



تطوير

BIOLOGY

Lec no:

File Title: Chapter 12

Done By: Leen Al-Ashram

وقل صرنا زكياتي علما



Biology : Chapter 12

cell cycle + mytosis

Done by: Leen AlAshram

Overview: The Key Roles of Cell Division

- The ability of organisms to produce more of their own kind best distinguishes living things from nonliving matter
- The continuity of life is based on the reproduction of cells, or cell division

cell division

for continuity of life.

chapter 12

Mitotic division Mitosis

- growth
- repair skin
- development of zygote
- asexual reproduction (Bacteria)

mother cell



diploid
خلية ثنائية المجموعة الكروموسومية

daughter cells



... genetically identical to each other & to the mother cell

* not reproductive cells [somatic cell]

خلية جسدية / خلية في العنبر / الكبد / ...

* increase number of cells without changes

sexual reproduction genetic variation large number of gametes

chapter 13 mitotic division meiosis

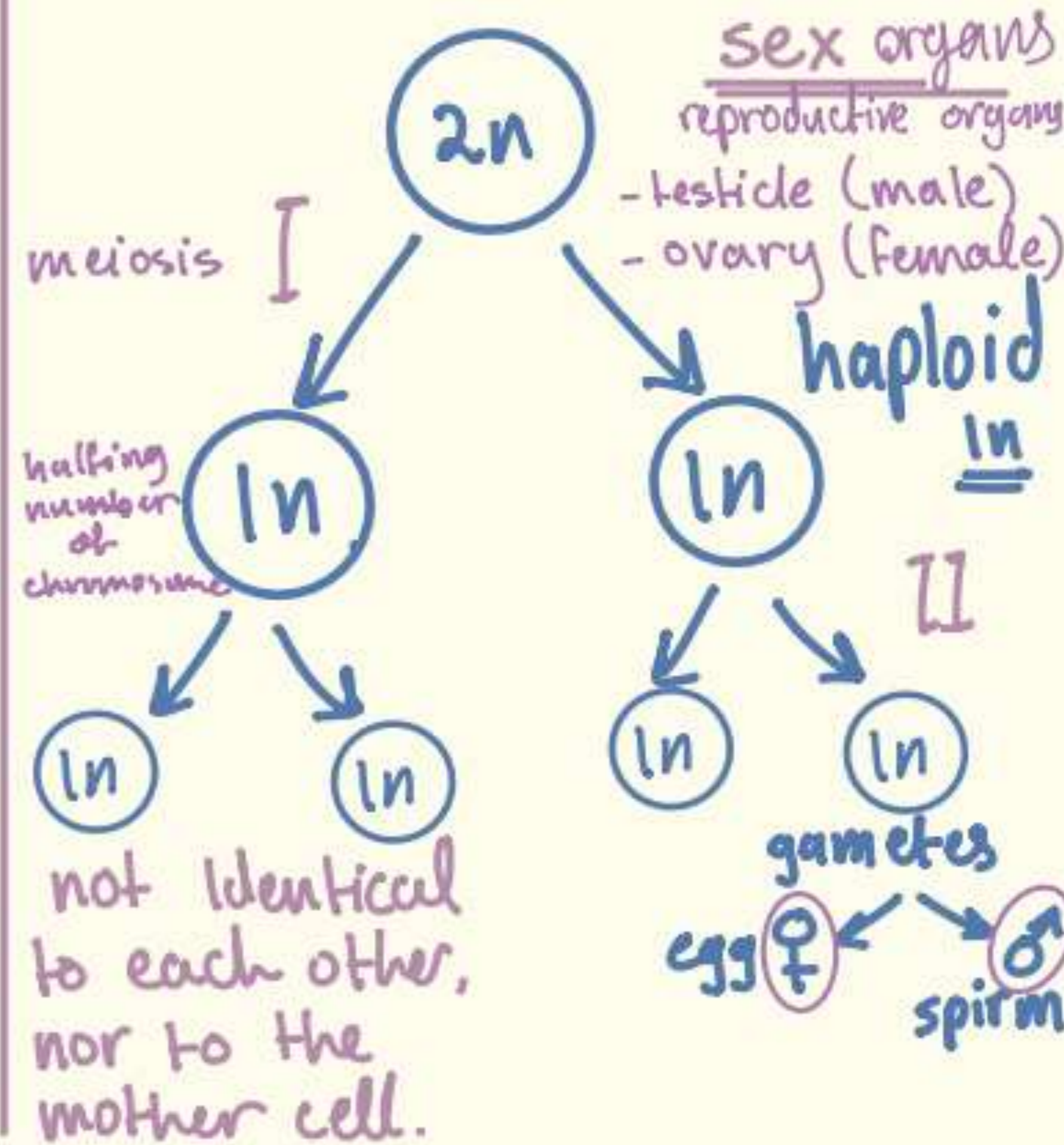
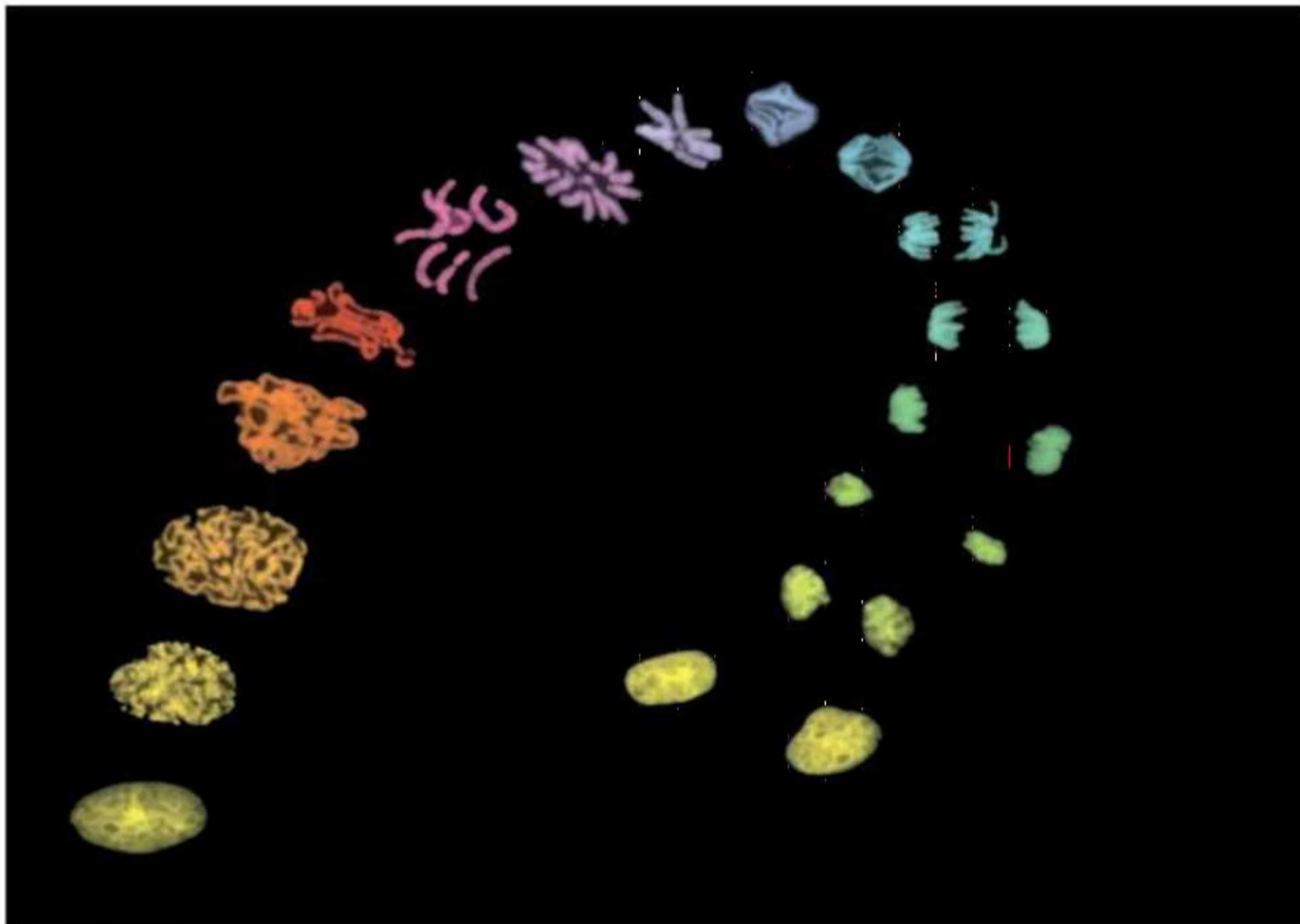
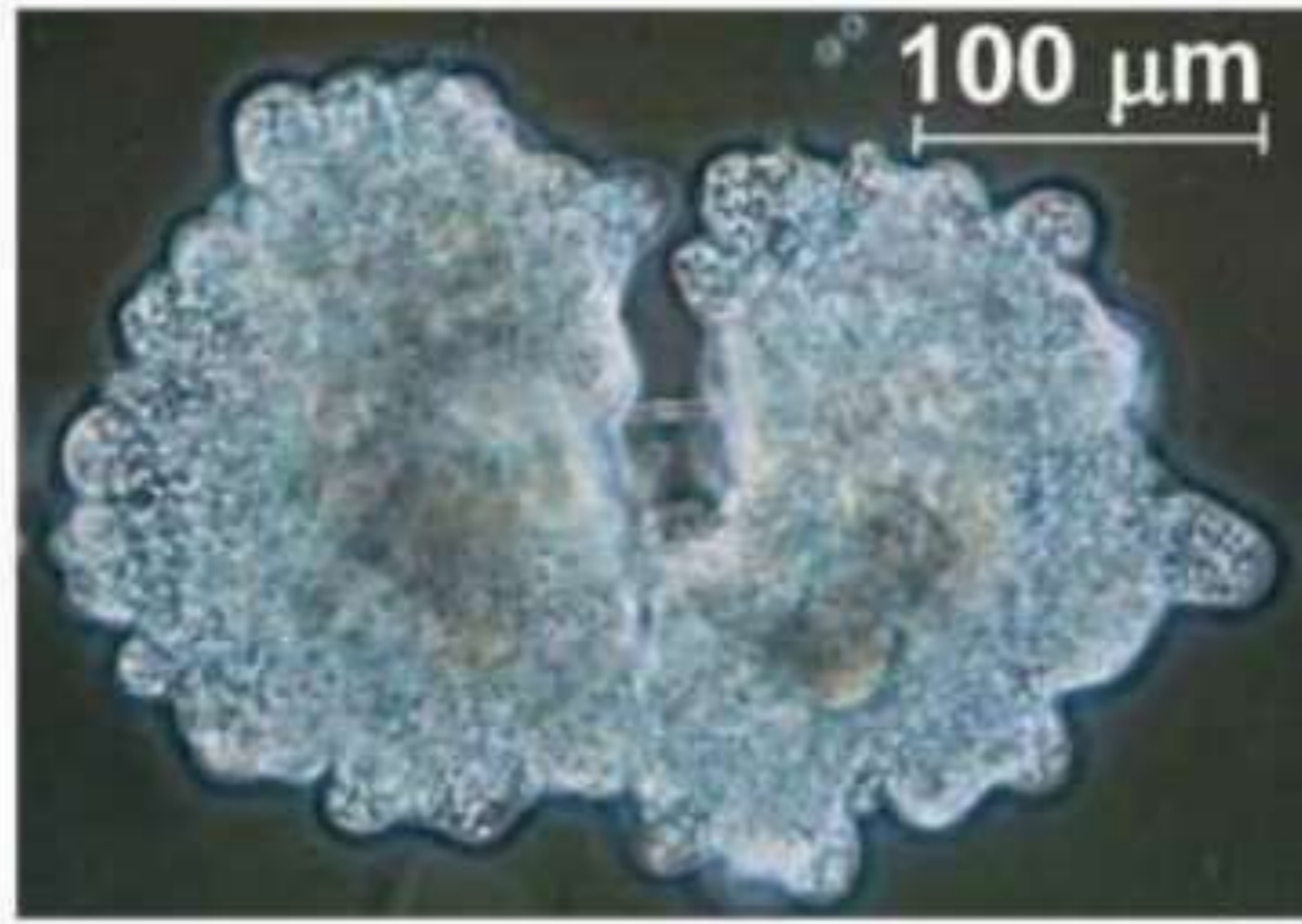


Figure 12.1



- In unicellular organisms, division of one cell reproduces the entire organism
- Multicellular organisms depend on cell division for
 - Development from a fertilized cell ^{zygote}
 - Growth
 - Repair
- Cell division is an integral part of the **cell cycle**, the life of a cell from formation to its own division

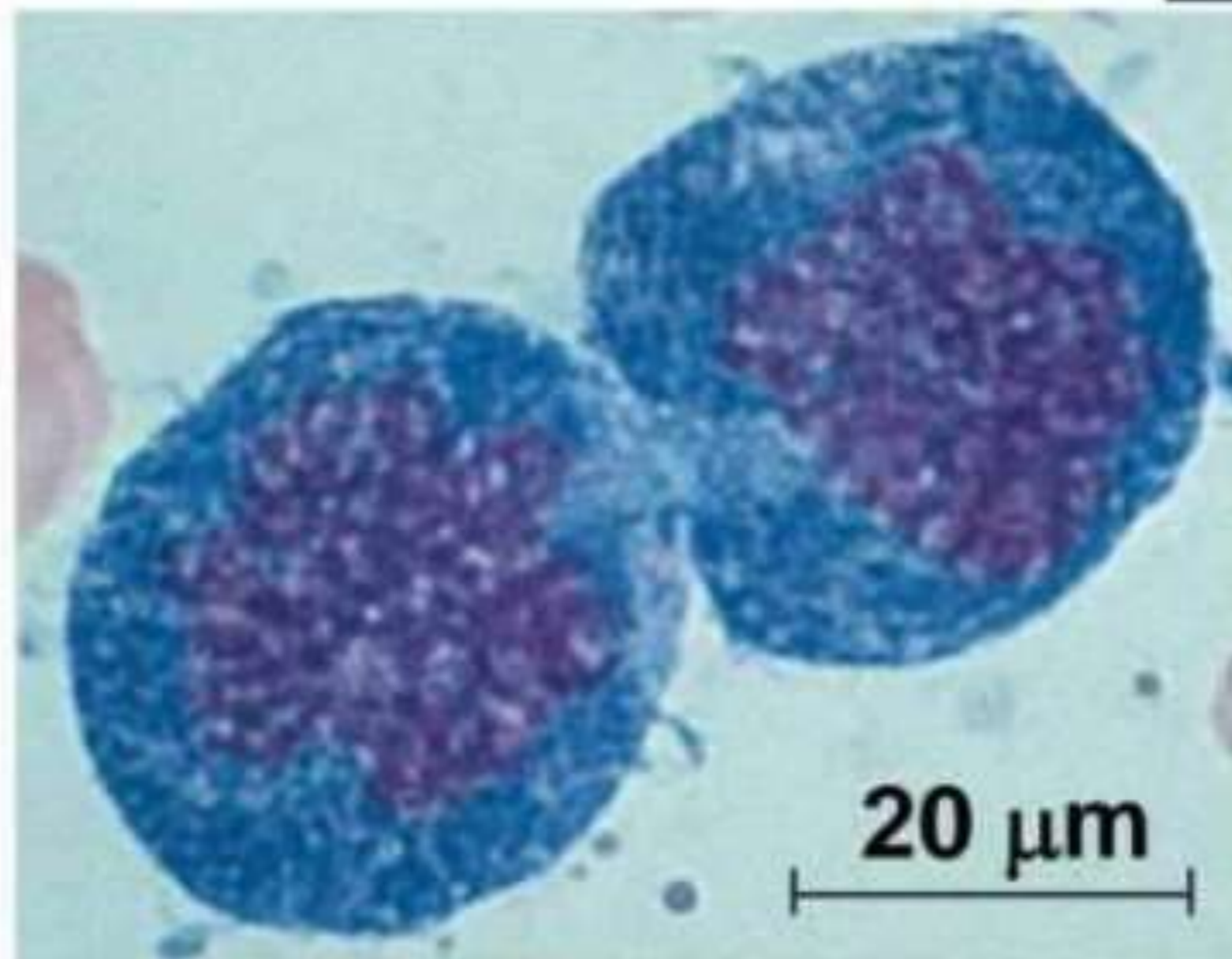
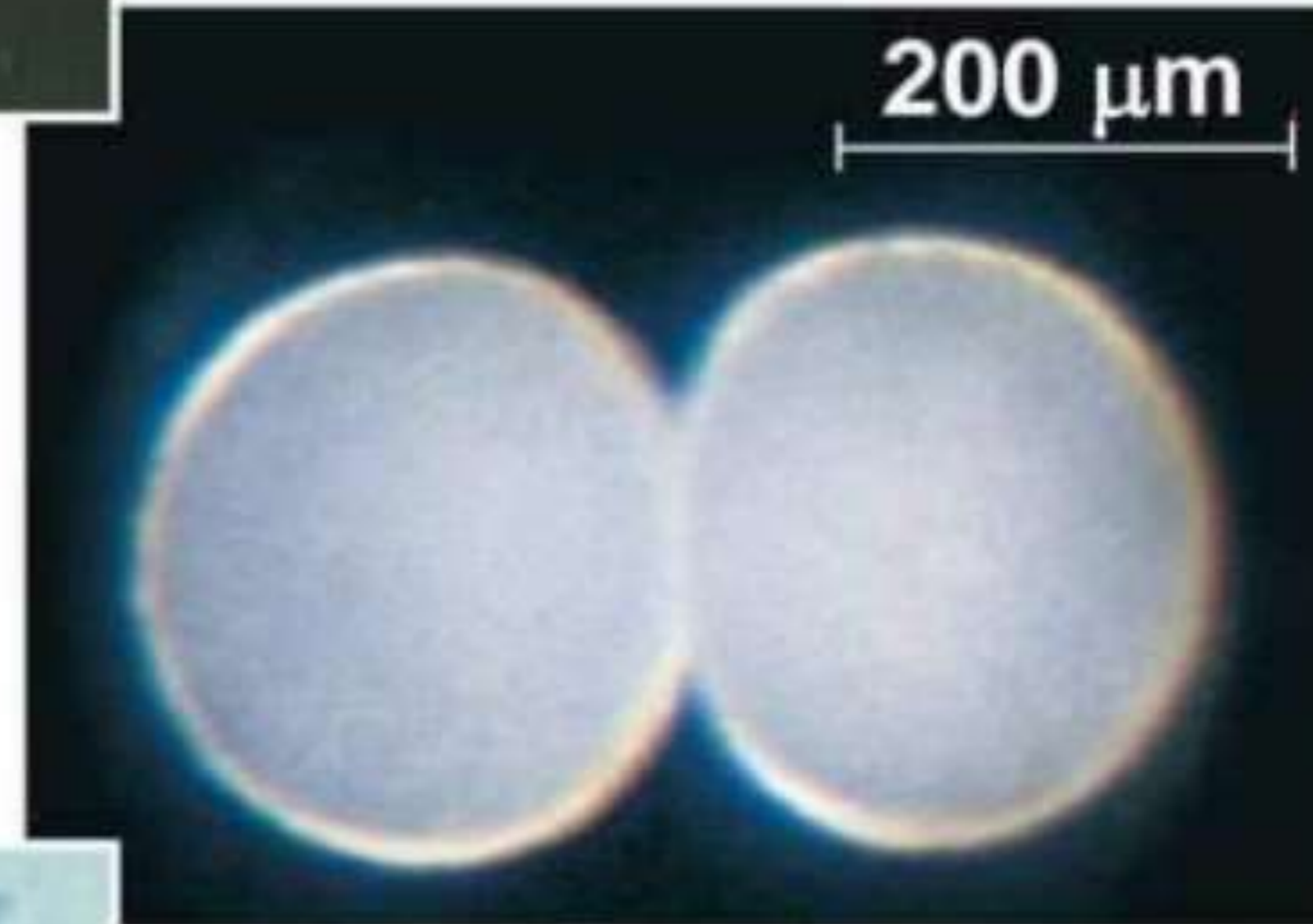
Figure 12.2



◀ (a) Reproduction

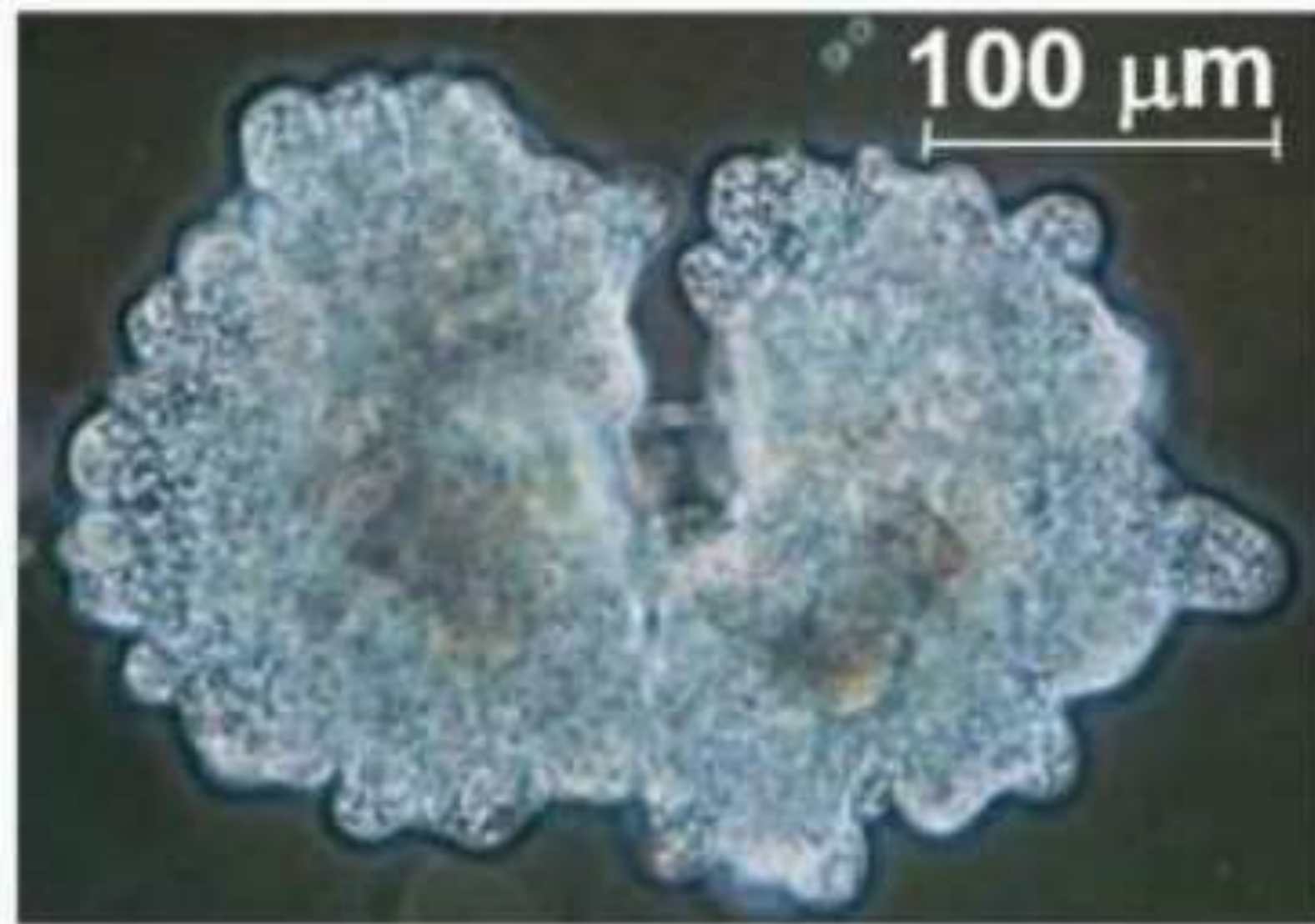
mitosis → asexual production
≠
not

▶ (b) Growth and development



↗ repair
◀ (c) Tissue renewal

Figure 12.2a



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◀ (a) Reproduction

▶ **(b) Growth and development**

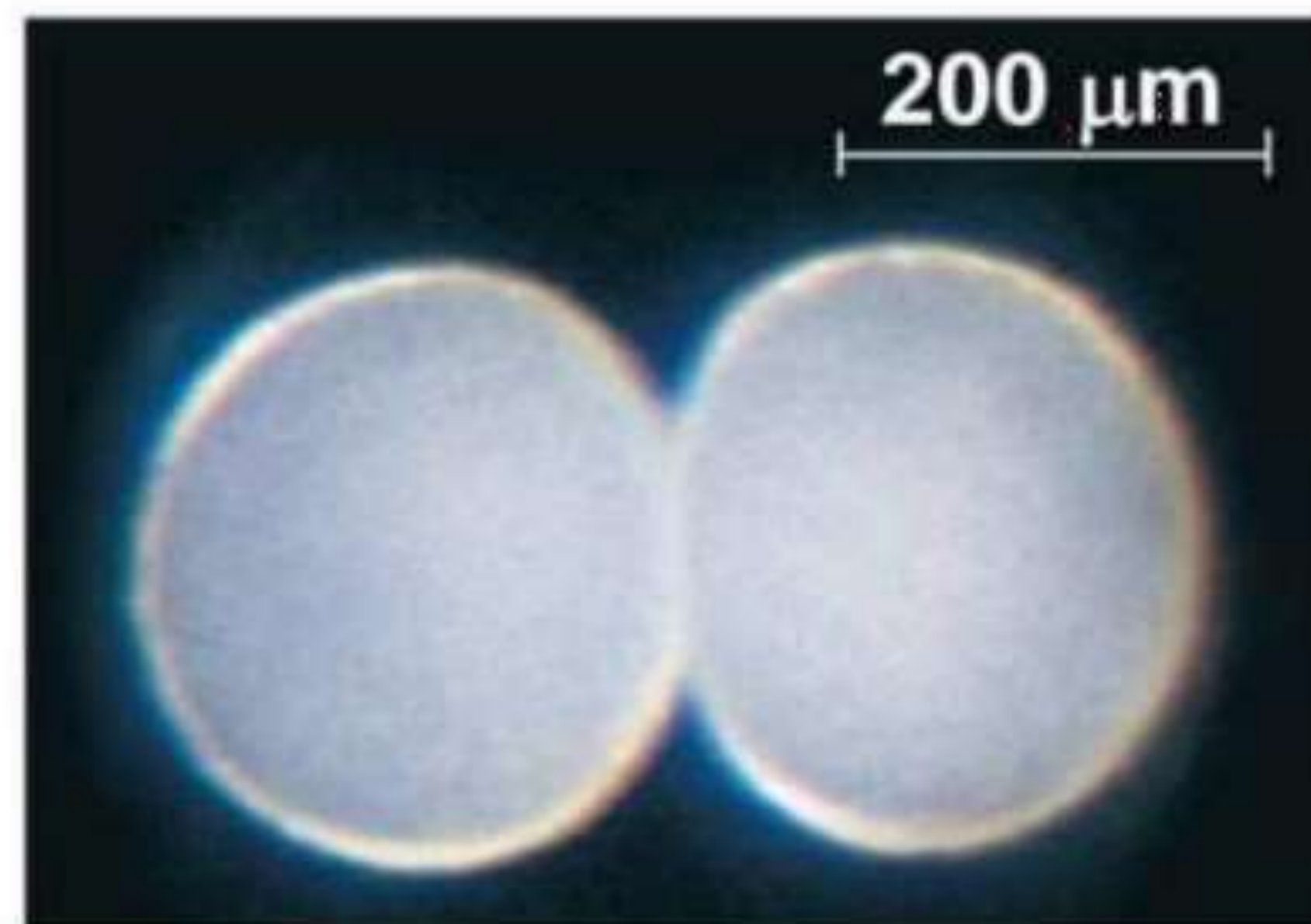
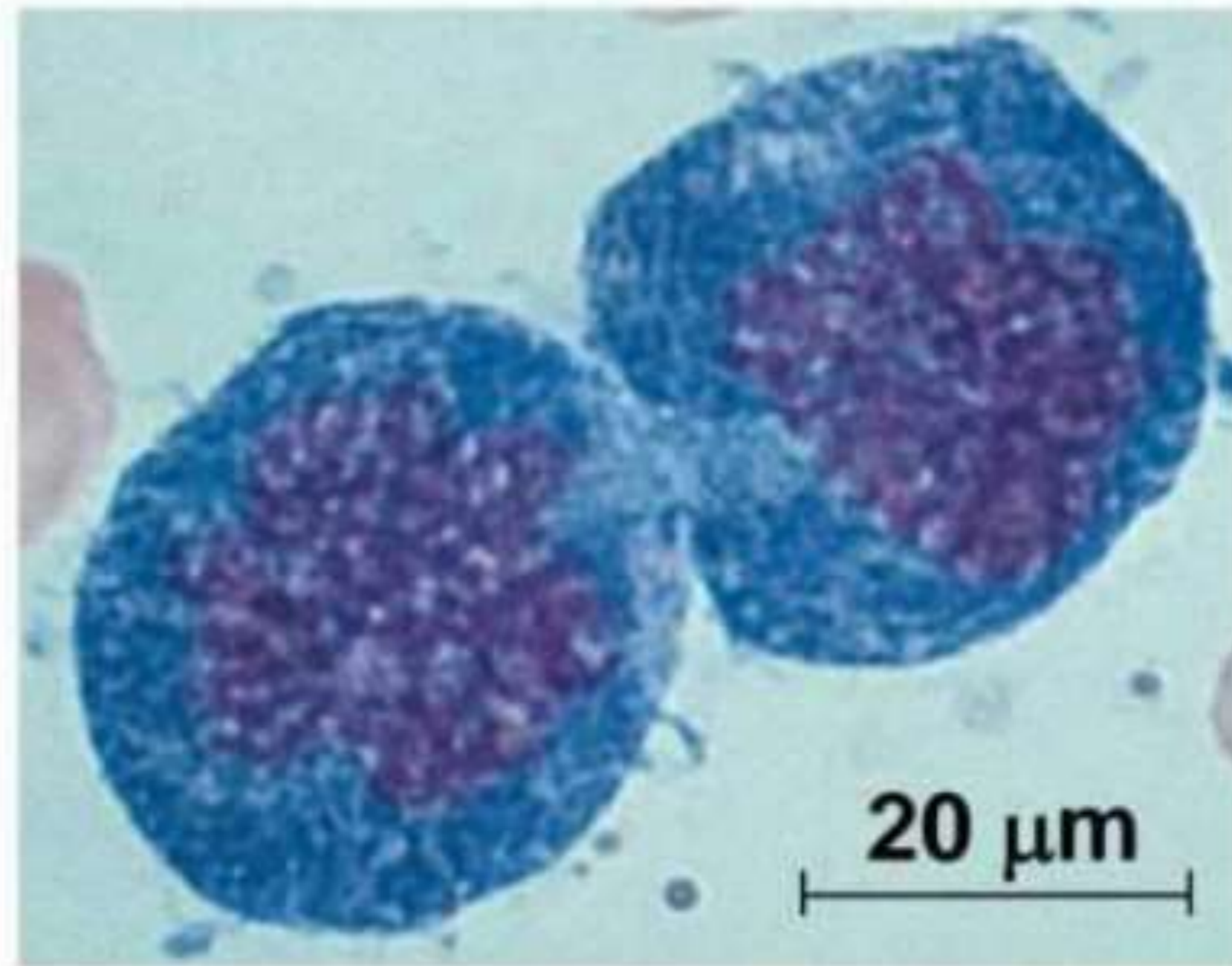


Figure 12.2c



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◀ (c) Tissue renewal

Concept 12.1: Most cell division results in genetically identical daughter cells

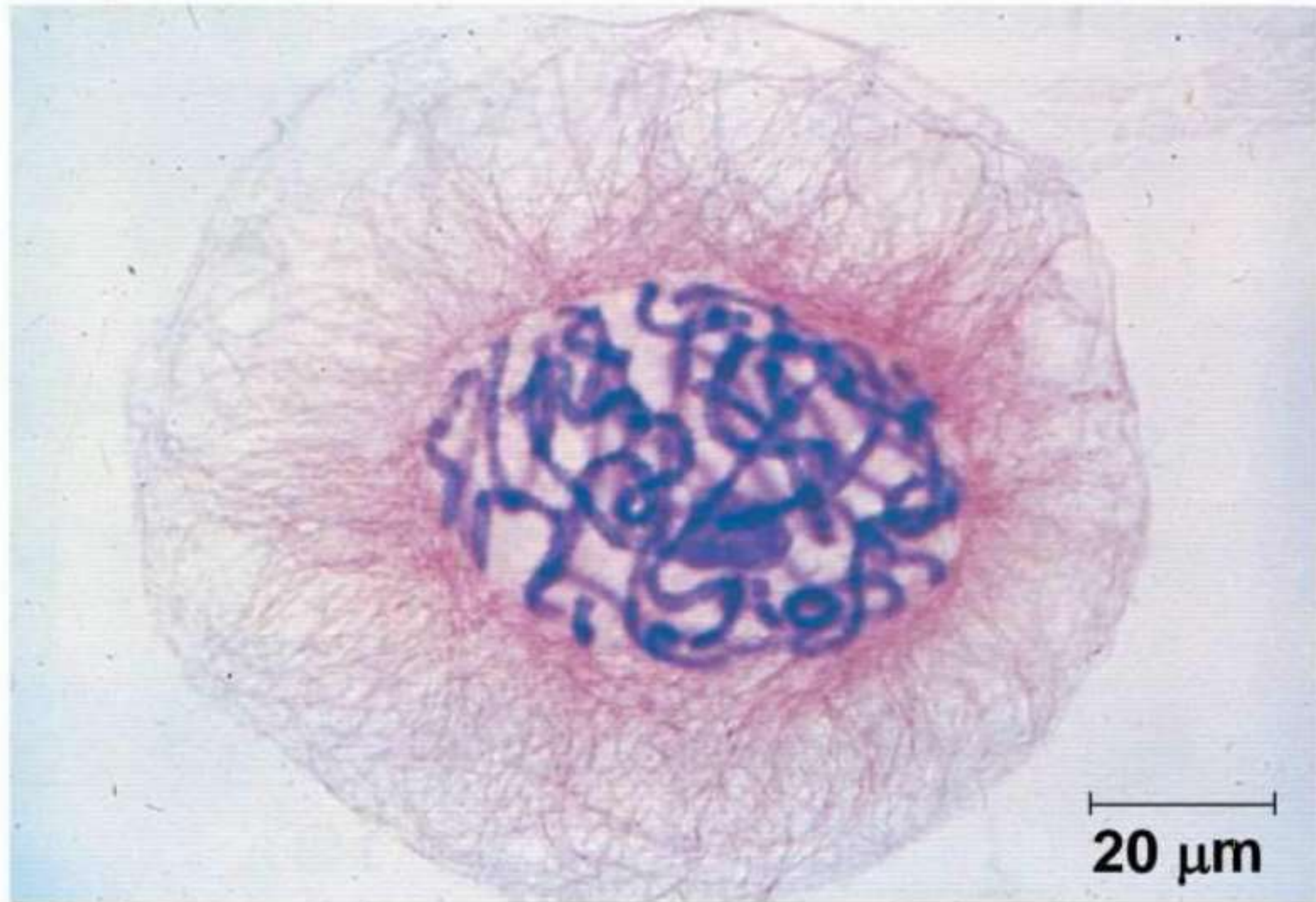
- Most cell division results in daughter cells with identical genetic information, DNA
- The exception is meiosis, a special type of division that can produce sperm and egg cells

Cellular Organization of the Genetic Material

23 pair of chromosome
"genetic makeup" ← الجينوم

- All the DNA in a cell constitutes the cell's **genome**
- A genome can consist of a single DNA molecule (common in prokaryotic cells) or a number of DNA molecules (common in eukaryotic cells)
- DNA molecules in a cell are packaged into **chromosomes**

Figure 12.3



- Eukaryotic chromosomes consist of **chromatin**, a complex of DNA and protein that condenses during cell division
- Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus
- Somatic cells (nonreproductive cells) have two sets of chromosomes
- Gametes (reproductive cells: sperm and eggs) have half as many chromosomes as somatic cells

Distribution of Chromosomes During Eukaryotic Cell Division

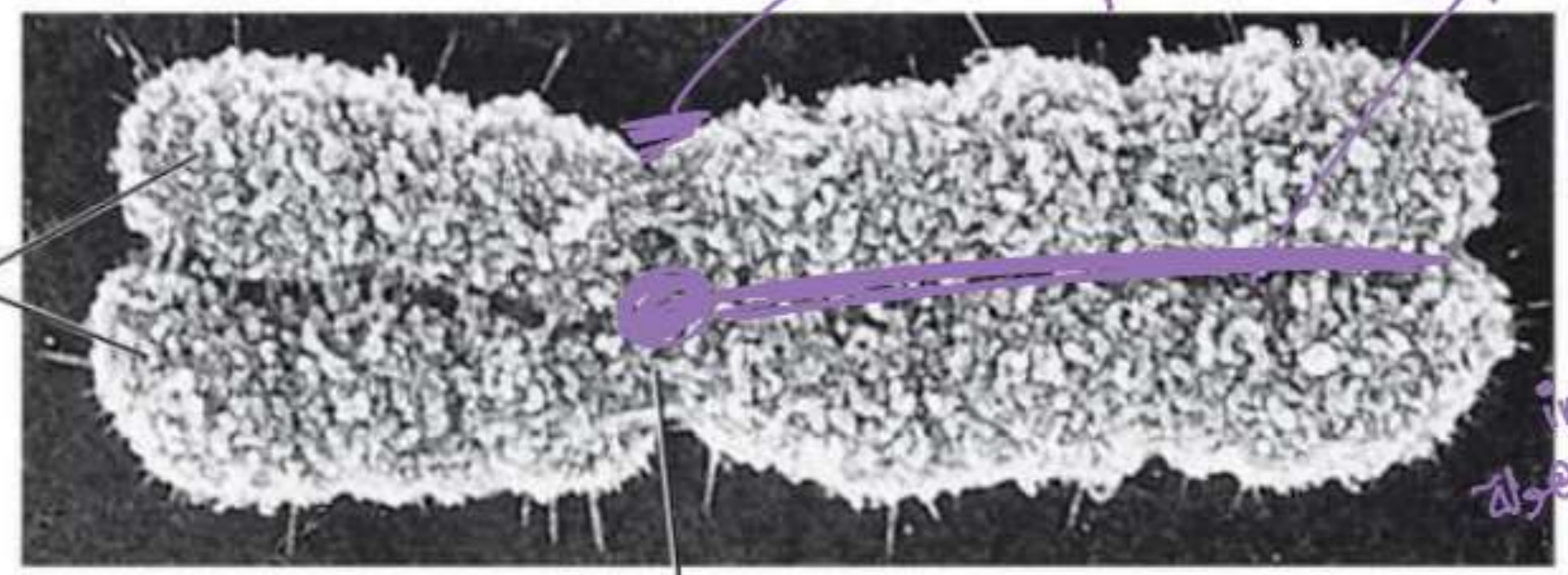
- In preparation for cell division, DNA is replicated and the chromosomes condense
- Each duplicated chromosome has two **sister chromatids** (joined copies of the original chromosome), which separate during cell division
- The **centromere** is the narrow “waist” of the duplicated chromosome, where the two chromatids are most closely attached

Figure 12.4

* chromosomes are thicker & shorter than chromatine

عوامل ثابتة مع بعض
① + ②

Sister chromatids



centromere المنطقة المركزية

kinetochore protein

② cohesin protein (gluing 2 sister chromatids) once it is active once it is inactive

① **Centromere**
 sister chromatide region/waste
 "التضييق" constriction

0.5 μm

↓
mitosis

- During cell division, the two sister chromatids of each duplicated chromosome separate and move into two nuclei
- Once separate, the chromatids are called chromosomes

cell cycle → stage make DNA replication
occurs before both meiosis & mitosis

Figure 12.5-1

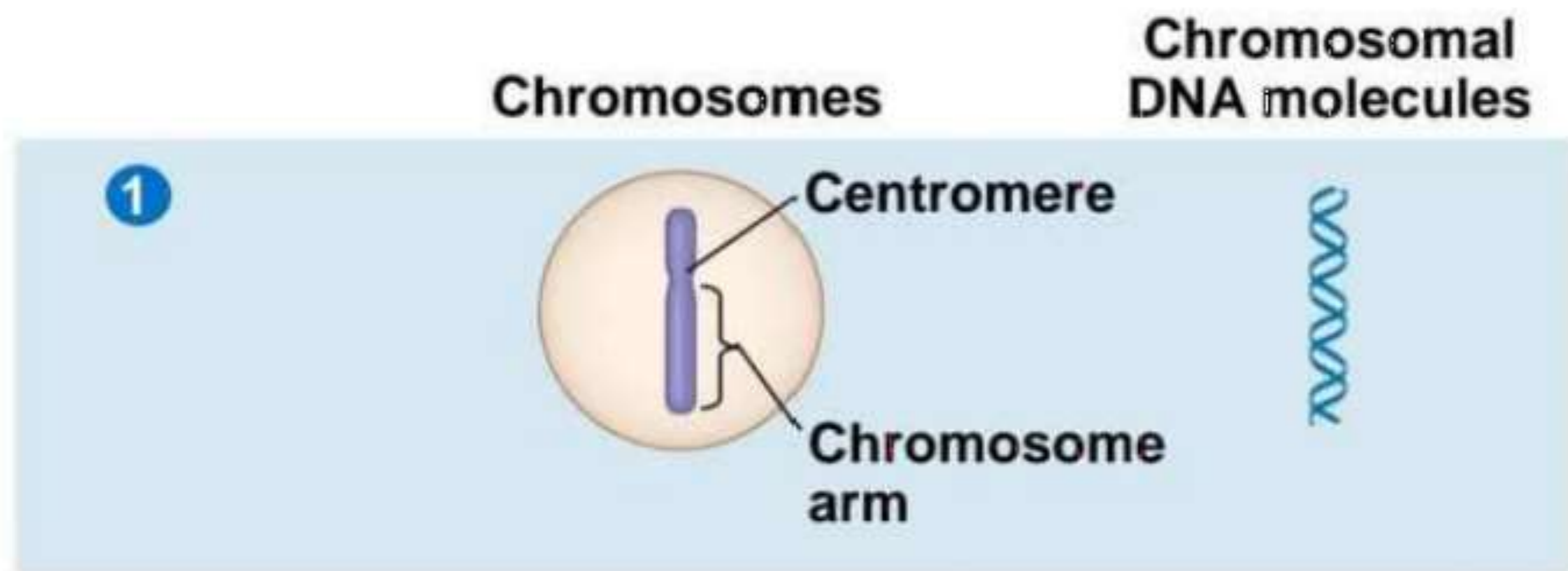


Figure 12.5-2

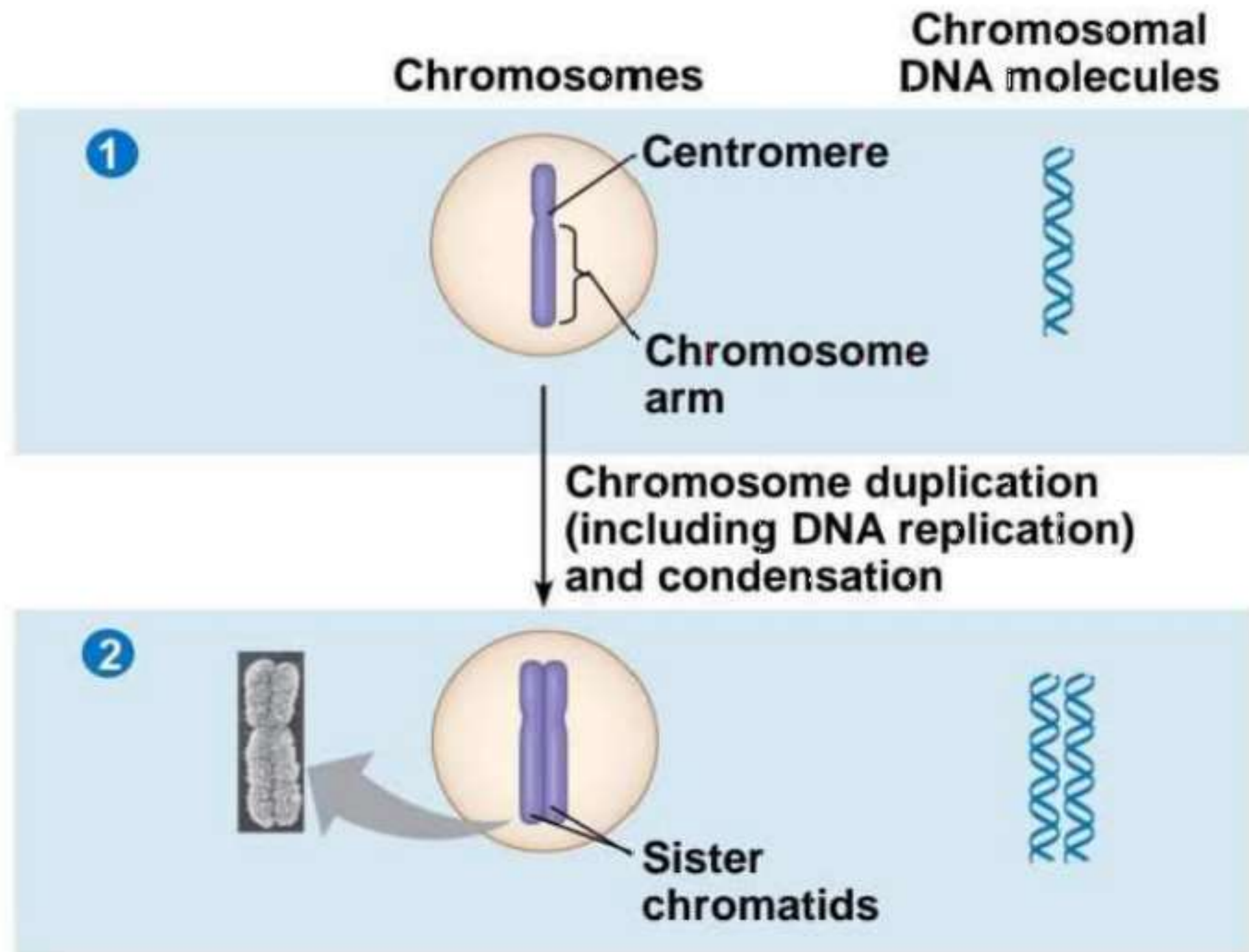
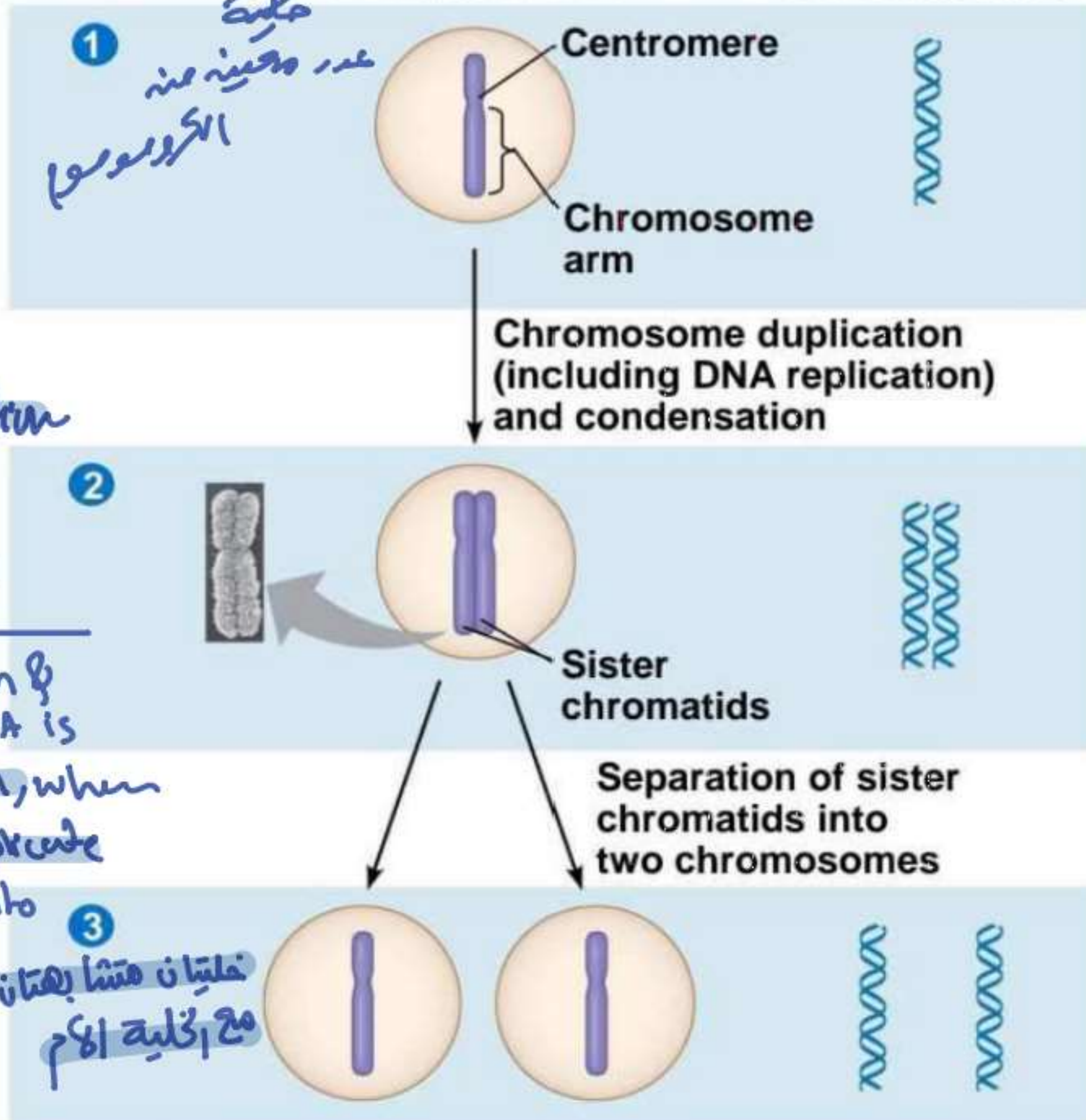


Figure 12.5-3

Chromosomes

Chromosomal DNA molecules



عشان تلبس وتنسجى بـ DNA لازم بتضاعف بالانز

DNA replication
one step on cell cycle

before division & replication, DNA is a **chromatin**, when it wants to **replicate** it turns into **chromosomes**

- Eukaryotic cell division consists of
 - 1st – **Mitosis**, the division of the genetic material in the nucleus
 - 2nd – **Cytokinesis**, the division of the cytoplasm
- Gametes are produced by a variation of cell division called **meiosis**
- Meiosis yields nonidentical daughter cells that have only one set of chromosomes, half as many as the parent cell

Concept 12.2: The mitotic phase alternates with interphase in the cell cycle

- In 1882, the German anatomist Walther Flemming developed dyes to observe chromosomes during mitosis and cytokinesis

Phases of the Cell Cycle

interphase + M phase

in every eukaryotic cell
same steps, But the length of the cycle differs, in human (24 h)

- The cell cycle consists of
 - **Mitotic (M) phase** (mitosis and cytokinesis)
 - **Interphase** (cell growth and copying of chromosomes in preparation for cell division)

بالكثير عشانها تدخل M phase تكون خالية من الاكسجين

- Interphase (about 90% of the cell cycle) can be divided into subphases

- **G₁ phase** ("first gap")

cell is bigger
 all orgunits x 2 / except DNA + centrosome
 200 mitochondria → 100 mitochondria
 prepares proteins & everything needed for S phase

everything needed for replication is already prepared in G₁

- **S phase** ("synthesis")

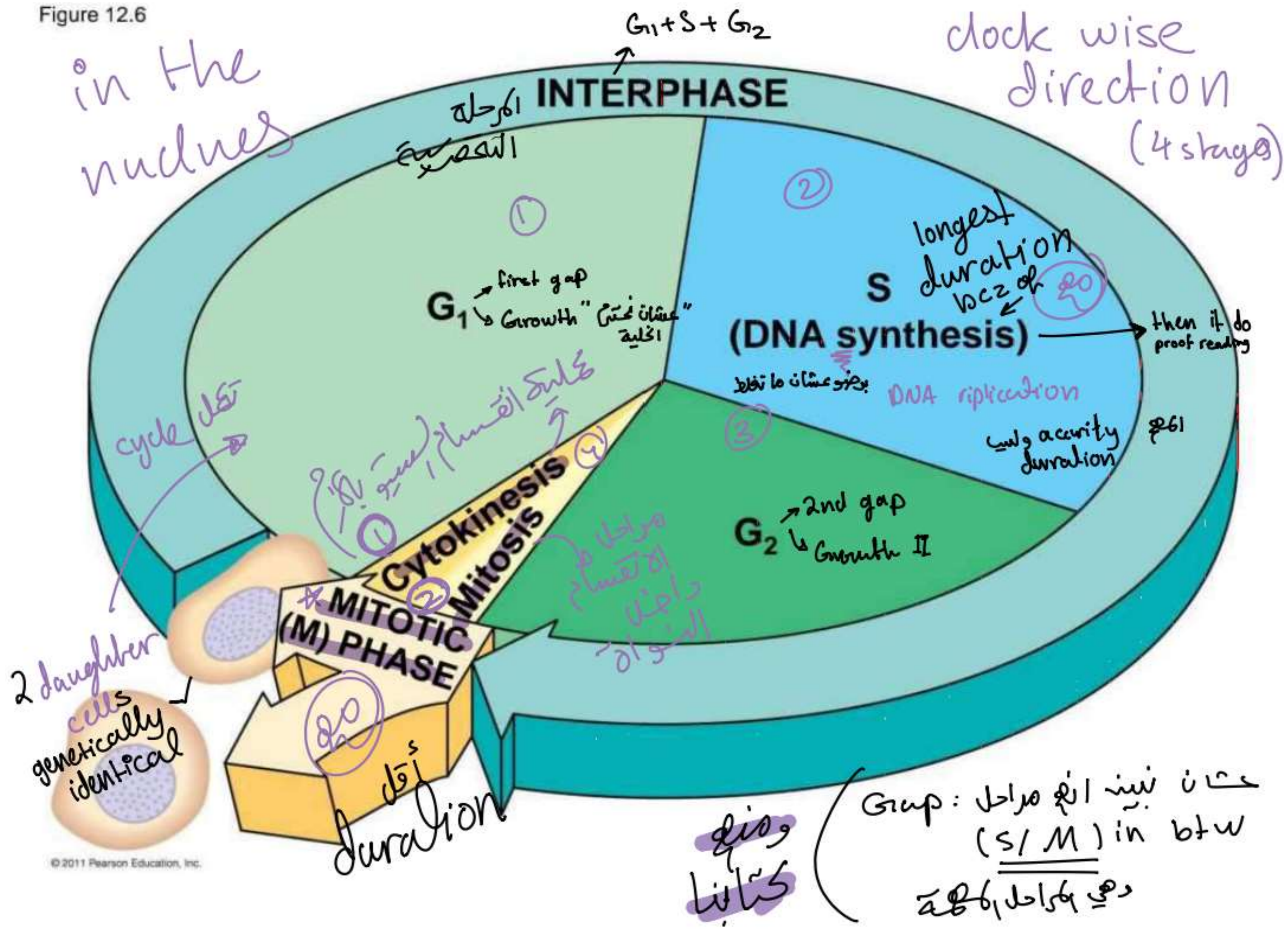
at end: 2 identical copies of DNA
 centrosome contains centrioles / DNA centrosome

- **G₂ phase** ("second gap")

checking up on having everything needed for (M) phase
 اي شي ناقص وقتها في M phase ترجع تصنع

- The cell grows during all three phases, but chromosomes are duplicated only during the S phase

Figure 12.6



M phase

- ① Mitosis is conventionally divided into five phases

تستغرق وقتاً طويلاً

Ⓐ **Prophase** beginning

Ⓑ **Prometaphase** in btw of Ⓐ + Ⓒ

Ⓒ **Metaphase** الاستواء

Ⓓ **Anaphase** انفصال

Ⓔ **Telophase** النهاية

- ② Cytokinesis overlaps the latter stages of mitosis



BioFlix: Mitosis

Figure 12.7

Mitosis stages in Animal cells

almost same in plant cell

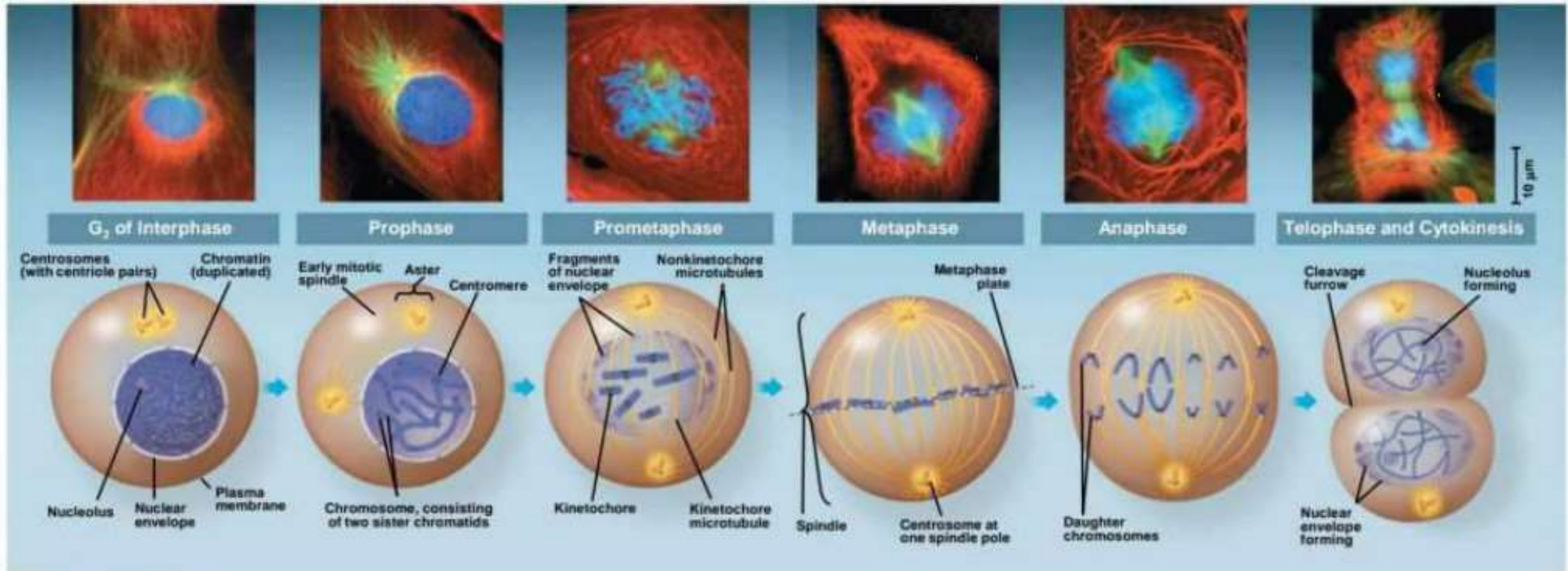
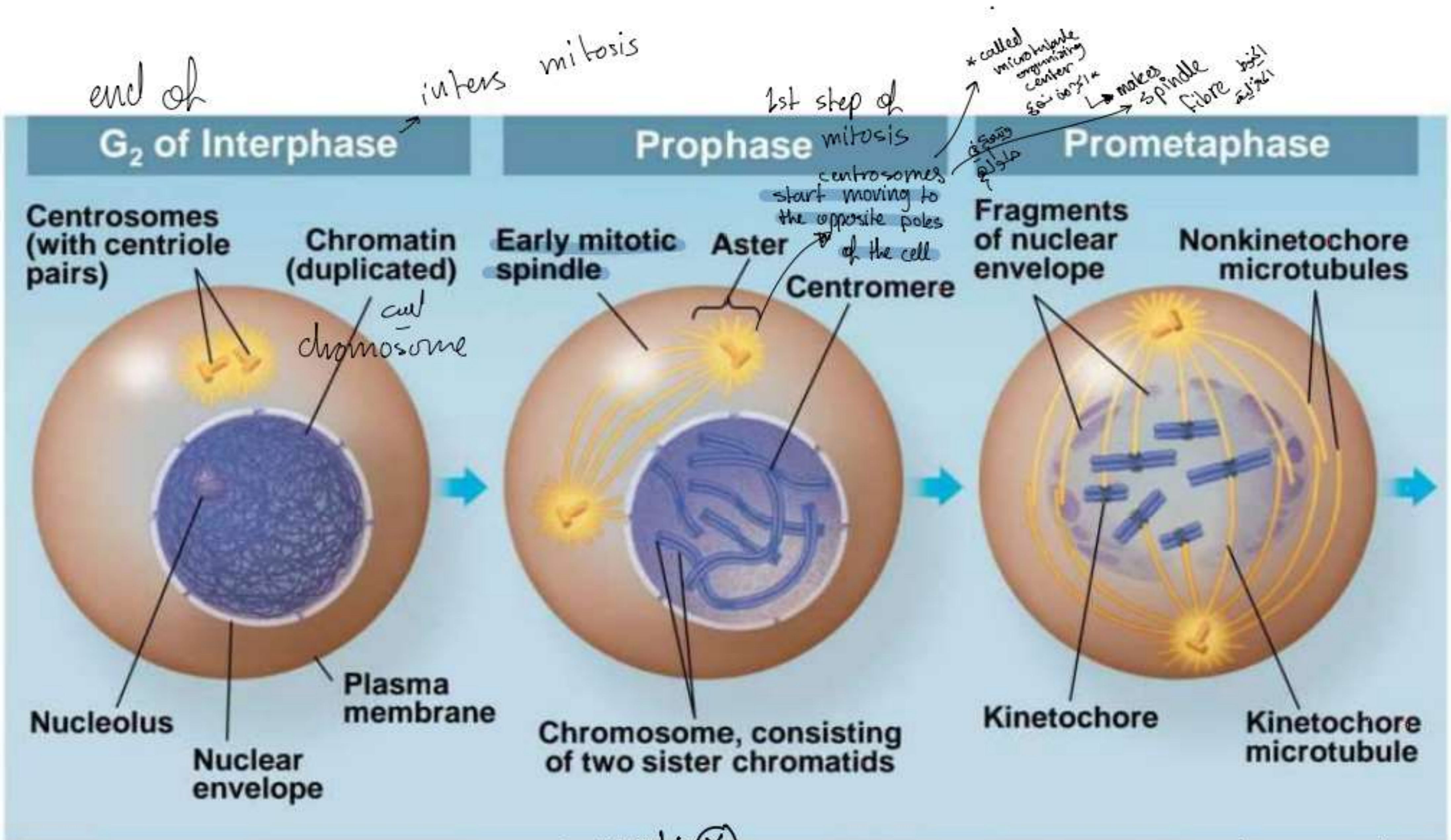


Figure 12.7a



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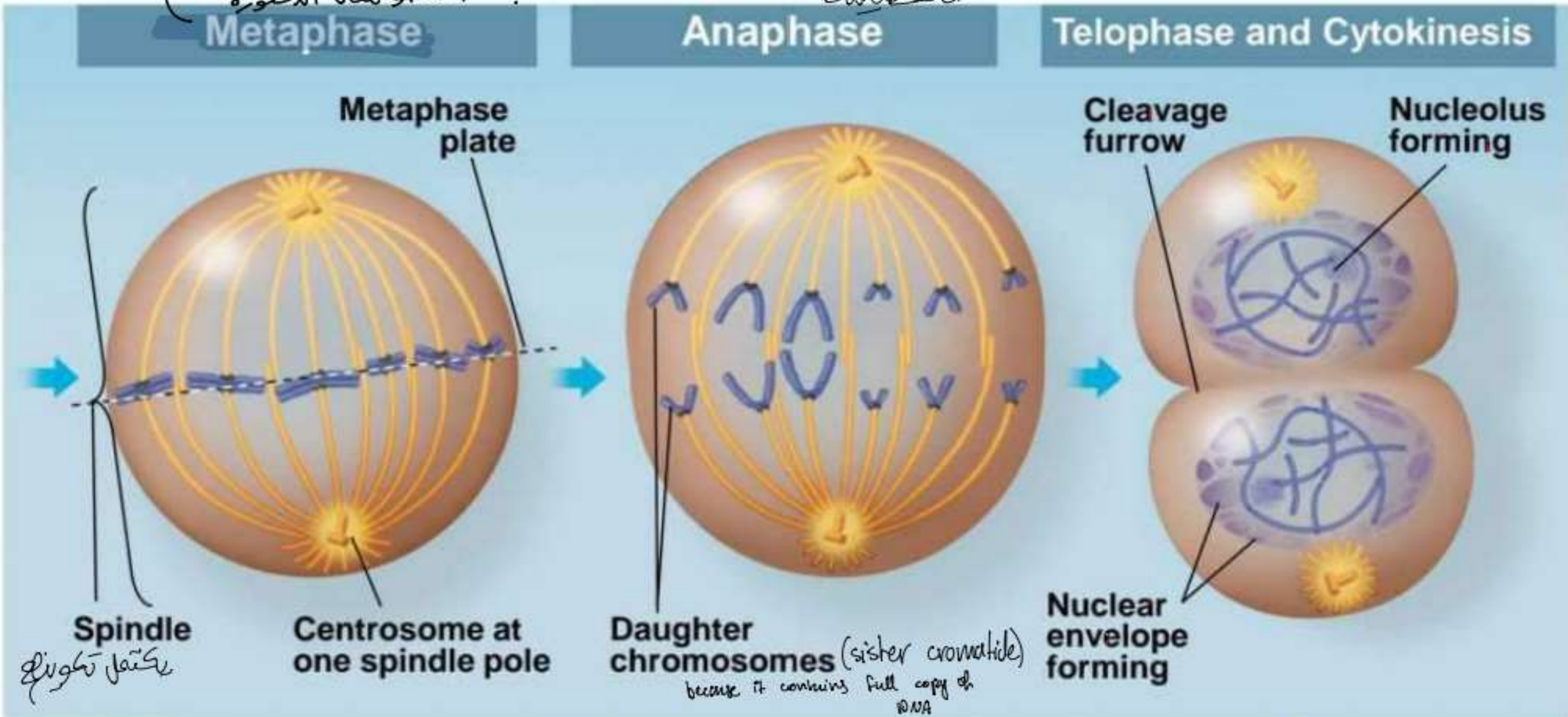
* chromatin (X)
 ↳ chromosomes ✓
 each chromosome consists of two sister chromatids & they become thicker + shorter & visible under microscope
 * nucleolus is gone: (→ disappear)

* No nuclear envelope
 * NO nucleus
 centrosomes is almost stable now on poles →
 spindle formation
 mitotic spindle
 spindle formation
 metaphase

Figure 12.7b

→ m phase: 1 hour
 metaphase: 15 minute
 احوال مرحلة في M phase
 ابعها / ما بروت اذا عليا صبح هيك
 سب هار هو مثال الكنتورة

انقسام خلية



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يكتفل تكويف
 * spindle → [two centrosomes found on opposite poles, + 3 types of spindle microtubules]
 * chromosomes will be lined at metaphase plate
 وهذا سبب تسمية المرحلة

* 2 sister chromatide seperates
 1. inactivation of cohesin protein
 2. shorting & contraction of kinetochore microtubule
 وذا سبب ما سكت / sister chromatide
 [centromeric division] /
 3. elongated / sister ...
 overlapping / non-kinetochore

* لار تكويف الانقسام
 - nucleolus
 - nuclear envelop
 - one cell / two nucleolus
 each one of them has same number of chromosome
 - sister chromatide → chromosome

Figure 12.7c

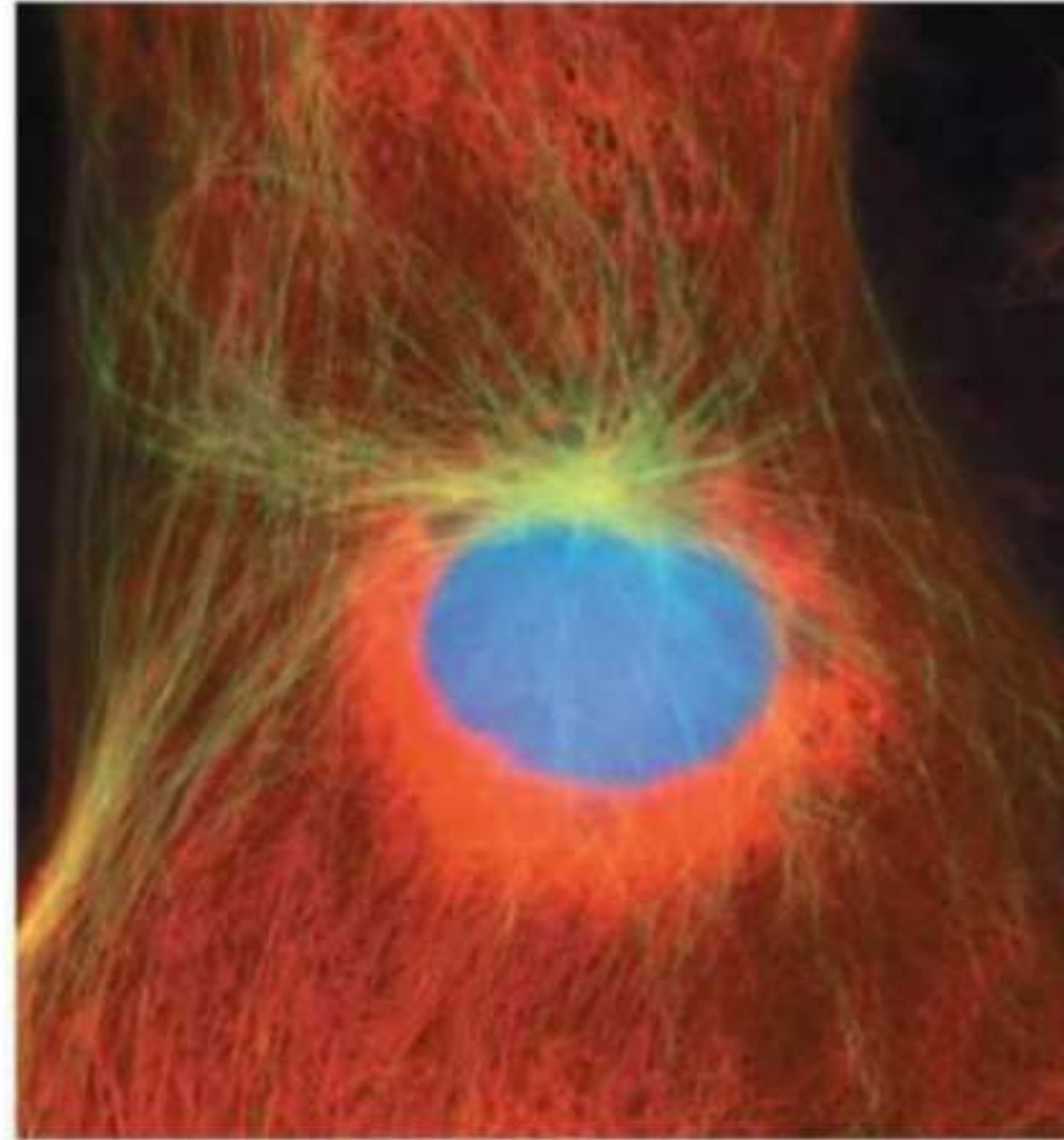
this permits
elongation of
the cell



Figure 12.7d

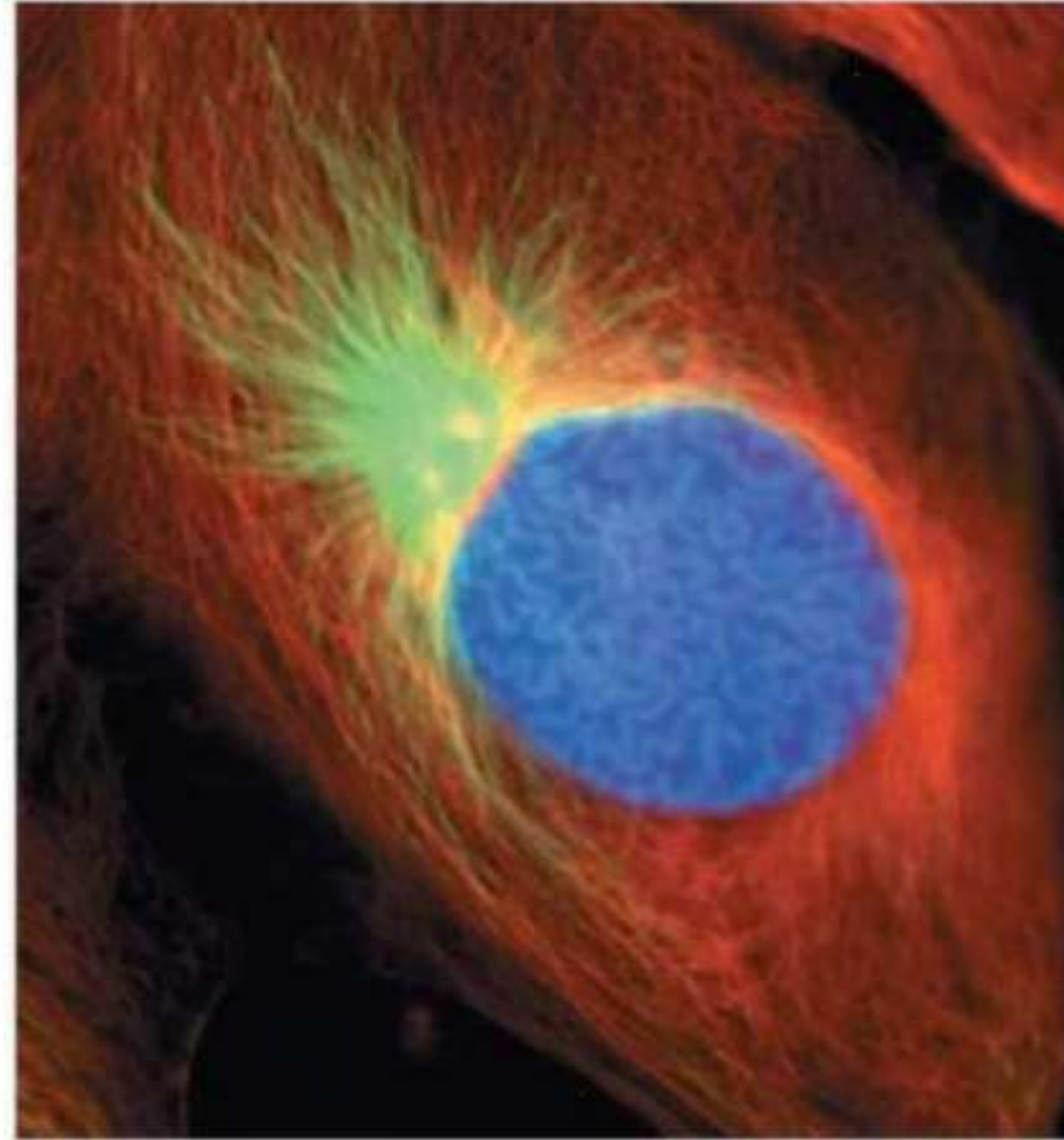


Figure 12.7e



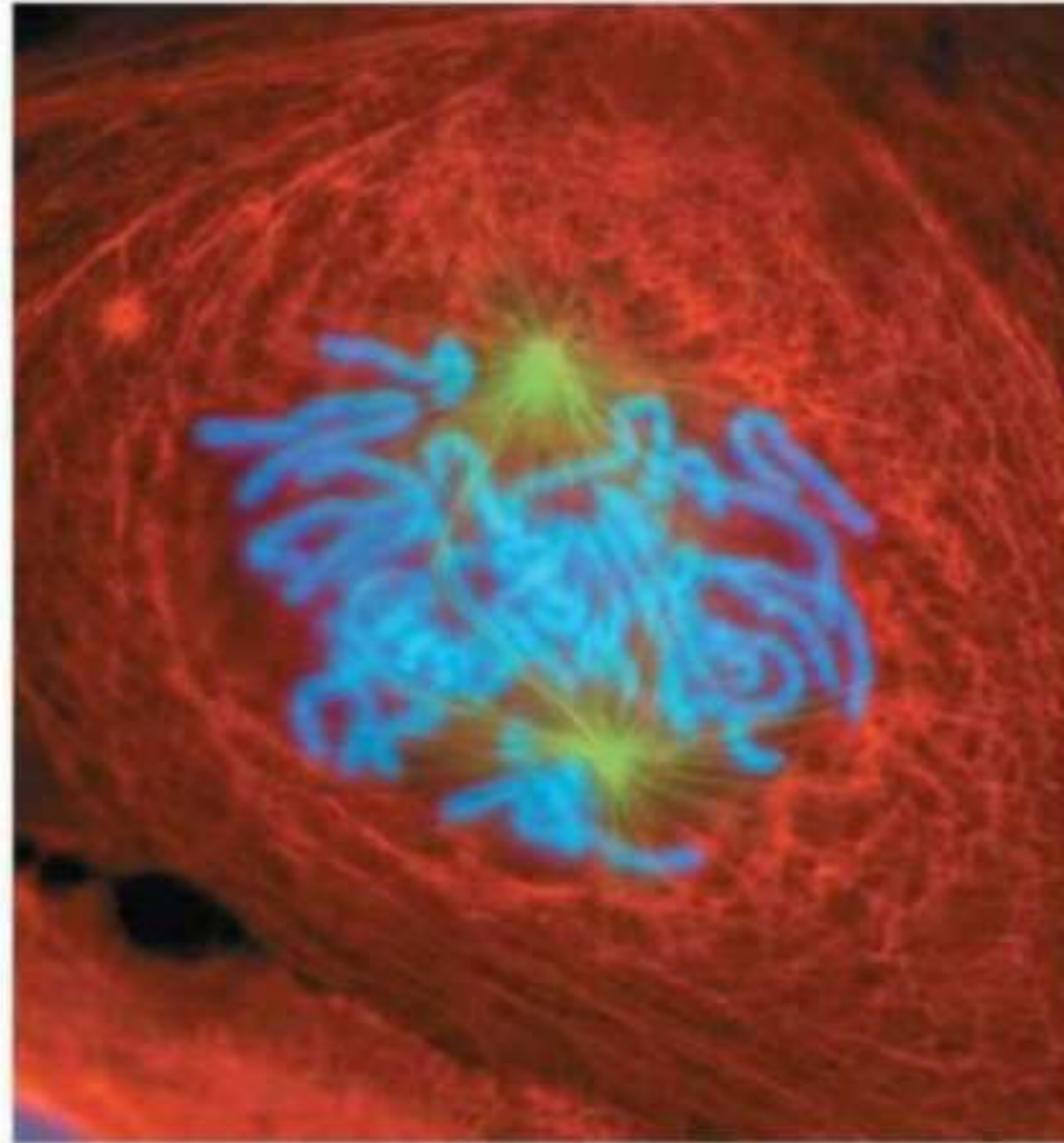
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Figure 12.7f



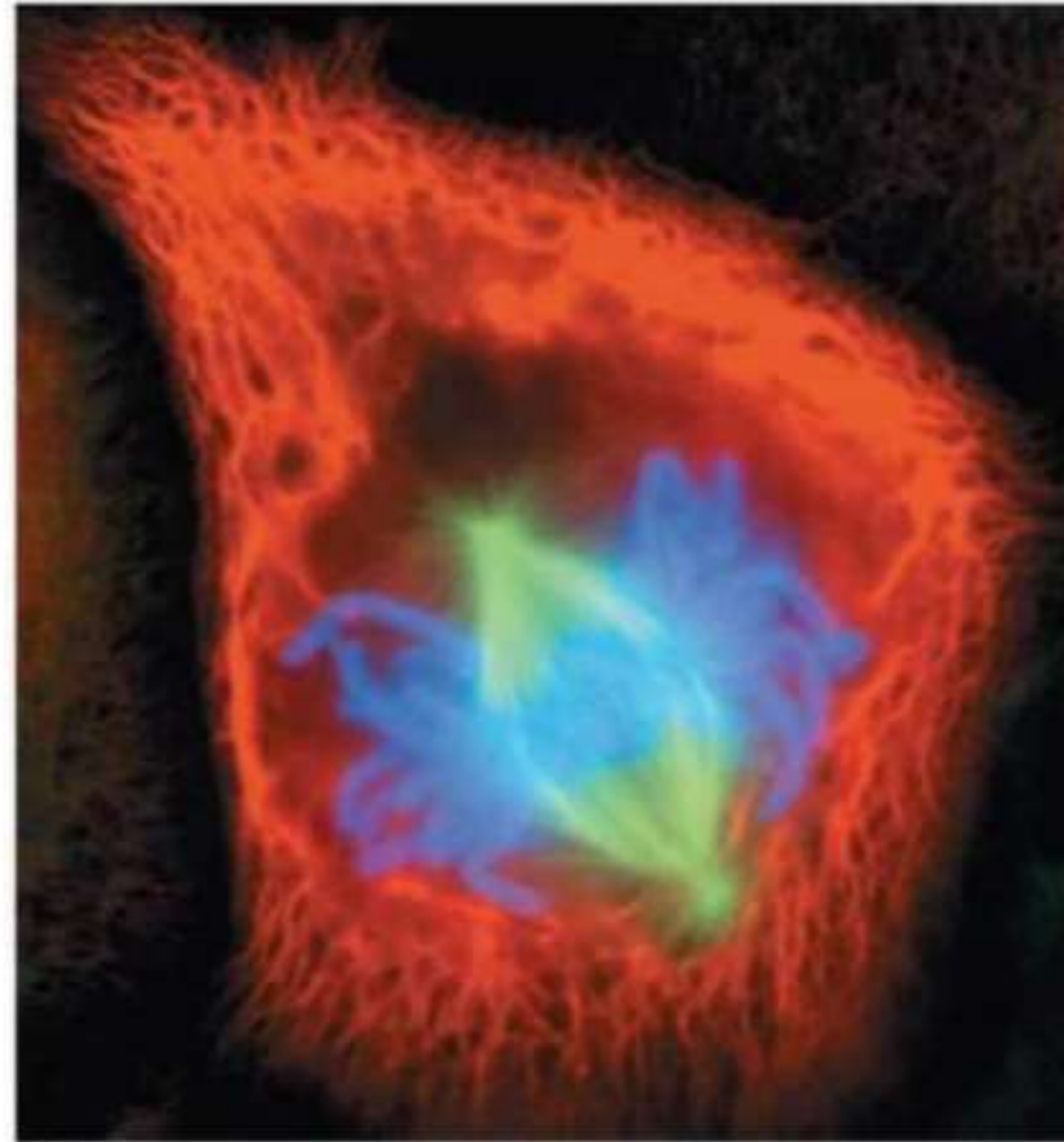
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Figure 12.7g



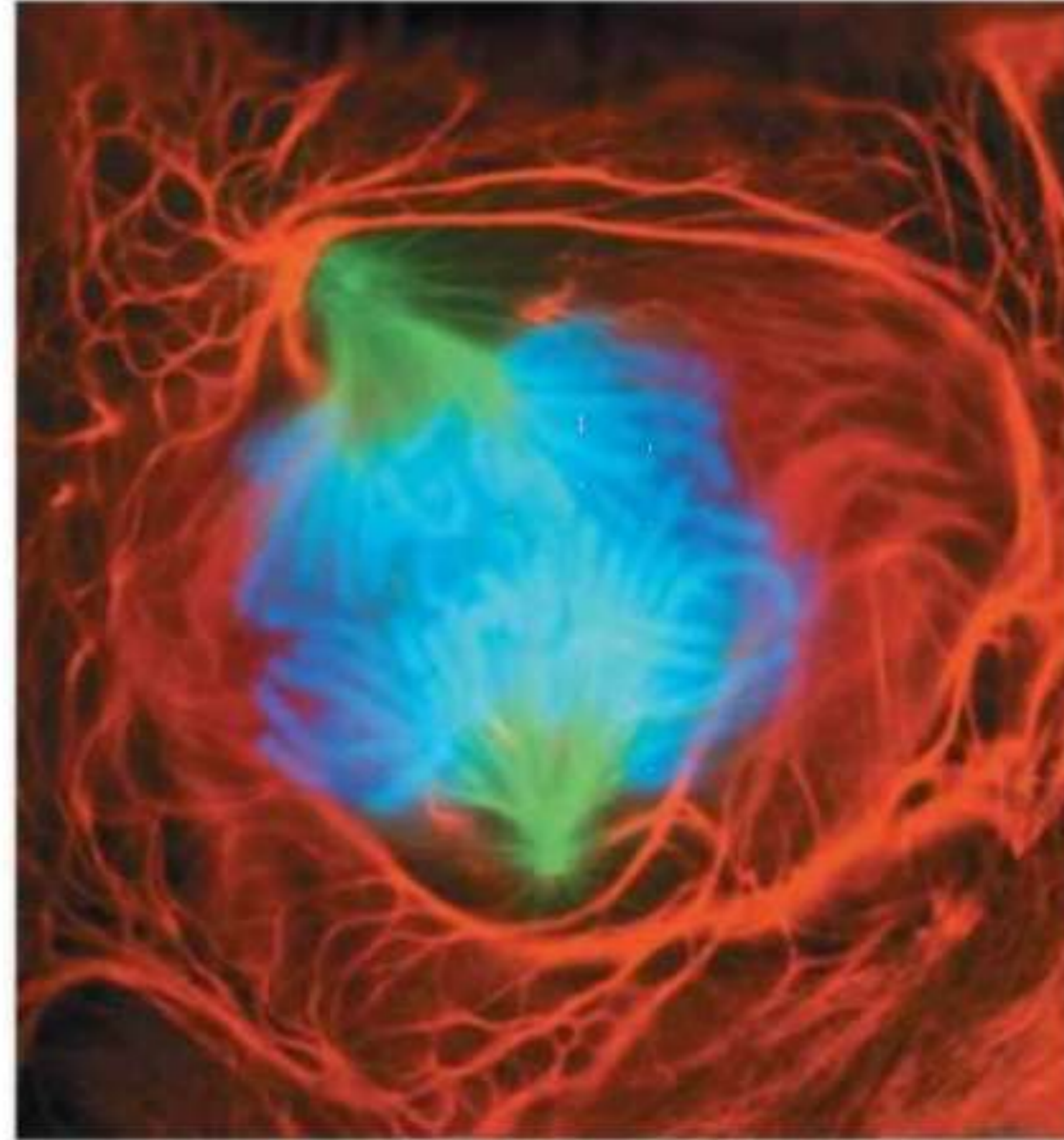
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Figure 12.7h



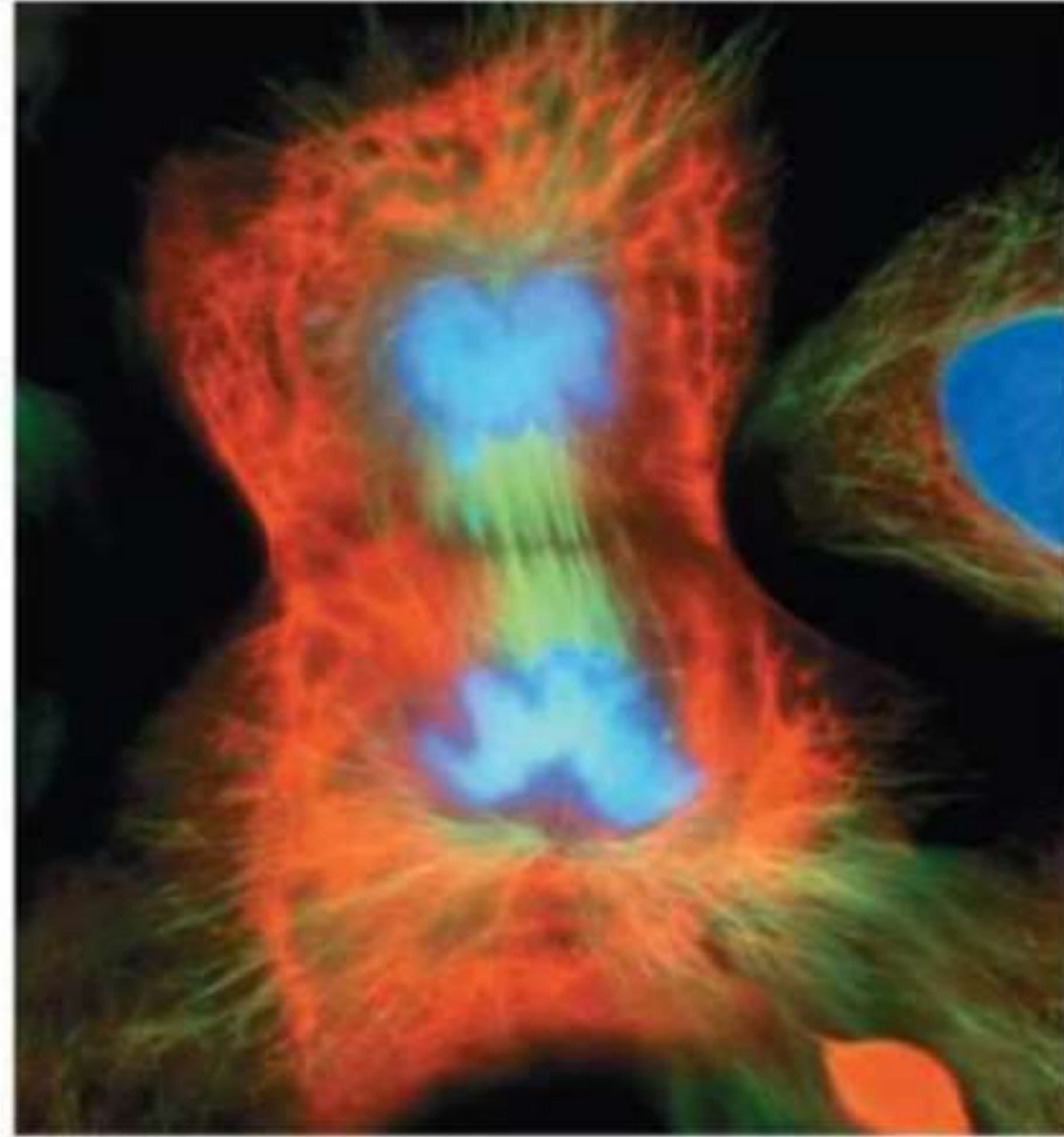
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Figure 12.7i



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Figure 12.7j



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The Mitotic Spindle: *A Closer Look*

- The **mitotic spindle** is a structure made of microtubules that controls chromosome movement during mitosis
- In animal cells, assembly of spindle microtubules begins in the **centrosome**, the microtubule organizing center
- The centrosome replicates during interphase, forming two centrosomes that migrate to opposite ends of the cell during prophase and prometaphase

- An **aster** (a radial array of short microtubules) extends from each centrosome
- The spindle includes the centrosomes, the spindle microtubules, and the asters

- During prometaphase, some spindle microtubules attach to the kinetochores of chromosomes and begin to move the chromosomes
- **Kinetochores** are protein complexes associated with centromeres
- At metaphase, the chromosomes are all lined up at the **metaphase plate**, an imaginary structure at the midway point between the spindle's two poles

Figure 12.8

3 types of spindle microtubules:

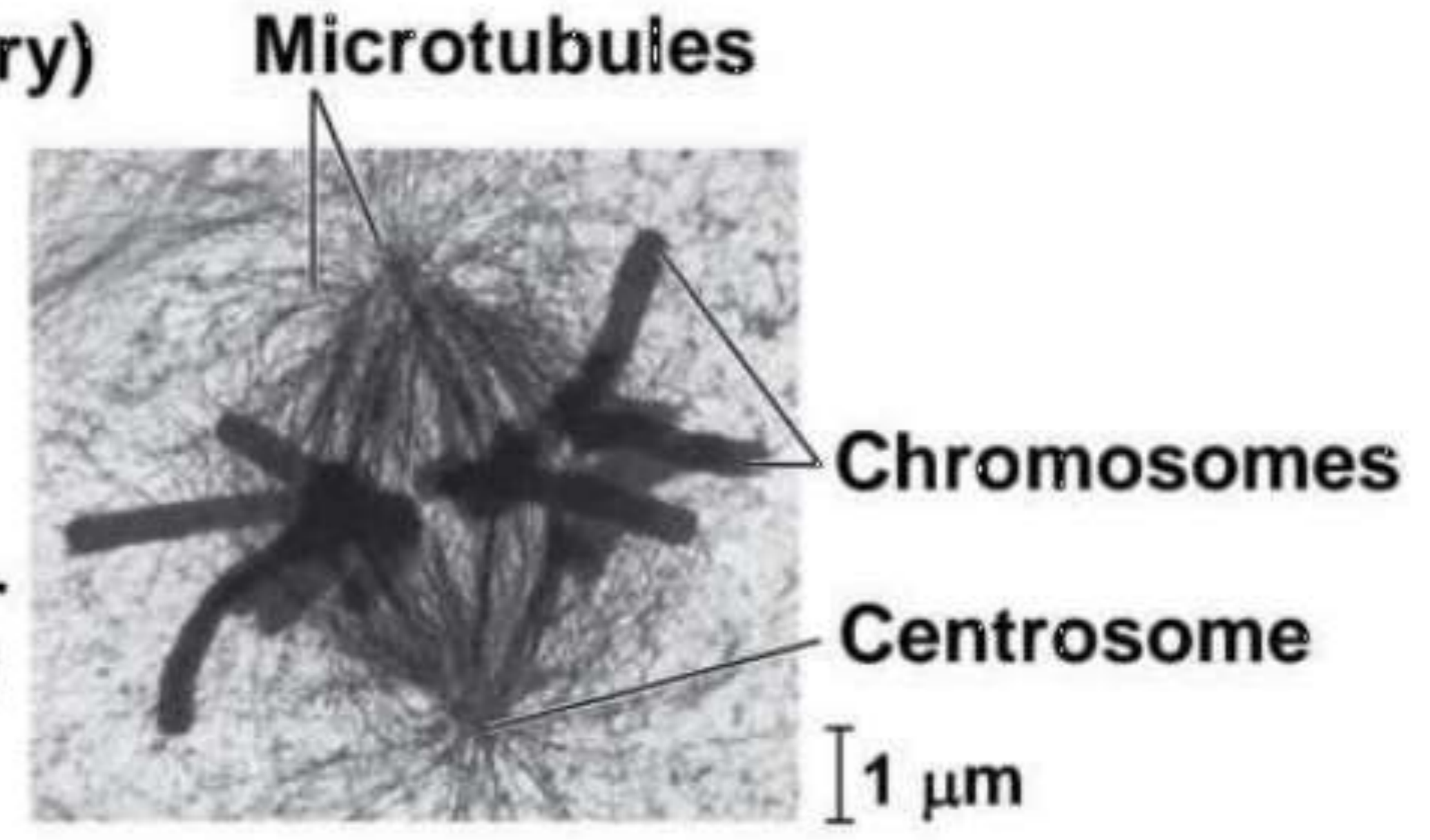
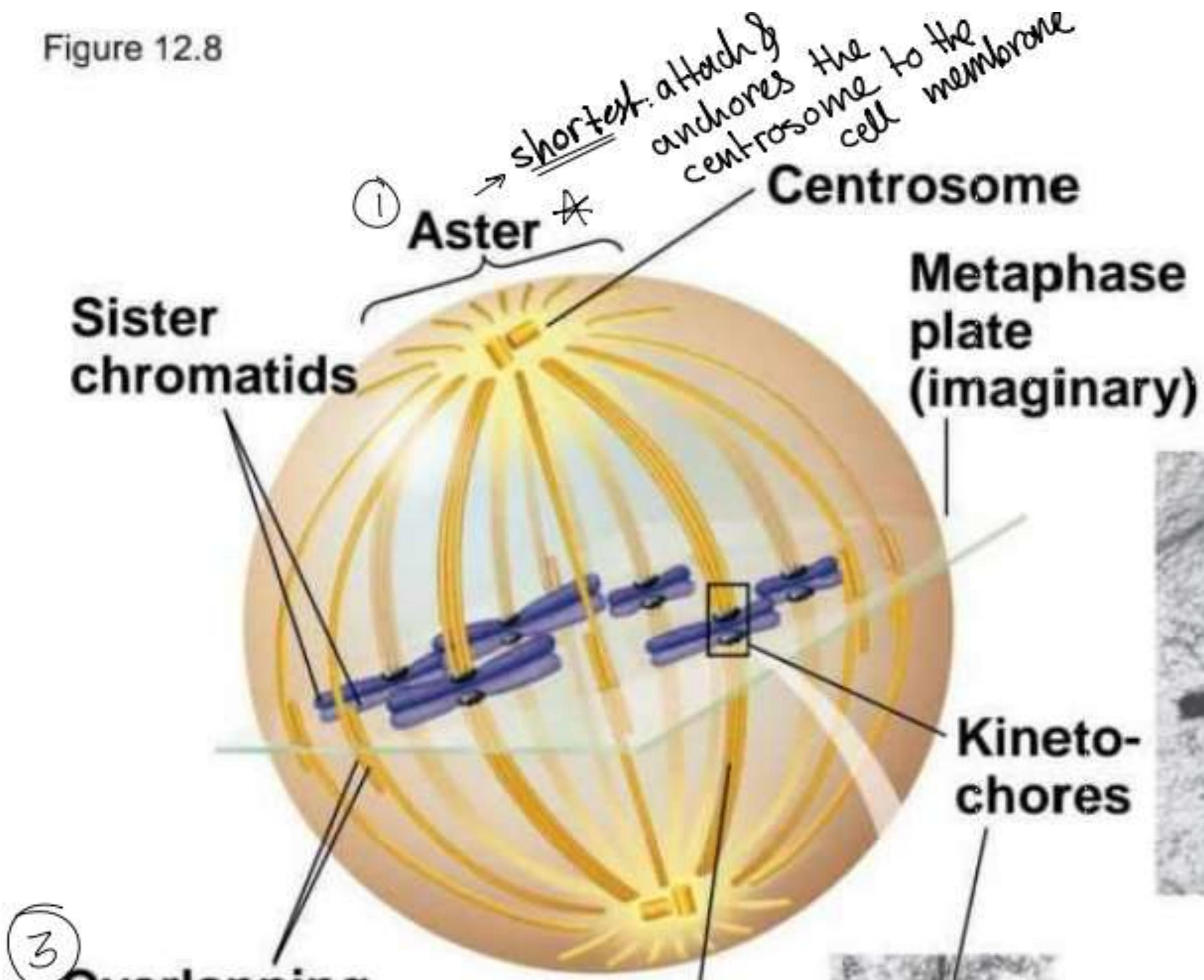


Figure 12.8a

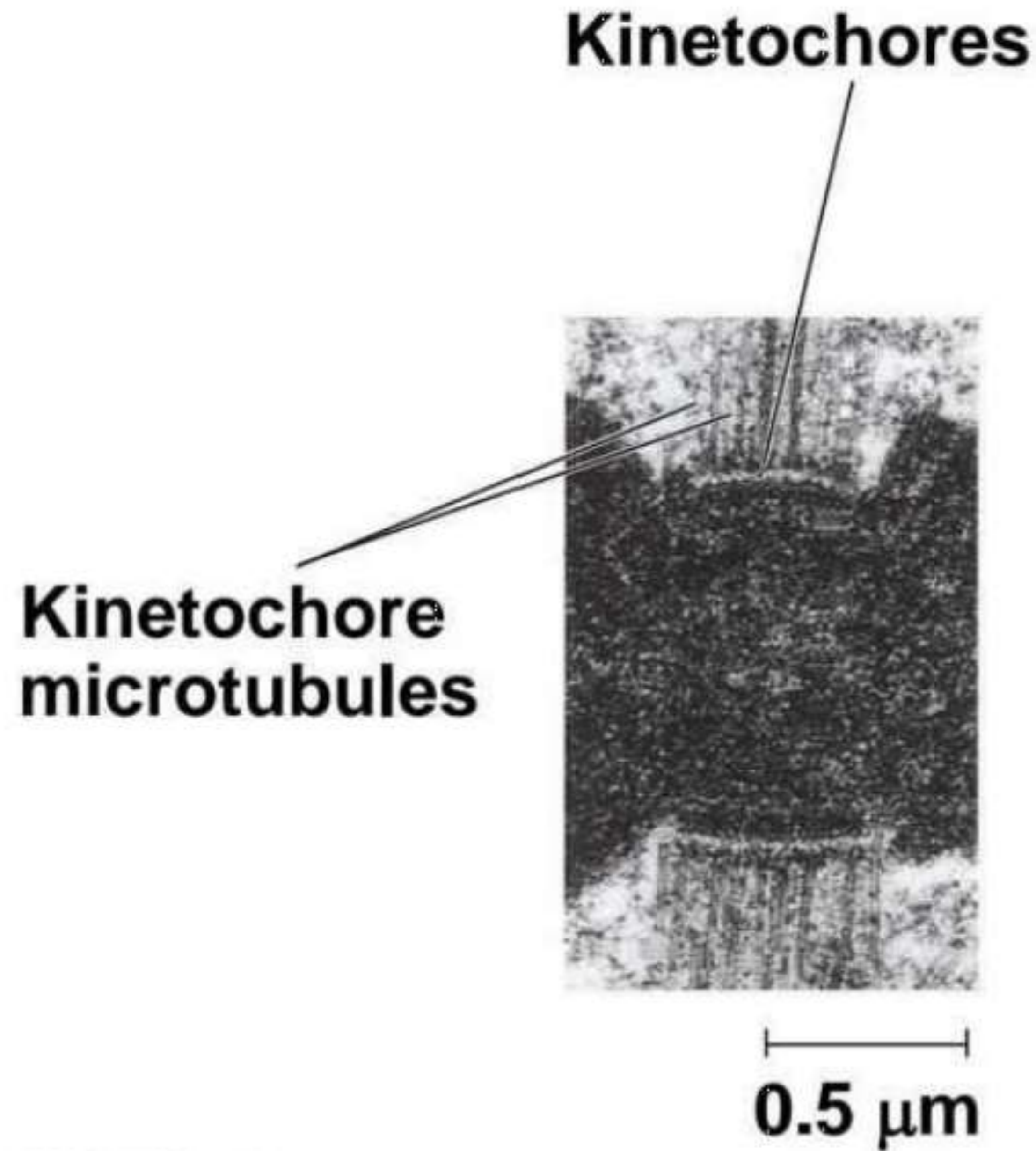
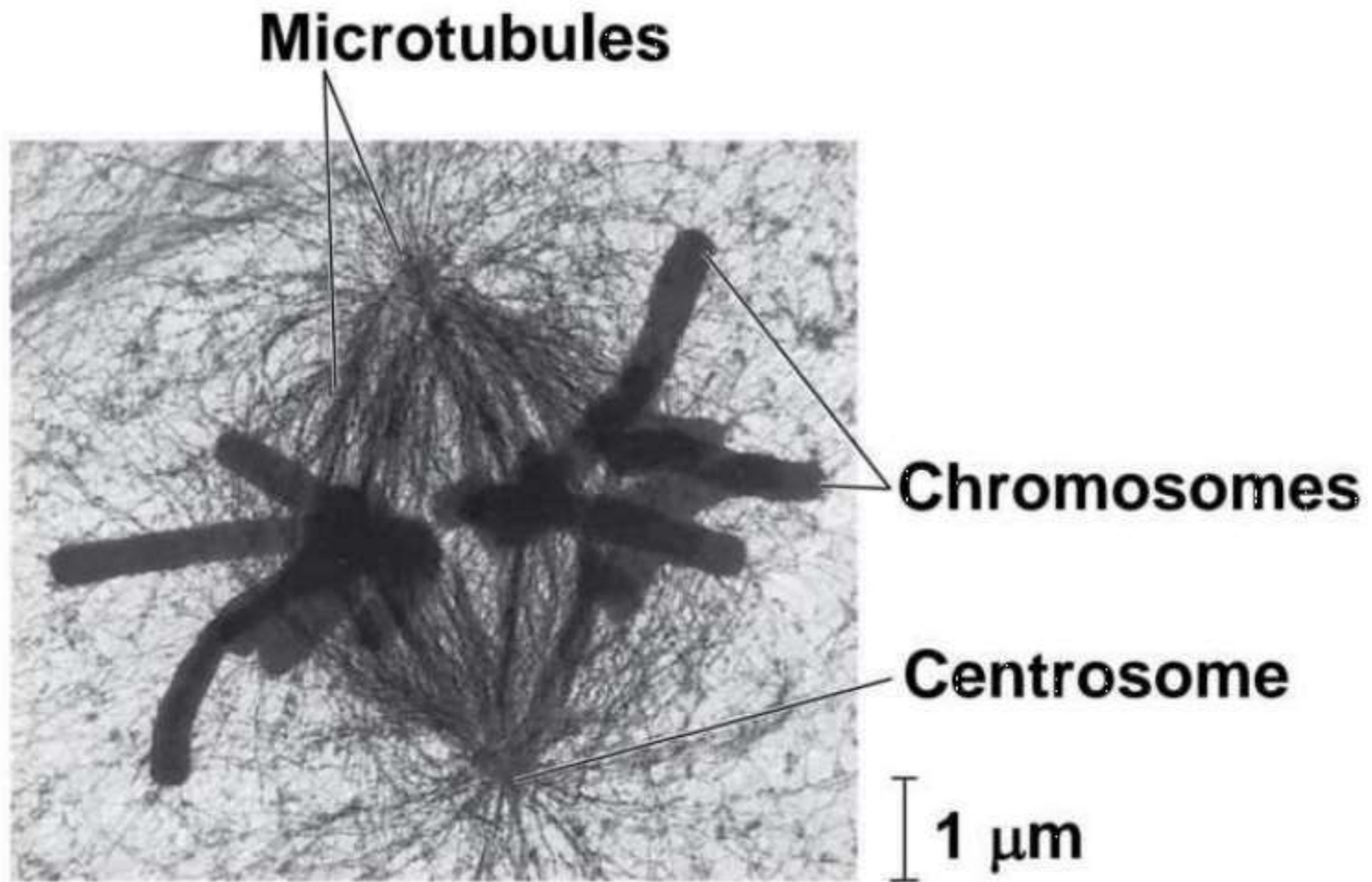


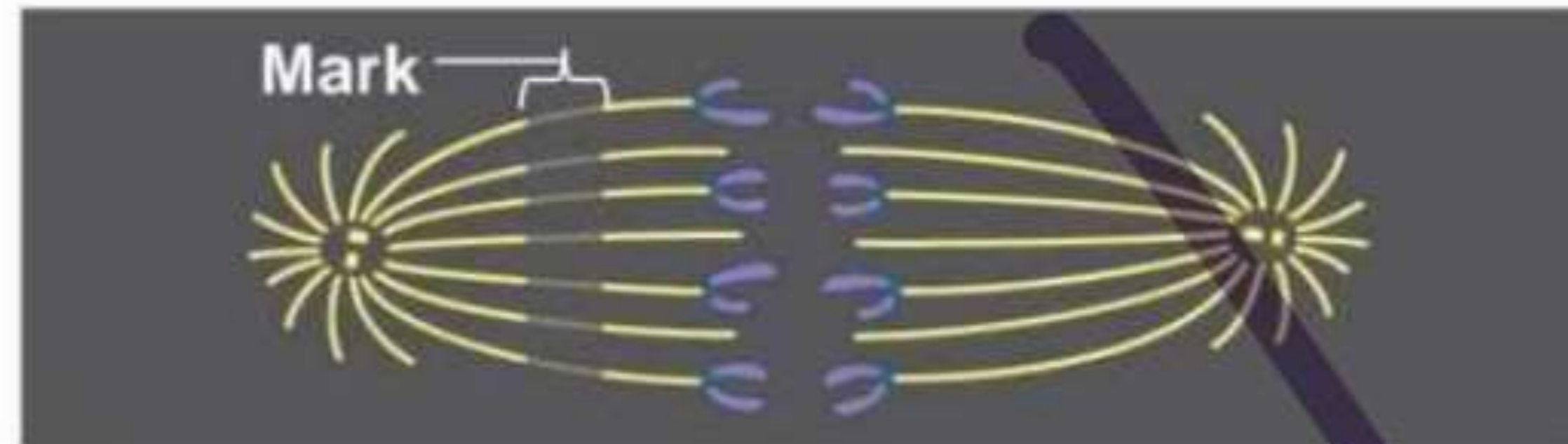
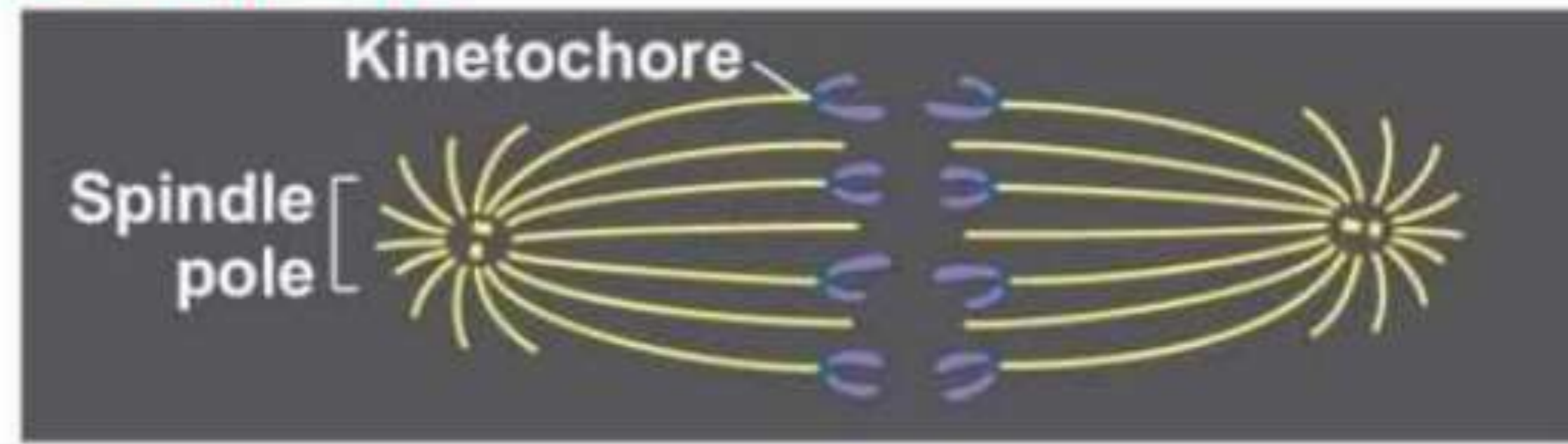
Figure 12.8b



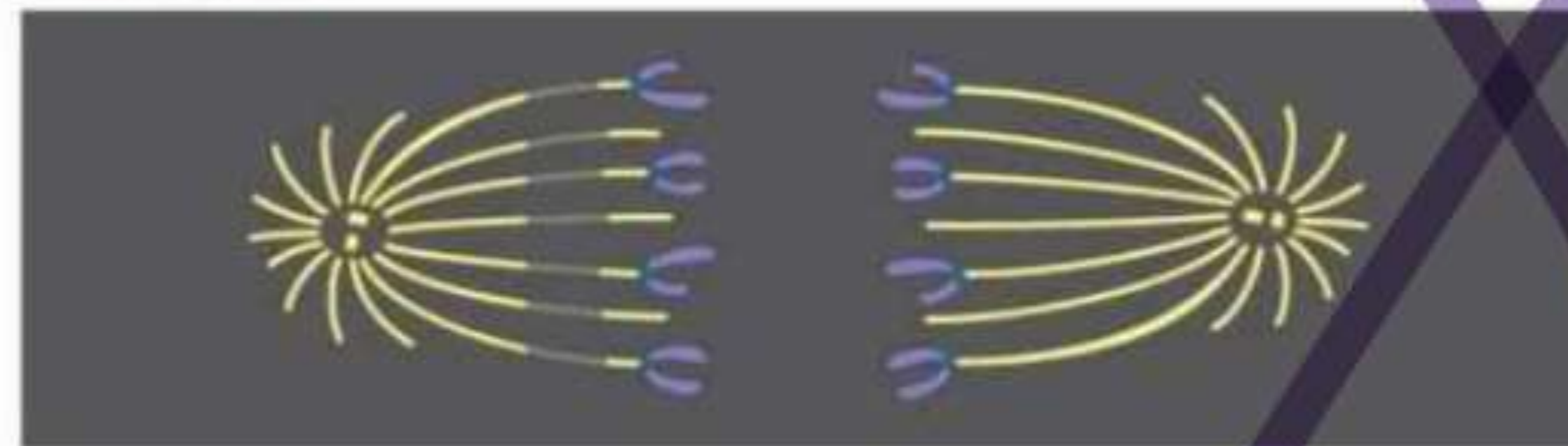
- In anaphase, sister chromatids separate and move along the kinetochore microtubules toward opposite ends of the cell
- The microtubules shorten by depolymerizing at their kinetochore ends

Figure 12.9

EXPERIMENT



RESULTS



CONCLUSION

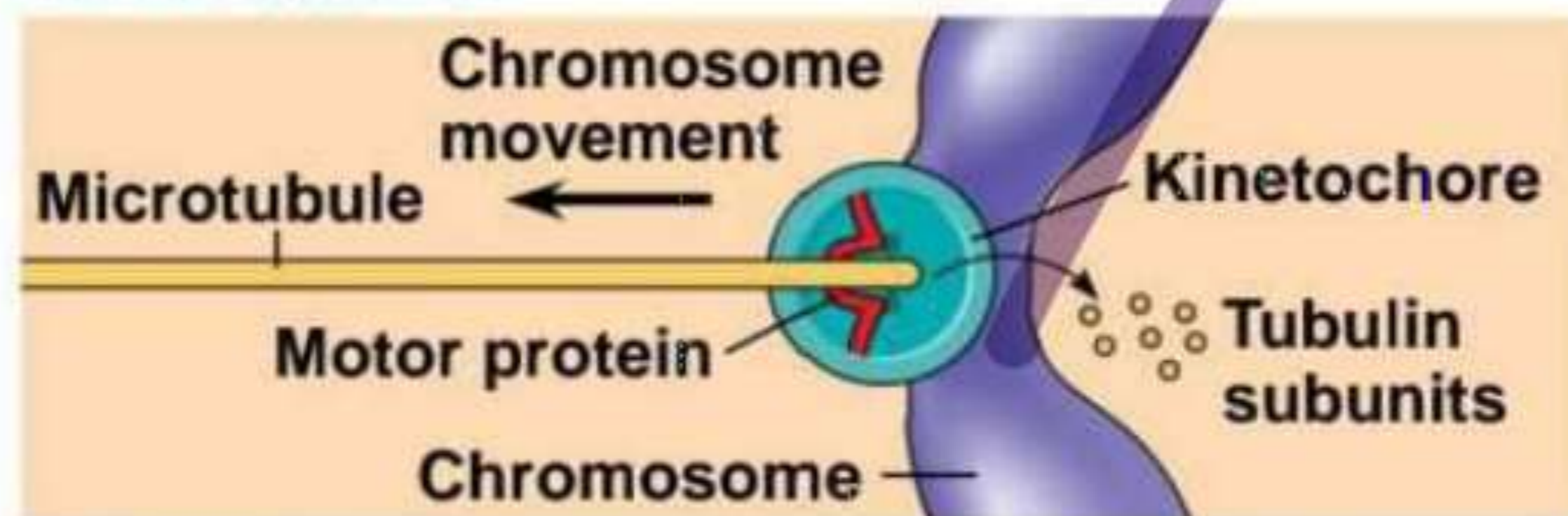
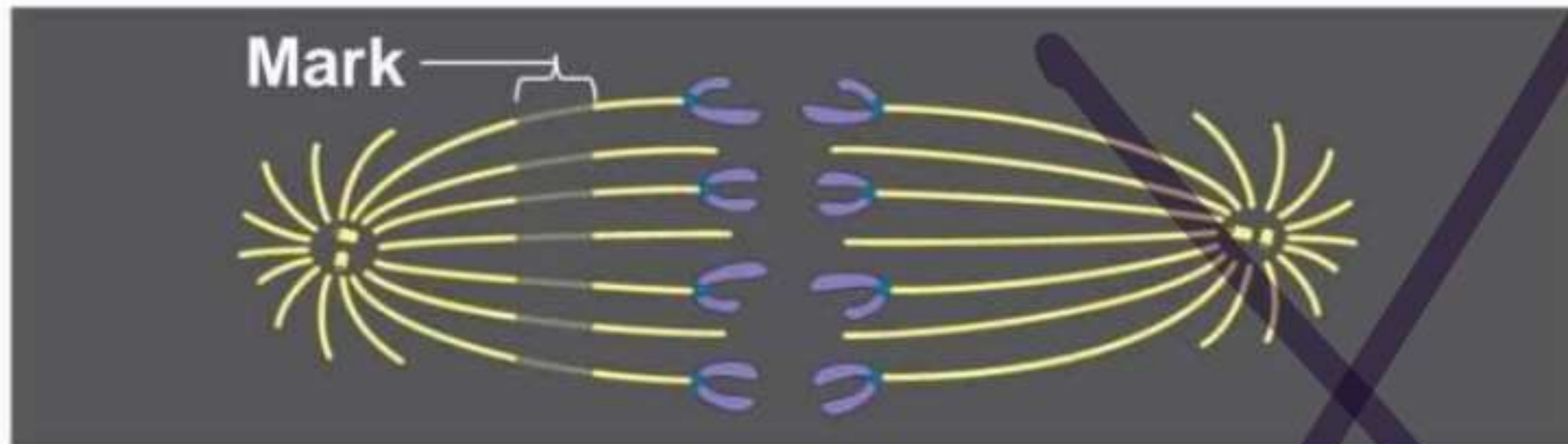
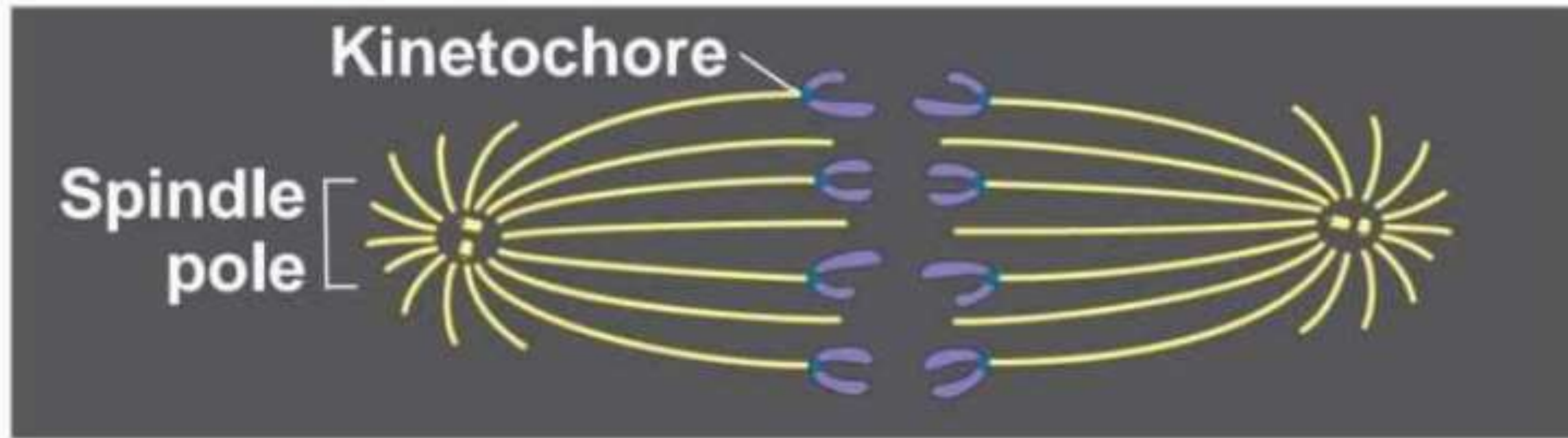


Figure 12.9a

EXPERIMENT



RESULTS

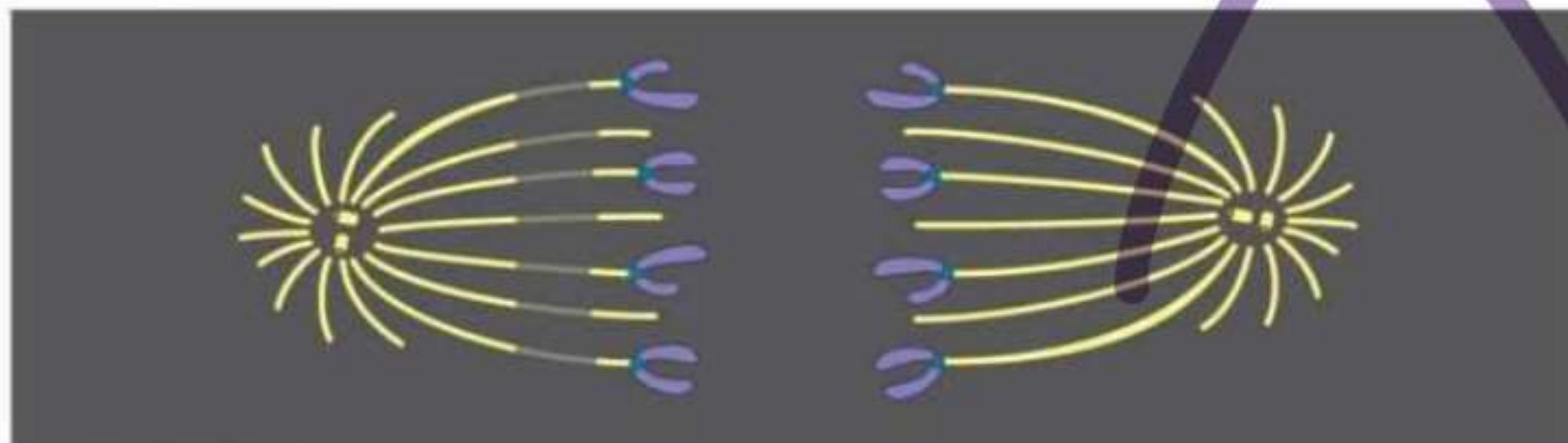
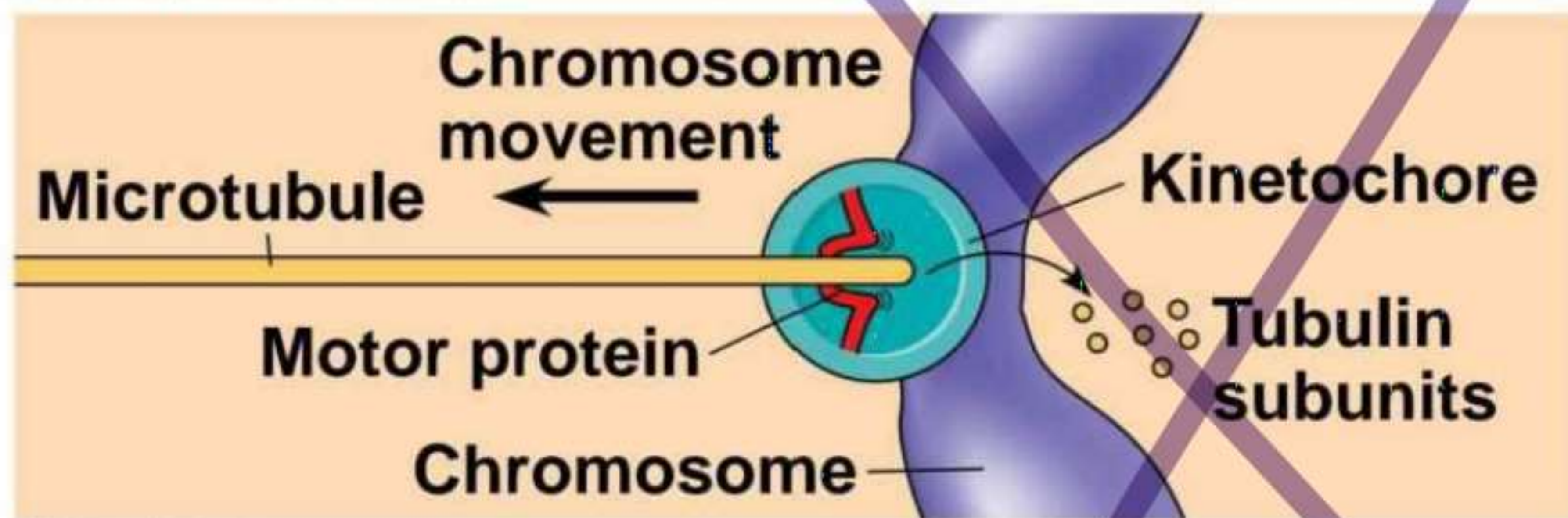


Figure 12.9b

CONCLUSION



- Nonkinetochore microtubules from opposite poles overlap and push against each other, elongating the cell
- In telophase, genetically identical daughter nuclei form at opposite ends of the cell
- Cytokinesis begins during anaphase or telophase and the spindle eventually disassembles

Cytokinesis: *A Closer Look*

in cells!
animal + plant
because of cell wall

- In animal cells, cytokinesis occurs by a process known as **cleavage**, forming a **cleavage furrow**
- In plant cells, a **cell plate** forms during cytokinesis



Animation: Cytokinesis



Video: Animal Mitosis



Video: Sea Urchin (Time Lapse)

Figure 12.10

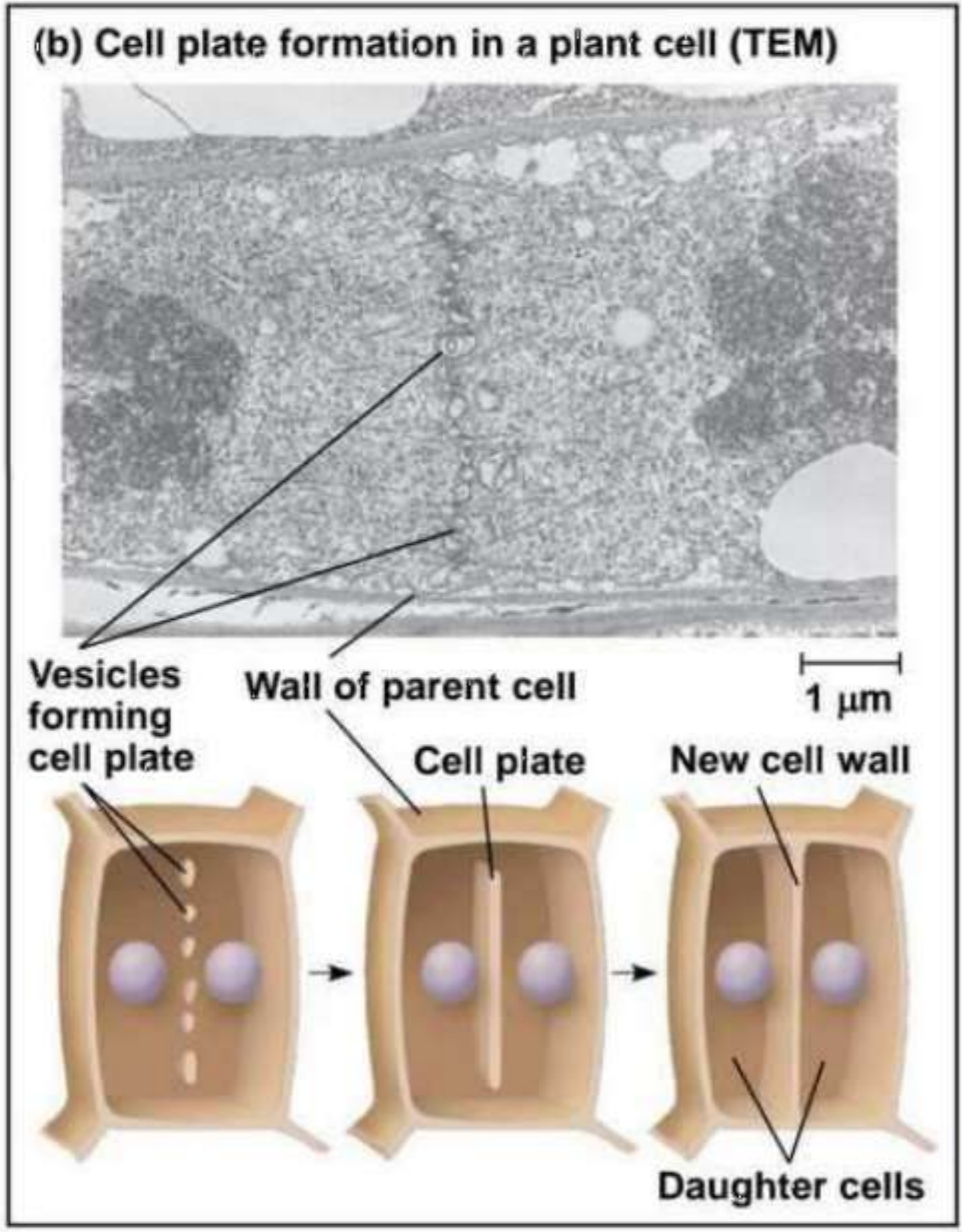
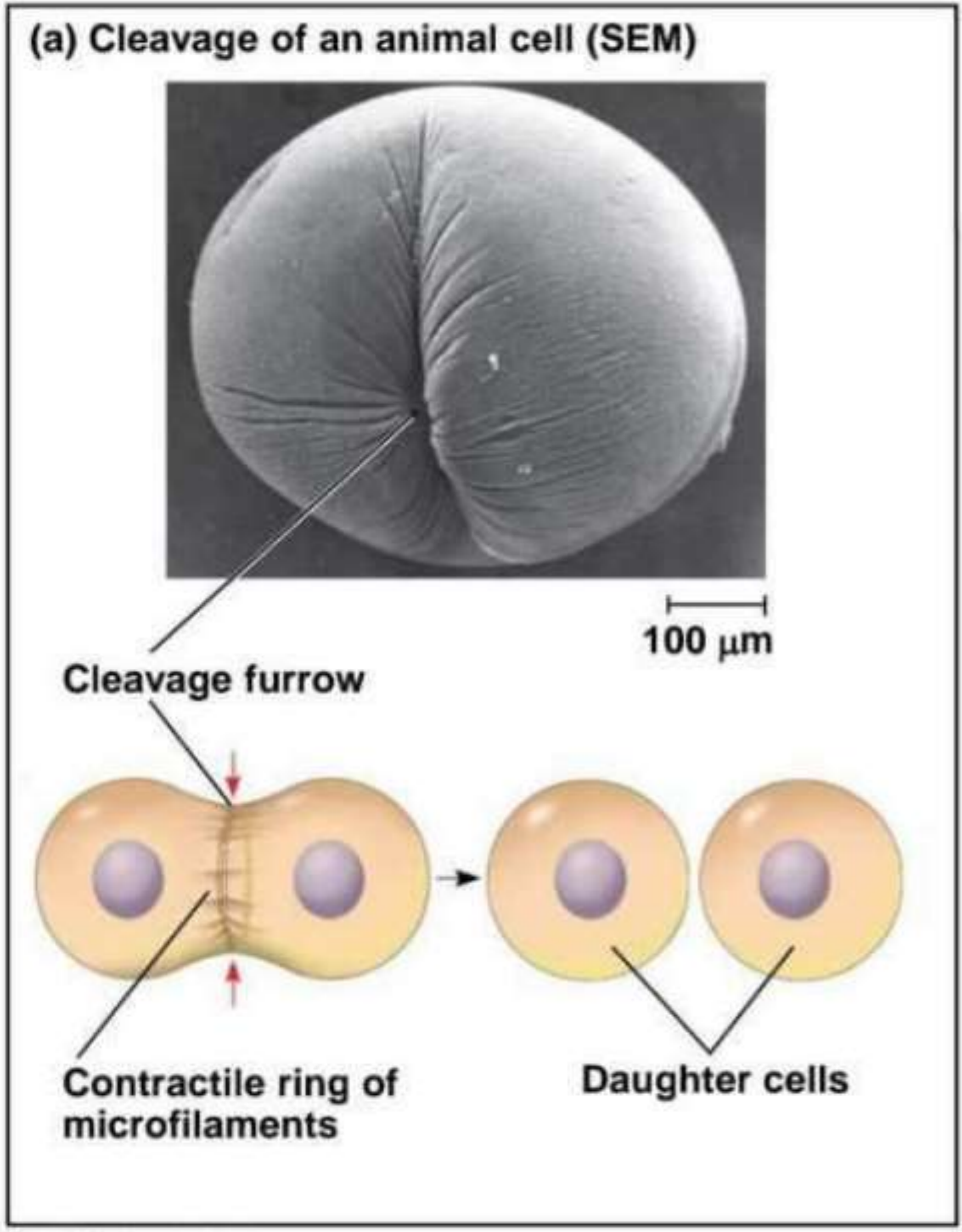
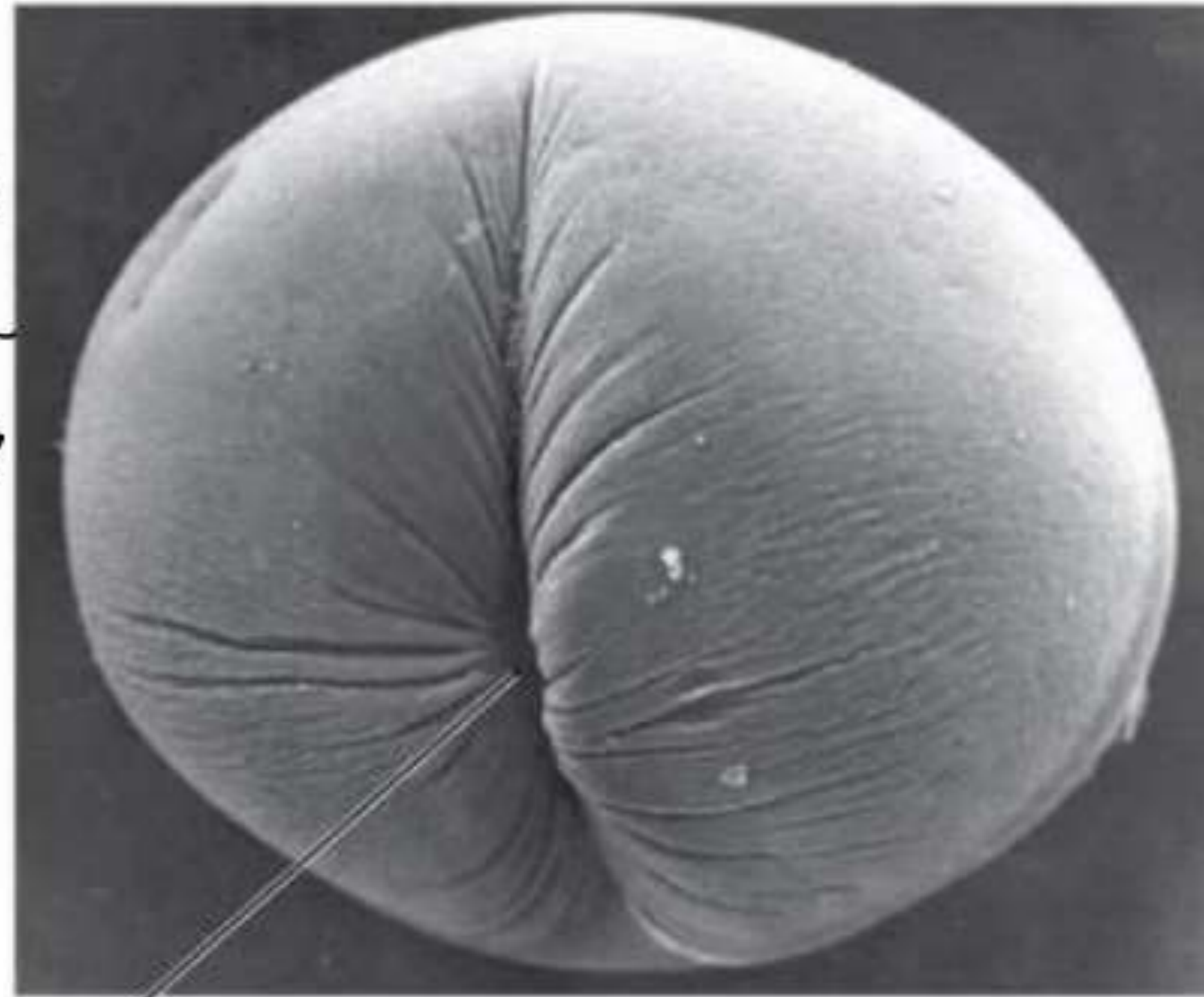


Figure 12.10a

(a) Cleavage of an animal cell (SEM)

cytokinesis in Animal cells: occurs by formation of cleavage furrow with help of microfilaments



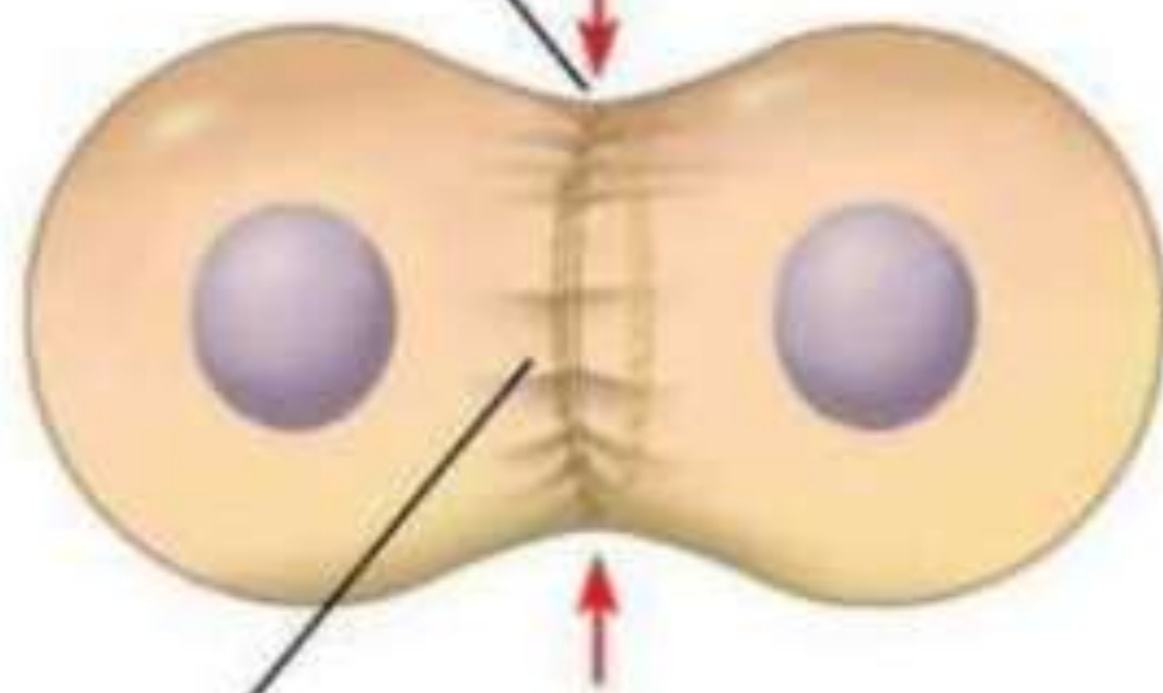
no hard protection (cell wall)

- microfilaments: contractile ring of actin

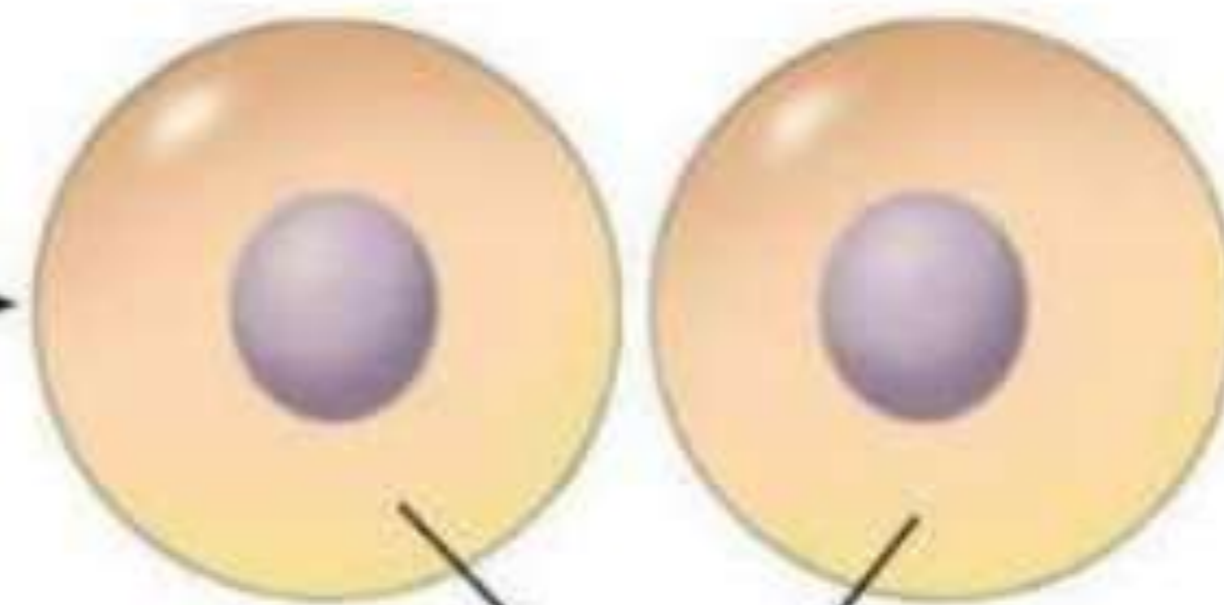
100 μm

Cleavage furrow

become cell



Contractile ring of microfilaments

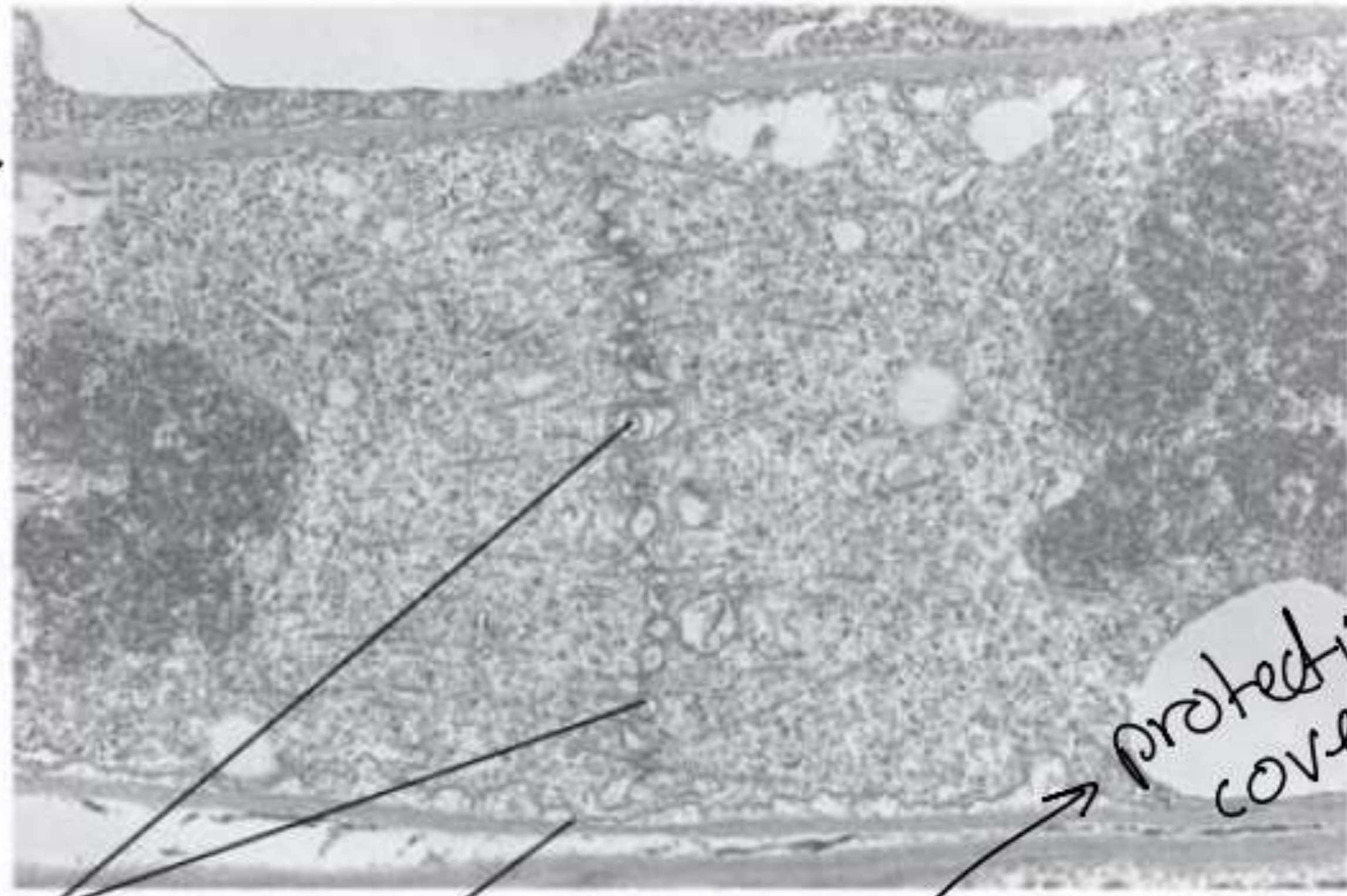


Daughter cells

Figure 12.10b

(b) Cell plate formation in a plant cell (TEM)

cytokinesis
by formation
of cell plate
↓ then
cell wall



protective covering

Vesicles forming cell plate

Wall of parent cell

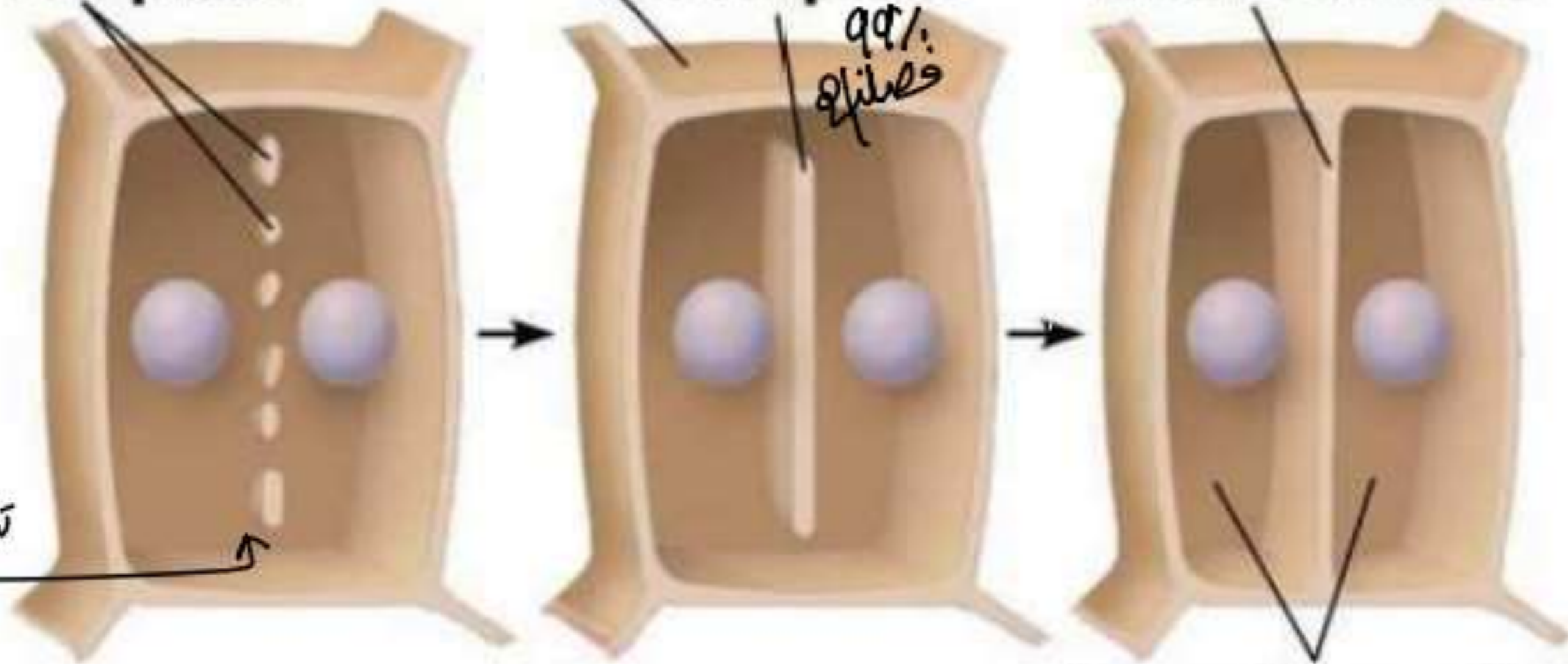
1 μm

Cell plate

New cell wall

*golgi apparatus manufactures type of carbohydrates that helps in cell wall synthesis

cellulose ...
vesicle containing carb.
Golgi apparatus
forming cell plate

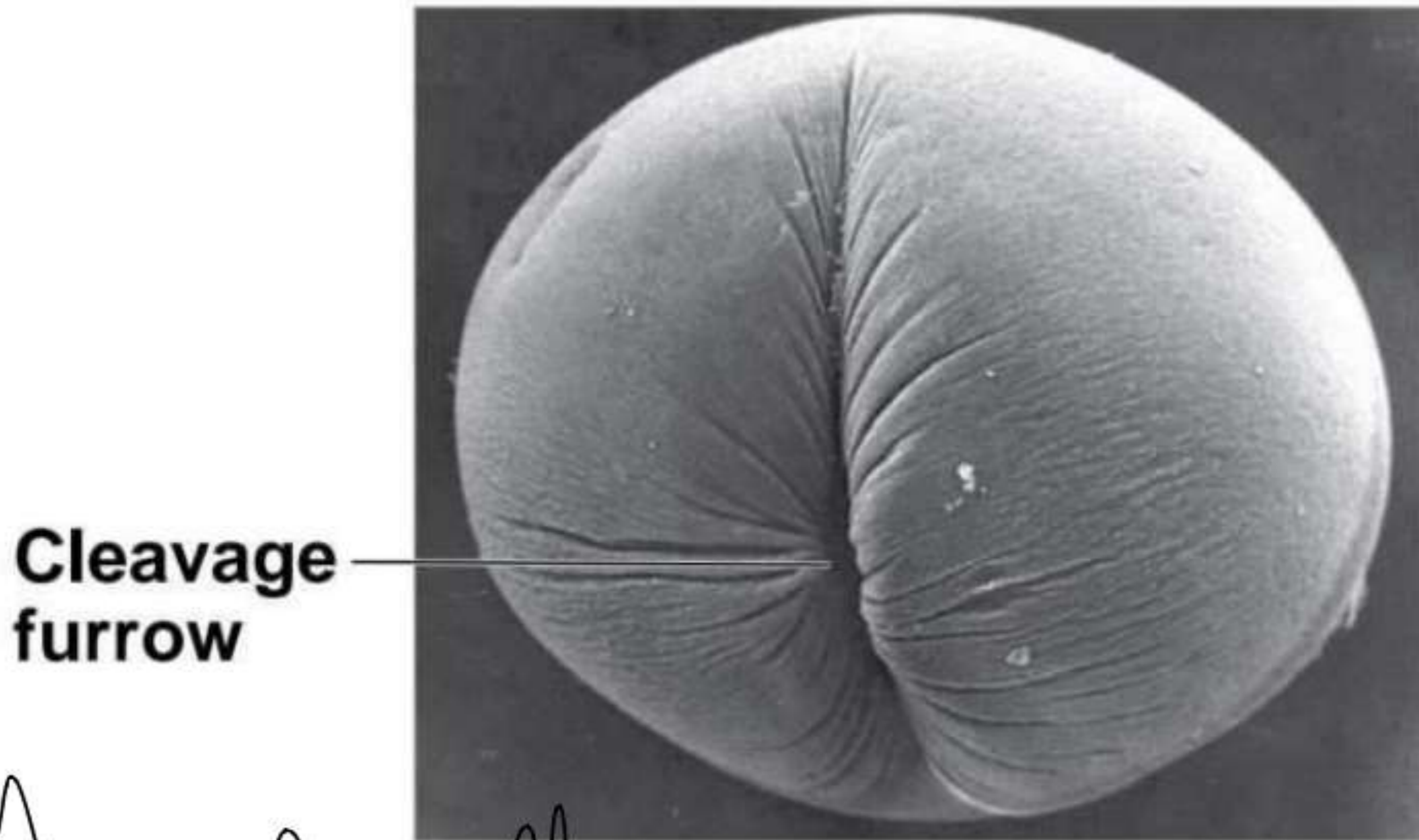


cellulose
99%
fibres

Daughter cells

membrane of vesicle is the membrane of cell wall of new cell

Figure 12.10c

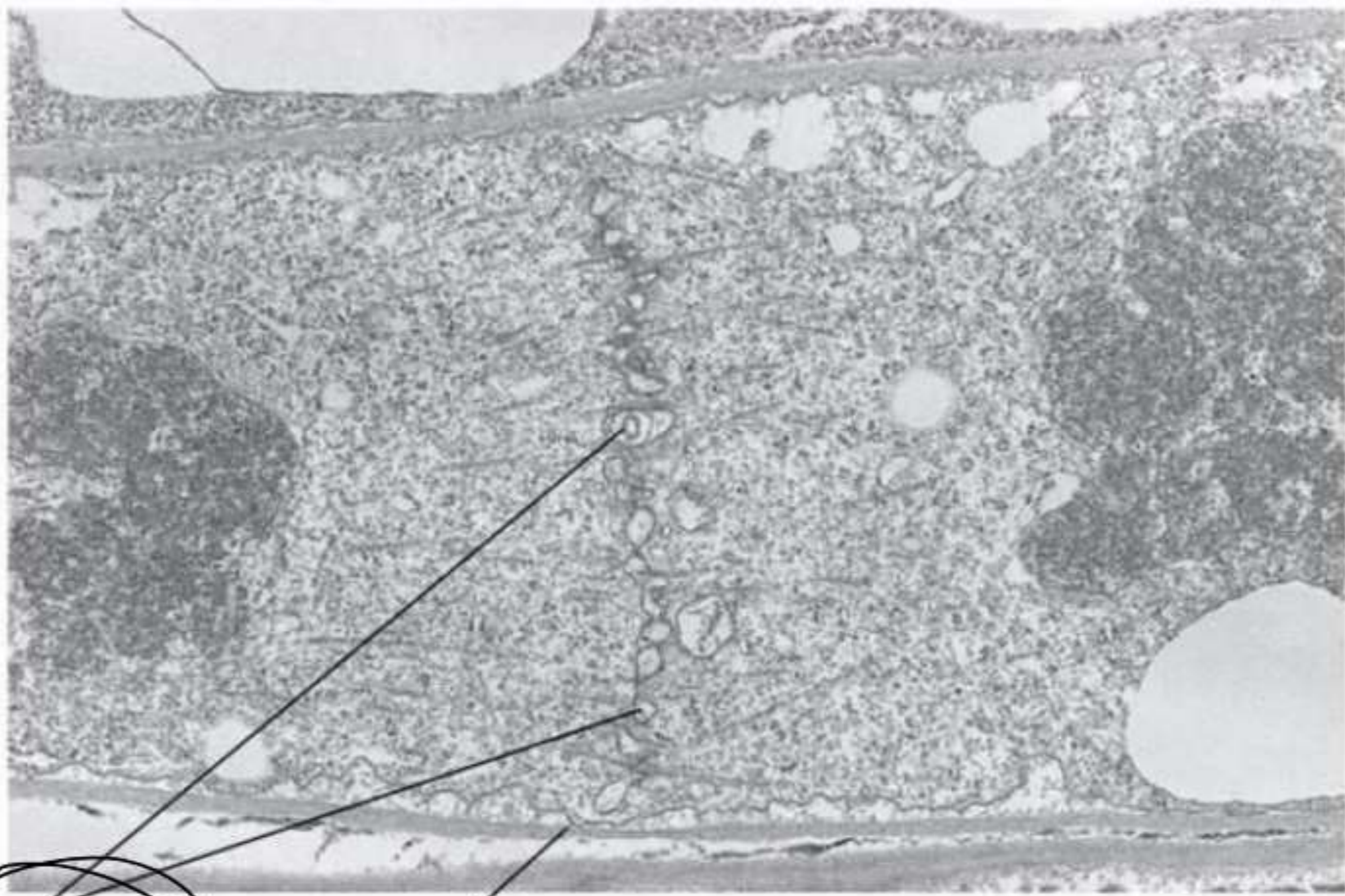


**Cleavage
furrow**

*in
animal cell*

100 μm

Figure 12.10d



*From
golgi*

**Vesicles
forming
cell plate**

Wall of parent cell

1 μm

Figure 12.11

Apical tips in plants

مراحل الانقسام
في
النبات

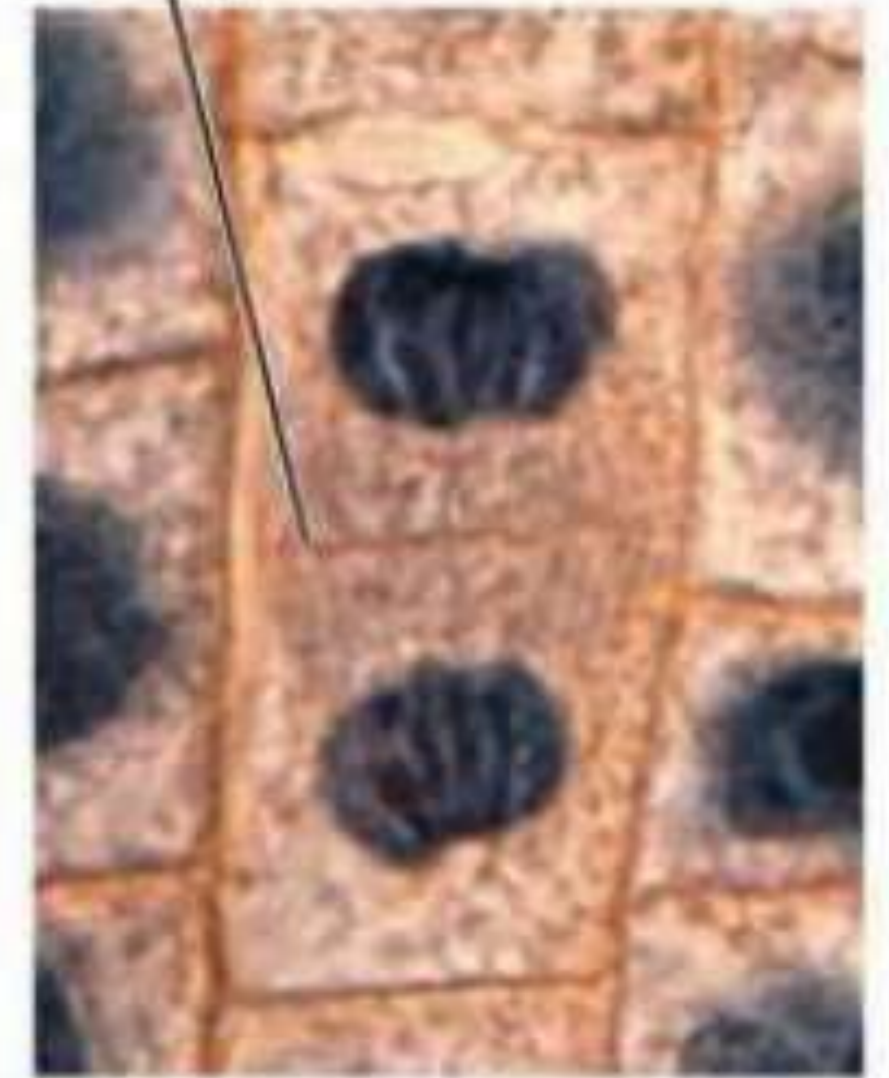
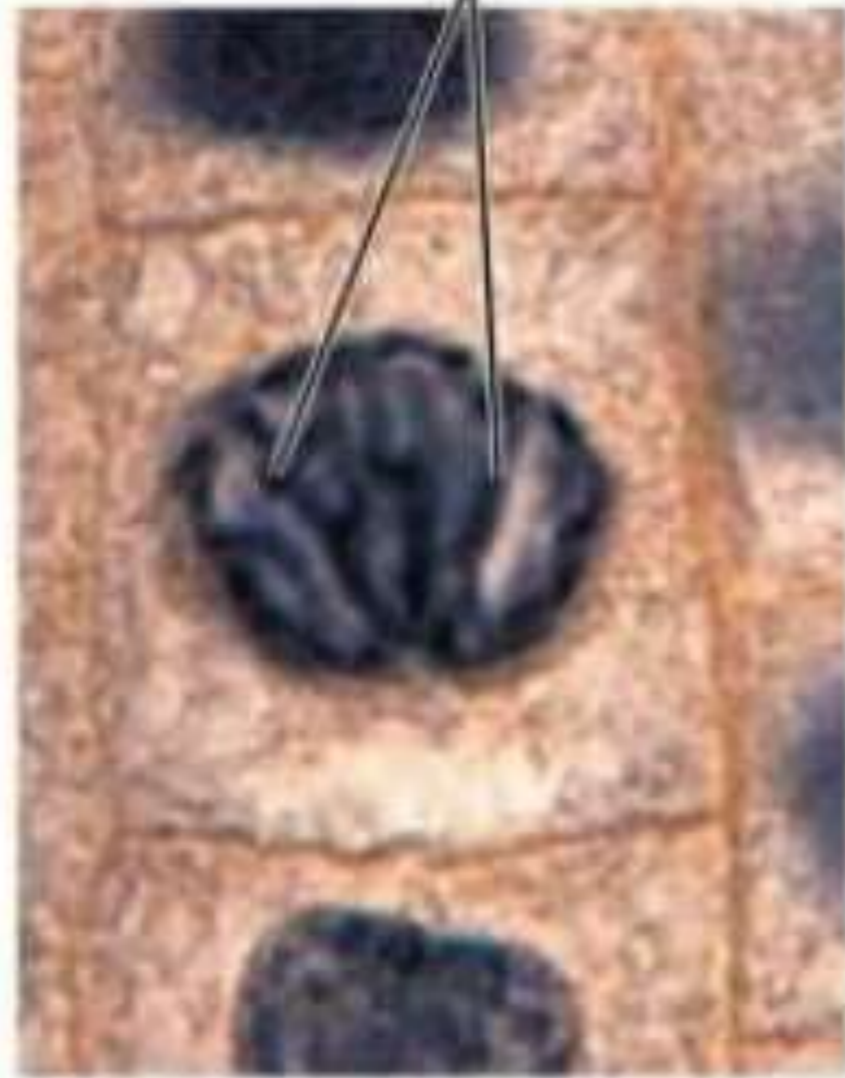
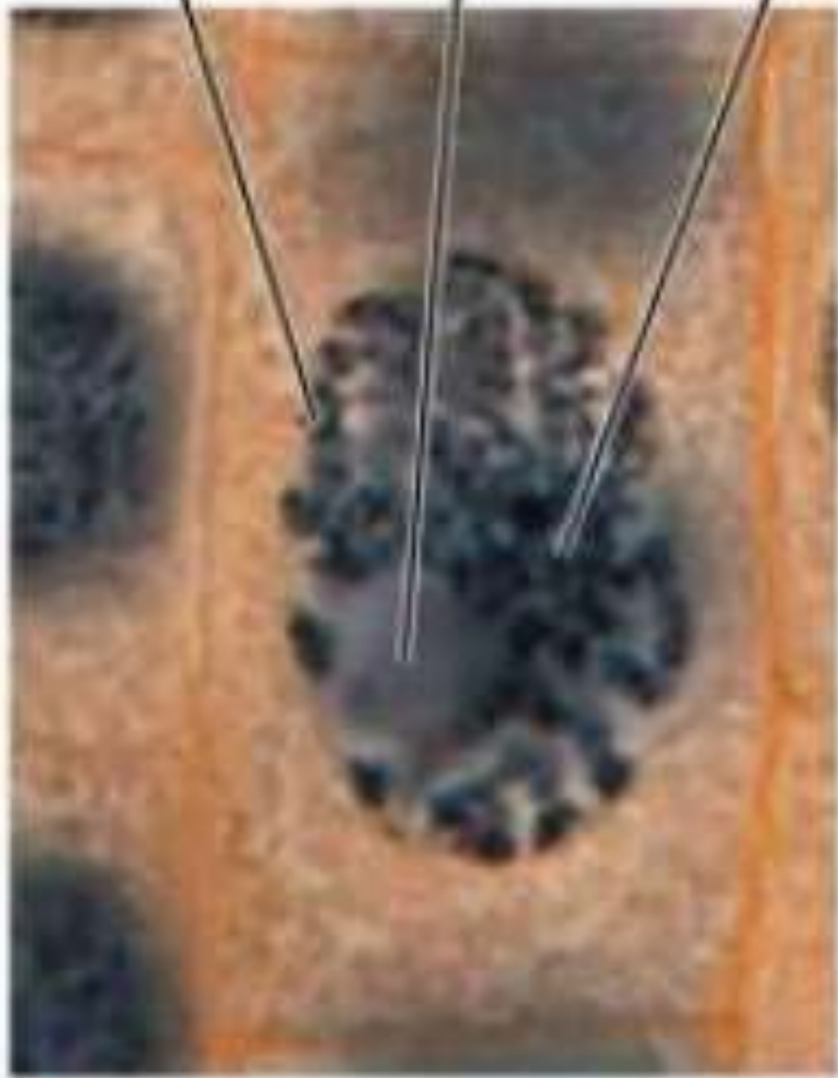
Shoot
tip
خوذة القمة
(ساعة التبريد)

اكتنوا جميع
مراحل
mitosis

Root tips
قمة ناصية تحت الأرض
تحتوي كبنو

Nucleus
Nucleolus
Chromatin
condensing
Chromosomes

Cell plate 10 μm



1 Prophase

2 Prometaphase

3 Metaphase

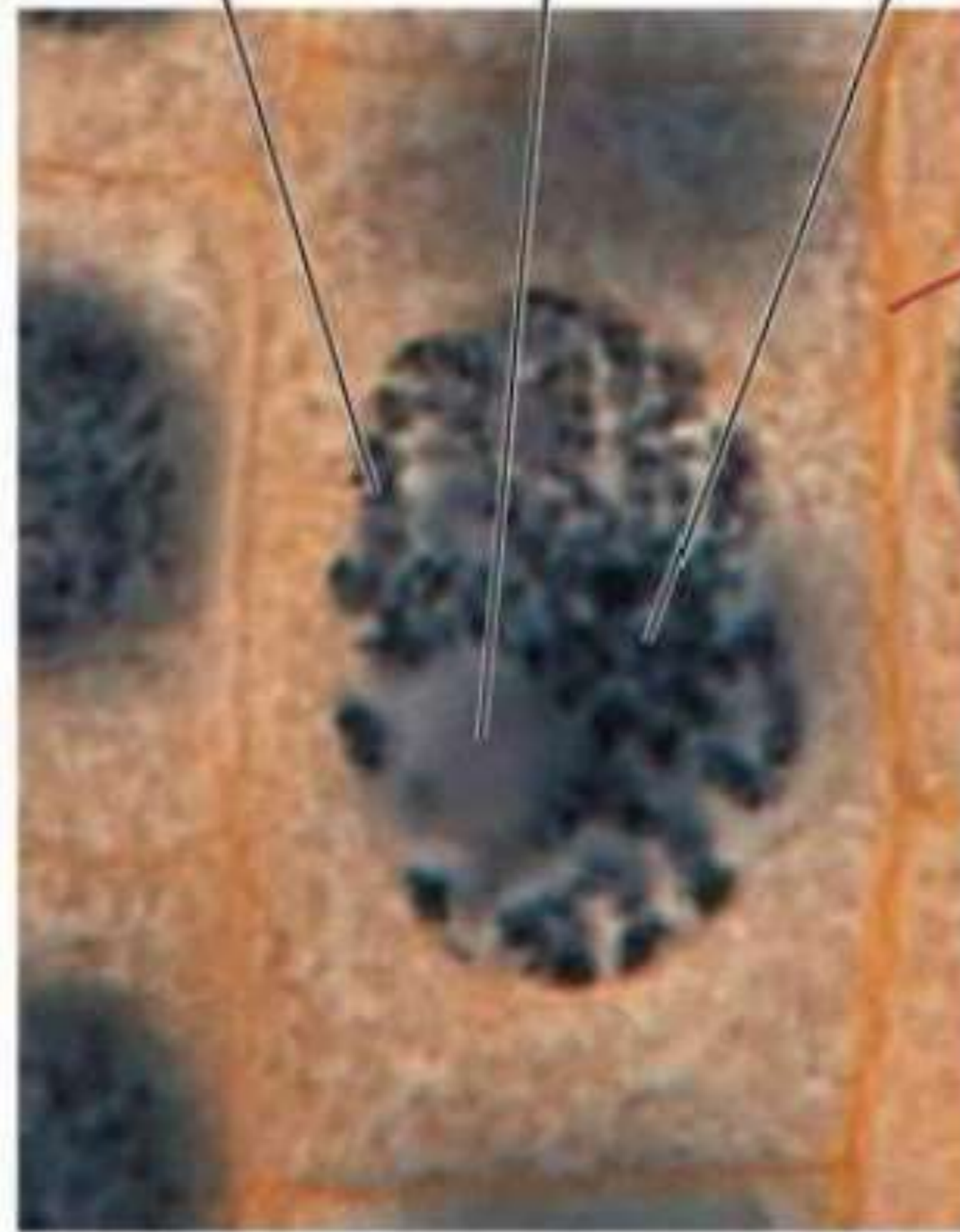
4 Anaphase

5 Telophase

Figure 12.11a

Nucleus **Chromatin condensing**

Nucleolus



cell wall

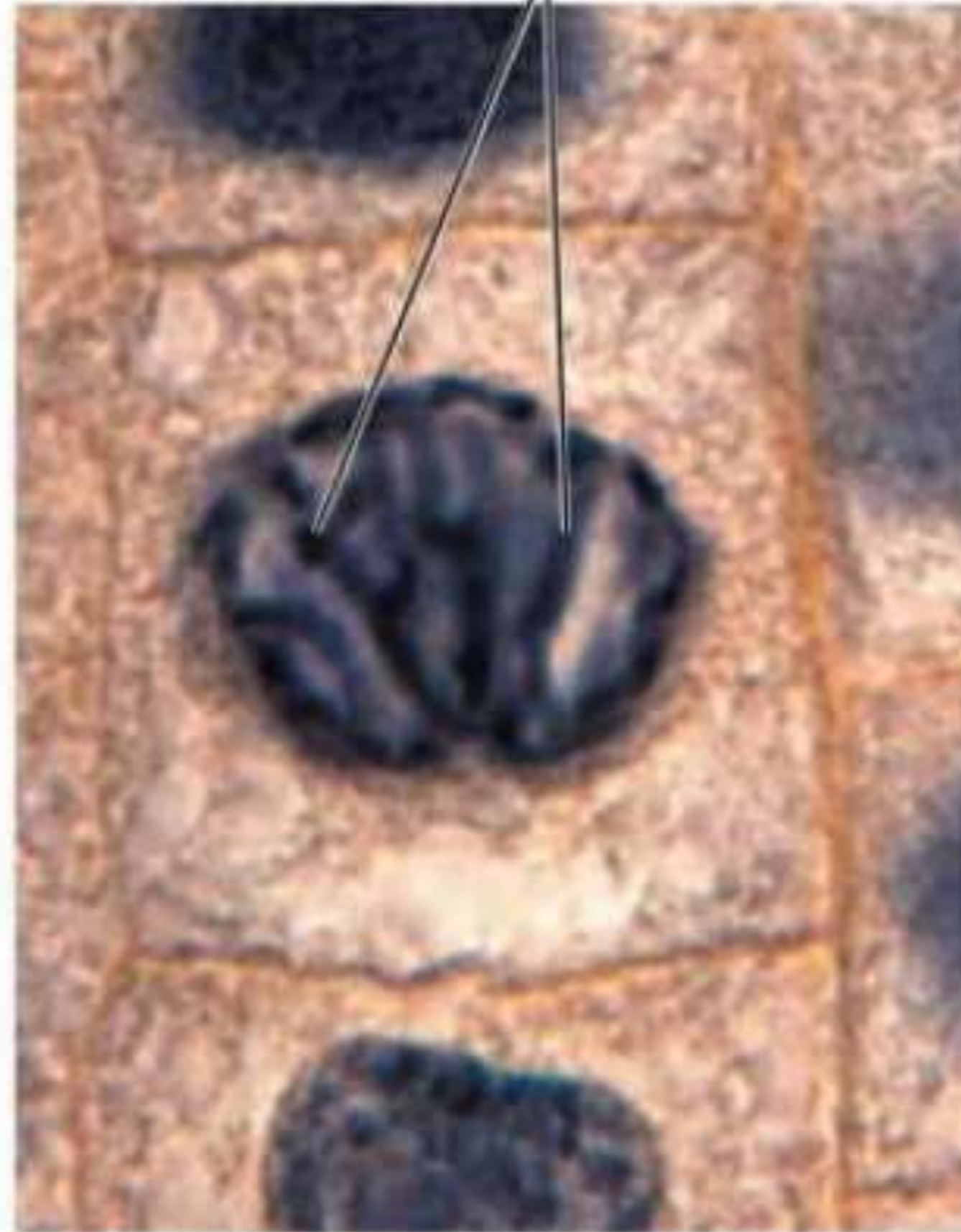
10 μm

1 Prophase

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chromosomes *3/19*

Chromosomes



no nuclear
envelope
no nucleolus

10 μm

2 Prometaphase

Figure 12.11c

10 μm



مرتب
metaphase
plate

3 Metaphase

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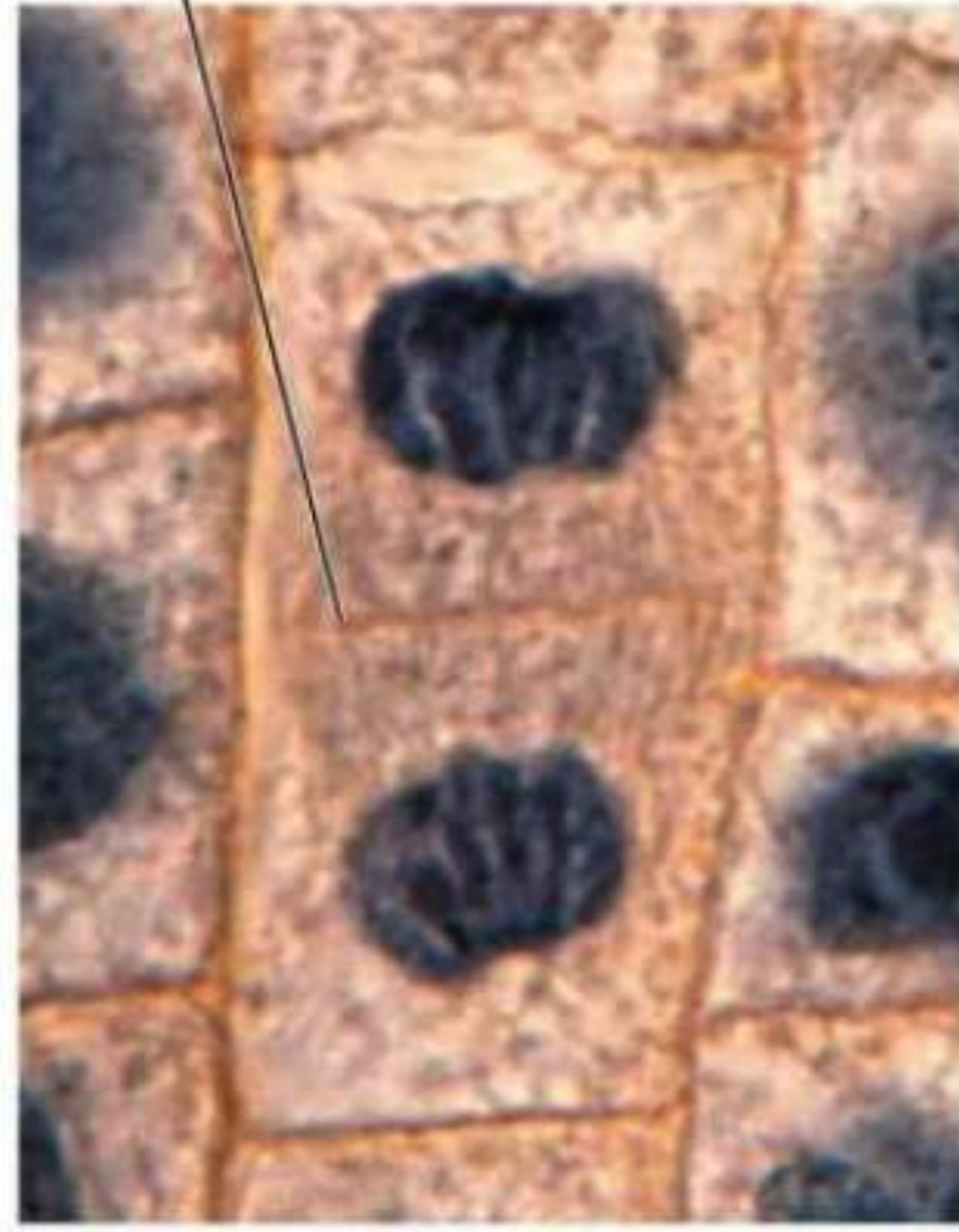
10 μm



separation of
sister chromatids

4 Anaphase

Cell plate 10 μm



5 Telophase

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rate of mitosis in young age is more



growth

Role of mitosis in cells: gts

- ① growth
- ② development
- ③ Repair [regeneration]
- ④ Asexual

Rep

Bacteria → simple → 2 cells

Binary Fission in Bacteria

- Prokaryotes (bacteria and archaea) reproduce by a type of cell division called **binary fission**
- In binary fission, the chromosome replicates (beginning at the **origin of replication**), and the two daughter chromosomes actively move apart
- The plasma membrane pinches inward, dividing the cell into two

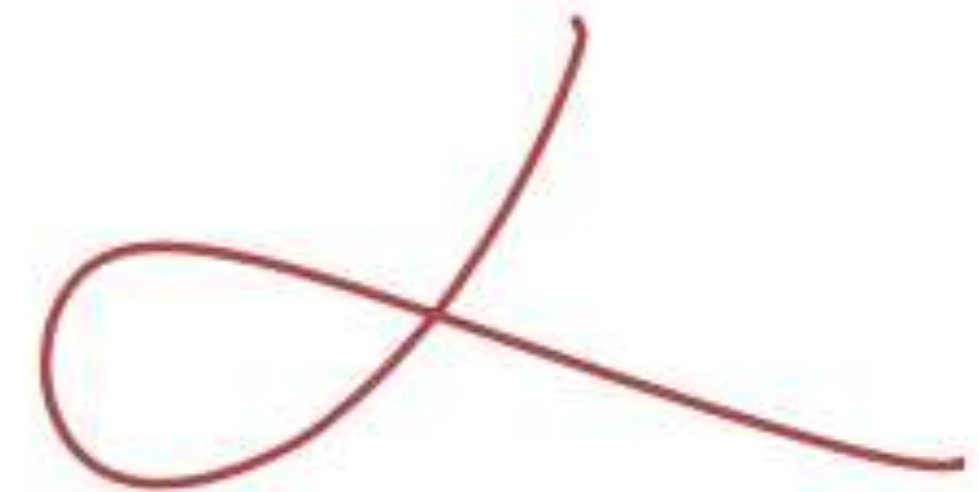
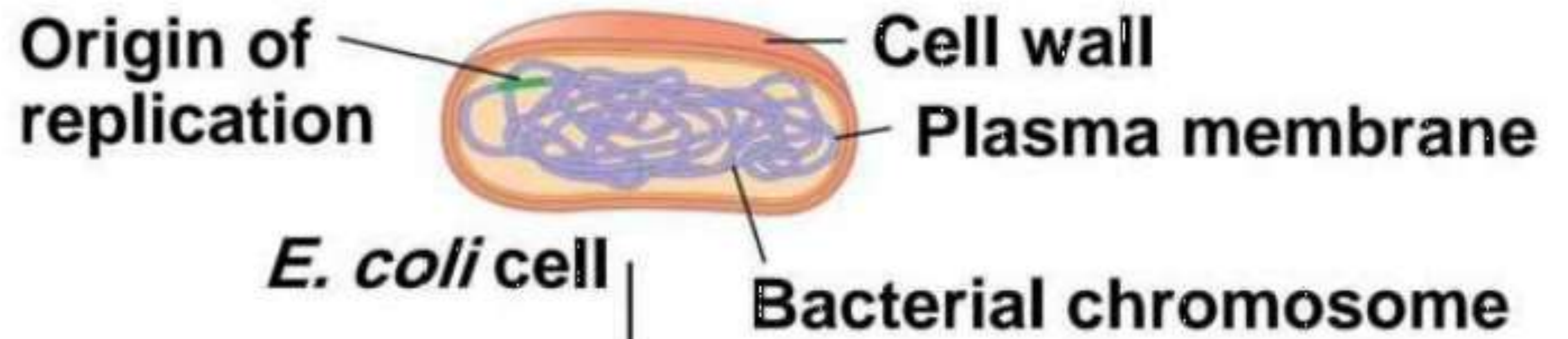


Figure 12.12-1



1 Chromosome replication begins.

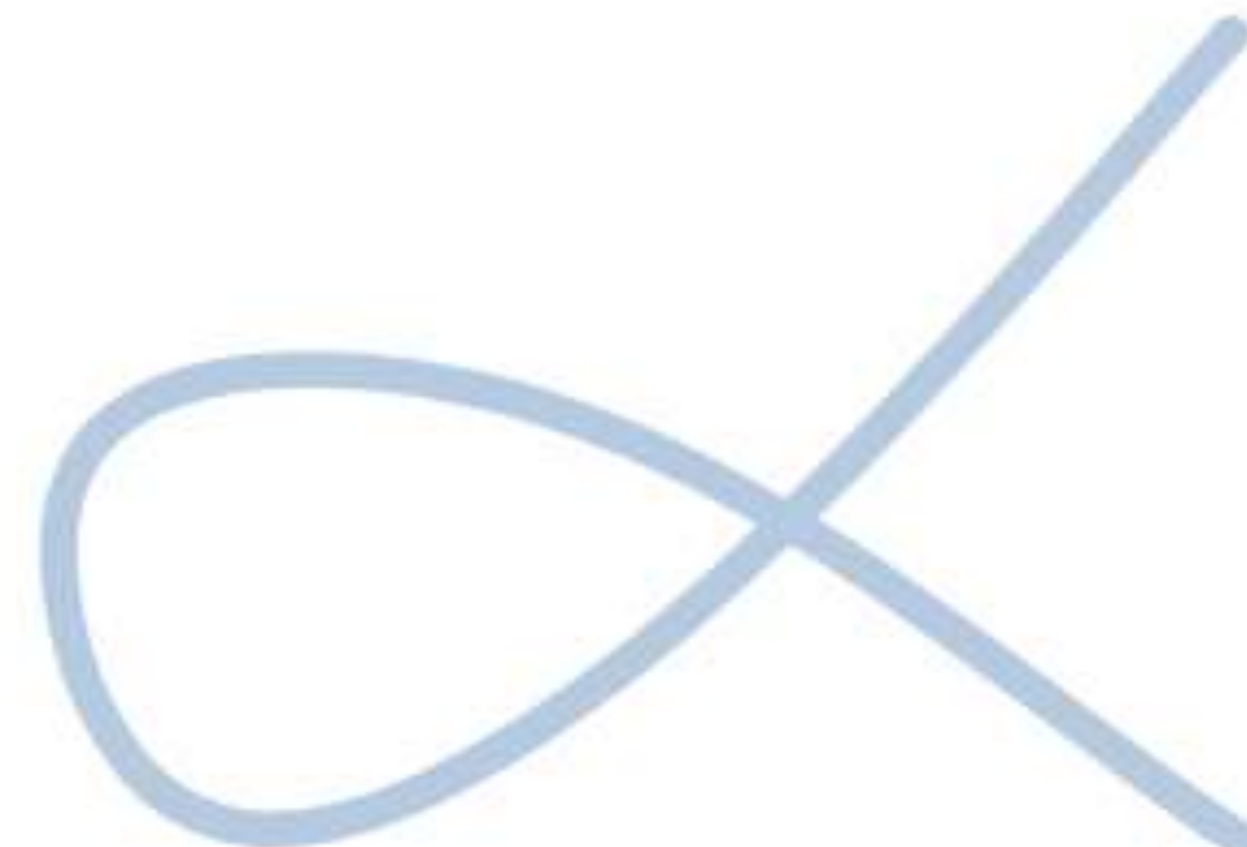
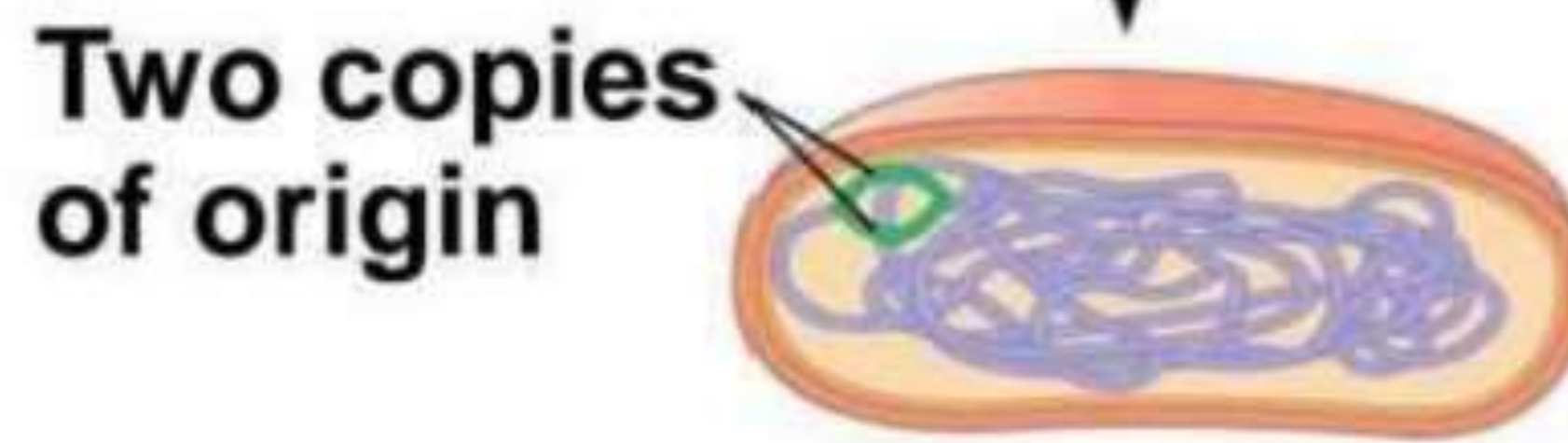


Figure 12.12-2

- 1 Chromosome replication begins.
- 2 Replication continues.

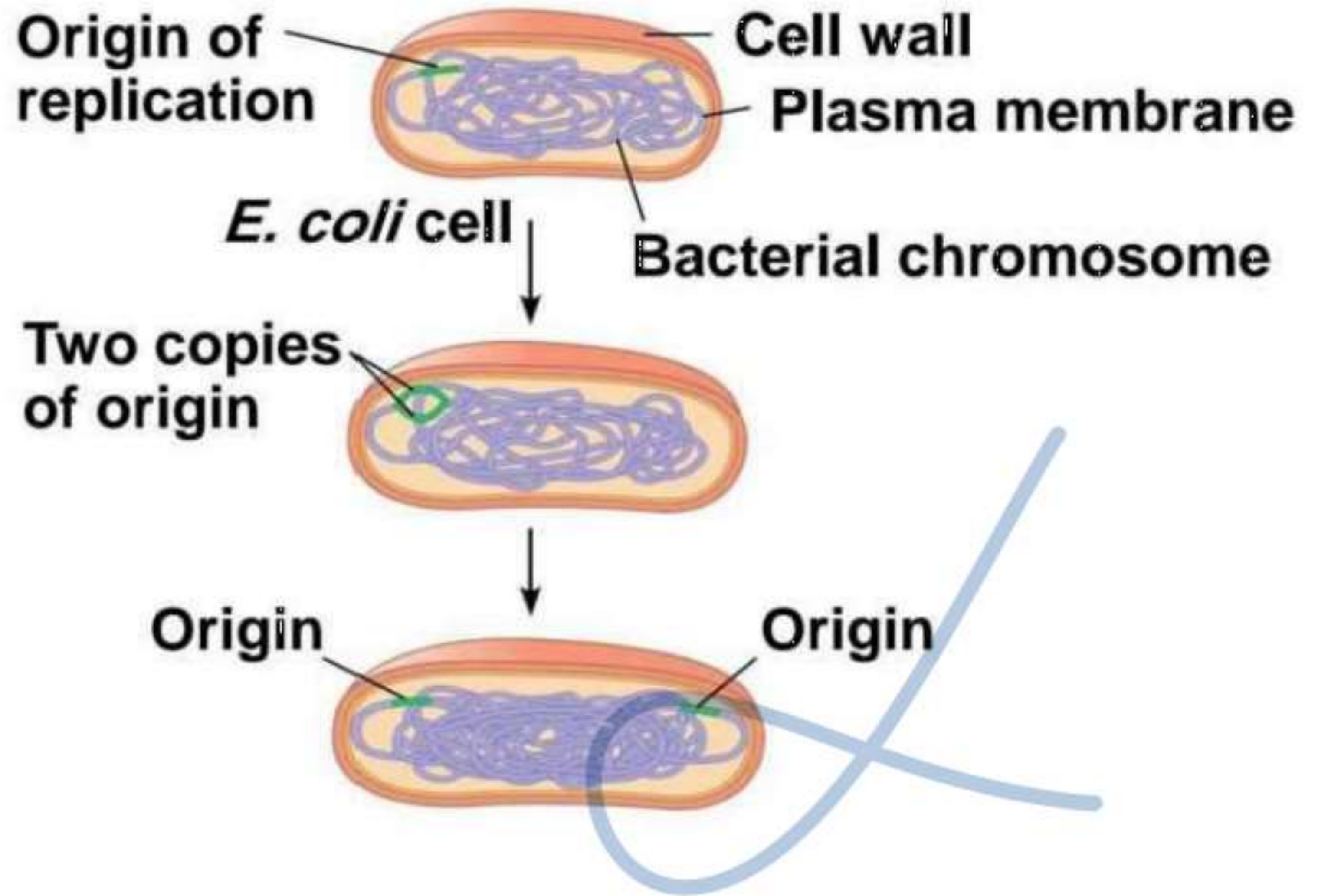


Figure 12.12-3

- 1** Chromosome replication begins.
- 2** Replication continues.
- 3** Replication finishes.

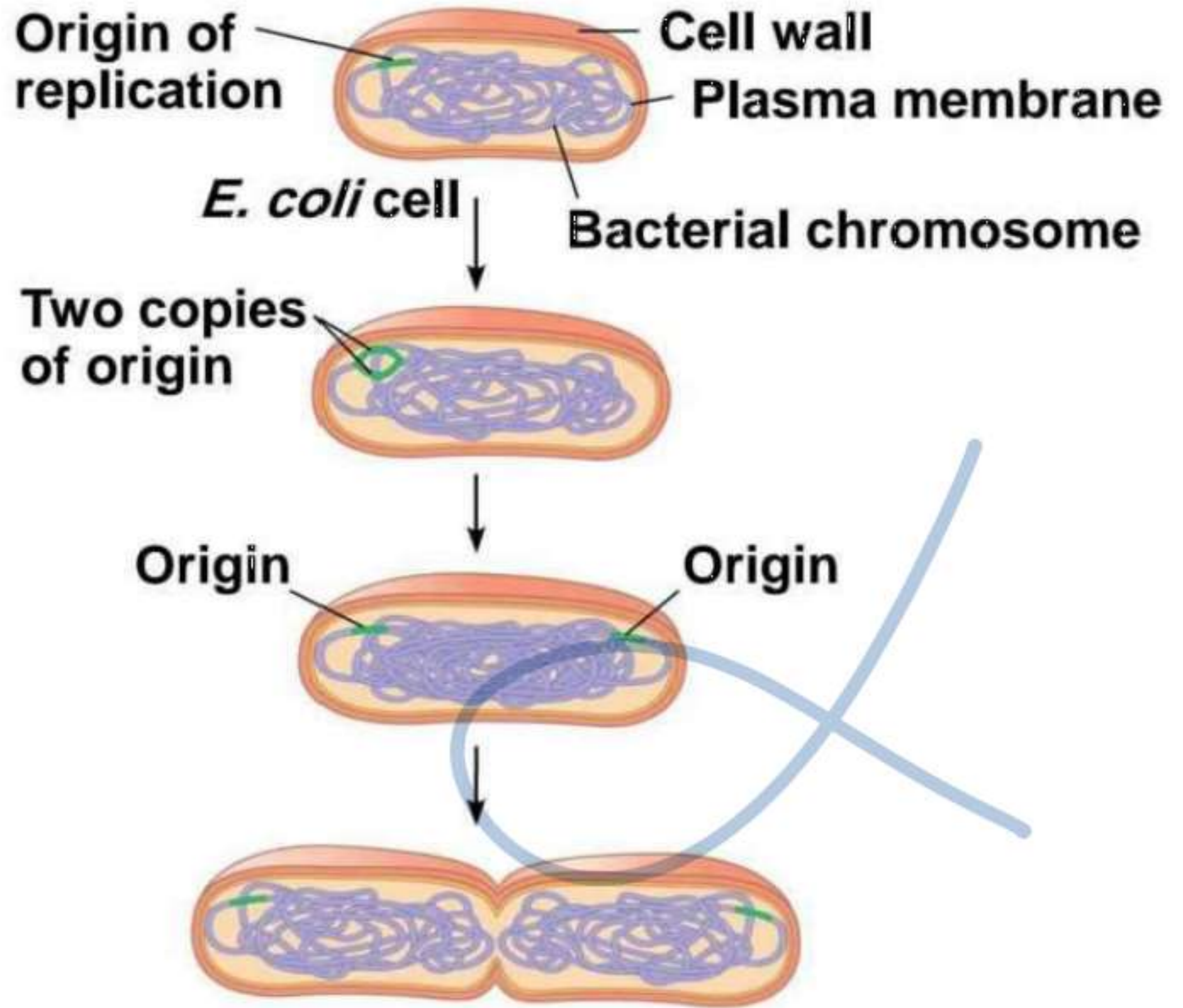
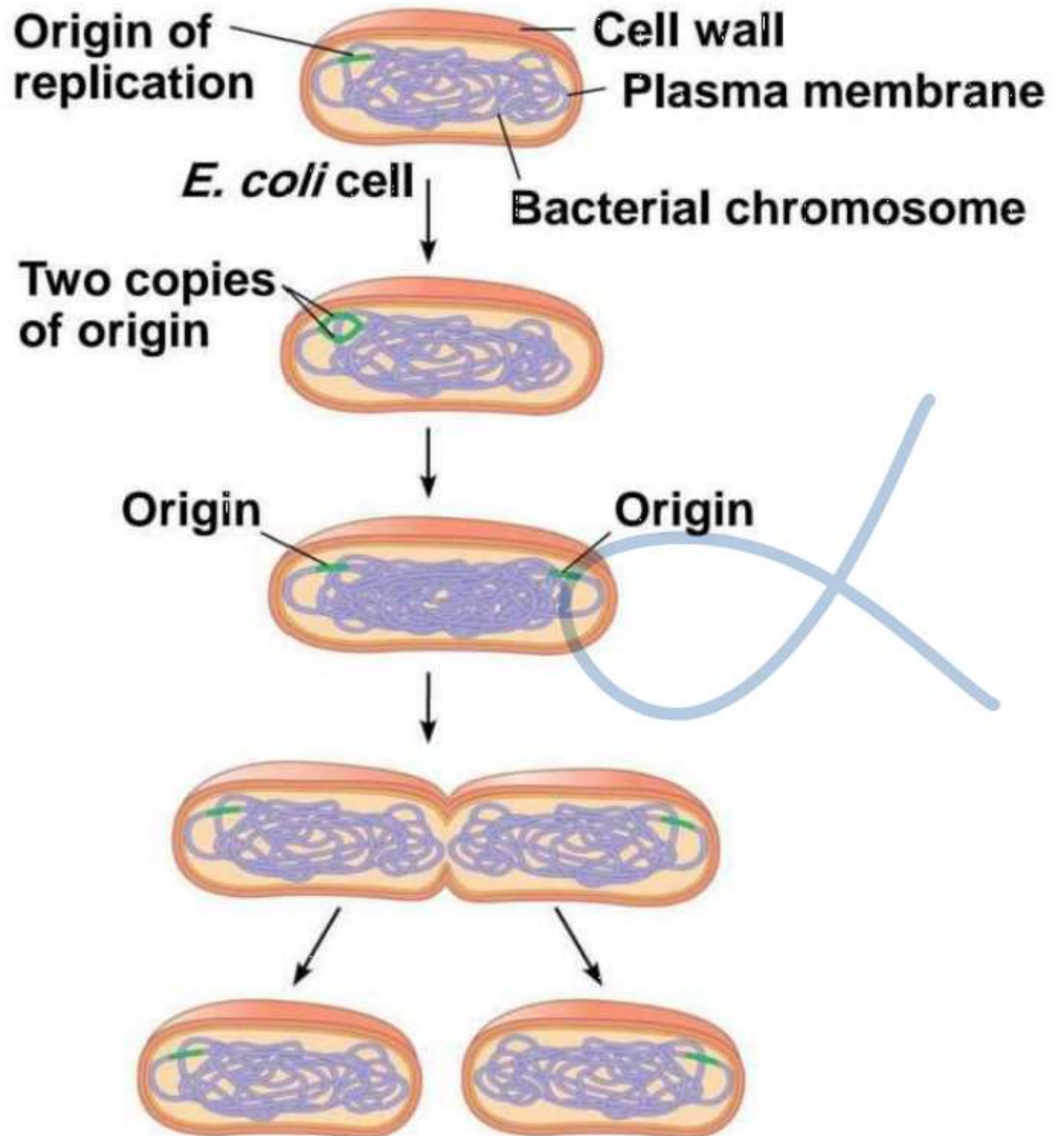


Figure 12.12-4

- 1** Chromosome replication begins.
- 2** Replication continues.
- 3** Replication finishes.
- 4** Two daughter cells result.



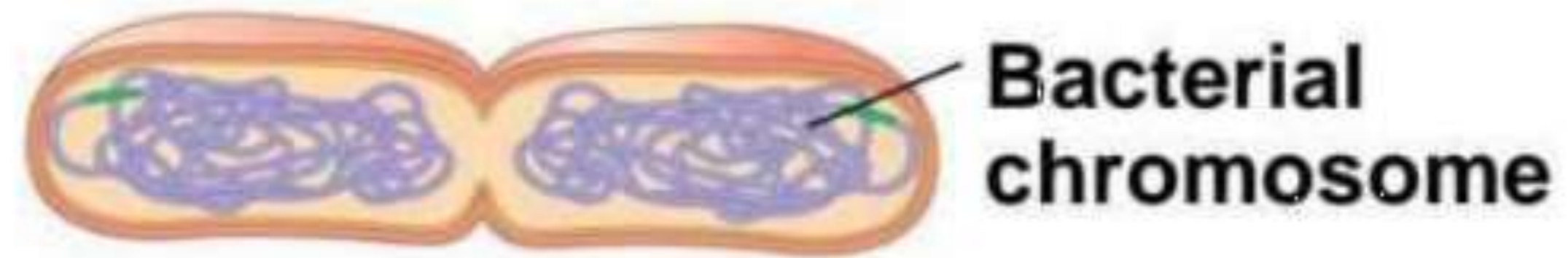
The Evolution of Mitosis

- Since prokaryotes evolved before eukaryotes, mitosis probably evolved from binary fission
- Certain protists exhibit types of cell division that seem intermediate between binary fission and mitosis

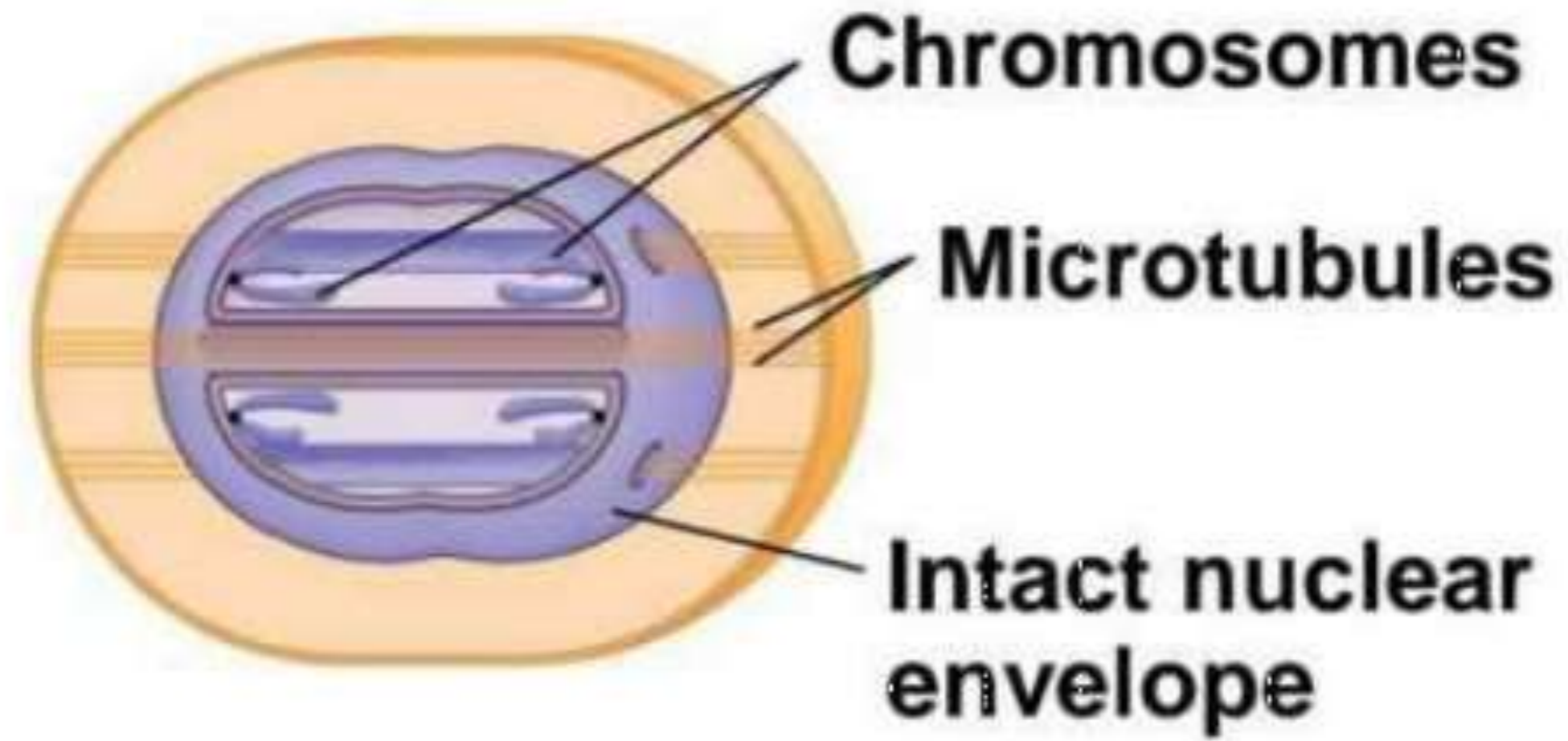


Figure 12.13

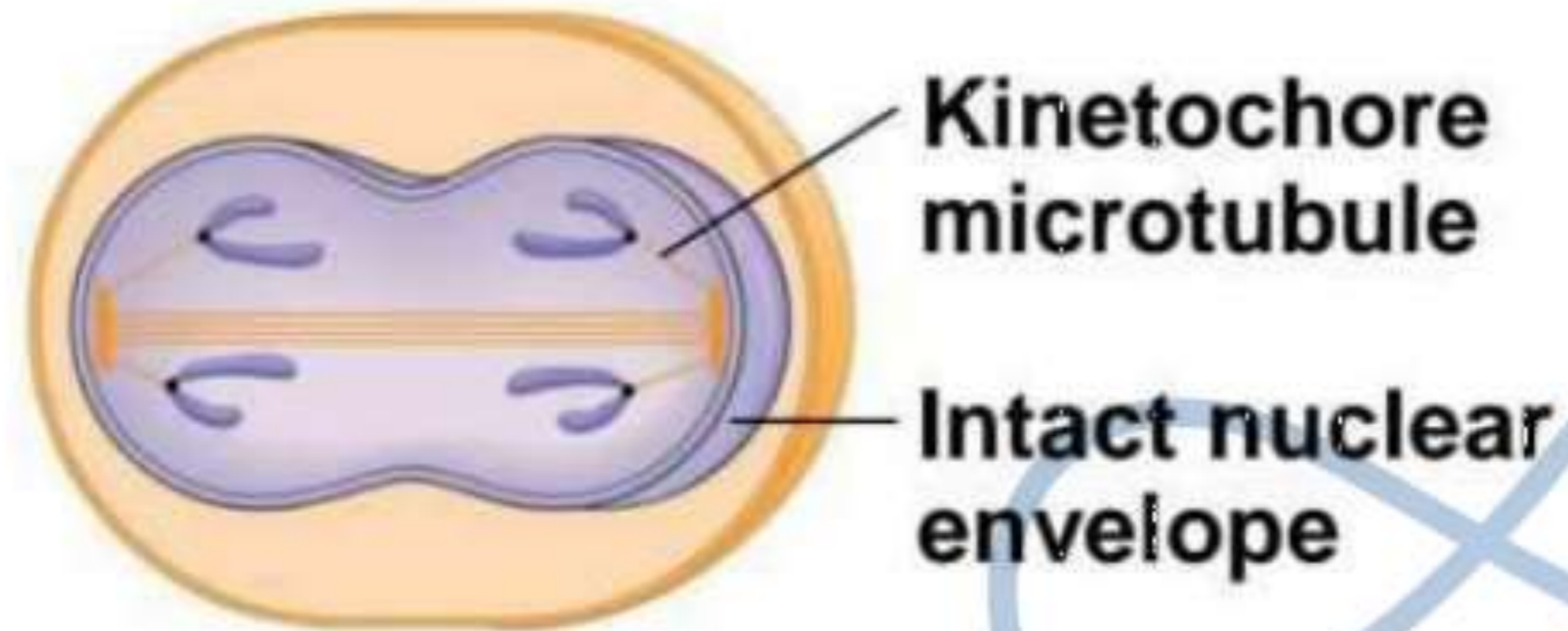
(a) Bacteria



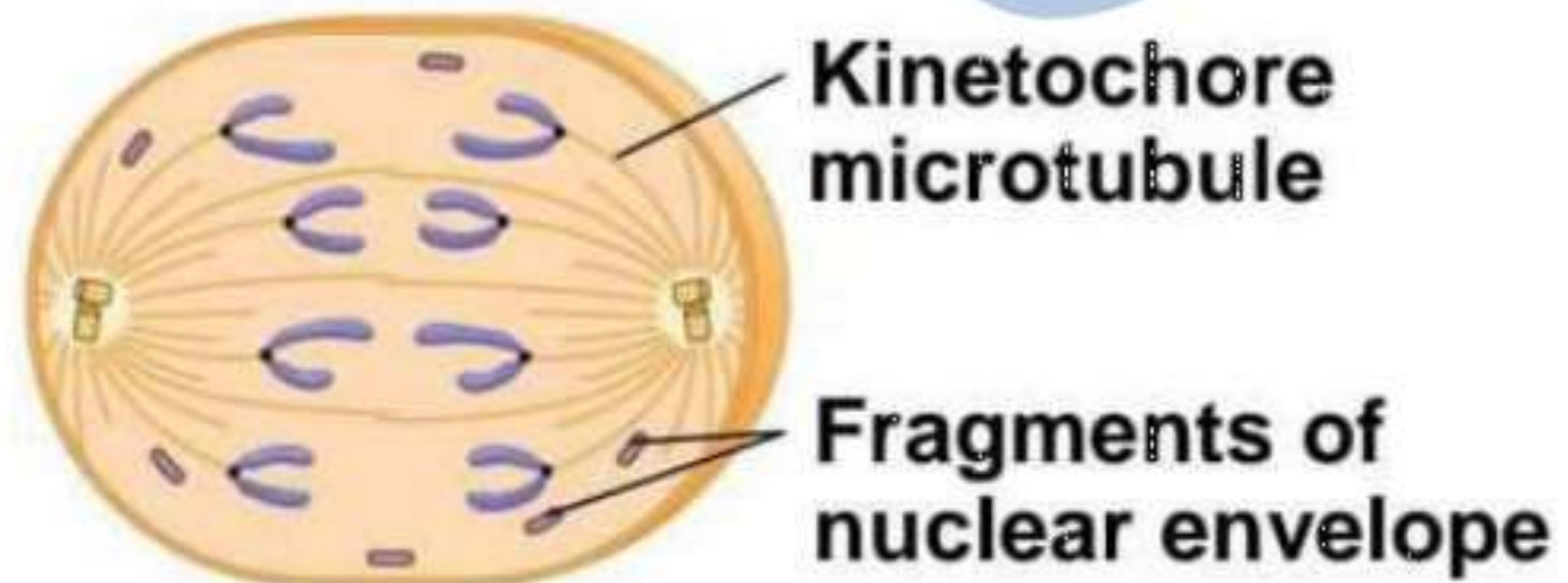
(b) Dinoflagellates

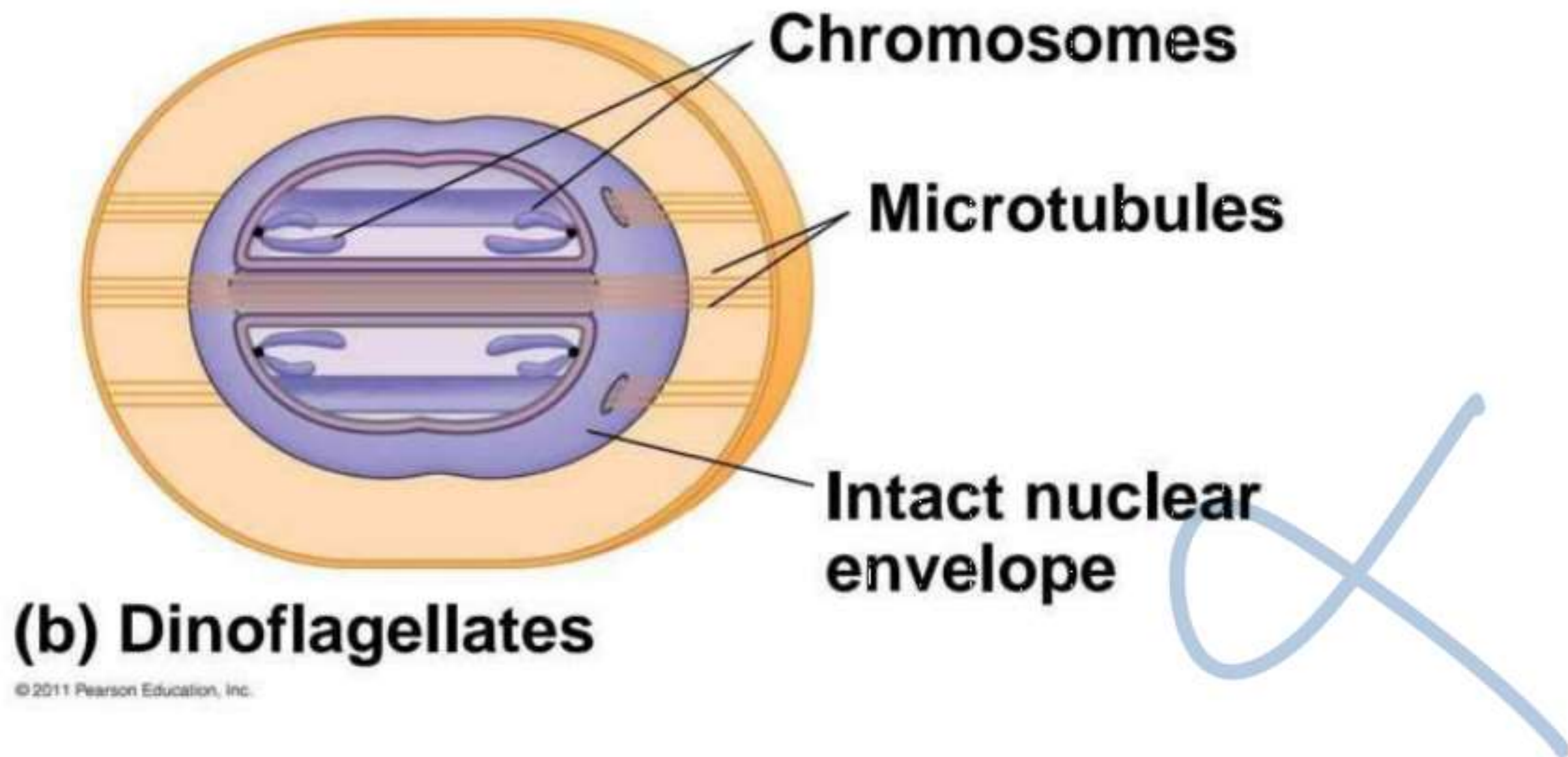
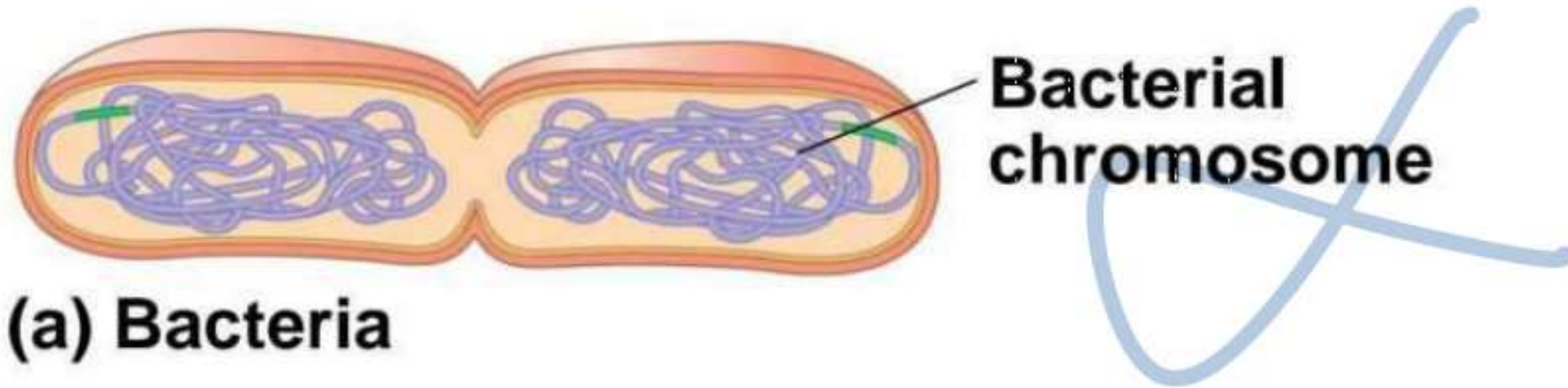


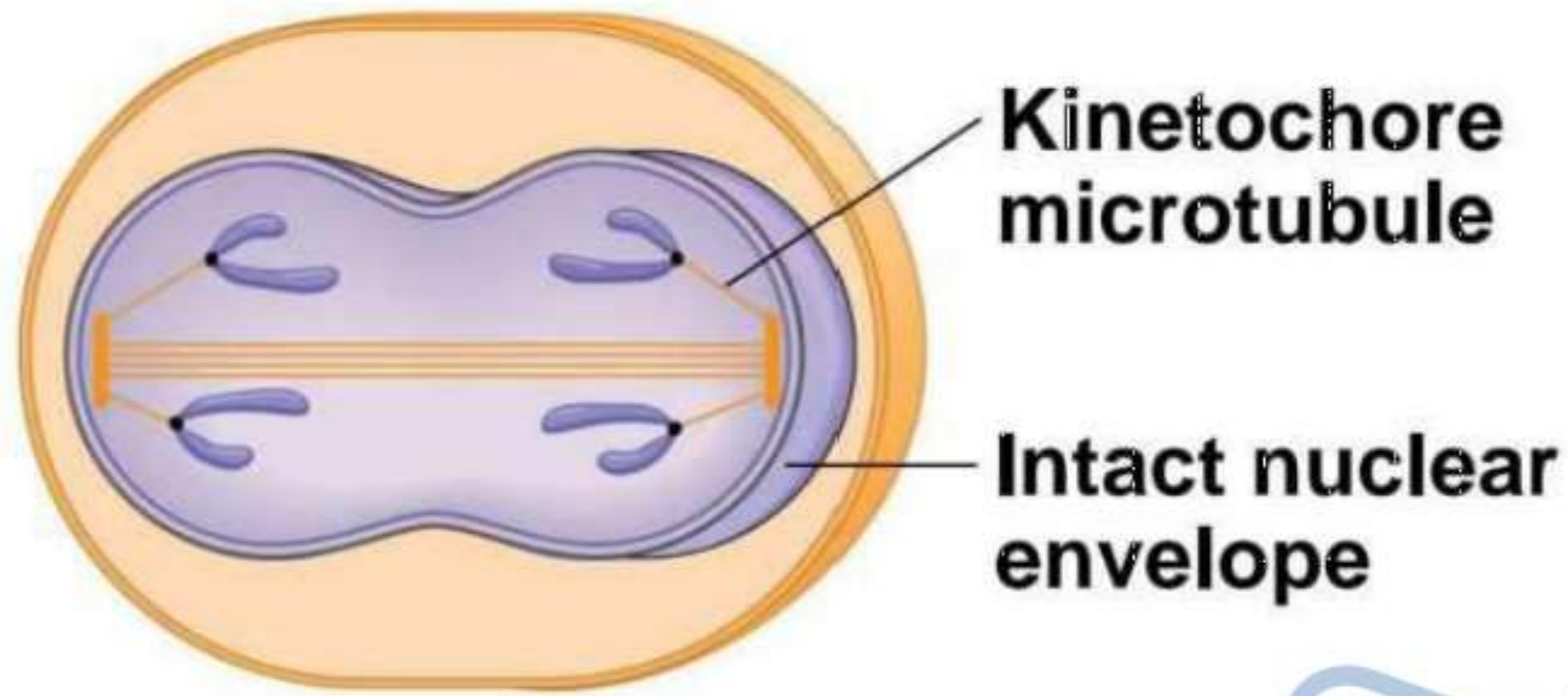
(c) Diatoms and some yeasts



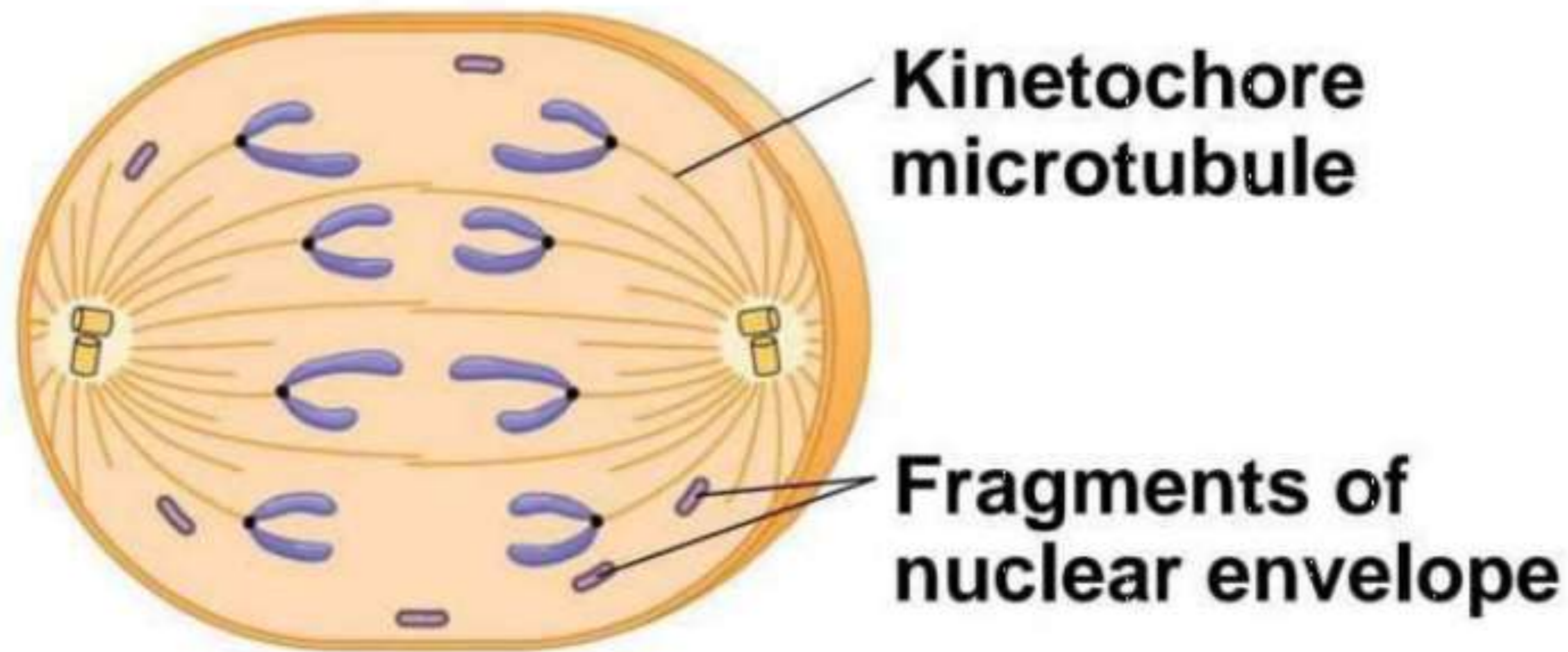
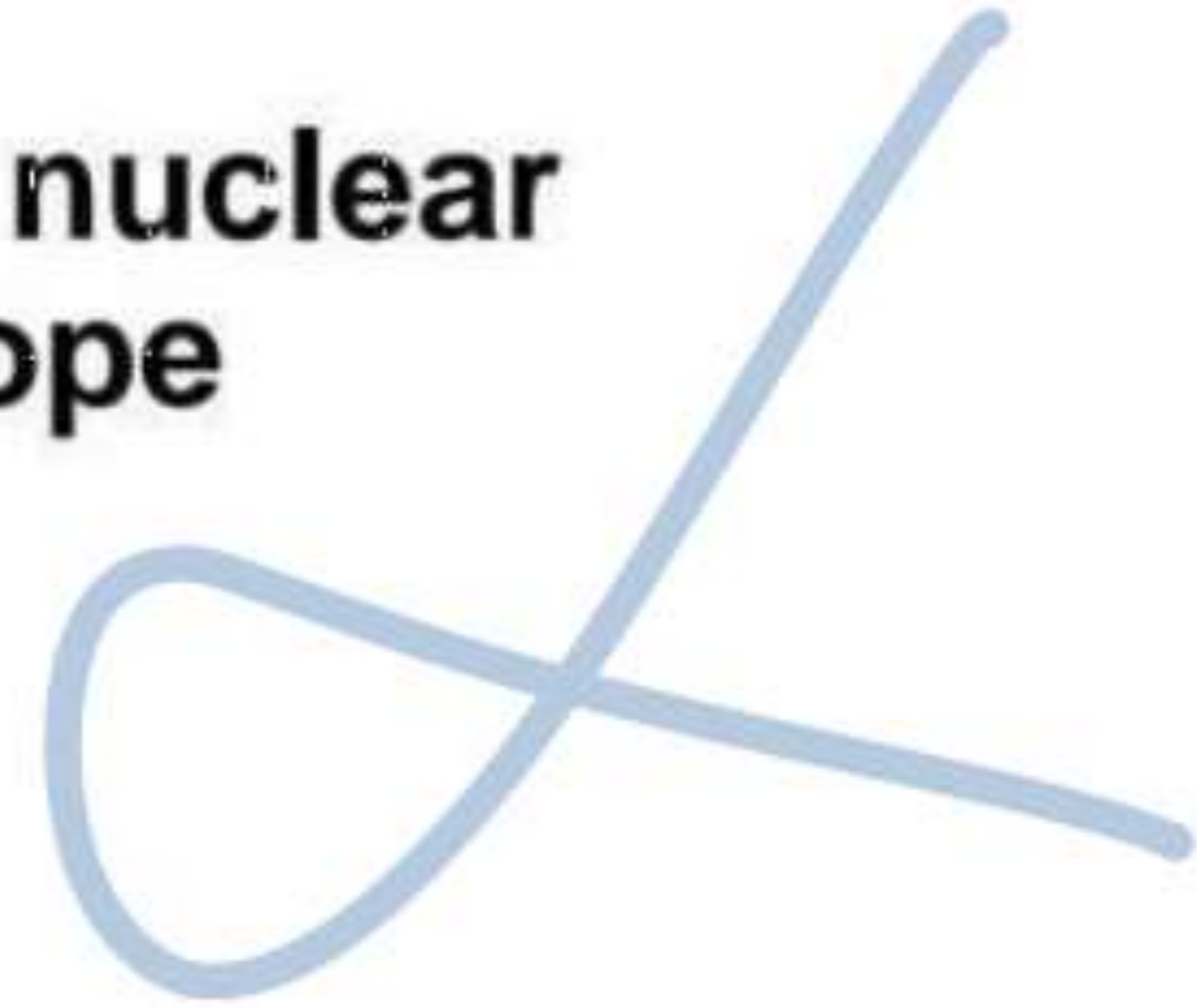
(d) Most eukaryotes







(c) Diatoms and some yeasts



(d) Most eukaryotes

How to regulate/control the cell cycle

Concept 12.3: The eukaryotic cell cycle is regulated by a molecular control system

- The frequency of cell division varies with the type of cell

مثلاً كل الخلايا تنقسم بنفس السرعة أو المعدل بسبب

- These differences result from regulation at the molecular level

على مستوى
الجزء

- Cancer cells manage to escape the usual controls (on the cell cycle)

لا يتحكم عليها
the normal regulation
system

تتقسم بسرعة كبيرة جداً

importance of cell cycle control

The timing and rate of cell division in different parts of a plant or animal are crucial to normal growth, development, and maintenance. The frequency of cell division varies with the type of cell. For example, human skin cells divide frequently throughout life, whereas liver cells maintain the ability to divide but keep it in reserve until an appropriate need arises—say, to repair a wound. Some of the most specialized cells, such as fully formed nerve cells and muscle cells, do not divide at all in a mature human. These cell cycle differences result from regulation at the molecular level. The mechanisms of this regulation are of great interest, not only to understand the life cycles of normal cells but also to learn how cancer cells manage to escape the usual controls.

liver cells have the ability for division, ولكن لا تنقسم 24 ساعة، كتنفذ بقدرتها تلك الى وقت الكافية (a)

خلايا الجلد تبقى تنقسم وتتجدد طوال العمر [لواخرج عموكبير ح يلقم ابرح]

الاهلية (a) + (b)

Evidence for Cytoplasmic Signals

من وينجابا قصة وجود molecules في cytoplasm التي تكثر على ال control of the cell cycle?

الكلمة
what do we mean by molecular level?

- The cell cycle appears to be driven by specific chemical signals present in the cytoplasm
- Some evidence for this hypothesis comes from experiments in which cultured mammalian cells at different phases of the cell cycle were fused to form a single cell with two nuclei

Conclusion The results of fusing a G₁ cell with a cell in the S or M phase of the cell cycle suggest that molecules present in the cytoplasm during the S or M phase control the progression to those phases.

التجربة للفح فقط / غير مطلوبة في الامتحان

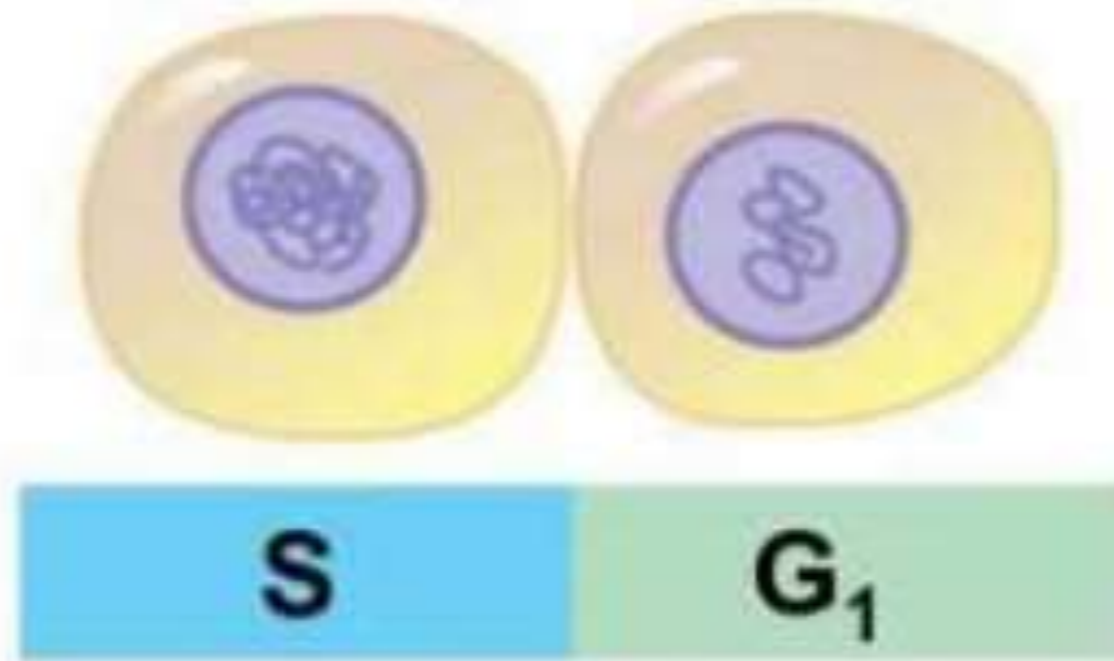
* حسب ما فهمت conclusion التجربة مطلوب

Figure 12.14

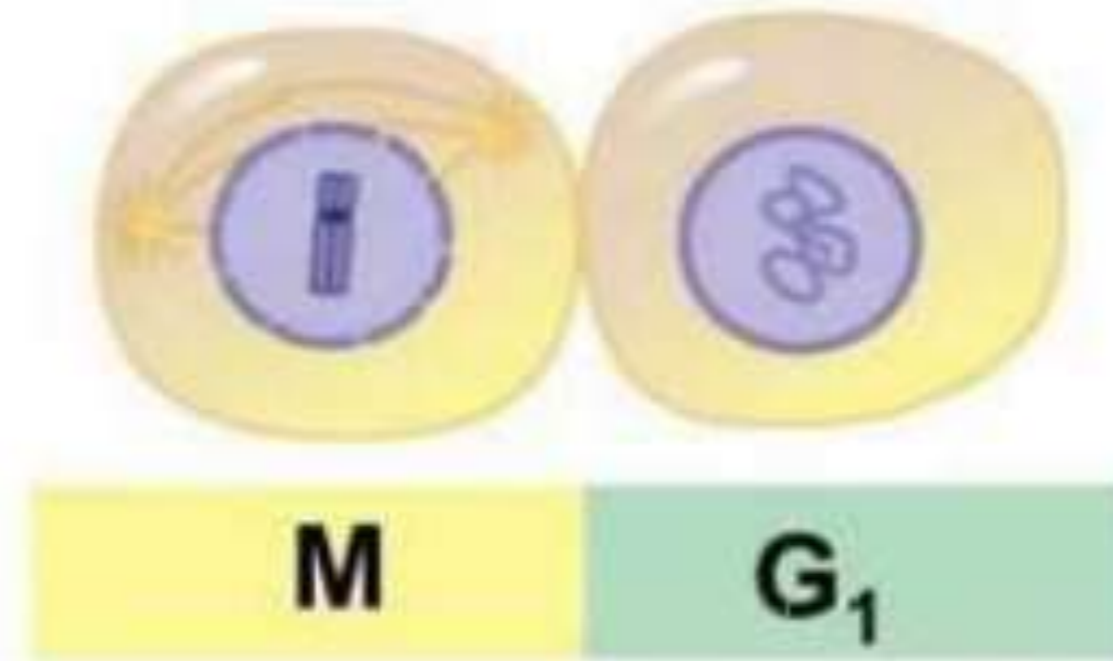


EXPERIMENT

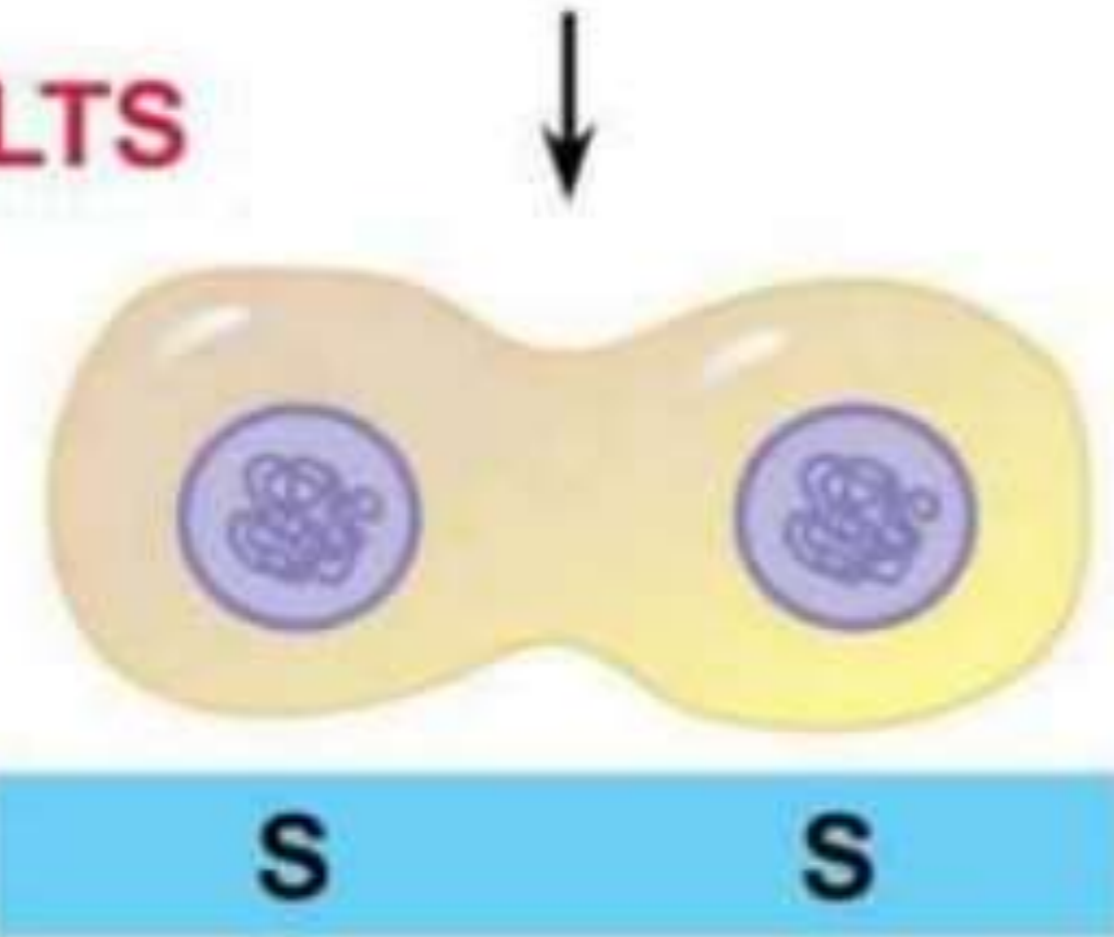
Experiment 1



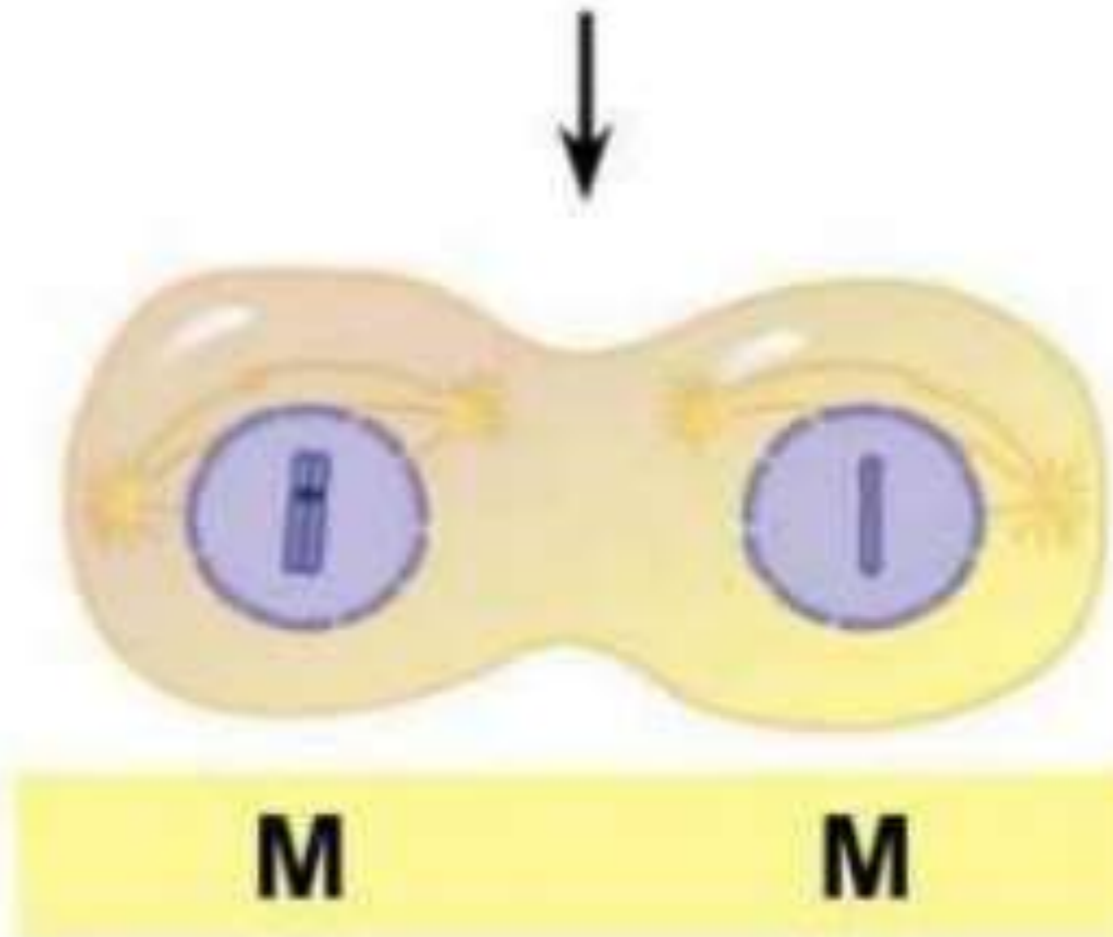
Experiment 2



RESULTS



When a cell in the S phase was fused with a cell in G_1 , the G_1 nucleus **immediately entered the S phase—DNA was synthesized.**



When a cell in the M phase was fused with a cell in G_1 , the G_1 nucleus **immediately began mitosis**—a spindle formed and chromatin condensed, even though the chromosome had not been duplicated. →

$G_1 \rightarrow$ M phase
skipped stages

ماہرقت
S phase لے

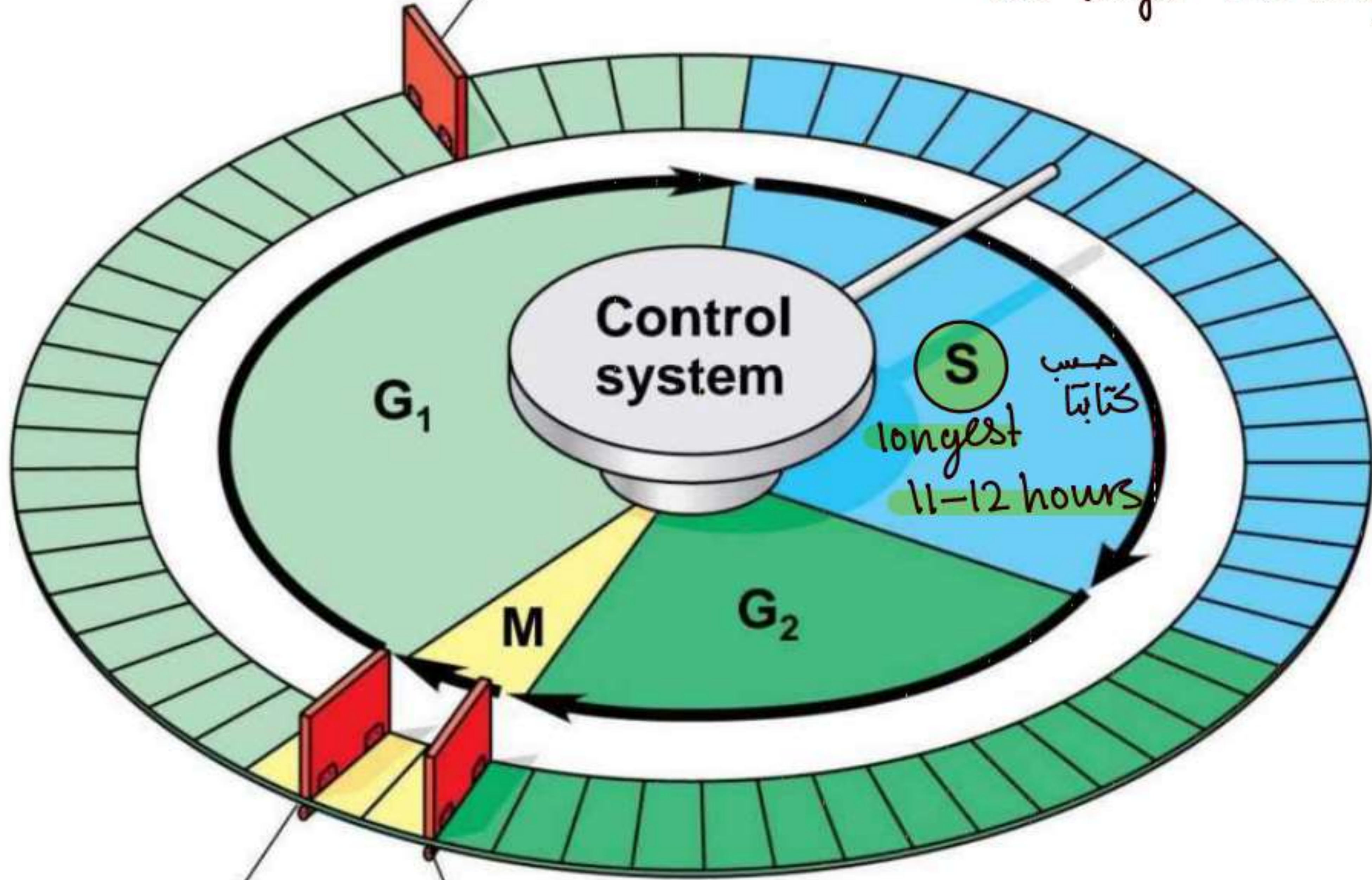
The Cell Cycle Control System

- The sequential events of the cell cycle are directed by a distinct **cell cycle control system**, which is similar to a clock [clock wise]
- The cell cycle control system is regulated by both internal and external controls → *منظورها ما ترجع بالاتجاه الواحد - unidirectional*
- The clock has specific **checkpoints** where the cell cycle **stops** until a **go-ahead** signal is received

* we have 3 checkpoints → **G₁ checkpoint** in G₁ phase
↳ **G₂ checkpoint** [btw G₂ & M]
↳ **M checkpoint** in M phase

Figure 12.15

G₁ checkpoint → most important checkpoint
- has larger role in regulation



S
longest
11-12 hours
حسب كتابا

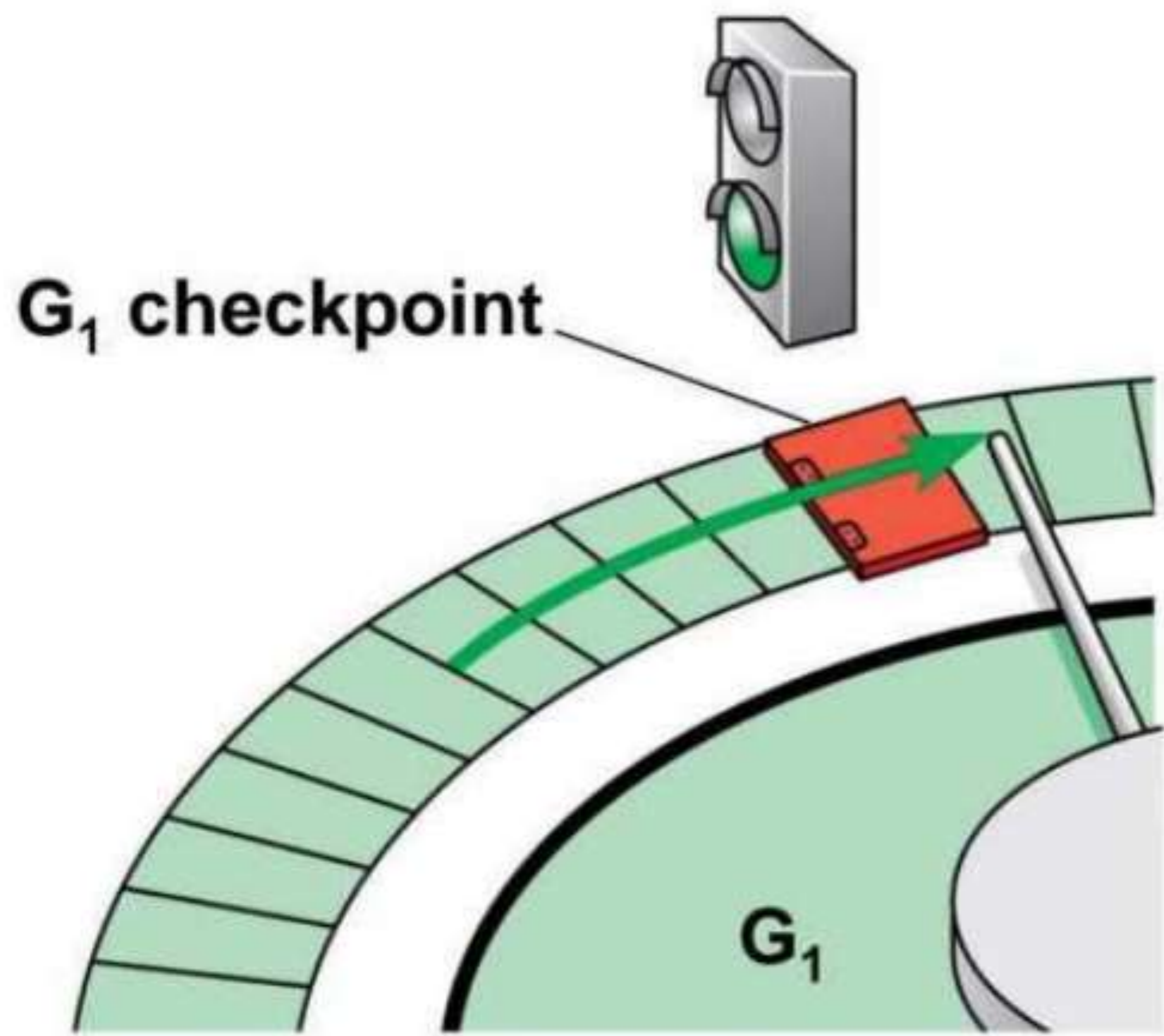
M checkpoint

G₂ checkpoint

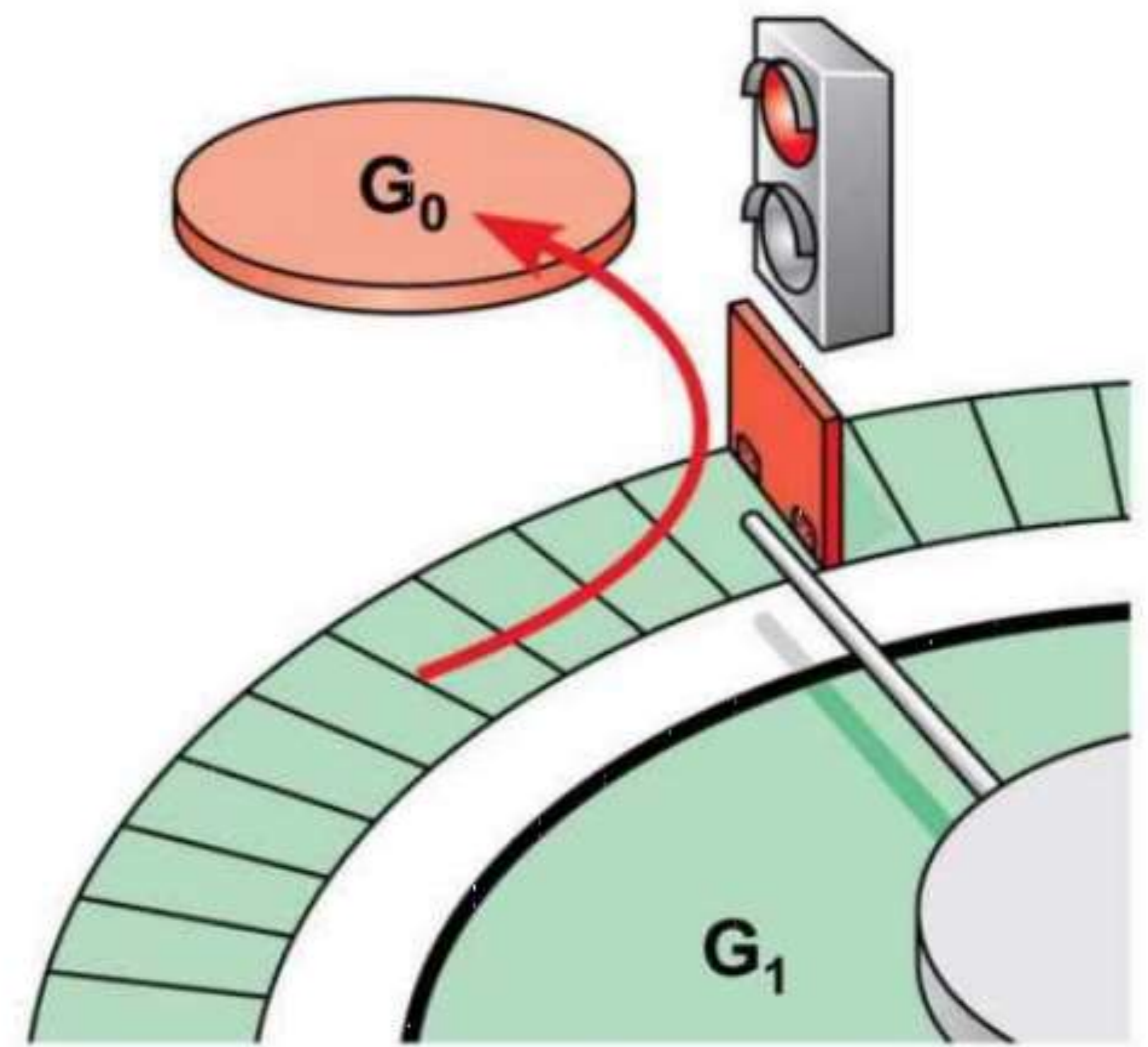
- For many cells, the G_1 checkpoint seems to be the most important
- ① If a cell receives a go-ahead signal at the G_1 checkpoint, it will usually complete the S, G_2 , and M phases and divide
- ② If the cell does not receive the go-ahead signal, it will exit the cycle, switching into a nondividing state called the **G_0 phase** ↓

ممكن تبقى فيه وممكن تطلع منه وتكمل دورة الخلية

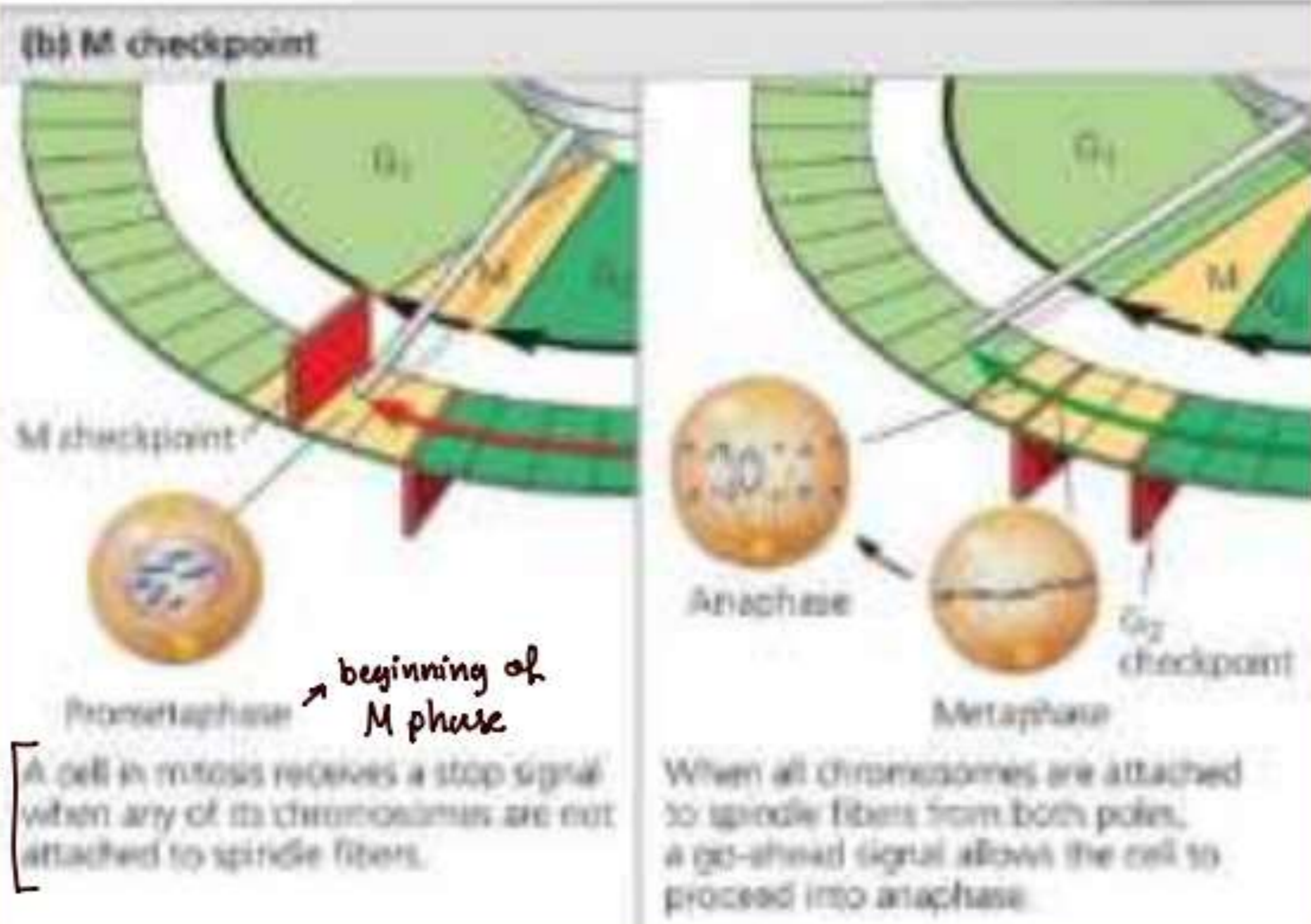
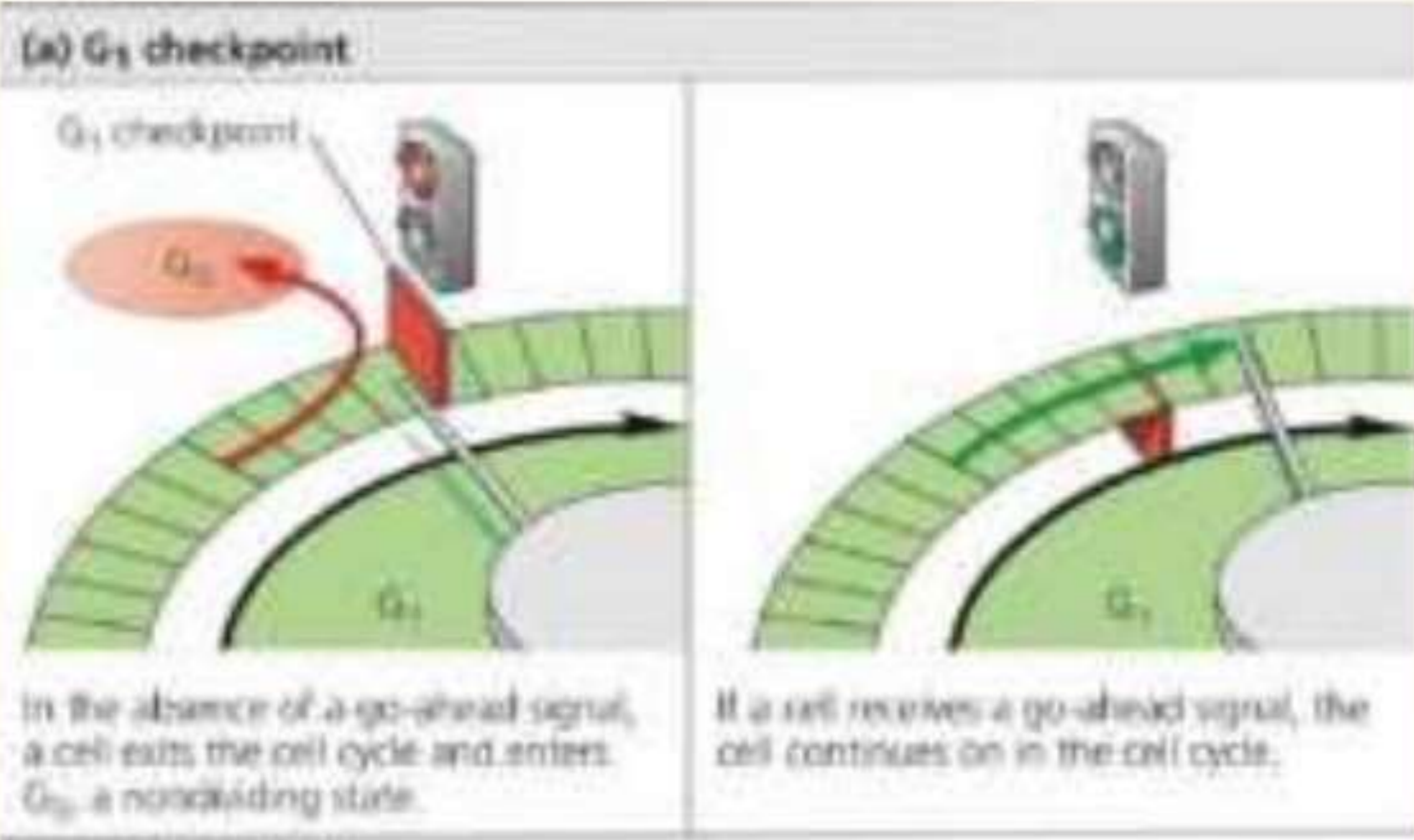
Figure 12.16



(a) Cell receives a go-ahead signal.



(b) Cell does not receive a go-ahead signal.
[stop signal]



The Cell Cycle Clock: Cyclins and Cyclin-Dependent Kinases

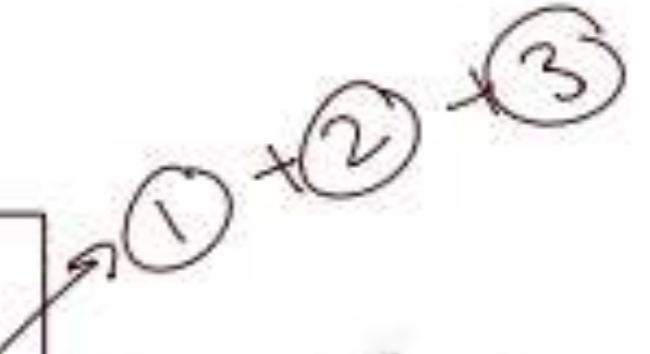
- Two types of **regulatory proteins** are involved in cell cycle control: **cyclins** and **cyclin-dependent kinases (Cdks)**

- Cdks** activity fluctuates during the cell cycle because it is controlled by **cyclins**, so named because their concentrations vary with the cell cycle

- MPF** (maturation-promoting factor) is a **cyclin-Cdk** complex that triggers a cell's passage past the G₂ checkpoint into the M phase

also called M-phase promoting factor

chemical signals



يُتذبذب

cyclin مختلف حسب cell cycle
Cdks مختلف حسب cyclin

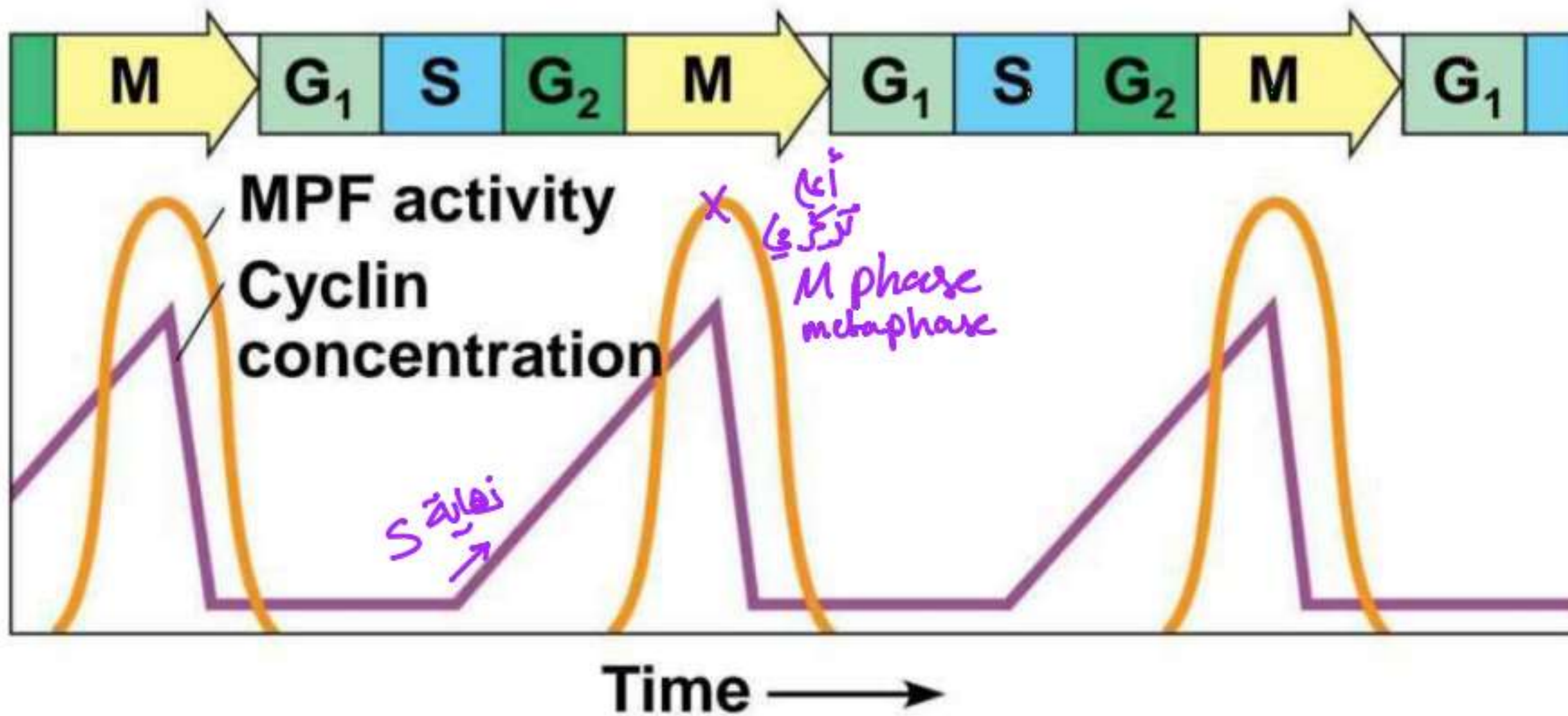
نتيجة من ارتباط

محفز

أي عند تكوينه

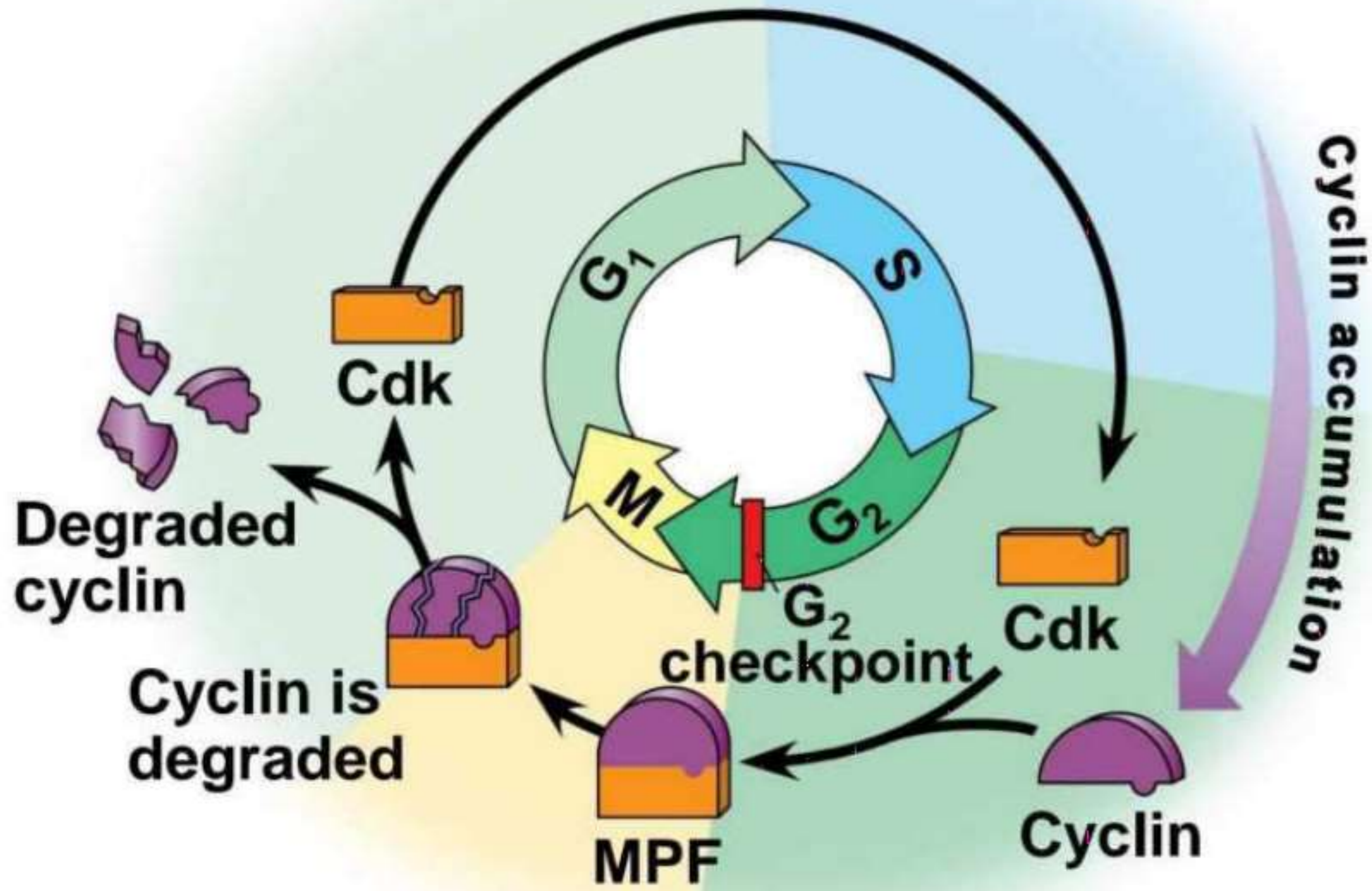
the cell will be matured

Figure 12.17a



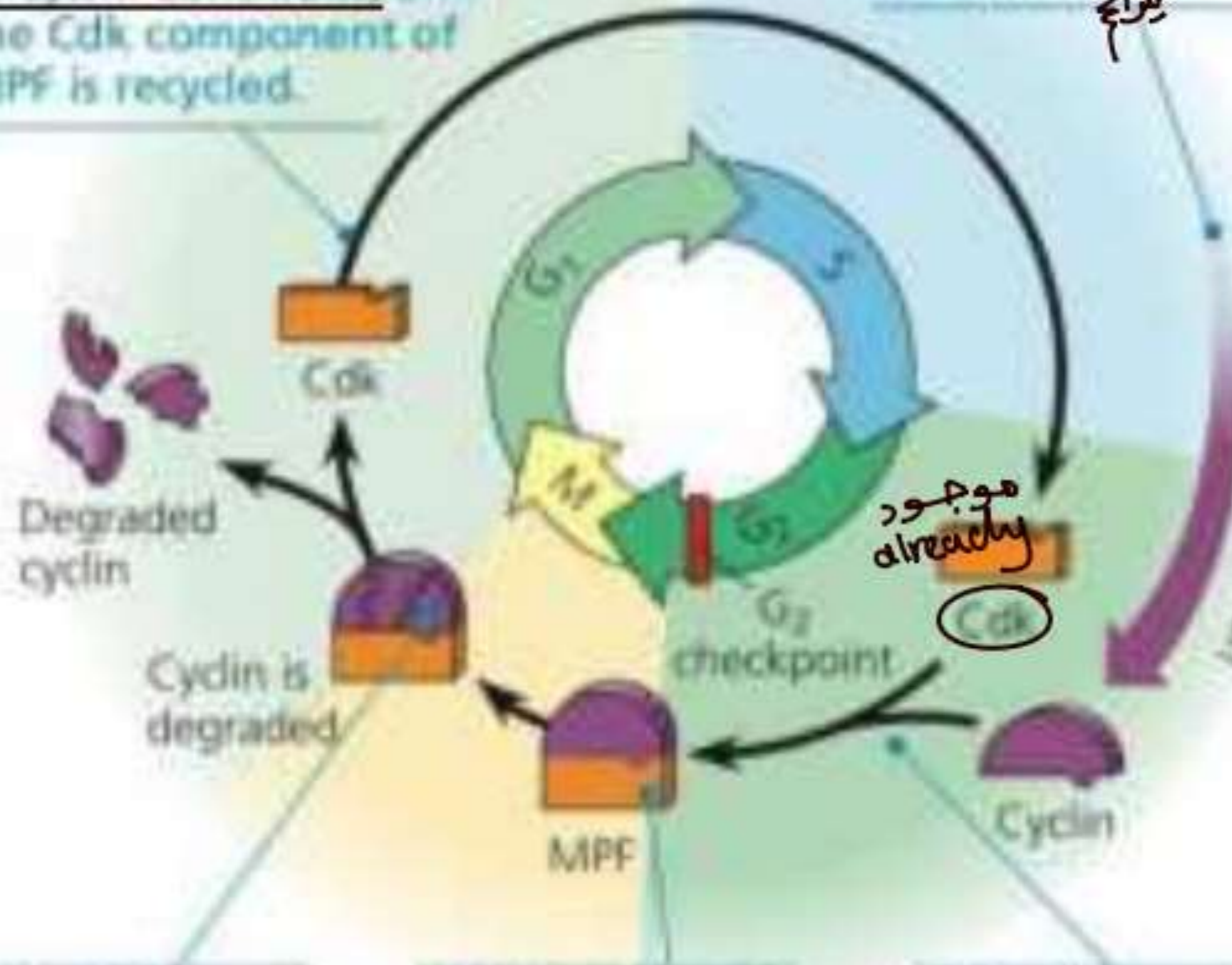
(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle

Figure 12.17b



(b) Molecular mechanisms that help regulate the cell cycle

5 During G_1 , the degradation of cyclin continues, and the Cdk component of MPF is recycled.



1 Synthesis of cyclin begins in late S phase and continues through G_2 . Because cyclin is protected from degradation during this stage, it accumulates.

S → G₂
خلال ذلك تصنع cyclin
يعطيها إشارة للذهاب إلى

4 During anaphase, the cyclin component of MPF is degraded, terminating the M phase. The cell enters the G_1 phase.

يتكسر إشارة الانقسام M phase ودخوله G₁

3 MPF promotes mitosis by phosphorylating various proteins. MPF's activity peaks during metaphase.

أي تركزه في metaphase

2 Cyclin combines with Cdk, producing MPF. When enough MPF molecules accumulate, the cell passes the G_2 checkpoint and begins mitosis.

تعتبرها إشارة للخروج من G₂ إلى M

Stop and Go Signs: Internal and External Signals at the Checkpoints

- An example of an **internal signal** is that kinetochores not attached to spindle microtubules send a molecular signal that delays anaphase
- Some **external signals** are **growth factors**, proteins released by certain cells that **stimulate** other cells to divide
- For example, **platelet-derived growth factor (PDGF)** stimulates the **division** of human fibroblast cells in culture

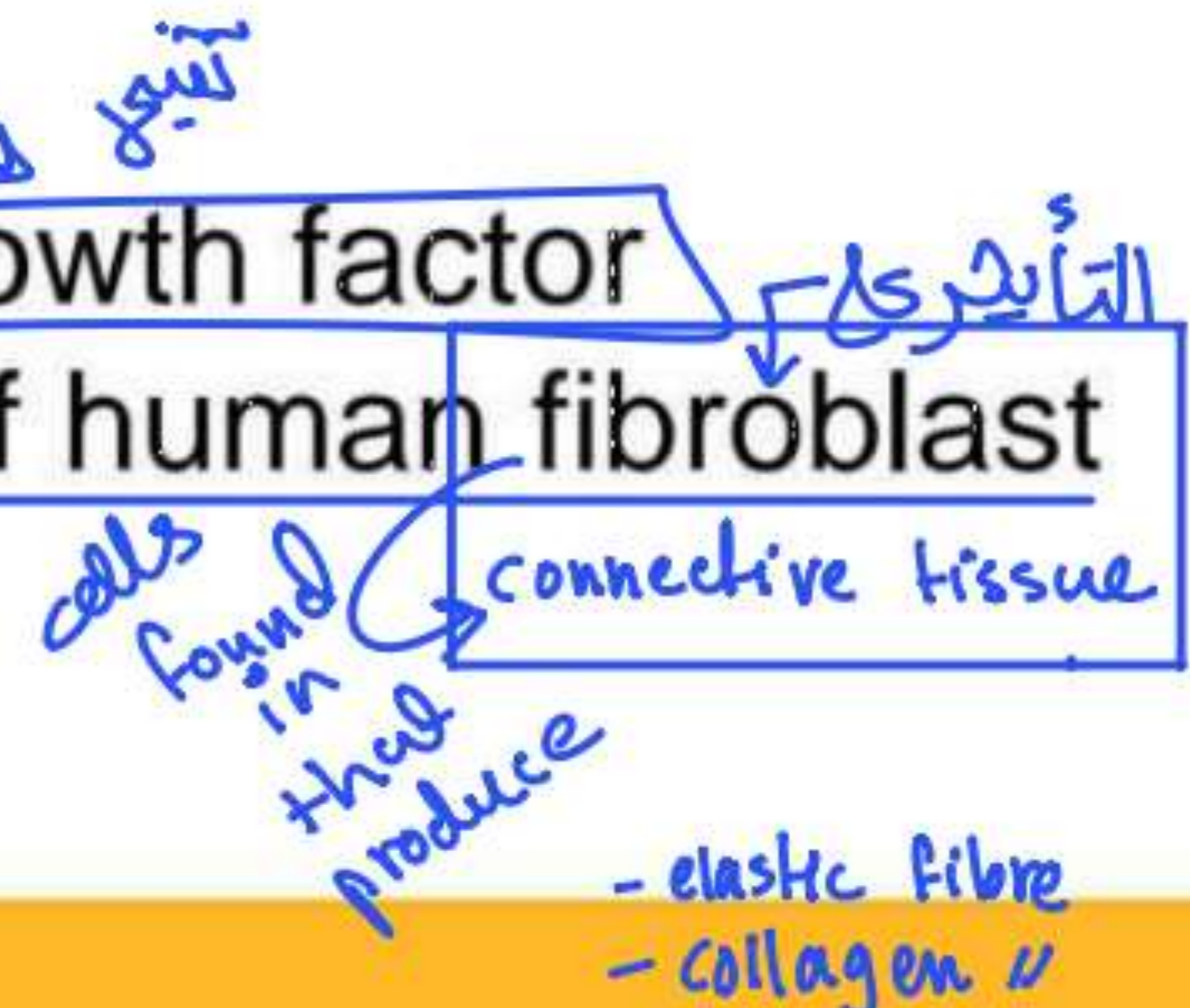
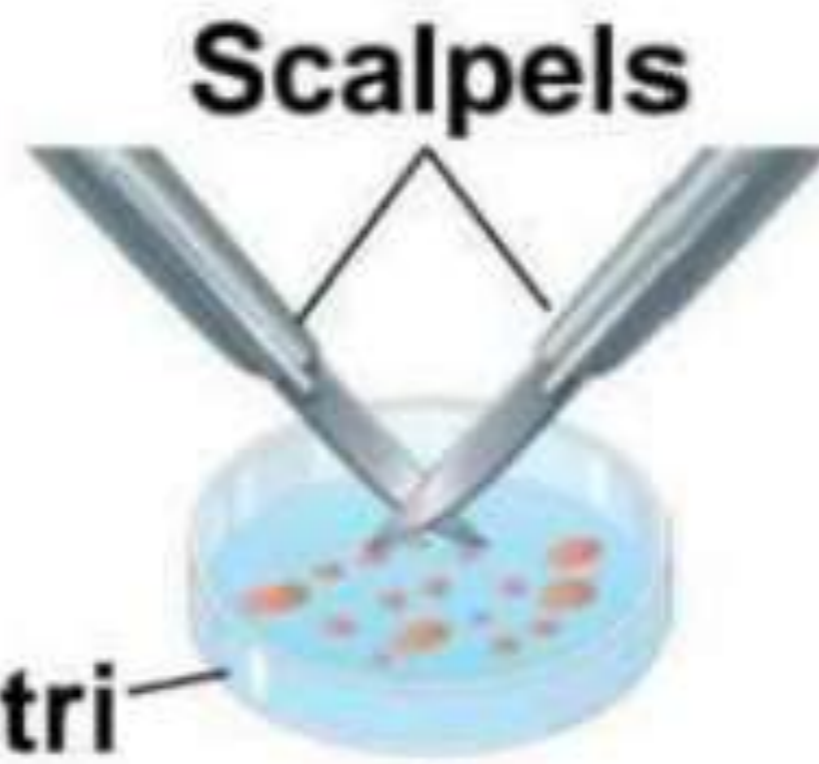


Figure 12.18

1 A sample of human connective tissue is cut up into small pieces. → ولكن مارجع خلايا



2 Enzymes digest the extracellular matrix, resulting in a suspension of free fibroblasts.

Petri dish



3 Cells are transferred to culture vessels.

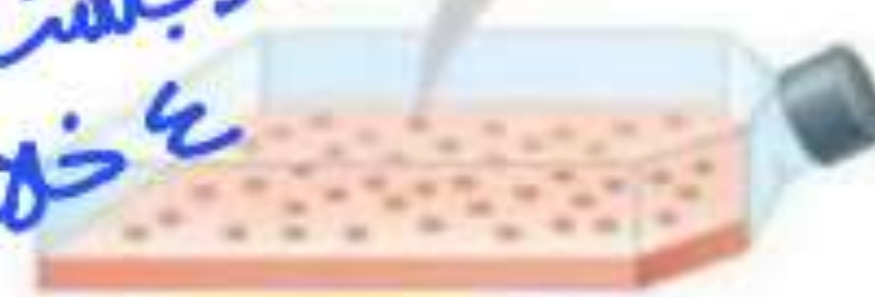
4 PDGF is added to half the vessels.

ع خلايا فقط + كل انسي
سكنا جوده الاقسام

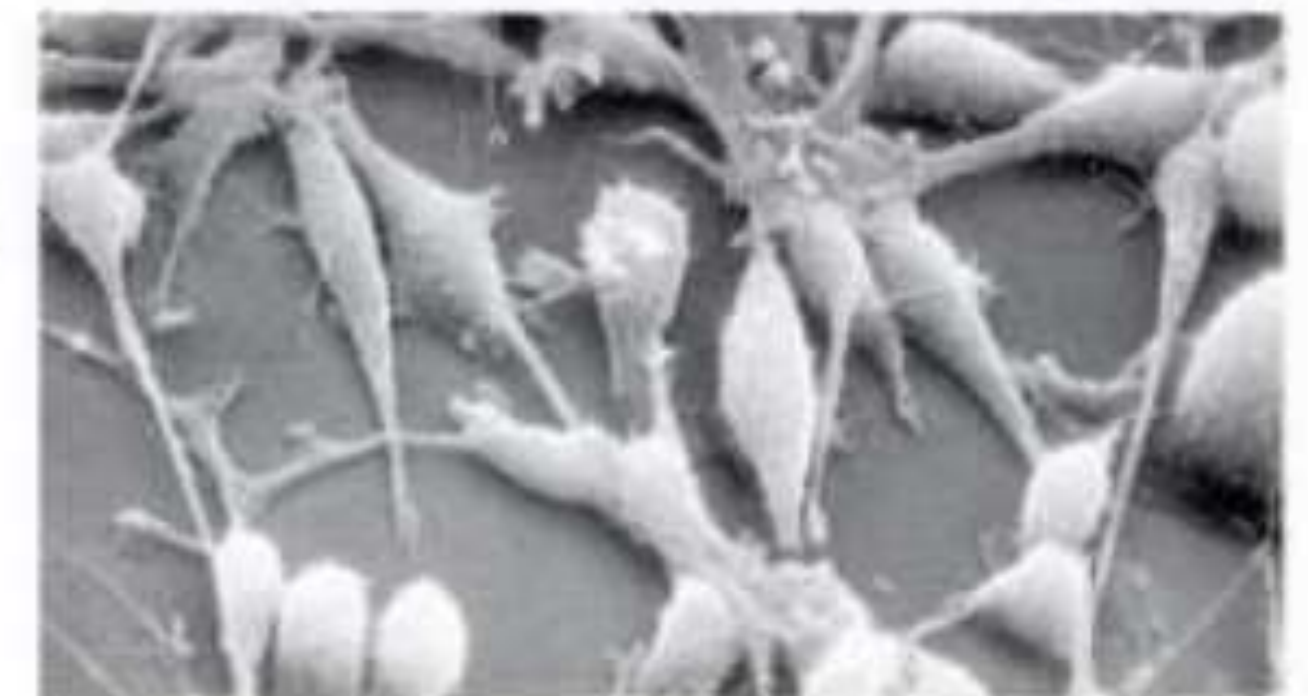


Without PDGF

بعضو بلنا ب
ع خلايا فقط



With PDGF

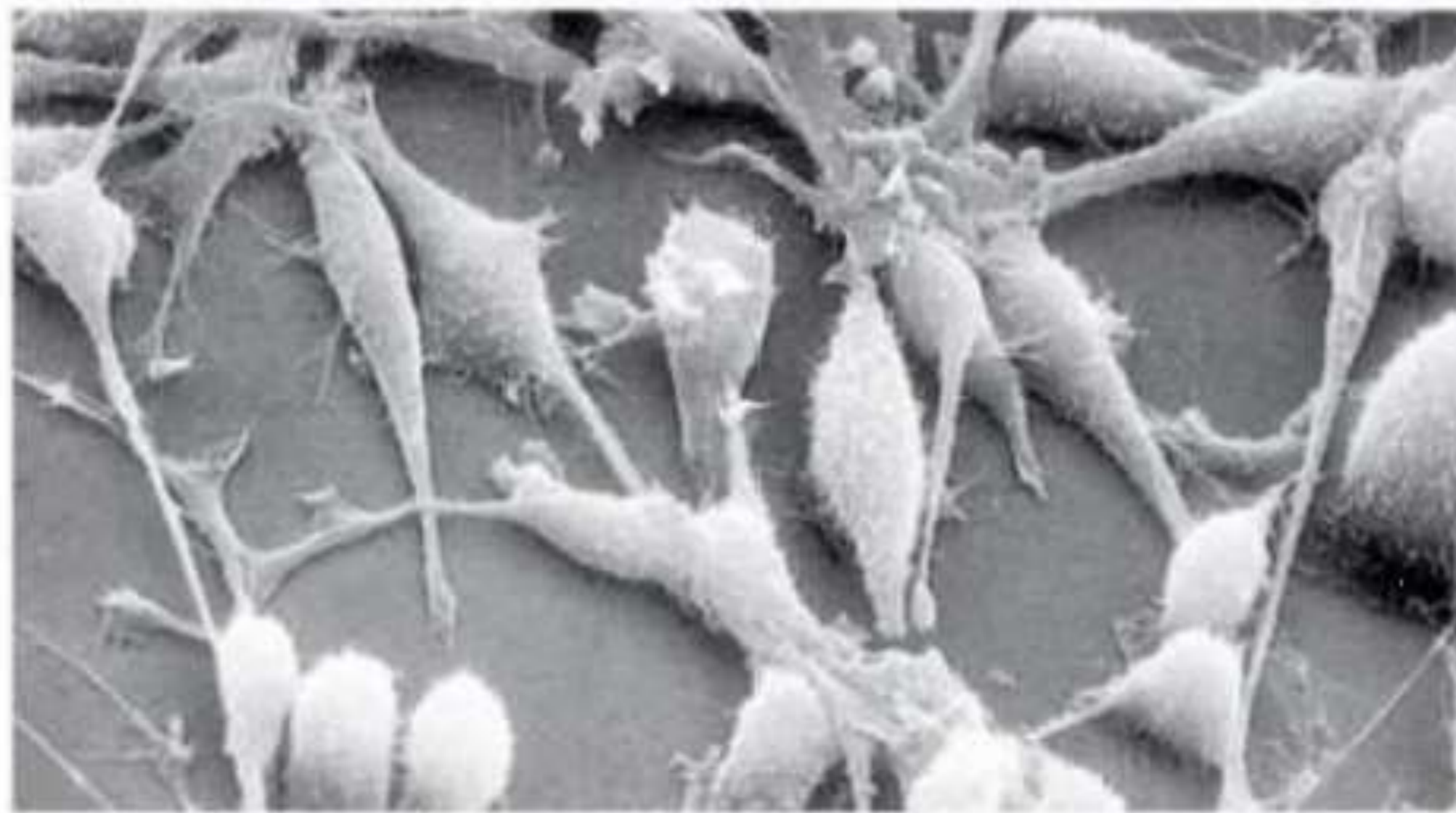


↓
خلايا 4 قسمه

↓
they divided + multiplied

Figure 12.18a

10 μm



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- A clear example of external signals is **density-dependent inhibition**, in which crowded cells

عشانه ما

يَكْسِرُوا

layers

قوة

بعض

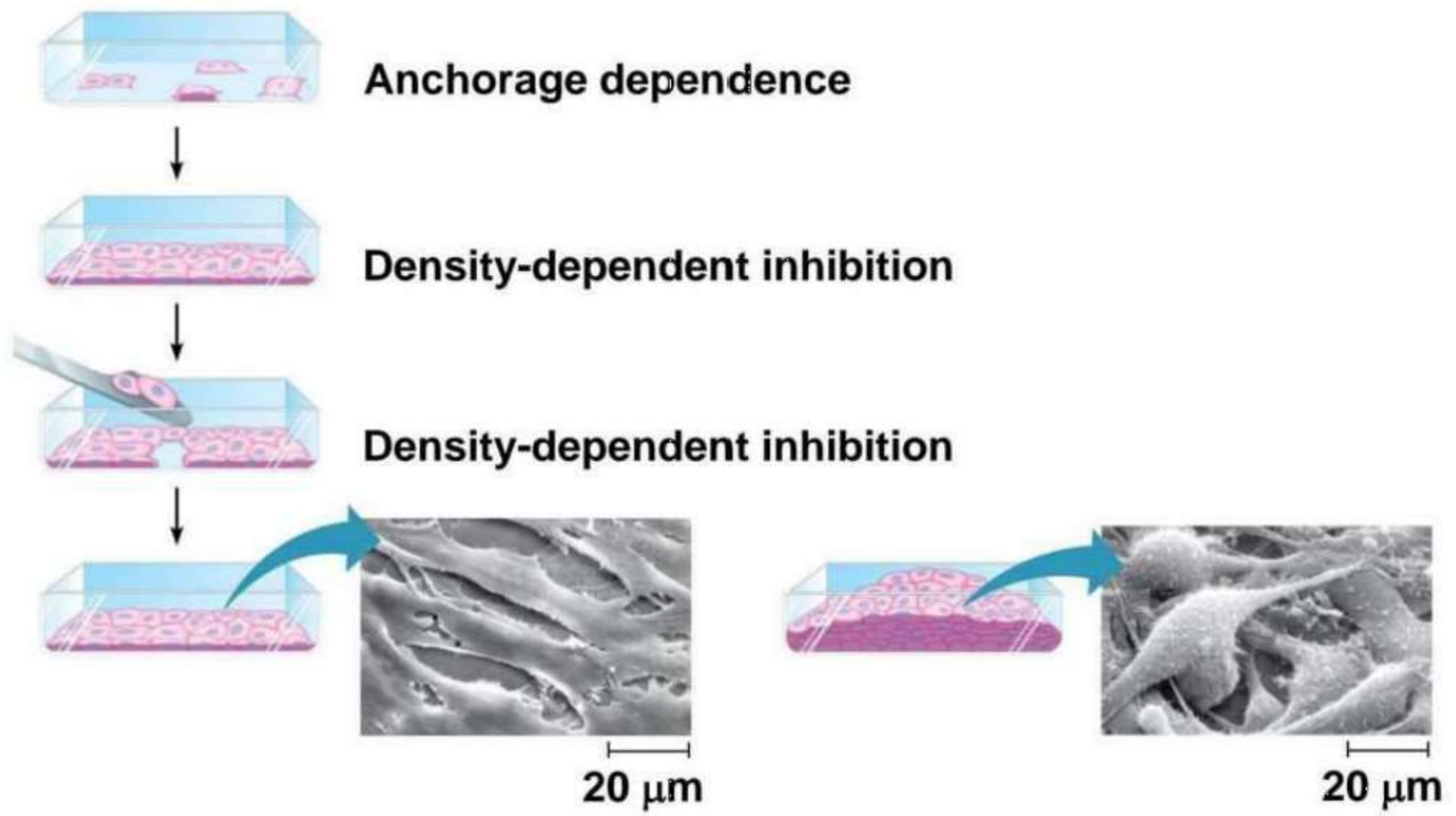
stop dividing → because of its density

Most animal cells also exhibit **anchorage dependence**, in which they must be attached to a substratum in order to divide

الخلايا اذا لقت انفسها
تثبت فيه / حيز دار
انفسها

- Cancer cells exhibit neither density-dependent inhibition nor anchorage dependence

Figure 12.19



(a) Normal mammalian cells

(b) Cancer cells



Cells anchor to dish surface and divide (anchorage dependence).

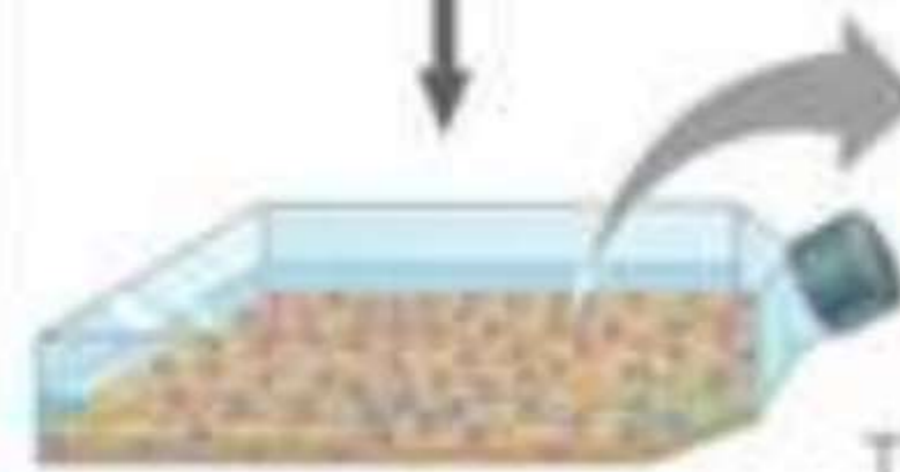


When cells have formed a complete single layer, they stop dividing (density-dependent inhibition).

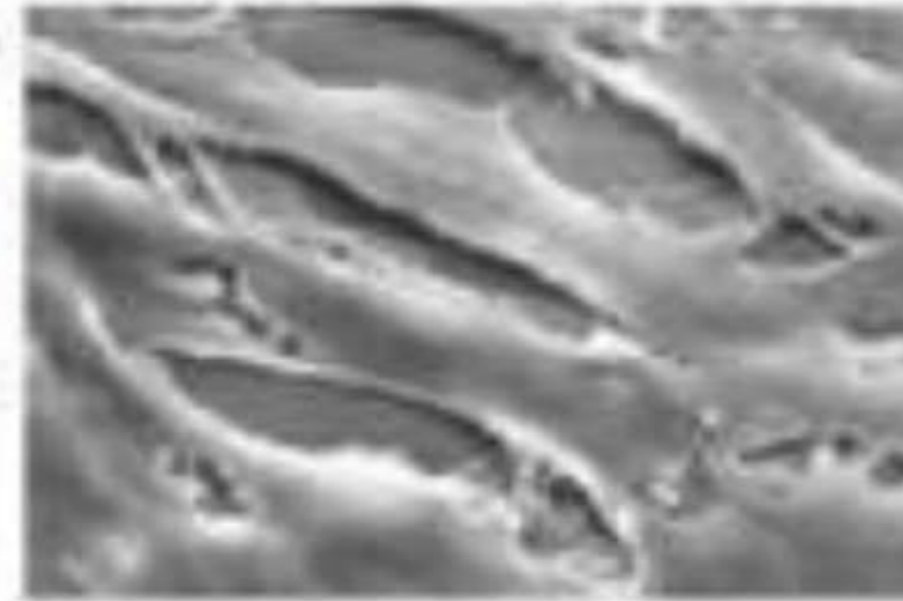


If some cells are scraped away, the remaining cells divide to fill the gap and then stop once they contact each other.

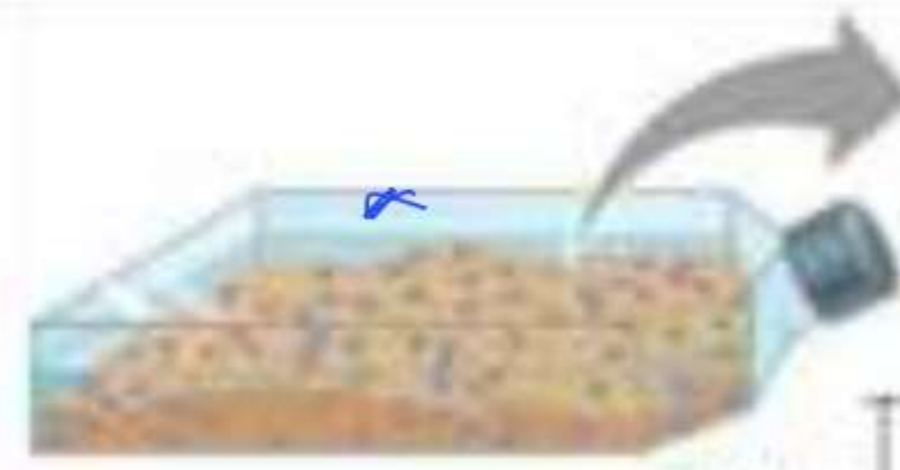
[density-dependent inhibition]



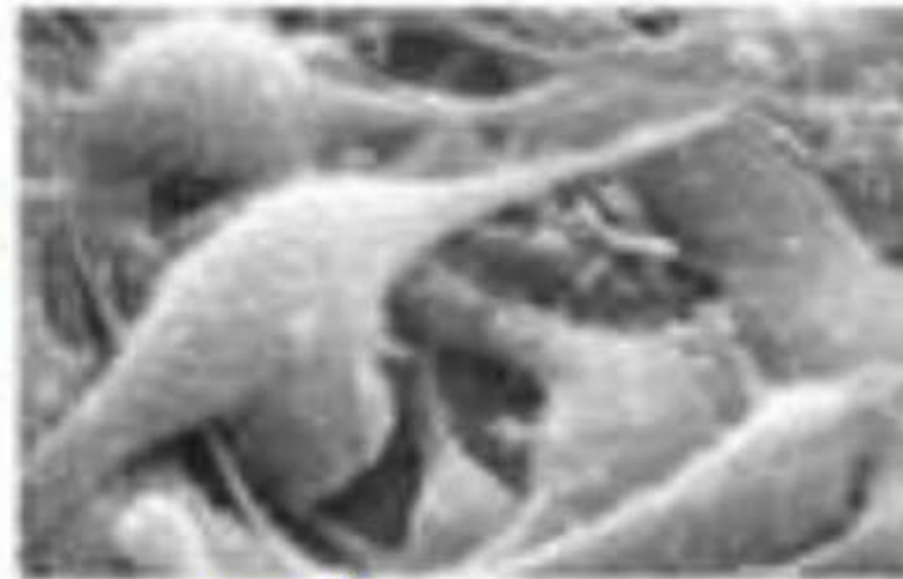
20 μm



(a) Normal mammalian cells. Cell density is limited to a single layer by contact with neighboring cells and the availability of nutrients, growth factors, and a substratum for attachment.



20 μm



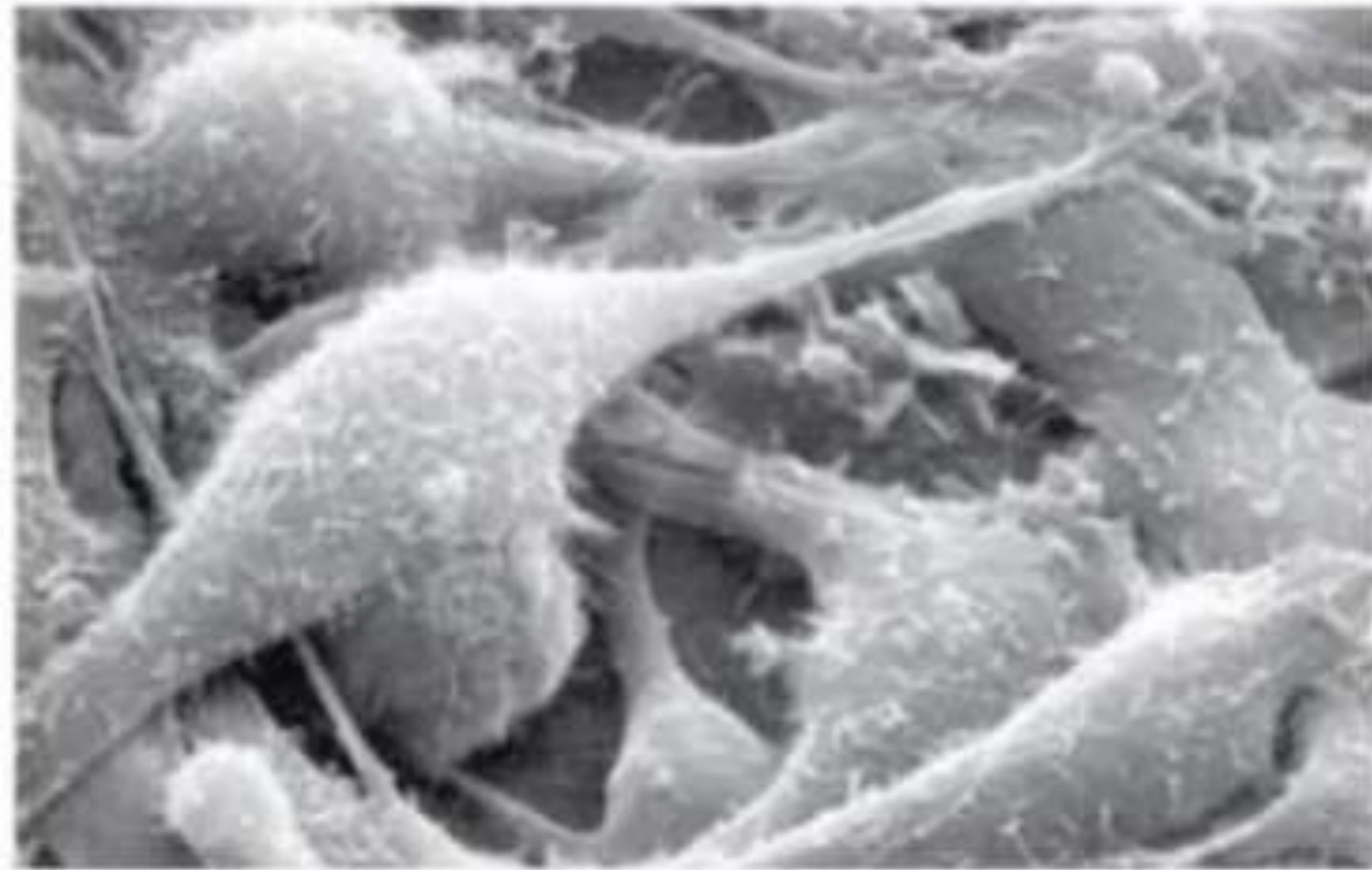
فوقه بعض

(b) Cancer cells. Cancer cells usually continue to divide well beyond a single layer, forming a dump of overlapping cells. They do not

[exhibit anchorage dependence or density-dependent inhibition]

لا يفتقرها حاجة

Figure 12.19b



20 μm

Loss of Cell Cycle Controls in Cancer Cells

- Cancer cells do not respond normally to the body's control mechanisms
- Cancer cells may not need growth factors to grow and divide
 - They may make their own growth factor
 - They may convey a growth factor's signal without the presence of the growth factor
 - They may have an abnormal cell cycle control system

تحت إلهام

- A normal cell is converted to a cancerous cell by a process called **transformation**

جهاز المناعة يحارب أي خلية غريبة سواء كانت داخلية أو خارجية [الخلايا السرطانية خلايا داخلية لأنها كانت طبيعية ثم تحولت] وهذه الخلية لا تتعدى

- Cancer cells that are not eliminated by the immune system form **tumors**, masses of abnormal cells within otherwise normal tissue

① قوة جهاز المناعة
② كمية الخلايا السرطانية

اورام

- ② If abnormal cells remain only at the original site, the lump is called a **benign tumor**

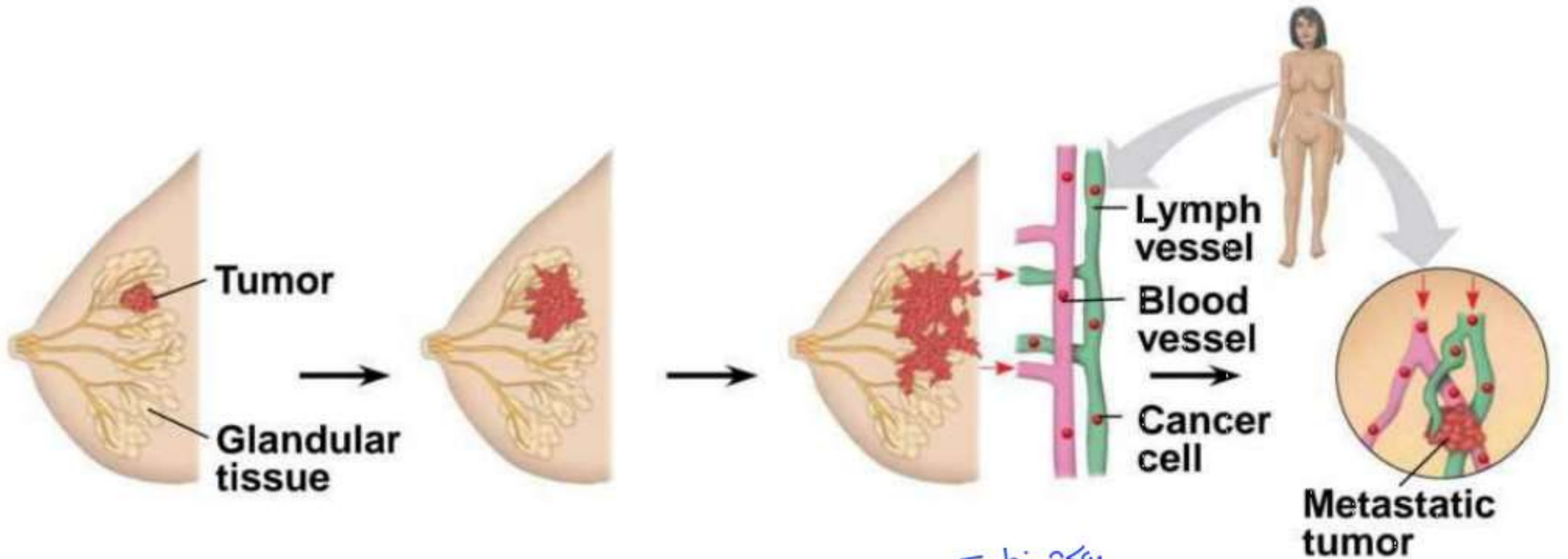
ضمت الكتلة بين الخلايا ولم يزد حجها/غير خبير

- ③ **Malignant tumors** invade surrounding tissues and can **metastasize**, exporting cancer cells to other parts of the body, where they may form additional tumors

→ to spread

Figure 12.20

* Breast cancer



1 A tumor grows from a single cancer cell.

لو اکتشف بعينه ابي كذا
ازال tumor و خذو ابي كذا

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2 Cancer cells invade neighboring tissue.

[still at the same organ]

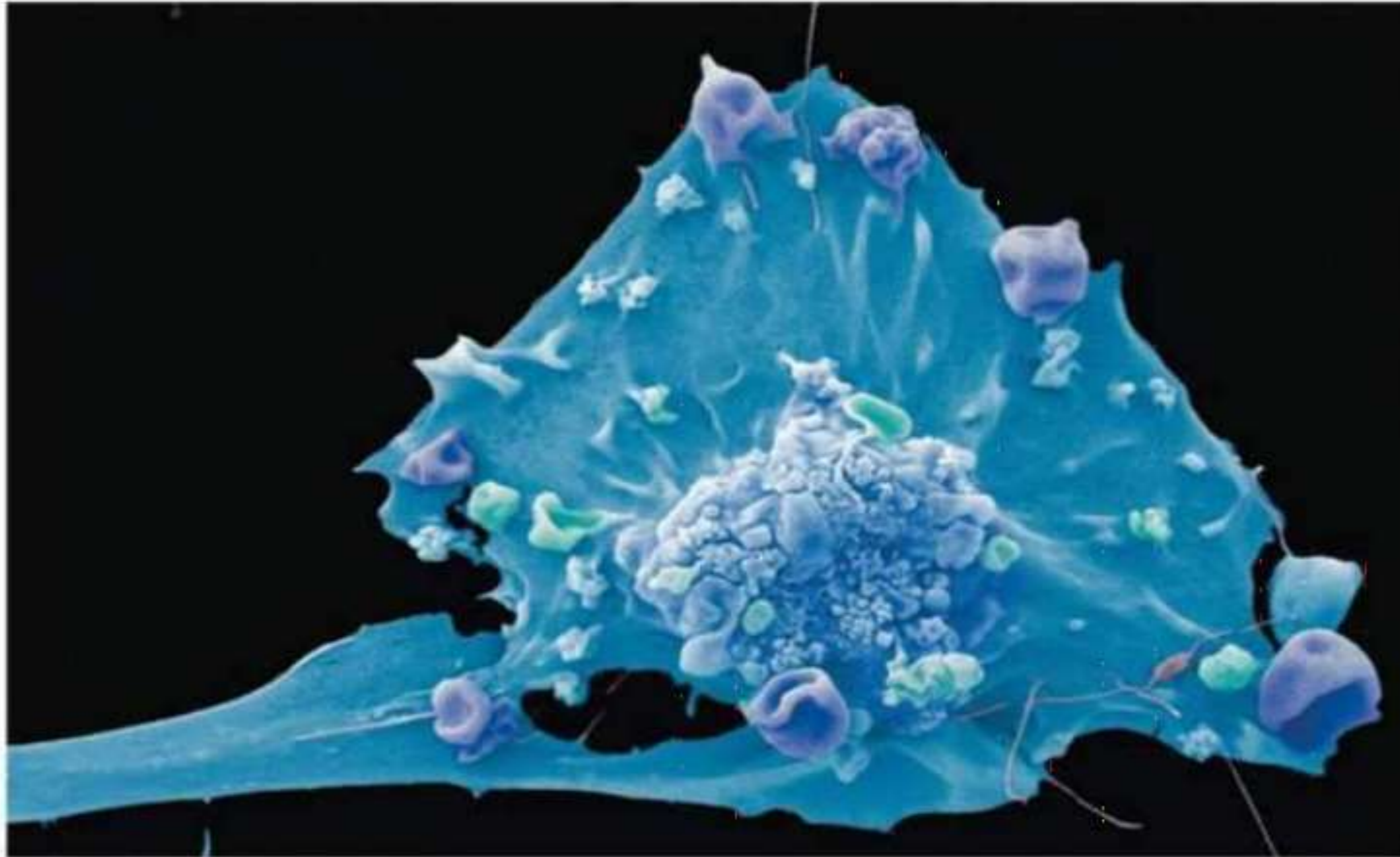
اكتر خطورة
the tissue
او امثال الـ... كذا

3 Cancer cells spread through lymph and blood vessels to other parts of the body.

4 Cancer cells may survive and establish a new tumor in another part of the body.

- Recent advances in understanding the cell cycle and cell cycle signaling have led to advances in cancer treatment

Figure 12.21



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Figure 12.UN01

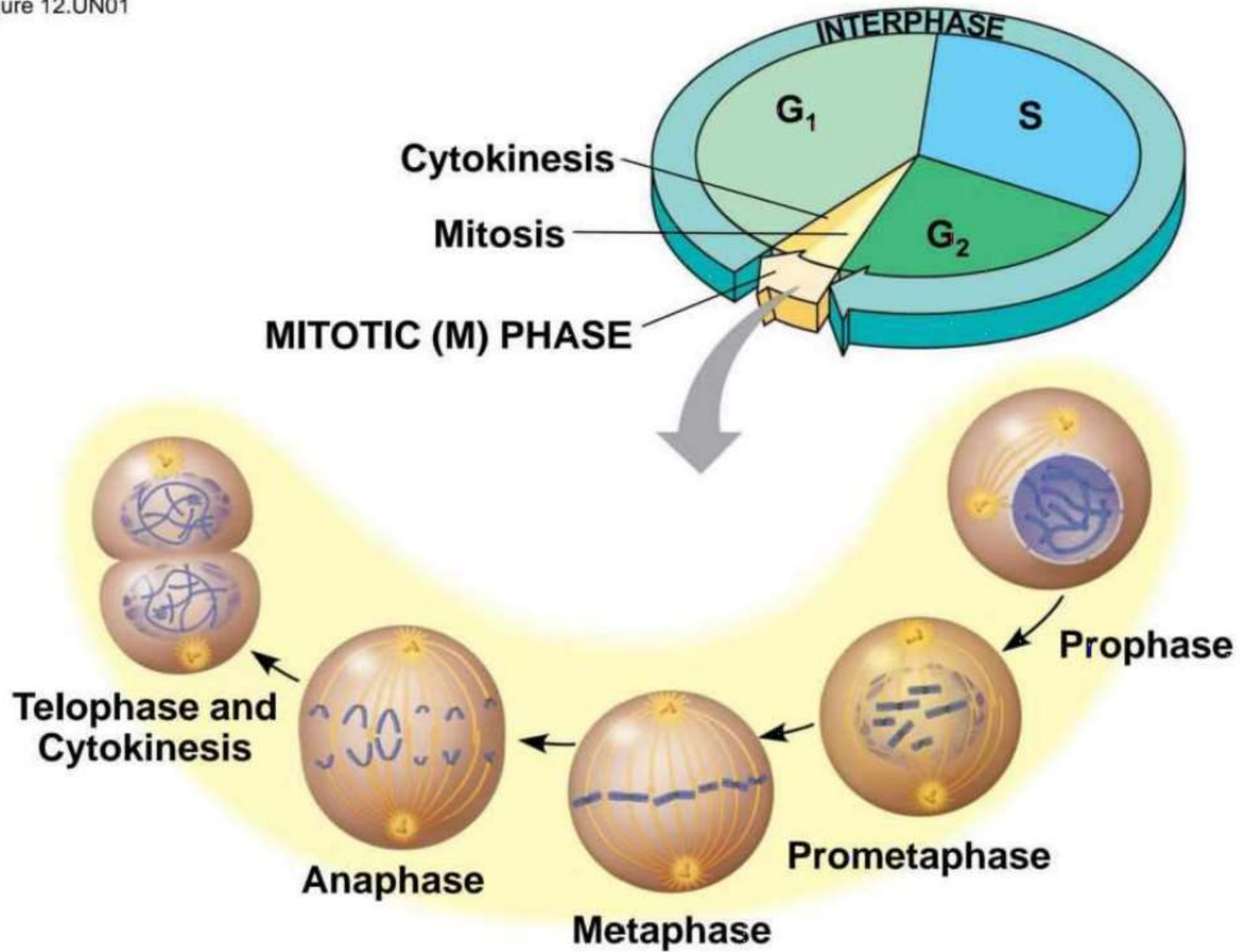
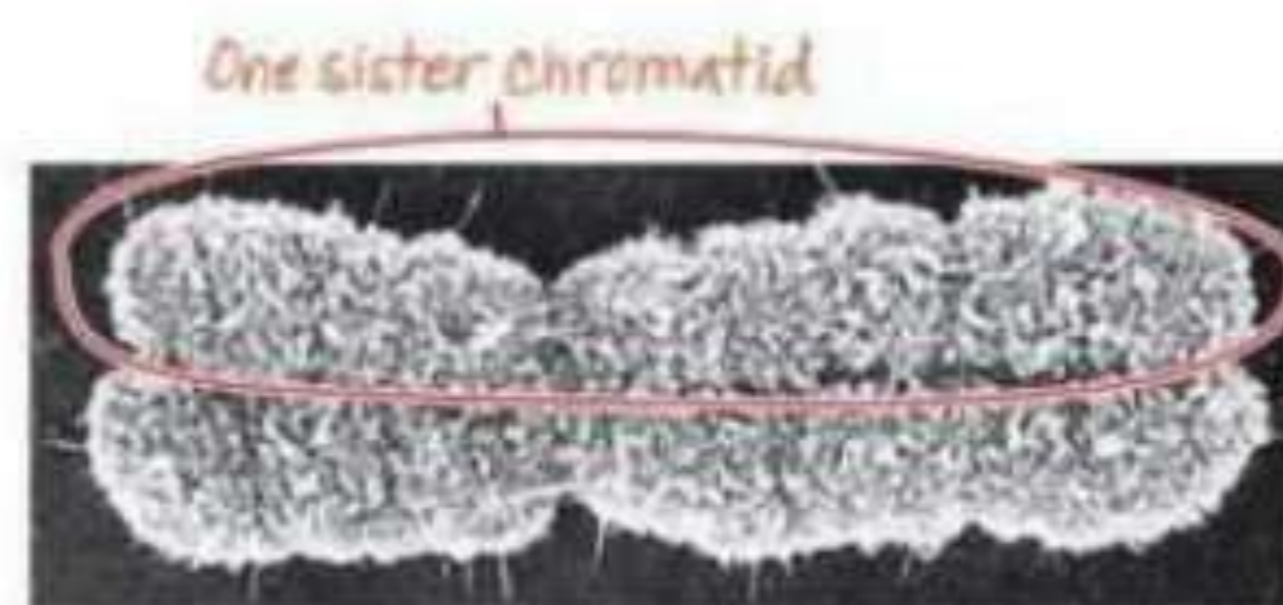


Figure 12.UN02



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Figure 12.UN03



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Figure 12.UN04

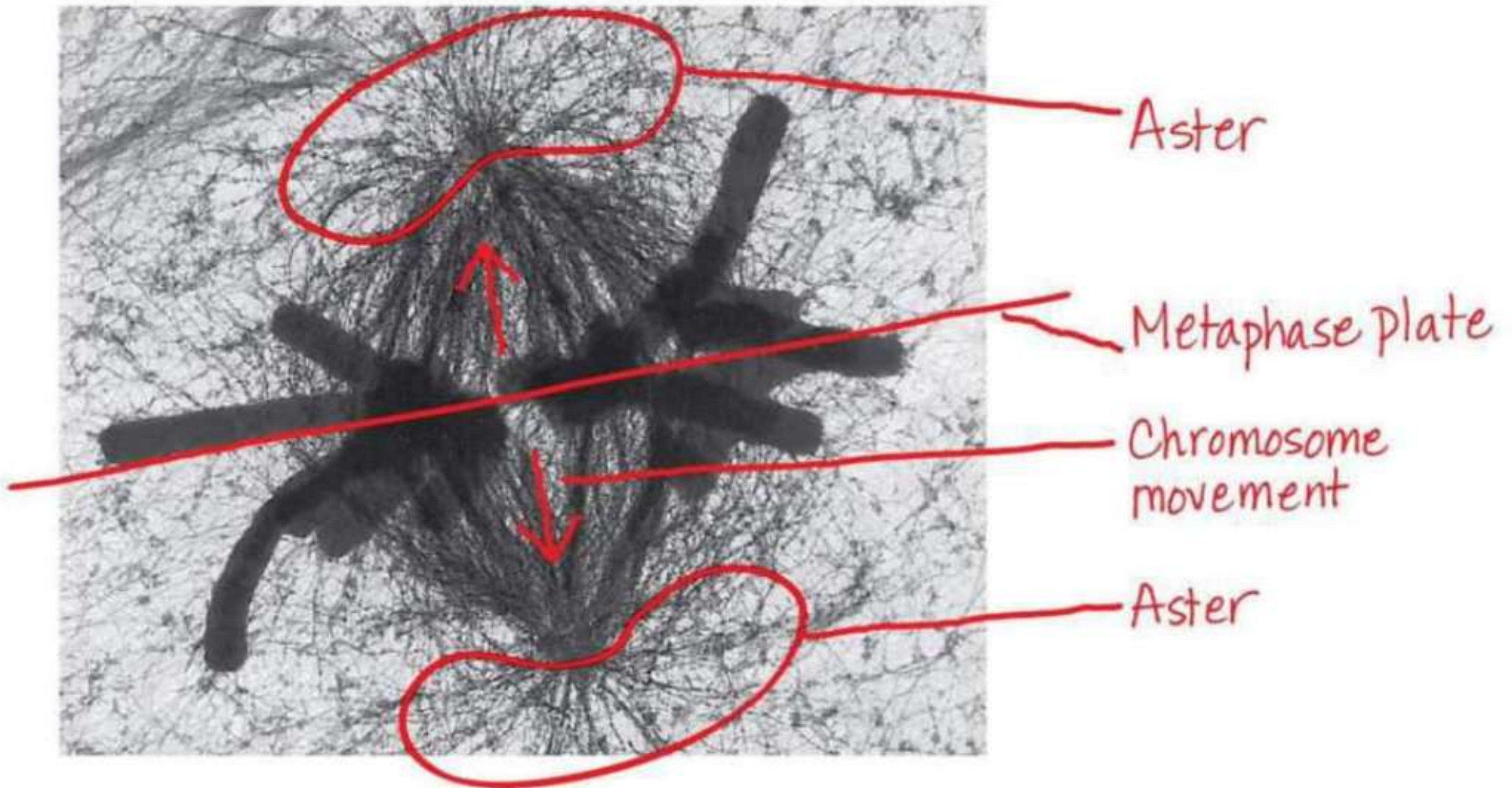


Figure 12.UN05

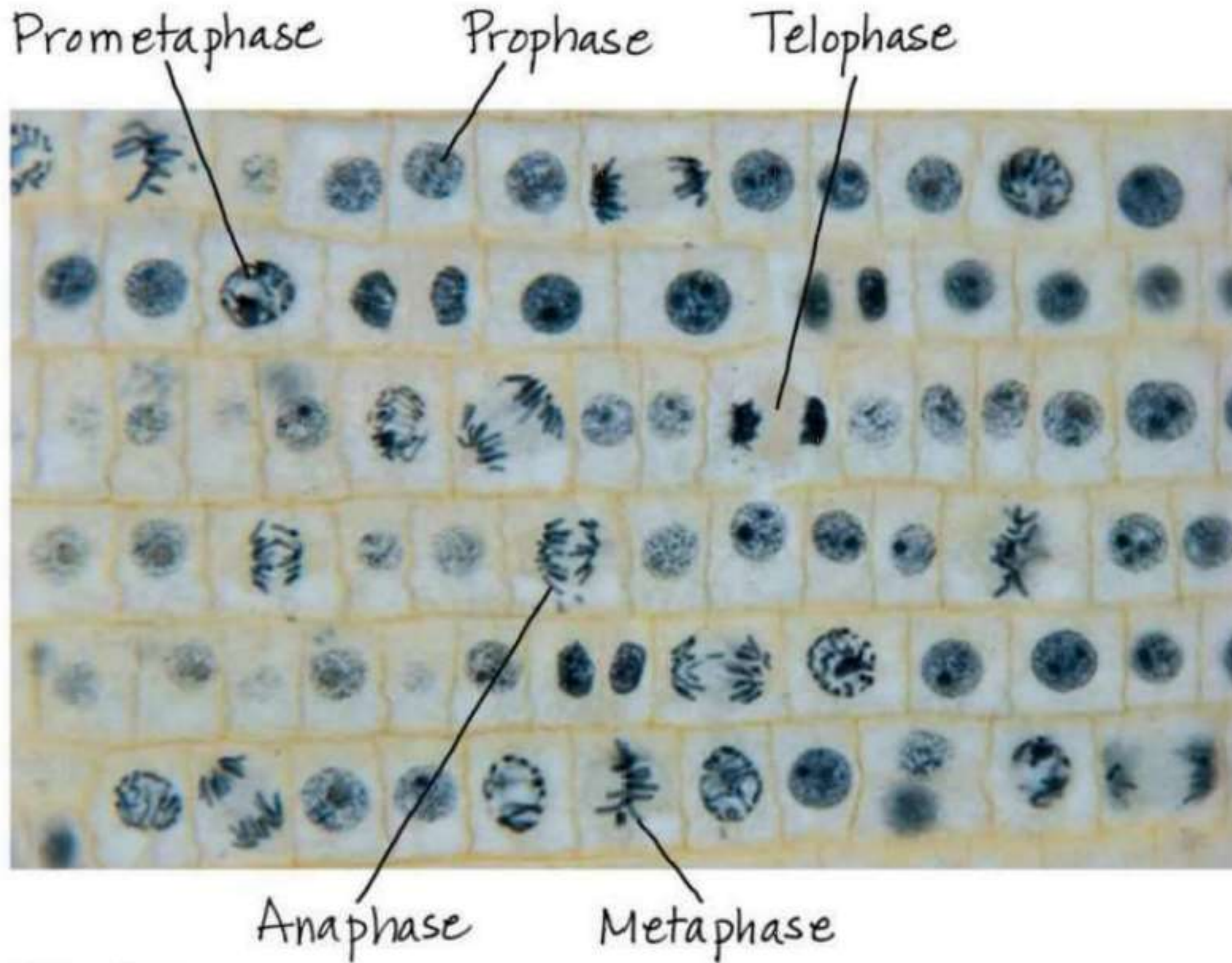


Figure 12.UN06

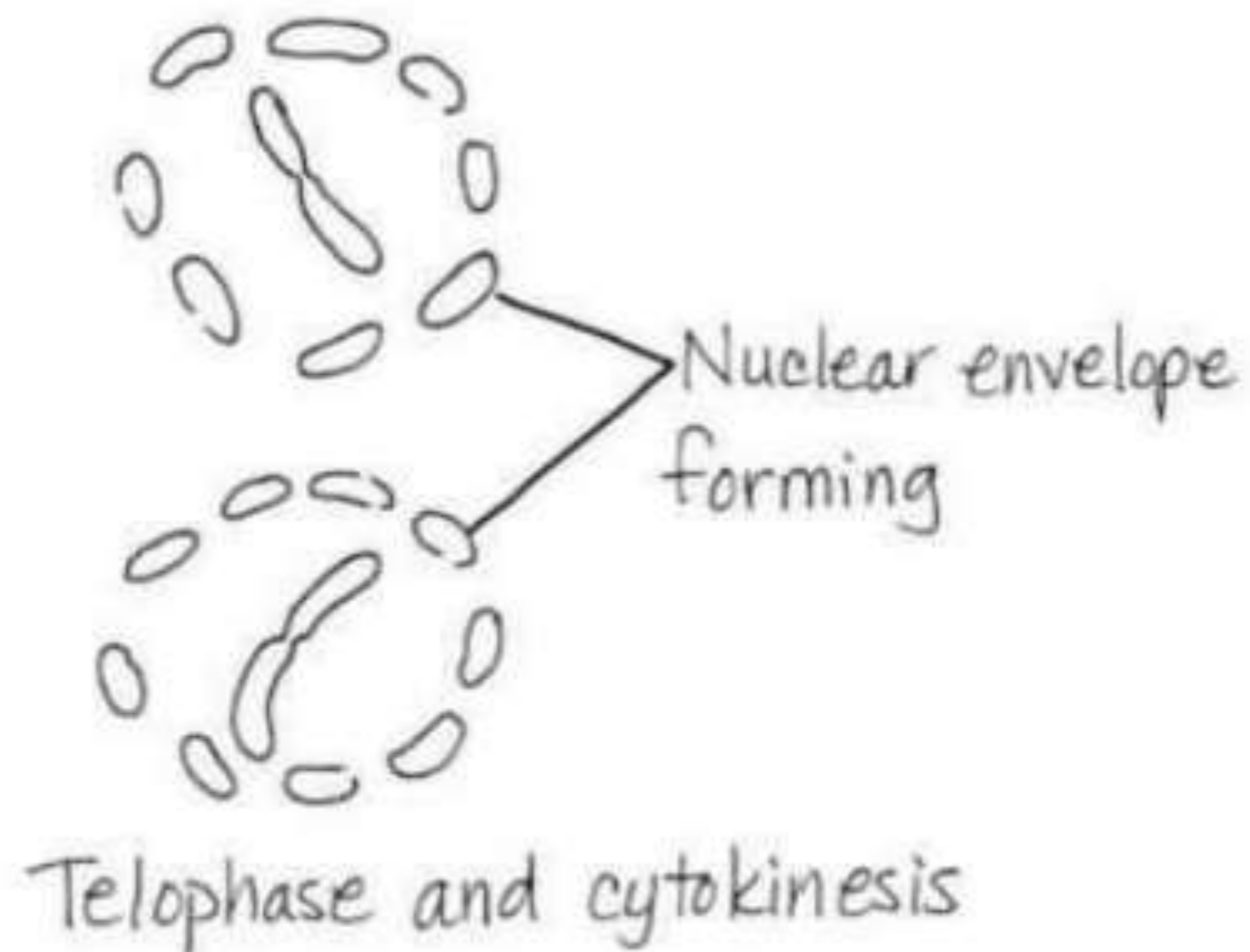
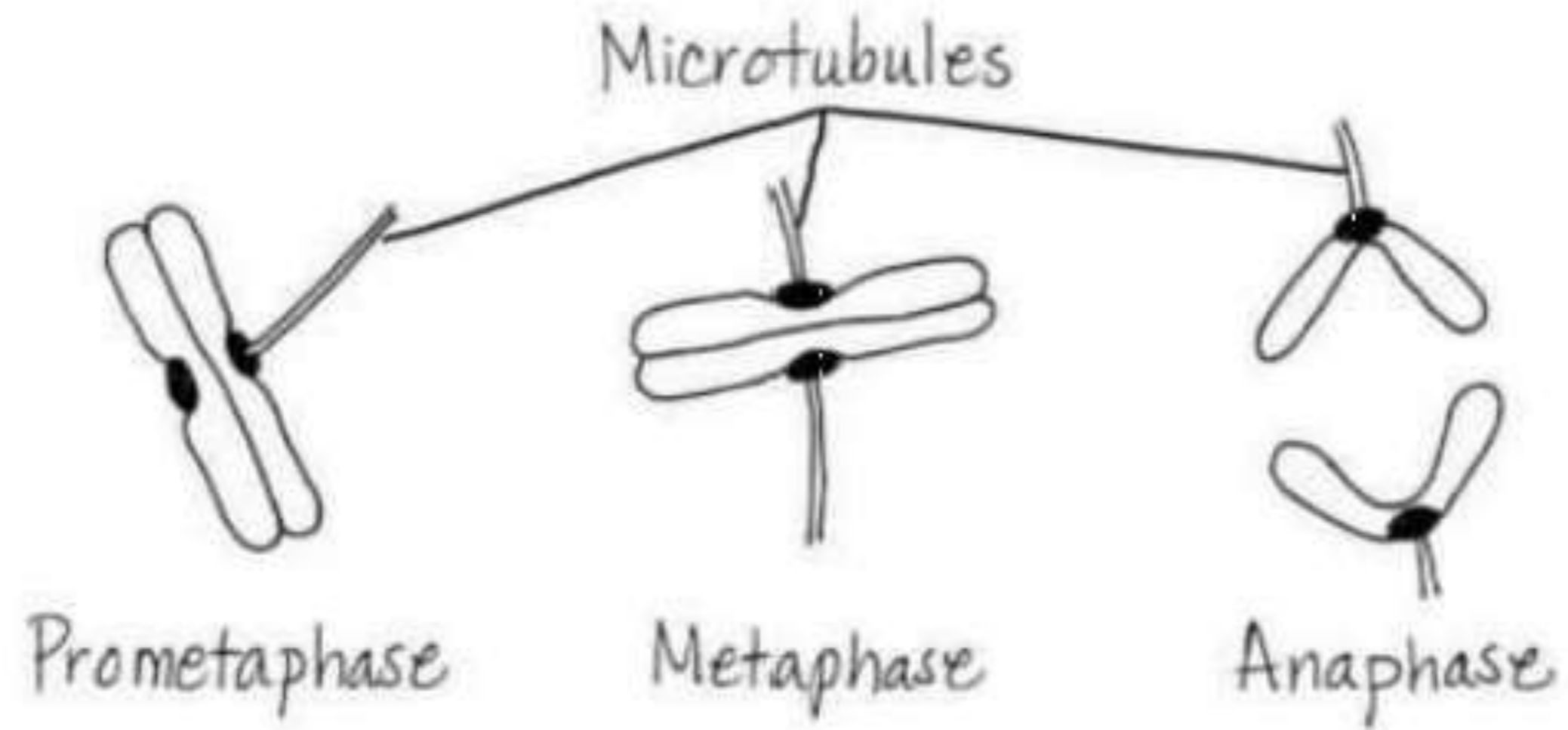
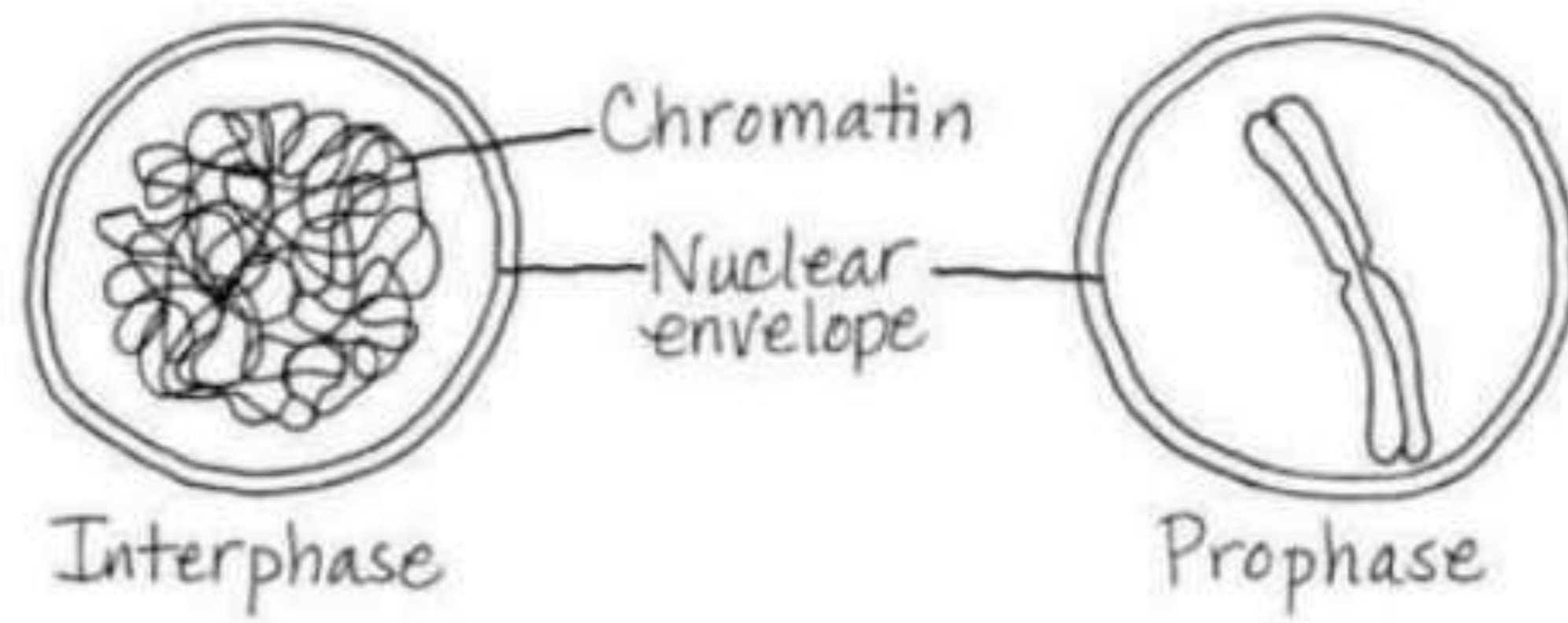


Figure 12.UN06

