The Cell Cycle Lecture-1

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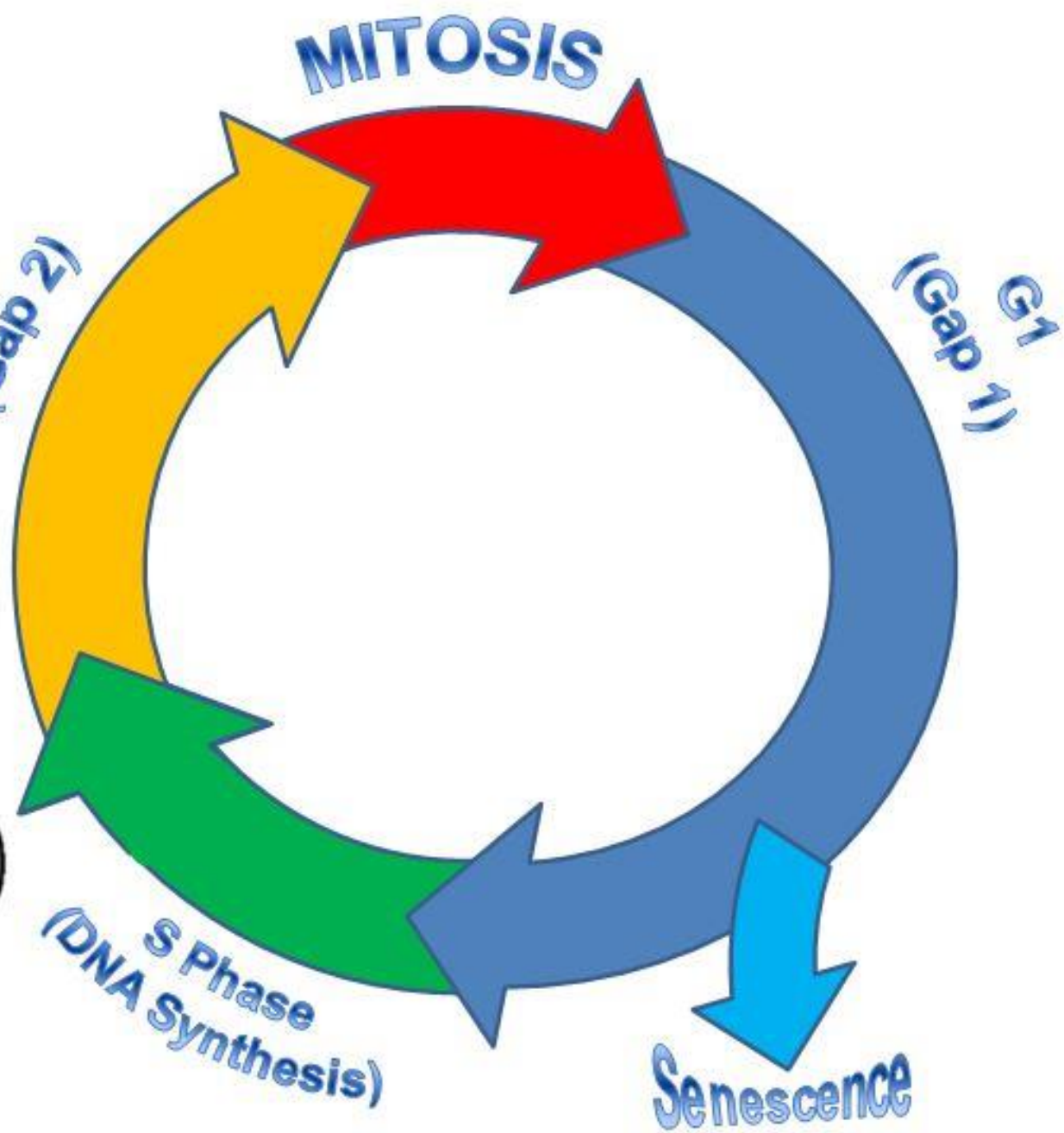
The Cell Cycle

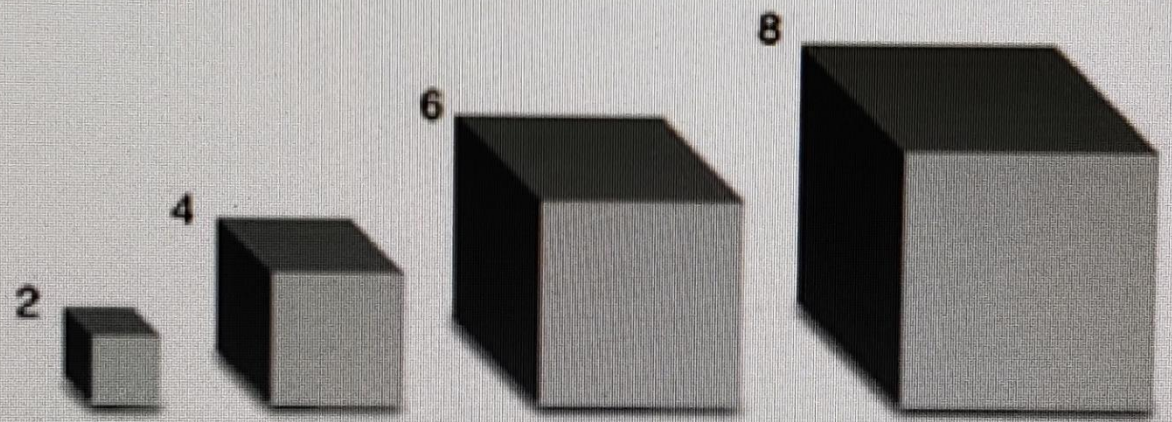


Why a cell needs to divide??

- When a cell is very small, it has a large surface area to volume ratio.
- As the cell grows, its surface area to volume ratio declines.
- This drop in surface area to volume ratio is unsuitable for normal functioning of cell. Because cells rely on diffusion to import and export many substances such as gases and nutrients or excretory products.
- However, as a cell grows, there is comparatively less membrane for the substances to diffuse through.
- This leads to inefficient diffusion and centre of the cell getting less substances than it needs. It can cause drop in cell activities and cell may stop growing.
- Thus, a cell divides.

Surface area refers to the outside area of an object, e.g. it is the area around the outside of a cell. Unit = cm^2.

Volume refers to the amount of space inside of the object, e.g. it is the space inside the cell. Unit = cm^3.



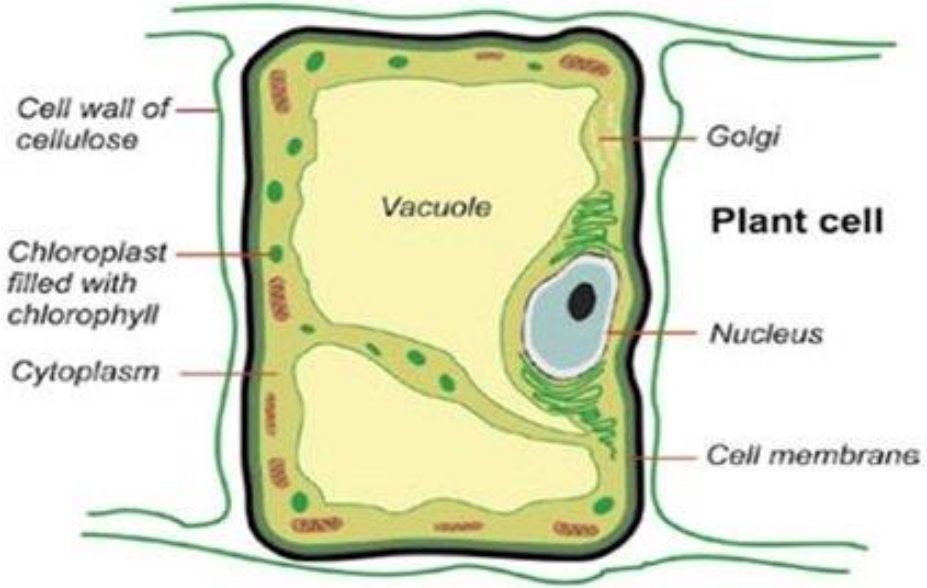
Cube size	Surface area	Volume	SA:V ratio
2 cm cube	$2 \times 2 \times 6 = 24cm^2$	$2 \times 2 \times 2 = 8cm^3$	24 to 8 = 3:1
4 cm cube	$4 \times 4 \times 6 = 96cm^2$	$4 \times 4 \times 4 = 64cm^3$	96 to 64 = 1.5:1
6 cm cube	$6 \times 6 \times 6 = 216cm^2$	$6 \times 6 \times 6 = 216cm^3$	216 to 216 = 1:1
8 cm cube	$8 \times 8 \times 6 = 384cm^2$	$8 \times 8 \times 8 = 512cm^3$	384 to 512 = 0.75:1

- Cells can also resort to alternative ways to have a higher surface area to volume ratio.
- These strategies are

1. Long thin shape or elongated shape. E.g. Neurons.

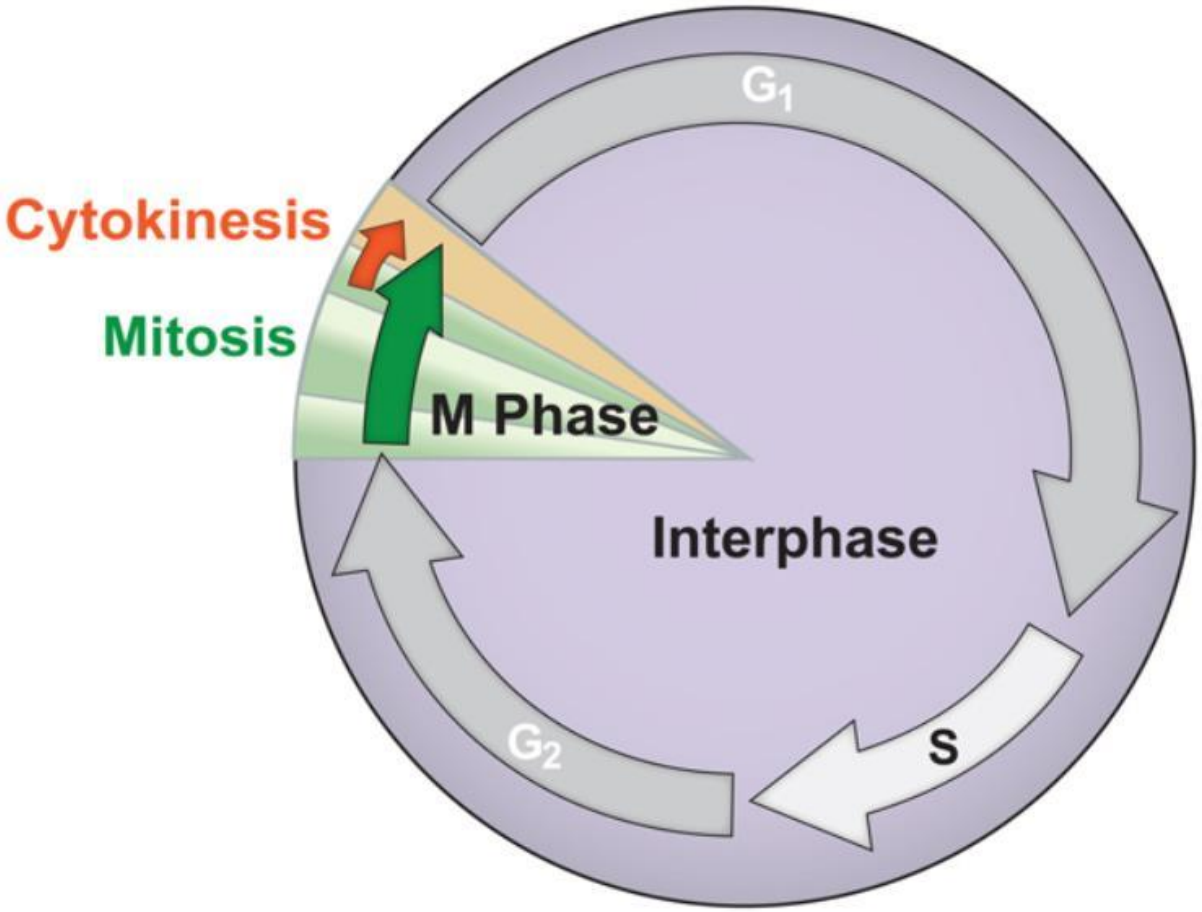
2. Folding of the surface of the cell membrane. E.g. Villi of the lining in the small intestines.

3. Plant cells are much larger than animal cells. They have a large vacuole which pushes the organelles to the edge of the cell where they get regular access to resources.

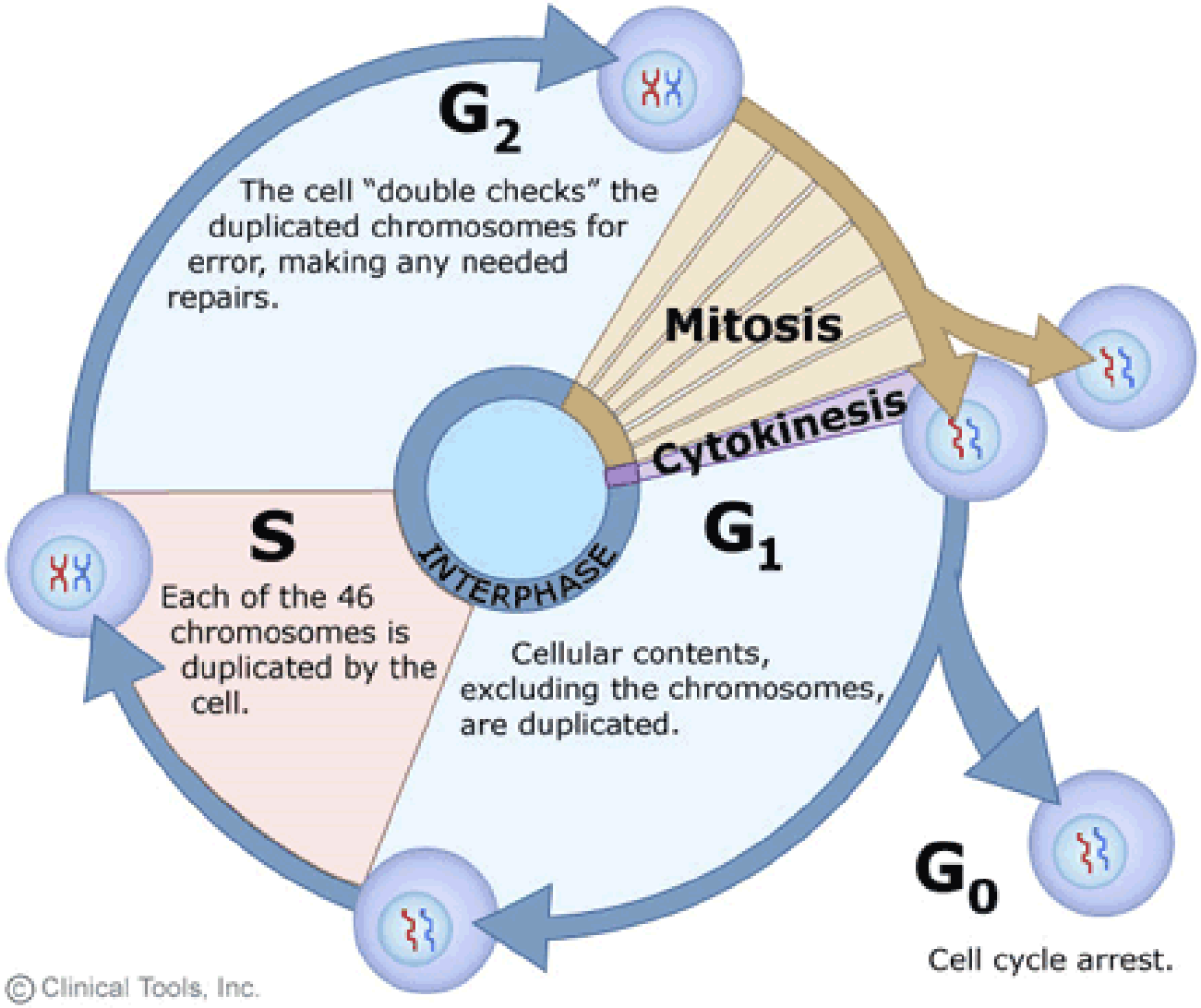


- **What is a cell cycle?**

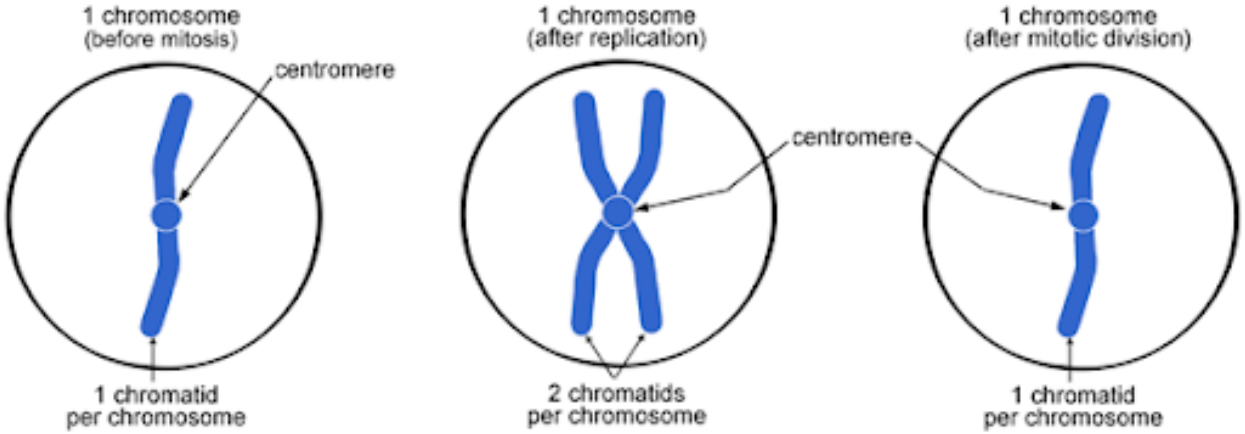
- It refers to the orderly events that take place over a fixed period of time while a cell divides into two.



Cell Type	Cell-Cycle Times
Early frog embryo cells	30 minutes
Yeast cells	1.5–3 hours
Intestinal epithelial cells	~12 hours
Mammalian fibroblasts in culture	~20 hours
Human liver cells	~1 year

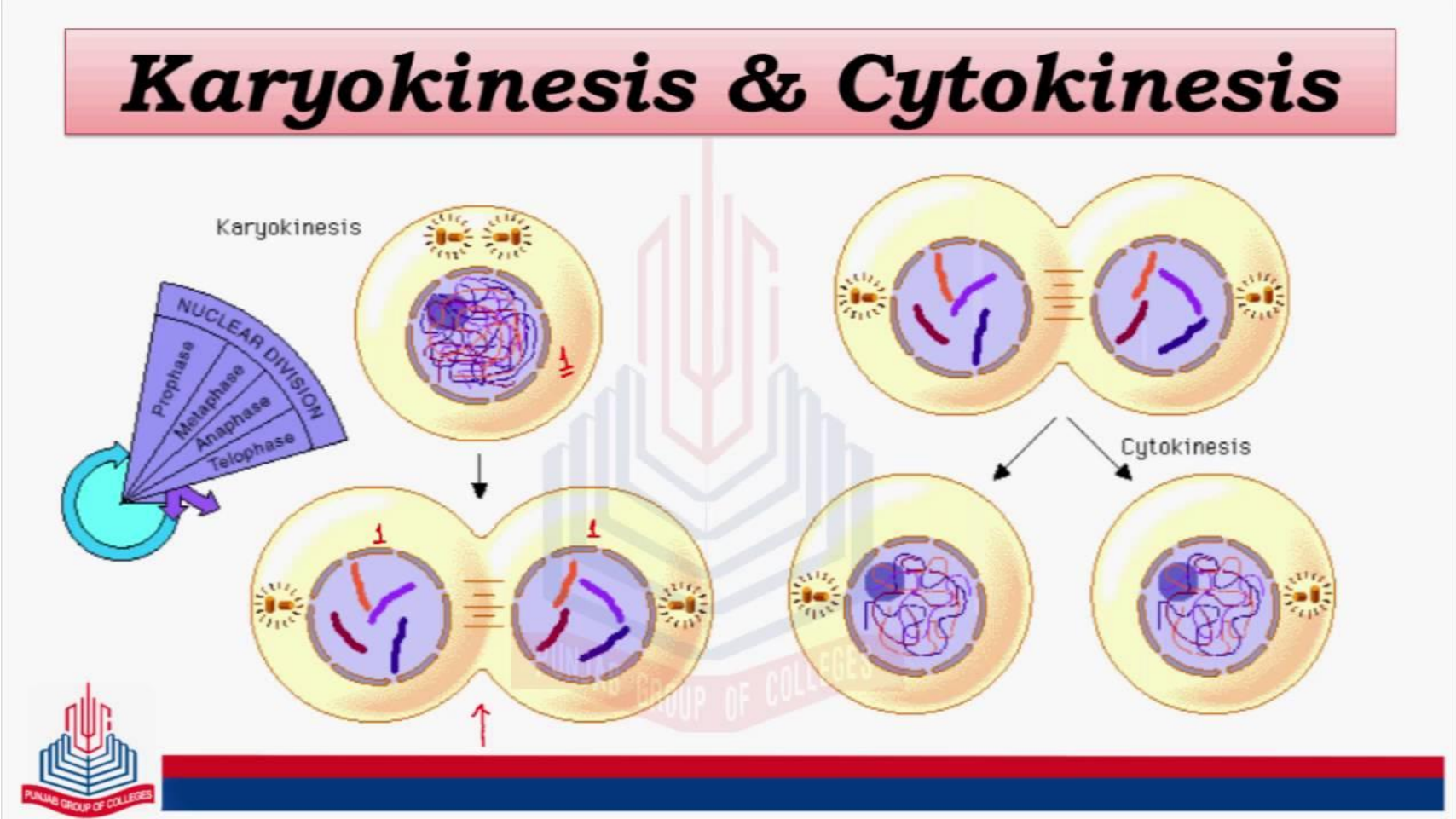


DNA content vs Number of chromosomes



- Every stage of cell cycle has specific functions and the mitotic phase is further divided into two stages

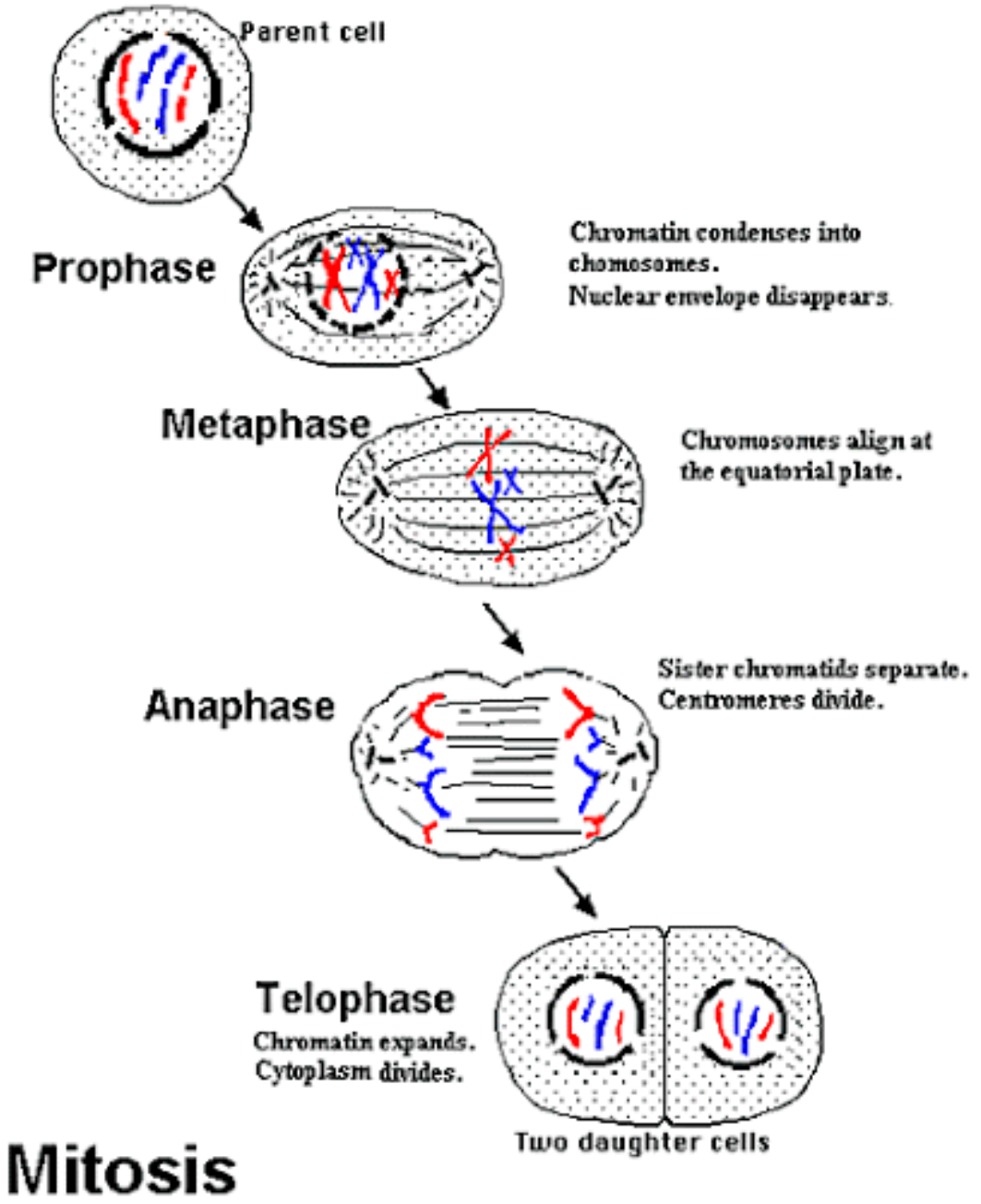
1. Karyokinesis, in this nucleus content, specifically chromosomes are divided equally.
2. Cytokinesis, in this the cell with two daughter nuclei is divided into two daughter cells.

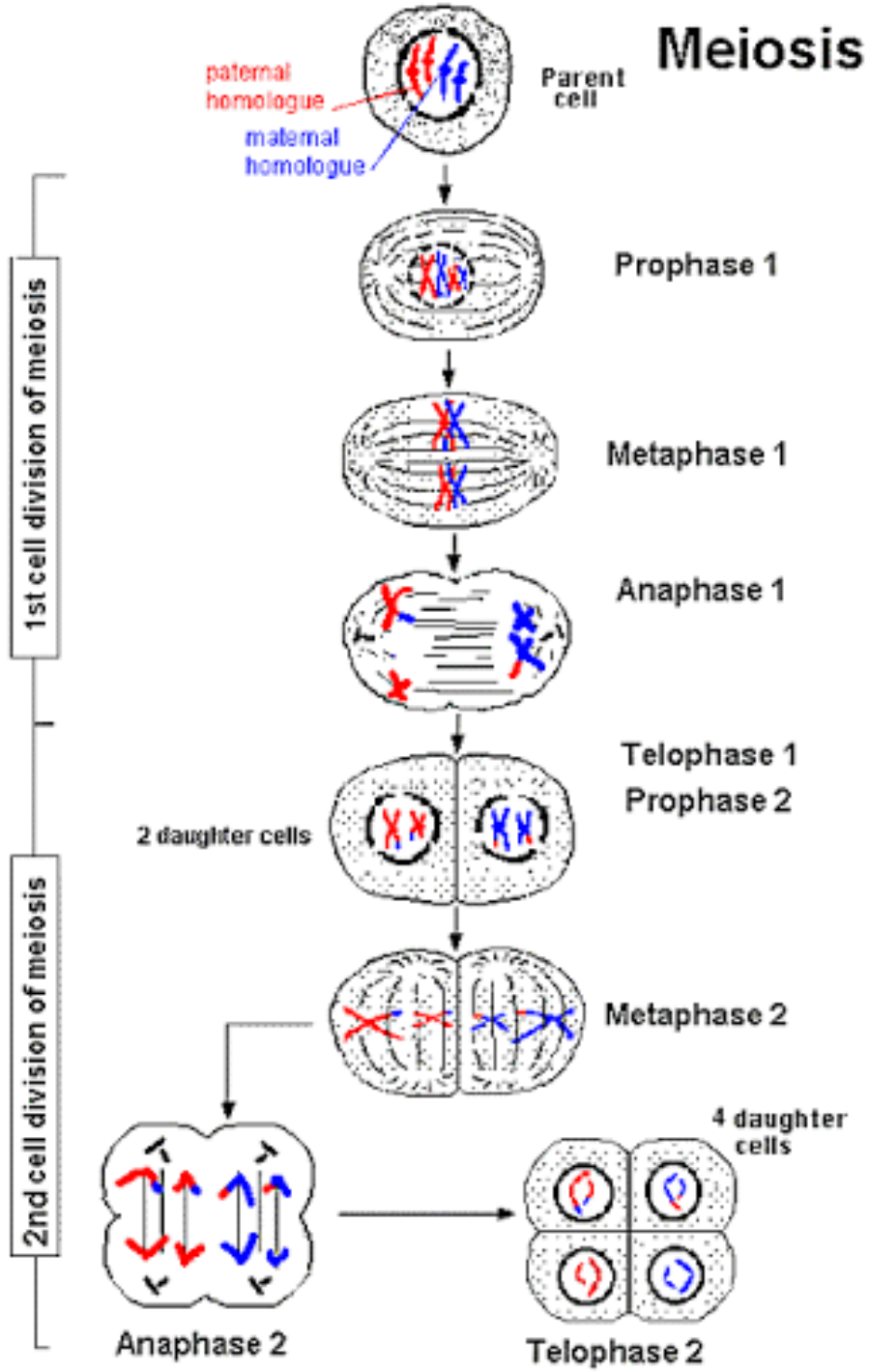


- However, there is a minor but significant difference between mitosis and meiosis when it comes to stages in cell cycle.

- In mitosis division, a cell will undergo complete sequence of cell cycle before it enters mitotic division again.

- But in case of meiosis, once meiosis I has been completed daughter cell immediately enters next round of cell division called as meiosis II and skips the route of cell cycle.




Meiosis
paternal homologue
maternal homologue
Parent cell
Prophase 1
Metaphase 1
Anaphase 1
Telophase 1
Prophase 2
2 daughter cells
Metaphase 2
4 daughter cells
Anaphase 2
Telophase 2
1st cell division of meiosis
2nd cell division of meiosis

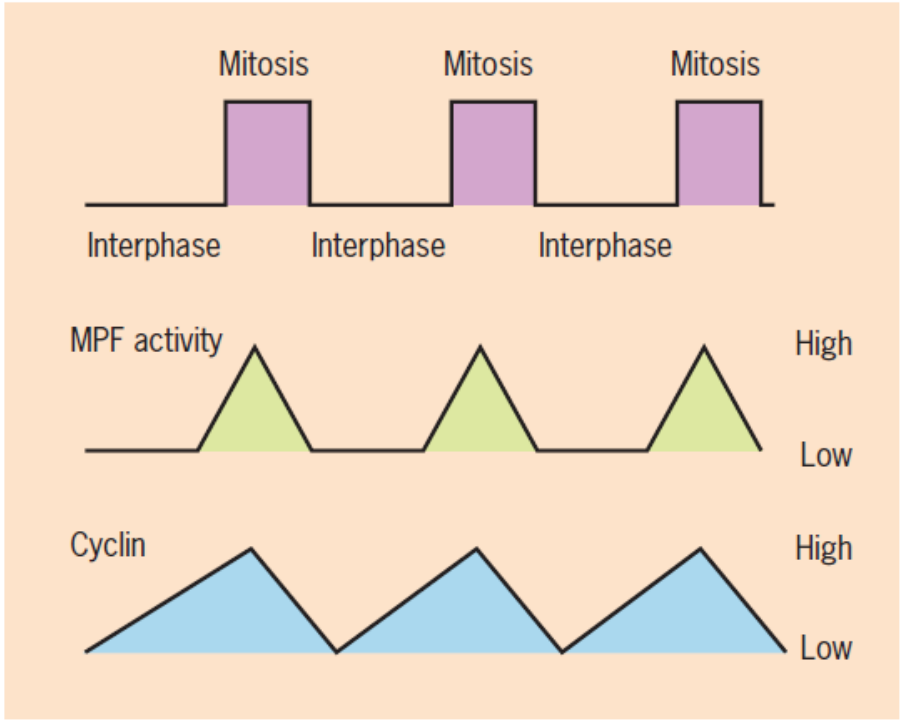
Regulation of cell cycle

- Movement of cell cycle from one phase into the next is carefully regulated.

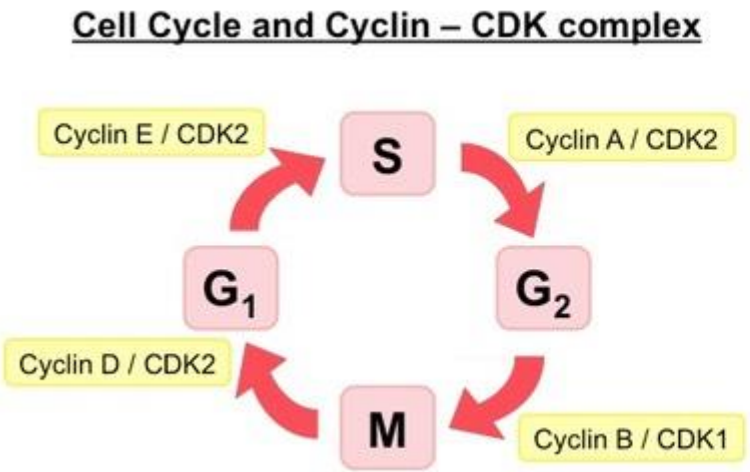
- This regulation occurs mainly by two set of proteins.

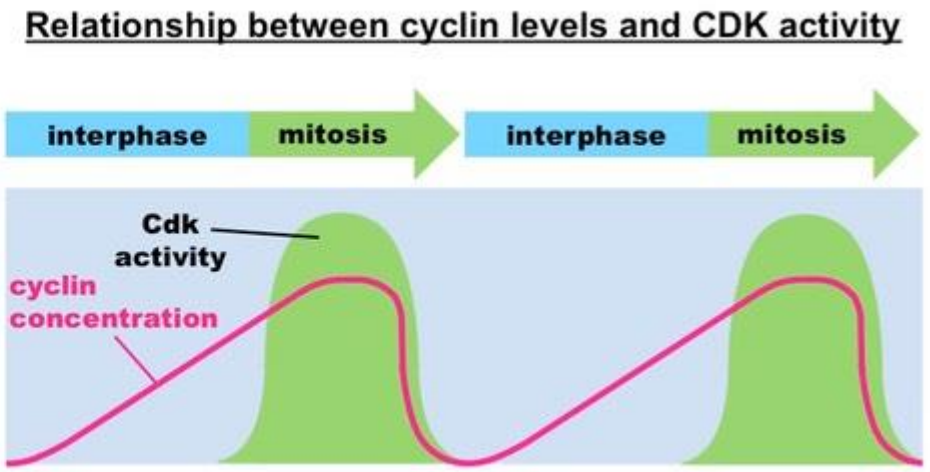
1. **Cyclin:** It is the regulatory protein whose concentration varies in a defined cyclical manner, hence, its name.
2. **Cyclin dependent kinases:** They are also abbreviated as CDKs and are the catalytic unit. But they are functional only when they combine with their partner cyclin protein. Thus, their name.

Once active they phosphorylate their target proteins and this regulates the entry of cell from one phase to the other phase of cell cycle.



Both the images show relation between cell cycle progress and cyclin-Cdk activity.





Potu Rao and Johnson`s experiment on cell fusion and regulation of cell cycle

- Their experiment is considered as landmark in the field of cell cycle regulation.
- Rao and Johnson wanted to know whether the cytoplasm of cells contains regulatory factors that affect cell cycle activities.
- They approached the question by fusing mammalian cells that were in different stages of the cell cycle.
- They performed following fusion experiments:

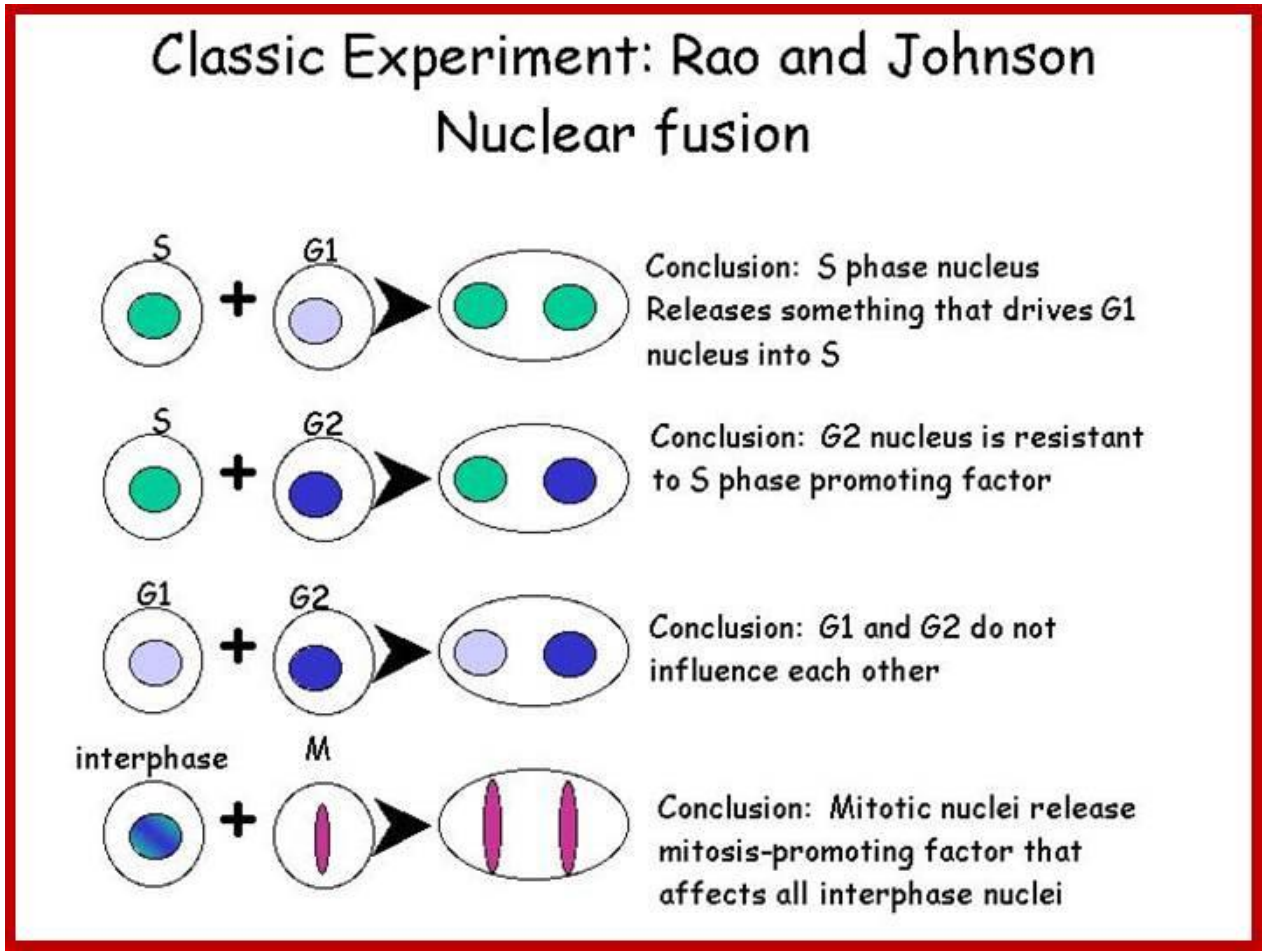
1. G_1-phase + M-phase.
2. G_2-phase + M-phase.
3. S-phase + M-phase.

In all these experiments, the fused cells were found to enter M-phase.

It led to the conclusion that M-phase cells have some properties that induce cells in other stages to enter M-phase.

- When further fusion experiments were performed, it was concluded that cells in each stage of the cell cycle have some defining factors.

- And the cell in advanced stages of cell cycle can induce the cells in early stages to move into the advanced stages even if its premature.



The Rao and Johnson Cell Fusion Experiments
Cell Cycle Regulation

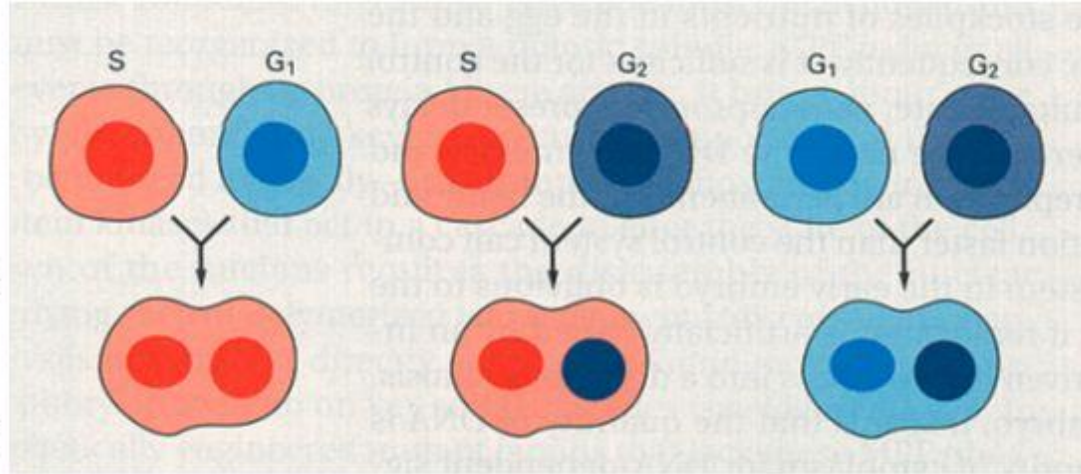
M cells + G1, S, or G2 cells ⟶ M
- **Mitotic state is dominant.**

S cells + G1 ⟶ G1 cells enter S

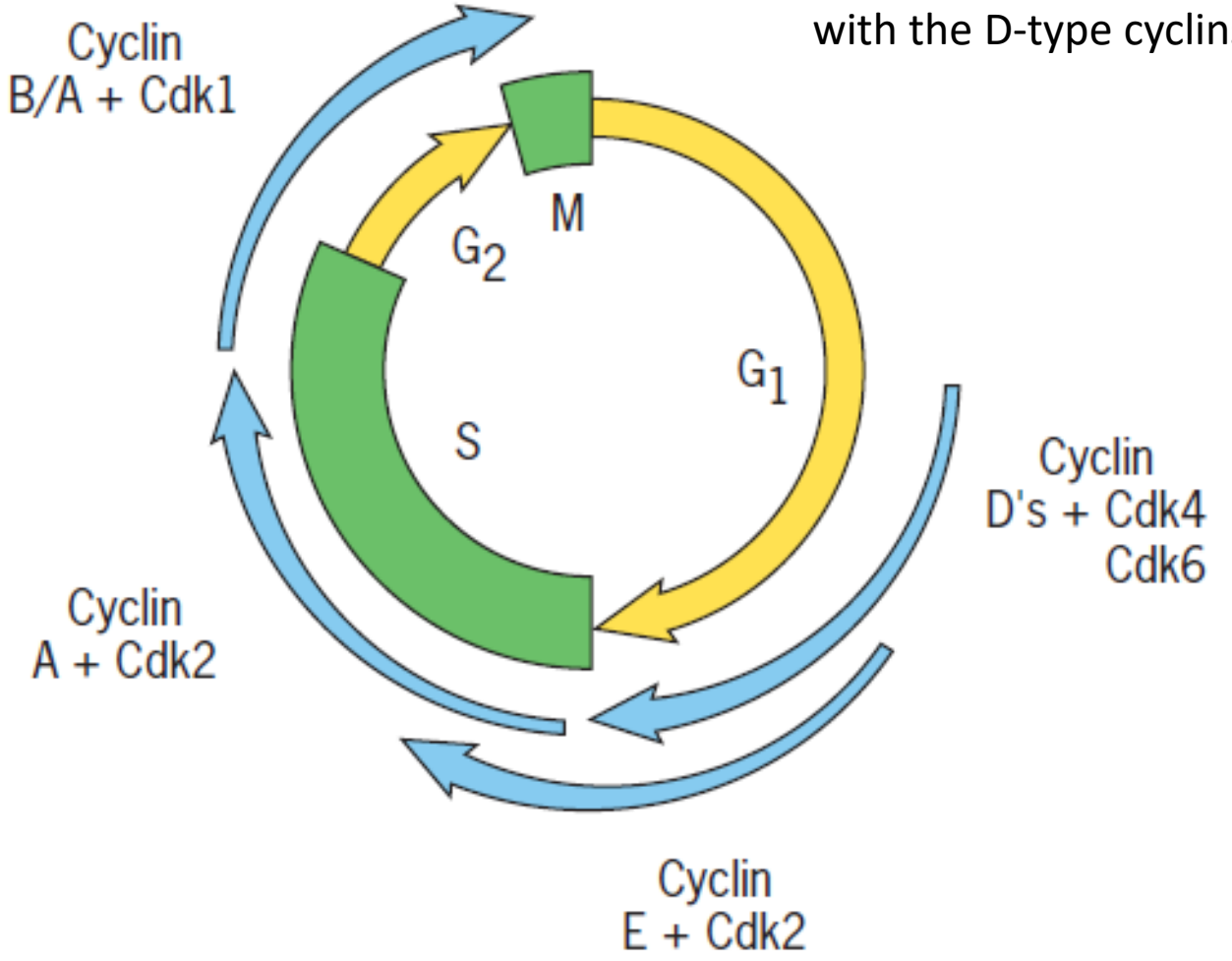
S cells + G2 ⟶

G2 cells do not enter S, but do not enter mitosis until the S-phase nucleus has entered G2.
- **Block to re-replication**
- **Inhibitor of mitosis produced by S phase cells**

G1 cells + G2 ⟶ Like S above.
- **G1 cells also block mitosis**



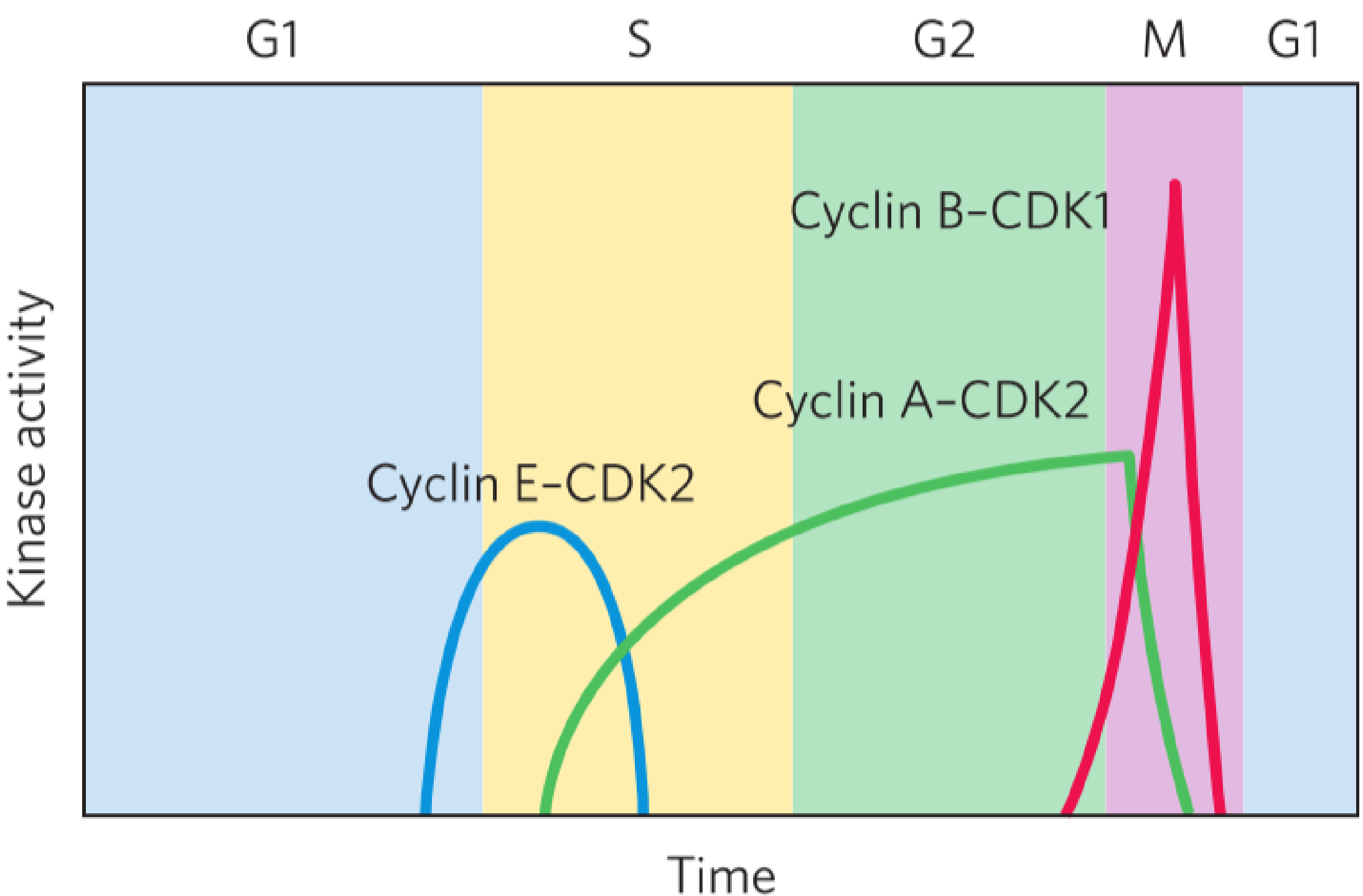
- A combination of specific cyclin and Cdk regulates the entry and exit into each phase of cell cycle as shown below.



- Cdk activity during early G1 is very low, which promotes the formation of prereplication complexes at the origins of replication.
- By mid-G1, Cdk activity is evident due to the association of Cdk4 and Cdk6 with the D-type cyclins (D1, D2, and D3).

- The G1–S transition, which includes the initiation of replication, is driven by the activity of the cyclin E–Cdk2 during early S-phase and cyclin A–Cdk2 complexe during late S-phase.

- The transition from G2 to M is driven by the sequential activity of cyclin A–Cdk1 and cyclin B1–Cdk1 complexes.


G1
S
G2
M
G1
Cyclin B–CDK1
Cyclin A–CDK2
Cyclin E–CDK2
Kinase activity
Time

M-phase and start of karyokinesis

- Once a cell has completed the cell cycle, it can decide to exit from the cell cycle and enter a phase of slow growth and no cell division. This stage is called as G_0-phase.

- However, if the cell decides to stay in cell cycle and enters G_1 phase then after completing all the stages it reaches the M-phase or mitotic phase.

- With this starts the process of karyokinesis.

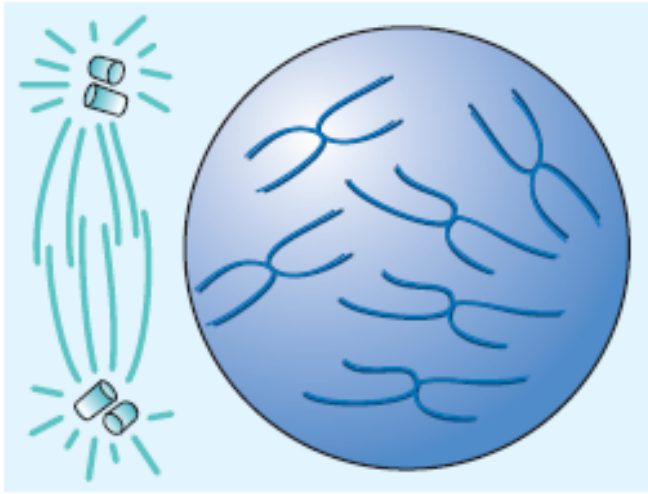
- Its stages and their basic features are discussed in subsequent slides.

Prophase

1. Chromosomal material condenses to form compact mitotic chromosomes. Chromosomes are seen to be composed of two chromatids attached together at the centromere.

2. Cytoskeleton is disassembled, and mitotic spindle is assembled.

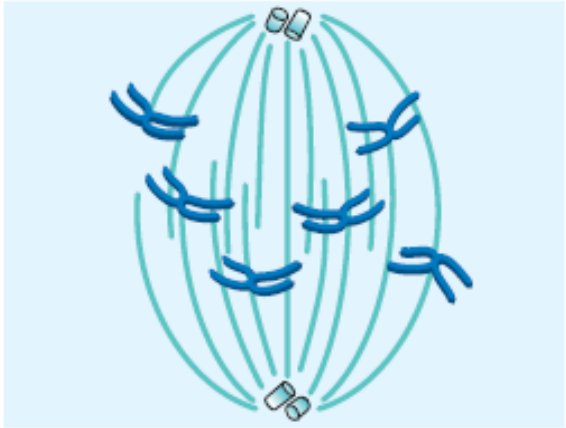
3. Golgi complex and ER fragment. Nuclear envelope disperses.



Prometaphase

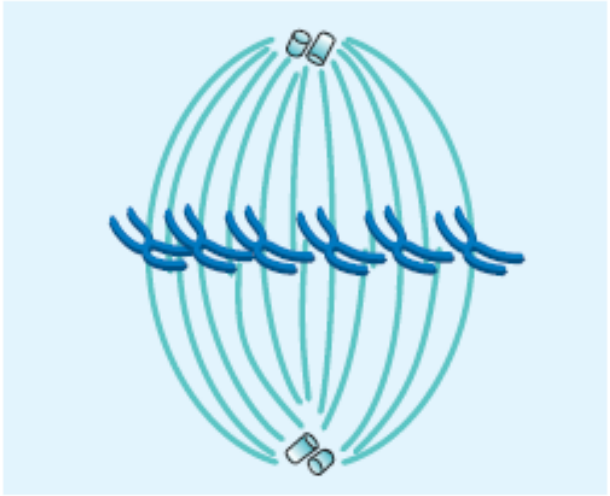
1. Chromosomal microtubules attach to kinetochores of chromosomes.

2. Chromosomes are moved to spindle equator.



Metaphase

1. Chromosomes are aligned along metaphase plate, attached by chromosomal microtubules to both poles.

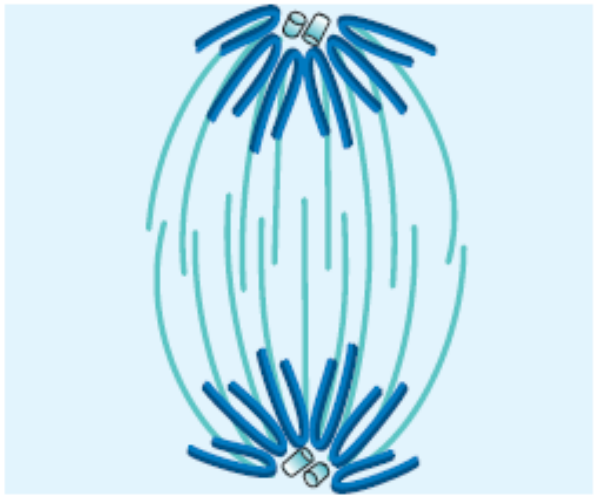


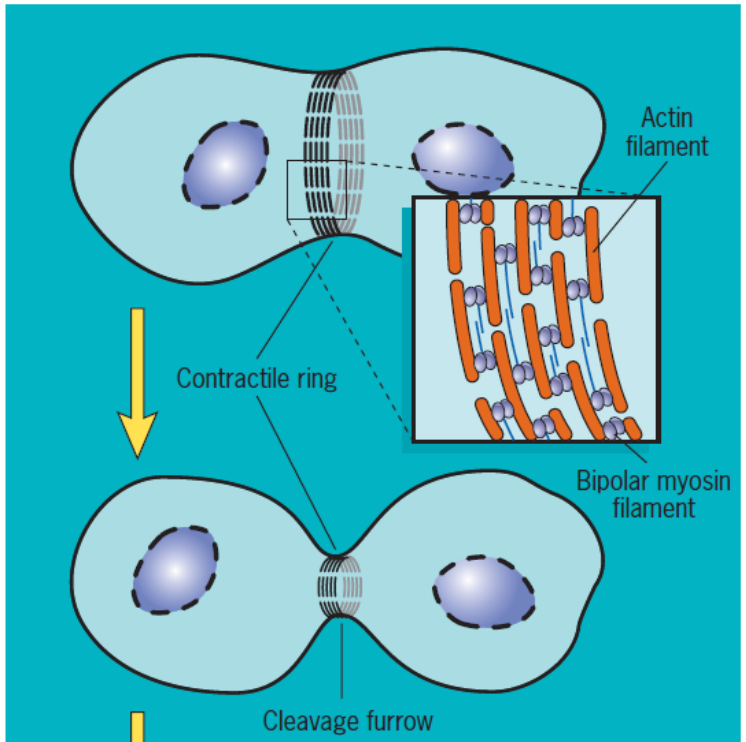
Anaphase

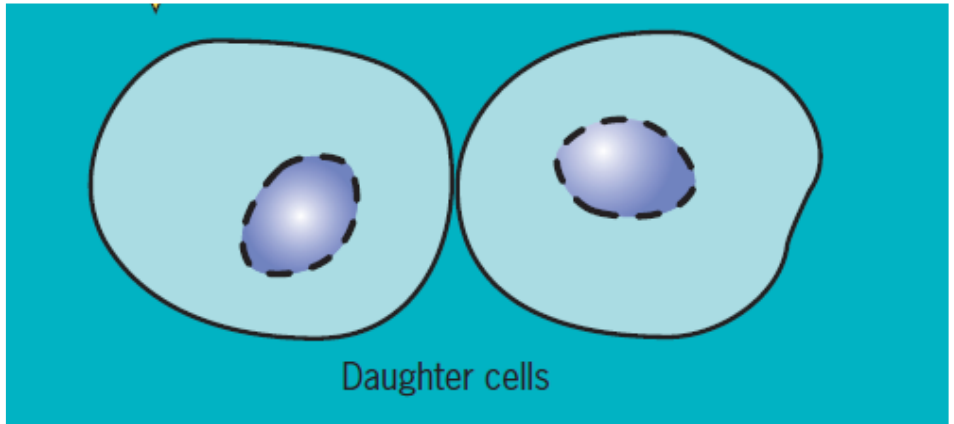
1. Centromeres split, and chromatids separate.
2. Chromosomes move to opposite spindle poles.
3. Spindle poles move farther apart.

Telophase

1. Chromosomes cluster at opposite spindle poles.
2. Chromosomes become dispersed.
3. Nuclear envelope assembles around chromosome clusters.
4. Golgi complex and ER reforms.
5. Daughter cells formed by cytokinesis.







Thank you