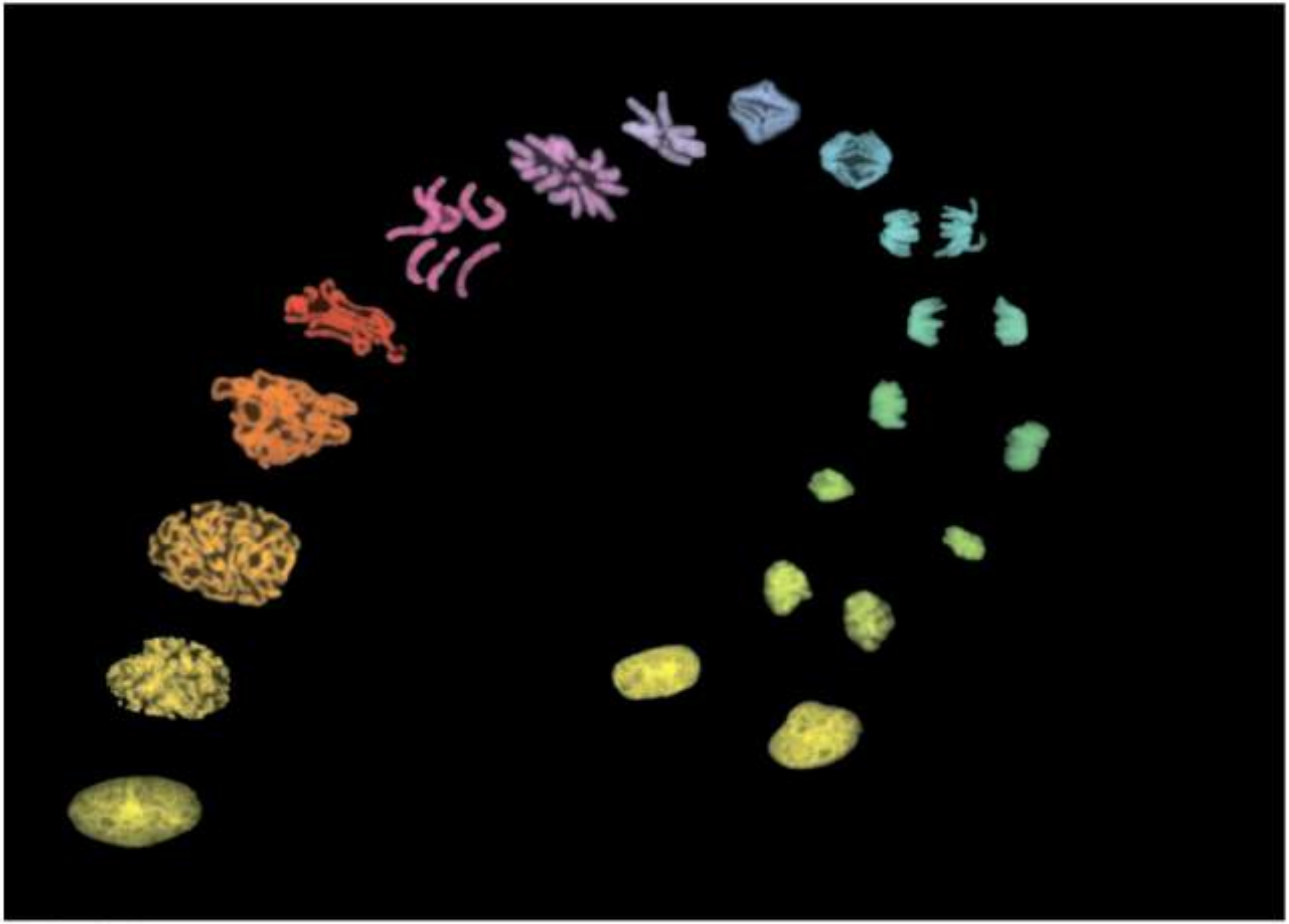
Overview: The Key Roles of Cell Division

- 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**

Figure 12.1



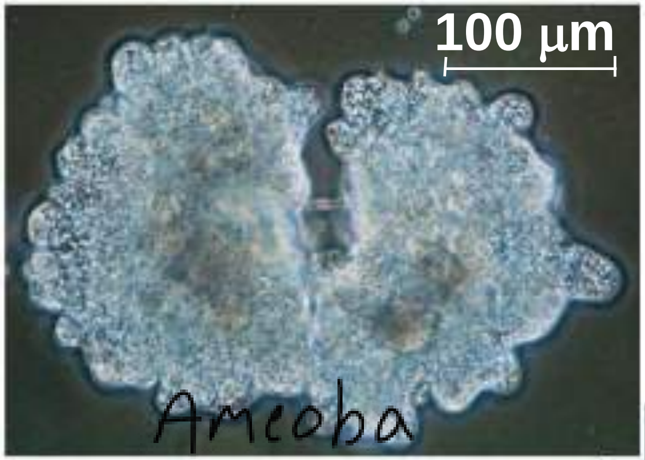
- In unicellular organisms, division of one cell reproduces the entire organism
- Multicellular organisms depend on cell division for
  - Development from a fertilized cell
  - Growth
  - Repair

جزء مهم

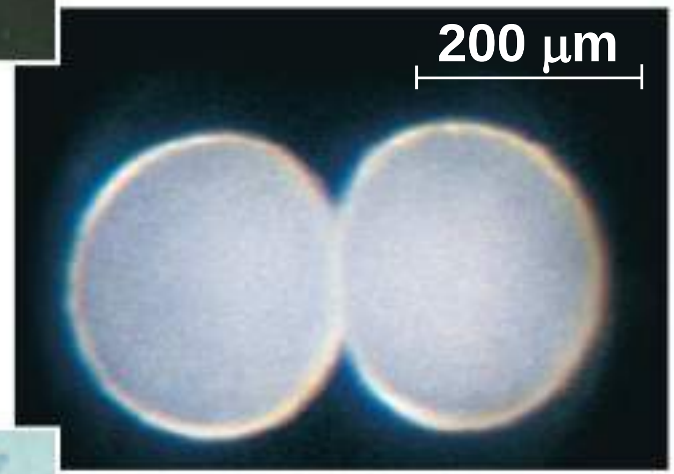
- Cell division is an integral part of the cell cycle, the life of a cell from formation to its own division

تعريف

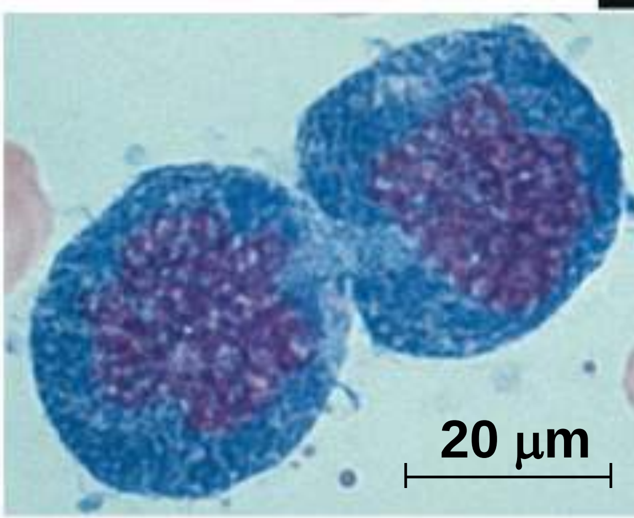
Figure 12.2



(a) Reproduction



(b) Growth and development

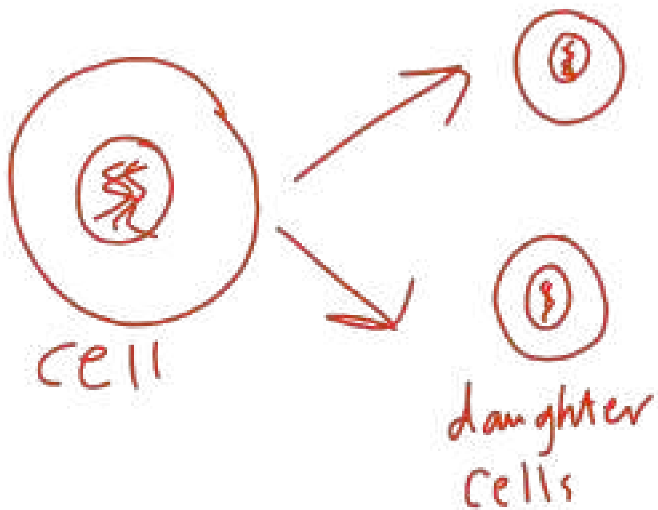


إصلاح

(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



(in human)

- somatic cells have 46 chromosoms
- sex cells (gametes) have 23 chromosoms

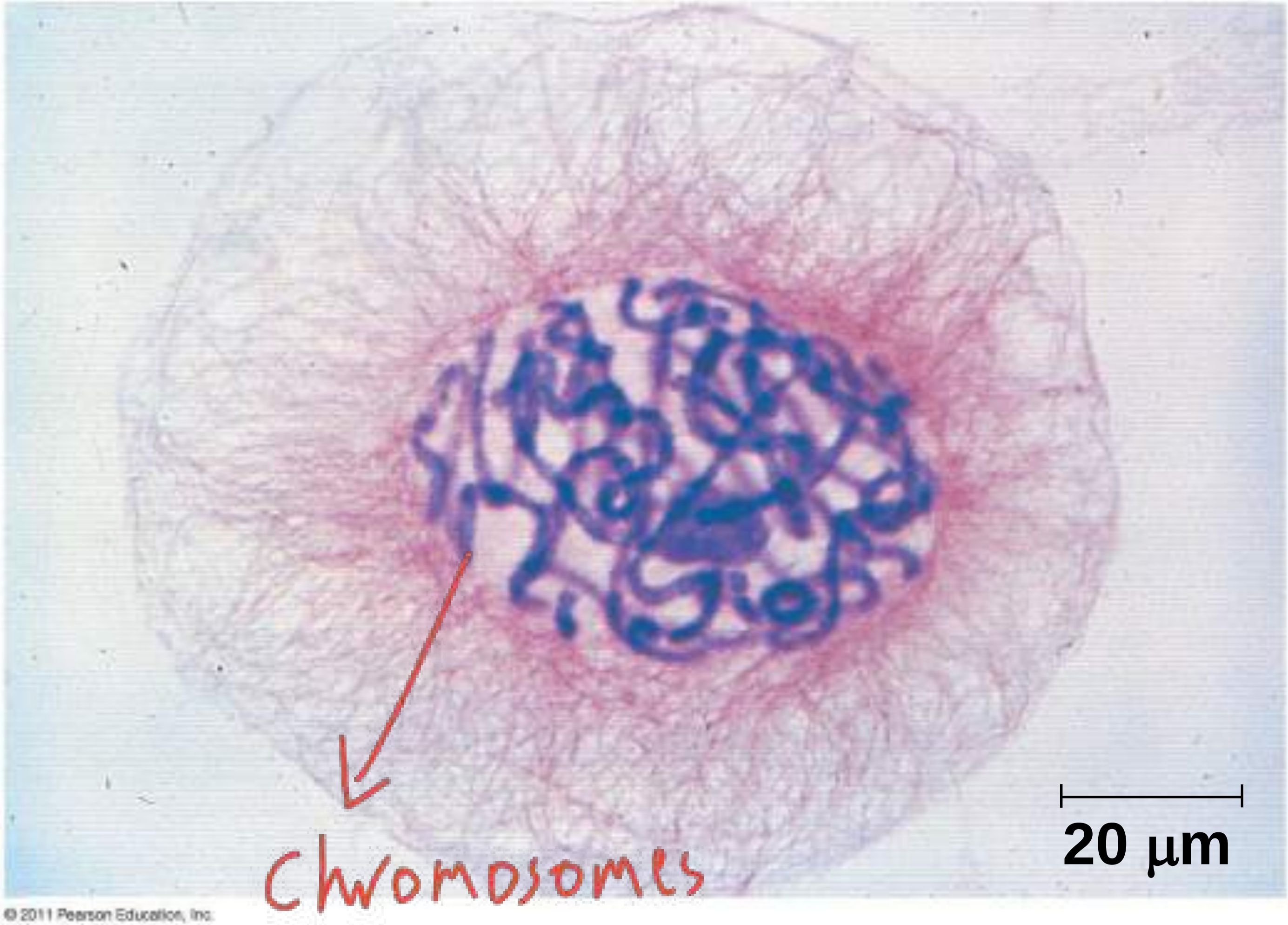
Cellular Organization of the Genetic Material

يشكل

- 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**

* chromosomes + protien = Chromatin

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 2n
- **Gametes** (reproductive cells: sperm and eggs) have half as many chromosomes as somatic cells

1n

Distribution of Chromosomes During Eukaryotic Cell Division

at s phase

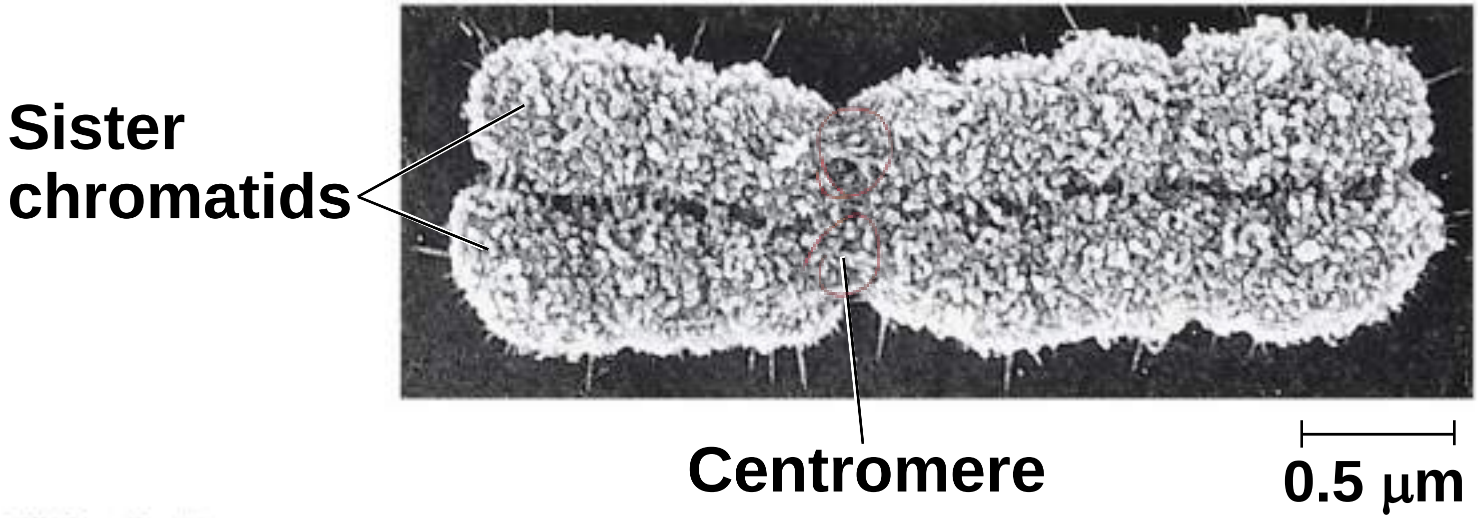
- In preparation for cell division, DNA is replicated and the chromosomes condense تتكثف
- Each duplicated chromosome has two **sister chromatids** (joined copies of the original chromosome), which separate during cell division

sister chromatides

- The **centromere** is the narrow "waist" of the duplicated chromosome, where the two chromatids are most closely attached

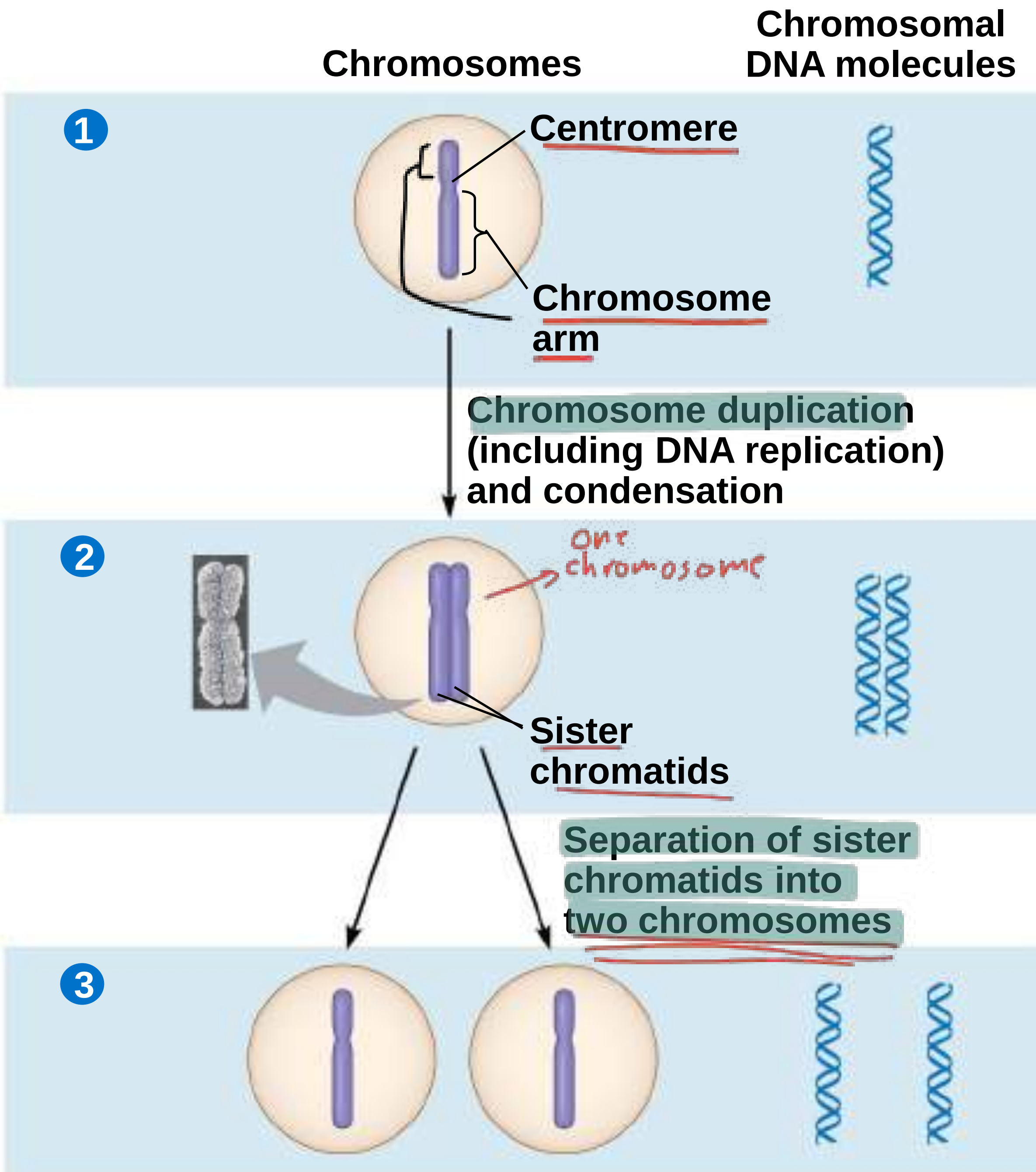
السنترومير هو المكان الي يكون فيه ال sister cromatids اكثر تلاصق

Figure 12.4



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

Figure 12.5-3


Chromosomes
Chromosomal DNA molecules
1
Centromere
Chromosome arm
Chromosome duplication (including DNA replication) and condensation
2
one chromosome
Sister chromatids
Separation of sister chromatids into two chromosomes
3

- Eukaryotic cell division consists of
  - **Mitosis**, the division of the genetic material in the nucleus
  - **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

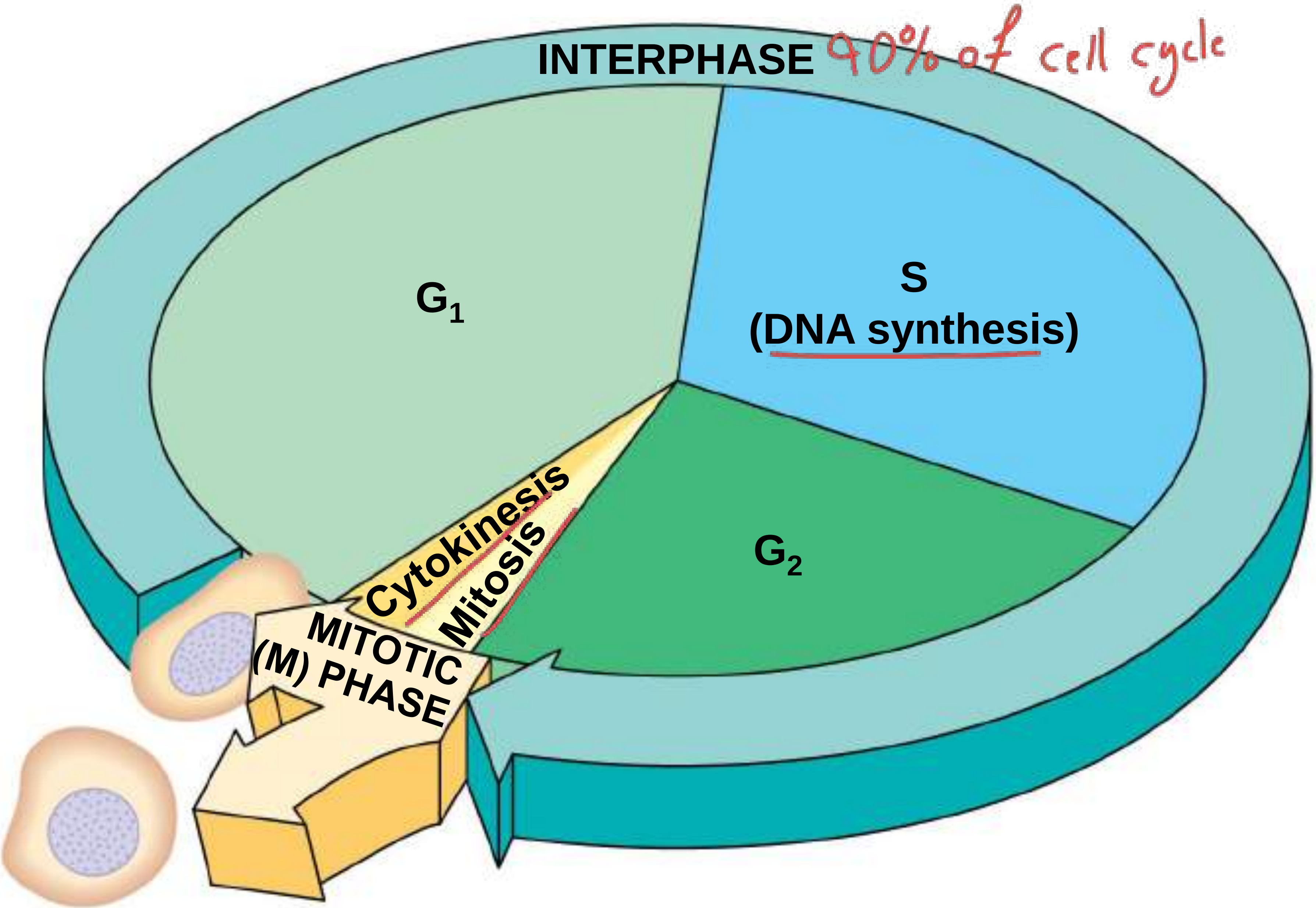
- In 1882, the German anatomist Walther Flemming developed dyes to observe chromosomes during mitosis and cytokinesis

Phases of the Cell Cycle

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

- Interphase (about 90% of the cell cycle) can be divided into subphases
  - **G_1 phase** (“first gap”)
  - **S phase** (“synthesis”)
  - **G_2 phase** (“second gap”)
- The cell grows during all three phases, but chromosomes are duplicated only during the S phase

Figure 12.6


INTERPHASE
90% of cell cycle
G_1
S
(DNA synthesis)
G_2
Cytokinesis
Mitosis
MITOTIC
(M) PHASE

- Mitosis is conventionally divided into five phases
  - **Prophase**
  - **Prometaphase**
  - **Metaphase**
  - **Anaphase**
  - **Telophase**

المراحل النهائيه

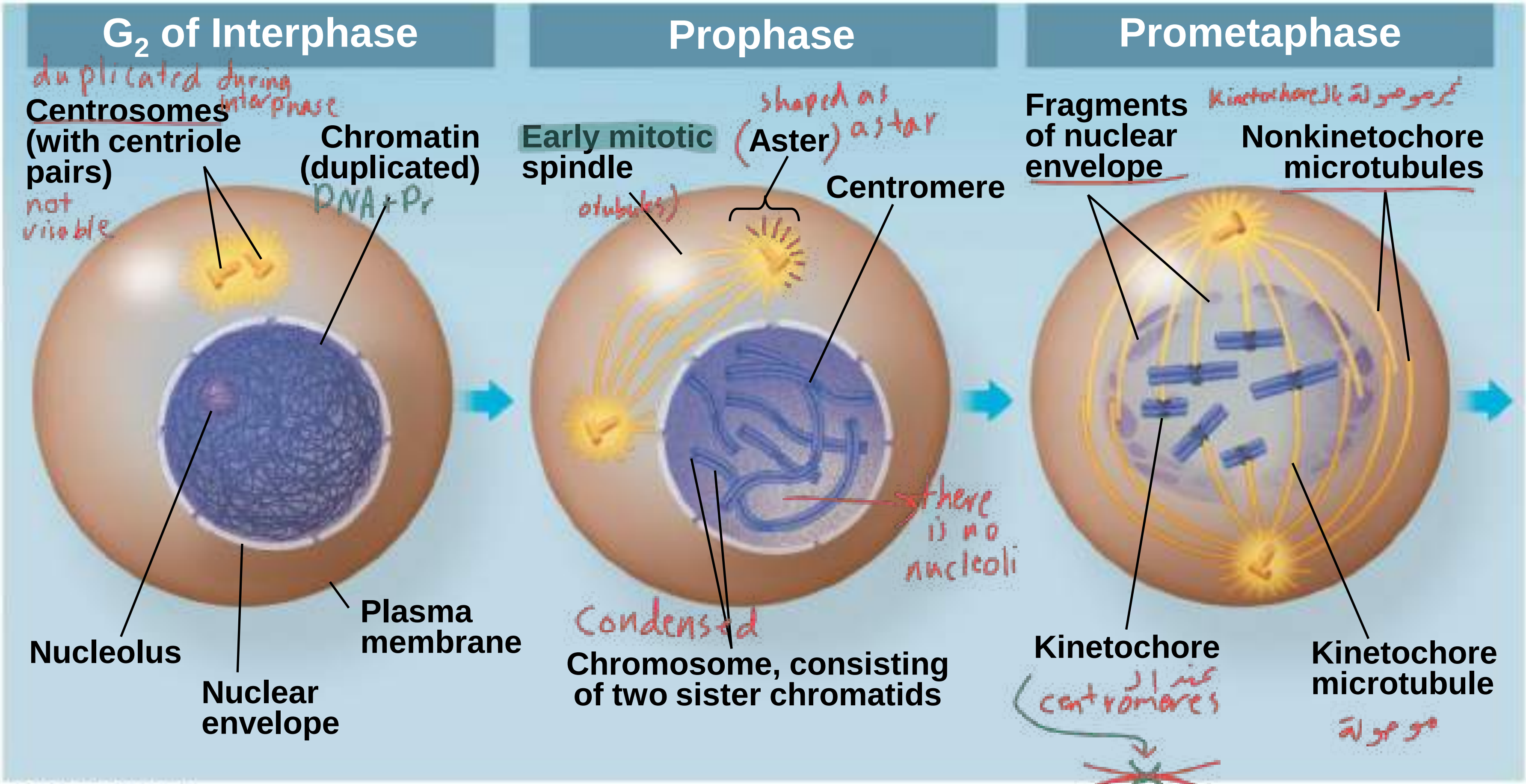
- Cytokinesis overlaps the latter stages of mitosis

يتداخل

يتداخل ال cytokinesis مع المراحل النهائية في ال mitosis
مثل ال anaphase وال telophase

PLAY BioFlix: Mitosis

Figure 12.7a



G2 of Interphase
Prophase
Prometaphase
duplicated during interphase
Centrosomes (with centriole pairs)
not visible
Chromatin (duplicated)
DNA+Pr
Early mitotic spindle
shaped as a star
Aster
Centromere
Fragments of nuclear envelope
Nonkinetochore microtubules
there is no nucleoli
Nucleolus
Nuclear envelope
Plasma membrane
Condensed
Chromosome, consisting of two sister chromatids
Kinetochore
centromeres
Kinetochore microtubule

Figure 12.7b

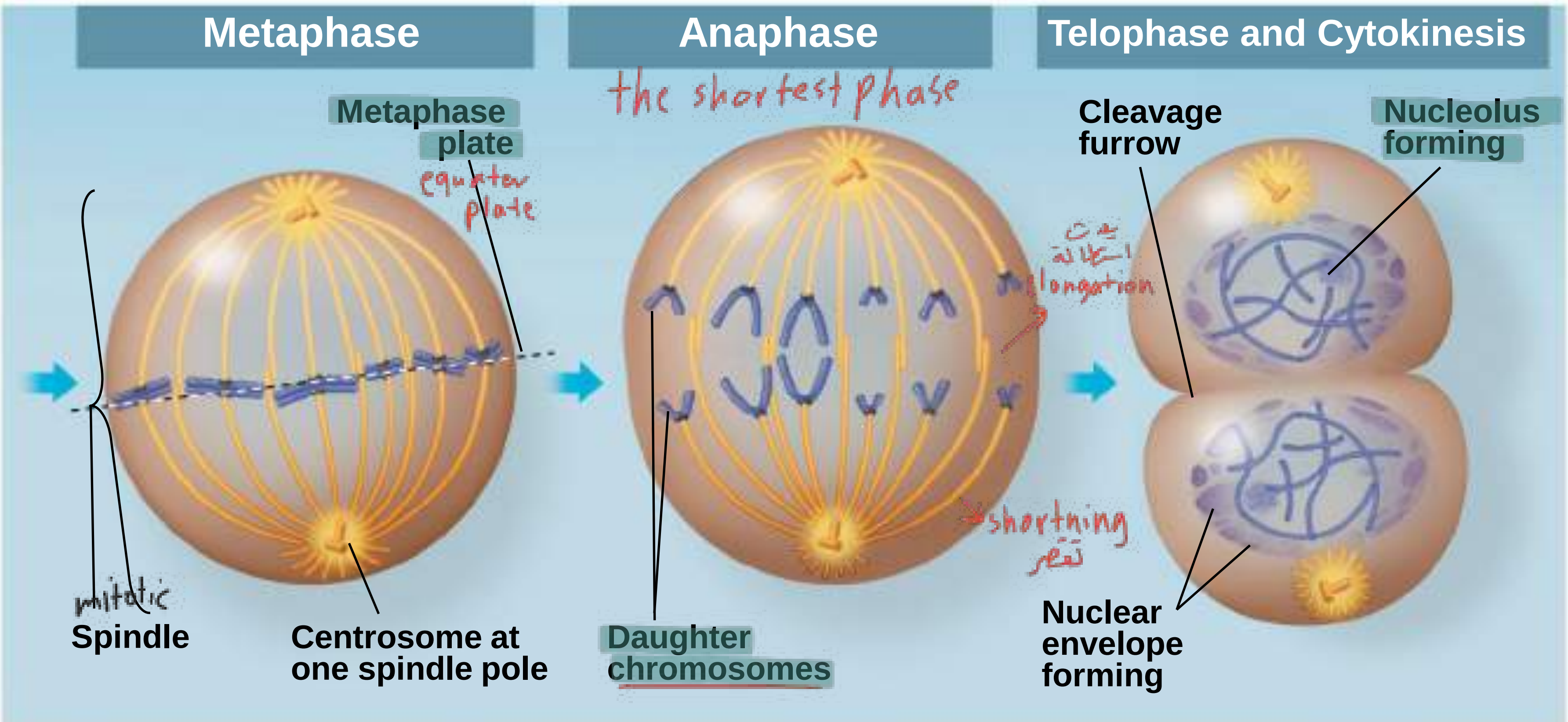
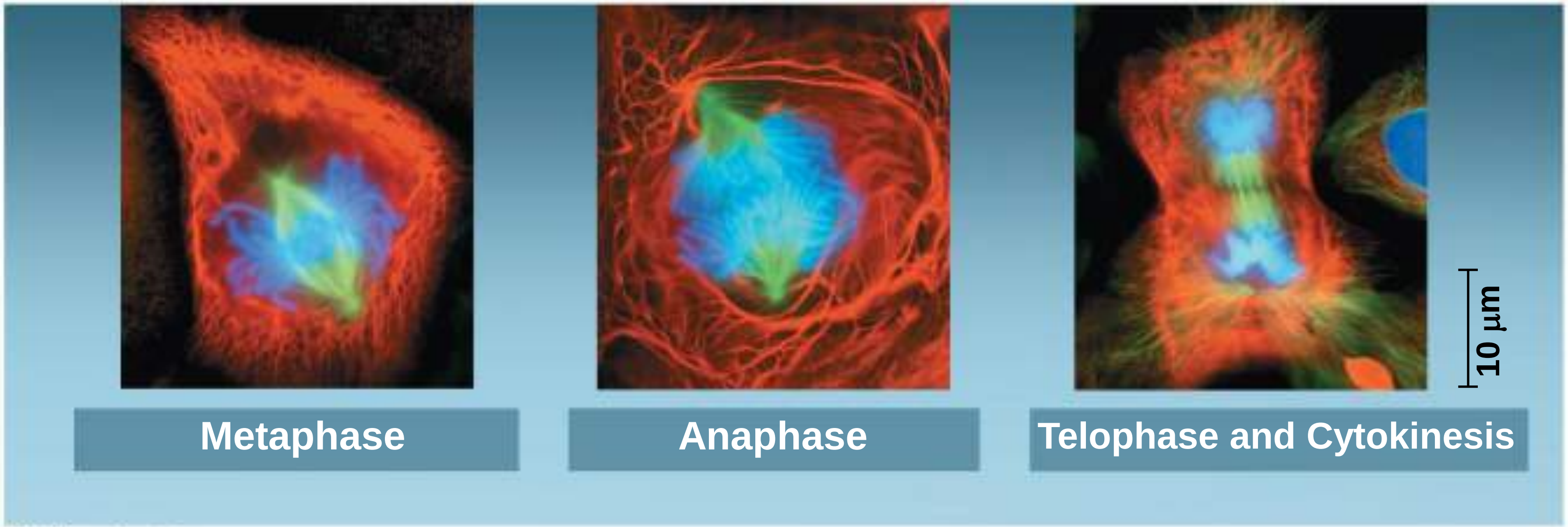
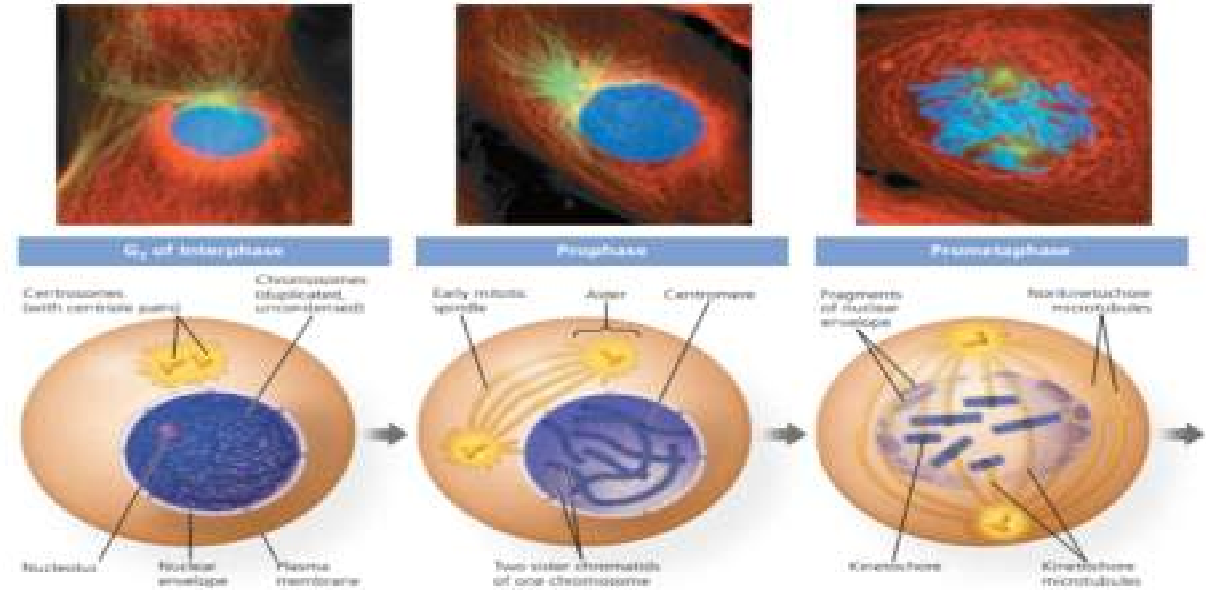

Metaphase
Anaphase
Telophase and Cytokinesis
Metaphase plate
equator plate
the shortest phase
Cleavage furrow
Nucleolus forming
elongation
shortning
mitotic
Spindle
Centrosome at one spindle pole
Daughter chromosomes
Nuclear envelope forming

Figure 12.7c

Figure 12.7d





G_2 of Interphase

- A nuclear envelope encloses the nucleus.
- The nucleus contains one or more nucleoli (singular, *nucleolus*).
- Two centrosomes have formed by duplication of a single centrosome. Centrosomes are regions in animal cells that organize the microtubules of the spindle. Each centrosome contains two centrioles.
- Chromosomes, duplicated during S phase, cannot be seen individually because they have not yet condensed.

The fluorescence micrographs show dividing lung cells from a newt; this species has 22 chromosomes. Chromosomes appear blue, microtubules green, and intermediate filaments red. For simplicity, the drawings show only 6 chromosomes.

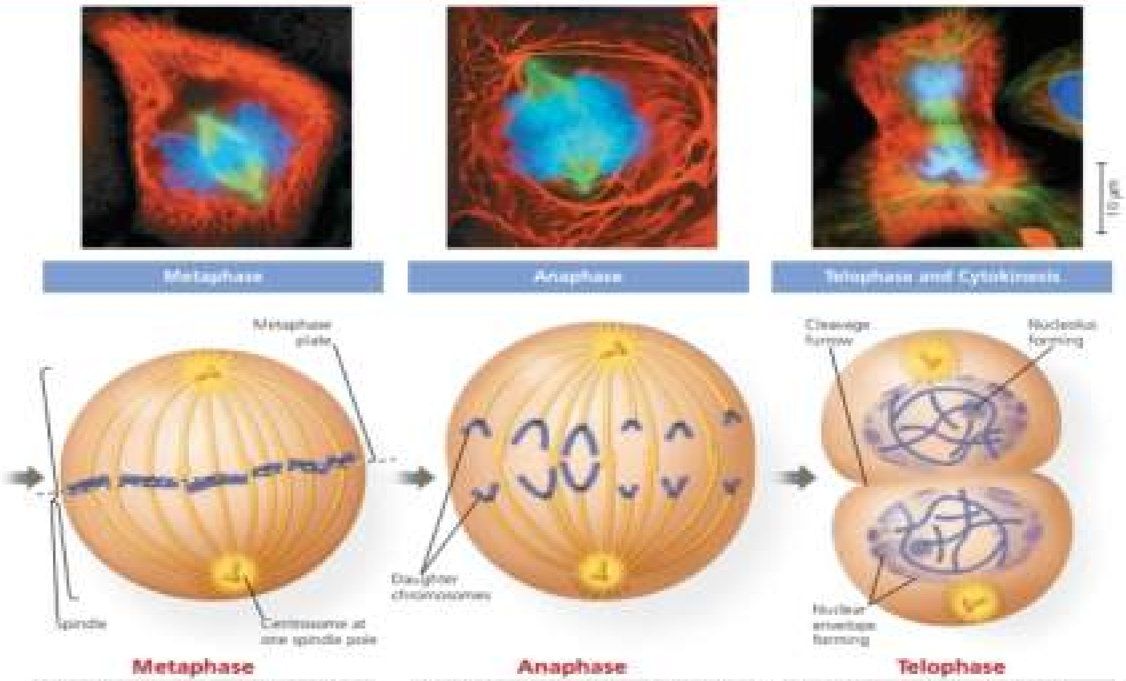
Prophase

- The chromatin fibers become more tightly coiled, condensing into discrete chromosomes observable with a light microscope.
- The nucleoli disappear.
- Each duplicated chromosome appears as two identical sister chromatids joined at their centromeres and, in some species, all along their arms by cohesins (sister chromatid cohesion).
- The mitotic spindle (named for its shape) begins to form. It is composed of the centrosomes and the microtubules that extend from them. The radial arrays of shorter microtubules that extend from the centrosomes are called asters ("stars").
- The centrosomes move away from each other, propelled partly by the lengthening microtubules between them.

Prometaphase

- The nuclear envelope fragments.
- The microtubules extending from each centrosome can now invade the nuclear area.
- The chromosomes have become even more condensed.
- A kinetochore, a specialized protein structure, has now formed at the centromere of each chromatid (thus, two per chromosome).
- Some of the microtubules attach to the kinetochores, becoming "kinetochore microtubules," which jerk the chromosomes back and forth.
- Nonkinetochore microtubules interact with those from the opposite pole of the spindle, lengthening the cell.

How many molecules of DNA are in the prometaphase drawing? How many molecules per chromosome? How many double helices are there per chromosome? Per chromatid?



Metaphase

- The centrosomes are now at opposite poles of the cell.
- The chromosomes have all arrived at the *metaphase plate*, a plane that is equidistant between the spindle's two poles. The chromosomes' centromeres lie at the metaphase plate.
- For each chromosome, the kinetochores of the sister chromatids are attached to kinetochore microtubules coming from opposite poles.

BioFlix® Animation: Mitosis
Video: Animal Mitosis (time-lapse)

Anaphase

- Anaphase is the shortest stage of mitosis, often lasting only a few minutes.
- Anaphase begins when the cohesin proteins are cleaved. This allows the two sister chromatids of each pair to part suddenly. Each chromatid thus becomes an independent chromosome.
- The two new daughter chromosomes begin moving toward opposite ends of the cell as their kinetochore microtubules shorten. Because these microtubules are attached at the centromere region, the centromeres are pulled ahead of the arms, moving at a rate of about 1 µm/min.
- The cell elongates as the nonkinetochore microtubules lengthen.
- By the end of anaphase, the two ends of the cell have equivalent—and complete—collections of chromosomes.

Telophase

- 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.
- Nucleoli reappear.
- The chromosomes become less condensed.
- Any remaining spindle microtubules are depolymerized.
- Mitosis, the division of one nucleus into two genetically identical nuclei, is now complete.

Cytokinesis

- 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.

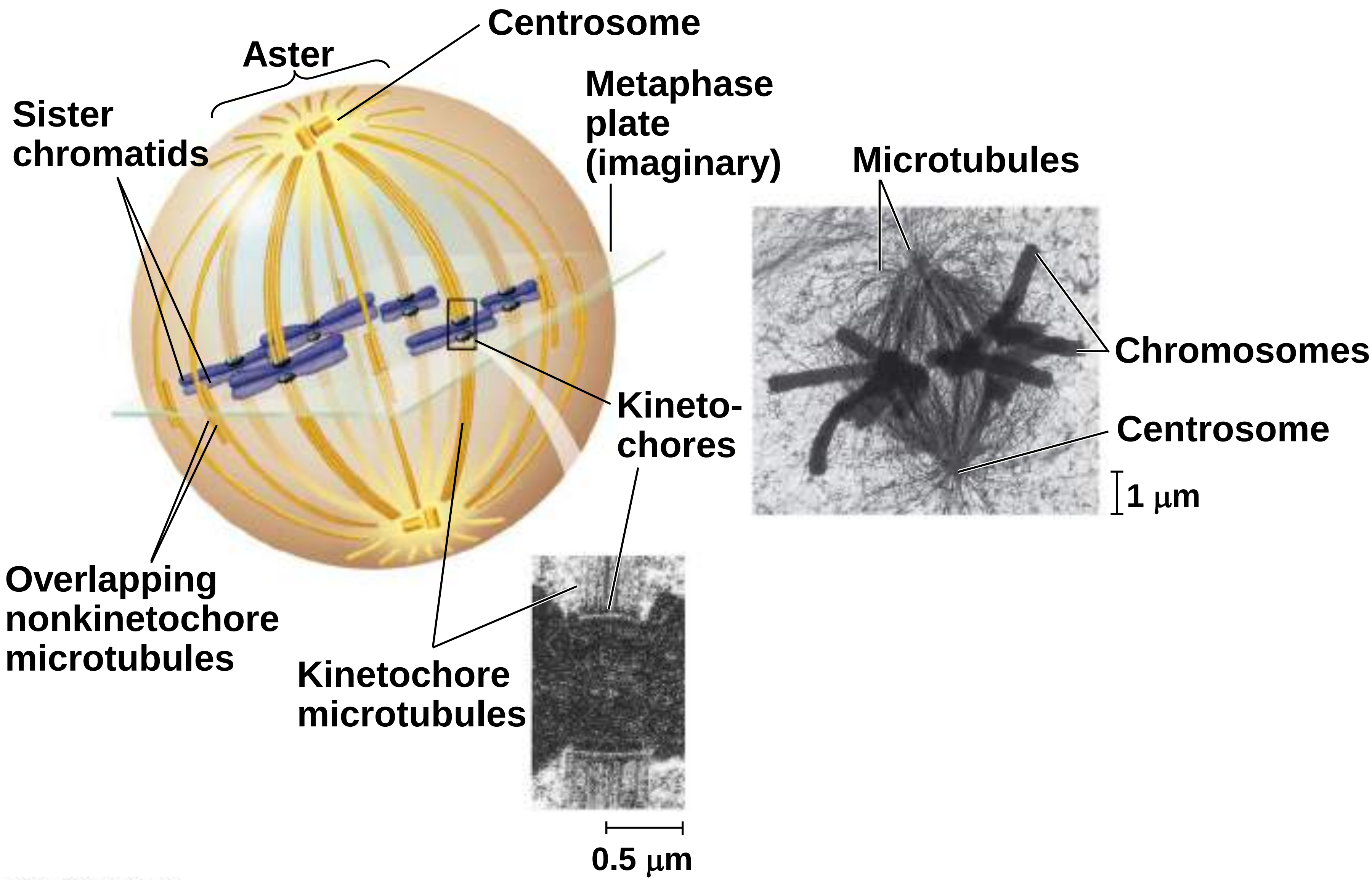
The Mitotic Spindle: *A Closer Look*

- 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



Centrosome
Aster
Metaphase plate (imaginary)
Sister chromatids
Microtubules
Chromosomes
Kineto-chores
Centrosome
1 μm
Overlapping nonkinetochore microtubules
Kinetochore microtubules
0.5 μm

Figure 12.8a

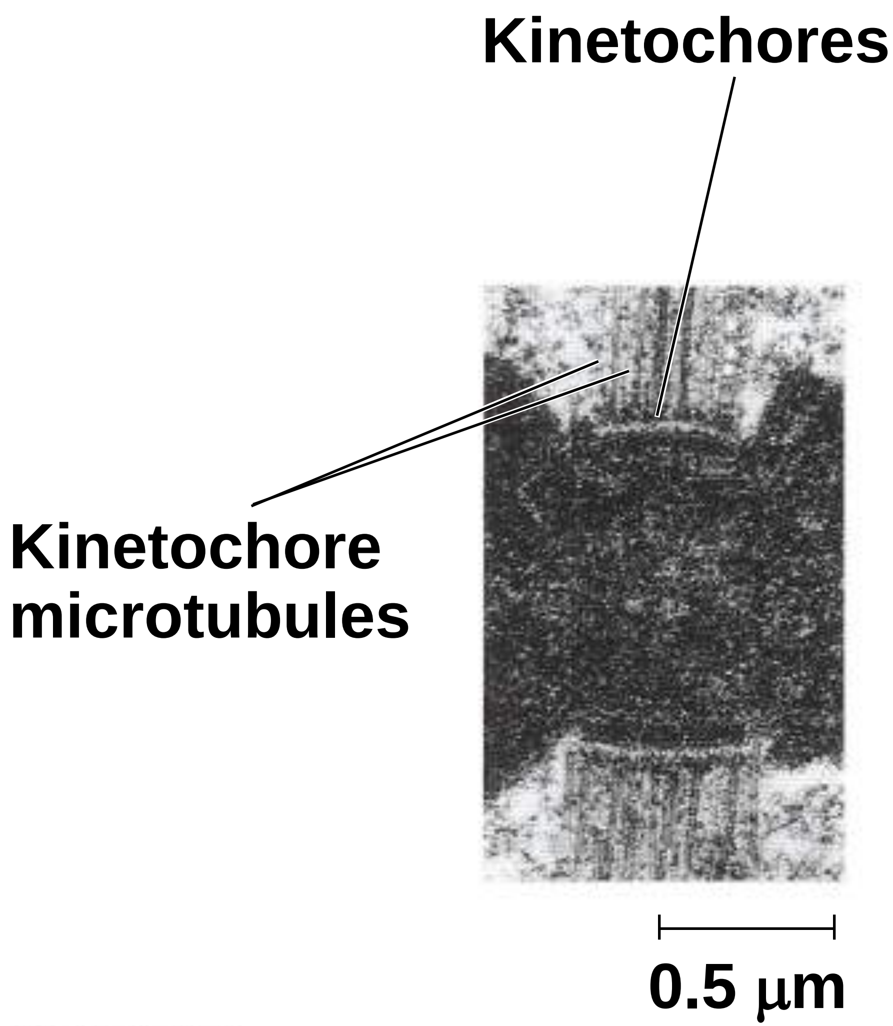
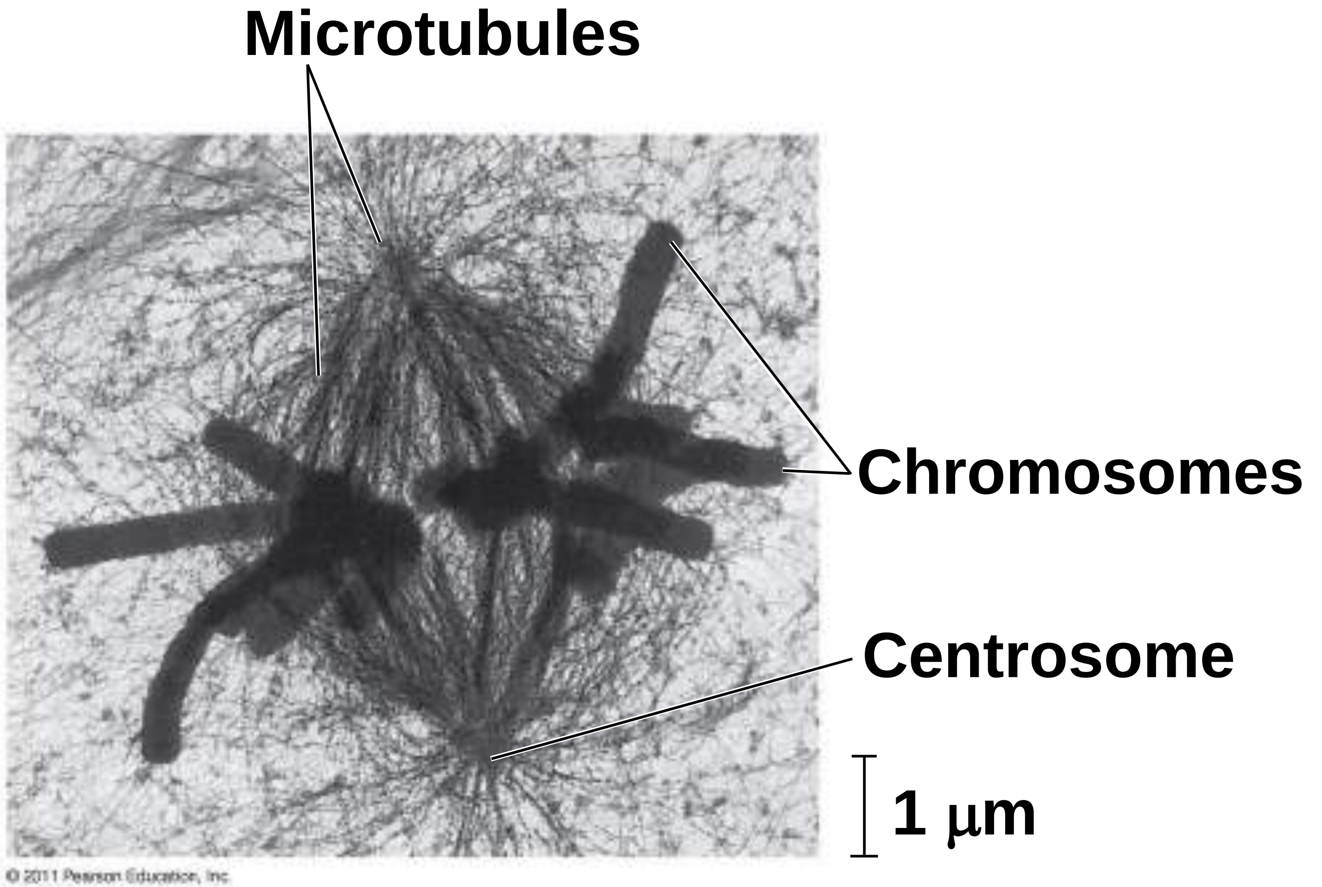


Figure 12.8b


Microtubules
Chromosomes
Centrosome
1 μm
© 2011 Pearson Education, Inc.

- 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

- 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

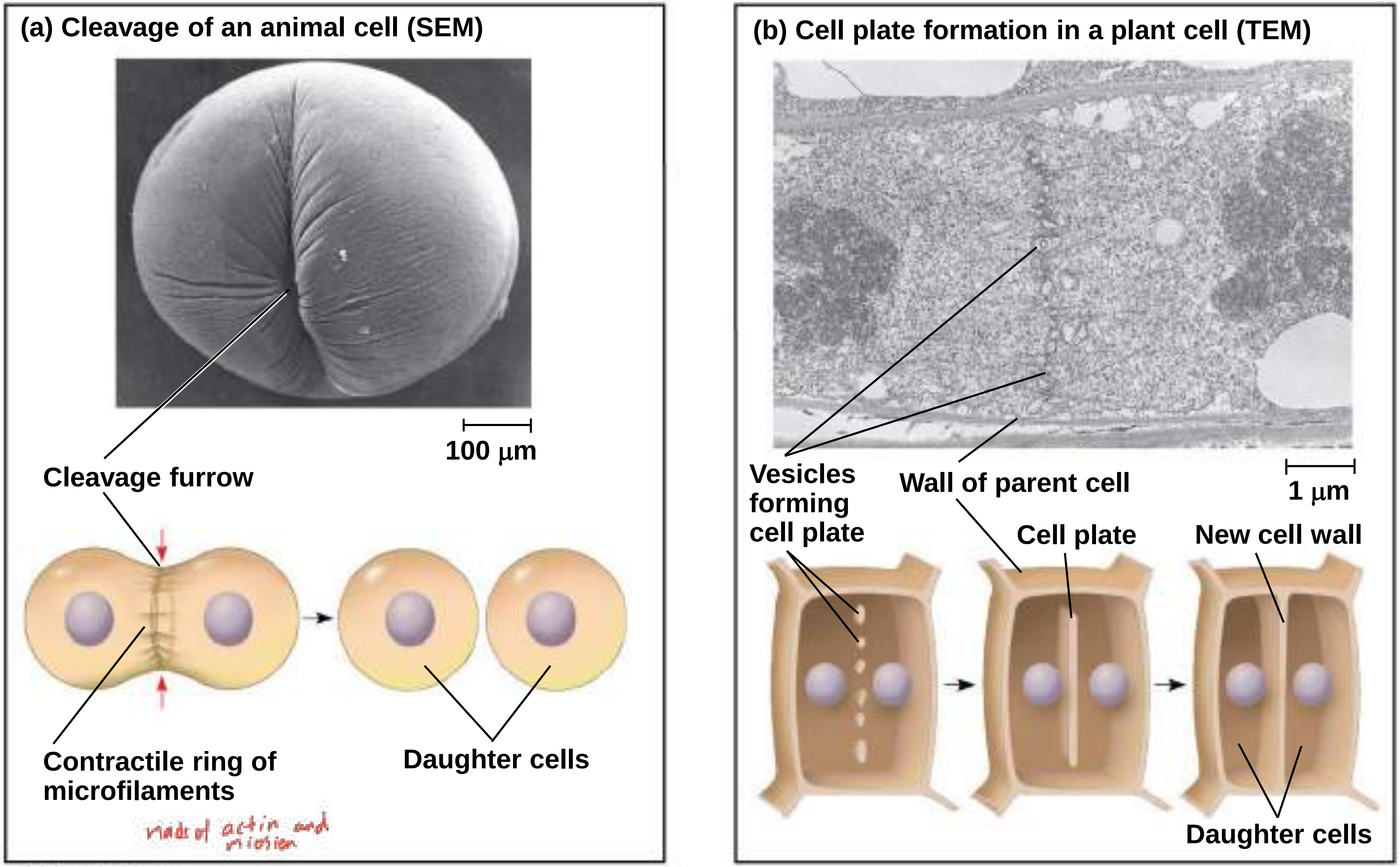
تتكسر

Cytokinesis: *A Closer Look*

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

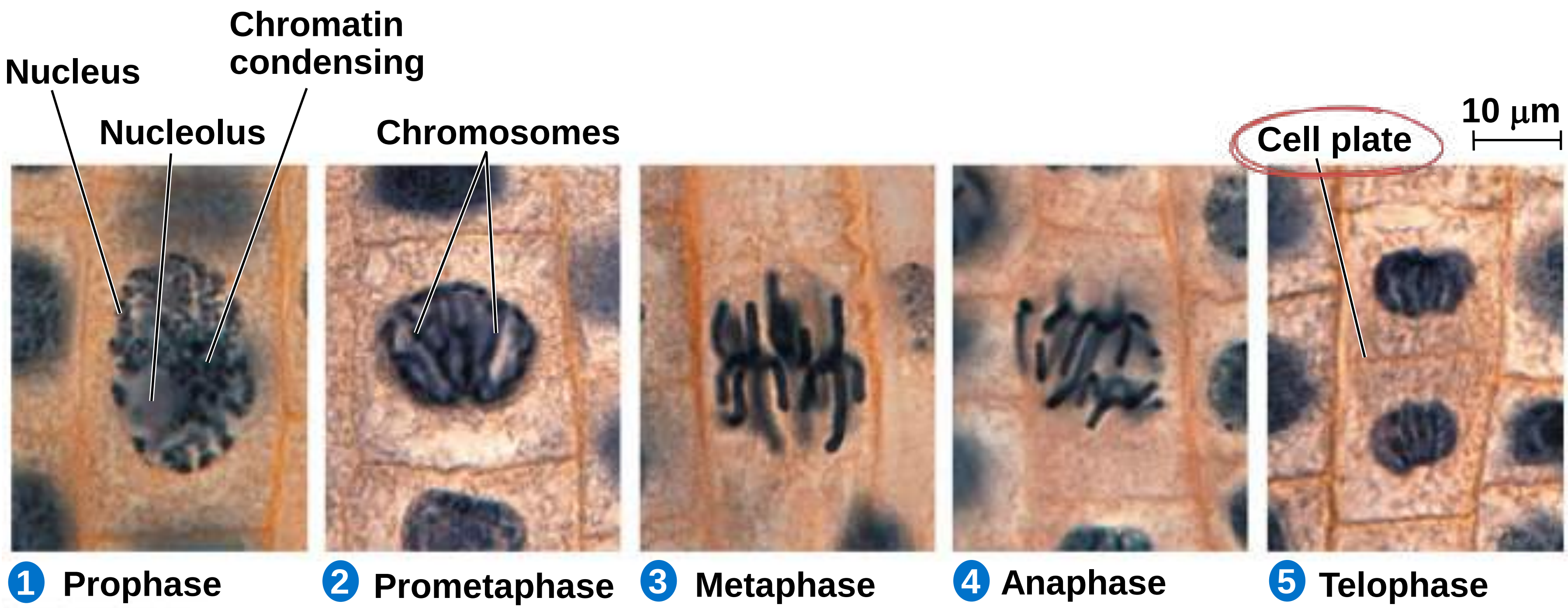
PLAY Animation: Cytokinesis

Figure 12.10



(a) Cleavage of an animal cell (SEM)
100 µm
Cleavage furrow
Contractile ring of microfilaments
made of actin and miosin
Daughter cells
(b) Cell plate formation in a plant cell (TEM)
Vesicles forming cell plate
Wall of parent cell
1 µm
Cell plate
New cell wall
Daughter cells

Figure 12.11


Chromatin
condensing
Nucleus
Nucleolus
Chromosomes
Cell plate
10 μm
1 Prophase
2 Prometaphase
3 Metaphase
4 Anaphase
5 Telophase

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
- These differences result from regulation at the molecular level
- Cancer cells manage to escape the usual controls on the cell cycle

Evidence for Cytoplasmic Signals

- The cell cycle appears to be driven by specific chemical signals present in the cytoplasm

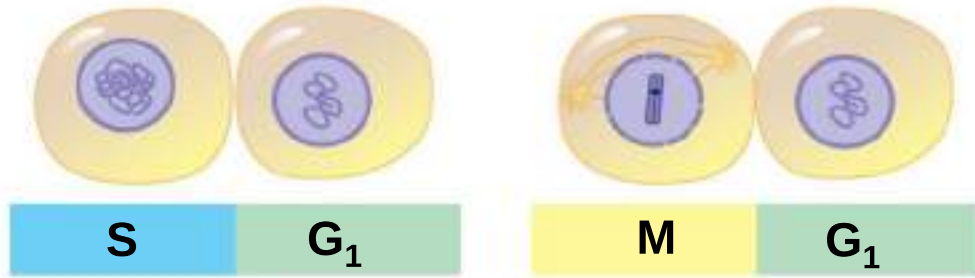
أدلة الفرضيه

- 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

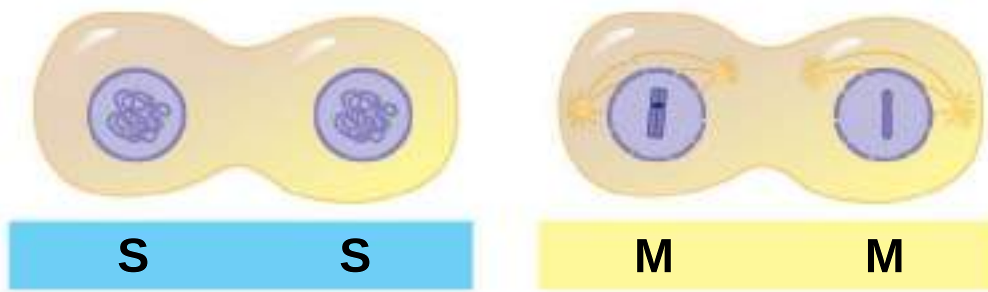
Figure 12.14

EXPERIMENT

Experiment 1 | Experiment 2



RESULTS



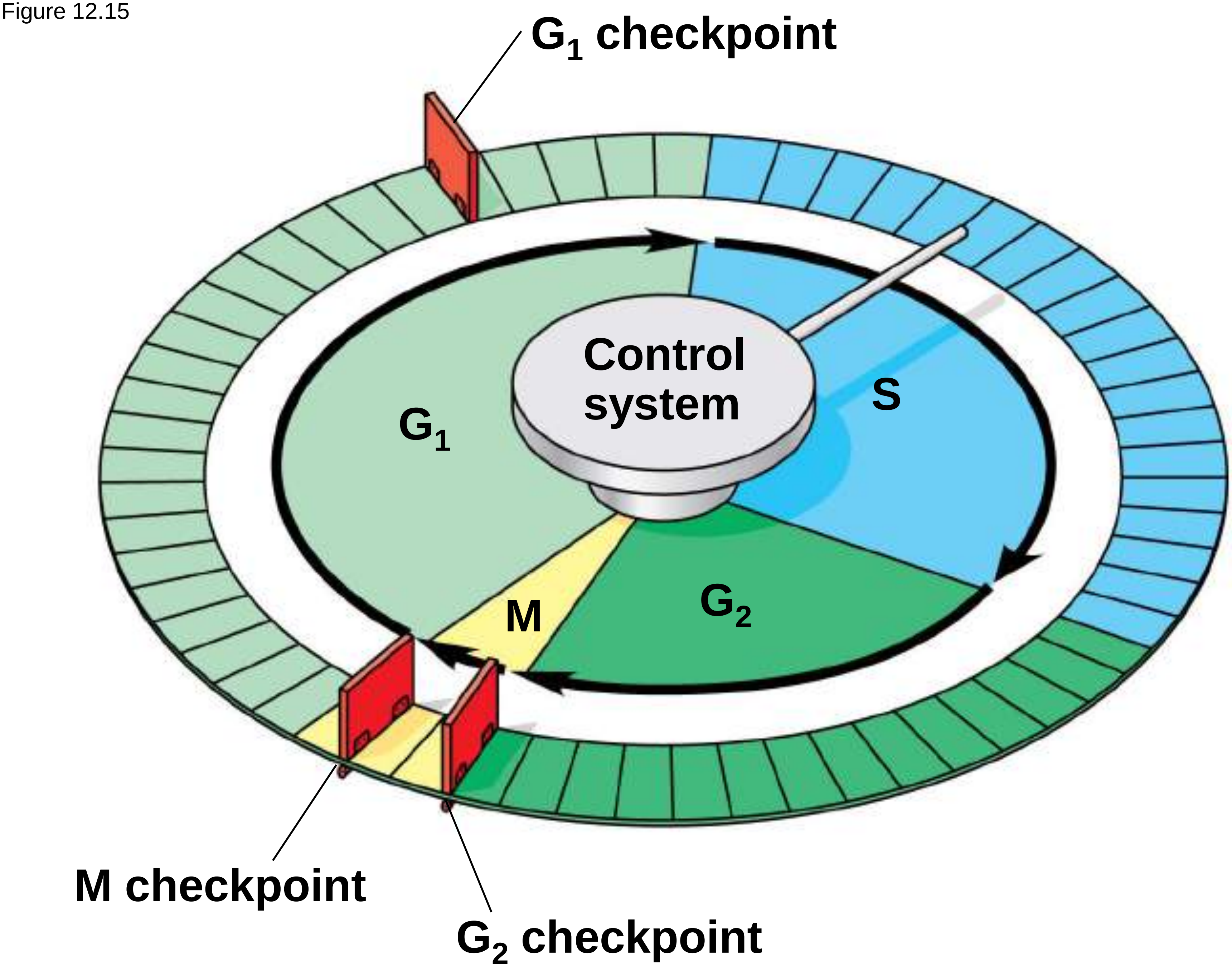
When a cell in the S phase was fused with a cell in G_1, the G_1 nucleus immediately entered the S phase—DNA was synthesized.

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.

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
- The cell cycle control system is regulated by both internal and external controls
- The clock has specific **checkpoints** where the cell cycle stops until a go-ahead signal is received

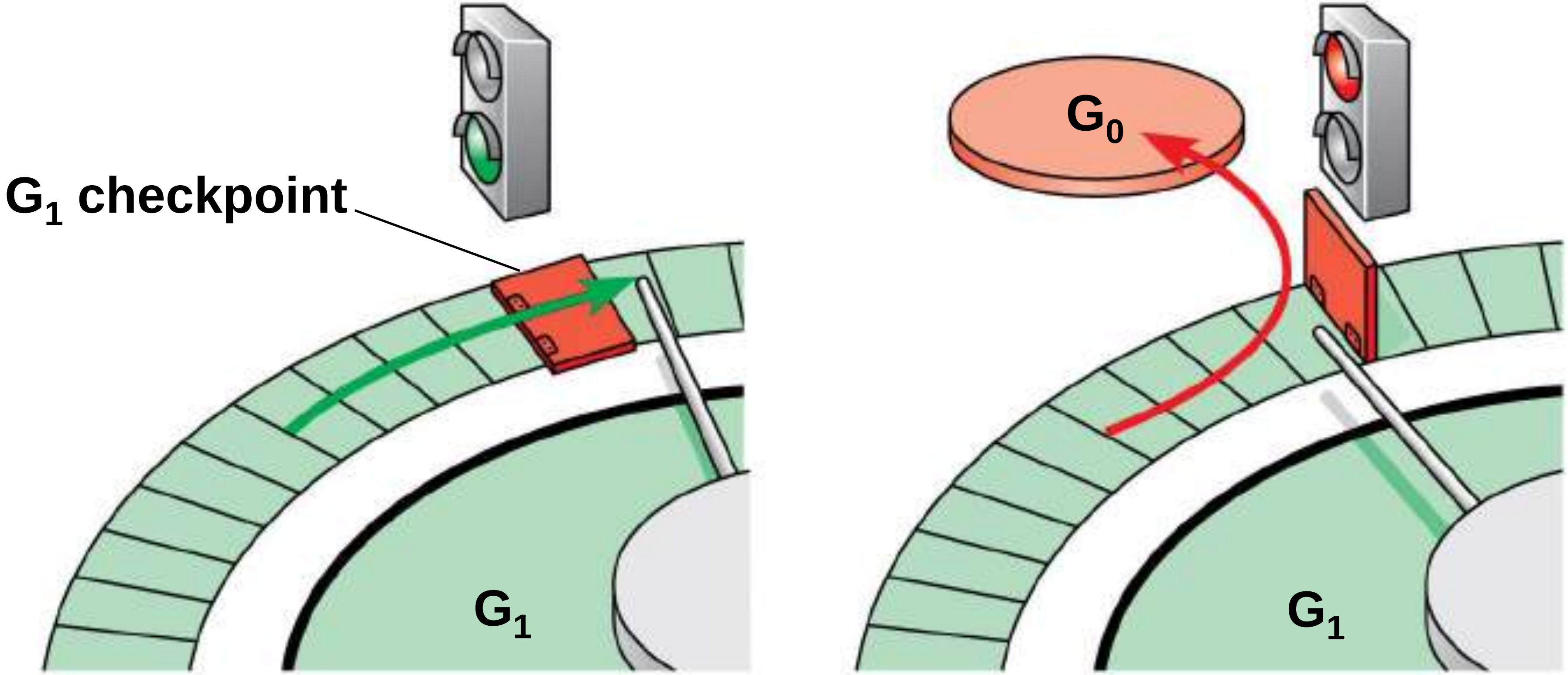
Figure 12.15



G1 checkpoint
Control
system
G1
S
M
G2
M checkpoint
G2 checkpoint

- For many cells, the G_1 checkpoint seems to be the most important why? 2
- 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
- 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**

Figure 12.16



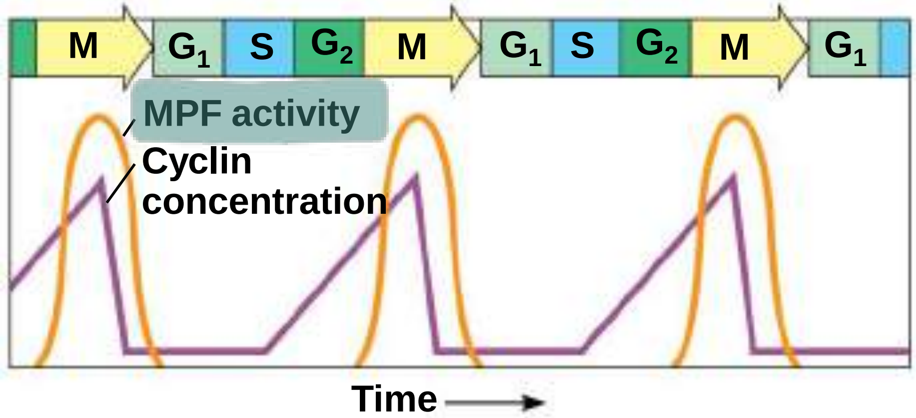
(a) Cell receives a go-ahead signal.

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

The Cell Cycle Clock: Cyclins and Cyclin-Dependent Kinases

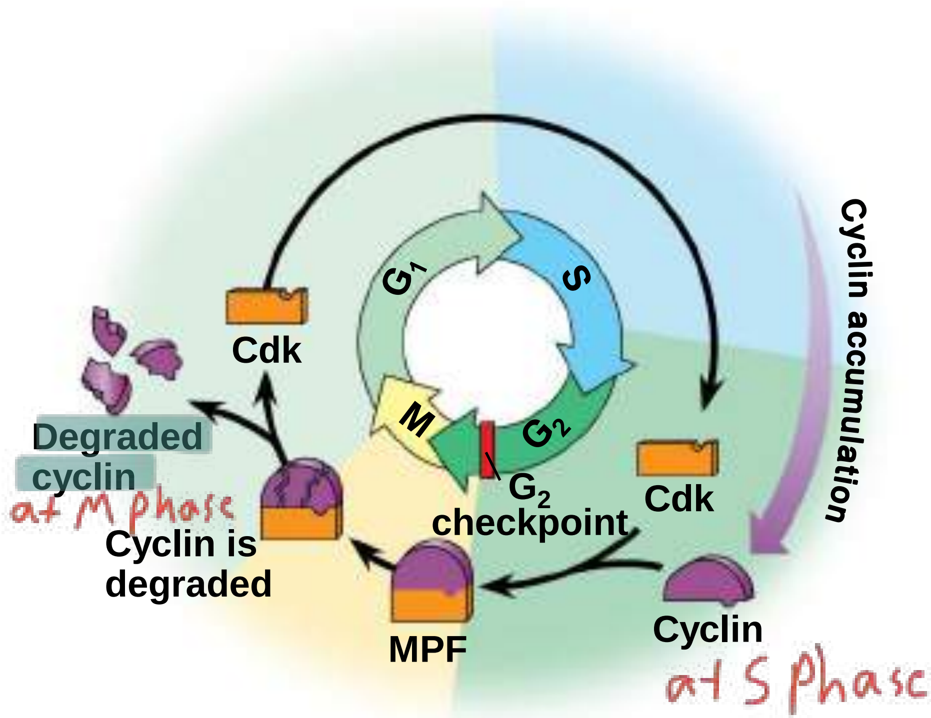
- Two types of regulatory proteins are involved in cell cycle control: **cyclins** and **cyclin-dependent kinases (Cdks)**
- Cdks activity fluctuates during the cell cycle because it is controled by cyclins, so named because their concentrations vary with the cell cycle
- **MPF** (maturation-promoting factor) is a cyclin-Cdk complex that triggers a cell's passage past the G_2 checkpoint into the M phase

Figure 12.17



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

Cyclin dependent kinase is always present in the cell

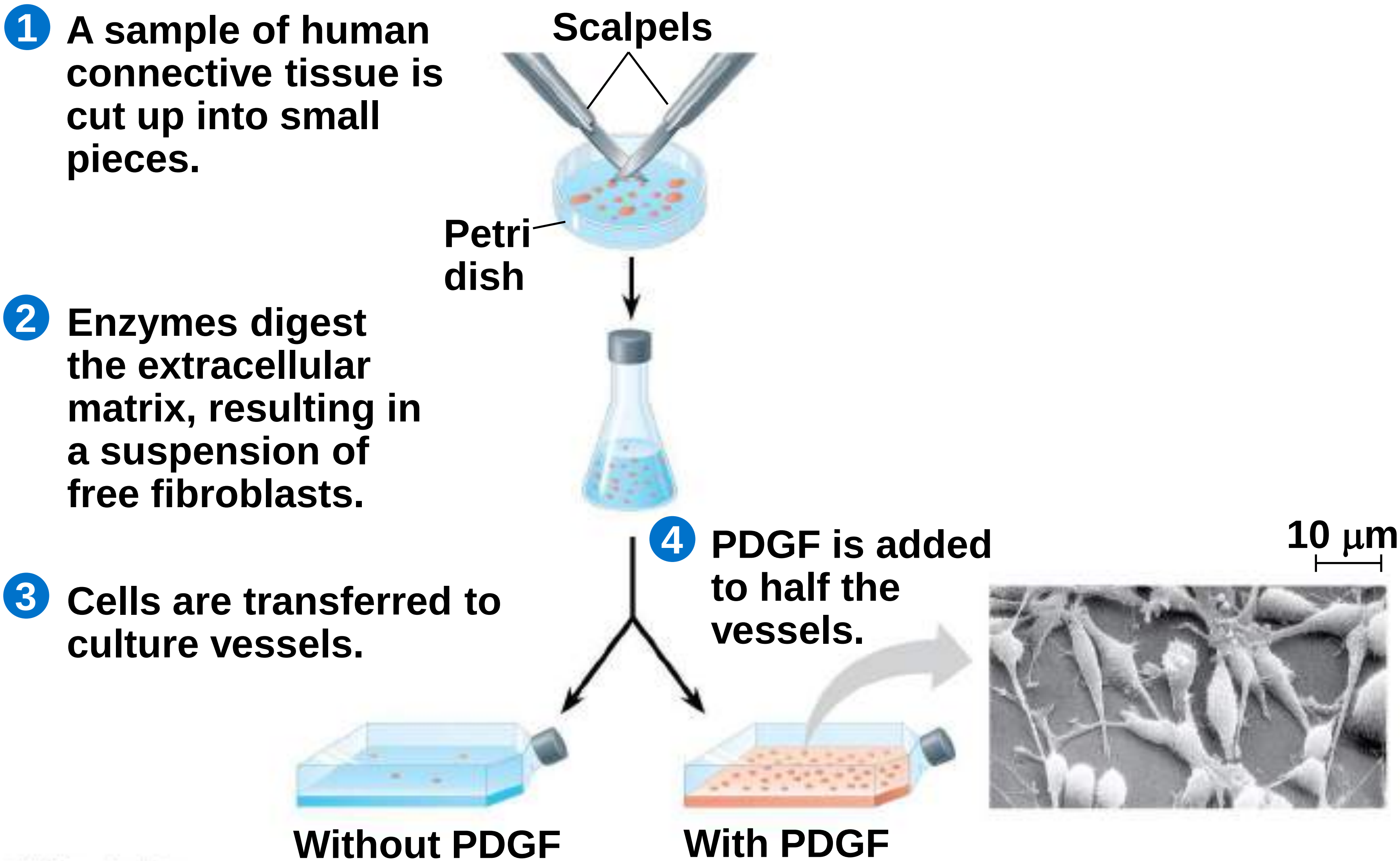


(b) Molecular mechanisms that help regulate the cell cycle

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

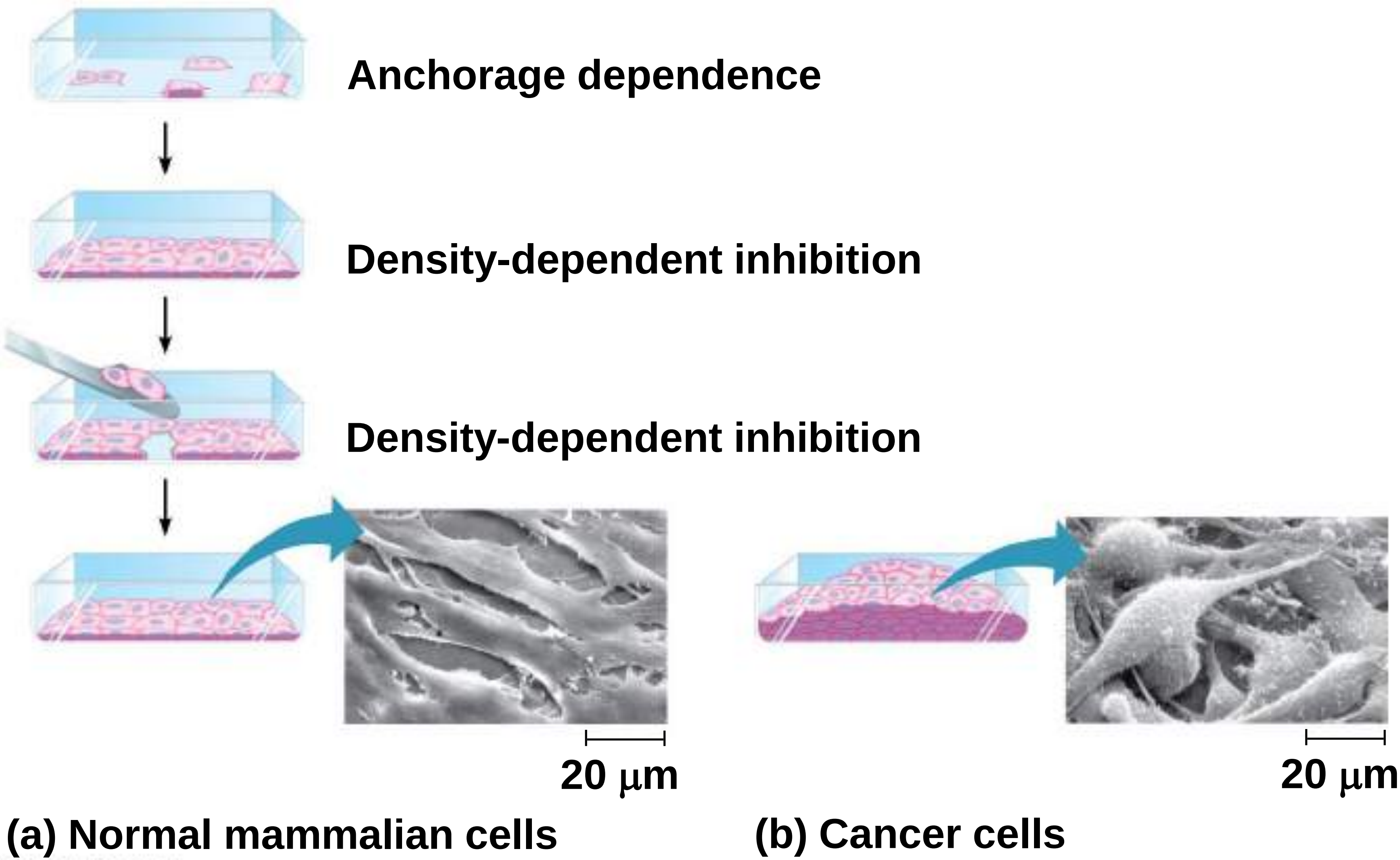
Figure 12.18



1 A sample of human connective tissue is cut up into small pieces.
Scalpels
Petri dish
2 Enzymes digest the extracellular matrix, resulting in a suspension of free fibroblasts.
3 Cells are transferred to culture vessels.
4 PDGF is added to half the vessels.
10 µm
Without PDGF
With PDGF

- A clear example of external signals is **density-dependent inhibition**, in which crowded cells stop dividing
- Most animal cells also exhibit **anchorage dependence**, in which they must be attached to a substratum in order to divide
- Cancer cells exhibit neither density-dependent inhibition nor anchorage dependence

Figure 12.19

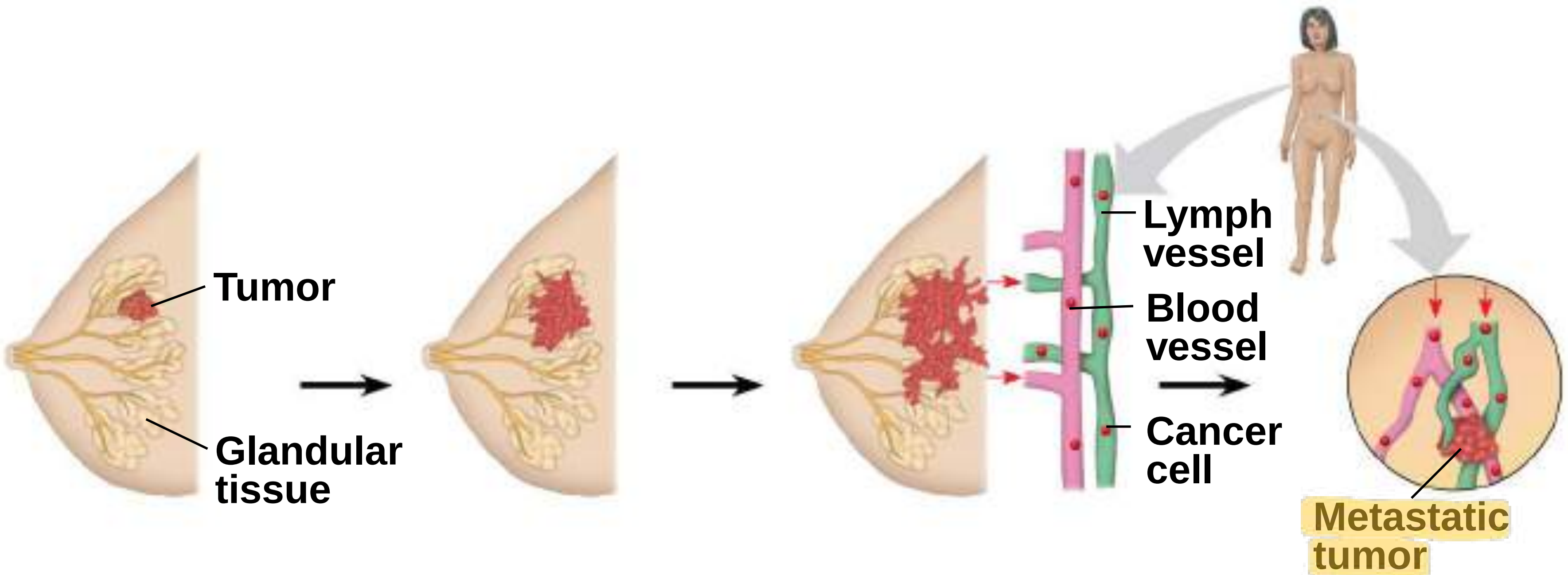

Anchorage dependence
Density-dependent inhibition
Density-dependent inhibition
20 μm
20 μm
(a) Normal mammalian cells
(b) Cancer cells

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 why?
  - 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

- A normal cell is converted to a cancerous cell by a process called **transformation**
- Cancer cells that are not eliminated by the immune system form tumors, masses of abnormal cells within otherwise normal tissue
- If abnormal cells remain only at the original site, the lump is called a **benign tumor**
- **Malignant tumors** invade surrounding tissues and can **metastasize**, exporting cancer cells to other parts of the body, where they may form additional tumors

Figure 12.20



1 A tumor grows from a single cancer cell.

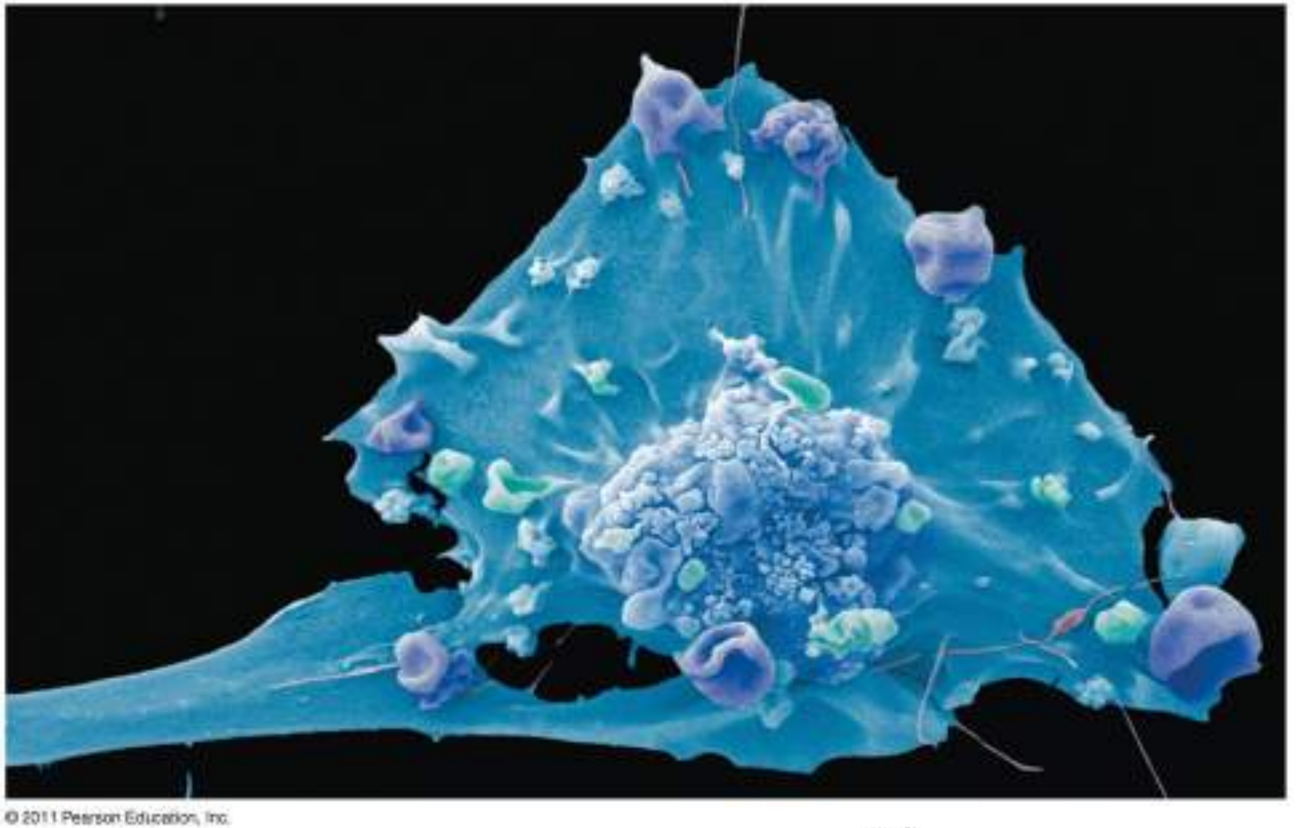
2 Cancer cells invade neighboring tissue.

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



Cancer cell

Figure 12.UN01

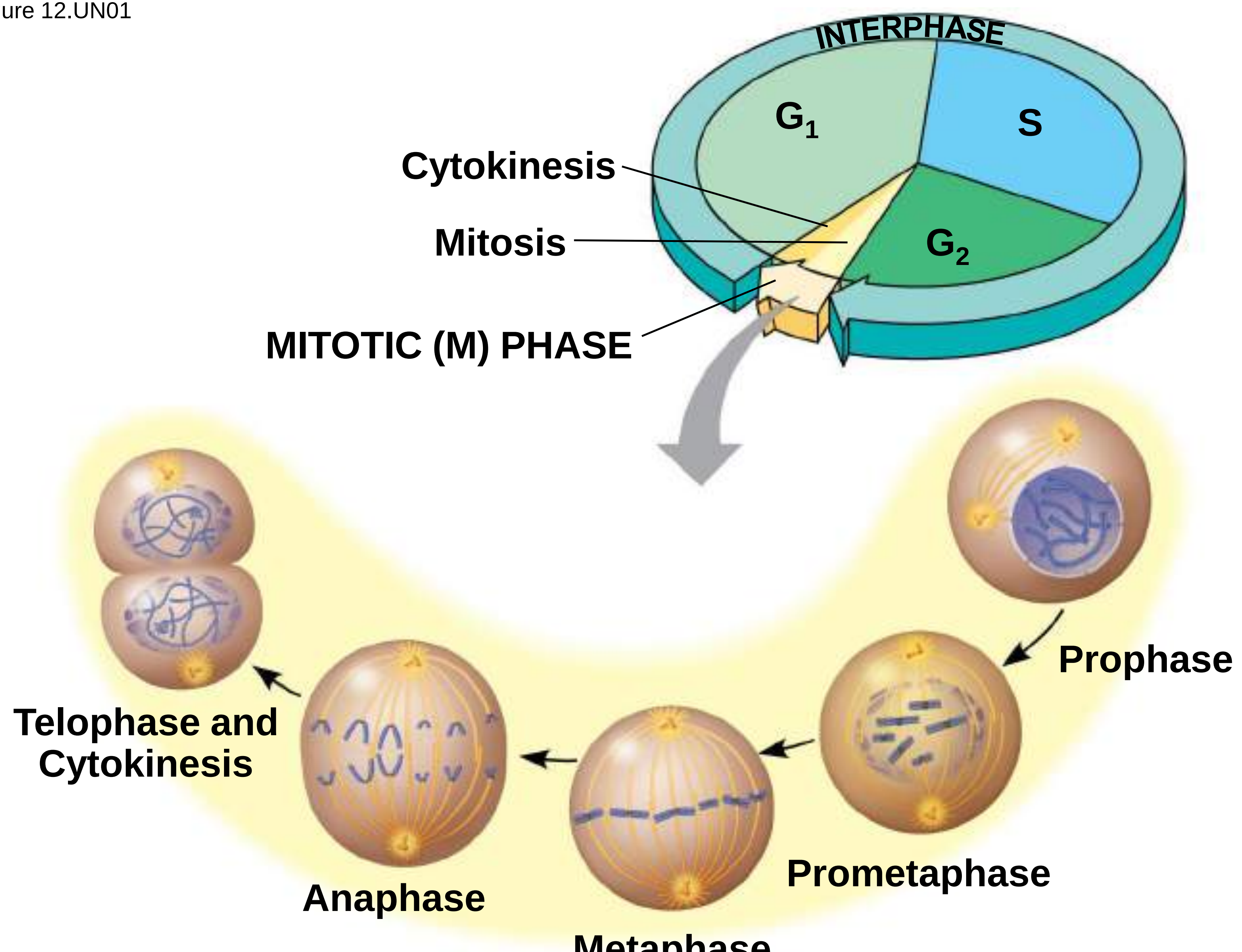


Figure 12.UN02

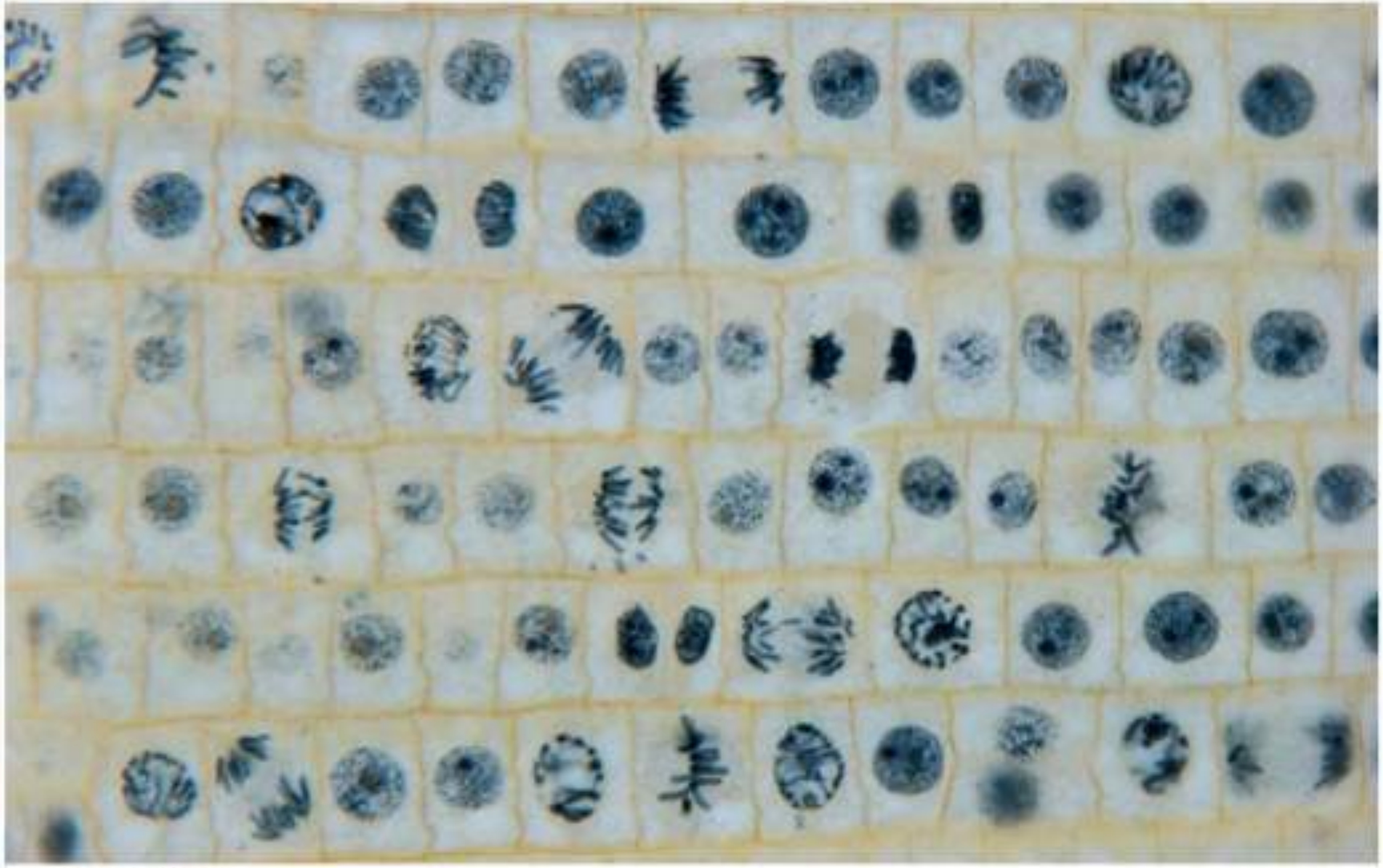


Figure 12.UN03

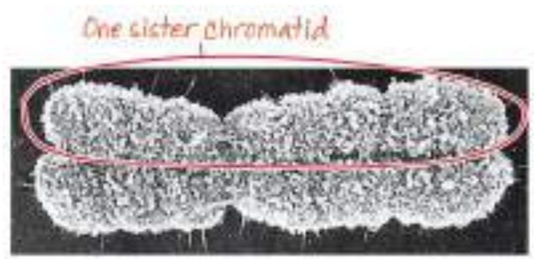


Figure 12.UN04

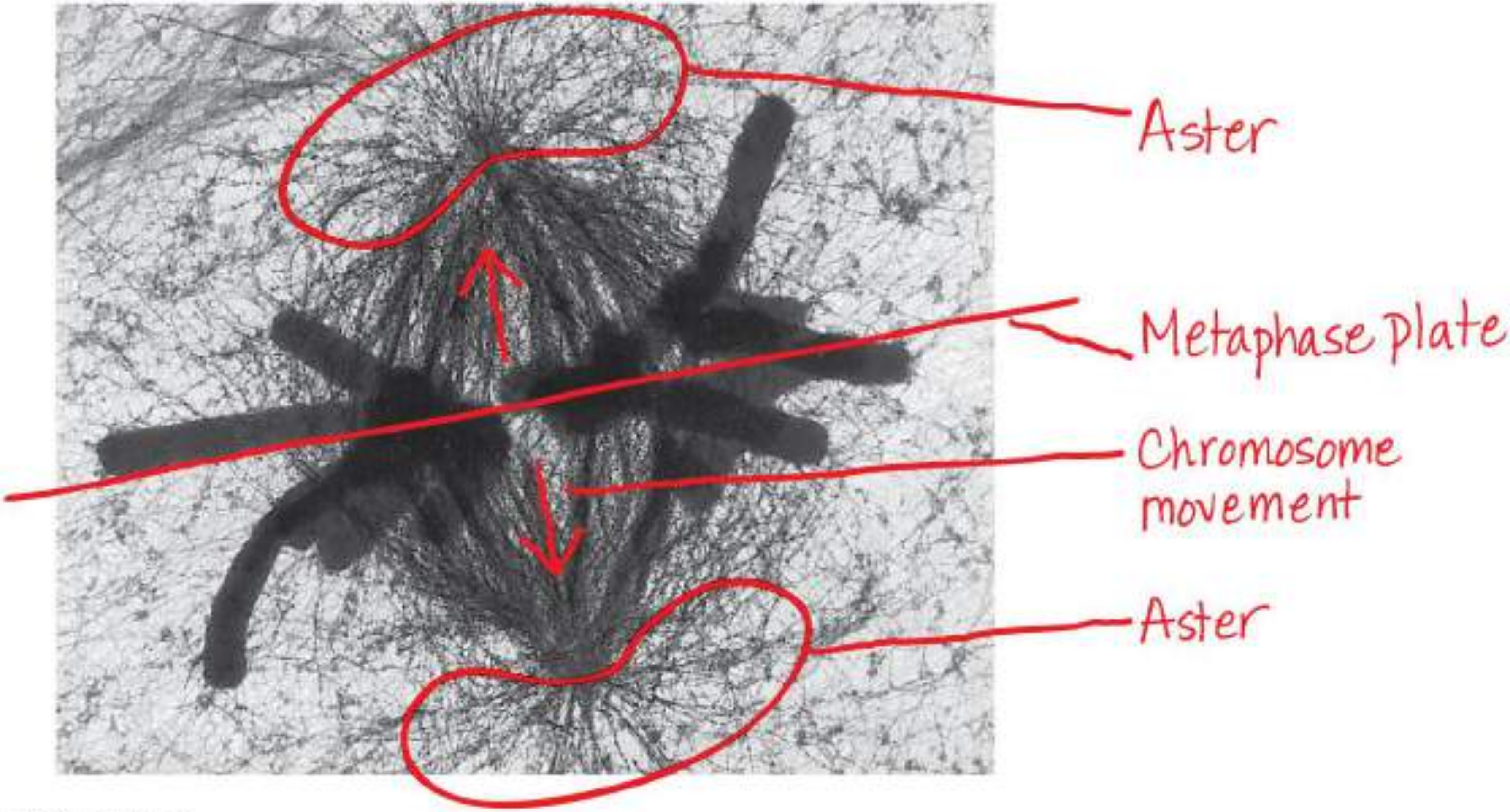


Figure 12.UN05

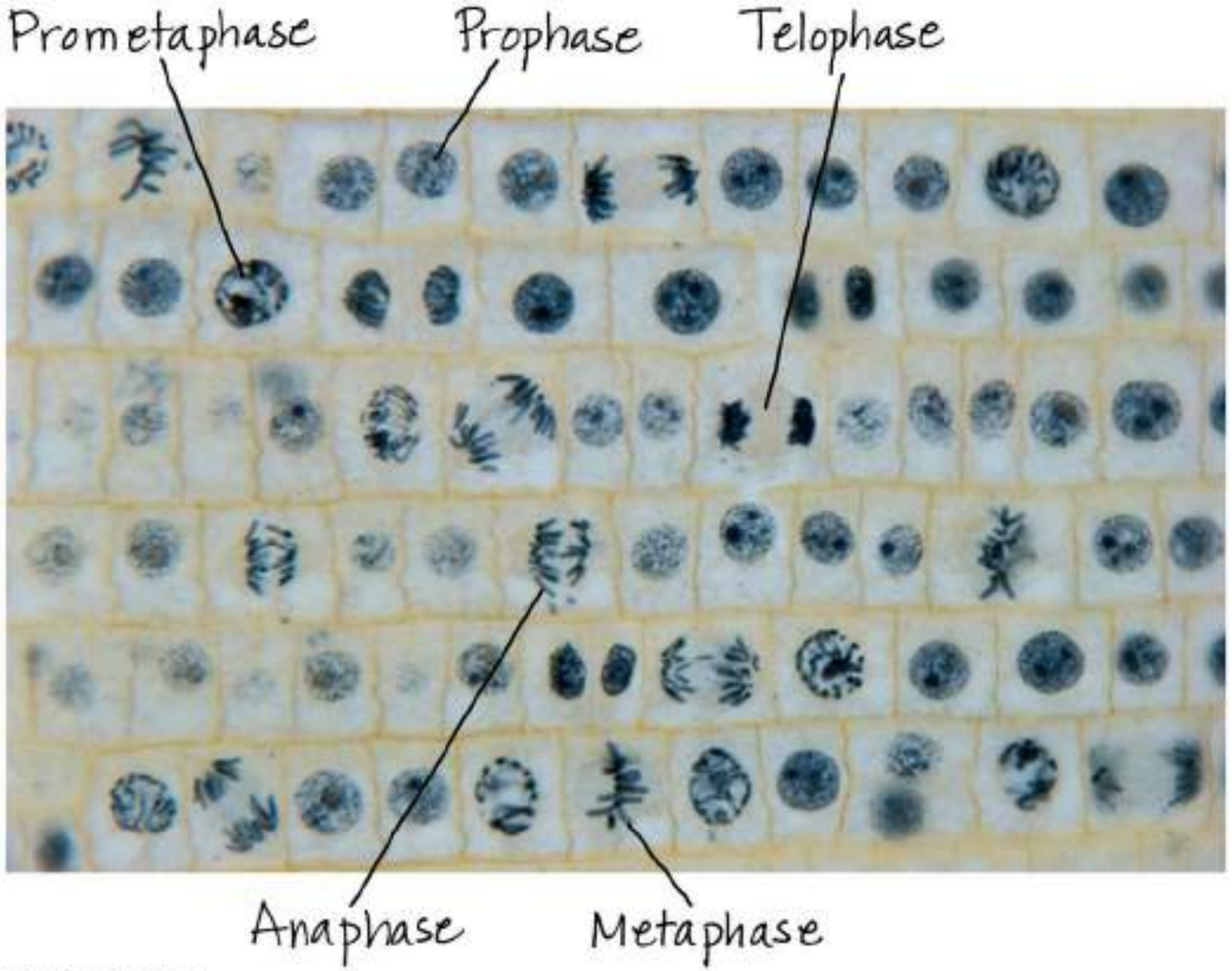


Figure 12.UN06