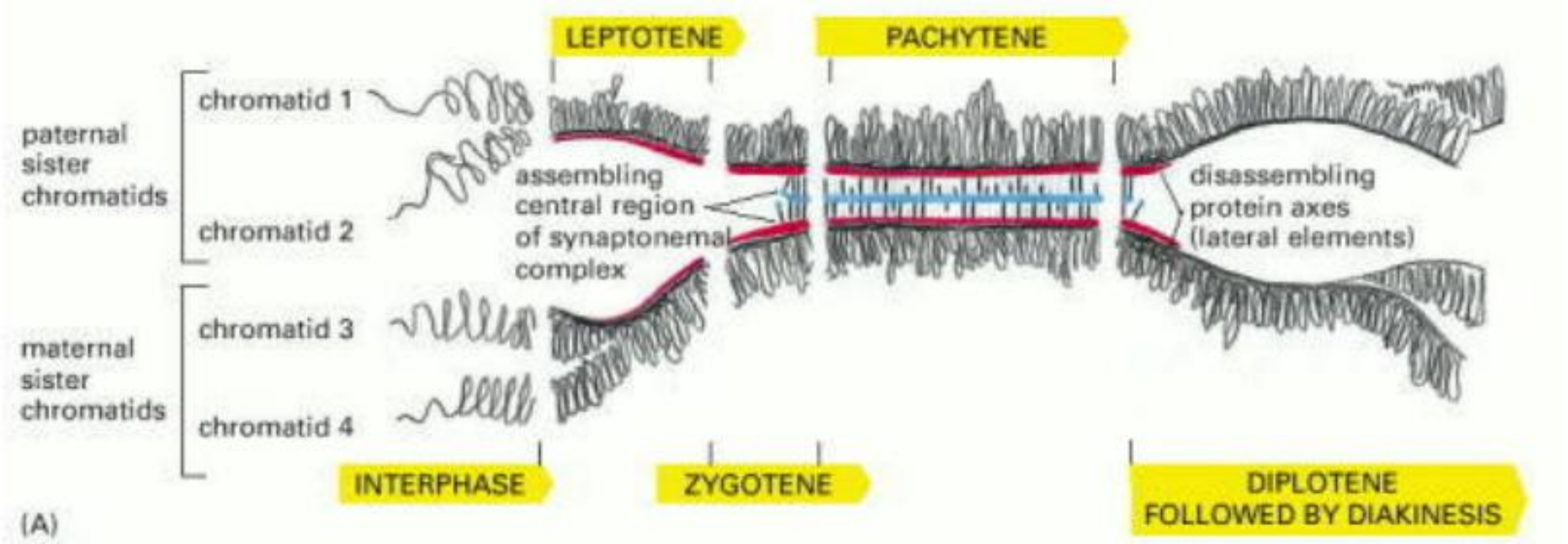
- In addition to reassorting genes, chromosomal crossing-over is crucial in most organisms for the correct segregation of the two duplicated homologs to separate daughter nuclei.
- This is because the chiasmata created by crossover events have a crucial role in holding the maternal and paternal homologs together until the spindle separates them at anaphase I.
- The duplicated homologs are held together at chiasmata only because the arms of sister chromatids are glued together along their length by proteins called *cohesins.*
- The arms of sister chromatids suddenly become unglued at the start of anaphase I, when the cohesins holding the arms together are degraded, allowing the duplicated homologs to separate and be pulled to opposite poles of the spindle.
- The sister chromatids of each duplicated homolog remain attached at the centromere by meiosis-specific cohesins, which are degraded at anaphase of meiotic division II (anaphase II); only then can the sister chromatids separate.

- In meiotic division II, as in a mitotic division, the kinetochores on each sister chromatid have attached kinetochore microtubules pointing in opposite directions, so that the chromatids are drawn into different daughter cells at anaphase.
- In meiotic division I, by contrast, the kinetochores on both sister chromatids behave as a single functional unit, as their attached kinetochore microtubules all point in the same direction so that the sister chromatids stay together when the duplicated homologs separate.



Meiosis I: Prophase I

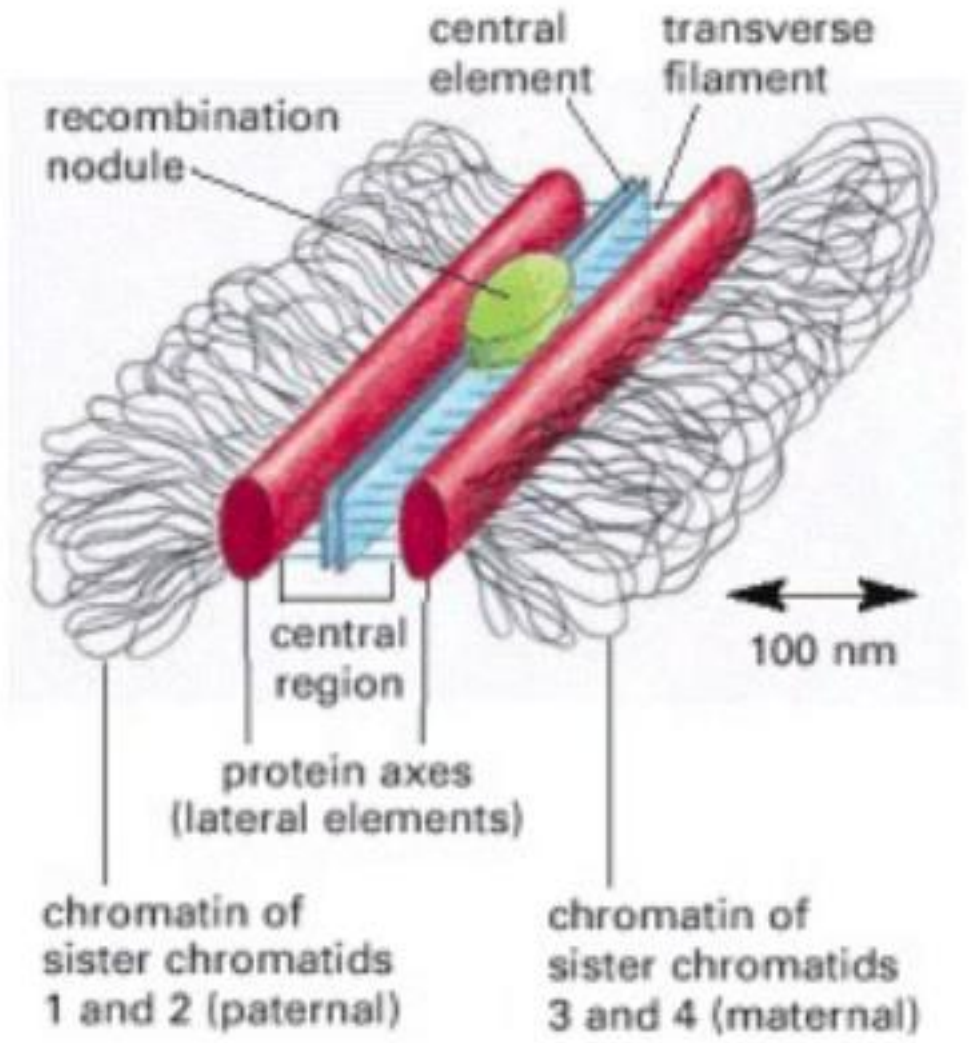
- **Prophase I:** The prophase of meiotic division I is traditionally divided into five sequential stages—*leptotene*, *zygotene*, *pachytene*, *diplotene*, and *diakinesis*—defined by the morphological changes associated with the assembly *(synapsis)* and disassembly *(desynapsis)* of the synaptonemal complex.
  - Leptotene: chromosomes start to condense.
  - Zygotene: homologous chromosomes become closely associated (synapsis) to form pairs of chromosomes (bivalents) consisting of four chromatids (tetrads).
  - Pachytene: crossing over between pairs of homologous chromosomes to form chiasmata (sing. chiasma).
  - Diplotene: homologous chromosomes start to separate but remain attached by chiasmata.
  - Diakinesis: homologous chromosomes continue to separate, and chiasmata move to the ends of the chromosomes.
- Prophase I can occupy 90% or more of the time taken by meiosis. Although it is traditionally called prophase, it actually resembles the G_2 phase of a mitotic cell division.
- The nuclear envelope remains intact and disappears only when the meiotic spindle begins to form, as prophase I gives way to metaphase I.
- After prophase I is completed, two successive cell divisions follow without an intervening period of DNA synthesis.



- (A) A single bivalent is shown. The pachytene stage is defined as the period during which a fully formed synaptonemal complex exists. At leptotene, the two sister chromatids condense, and their chromatin loops each extend from a common protein axis *(red)*.
- As meiosis progresses, the two homologs become tightly connected by proteins that form the central region of the synaptonemal complex, composed of a central element *(blue),* transverse filaments *(thin black lines),* and the lateral elements *(red)* that anchor the chromatin loops.
- In the gametes of many female animals, but not those of mammals, the subsequent diplotene stage is an enormously prolonged period of cell growth, during which the chromosomes are decondensed and very active in transcription.
- Diplotene ends with diakinesis—the stage of transition to metaphase,in which the chromosomes recondense and transcription halts.

Synaptonemal Complex

- The synaptonemal complex consists of a long, ladderlike protein core, on opposite sides of which the two duplicated homologs are aligned to form a long linear chromosome pair.
- The sister chromatids in each homolog are kept tightly packed together, with their DNA extending from their own side of the protein ladder in a series of loops.
- In the central region, a central element is connected by transverse filaments to lateral elements that run along each pair of sister chromatids, forming the sides of the ladder.



Recombination Nodules Mark the Sites of Genetic Recombination

- The crossover events that take place during the prophase of meiotic division I can occur nearly anywhere along a chromosome.
- They are not distributed uniformly, however: there are recombination "hot spots," where double-stranded DNA breaks seem to be preferentially induced by the meiotic endonuclease called *Spo*11.
- The occurrence of one crossover event decreases the probability of a second occurring at a nearby chromosomal site.
- This "interference" seems to ensure that the limited number of crossovers are spread out so that even small chromosomes get at least one, as required for the homologs to segregate normally.
- There is strong indirect evidence that the general genetic recombination events in meiosis are catalyzed by **recombination nodules**.
- These are very large protein complexes that sit at intervals on the synaptonemal complex, placed like basketballs on a ladder between the two homologous chromosomes (see Figure 20-13).
- These nodules contain Rad51, which is the eucaryotic version of the RecA protein, which mediates general recombination in *E. coli*.
- This process generates single stranded DNA filaments (cut by endonuclease spo11) coated by RAD51 and DMC1 which invade the homologous chromosomes, forming inter-axis bridges, and resulting in the pairing/co-alignment of homologues.
- They seem to mark the site of a multienzyme "recombination machine" that interacts with local regions of DNA on the maternal and paternal chromatids across the 100-nm-wide synaptonemal complex.

- **Prometaphase I**
- Spindle apparatus formed, and chromosomes attached to spindle fibres by kinetochores.
- **Metaphase I**
- Homologous pairs of chromosomes (bivalents) arranged as a double row along the metaphase plate.
- The arrangement of the paired chromosomes with respect to the poles of the spindle apparatus is random along the metaphase plate.
- This is a source of genetic variation through random assortment, as the paternal and maternal chromosomes in a homologous pair are similar but not identical.
- **Anaphase I**
- The homologous chromosomes in each bivalent are separated and move to the opposite poles of the cell
- **Telophase I**
- The chromosomes become diffuse and the nuclear membrane reforms.
- **Cytokinesis**
- The final cellular division to form two new cells, followed by Meiosis II. Meiosis I is a reduction division: the original diploid cell had two copies of each chromosome; the newly formed haploid cells have one copy of each chromosome.

Meiosis II

- When meiotic division I ends, nuclear membranes re-form around the two daughter nuclei, and the brief interphase of division II begins.
- During this period, the chromosomes may decondense somewhat, but usually they soon recondense and prophase II begins. (Because there is no DNA synthesis during this interval, in some organisms the chromosomes seem to pass almost directly from one division phase into the next.)
- Prophase II is brief: the nuclear envelope breaks down as the new spindle forms, after which metaphase II, anaphase II, and telophase II usually follow in quick succession.
- After nuclear envelopes have formed around the four haploid nuclei produced at telophase II, cytokinesis occurs, and meiosis is complete.