Cell Cycle and apoptosis

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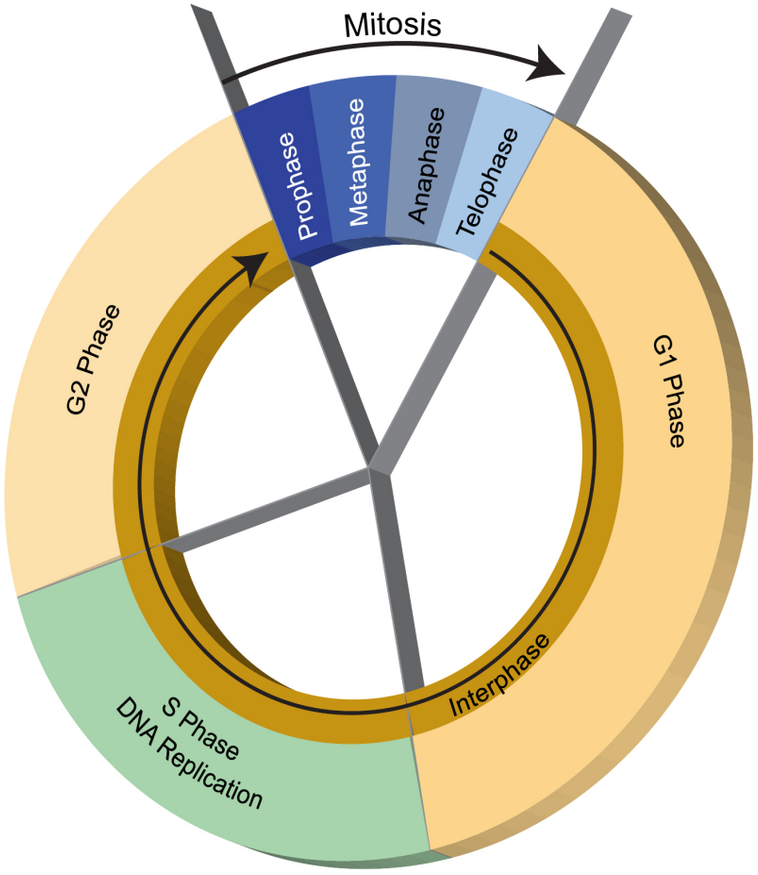

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Cell Cycle

is the series of events that take place in a cell

leading to its division and duplication of its DNA

to produce two daughter cells.

Transmission of genetic information from one cell

generation to the next requires genome replication

during the S-phase, and its segregation to the two

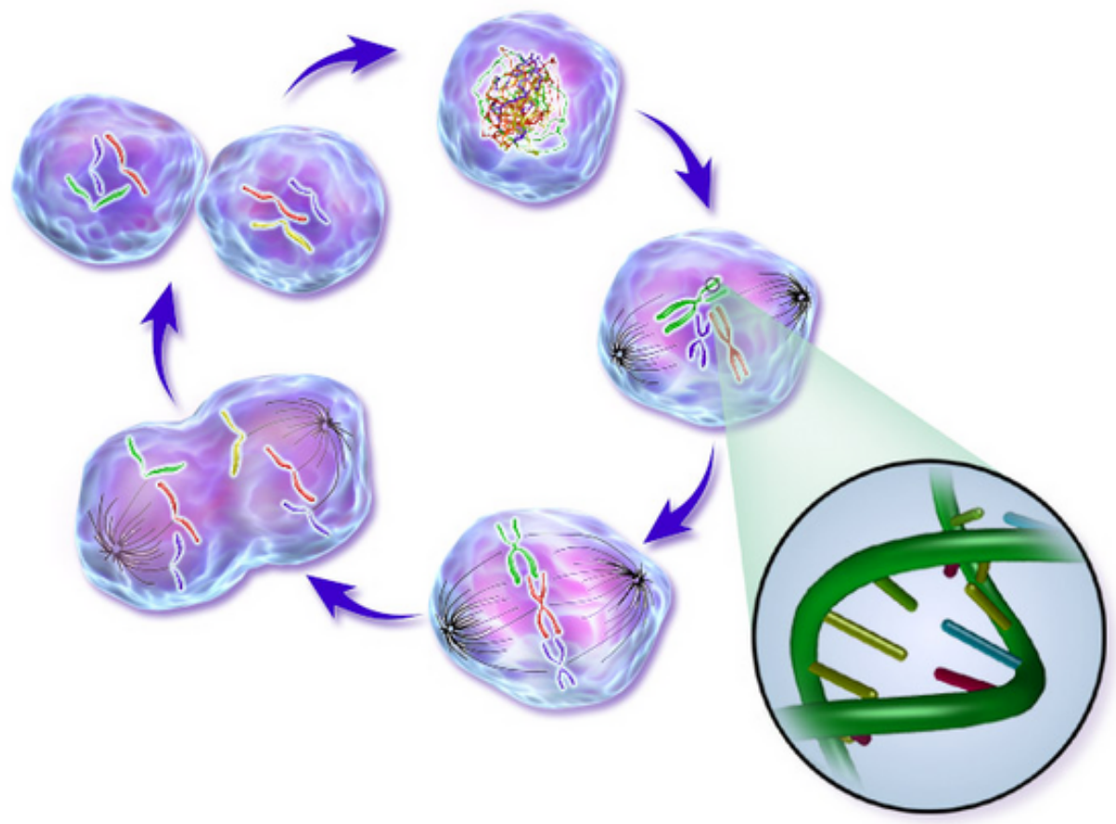
new daughter cells during mitosis or M-phase

The cell cycle has four distinct phases:

1- M mitosis,

2- three interphase periods termed:

- **G_1 (the time gap between mitosis and DNA replication),**
- **S (the period of DNA synthesis),**
- **G_2 (the gap between DNA duplication and the next mitosis)**



• **During the G_1 phase : there is active synthesis of RNA**

and proteins, including proteins that control the cell cycle,

and the cell volume, reduced to one-half by mitosis, grows

to its previous size.

• **The S phase : is characterized by the synthesis of DNA and histones and by the beginning of centrosome duplication.**

• **G_2 phase: relatively short, proteins required for mitosis accumulate.**

• **G0 phase: cell cycle activities may be temporarily or**

permanently suspended and the new cells exits from the G1

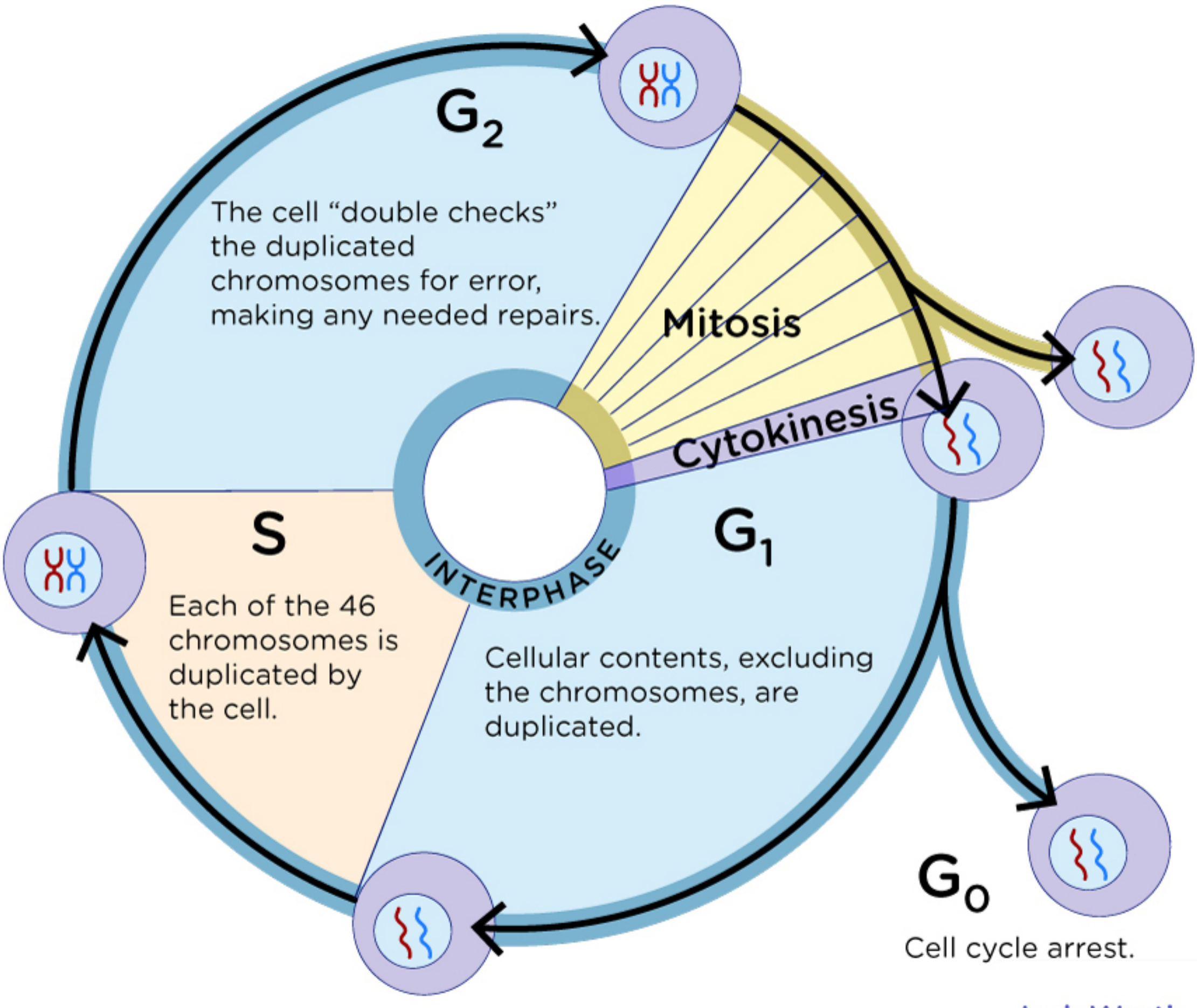
phase of the cell cycle to enter into a quiescent state and begin

to specialize and differentiate

• **some differentiated cells, such as those of the liver, renew**

cycling under certain conditions; others, including most muscle

and nerve cells are terminally differentiated


G_2
The cell "double checks" the duplicated chromosomes for error, making any needed repairs.
Mitosis
Cytokinesis
S
Each of the 46 chromosomes is duplicated by the cell.
INTERPHASE
G_1
Cellular contents, excluding the chromosomes, are duplicated.
G_0
Cell cycle arrest.
Jack Westin

Cell division, or MITOSIS, is the division of **somatic** cells and can be observed with the light microscope.

During this process:

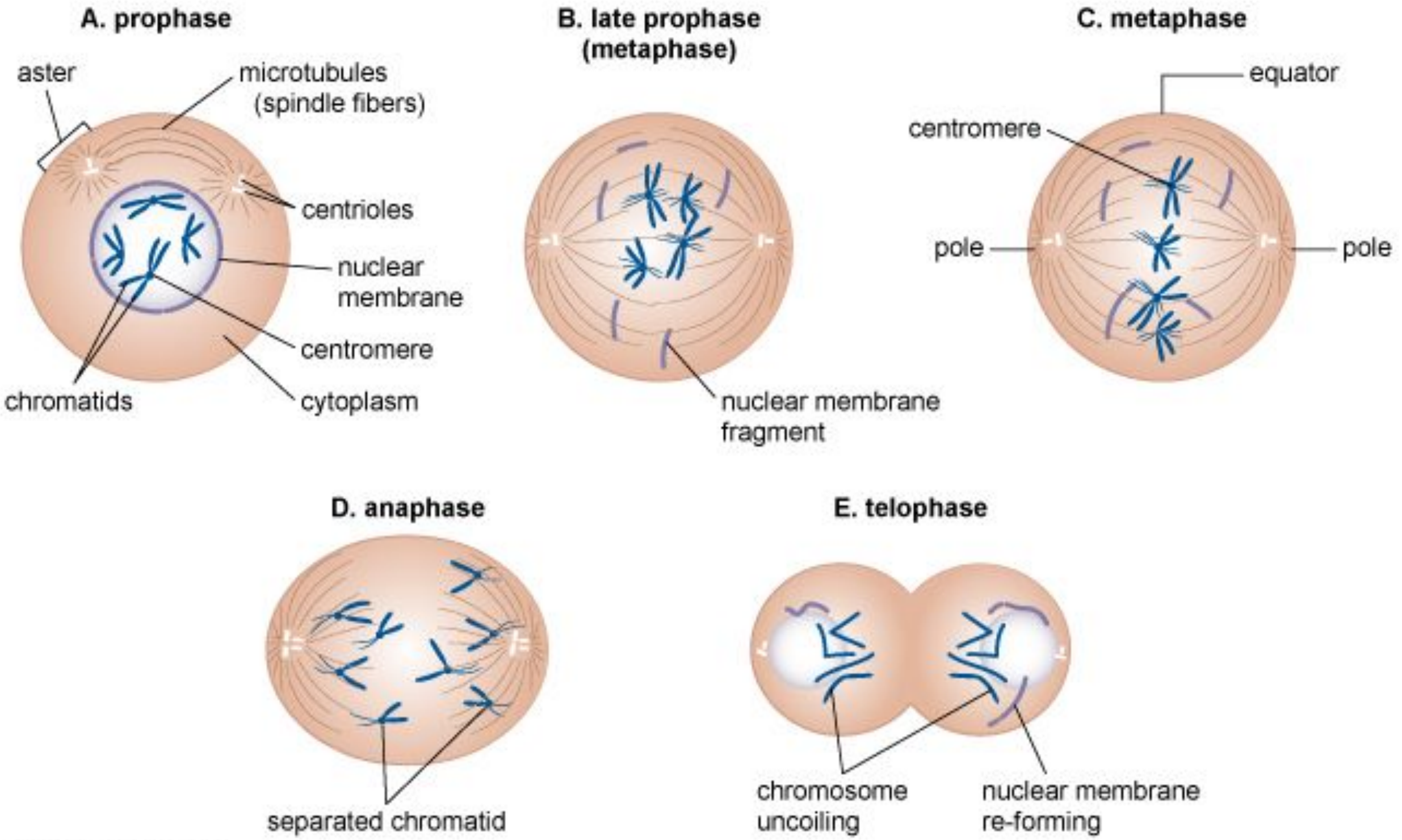
- The parent cell divides,
- Each of the daughter cells receives a **chromosomal set identical to that of the parent cell**

• longitudinal duplication of the chromosomes takes place, and these chromosomes are distributed to the daughter cells.

• The period between mitoses is called **Interphase**, during which the DNA is replicated and the nucleus appears as it is most commonly seen in histological preparations.

The process of mitosis is subdivided into four **phases**

- **Prophase**
- **Metaphase**
- **Anaphase**
- **Telophas**



PROPHASE

1. The nuclear envelope begins to disaggregate

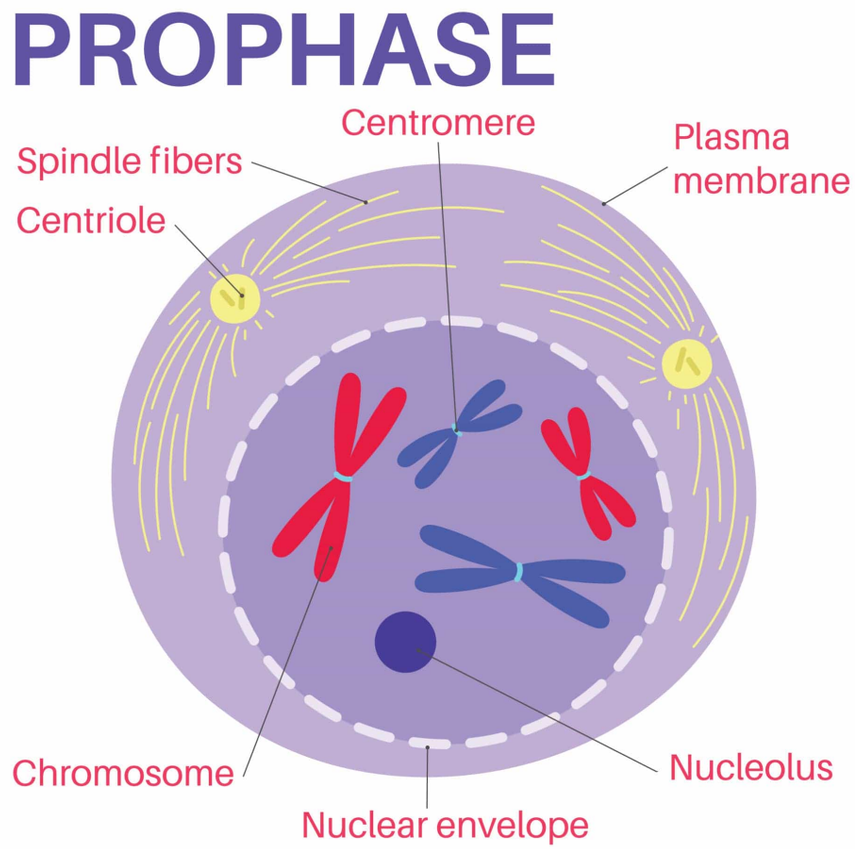
2. The chromatin in the nucleus begins

to condense and becomes visible by

light microscopy as elongated,

spindly chromosomes.

3. The nucleolus disappears.



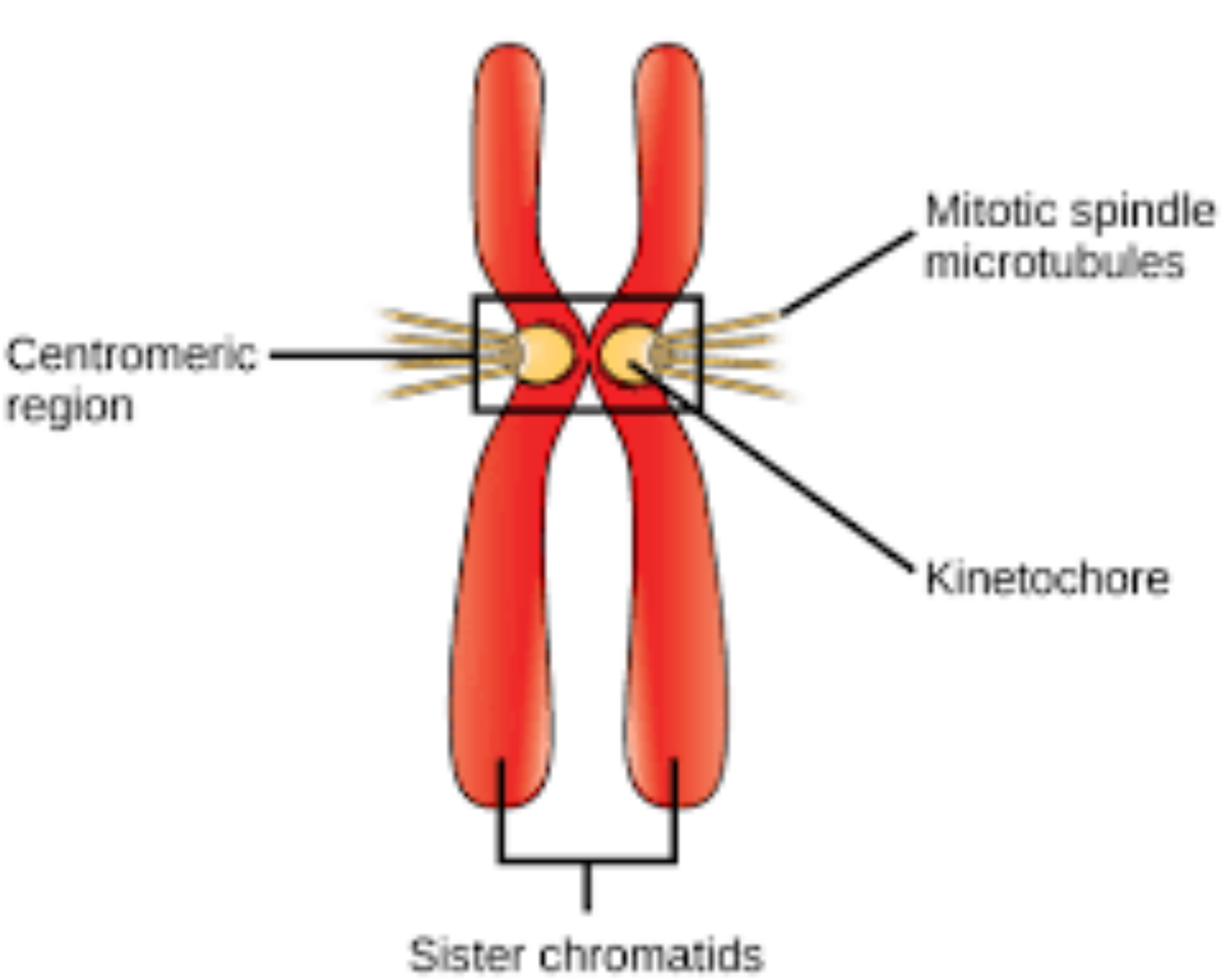
4. Centrosomes begin migrating to opposite poles of the cell, and

microtubule fibers extend from centrosome to centrosome and

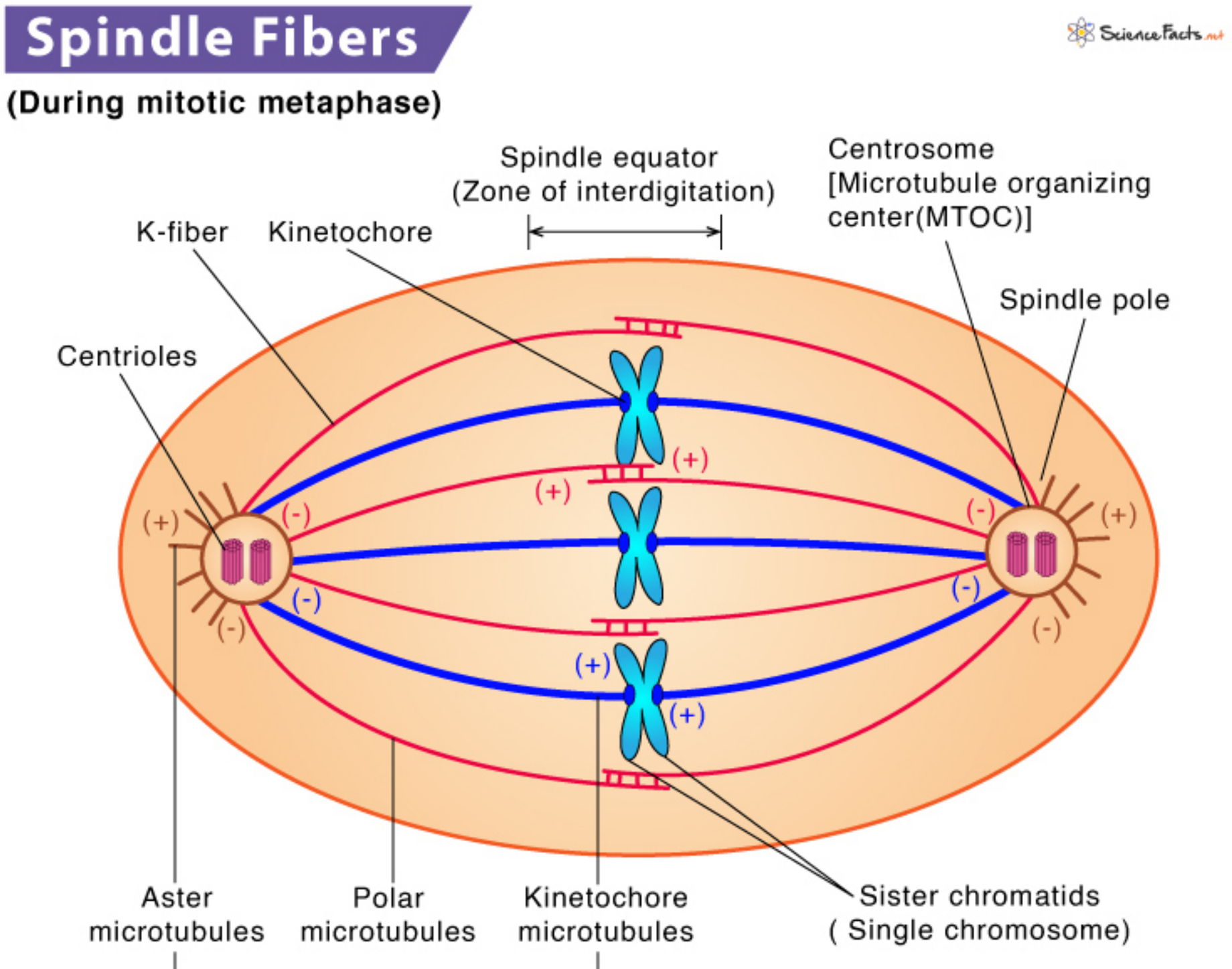
from centrosome to the kinetochore of the centromere of each

chromosome to form the mitotic spindle

Simultaneously with centrosome migration, the microtubules of the mitotic spindle appear between the two centrosomes


Mitotic spindle microtubules
Centromeric region
Kinetochore
Sister chromatids

Spindle Fiber attached to Chromosome



METAPHASE

- The chromatids attach to the microtubules of the mitotic spindle at the **kinetochore**, located close to the **centromere**
- Chromosomes migrate to the equatorial plane of the cell

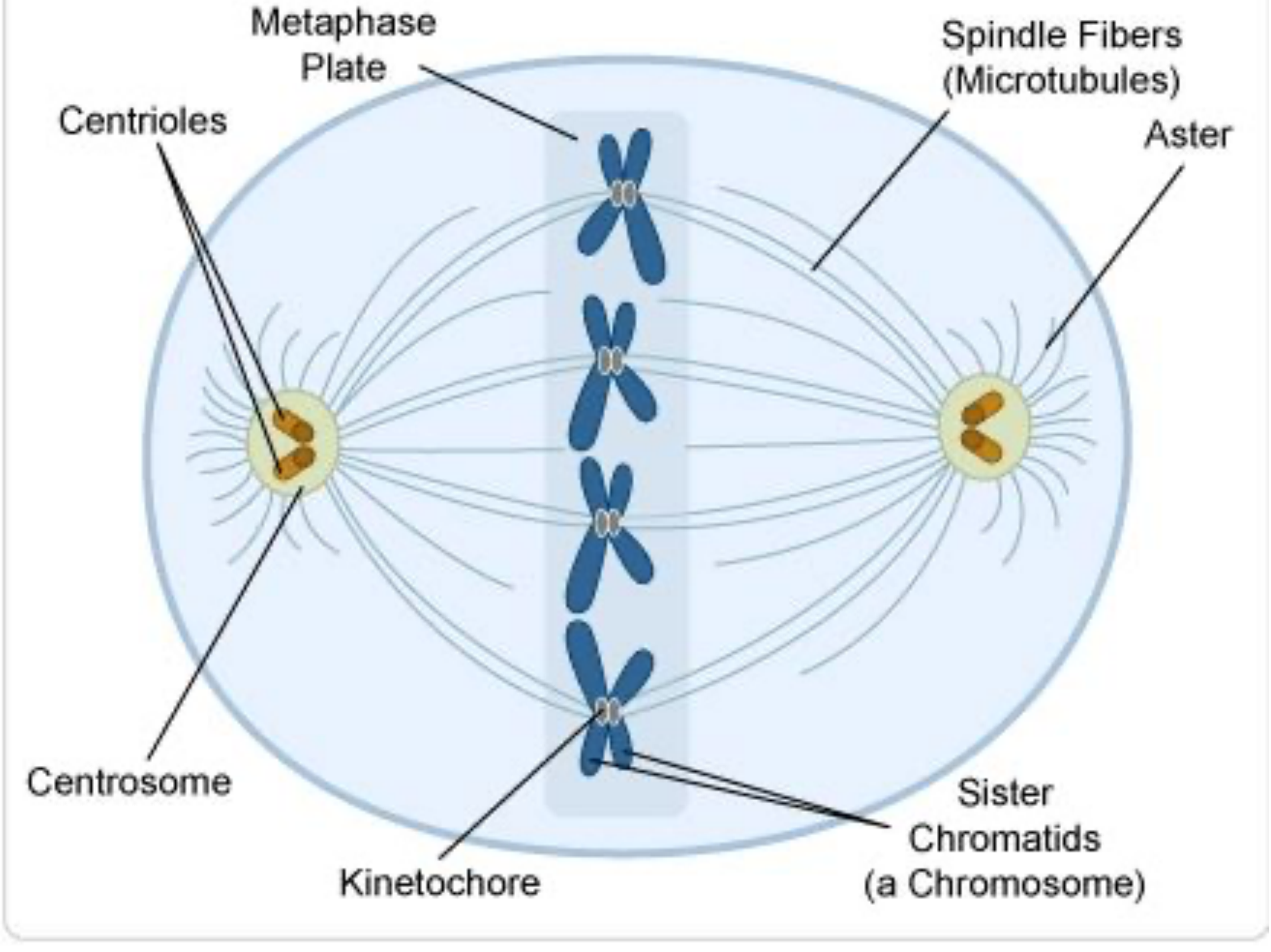
SPINDLE FIBRES line the chromosomes along the middle of the cell nucleus. This line is referred to as the **metaphase plate.**

Polar microtubules extend from the pole to the equator, and typically overlap

Kinetochore microtubules extend from the pole to the kinetochores

This organization helps to ensure that in the next phase, when the chromosomes are separated, each new nucleus will receive one copy of each chromosome

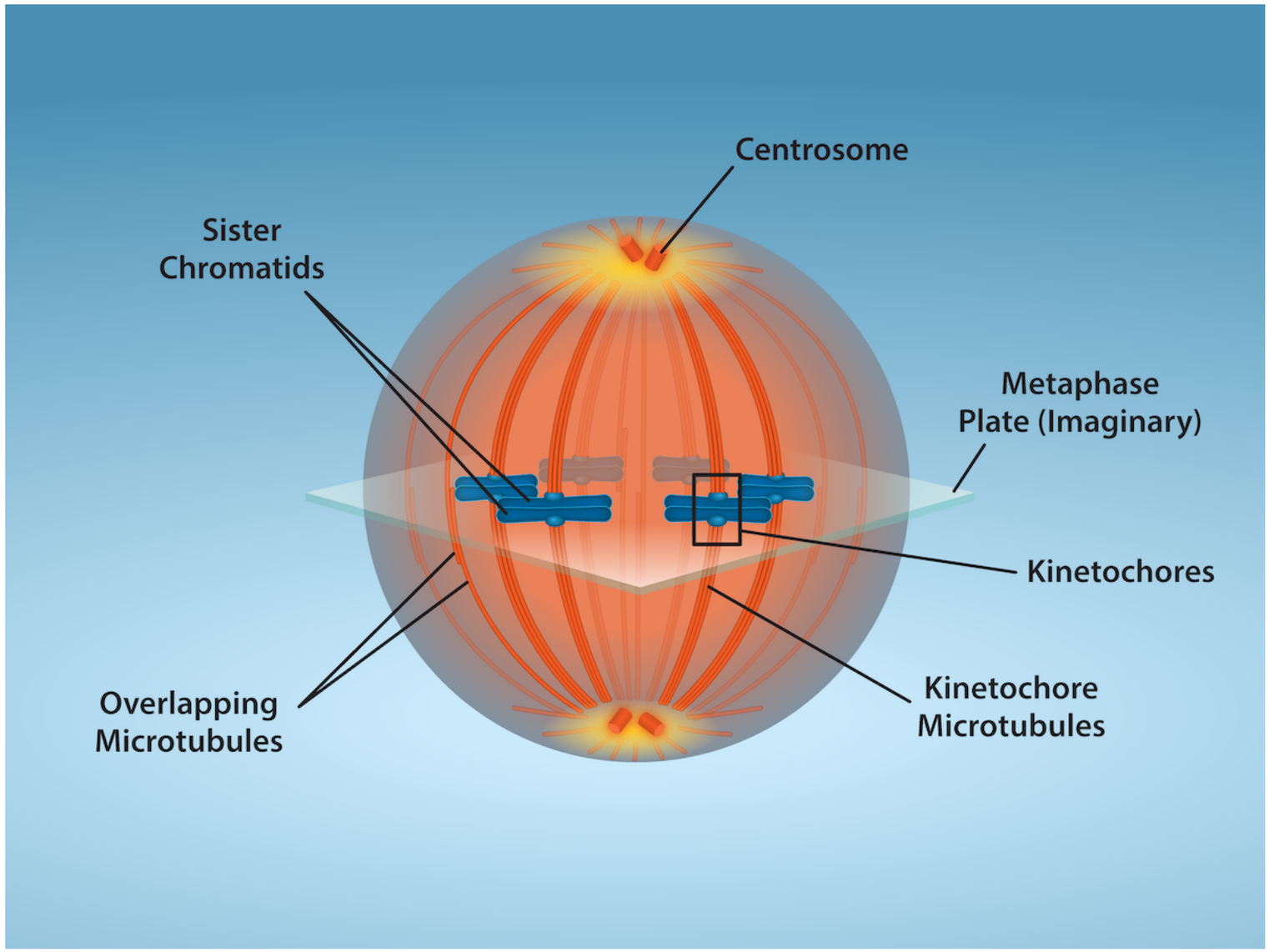
Metaphase


Metaphase Plate
Spindle Fibers (Microtubules)
Centrioles
Aster
Centrosome
Kinetochore
Sister Chromatids (a Chromosome)

Chromosomes, attached to the kinetochore fibers,

move to the center of the cell.

- **Chromosomes are now lined up at the equator**



ANAPHASE

1. The sister chromatids separate from each other and

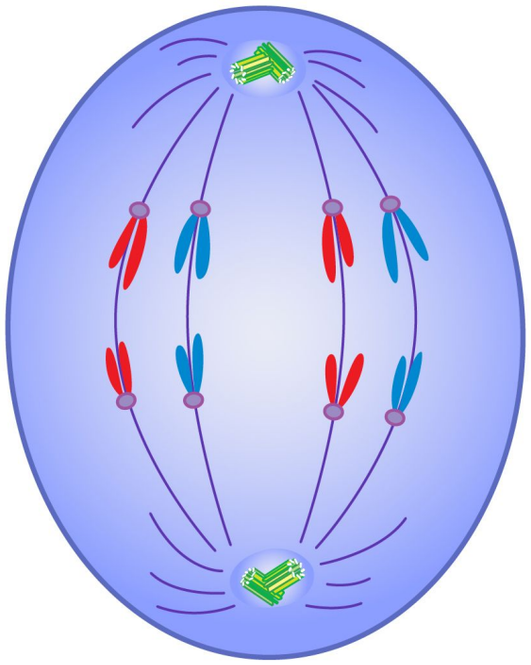
migrate toward the opposite poles of the cell,

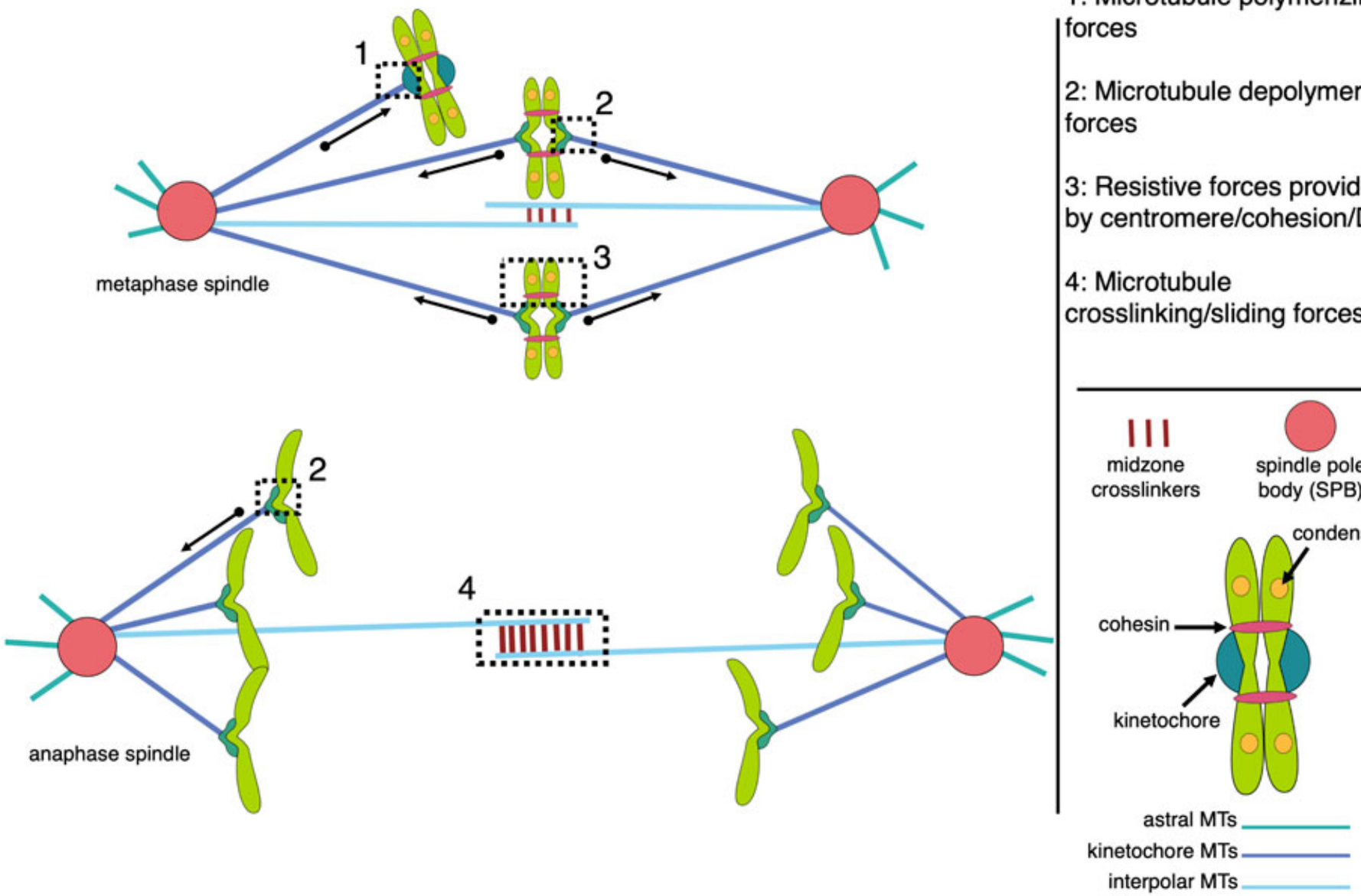
pulled by microtubules.

2. Throughout this process, the centromeres move

away from the center, pulling the remainder of the

chromosome along





The chromosomes are pulled by the kinetochore microtubules to the poles and form a "V" shape

Motion results from a combination of kinetochore movement along the spindle microtubules and through the
physical interaction of polar microtubules

TELOPHASE

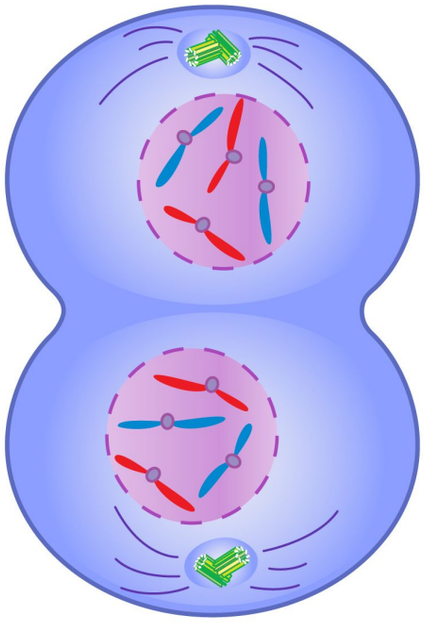
1. The reappearance of nuclei in the daughter cells.

2. The chromosomes revert to their

semidispersed state, the nucleoli,

chromatin, and nuclear envelope reappear.

The spindle fibers disperse, and **cytokinesis** will start



A constriction develops at the equatorial plane of the parent cell and progresses until the cytoplasm and its organelles are divided in two, this called the **cytokinesis**. In animal cells, cytokinesis results when a fibre ring composed of a protein called actin around the centre of the cell contracts

dividing the cell into two daughter cells, each with one nucleus

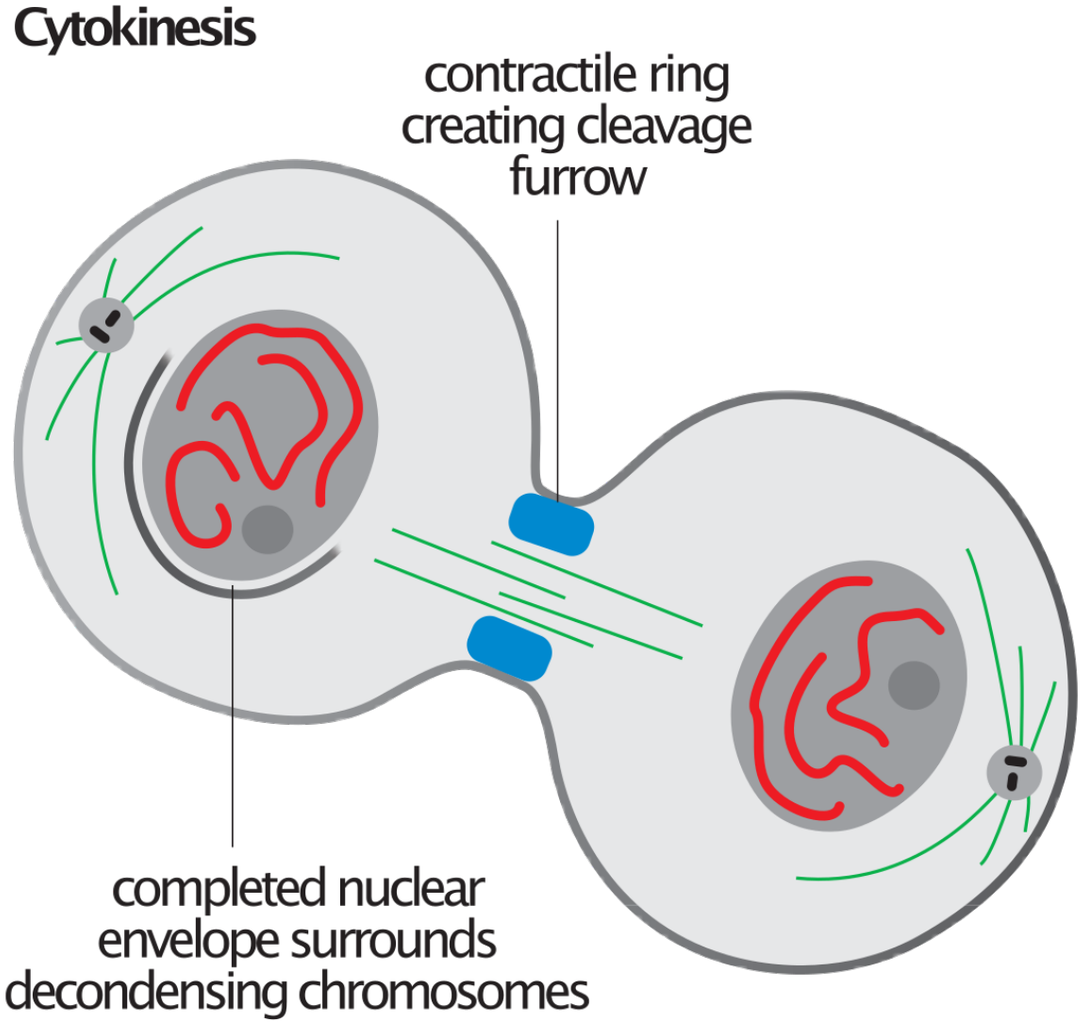
cytokinesis

Means division of the cytoplasm

Division of cell into two, identical halves called daughter cells

In animal cells, cleavage furrow forms to split cell

Cleavage furrow in animal cell



• Most tissues undergo constant cell turnover because of continuous cell division and the ongoing death of cells. Nerve tissue and cardiac muscle cells are exceptions.

• The turnover rate of cells varies greatly from one tissue to another, rapid in the epithelium of the digestive tract and the epidermis and slow in the pancreas and the thyroid gland

Cell cycle checkpoints

- a series of control systems enabling proliferation only in the presence of stimulatory signals such as growth factors.

- The timing and order of cell cycle events are monitored during cell cycle checkpoint

The main checkpoints are:

1. G1/S boundary, also knowing as restriction point, As the cell progresses through G1, depending on internal and external conditions, it can either delay G1, enter a quiescent state (G0), or cross the restriction point to enter S phase

2- In S-phase, also known as the DNA

damage checkpoint, ensures that the cell

underwent all of the necessary changes

during the S and G2 phases and is ready to divide

3. G2/M-phases: ensures that DNA replication is complete

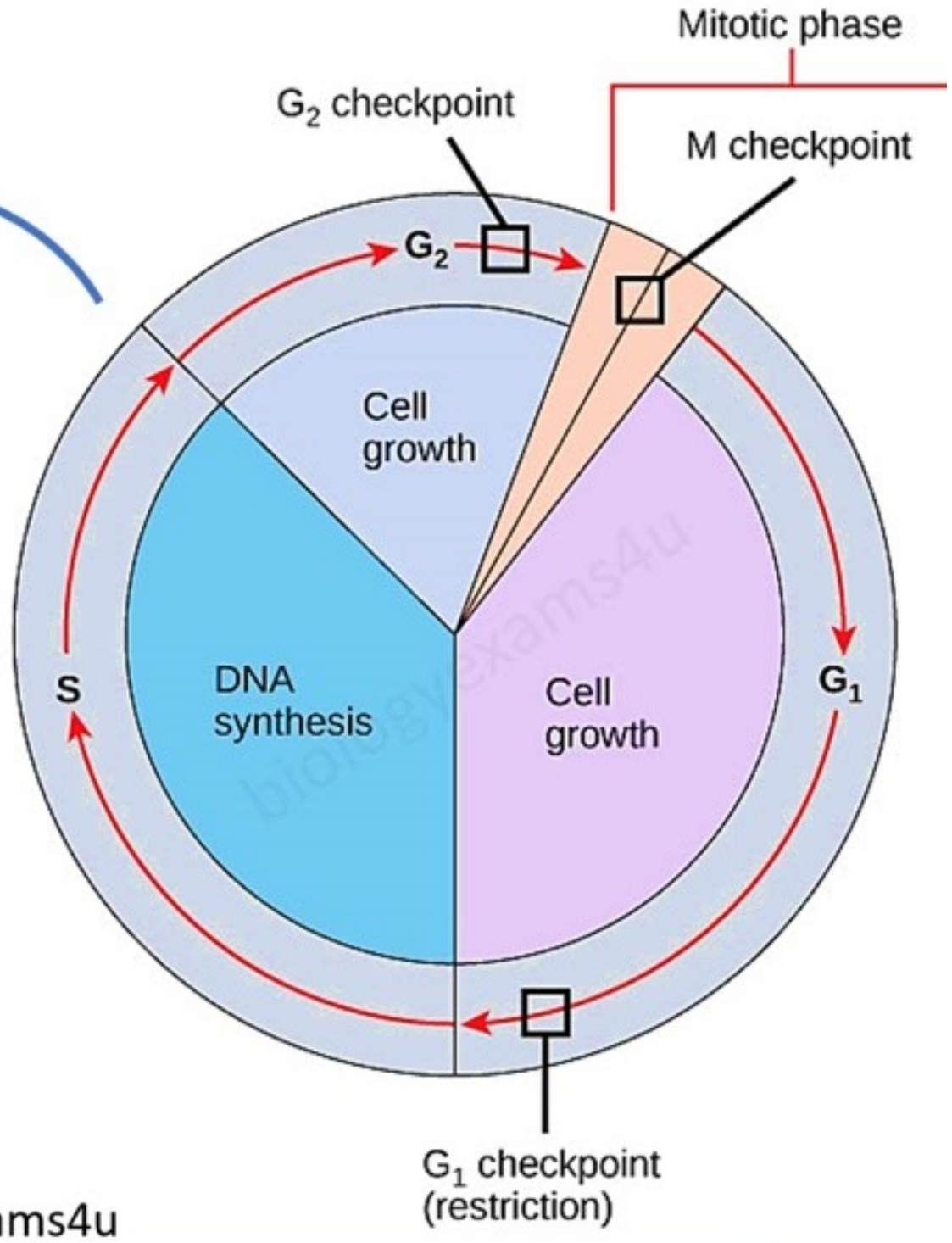
4. M-phase: (The mitotic spindle checkpoint),

Check that all the chromosomes should be

aligned at the mitotic plate and be under bipolar tension

Purpose:

- **DNA integrity**
- **Proper chromosome alignment**
- **Adequate cell size and nutrient availability**



Key Checkpoints:

- **G1 checkpoint**
- **G2 checkpoint**
- **M checkpoint**

Cell cycle checkpoints are critical regulatory points in the cell cycle that ensure the proper progression of cell division through different

The cell cycle checkpoints

? The checkpoints are activated by:

1. Cell volume reduction

2. DNA damage or incomplete DNA replication

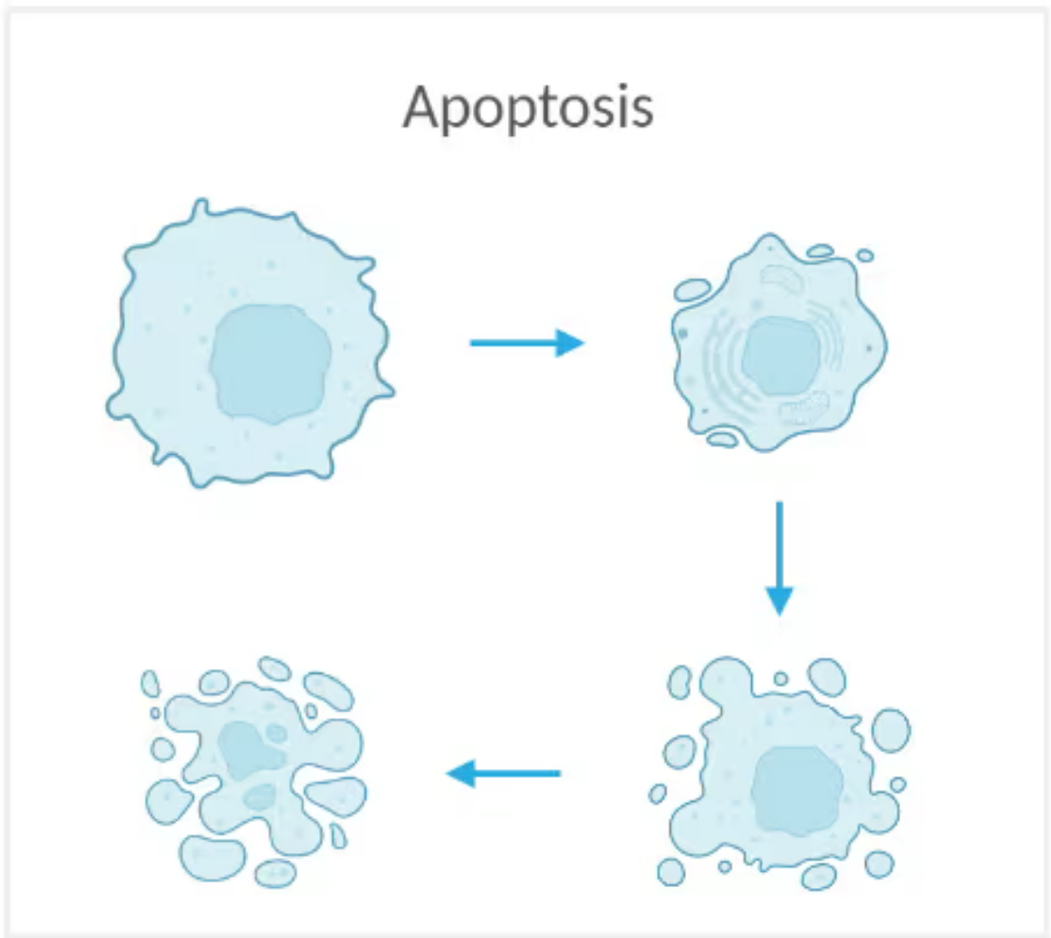
3. Mis-aligned chromosomes at the mitotic spindle.

In this case, the growth arrest caused by checkpoints allows the cell to repair the damage. After damage repair, progression through the cell cycle resumes. If the damage cannot be repaired, the cell is eliminated through apoptosis

Apoptosis

Programmed cell death serves as a major mechanism for the precise regulation of cell numbers and as a defense mechanism to remove unwanted and potentially dangerous cells.

the execution of the death program is often associated with characteristic morphological and biochemical changes, and this form of programmed cell death has been termed apoptosis



Apoptosis is an important means of eliminating cells

whose survival is blocked by

lack of nutrients,

damage caused by free radicals or radiation,

action of tumor suppressor proteins.

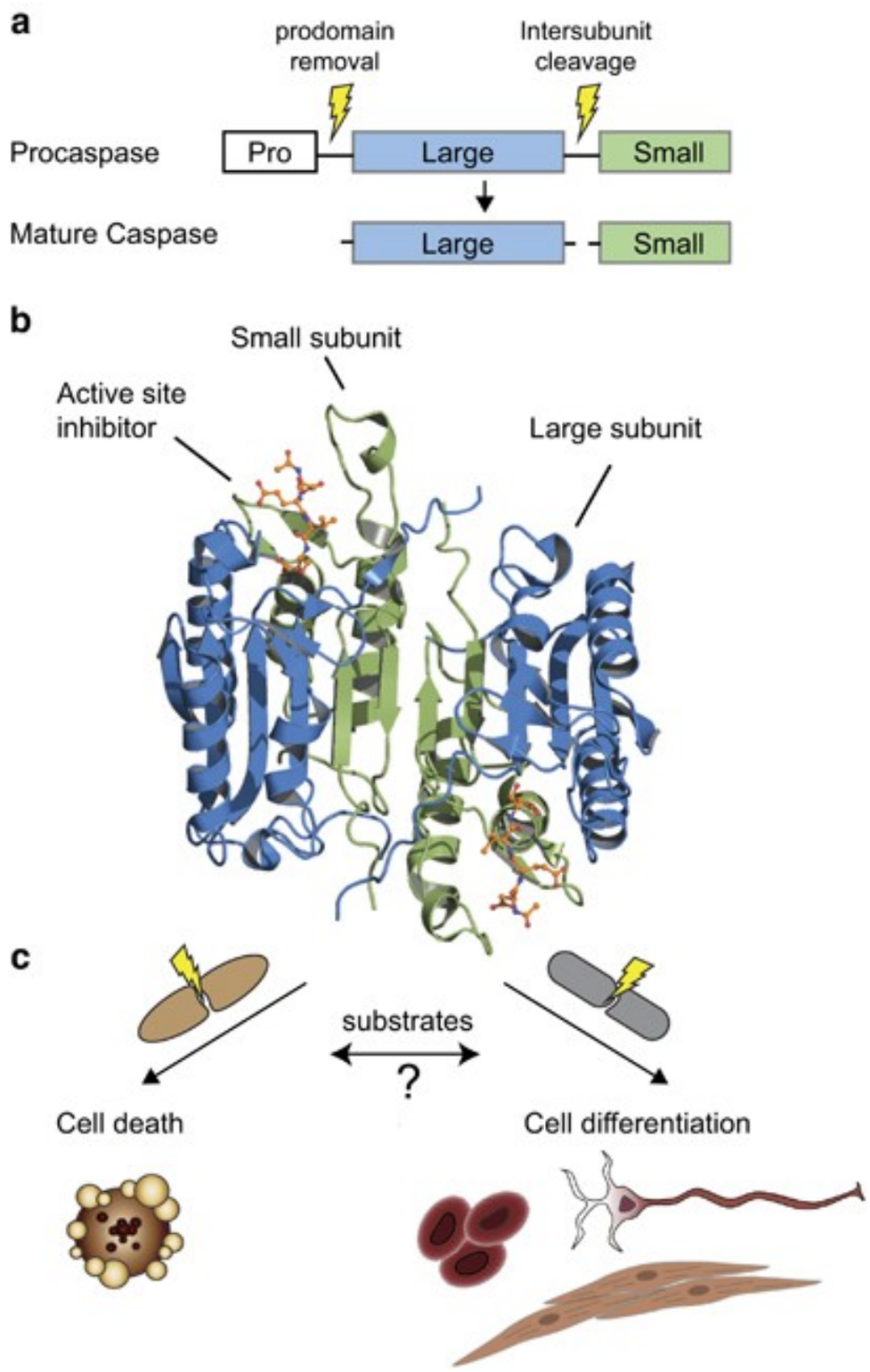
In all examples studied apoptosis occurs very rapidly, in

less time than required for mitosis, and the affected cells

are removed without a trace

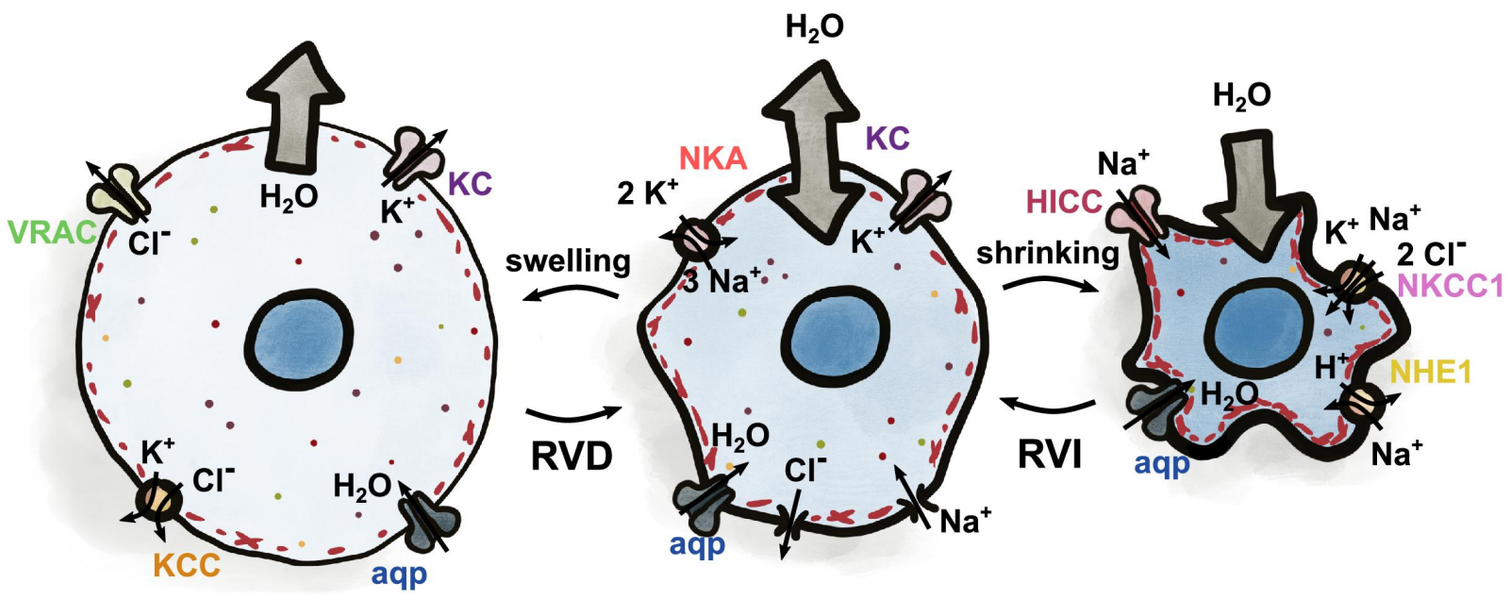
The main important features of apoptosis are summarized as:

Loss of mitochondrial function: Mitochondrial membrane integrity is not maintained, causing the end of normal activity and release of cytochrome c into the cytoplasm where it activates proteolytic enzymes called caspases .The initial caspases activate a cascade of other caspases, resulting in protein degradation throughout the cell



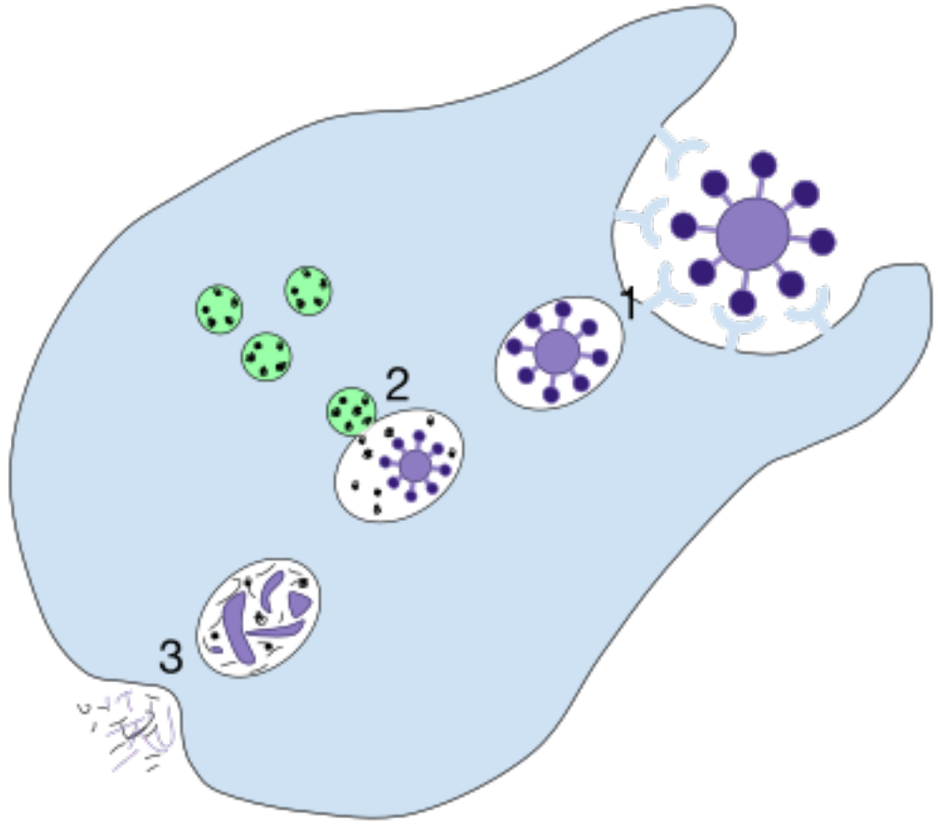
Fragmentation of DNA: Endonucleases are activated which cleave DNA between nucleosomes into small fragments.(The new ends produced in the fragmented DNA allow specific histochemical staining of apoptotic cells using an appropriate enzyme that adds labeled nucleotides at these sites.)

Shrinkage of nuclear and cell volumes: Small dark-stained (pyknotic) nuclei can sometimes be identified with the light microscop



Cell membrane changes: the cell undergoes dramatic shape changes, such as "blebbing", as membrane proteins and cytoskeleton are degraded. Phospholipids normally found only in the inner layer move to the outer layer, serving as signals to induce phagocytosis.

Formation and phagocytic removal of these apoptotic bodies



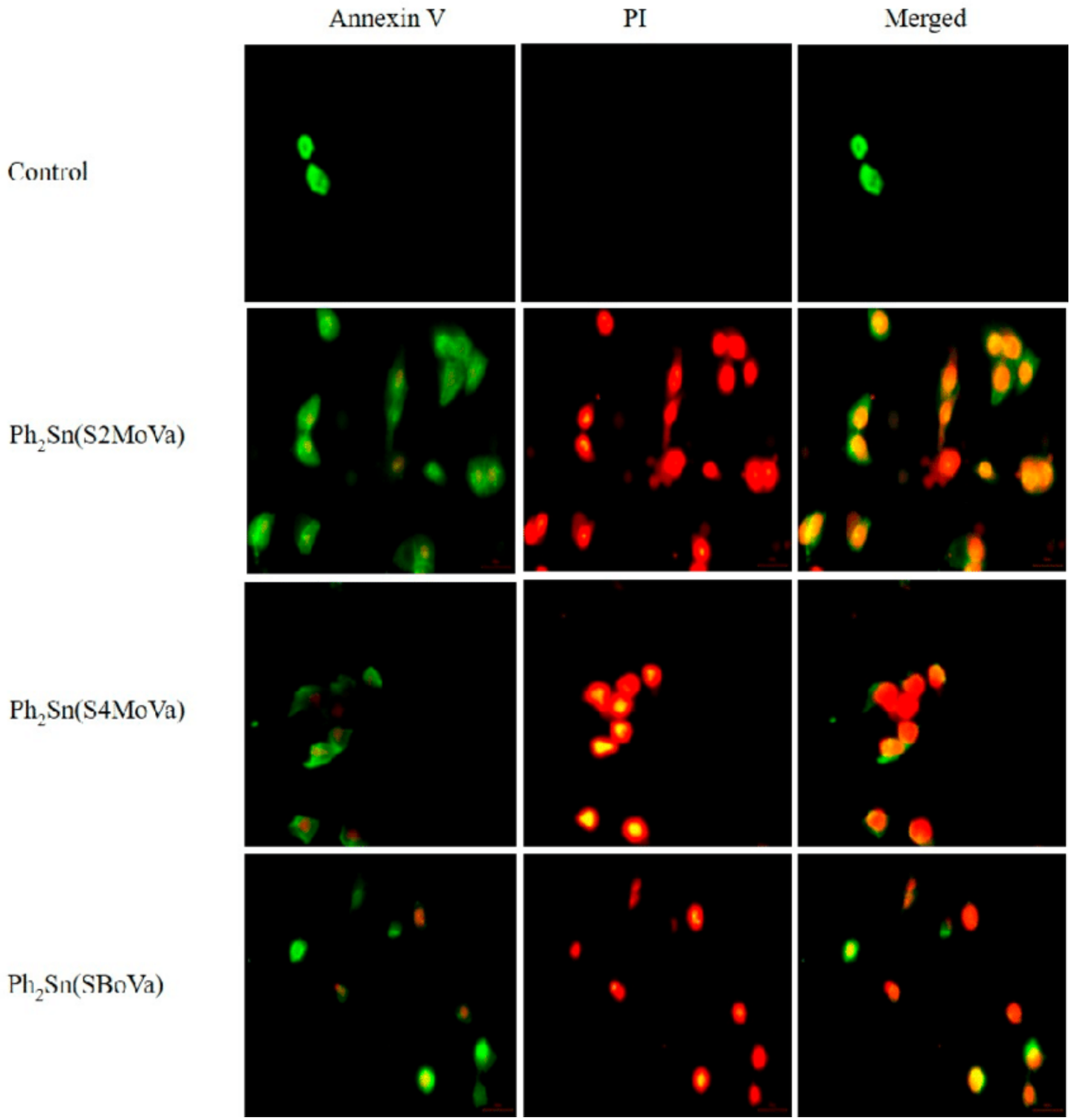
The study of apoptosis under fluorescence microscopy is classified into five different categories (stages), which are;

- **viable non-apoptotic (viable) cells,**
- **viable apoptotic (early apoptotic) cells,**
- **non-viable apoptotic (late apoptotic) cells,**
- **necrotic cells**
- **chromatin free (ghost) cells**

as shown below

Apoptosis stains

Acridine orange (AO) and propidium iodide (PI) are nucleic acid specific fluorochromes which emit green and orange fluorescences, respectively, when they are bound to DNA. Only AO can cross the plasma membrane of viable and early apoptotic cells. Late apoptotic cells and necrotic cells will stain with both AO and PI



showed the fluorescence microscopy images of cells.
where V: viable cells; E: early apoptotic cells; L: late apoptotic cells; AB: apoptotic bodies; D: dead cells


Thank
you!