INTRODUCTORY BIOLOGY AND MICROBIOLOGY

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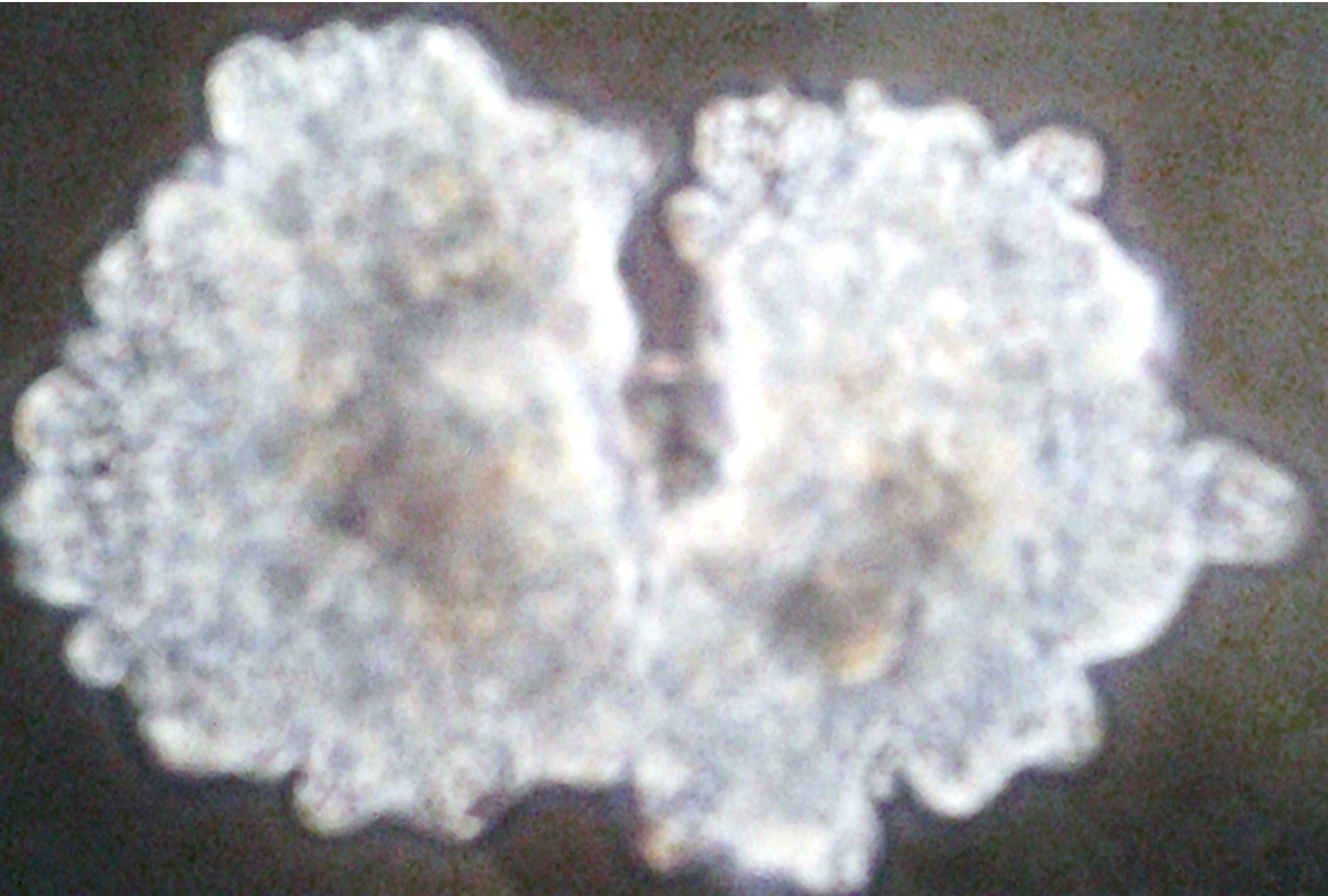
The Cell Cycle

Introduction

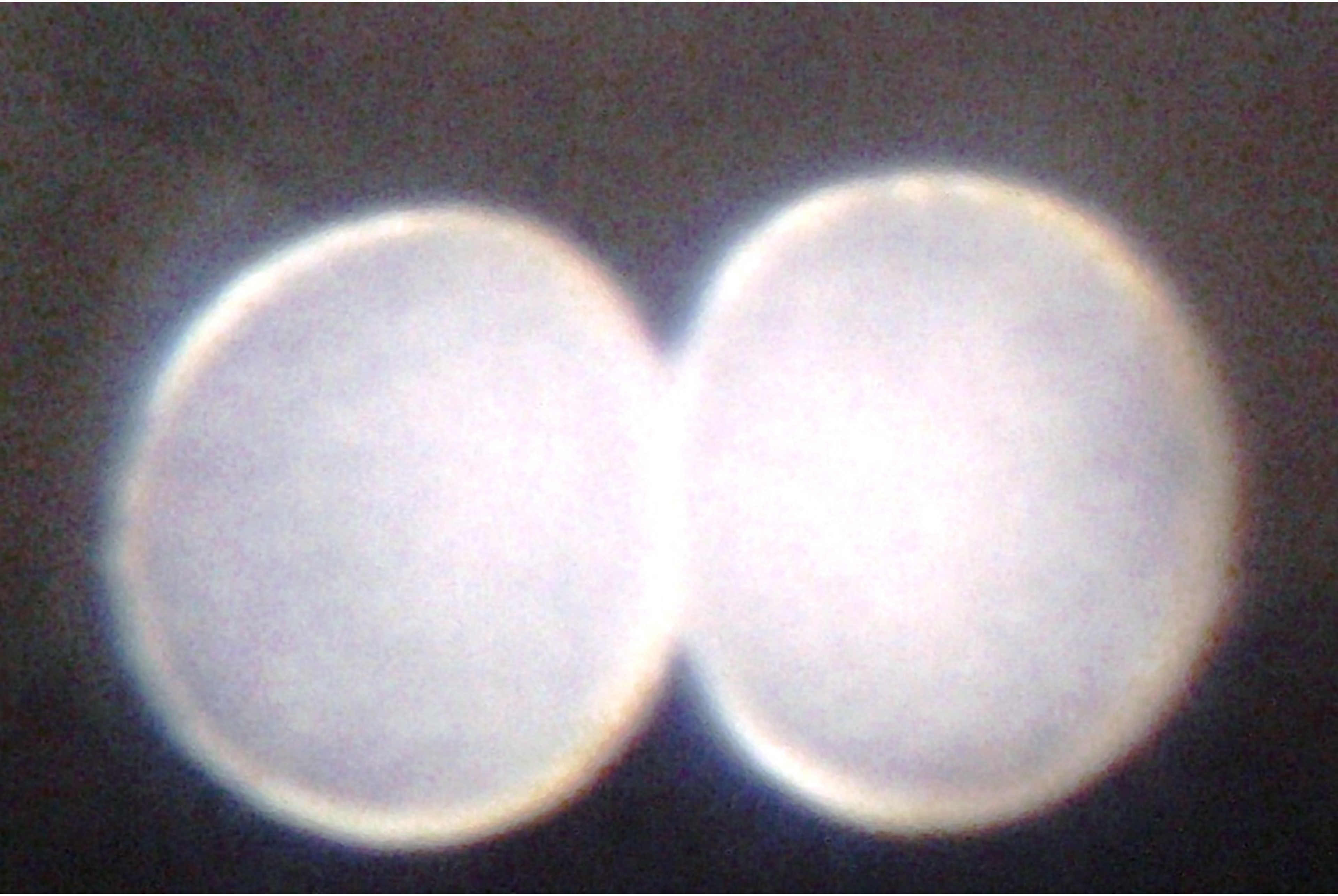
- The ability of organisms to reproduce their own kind is the one characteristic that best distinguishes living things from non-living matter.
- This capacity to procreate, like all biological functions, has a cellular basis.
- Rudolf Virchow of German in 1855 said: where a cell exists, there must have been a pre-existing cell.

- He summarized this concept with the latin words: “*Omnis cellula e cellula*”, meaning every cell from a cell.”
- The continuity of life is based on the reproduction of cells, or cell division.
- Cell division plays several important roles in the life of an organisms.
- When a unicellular organism, such as an amoeba, divides and forms a duplicate offspring, the division of one cell reproduces the entire organism



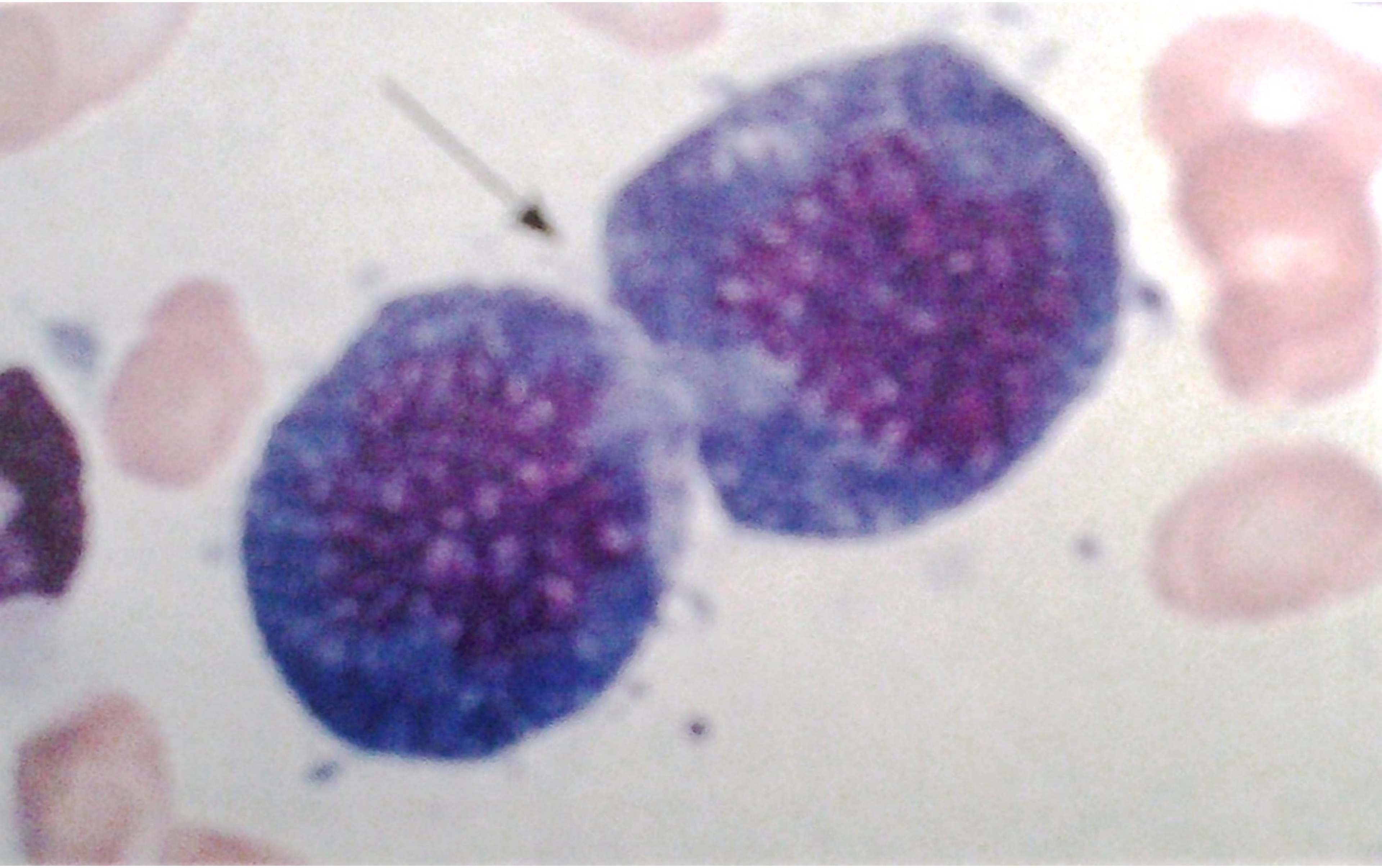
Reproduction; An amoeba a single-celled eukaryote is dividing into two cells. Each new cell will be an individual organism.

- Cell division on a larger scale can produce progeny from some multicellular organism.
- Cell division also enables sexually reproducing organisms to develop from a single cell – the fertilized egg, or zygote.



Micrograph of a sand dollar embryo shortly after the fertilized egg divided forming two cells.

- After an organism is fully grown, cell division continues to function in renewal and repair, replacing cells that die from normal wear and tear.
- For instance dividing cells in human bone marrow continuously make new blood cells



Tissue renewal: These dividing bone marrow cells (arrow) will give rise to new blood cells

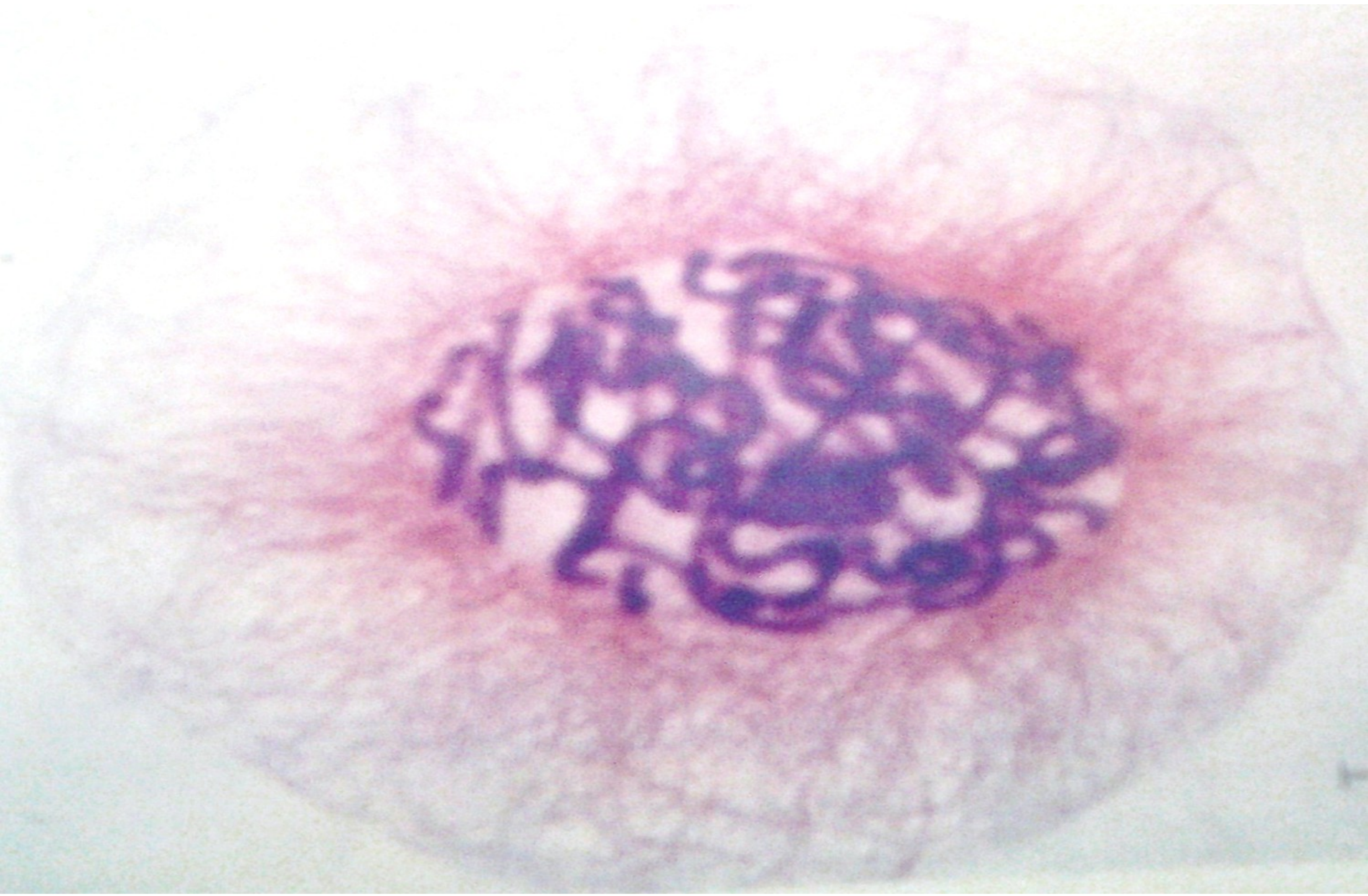
- Cell division process is an integral part of the cell cycle, the life of a cell from the time it is first formed from dividing parent cell until its own division into two cells.
- Passing identical genetic material to cellular off-springs is an important function of cell division.

Cell Division and Transfer of Genetic material to daughter cells

- Most cell division involves the distribution of identical genetic material – DNA – to two daughter cells.
- The most remarkable fact about cell division is the reliability with which the DNA is passed along from one generation of cells to the next.
- A dividing cell duplicates its DNA, allocates the two copies to opposite ends of the cell, and only then splits into daughter cells.

Cellular organization of the genetic Material

- A cell's endowment of DNA, its genetic information, is called its genome. A Prokaryotic genome contains a single long DNA molecule whereas eukaryotic genome consists of a number of DNA molecules.
- For example a human cell has about 2 m of DNA, which is 250, 000 times greater than the cells diameter.
- The DNA molecules is packaged into chromosomes – Greek Chroma meaning dye and soma - body.



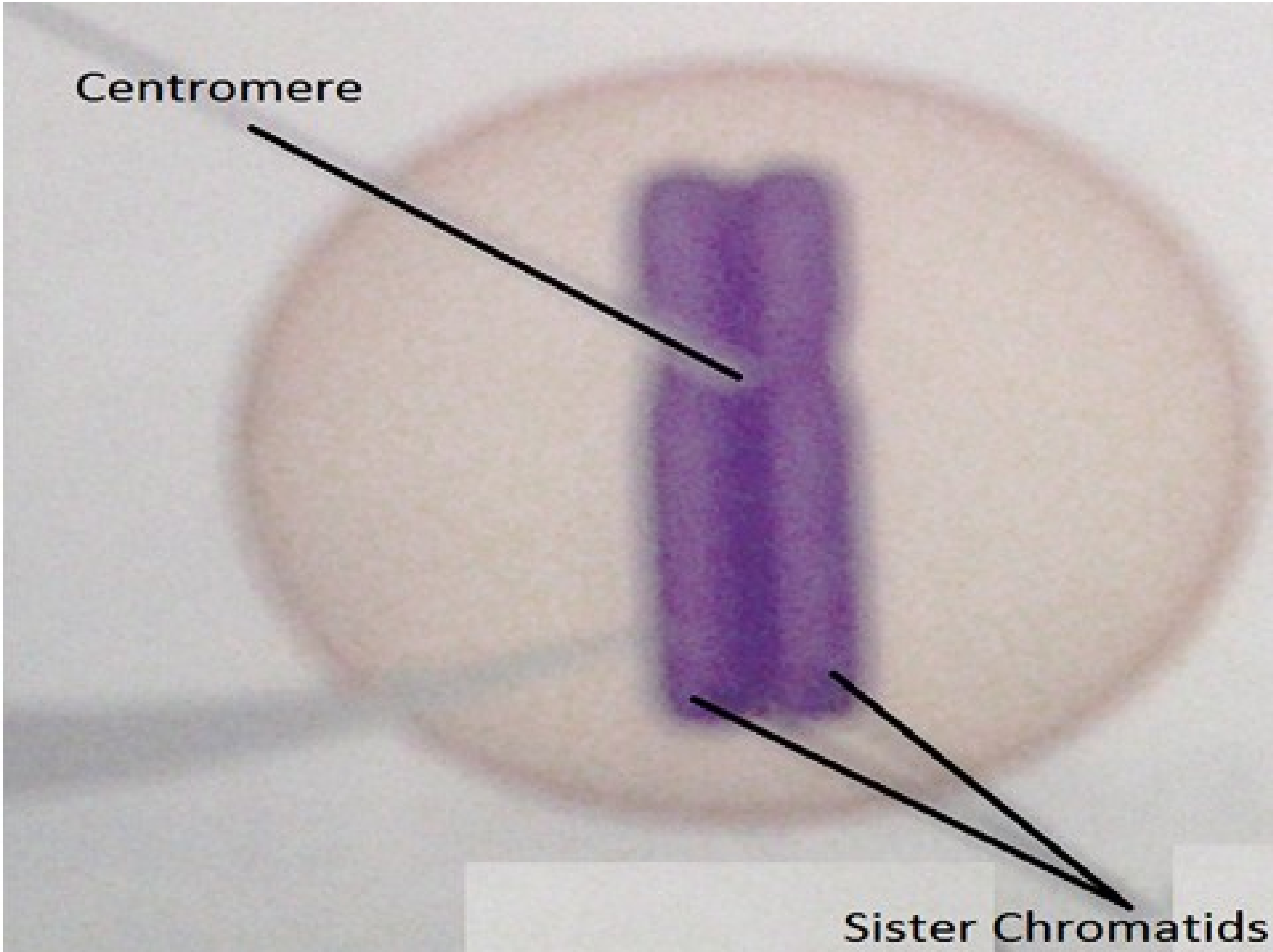
Eukaryotic chromosomes. Chromosomes (stained purple) are visible within the nucleus of this eukaryotic cell.

- Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus.
- For example, the nuclei of human somatic cells (all body cells except the reproductive cells) each contain 46 chromosomes made up of 23, one set inherited from each parent.
- Reproductive cells or gametes – sperms and eggs – have half as many chromosomes as somatic cells, or one set of 23 chromosomes in humans.
- The number of chromosomes are species dependent e.g. cabbages has 18; elephant has 56; hedgehogs has 90 etc.

- Eukaryotic chromosomes are made of chromatin, which is a complex of DNA and associated protein molecules.
- A single chromosome contains a long linear DNA molecule that caries on it several hundreds to a few thousands of genes.
- Genes are units that specify an organism’s inherited traits.
- The associated proteins maintain the structure of the chromosome and controls the activities of the genes.

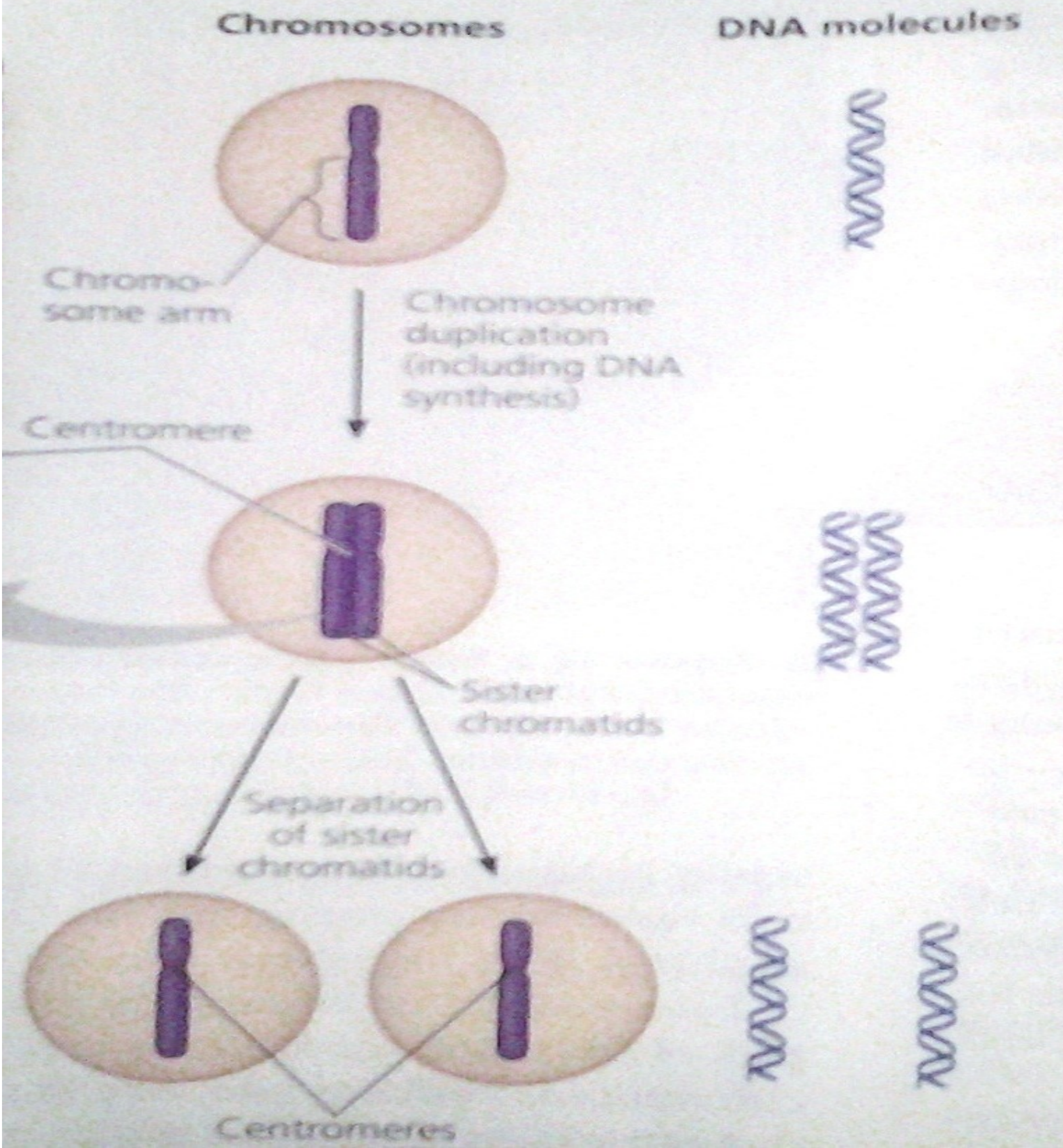
Distribution of Chromosomes During Eukaryotic Cell Division: Mitosis

- When a cell is not dividing the chromosome is in the form of a long, thin chromatin fiber.
- After DNA duplication, the chromosome condense: each chromatin fiber becomes densely coiled and folded, making the chromosome much shorter and thick such that they can be seen with the aid of a light microscope.
- Each duplicated chromosome has two sister chromatids, with identical DNA. The chromatids are held along their lengths by adhesive protein complex called ***sister chromatid cohesion***.


Centromere
Sister Chromatids

- In the condensed form the chromosome has a narrow “waist” at the centromere, a region where the two chromatids are most closely attached.
- The part of the chromatid on either side of the centromere is called the arm of the chromatid or chromosome arm.
- During cell division the two sister chromatids of each duplicated chromosome separate and move into two new nuclei, one forming at each end of the cell. Once the chromatids separate they are considered individual chromosomes.

- This means that each newly formed nucleus receives a collection of chromosomes that are identical to that of the parent cell.



1. Before duplication, each chromosome has a single DNA molecule.

2. Once replicated, a chromosome has 2 sister chromatids connected by centromere.

3. Mechanically the sister chromatids separate into two chromosomes and distribute them to 2 daughter cells.

- The division of the nucleus is called mitosis. Mitosis is immediately followed by cytokinesis, which is division of the cytoplasm i.e., where there was one cell, there are now two cells with genetic material equivalent to the parent cell.

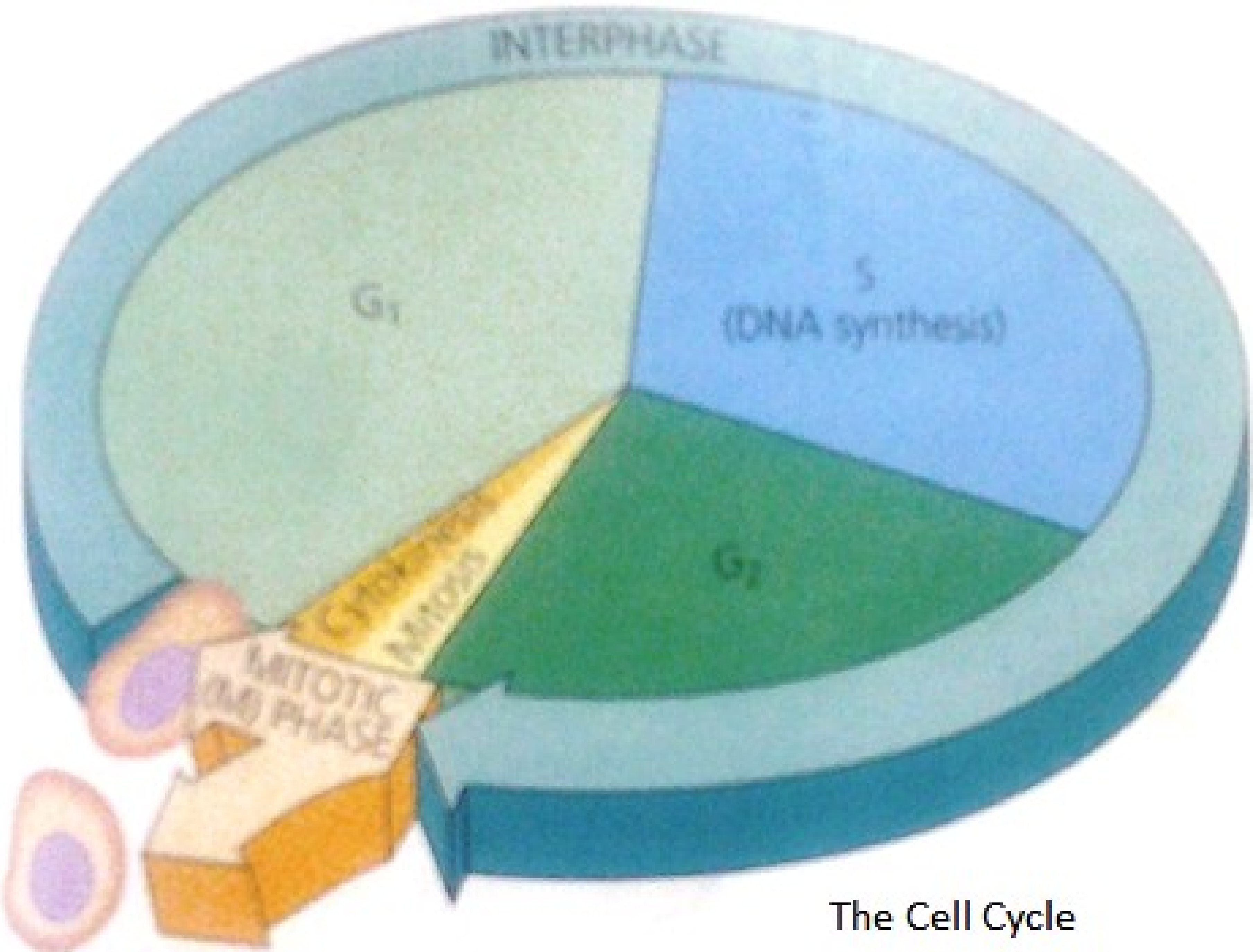
Phases of the Cell Cycle

- Many critical events occur during the cell cycle.
- Mitosis is just one part of the cell cycle. The cell cycle is divided into interphases which are divided into sub-phases namely:
  - The G1 phase, the first part of the interphase, the cell grows. The G1 would take 5 – 6 hours.
  - The S phase the cell continues to grow as it also copies its chromosomes - DNA synthesis. The S phase takes about 10 – 12 hours i.e. half the cycle.

- Phase G2, which is the second part of the interphase. The cell grows more as it completes preparation for cell division.
- The G2 phase usually takes 4 – 6 hours.
- Mitosis (M – phase), the nucleus divides and distributes its chromosomes to the daughter nuclei and cytokinesis divides the cytoplasm producing two daughter cells.
- The M phase usually takes less than 1 hour.

G2 Phase of the Interphase

- A nuclear envelope bounds the nucleus
- The nucleus contains one or more nucleoli (singular, nucleolus).
- Two centrosomes have formed by replication of a single centrosome.
- In animals cells, each centrosome features two centrioles.
- Chromosomes, duplicated during S phase, cannot be seen individually because they have not yet condensed.



The Cell Cycle

The mitotic spindle

- The mitotic spindle is the microtubule-based bipolar structure that segregates the chromosomes in mitosis process.
- The poles of the mitotic spindle are made up of centrosomes and the chromosomes are lined up at the spindle equator to ensure their correct bi-orientation and segregation.
- In animal cells, the assembly of the spindle microtubules start from the centrosome, which is also called the microtubule organizing center.
- During interphase in animal cells, the single centrosome replicates and remain near the nucleus.

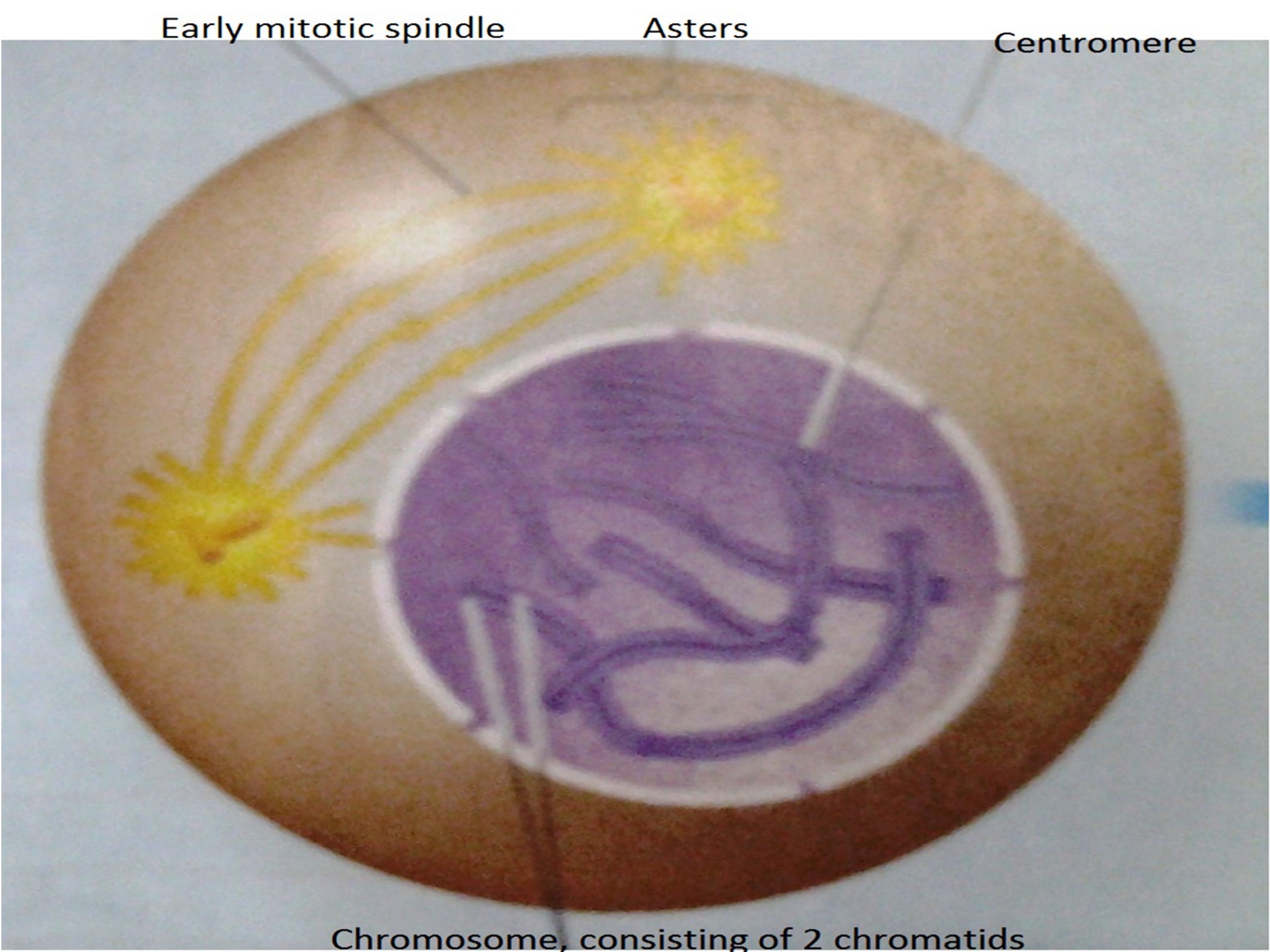
- The two centrosomes move apart during prophase and prometaphase of mitosis as the spindle microtubules grow out from them.
- By the end of prometaphase the two centrosomes, one at each pole of the spindle, are at the opposite ends of the cell.
- An aster, a radial array of short microtubules, extends from each centrosome.

- Each of the chromatids of a replicated chromosome has a kinetochore, which is a structure of proteins associated with centromere of the chromosomal DNA.

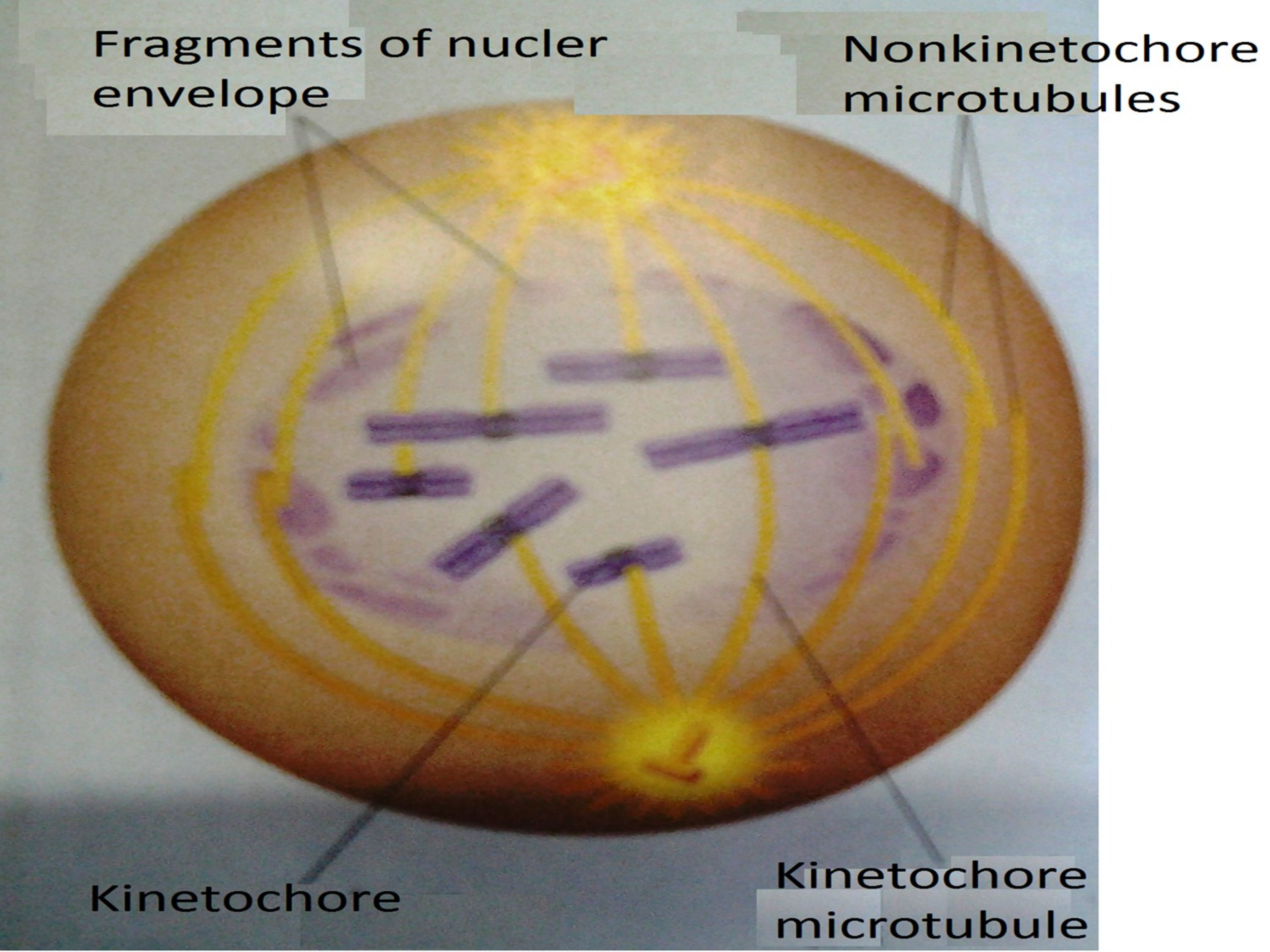
Mitosis Stages

- Mitosis is conventionally broken down into five stages:
  - Prophase
  - Prometaphase
  - Metaphase
  - Anaphase
  - Telophase and Cytokinesis

- **1. Prophase**
  - The chromatin fibers become more tightly coiled, condensing into discrete chromosomes.
  - The nucleoli disappears
  - Each duplicated chromosome appears as two identical sister chromatids joined at their centromeres and all along their arms by cohension.
  - The mitotic spindle begins to form. It is composed of the centrosomes and the microtubules that extend from them.
  - The centrosome move away from each other due to the lengthening of microtubules between them.


Early mitotic spindle
Asters
Centromere
Chromosome, consisting of 2 chromatids

- **2. Prometaphase**
  - The nuclear envelop fragments.
  - The microtubules extending from each centrosome can now invade the nuclear area.
  - The chromosomes have become more condensed.
  - Each of the two chromatids of each chromosome now has a kinetochore, which is a protein structure located at the centromere.
  - Some of the microtubules attach to the kinetochores, becoming “kinetochore microtubules”; which jerk the chromosomes back and forth.
  - Non-kinetochore microtubules interact with those from the opposite pole of the spindle.



Fragments of nucler envelope
Nonkinetochore microtubules
Kinetochore
Kinetochore microtubule

- **3. Metaphase**
  - Metaphase is the longest stage of mitosis lasting for about 20 minutes.
  - The centrosomes are now at opposite poles of the cell
  - The chromosomes convene on the metaphase plate, an imaginary plane equidistant between the spindle’s two poles.
  - The chromosomes centromere lie on the metaphase plate.
  - For each chromosome, the kinetochores of the sister chromatids are attached to kinetochore microtubules coming from opposite poles.

Metaphase Plate

Centrosome at spindle pole

Spindle

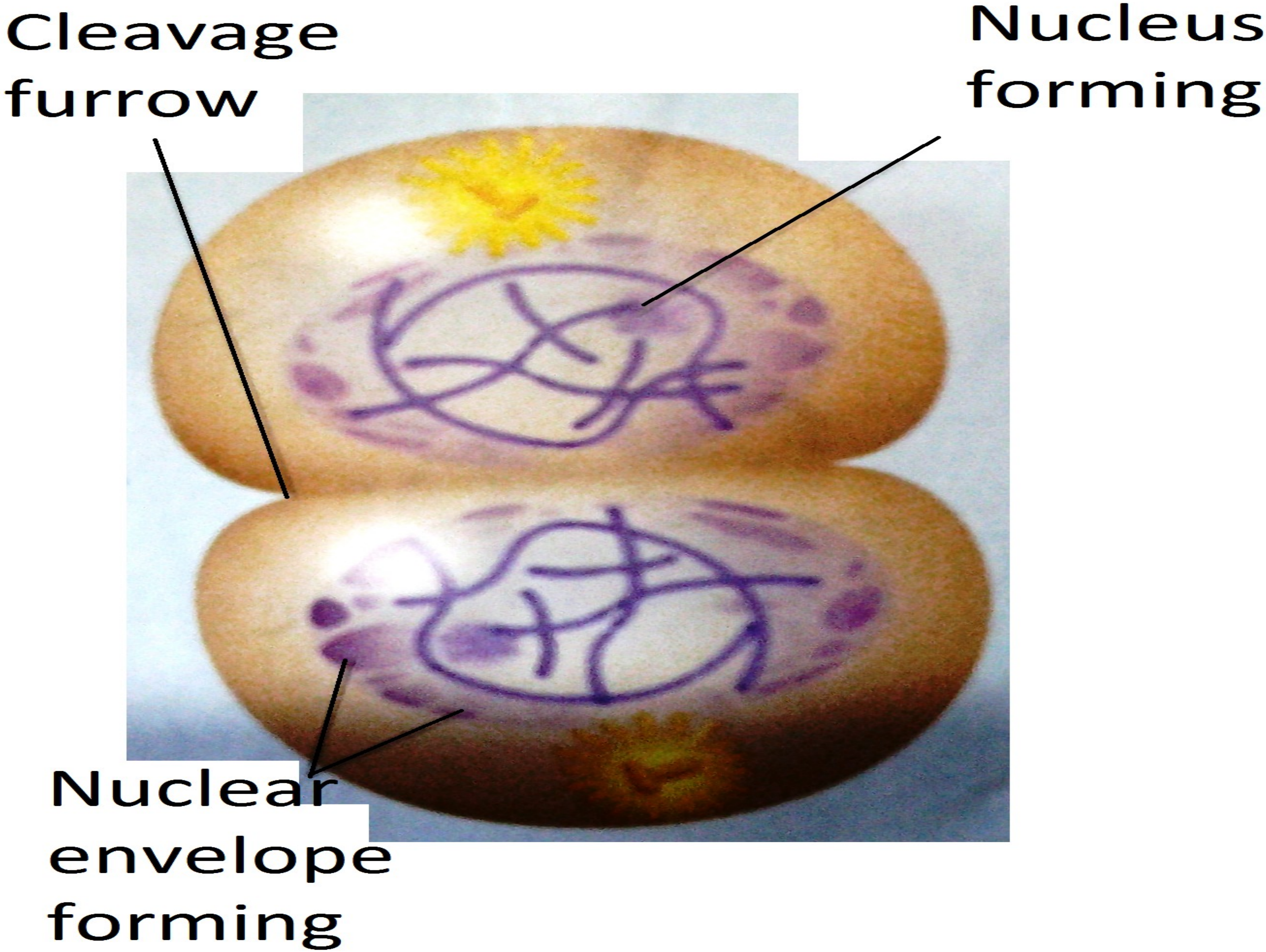
- **4. Anaphase**
  - Anaphase is the shortest stage of mitosis.
  - Anaphase begins when the cohesion proteins are cleaved. This allows the two sister chromatids to part suddenly.
  - Each chromatid thus become a fully fledged chromosome.
  - The two liberated chromosome begin moving toward opposite ends of the cell as their kinetochore microtubules shorten. Because these microtubules are attached at the centromere region, the chromosomes move centromere first at about 1 μm/min.

- The cell elongates as the kinetochore microtubules begin to lengthen.
- By the end of the anaphase, the two ends of the cell have equivalent and complete collection of chromosomes.


Daughter
chromosomes

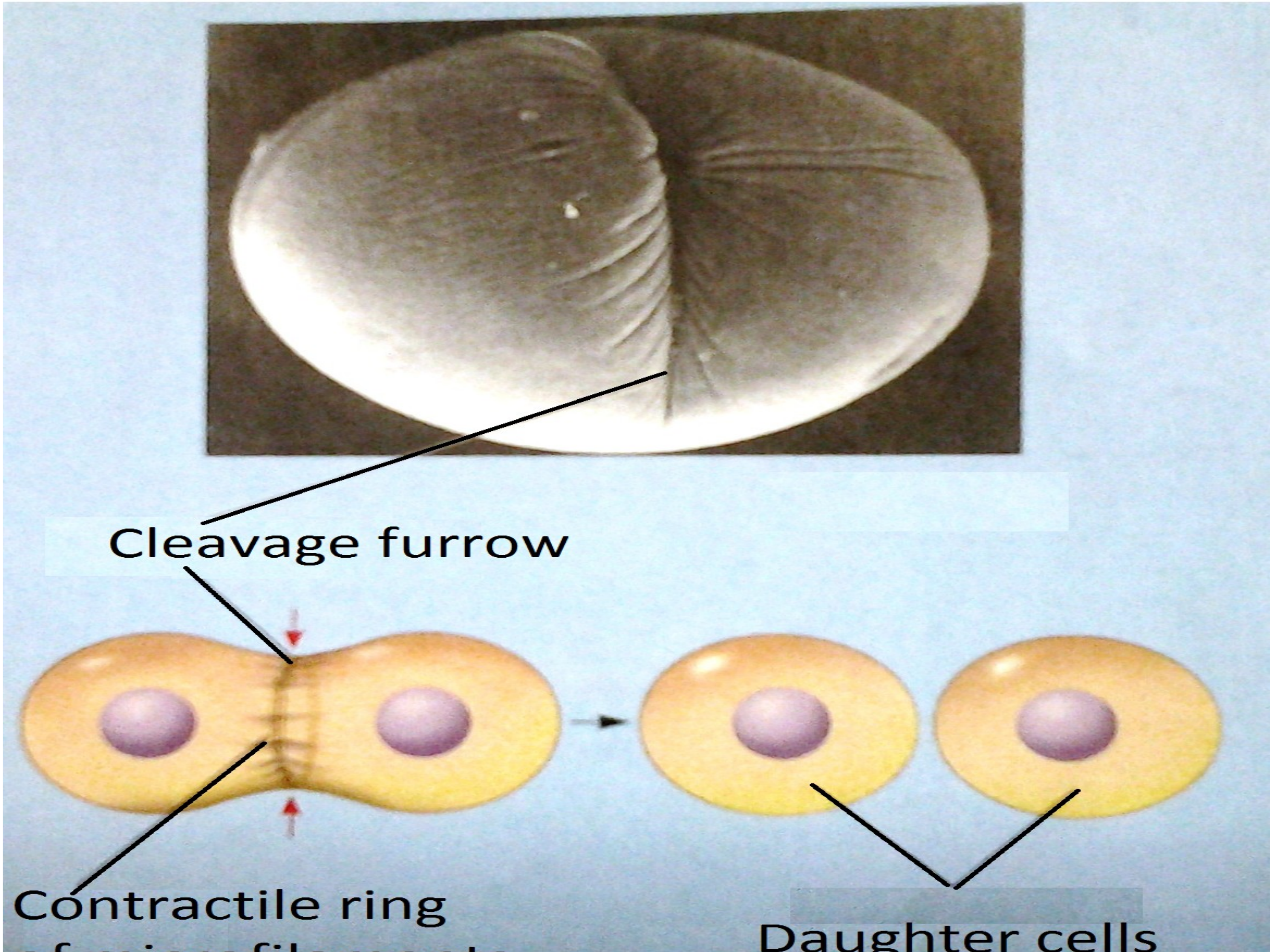
- **5. Telophase and Cytokinesis**
  - Two daughter nuclei form in the cell
  - Nuclear envelopes arise from the fragments of the parent cell's nuclear envelope and other portions of the endomembrane system.
  - The chromosomes become less condensed.
  - Mitosis, the division of the nucleus into two genetically identical nuclei is now complete.

- The division of the cytoplasm is usually well under way by late telophase, so the two daughter cells appear shortly after the end of mitosis.
- In animal cells, cytokinesis involves the formation of a cleavage furrow, which pinches, the cell in two.


Cleavage furrow
Nucleus forming
Nuclear envelope forming

Process of Cytokinesis in Animal and Plant Cells

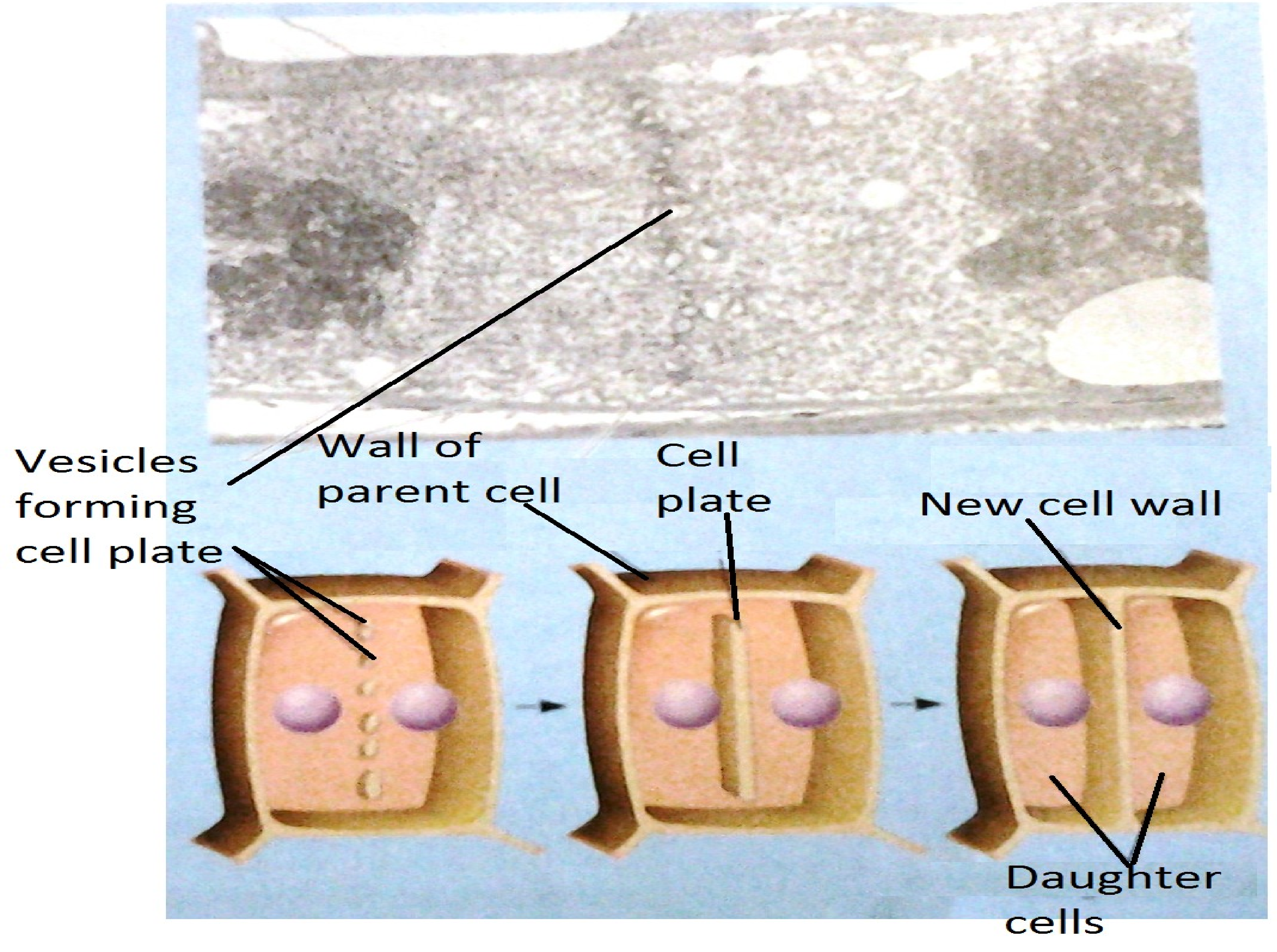
- In animal cells cytokinesis occurs by a process called cleavage.
- First signs of cleavage is the appearance of a cleavage furrow., a shallow groove on the cell surface near the old metaphase plate.
- On the cytoplasmic side of the furrow is a contractile ring of actin microfilaments associated with molecules of the protein myosin.


Cleavage furrow
Contractile ring
Daughter cells

- The actin microfilaments interact with the myosin molecules, causing the ring to contract.
- The cleavage furrow deepens until the parent cell is pinched in two, producing two completely separated cells, each with its own nucleus and share of cytosol, organelles and other subcellular structures.

- Cytokinesis in plant cells, which has cell walls, is different in that there is no cleavage furrow. Instead during telophase vesicles derived from Golgi apparatus move along microtubules to the middle of the cell to form a cell plate.
- Cell wall materials carried in the vesicles collect in the cell plate as it grows. The cell plate then enlarges and its surrounding membrane fuses with the plasma membrane along the perimeter of the cell.

- The two daughter cells result, each with its own plasma membrane and a cell wall is formed from the materials arising from the cell plate between the two daughter cells.

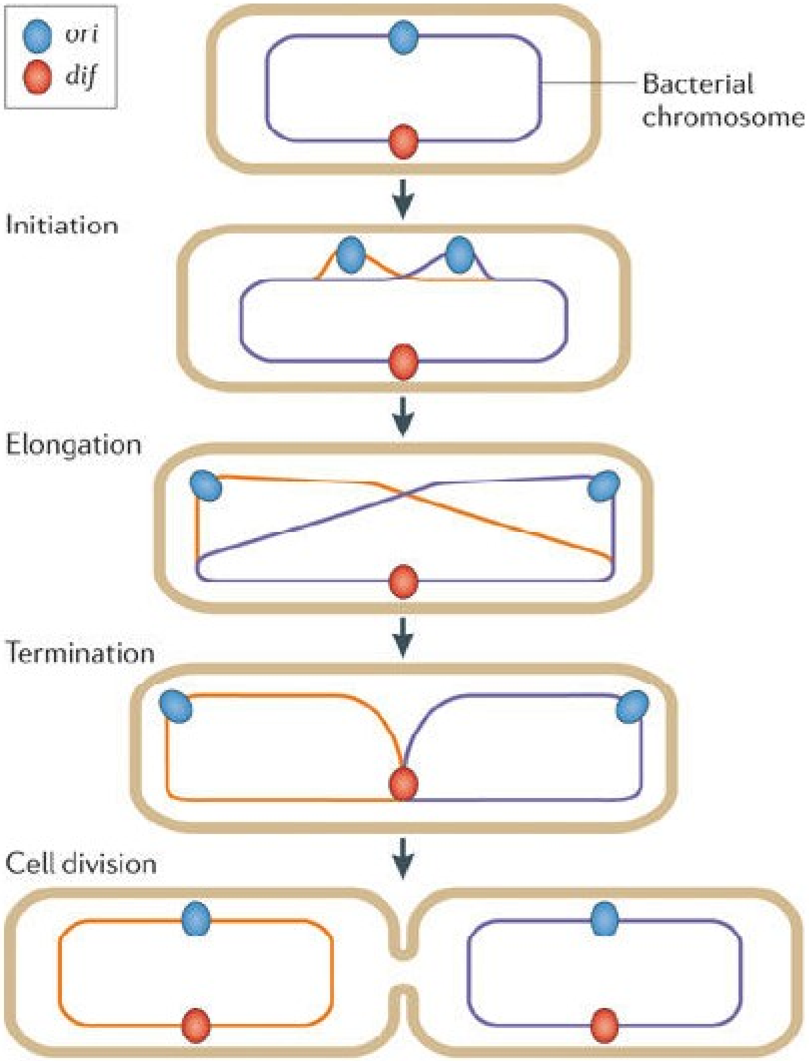

Vesicles forming cell plate
Wall of parent cell
Cell plate
New cell wall
Daughter cells

Cell Division by Prokaryotic Cells

- The asexual reproduction in single - celled eukaryotes, such as amoeba includes mitosis and take place by binary fission, meaning "division in half".
- Prokaryotes (bacteria and archae) also reproduce by binary fission only that mitosis does not take place.
- In bacteria, most genes are carried on a single chromosome that consists of a circular DNA molecule and associated proteins.

- In bacteria the process of cell division is initiated when the DNA of the bacterial chromosome begins to replicate at a specific place on the chromosome called the origin of replication, producing two origins.
- Replication process is completed at a site called terminus, which is directly opposite the origin
- As the chromosome begins to replicate the origin moves rapidly towards the opposite end of the cell.

- While the chromosome is replicating the cell elongates.
- Proteins referred to as replisome are needed for DNA replication.
- DNA replication proceeds from the origin as the parent DNA spools through the replisome, which remains stationary.
- This results in the formation of two progeny chromosomes each with an origin.
- (See Biology by Campbell and Reece, 8th Ed. Page 237)



Chromosome replication and partitioning

- MreB protein is responsible for cell shape and chromosome movement.
- MreB protein polymerizes to form a spiral around the inside periphery of the cell.
- When replications is complete and the bacterium has reached about twice its initial size, its plasma membrane grows inward, dividing the parent bacterial cell into two daughter cells through septation with each inheriting a complete genome.

Septation

- Septation is the process of forming a cross wall between two daughter cells.
- Septation is divided into several steps:
  - Selection of the site where the septation will be formed
  - Assembly of specialized structure called the Z ring, divides the cell into 2 by constriction.
  - Linkage of the Z ring to the plasma memberane and the cell wall
  - Assembly of cell wall synthesizing machinery and
  - Constriction of Z ring and septum formation

- FtsZ protein tubulin is responsible for Z ring formation
- Another protein called the MinCD, which oscillates its position from one end of the cell to the other ensures that the Z- ring is only formed at the centre of the cell.

-END-