GENETICS

Done By:

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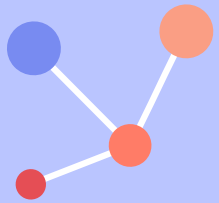
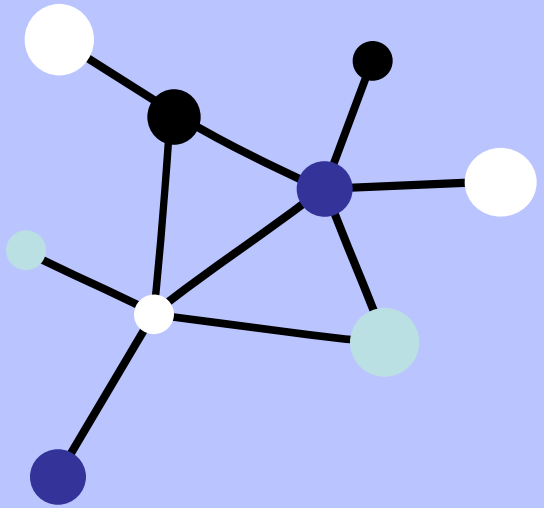




History of Cytogenetics

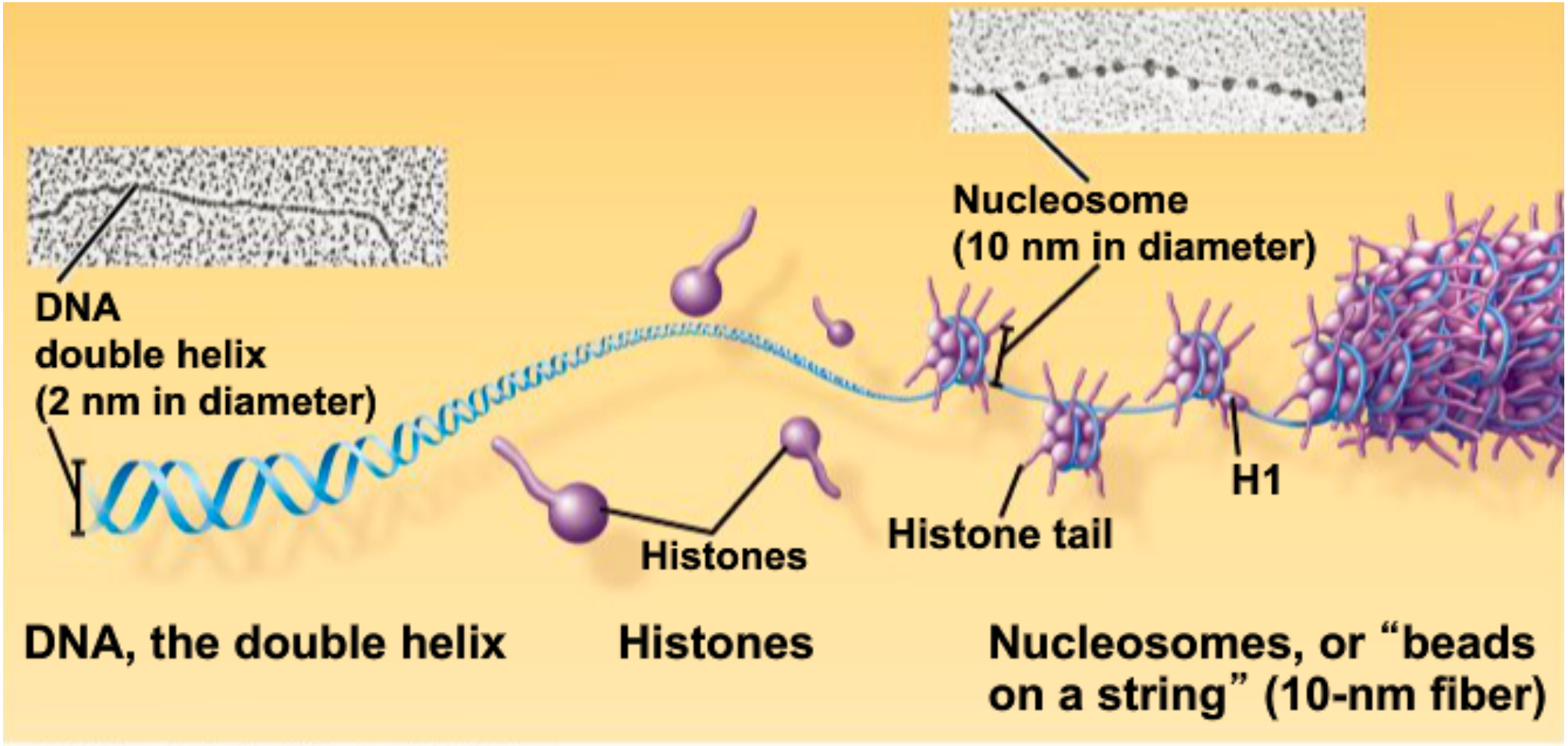
It is the study of chromosomes not to confused with cytology which is the study of cells.

True chromosome number established in 1956

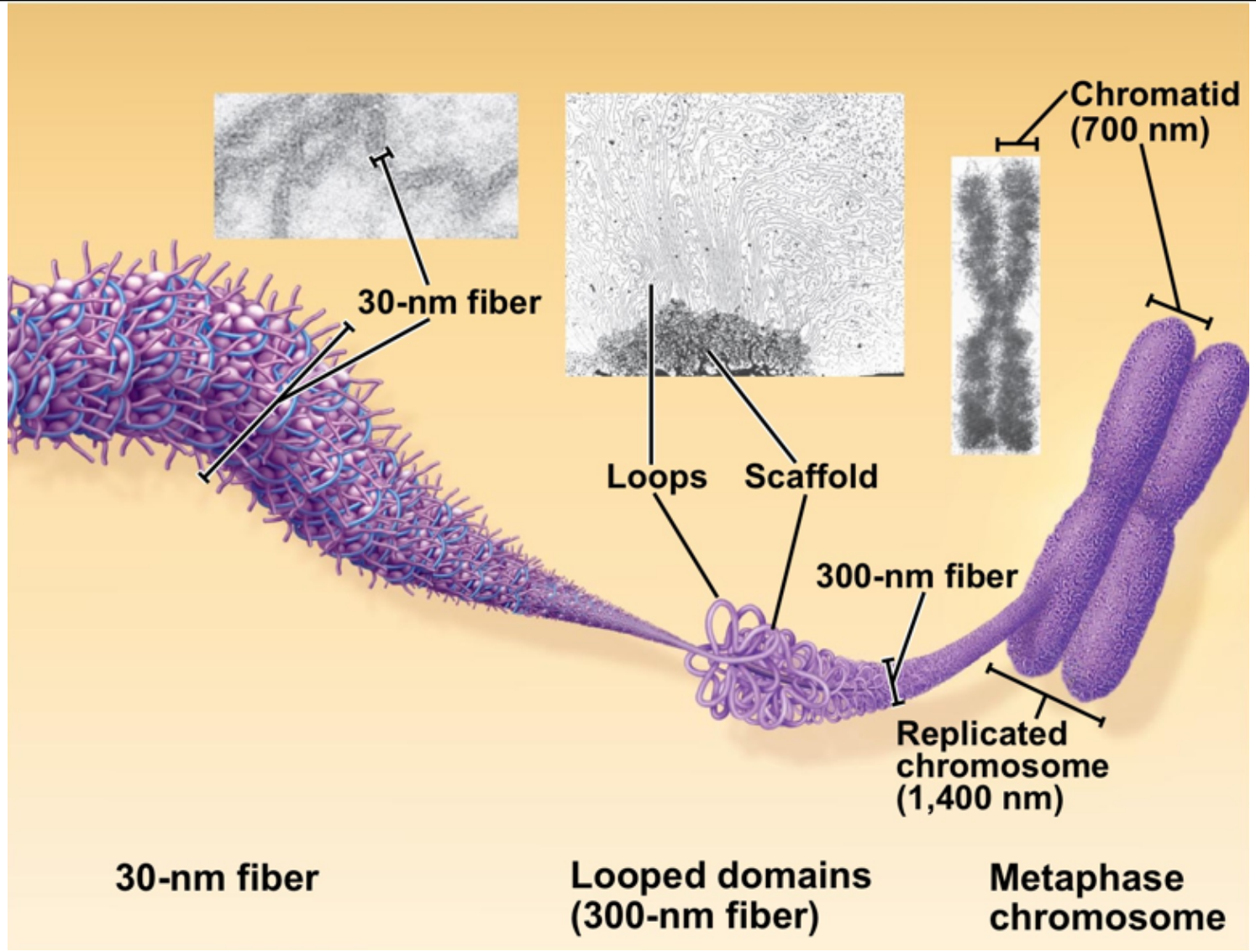
Before that we had no idea about the human number of chromosomes.

" From their vantage through the microscope, the cytogeneticists' view of the genome is still unrivalled in its scope, detail and color."

Barbara J. Trask, 2002

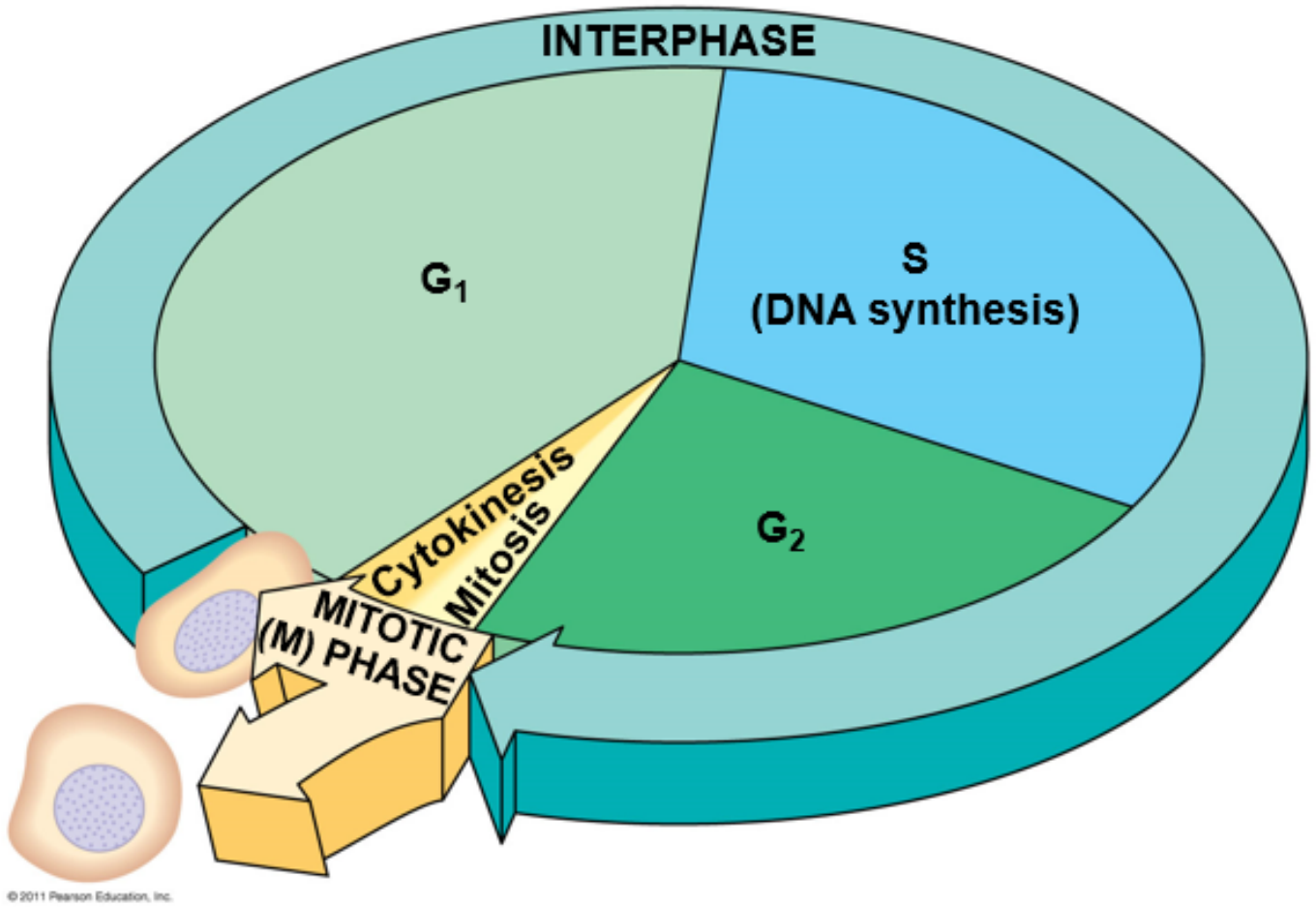


Whenever we say DNA molecule, we mean double-stranded DNA. The DNA molecule is wrapped around a group of proteins and these proteins are called histones and the complex of the proteins wrapped in DNA are called nucleosomes.



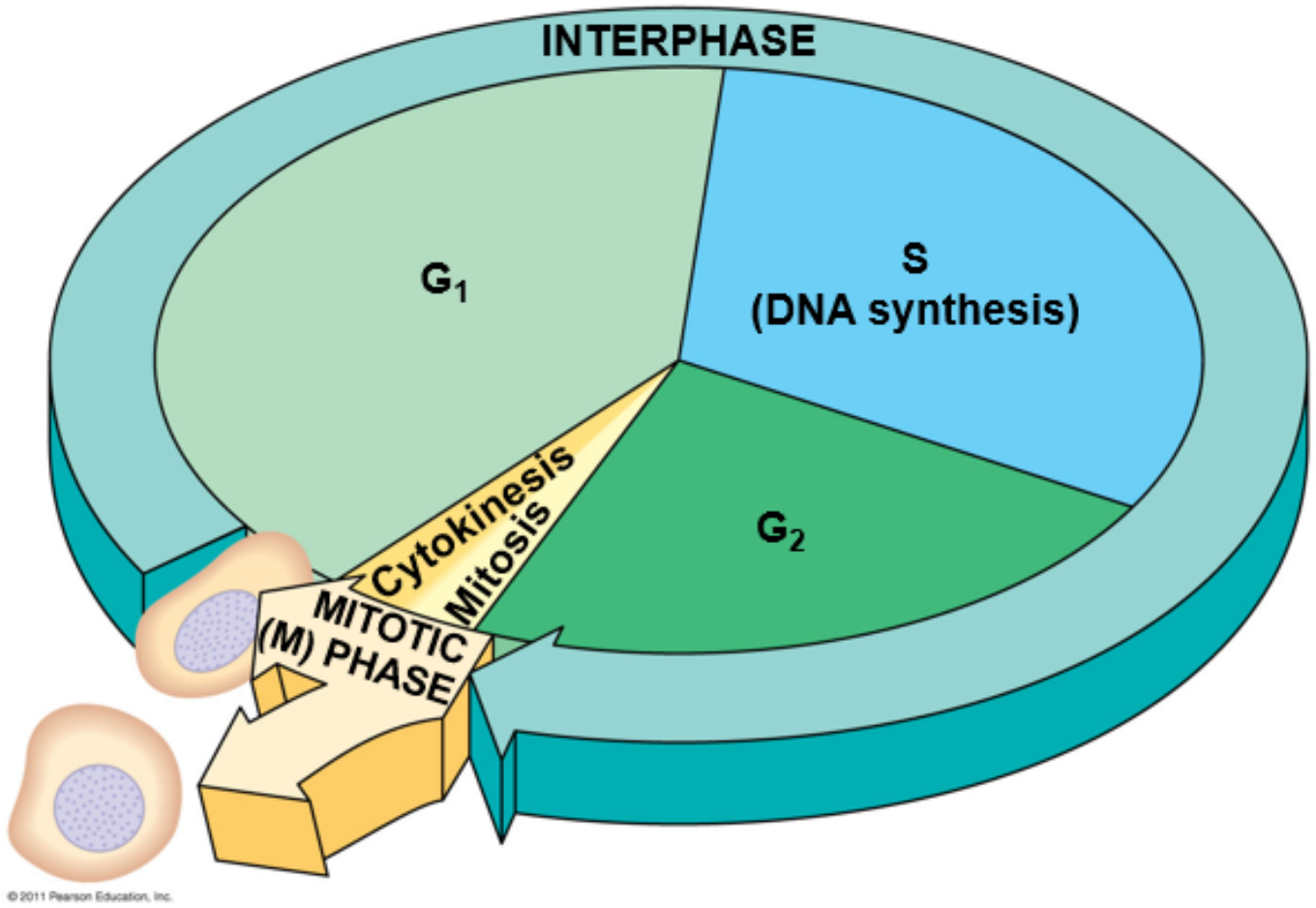
When the nucleosome are arranged together they form chromatin, which is a thread-like structure and it is then arranged on a scaffold and forms a chromatid. Then the two sister chromatids (which have an identical DNA sequence) form a chromosome

Figure 12.6



- DNA replication in the cell cycle occurs in the s phase, and in this phase the DNA polymerase attaches to the ds DNA and each of the two strands will be used as a template to synthesize daughter strands, and eventually two new DNA molecules will result from the first DNA molecule.
- In the interphase, the DNA itself needs to be accessible; the DNA must be loose in the 3D structure and available for attachment.
- In these phases there is growth of the cell, which means there are more organelles and proteins, and these proteins need transcription and translation. This means that the DNA needs to be available for the binding of the RNA polymerase and transcription factors and other proteins.
- If they cannot access the DNA then that means that there will be no gene expression and there will be no protein synthesis and growth of the cell.

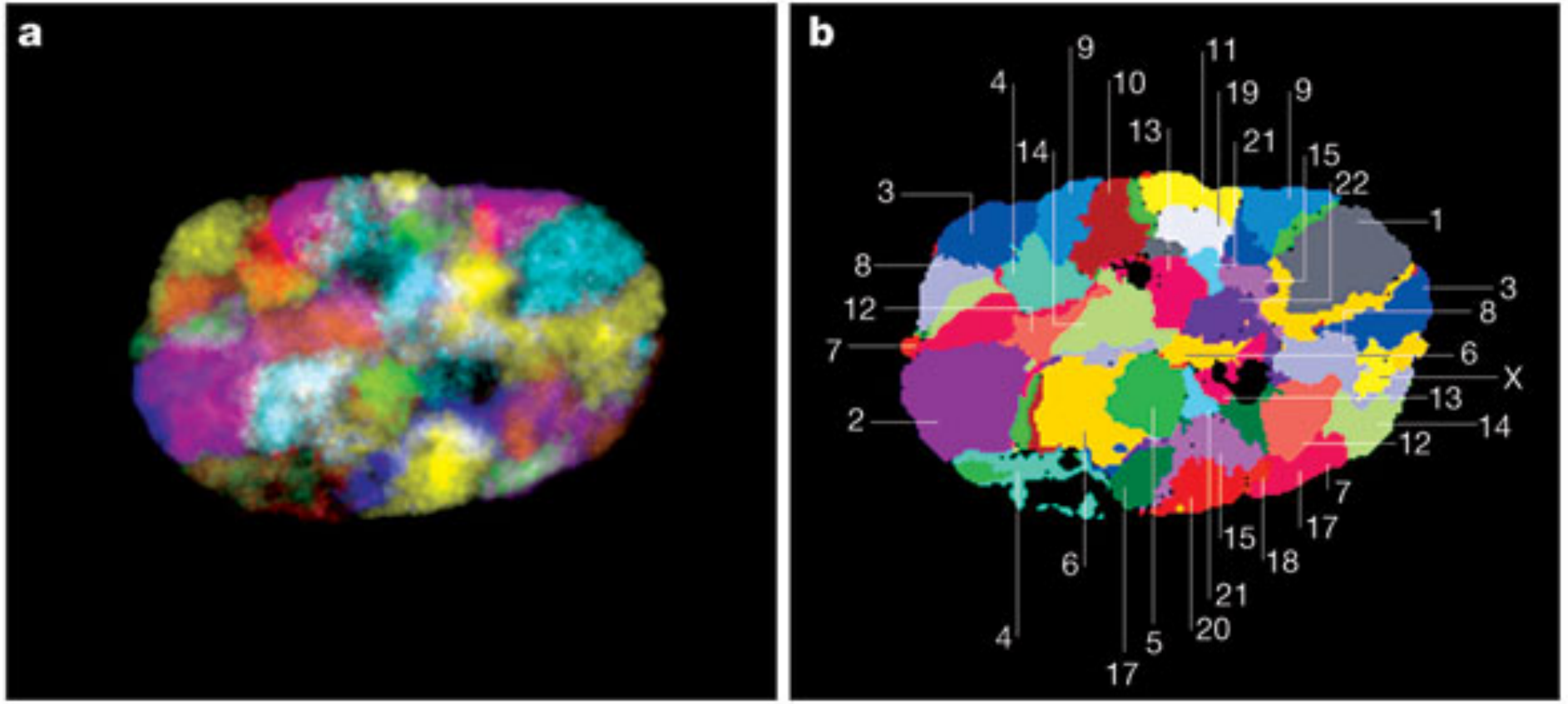
Figure 12.6



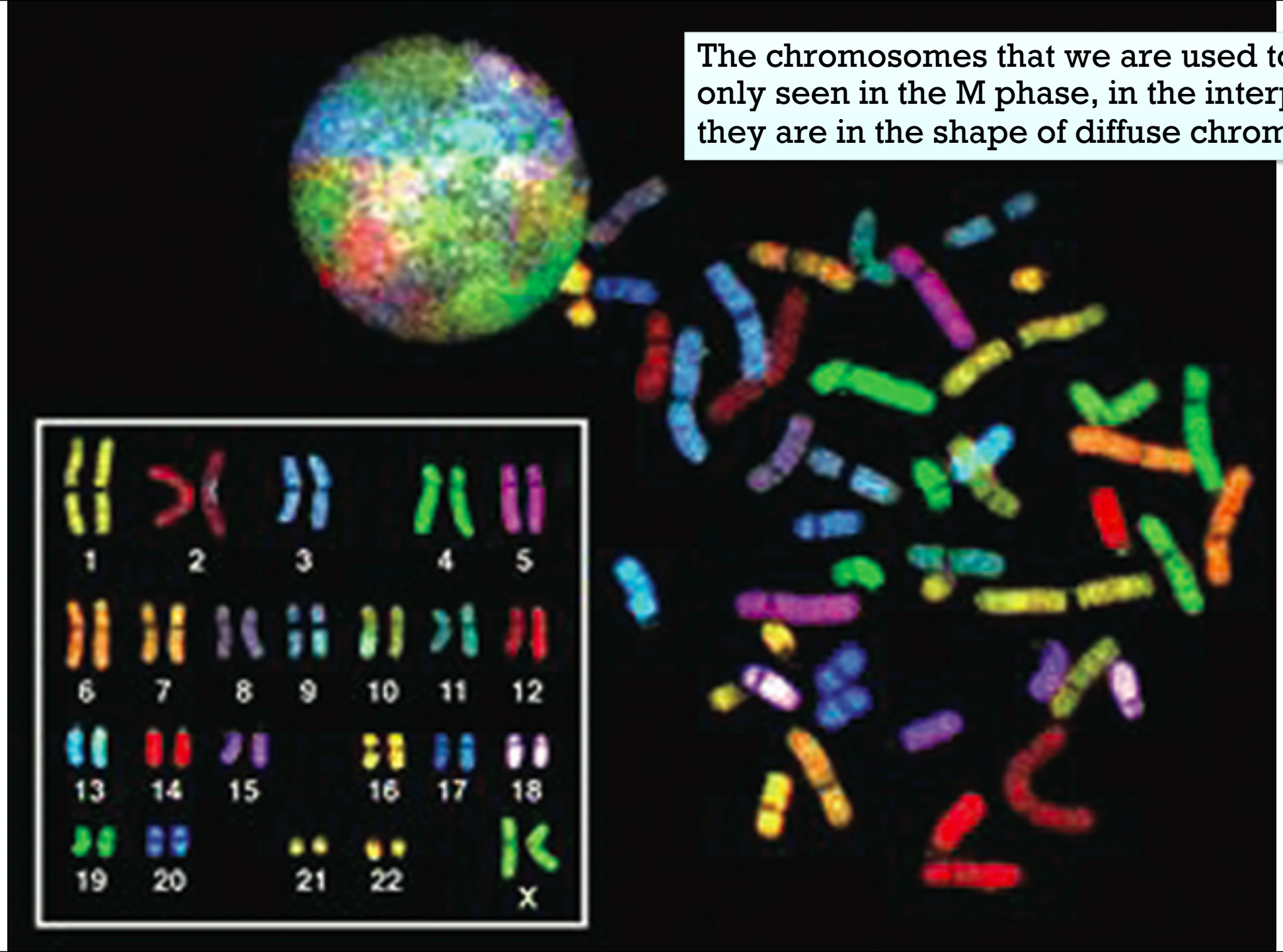
- The same thing goes for S phase. There is a group of proteins (DNA polymerase, helicase, topoisomerase) that that needs to have access to the DNA in order for replication to occur.

- In summary, in the interphase, the chromatin needs to be diffuse, not condensed and compact because otherwise, this will hinder the function of the interphase.
In the M phase , it is very different, we are not replication DNA , we are not expressing genes. In this phase, the purpose is to form two daughter cells (with two nuclei) each with the correct number of chromosomes. This is made easier by the condensation of the chromatin into chromosomes.

This is an image of the nucleus and the chromosomes are each labelled with a different color. The image on the right is a digital enhancement of the one on the left.

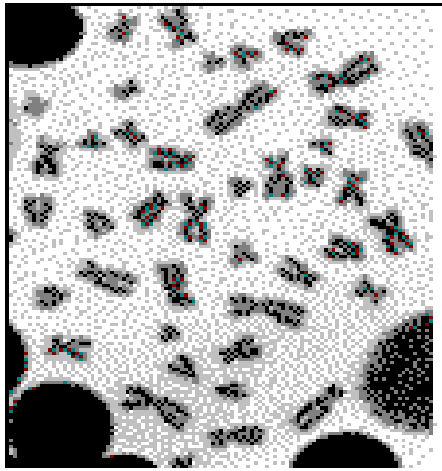


There are no clear shapes of chromosomes and this is how the nucleus looks like in the interphase

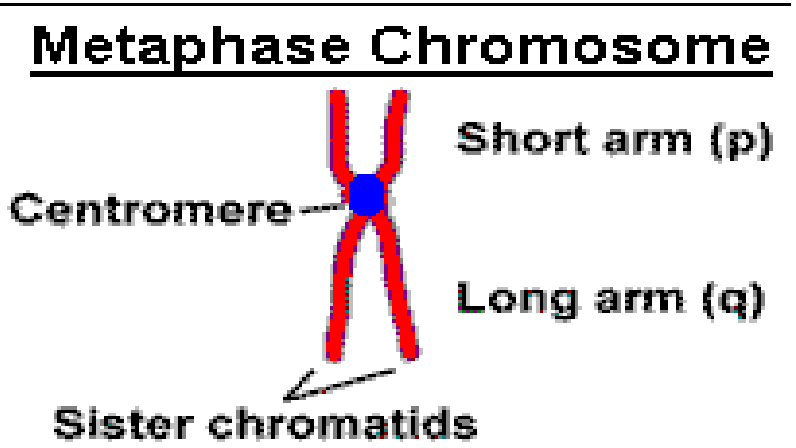


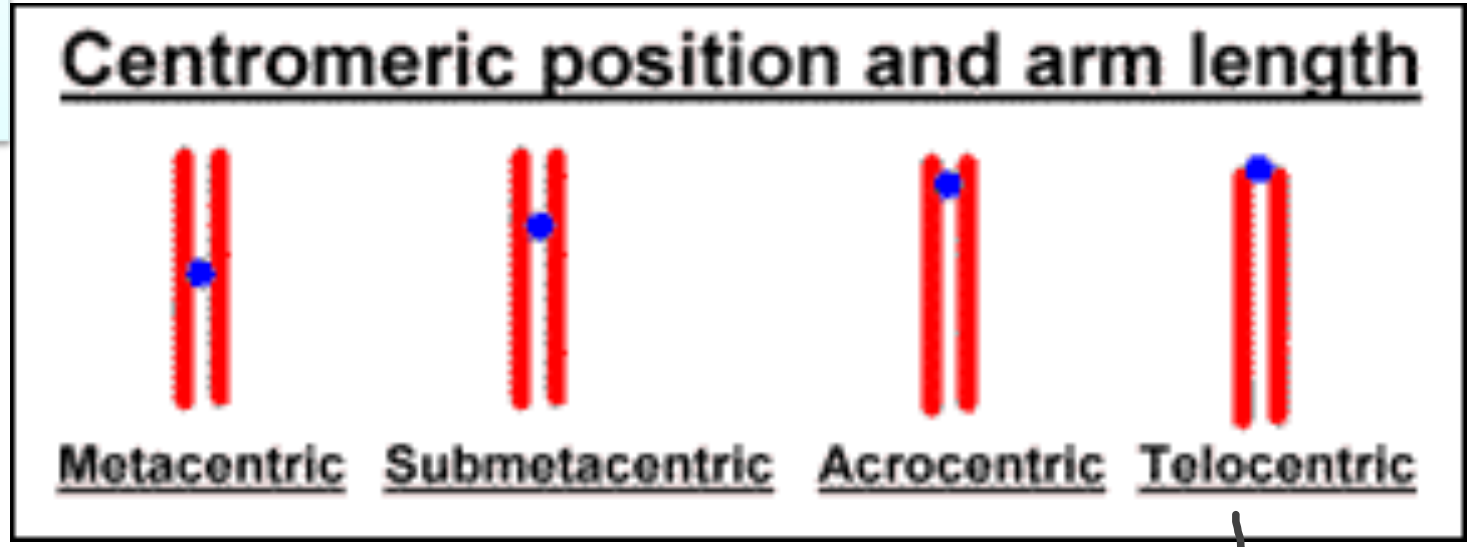
The chromosomes that we are used to are only seen in the M phase, in the interphase they are in the shape of diffuse chromatin.

Nomenclature of chromosomes



This picture was taken in the M phase, and more specifically in the metaphase (most condensed)



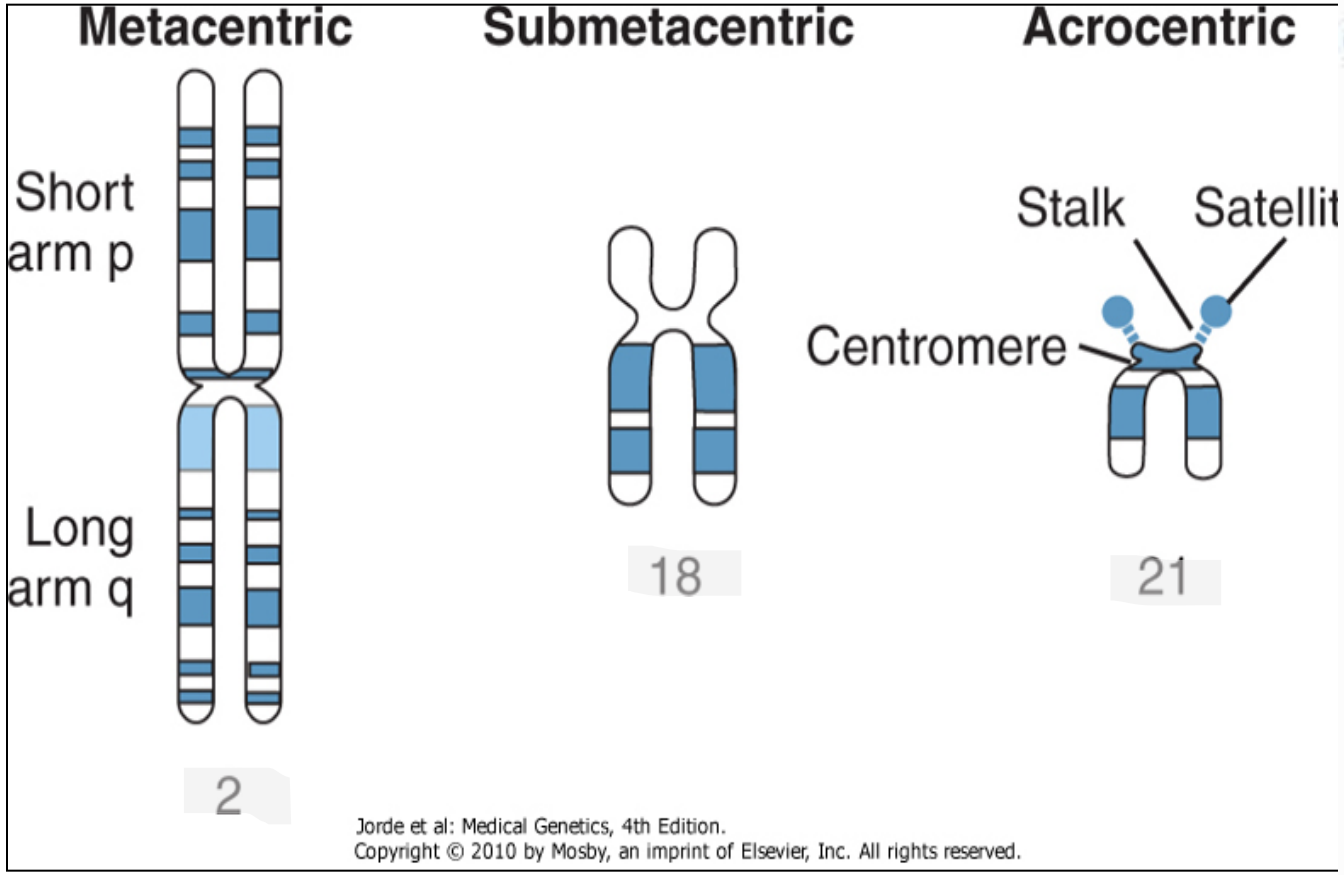


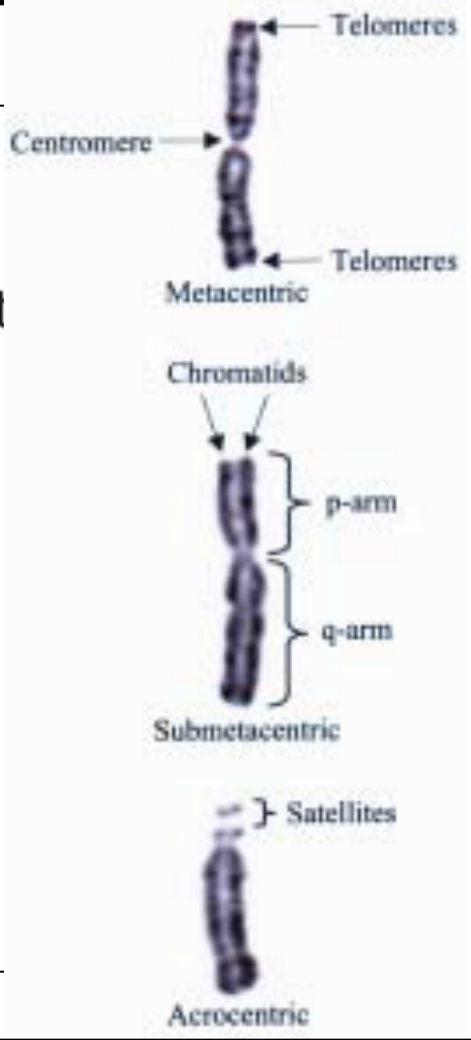
We can classify autosomes (the 22 chromosomes other than the sex chromosomes) based on the location of the centromere

Not in humans, or exists in abnormal cases

Chromosome Shape

Metacentric- centromere is located in the middle of chromosome
Submetacentric- centromere is displaced from the center
Acrocentric – centromere is placed near the end



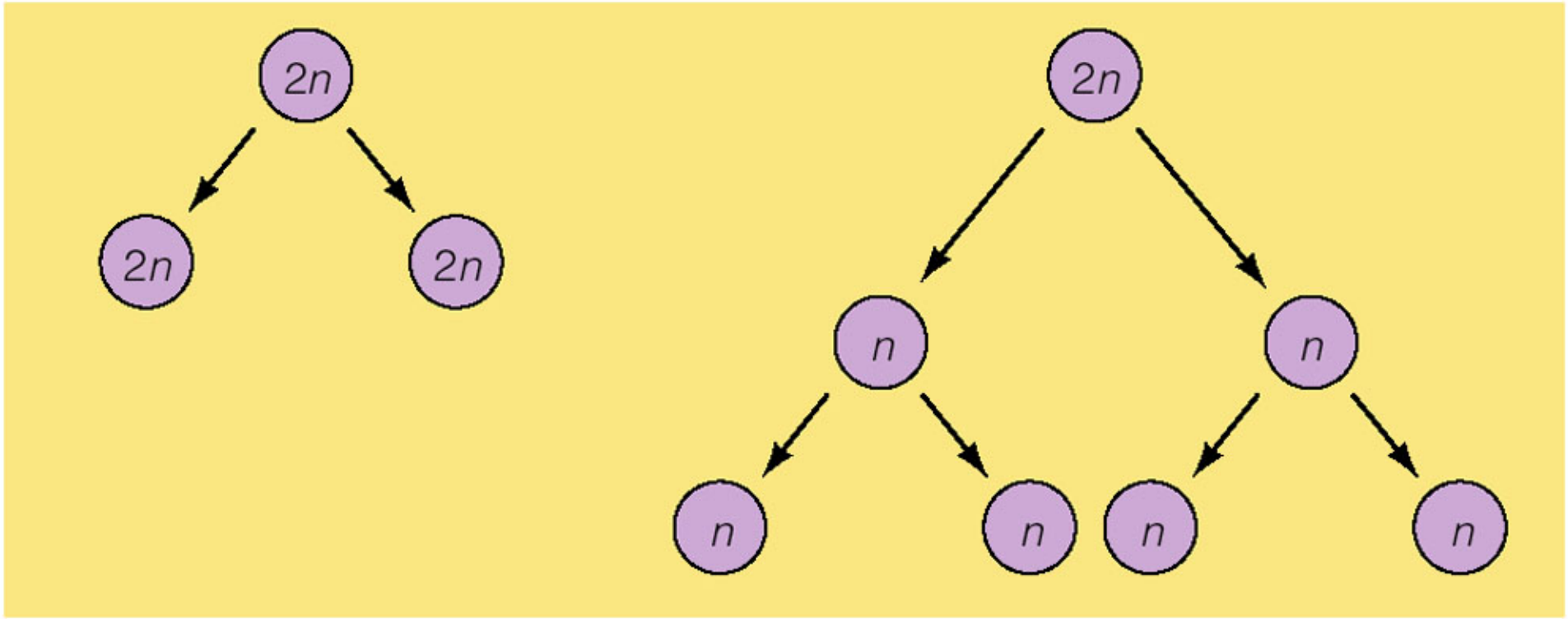


Human chromosomes

- DNA and associated proteins are organized into chromosomes
- Human somatic cells are **diploid** and have 22 pairs of **autosomes** AND 1 set of **sex** chromosomes (XX or XY)= total of 46
  - Females XX
  - Males XY
- Germ cells are haploid and contain 22 chromosomes plus 1 sex chromosome (X or Y)

Mitosis

Meiosis



In mitosis, there is division on the genetic level, not the cytoplasmic level, and it results in identical daughter cells to the parental cell; the number of chromosomes and their sequence is identical.
In meiosis, we have daughter cells with half the number of chromosomes, and they have a different DNA sequence compared to each other.

Interphase

- **Gap 1** (G1)– many cytoplasmic organelles are constructed; RNA, protein and other molecules are synthesized; cell almost doubles in size
- **Synthesis** (S)– DNA is replicated and chromosomes duplicate, forming 2 sister chromatids attached at the centromere
- **Gap 2** (G2)– more cell growth; mitochondria divide; spindle precursors form

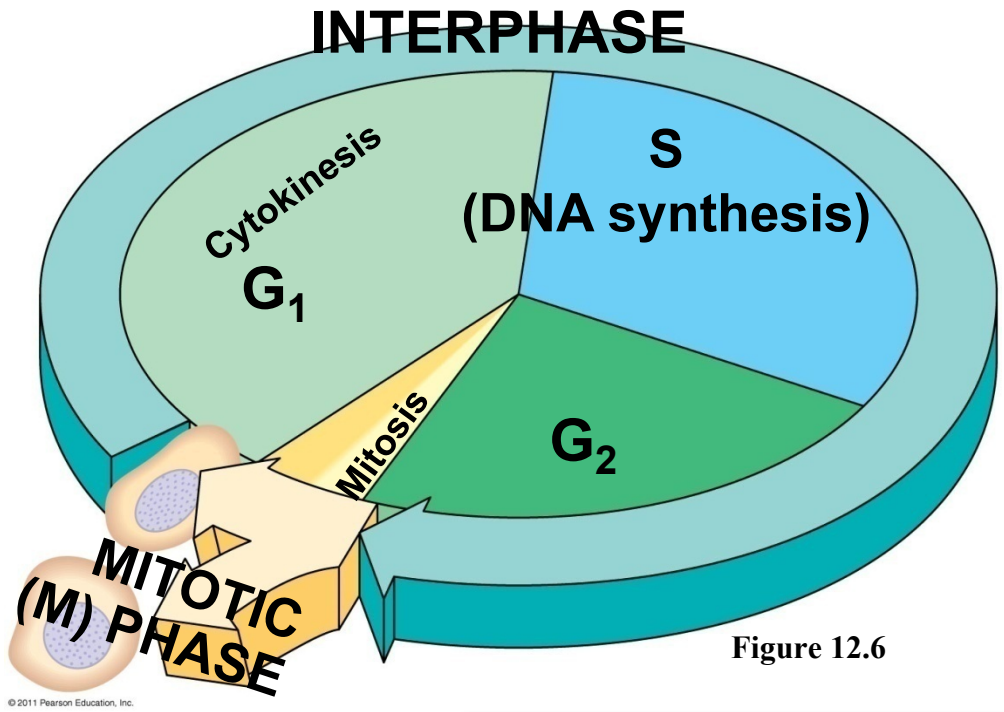


Figure 12.6

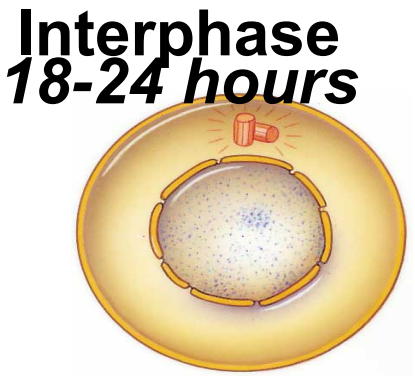
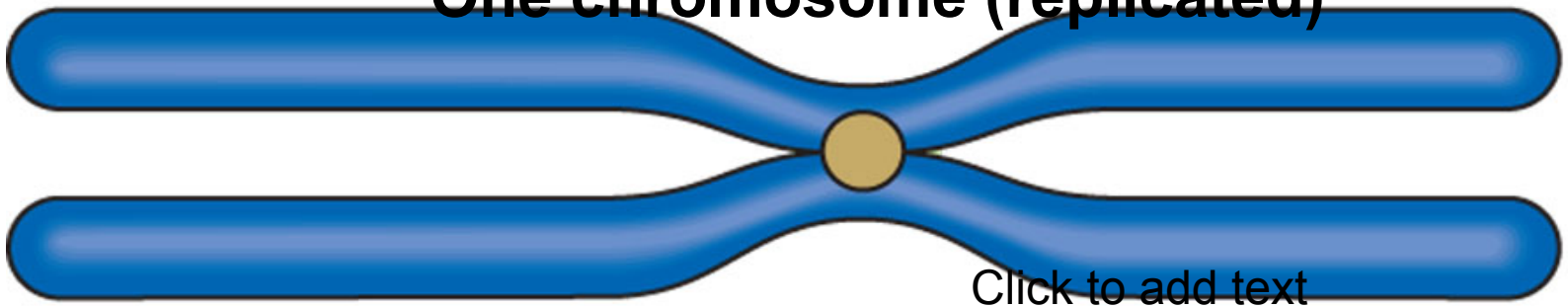


Fig. 2.8a

In the S phase, the DNA polymerase binds to the template molecule and binds to each of the two strands of DNA, (the leading and lagging strands), and from each DNA molecule we will have two daughter DNA molecules, and these are the sister chromatids of the original chromosome.
When we go towards the M phase, the 46 chromosomes are each composed of two sister chromatids.

One chromosome (unreplicated)

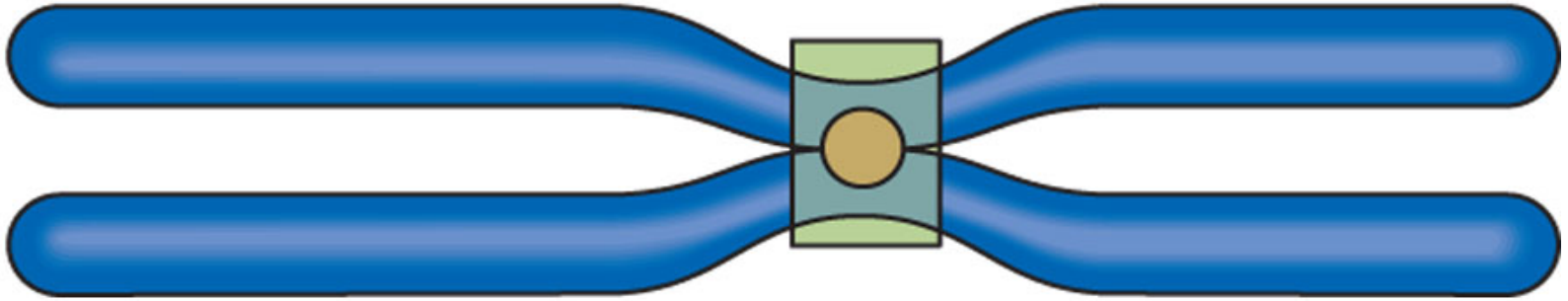
One chromosome (replicated)



A chromatid

Its sister chromatid

Click to add text

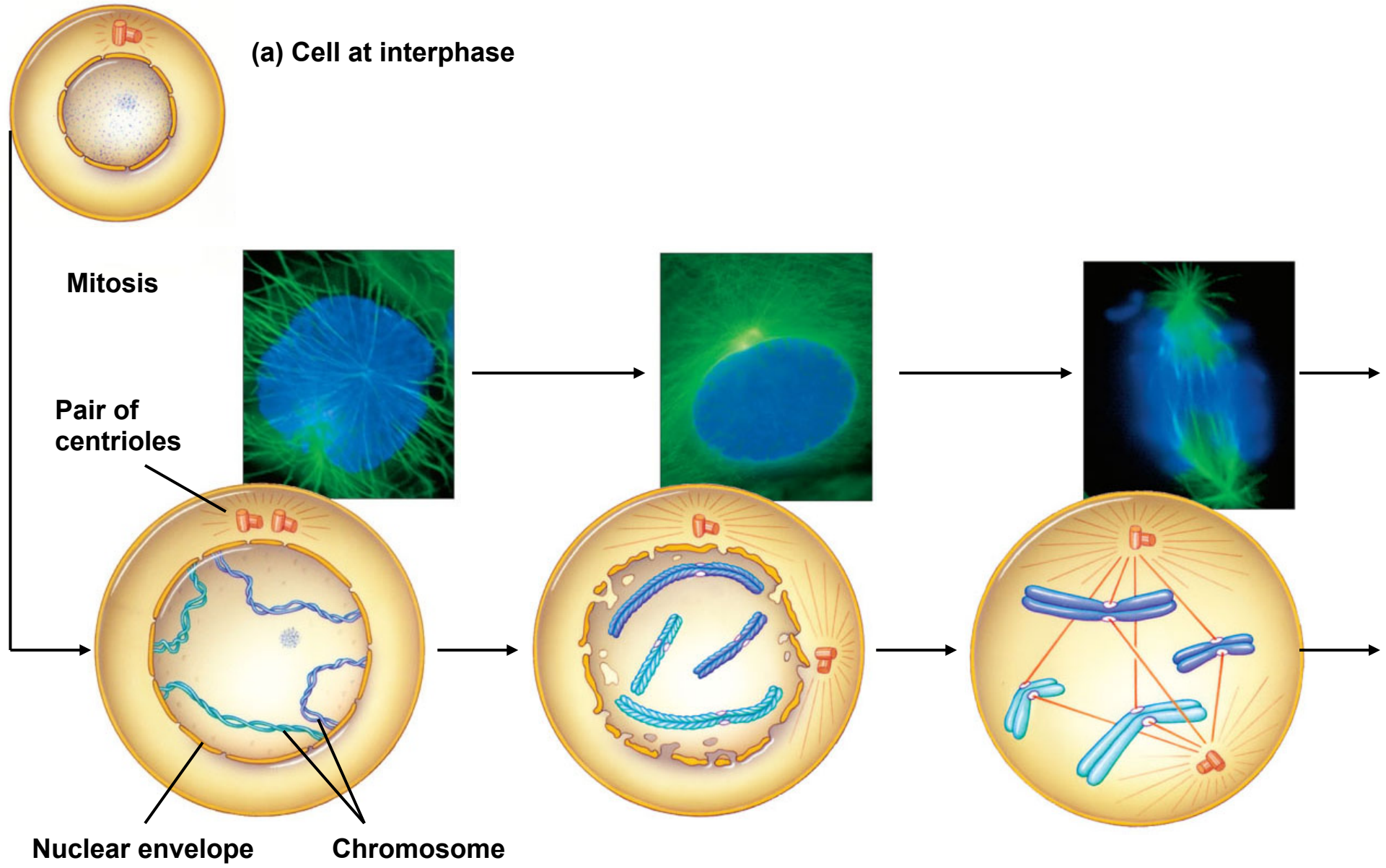


Centromere

Before the S phase we have 46 chromosomes in our cells and after the S they stay the same. Before the S phase, the chromosome consists of 1 DNA molecule (ds), and after the S phase it becomes two sister chromatids, and their sequence is identical.

Mitosis

- Produces identical daughter cells
  - (46 chromosomes)
- It must be accurate for cells to function properly
- Continuous process but divided into distinct steps:
  - Prophase
  - Metaphase
  - Anaphase
  - Telophase


(a) Cell at interphase
Mitosis
Pair of centrioles
Nuclear envelope
Chromosome
(b) Early Prophase
(c) Late Prophase
(d) Transition to Metaphase

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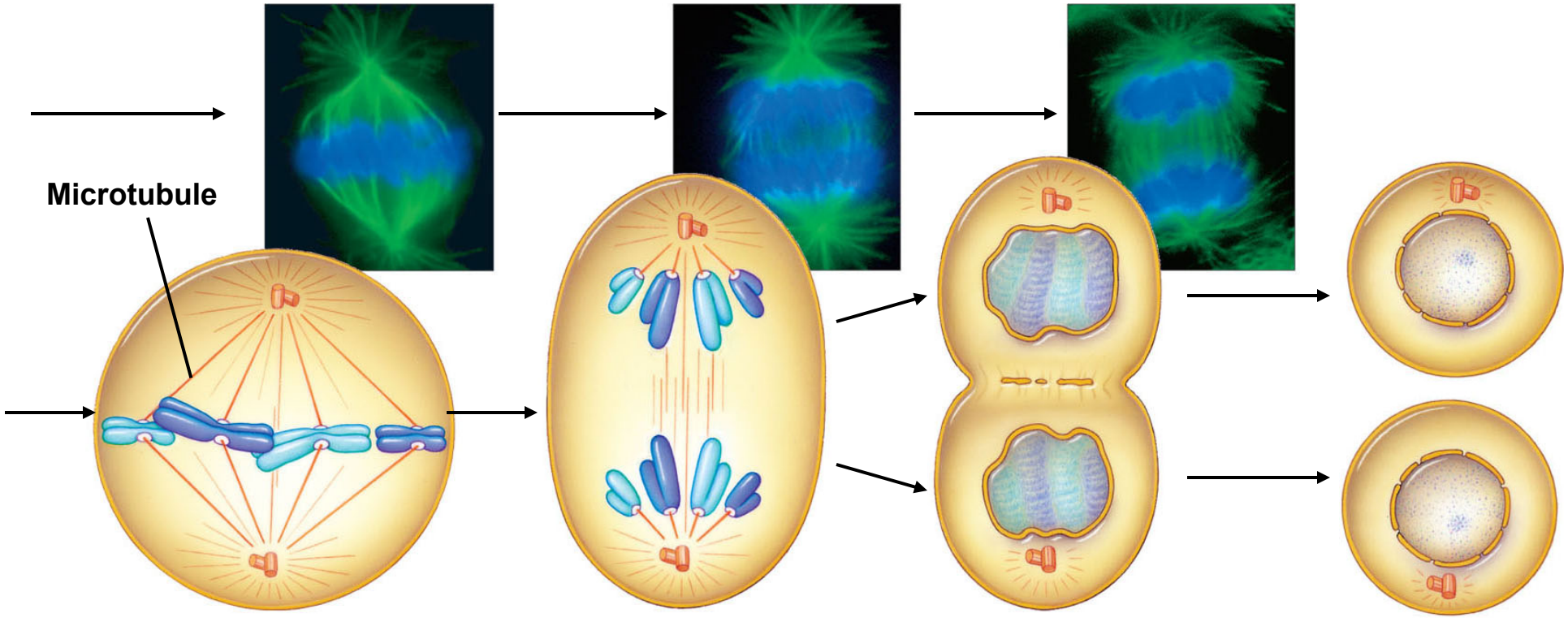
Microtubule
(e) Metaphase
(f) Anaphase
(g) Telophase
(h) Interphase

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Explanation to the previous figures

- Prophase is the first step in mitosis and there is condensation of chromatin into chromosomes. The nuclear envelope will start fragmenting and then two pairs of centrioles (centrosomes) which will migrate to the opposite poles and then mitotic spindles come out of them and each one holds onto every chromosome from each side.
- Metaphase: chromosomes align **individually** on the plate, and each chromosome is attached to spindle fibers from both sides of the cell.
- Anaphase: sister chromatids disjoin, they separate, and once this happens, each chromatid by itself is considered a chromosome. (2x of the number of chromosomes in the cell).
- Telophase: there are two daughter nuclei and cytokinesis occurs. The chromosomes are decondensed, and the nuclear envelope for each nucleus is regenerated. Results in two identical daughter cells after cytokinesis is complete.

The Stages of Meiosis

- After chromosomes duplicate, two divisions follow
  - Meiosis I (reductional division): homologs pair up and separate, resulting in two haploid daughter cells with replicated chromosomes
  - Meiosis II (equational division) sister chromatids separate
- The result is four haploid daughter cells with unreplicated chromosomes

Figure 13.7-1

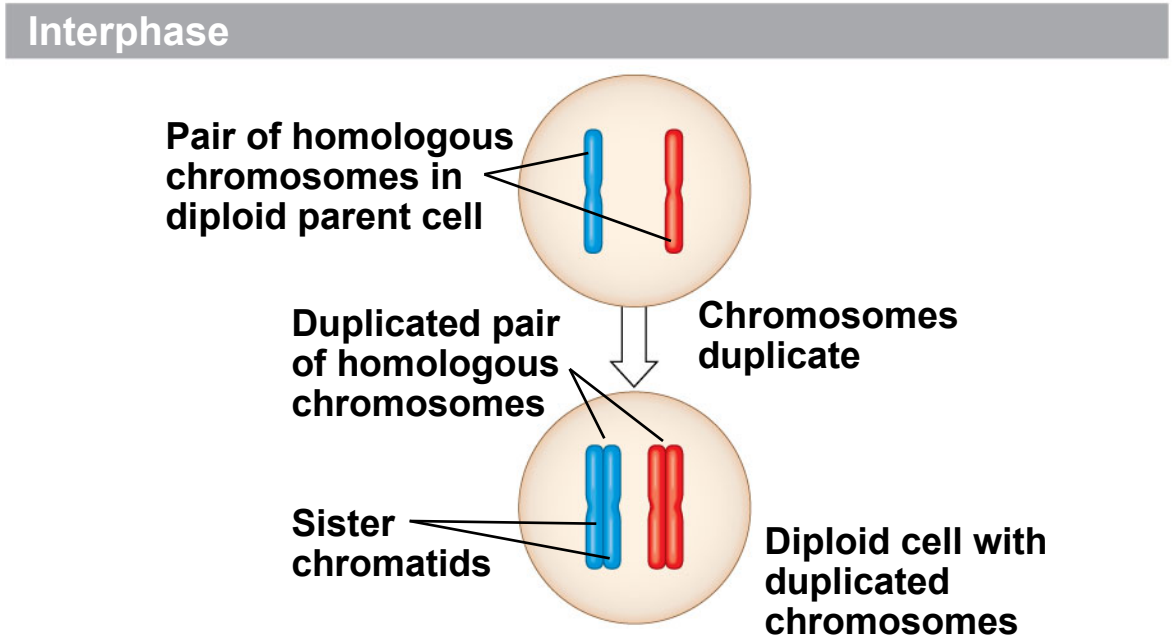


Figure 13.7-2

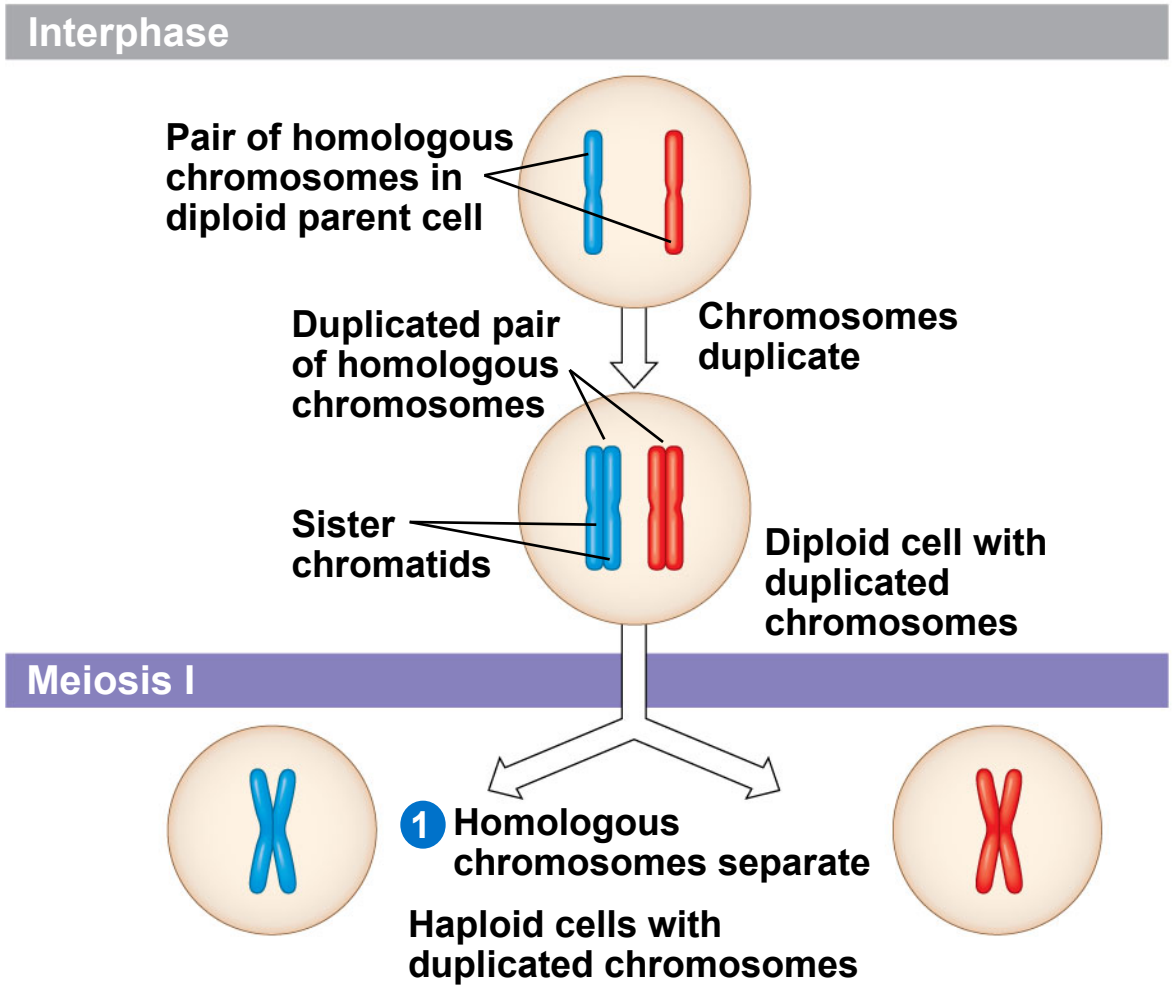
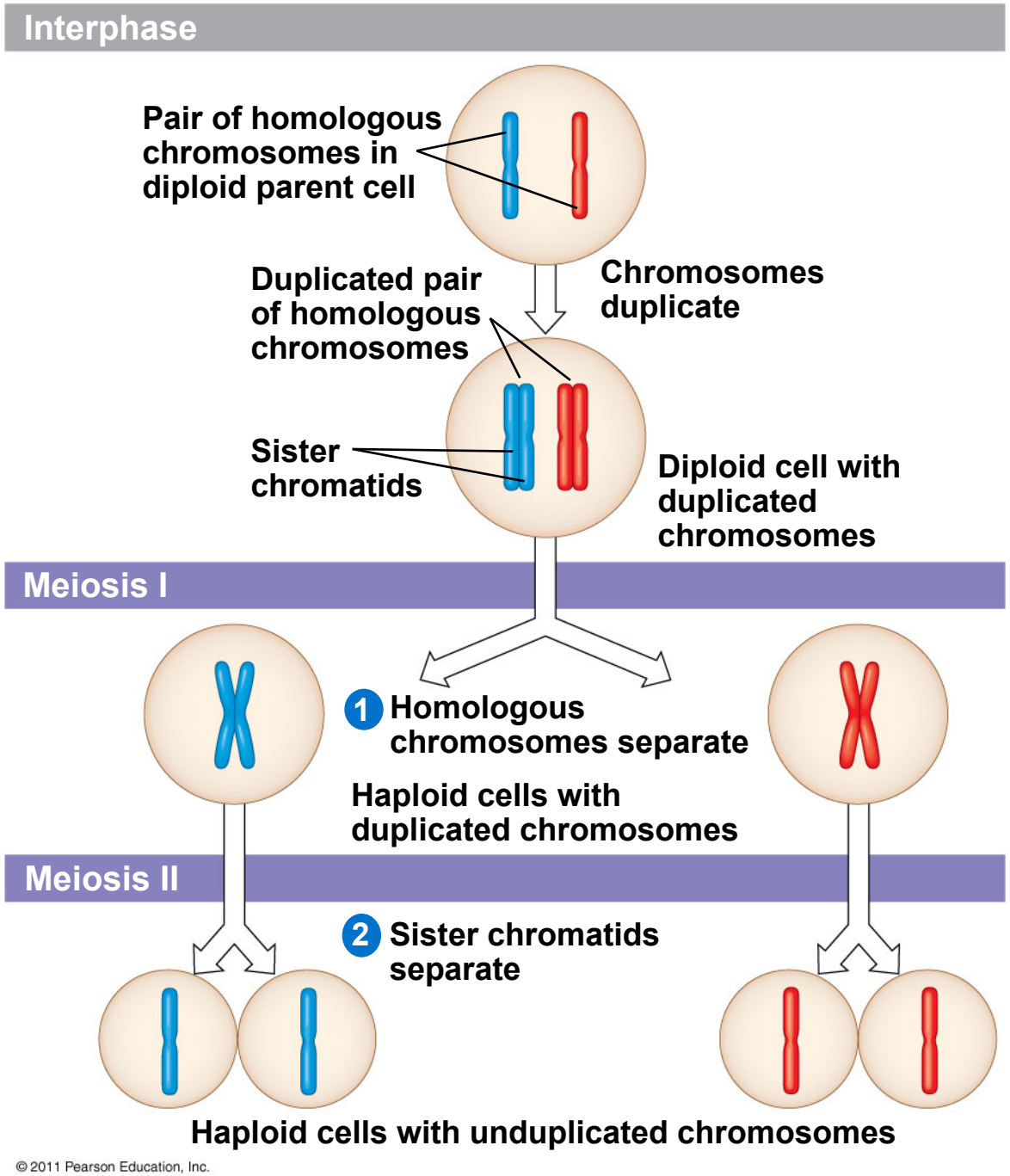


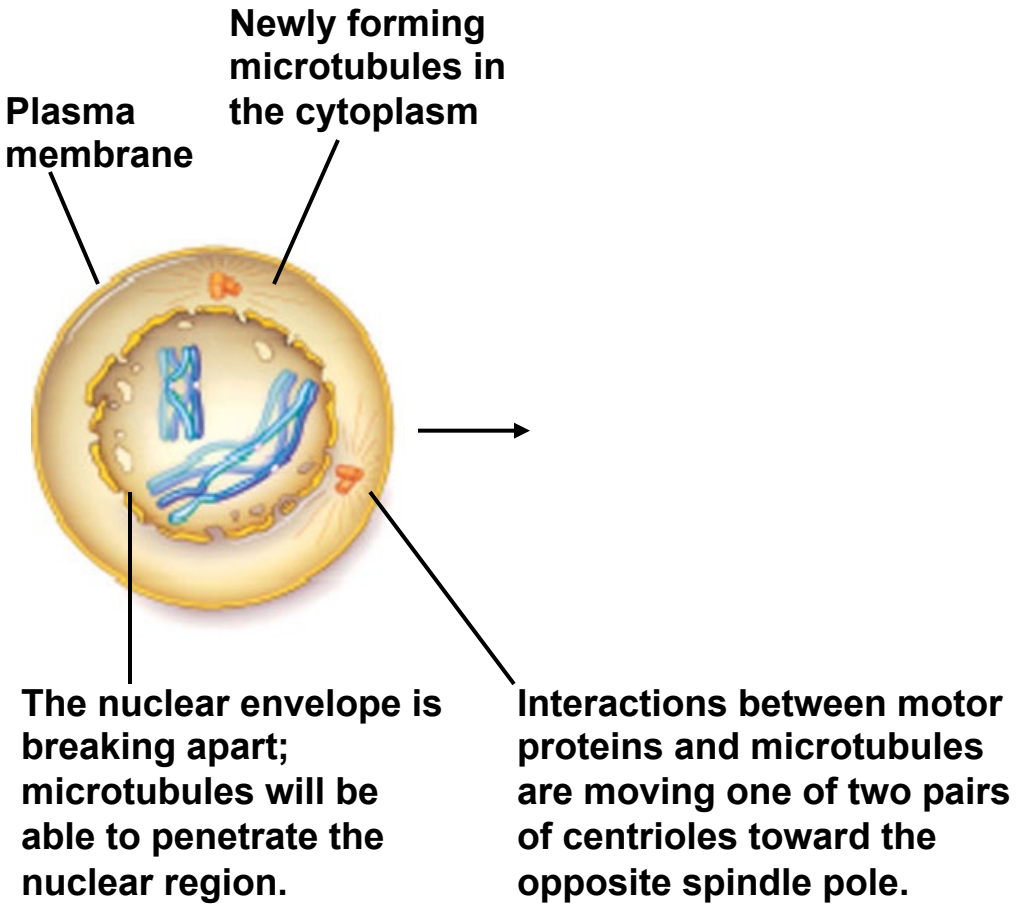
Figure 13.7-3

In miosis I, the homologous chromosomes separate and each one goes to a daughter cell, and in miosis II, these two chromatids disjoin and each go into two other new daughter cells



The reduction of the number of chromosomes occurs in miosis I; in the first cell we have two chromosomes which then become one in each daughter cell, and after the second division we also have only one chromosome that consists of one chromatid each.

Meiosis I



(a) Prophase I

Chromosomes begin to condense, the spindle fibers come out of the centrioles and the centrioles migrate to the opposite poles and the nuclear envelope will disappear, and then crossing over occurs.

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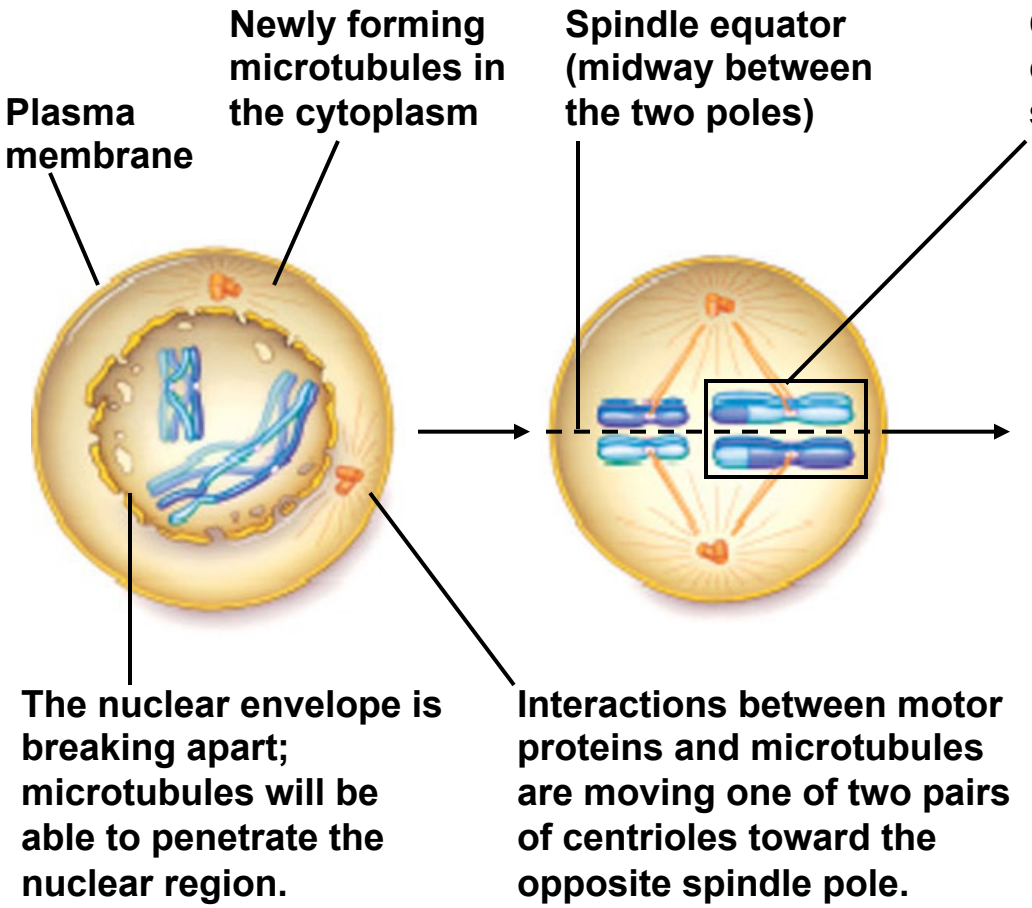
Meiosis I



- The homologous chromosomes align in the form of pairs at the metaphase plate, not individually like in mitosis.
- Notice the fact that each chromosome has one centromere that is attached to it by spindle fibers from one side of the cell.

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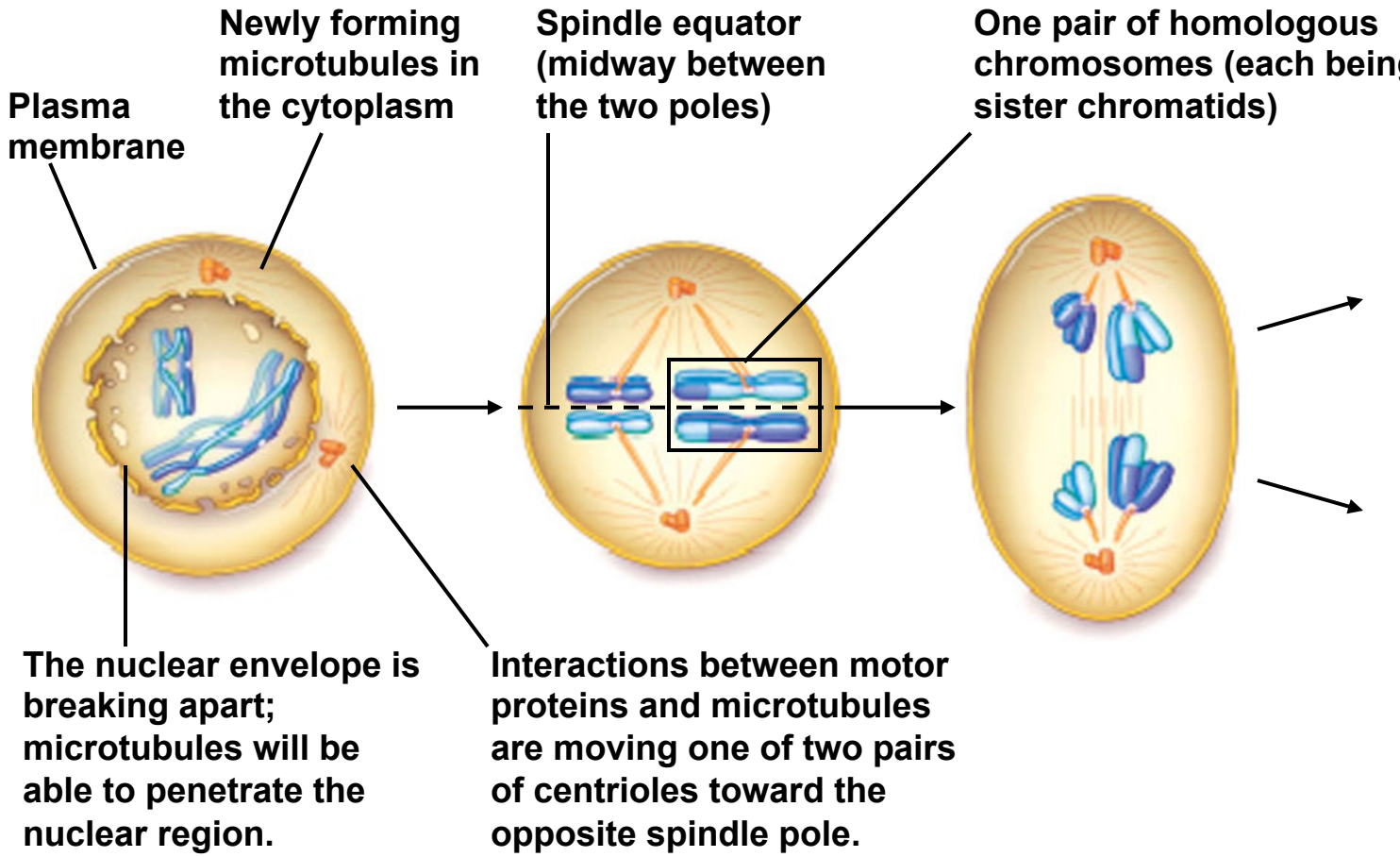
Meiosis I



This means that when anaphase happens, the homologous chromosomes will migrate to the opposite side of the cells and each chromosome will be composed of two sister chromatids.

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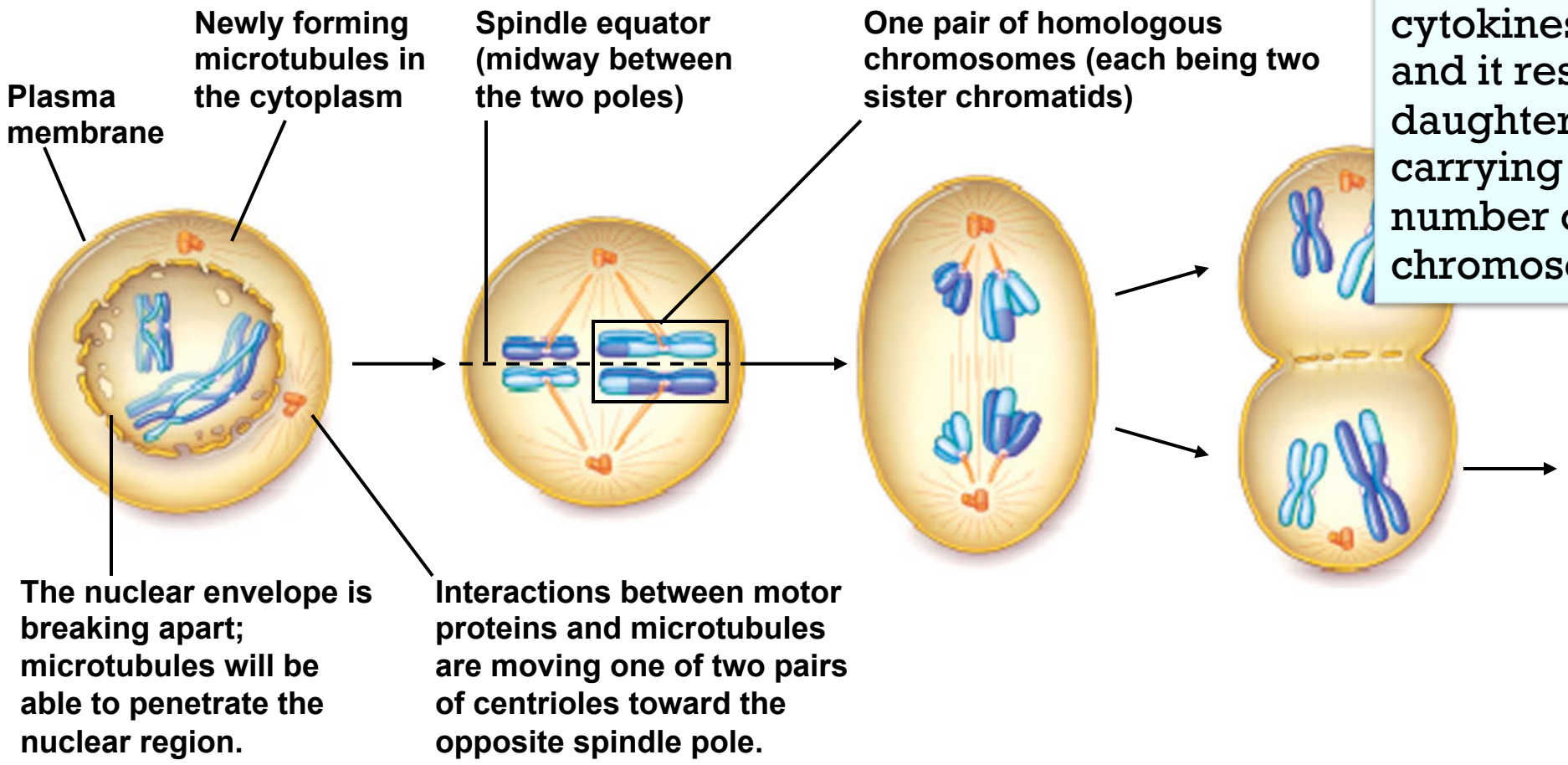
Meiosis I



In telophase we have two nuclei and then cytokinesis occurs and it results in two daughter cells carrying half the number of chromosomes

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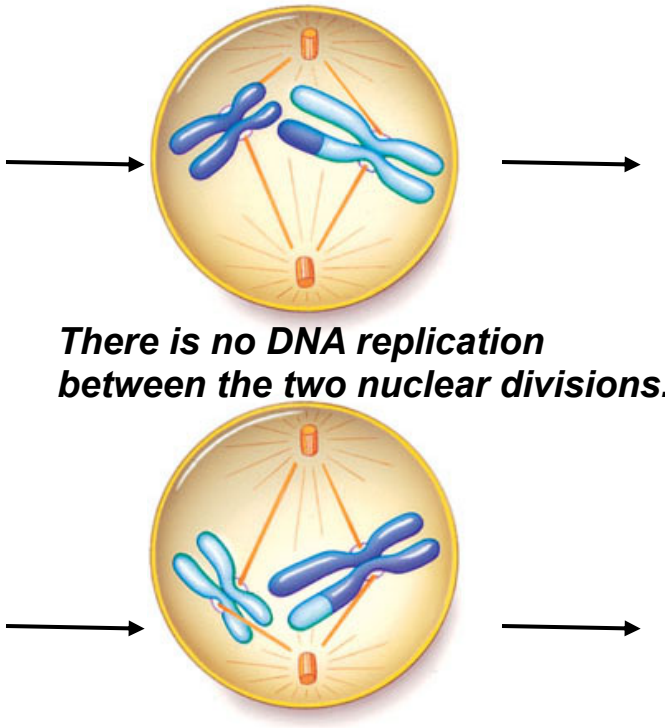
Meiosis II

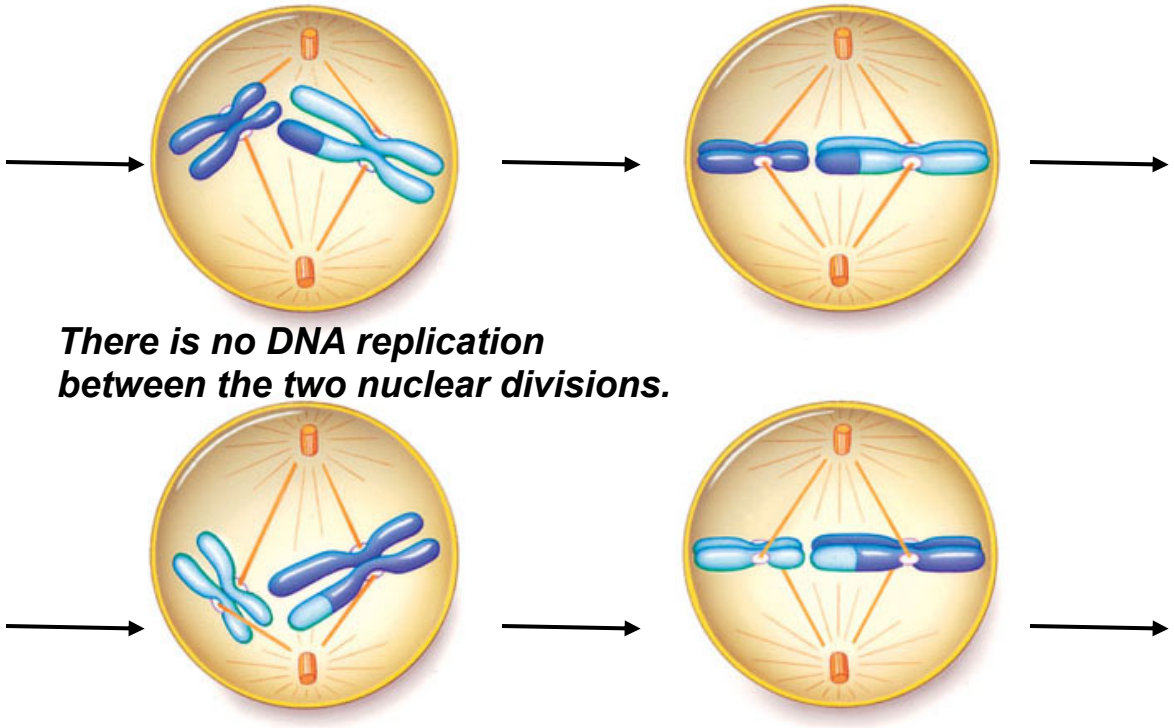


There is no DNA replication between the two nuclear divisions.

(e) Prophase II

There is no interphase (G and S phases) between meiosis I and meiosis II. When the first one is complete, meiosis II immediately starts.
Prophase II starts immediately after telophase I.

Meiosis II



There is no DNA replication between the two nuclear divisions.

(e) Prophase II

(f) Metaphase II

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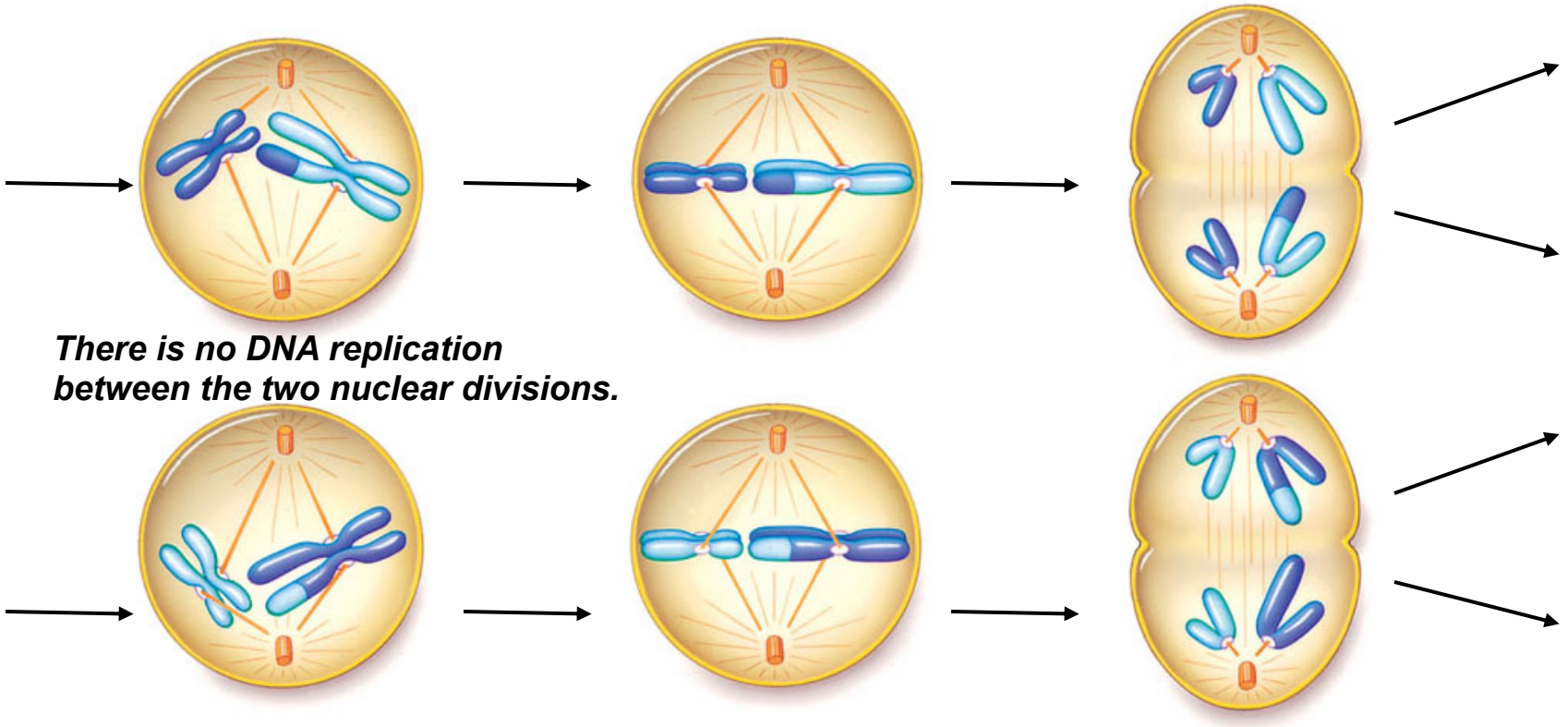
Meiosis II

In anaphase II, the sister chromatids separate from each other



There is no DNA replication between the two nuclear divisions.

(e) Prophase II (f) Metaphase II (g) Anaphase II

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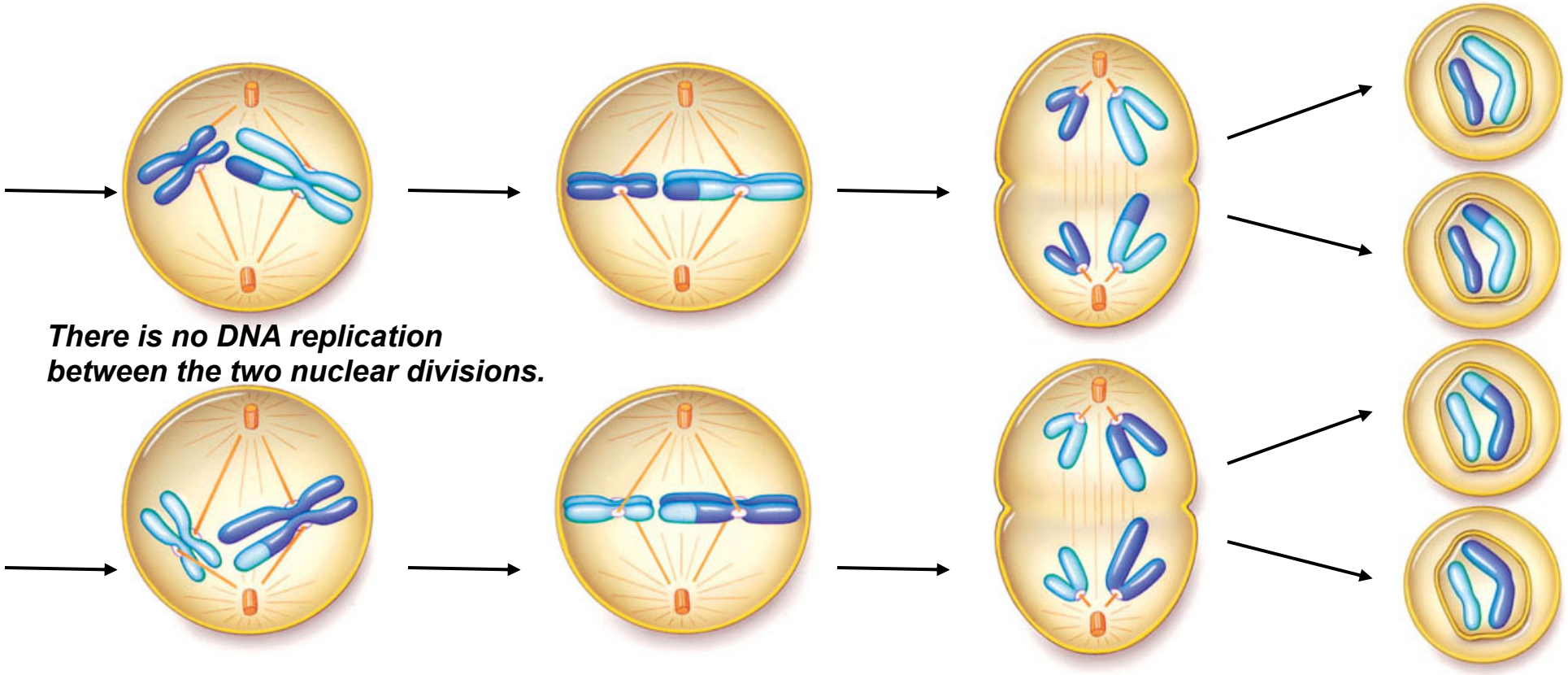
Meiosis II



There is no DNA replication between the two nuclear divisions.

(e) Prophase II (f) Metaphase II (g) Anaphase II (h) Telophase II

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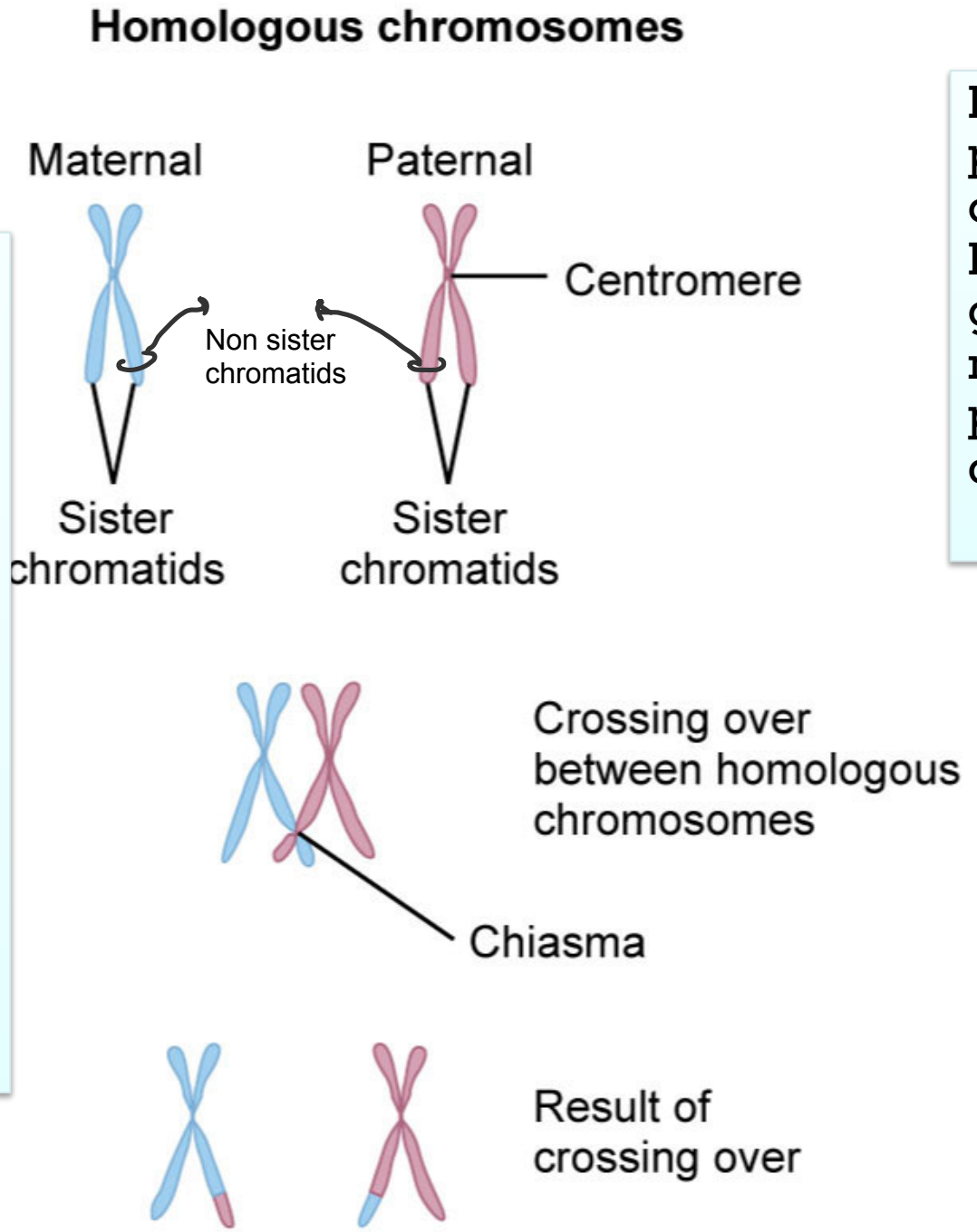
There are two copies from each chromosome, one from each parent.

The progenitor cell for the germ cells in the testis and ovaries contains 46 chromosomes, and this cell undergoes meiosis so that it produces a gamete carrying half the number of chromosome as the progenitor cell.
The maternal and paternal chromosomes are divided when the gametes are produced, so 50% of the gametes will contain maternal chromosomes and 50% contain paternal chromosomes.

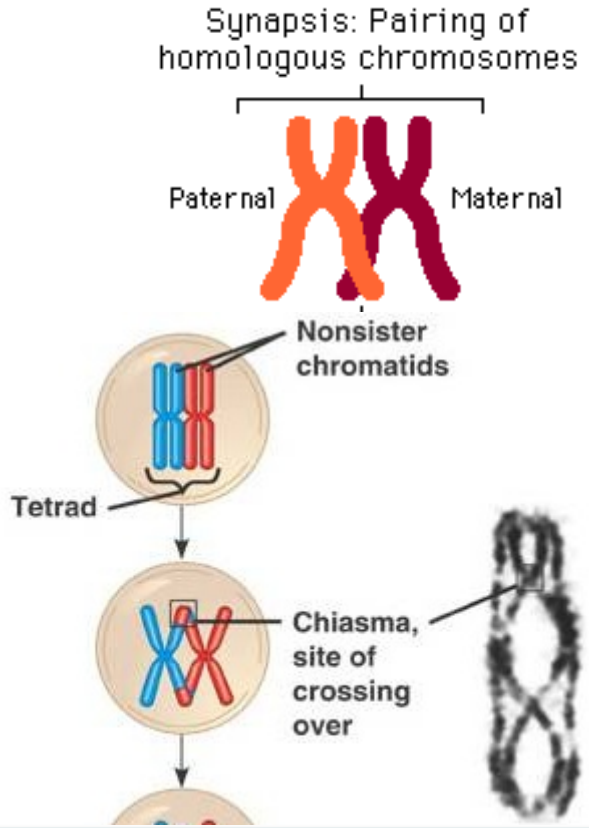


In prophase I there is a process called crossing over or recombination. It is the exchange of genetic material between non-sister chromatids of a pair of homologous chromosomes.

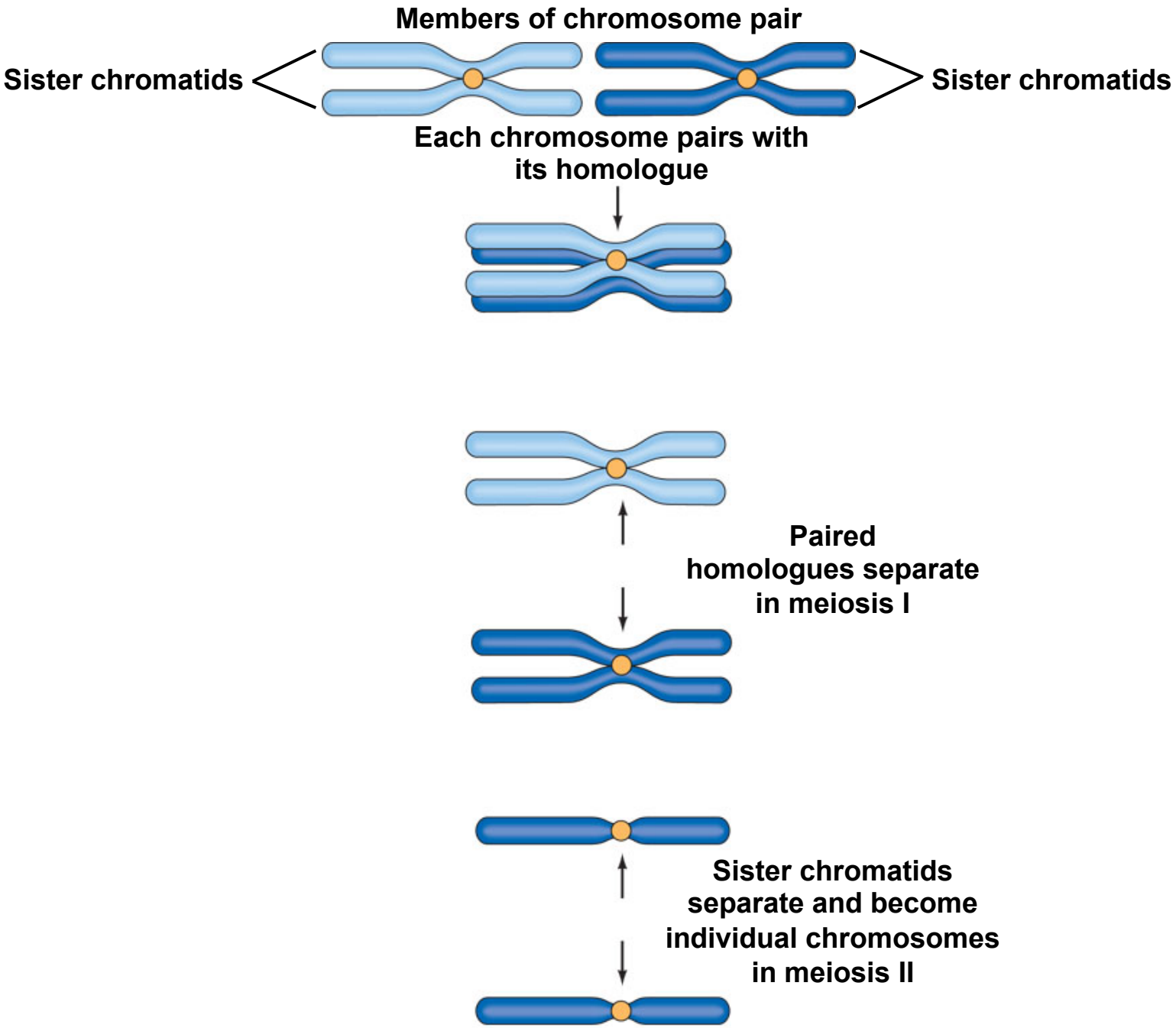
Prophase I

IMPORTANT SLIDE

- Leptotene
  - Replicated chromosomes align and begin to condense
- Zygotene
  - homologous chromosomes pair along entire length (**synapsis**)
  - synaptonemal complex forms
- Pachytene
  - Synapsis is complete and each pair of homologues is called a **tetrads** (**bivalent**)
  - **Crossing over** occurs (recombination at **chiasmata**)
- Diplotene
  - Homologous chromosomes separate some but remain bound at chiasmata
    - usually 2 chiasmata/chromosome, more frequent in females)
- Diakinesis
  - Further chromosome condensation; tetrads viable



Why would the homologous chromosomes remain attached at the chiasmata in diplotene if the crossing over is complete?
This is because there is no need for separation since in the next phase (metaphase) the chromosomes will align, so it makes sense to remain attached in preparation for metaphase.



Genetic consequences of meiosis

- Reduction of chromosome number
- Diploid to haploid (essential for gametes)
- Random assortment of maternal and paternal chromosomes
  - genes on different chromosomes
  - maternal/paternal chromosomes
  - Number of possible chromosomal combinations = 2^{23} or 8,388,608 (2^n)
  - Recombination between chromosome pairs increases the possible combinations
- Segregation of alleles
- Recombination/crossing-over
  - Allows new combinations of genes to be produced
  - Important for normal chromosome disjunction
  - Ensures genetic diversity

- At the time of Gregor Mendel there was no knowledge about chromosomes or DNA or genes, but he said two laws
- First law: law of segregation, (in the context of chromosomes), on meiosis, the homologous chromosomes, when producing the gametes, each of them will end up being in a different daughter cell.
- Second law: law of independent assortment, in meiosis I, the chromosomes align in the form of pairs at the metaphase plate, and they align independently of the parent of origin.

Chromosome combinations: independent assortment