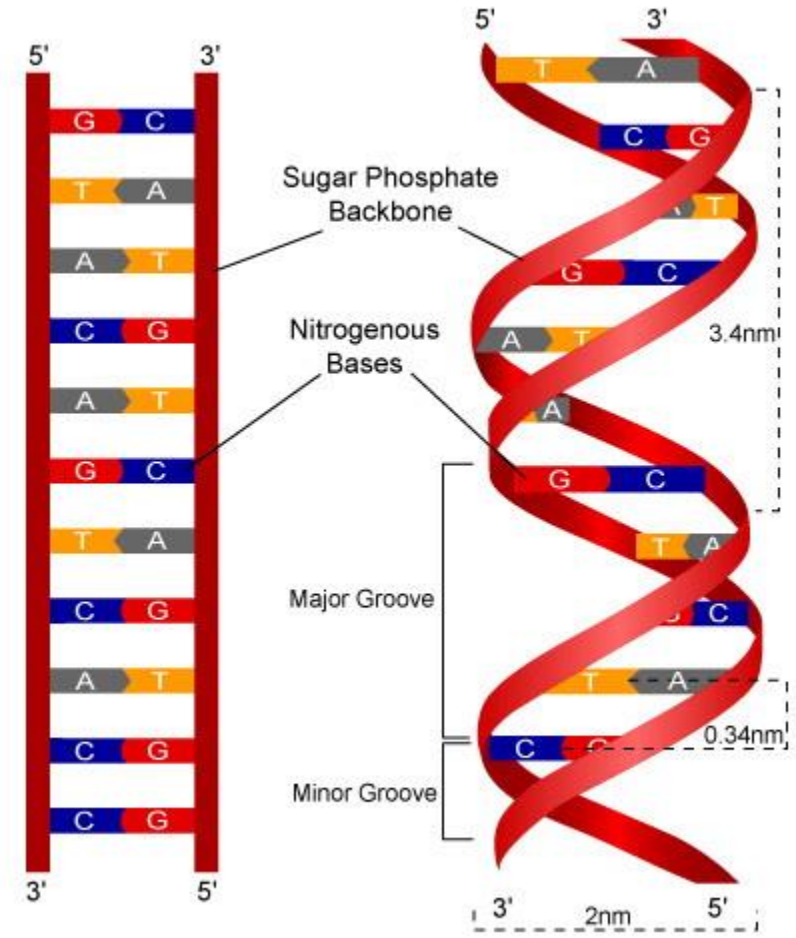
Cell cycle

Ass. Prof Dr. Heba Hassan Abd El-Gawad

Chemical (Molecular) structure of chromatin

- Chromatin is composed mainly of **DNA** (2nm) combined with basic proteins known as **histones**. There are five types of histones which are H_1, H_2A, H_2B, H_3 and H_4 They are packaged together in special manner named order of condensation.

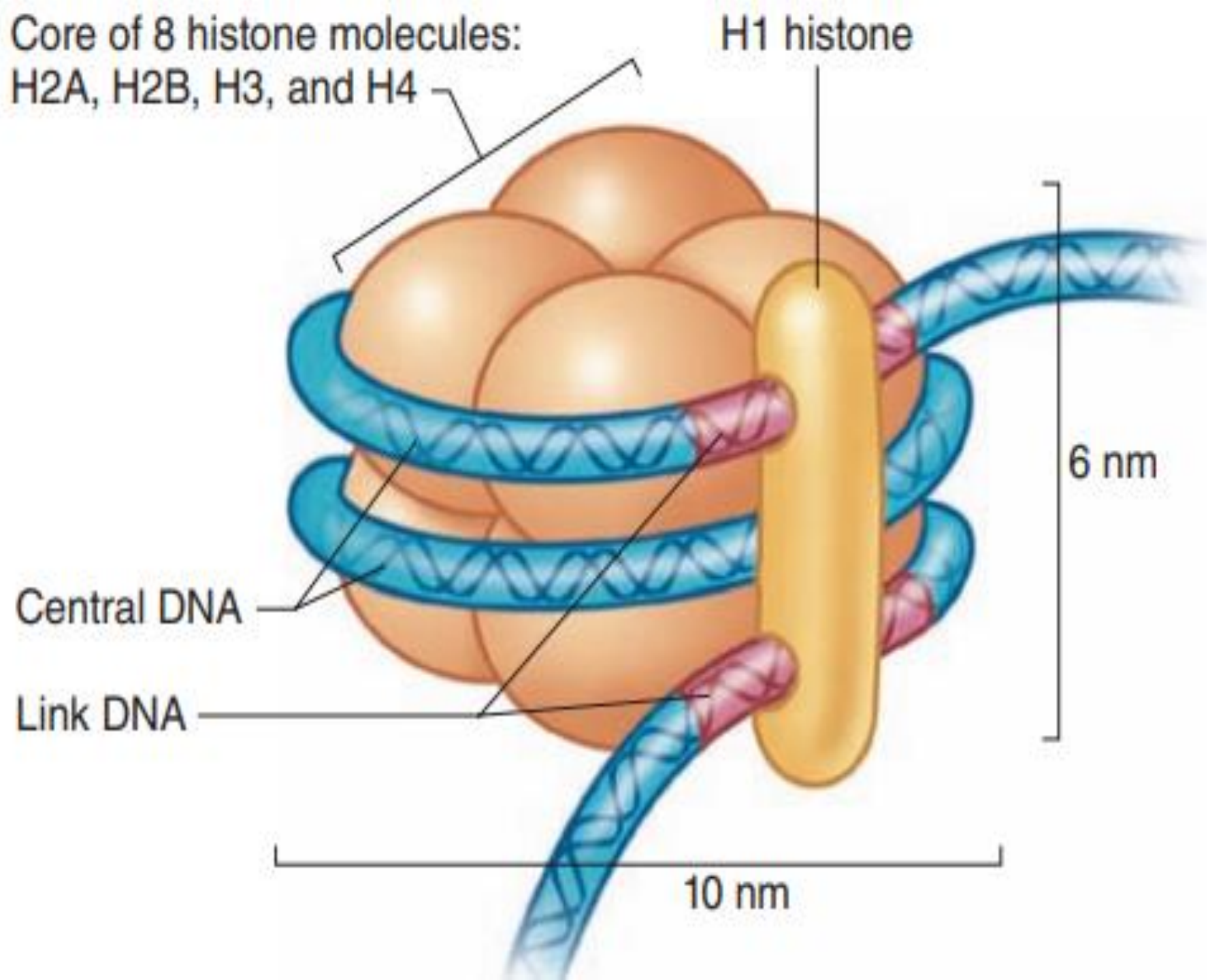


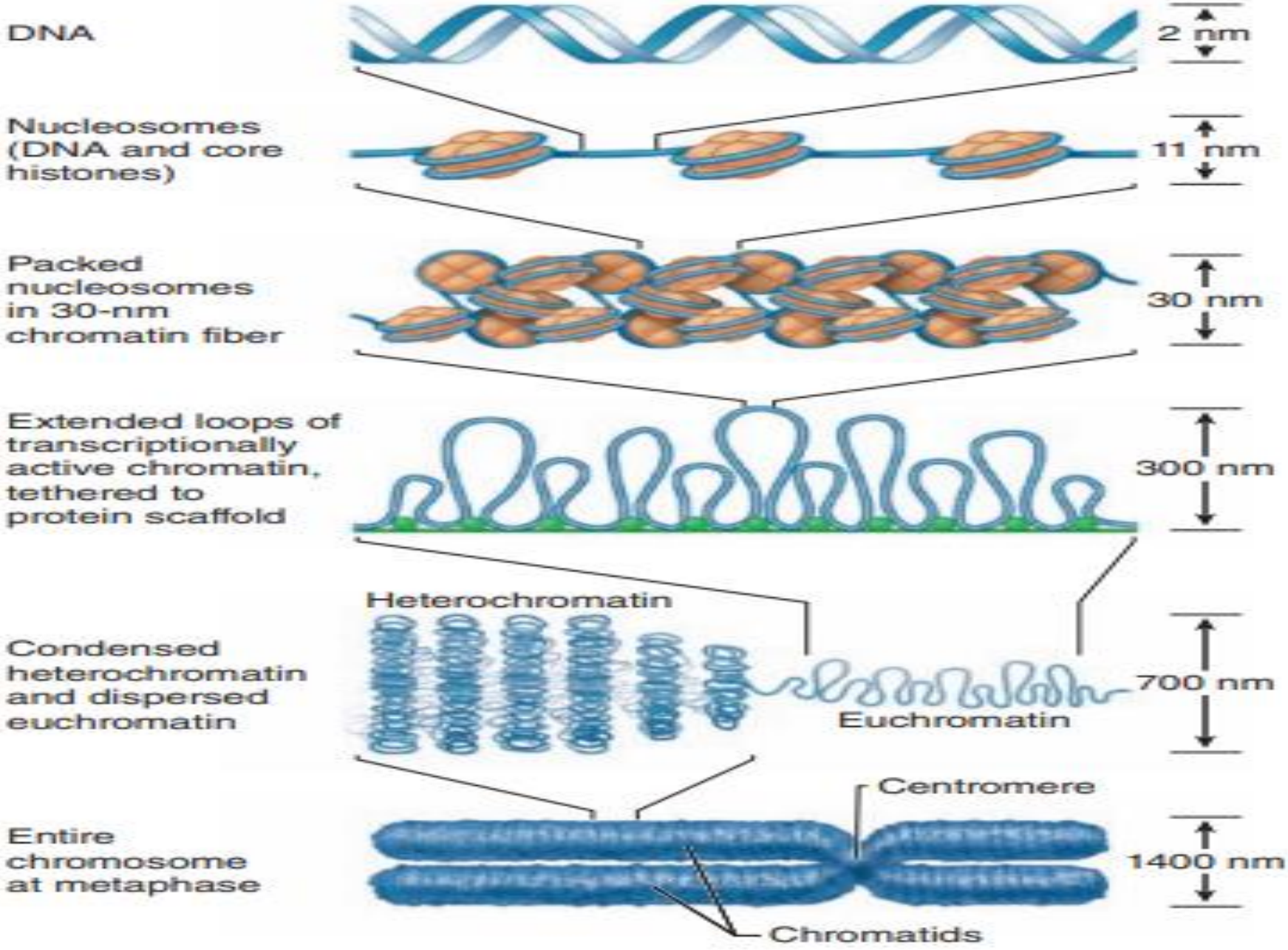
Packaging of DNA into chromatin & chromosome

(Order of condensation)

1-<u>Nucleosome</u> is the basic structural unit of chromatin. DNA filament is wrapped twice around a core of eight histones (octamer). The octamer is formed of two molecules of the 4 histones ; H_2A, H_2B, H_3 and H_4. The segment of DNA between two successive nucleosomes is known as linker DNA which is attached to histones H_1.

2-Nucleosomes and linker DNA constitute what is known as **<u>Beads-on-a string form</u>** of chromatin, which is <u>10-11 nm in diameter</u> .

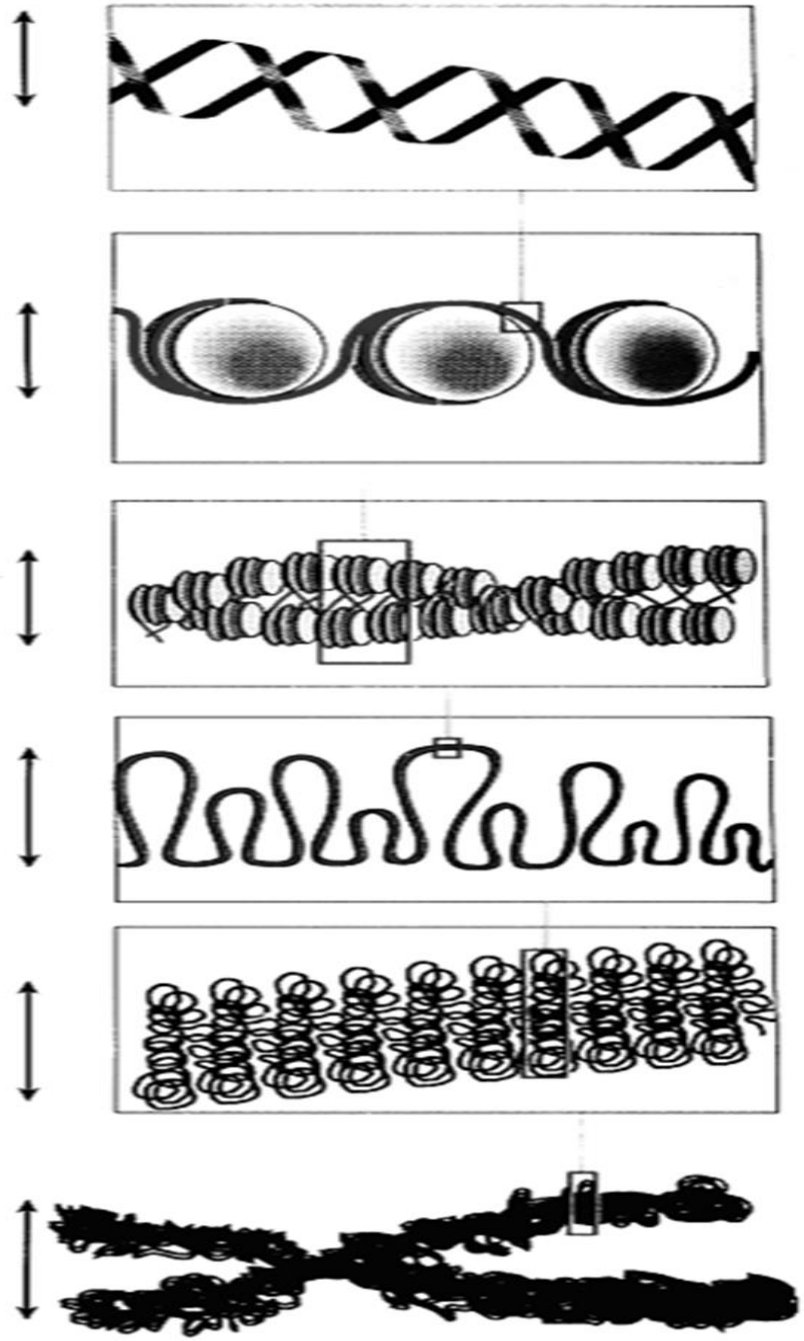

Core of 8 histone molecules:
H2A, H2B, H3, and H4
H1 histone
6 nm
Central DNA
Link DNA
10 nm


DNA
2 nm
Nucleosomes (DNA and core histones)
11 nm
Packed nucleosomes in 30-nm chromatin fiber
30 nm
Extended loops of transcriptionally active chromatin, tethered to protein scaffold
300 nm
Heterochromatin
Condensed heterochromatin and dispersed euchromatin
Euchromatin
700 nm
Centromere
Entire chromosome at metaphase
1400 nm
Chromatids

3-Solenoid or 30 nm fibers: It is the next higher order of organization of chromatin. In this structure, nucleosomes become coiled around an axis, with six nucleosomes per turn .

4- Looped domain of chromatin (300nm) is formed due to further coiling of the 30 nm fiber forming series of loops**.**

5- Heterochromatin (700nm) and **metaphase chromosomes (1400)** are formed during mitosis due to further coiling and condensation of the looped domains.



DNA Double Helix 2 nm

Beads-on- a-string form of chromatin 11nm (nucleosome)

30nm chromatin fiber of packed nucleosomes (Solenoid)

Looped domain (300nm)

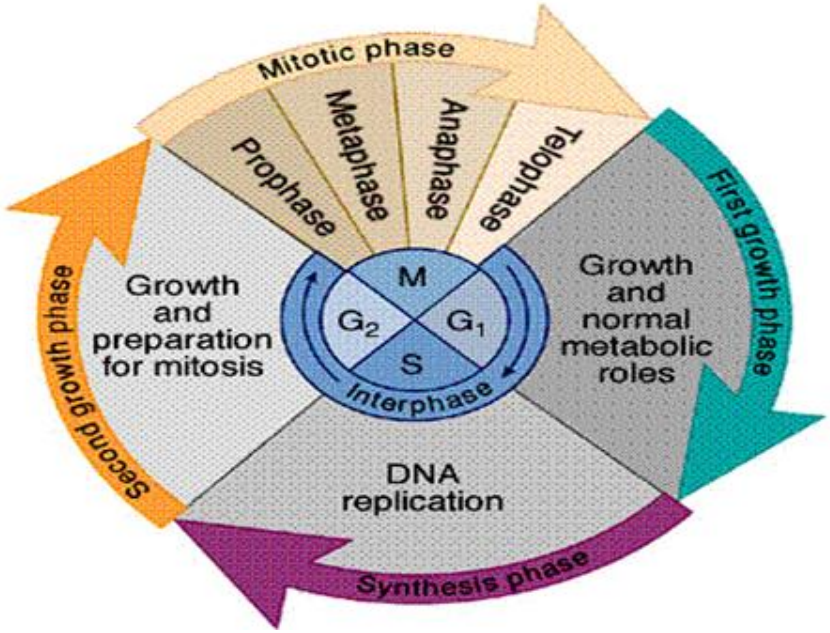
Prophase chromosome 700nm

Metaphase chromosome 1400nm

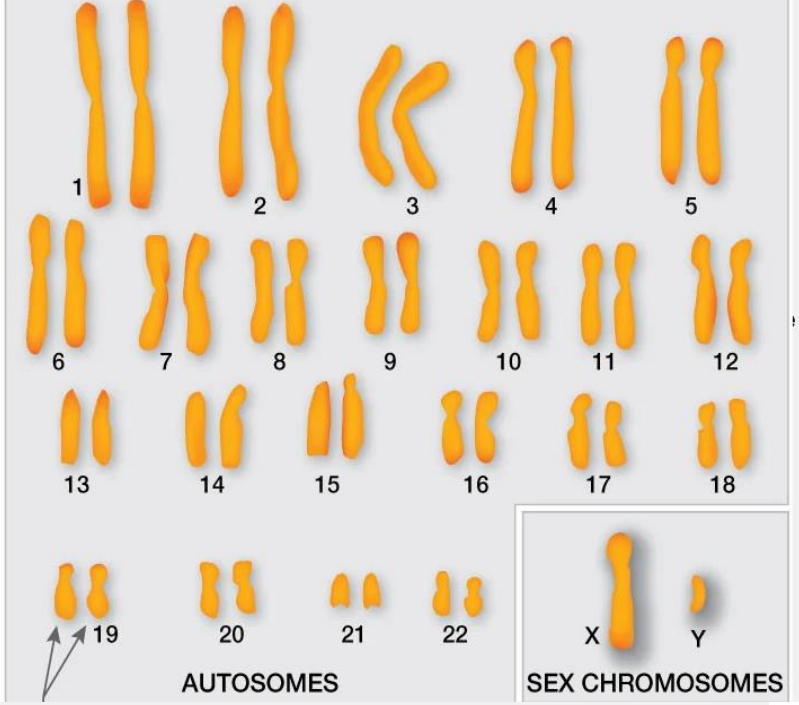
CELL CYCLE

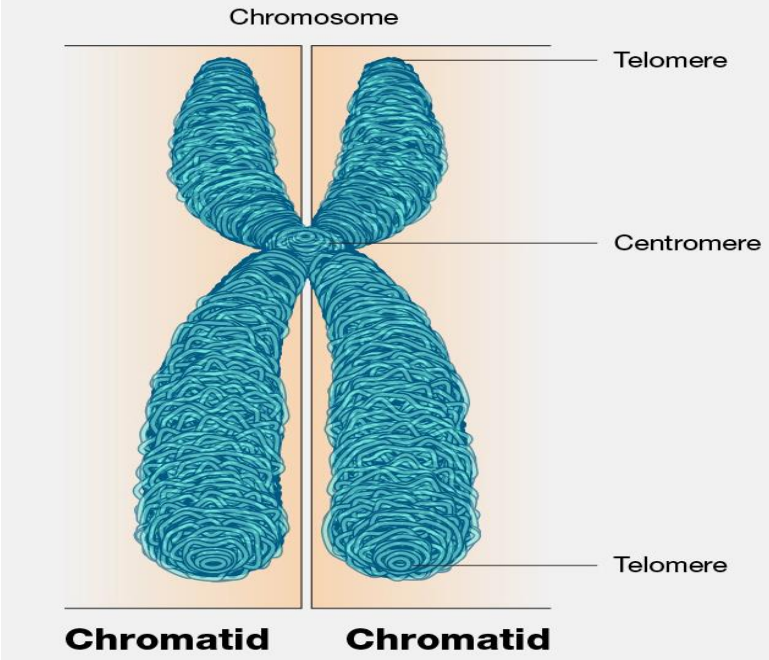
1- Mitosis: is the short period of time (1- 2 1 /2 hour) during which the cell divides its nucleus and cytoplasm giving rise to two daughter cells.

2- Interphase, a longer+ period of time (20 hours) between two successive divisions, during which the cell increases its size and content and replicates its genetic material.



- **Haploid number:**
  - **23 s-chromosomes = 23 chromatids (ovum & sperm)**
- **Diploid number:**
  - **46 s-chromosomes = 46 chromatids**
  - **46 d-chromosomes = 92 chromatids**
- **Amount of DNA=n**
  - **1n: in germ cells (ovum & sperm)**
  - **2n: in somatic cells (46s)**
  - **4n: in S-phase (46 d)**





INTERPHASE

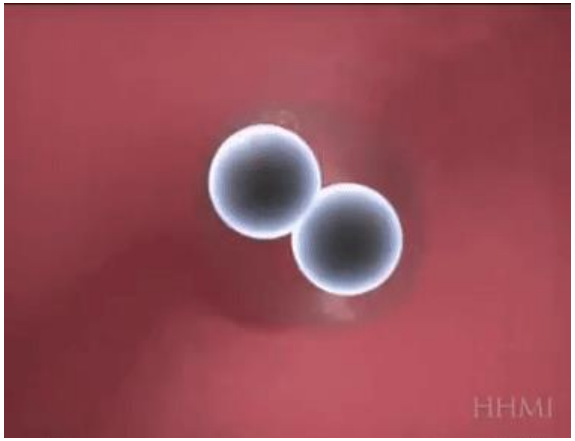
- **<u>is subdivided into three phases:</u>**
- ***G1 (gap1):*** cell prepare for DNA duplication.
- ***S (synthetic):*** DNA duplicatation.
- ***G2 (gap2):*** cell prepare for mitosis.

G1 phase (pre-duplication)

- It is the period between the end of mitosis and the beginning of S- phase. It takes 8 hours.
- **During this phase:**
  - **The cell increases in size.**
  - **Starts to synthesize RNA and protein to build themselves**
  - **The cell contains 46 s-chromosomes (diploid number) = 2n (amount of DNA).**

G1 phase (pre-duplication)

The duration of G1 phase may vary from one cell to another according to the main function of the cell :



Highly proliferated cells:

have short G_1 phase e.g. stem cells of bone marrow and germinal epithelium

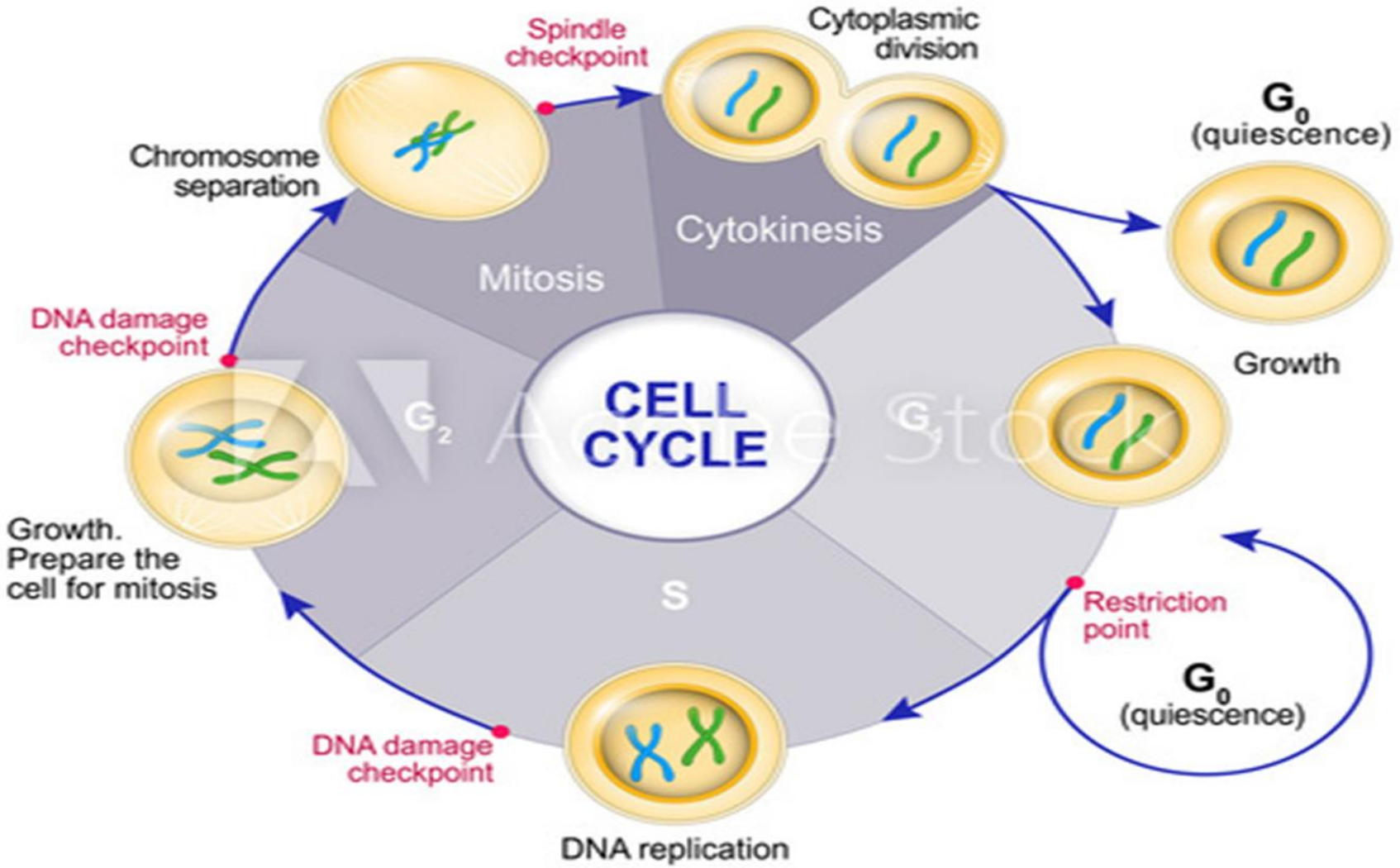
G1 phase (pre-duplication)

Highly differentiated cells:

after the last mitosis may leave the cell cycle at G_1 phase either:

1. ***Temporarily*** (e.g. hepatocyte): The cells perform their specific functions and some of them may enter the cycle again to repair and regenerate damaged cells (Prolonged G_1 phase).

2. ***Permanently*** (e.g. nerve cells and cardiac muscle); there is no repair if the cells are damaged, these cells are said to be in resting stage, the G0 phase.

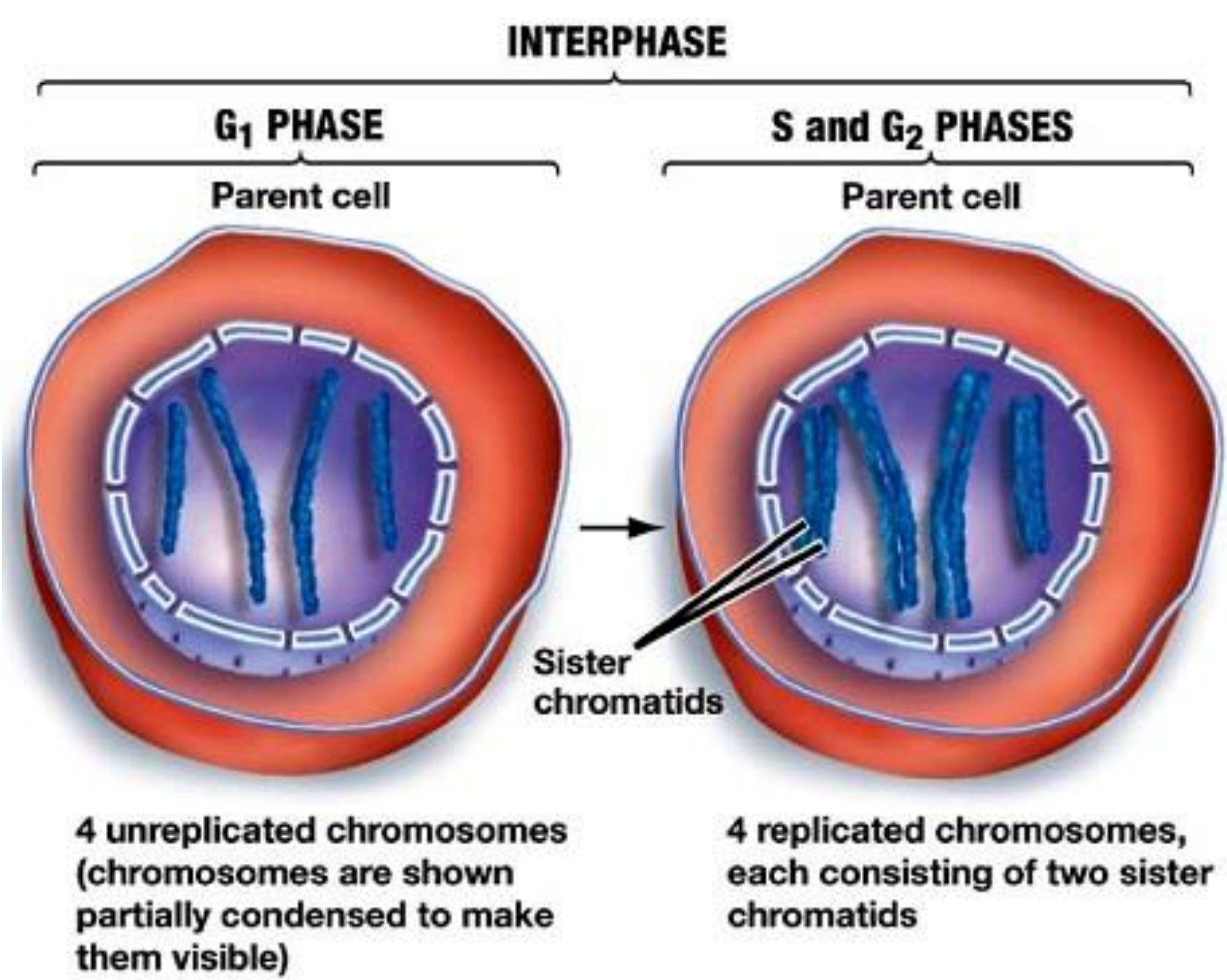

Spindle checkpoint
Cytoplasmic division
G_0 (quiescence)
Chromosome separation
Cytokinesis
Mitosis
DNA damage checkpoint
Growth
CELL CYCLE
G_2
G_1
Growth. Prepare the cell for mitosis
S
Restriction point
G_0 (quiescence)
DNA damage checkpoint
DNA replication

S-Phase (DNA synthesis)

- **Definition:** The period that follows G1 phase
- **Duration:** It takes 8 hours.
- -During this phase:

a. DNA is duplicated (DNA replication). Thus, each somatic cell having 46 s-chromosme and 2n DNA after duplication will contain 46 d-chromosomes and double the amount of DNA (4n).

b. Duplication of the 2 centrioles into 2 pairs


INTERPHASE
G1 PHASE
S and G2 PHASES
Parent cell
Parent cell
Sister chromatids
4 unreplicated chromosomes (chromosomes are shown partially condensed to make them visible)
4 replicated chromosomes, each consisting of two sister chromatids

G2 Phase (post-DNA duplication)

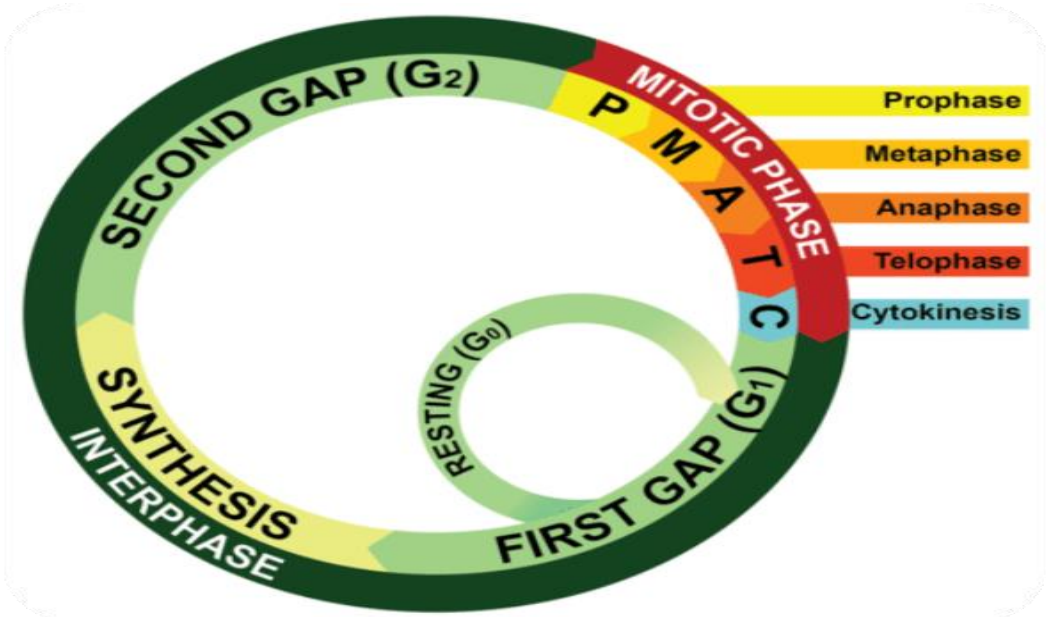
- **Definition:** It is the period between S-phase and the beginning of the next mitosis.
- **Duration:** It takes 4 hours.
- **During this phase**: the cell prepares itself for mitosis by:

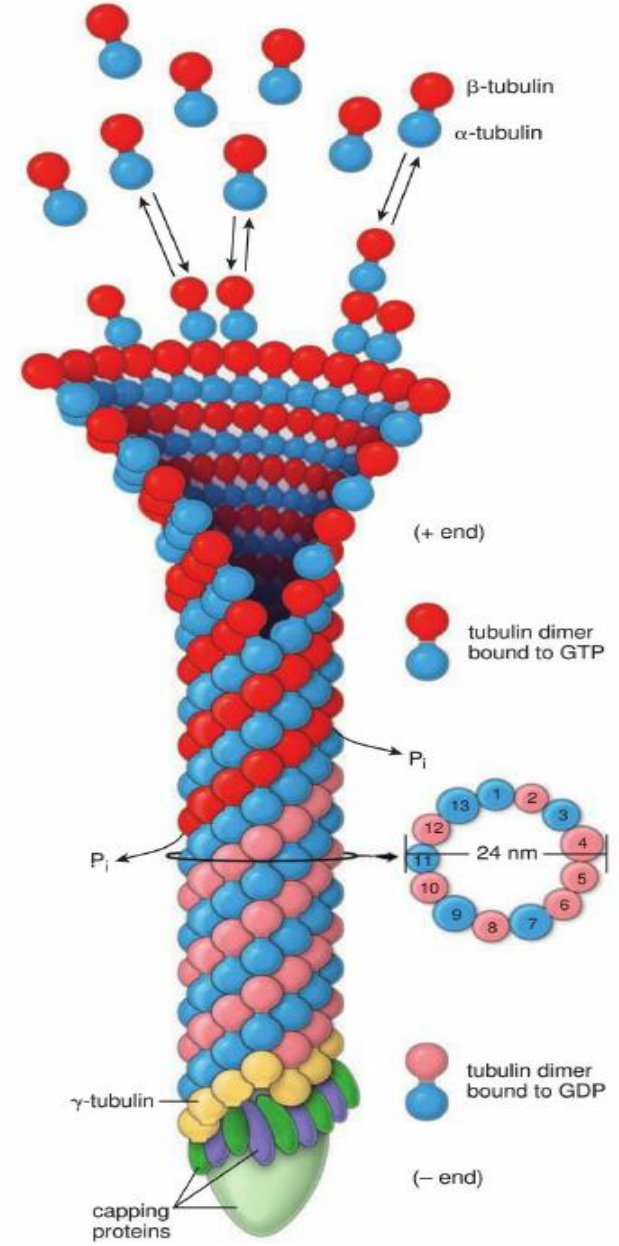
a. Synthesis of RNA and proteins essential to cell.

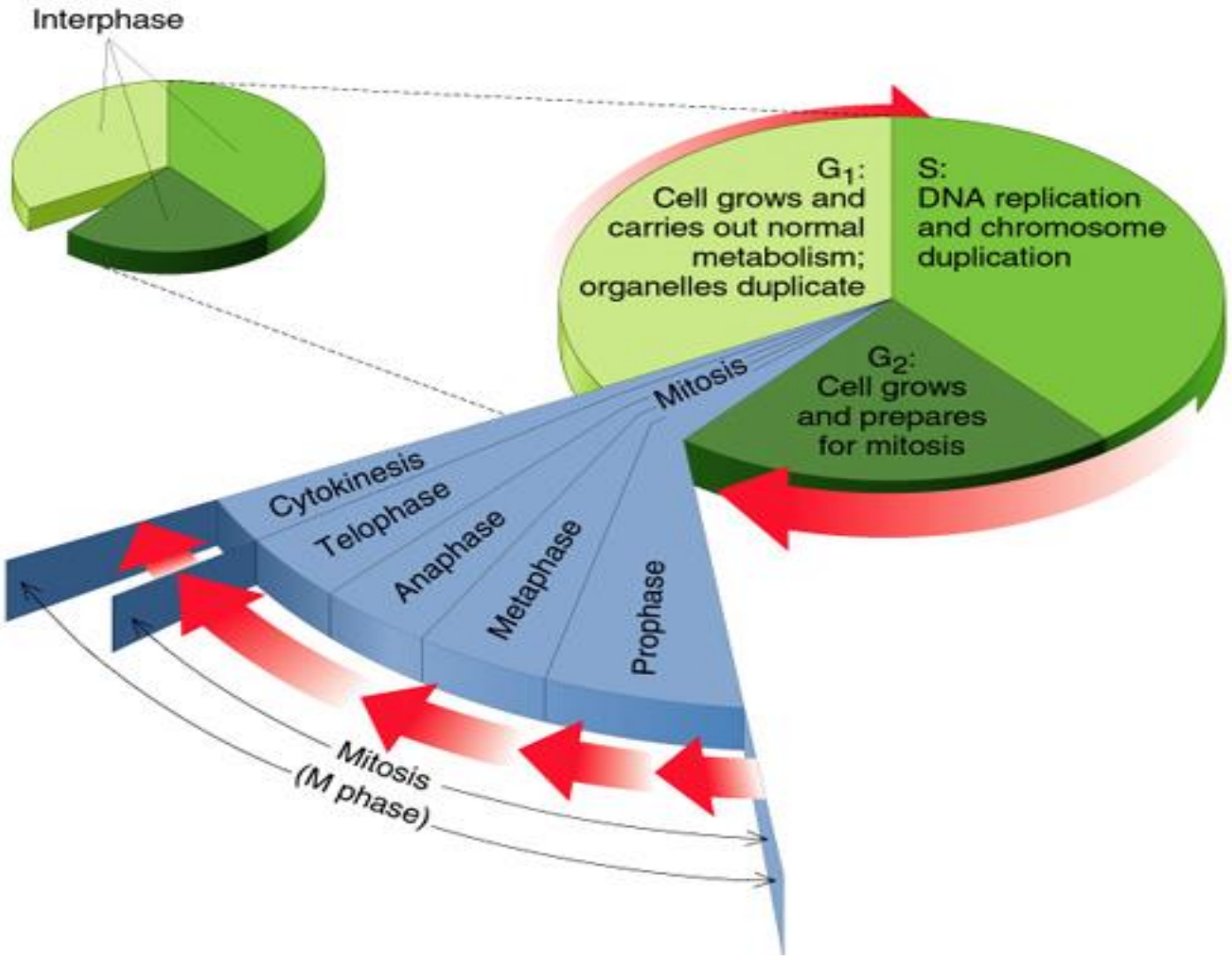
b. Storage of energy for mitosis.

c. Synthesis of tubulin that is essential for formation of microtubules required for the mitotic spindle.

G2 Phase (post-DNA duplication)






Interphase
G1:
Cell grows and carries out normal metabolism; organelles duplicate
S:
DNA replication and chromosome duplication
G2:
Cell grows and prepares for mitosis
Mitosis
Prophase
Metaphase
Anaphase
Telophase
Cytokinesis
Mitosis
(M phase)

MITOSIS

Definition: It is the process by which the cytoplasm & nucleus of somatic cell are divided **equally** into two **identical** daughter cells, each cell having the **same** number of chromosomes (46 = 23 pairs) s chromosome as the parent cell.

Duration: 1- $2^{1}/_{2}$ hours.

PHASES

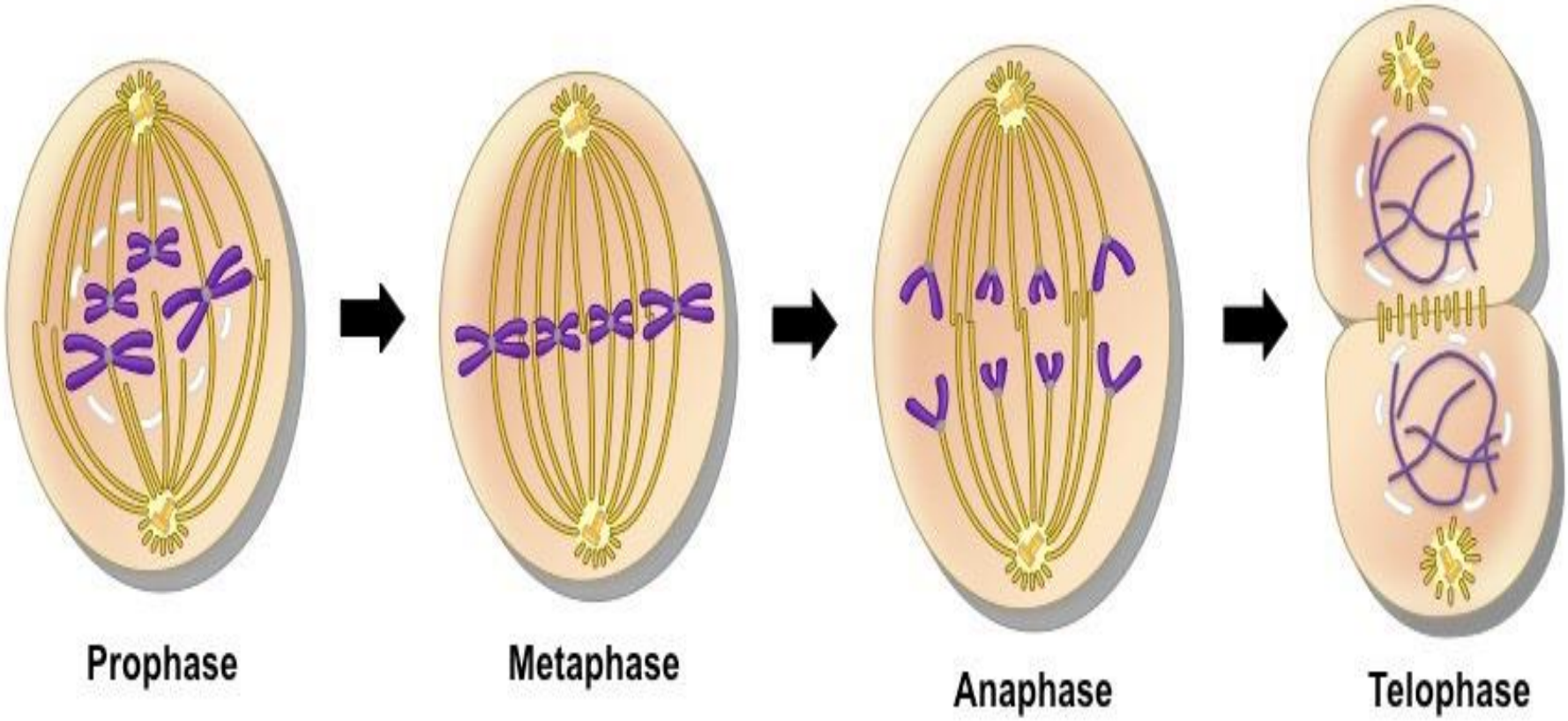
Karyokinesis

- Division of the nuclear material

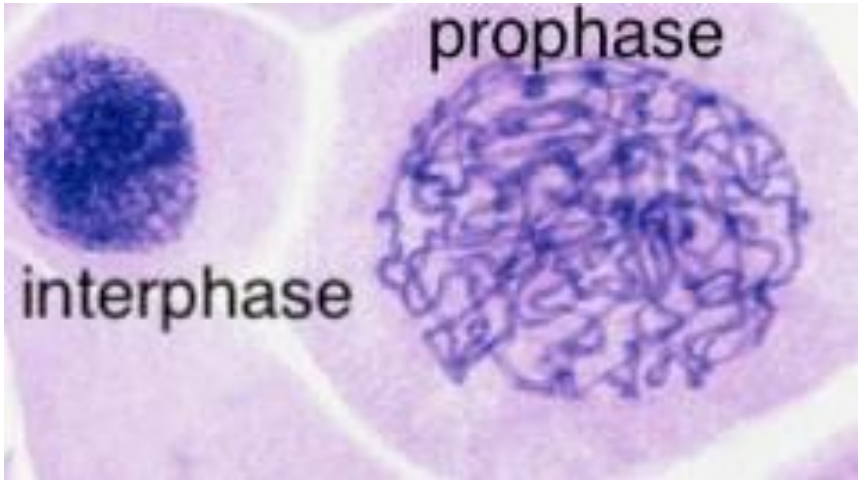
Cytokinesis

- Division of the cytoplasm

Karyokinesis



PROPHASE

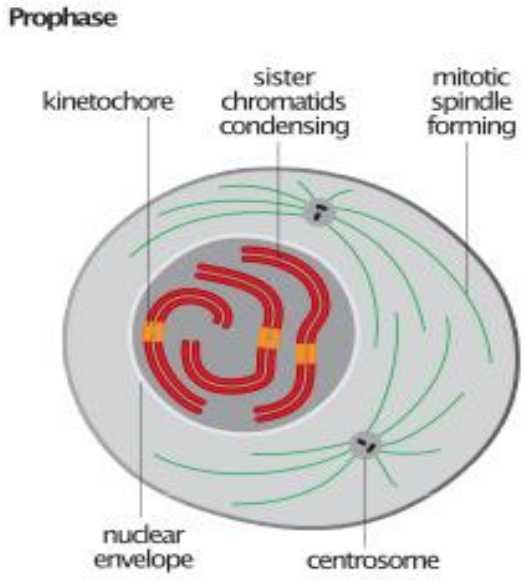


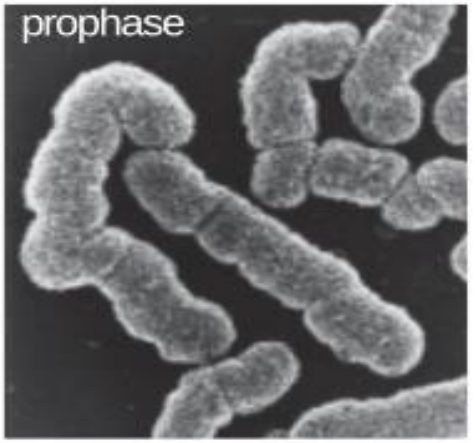
- It is characterized by:-

1.Disappearance of the nucleolus.

2.The chromosomes are condensed and become visible with L/M.

3.The nuclear envelope remains intact until late in this phase, and then starts to disappear.





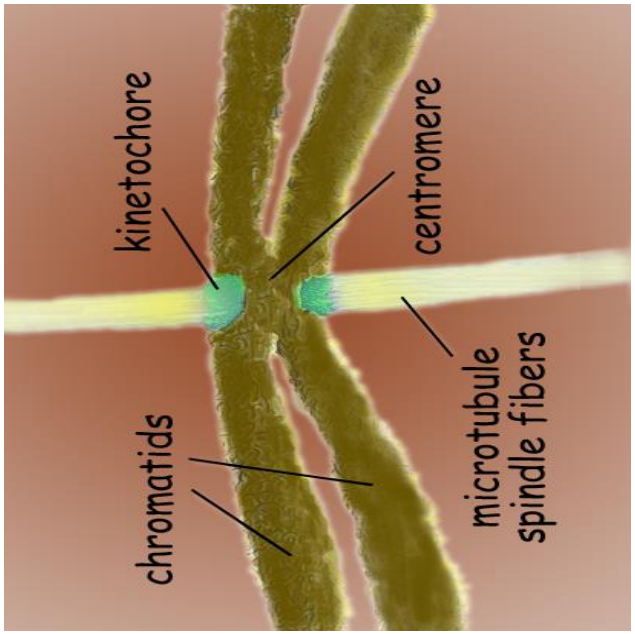
PROPHASE

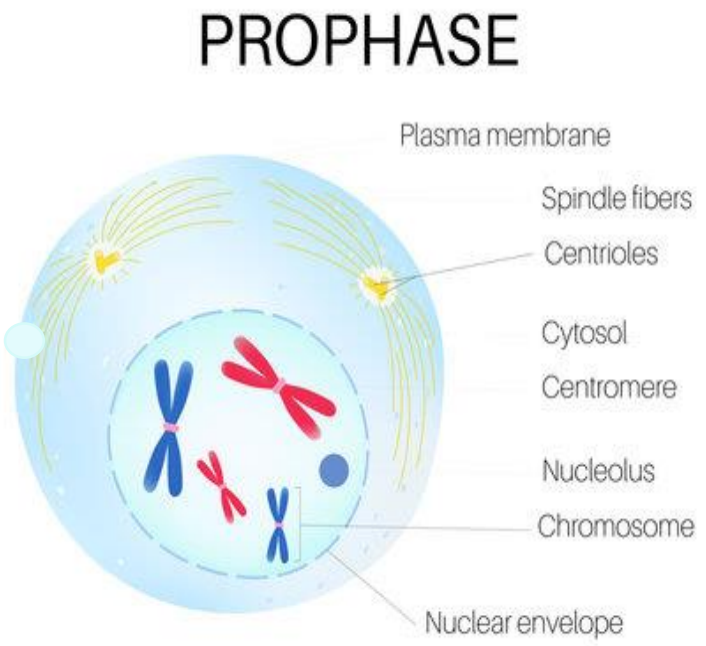
- It is characterized by:-

4. Each chromosome consists of two sister chromatids joined together by centromere.

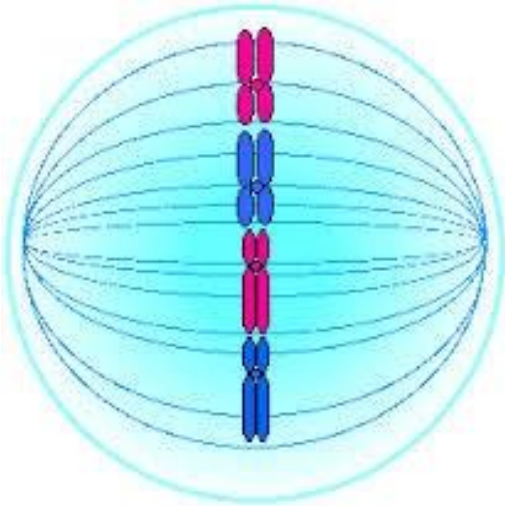
5. At the centromere region of each chromatid the kinetochore develops which is a microtubule-organizing center (MTOC).

6. Each pair of centrioles moves towards one pole of the cell to form mitotic spindle.





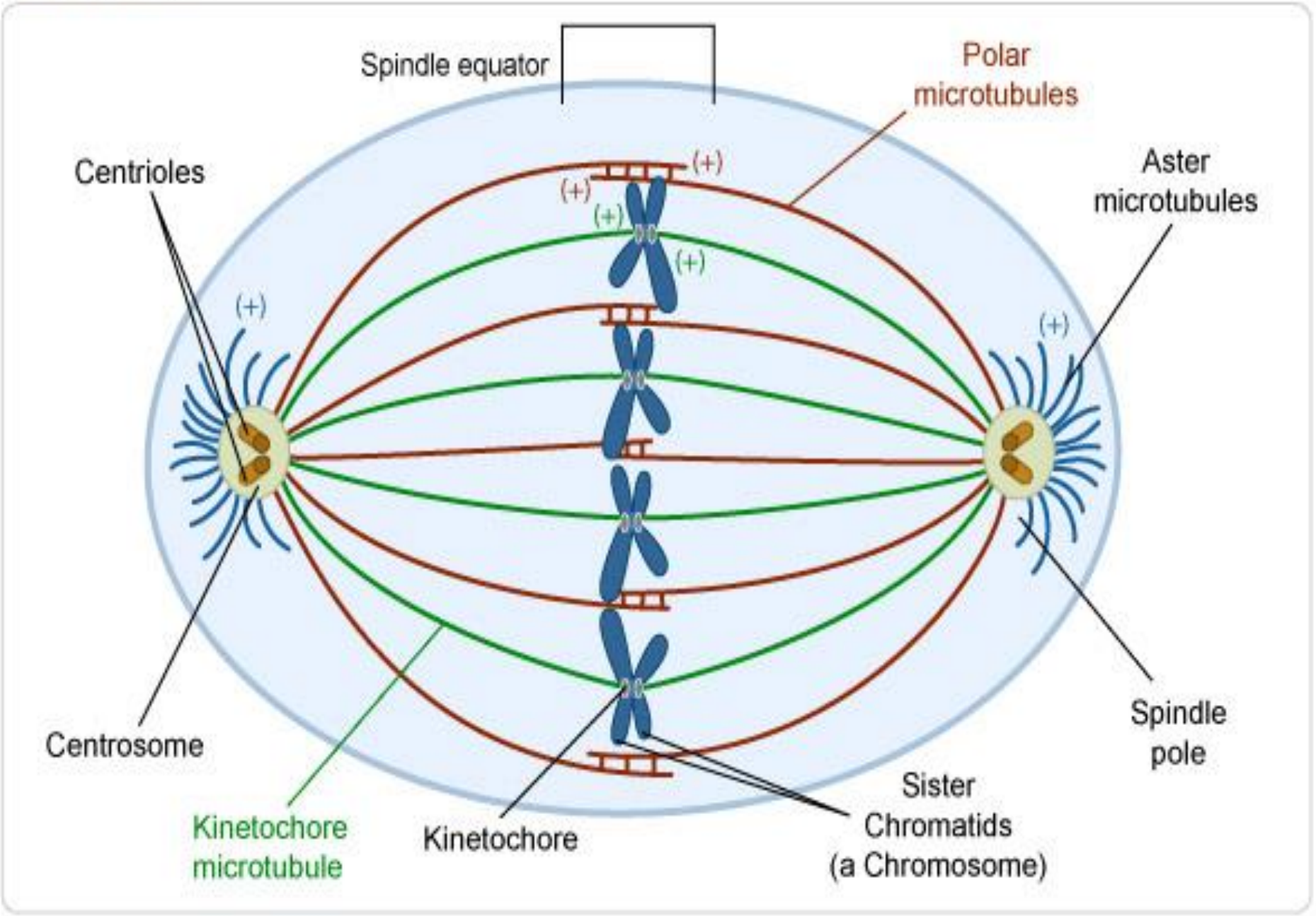
METAPHASE



- It is characterized by:-

1. Complete disappearance of nuclear envelope.
2. Migration of chromosomes to equatorial plane of the cell.

Metaphase



METAPHASE

1.Mitotic spindle at this stage consist of :

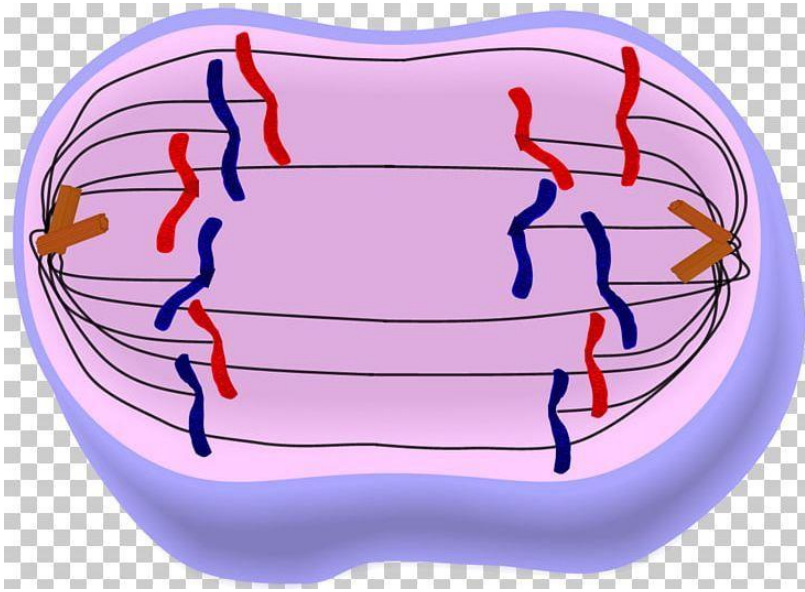
a.Chromosomal microtubules that become attached to kinetochores. They assist in migration of each set of chromatids to one pole of the cell.

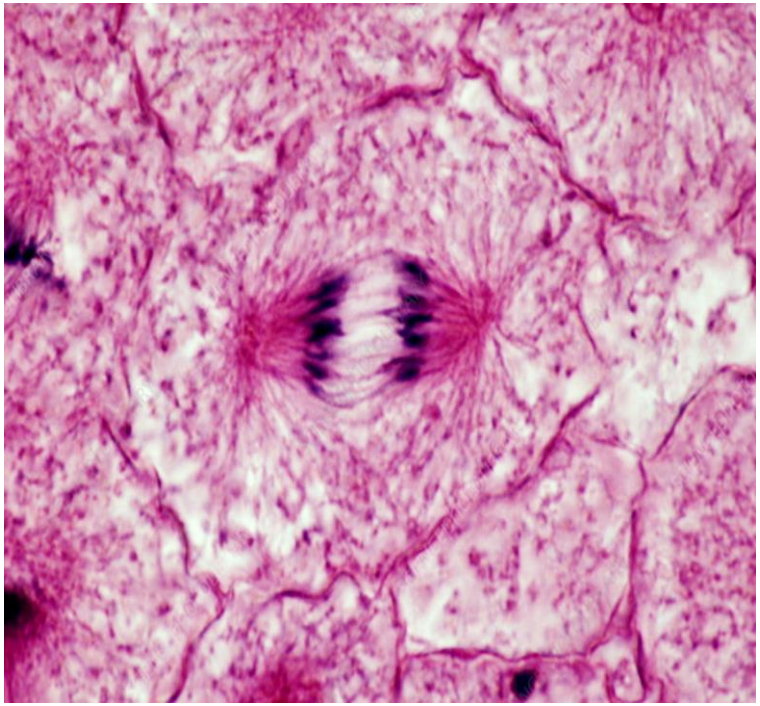
b.Polar microtubules are not attached to kinetochores and extend between the two pairs of centrioles. They are responsible for maintaining the spacing between the two poles during mitotic events.

c.Astral microtubules are originating from the centrosome and organized into radial arrays around it and are not connected to a kinetochores

ANAPHASE

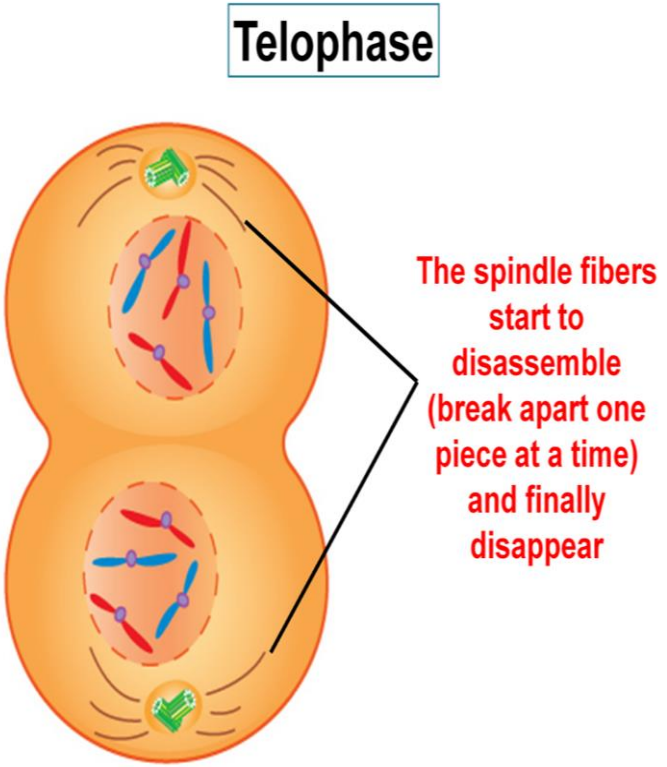
1. It begins when sister chromatids separate from each other. Now the cell contains 92 chromatids (s-chromosomes). They begin to migrate, so that 46 chromatids move to one pole of the cell and the other 46 chromatids move to the other pole.
2. In late anaphase a cleavage furrow begins to form at cell membrane.

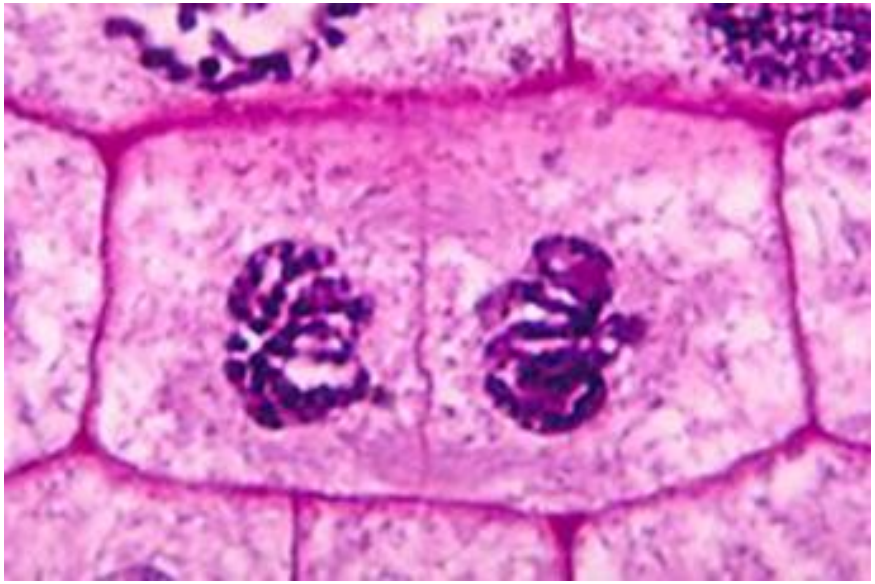




TELOPHASE

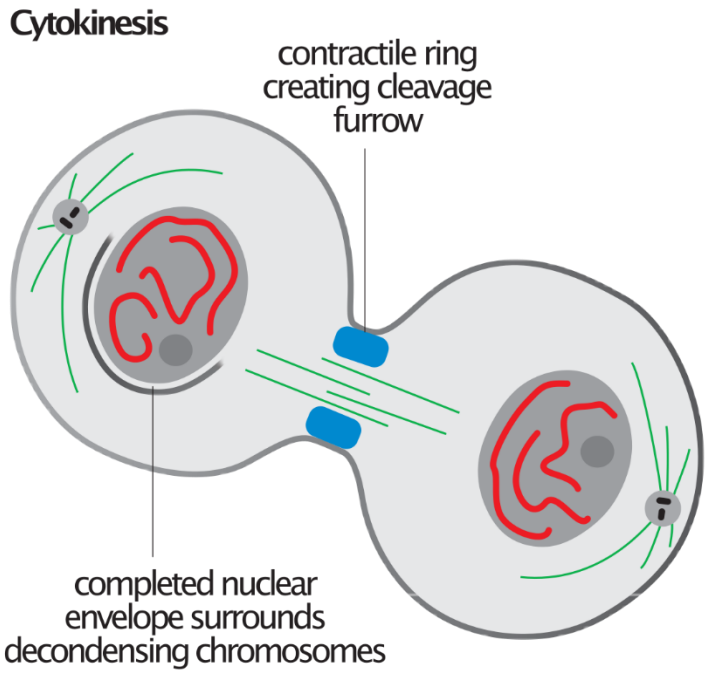
1. Each set of chromosomes has **reached** its respective pole.
2. Reappearance of **nuclei** in the daughter cells.
3. The chromosomes **uncoil** and become organized into heterochromatin and euchromatin of the interphase cell.
4. Nuclear **envelope** is reconstituted.

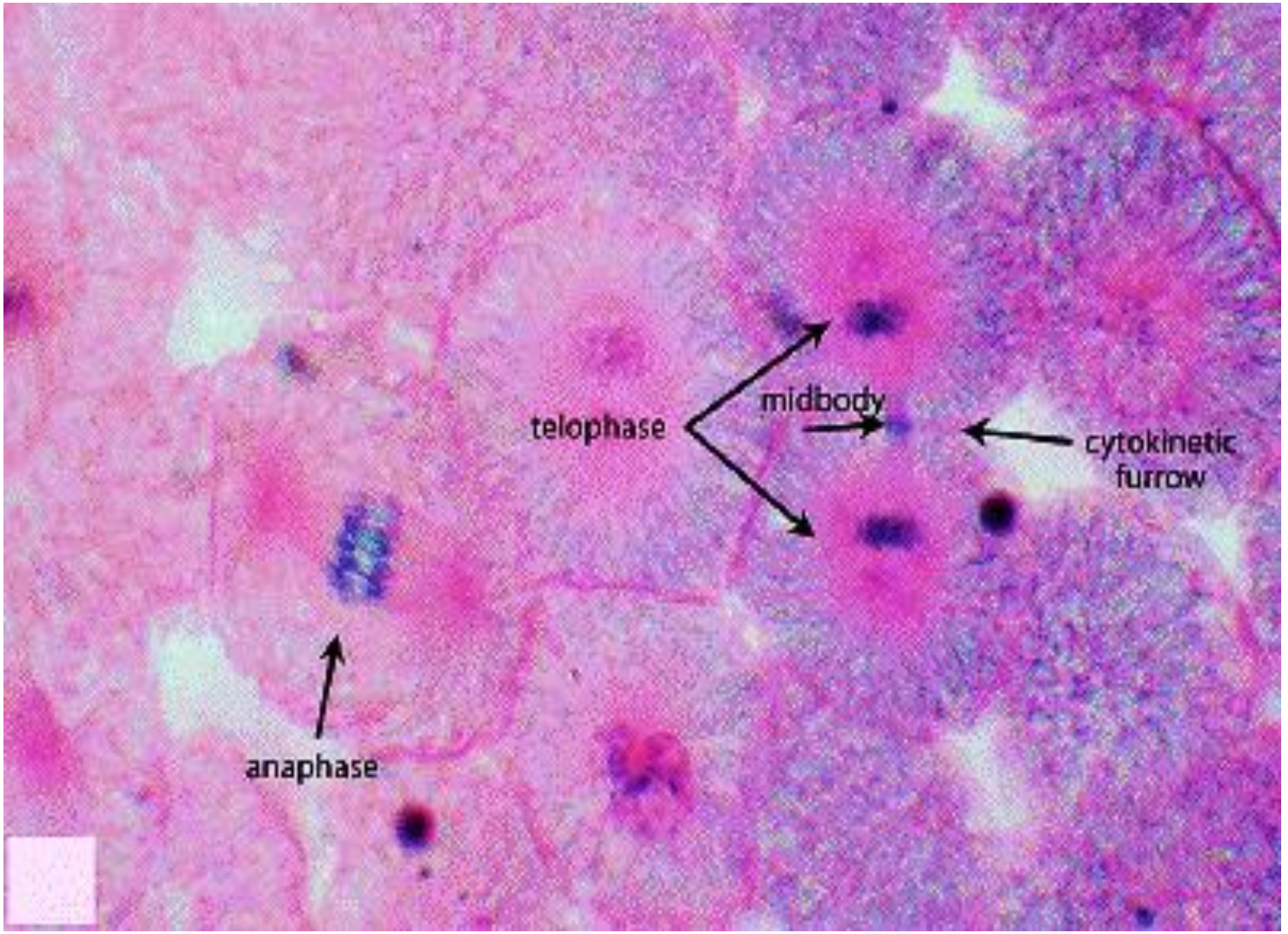


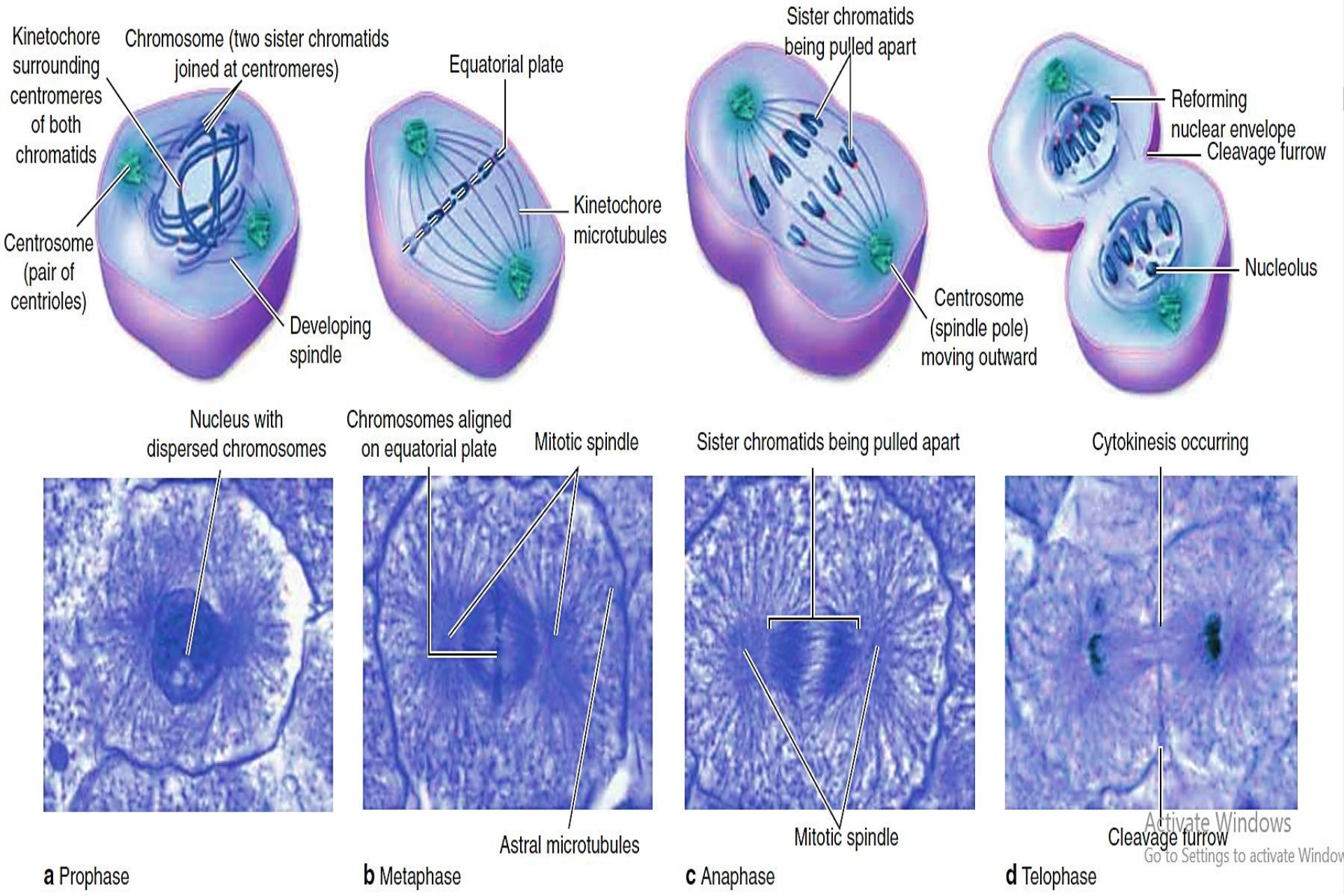


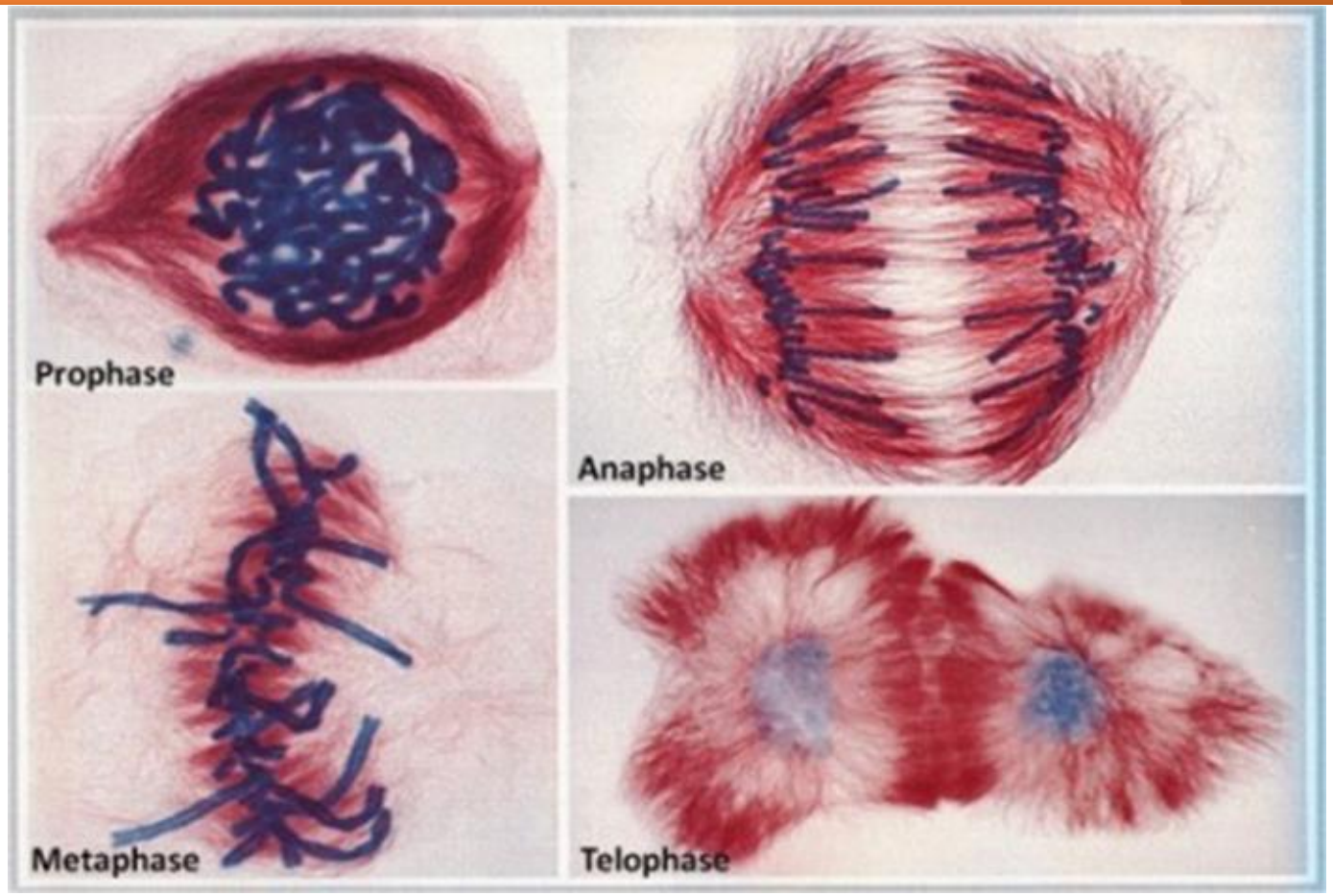
Cytokinesis

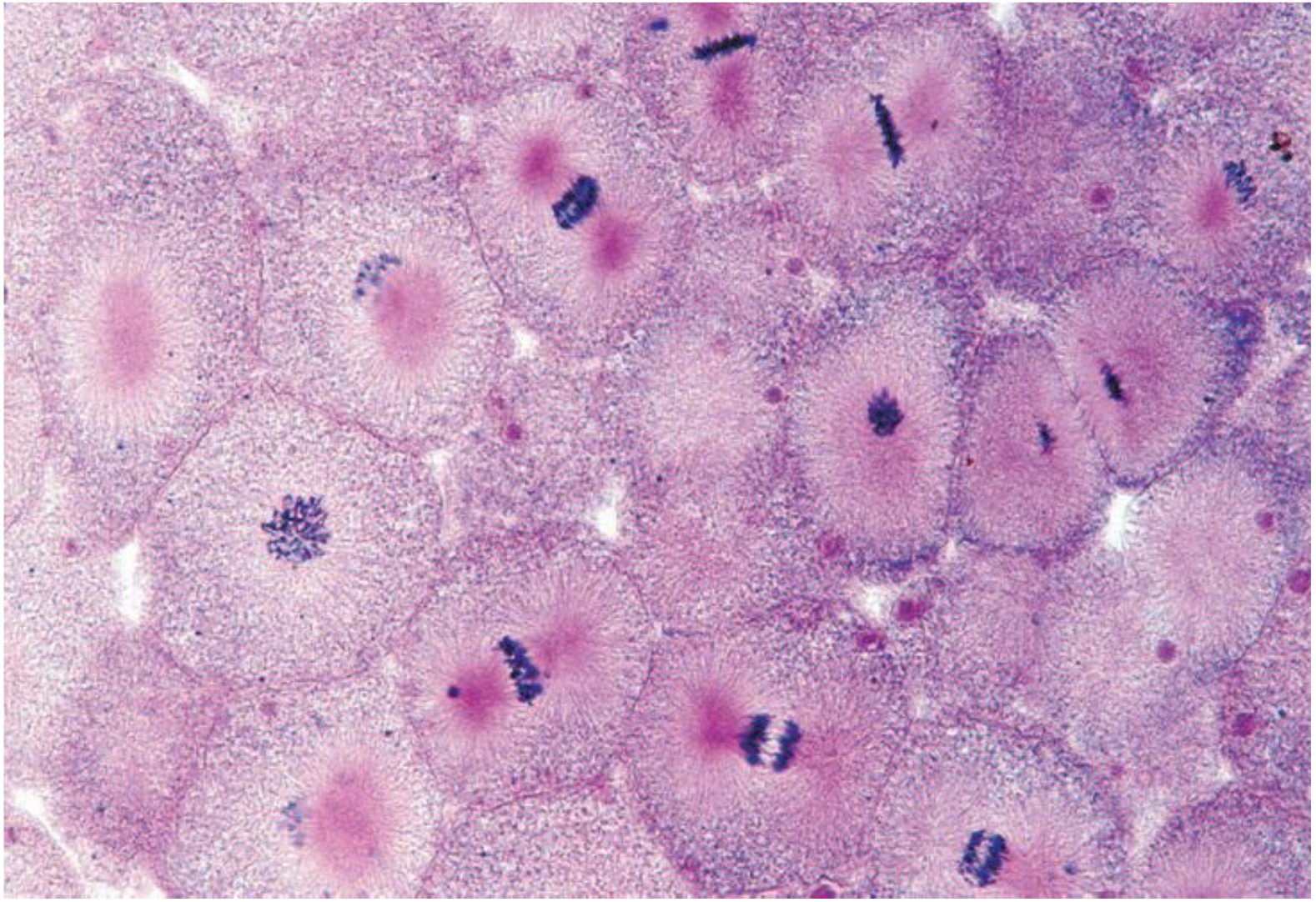
1. The cleavage furrow continues to deepen until the mid body.
2. Mid body is a small bridge of cytoplasm connecting the two daughter cells together. It is formed of polar microtubules and surrounded by contractile ring.
3. Contractile ring is composed of actin and myosin filaments.
4. Constriction of the ring is followed by separation of the two daughter cells. Each cell contains 46 s-chromosomes.




telophase
midbody
cytokinetic furrow
anaphase




Prophase
Anaphase
Metaphase
Telophase



A genome is the complete set of genetic information in an organism. It provides all of the information the organism requires to function.

Gene: Segment of chromosomal DNA which controls the production of a particular polypeptide chain.

Mitotic figures

- Cells in mitosis
- Appear in rapidly growing tissues (eg. Intestinal epithelium)

Clinical application

-Increased number of mitotic figures & abnormal mitosis **in tumors** is important to distinguish malignant from benign tumors

-Mitotic figures are important also in prognosis of tumors.