CAMPBELL BIOLOGY IN FOCUS

URRY • CAIN • WASSERMAN • MINORSKY • REECE

9

The Cell Cycle

Lecture Presentations by
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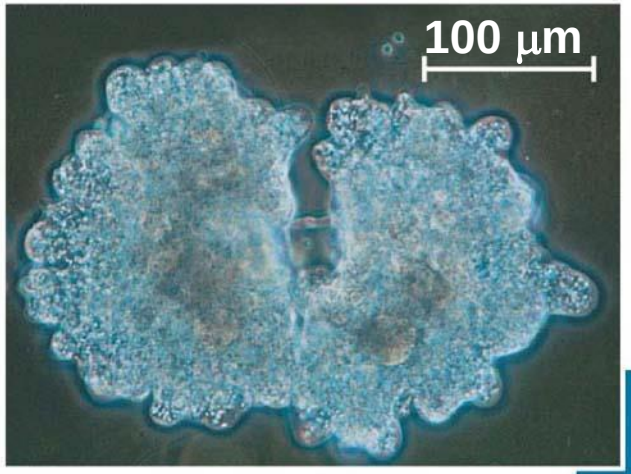
SECOND EDITION

Overview: The Key Roles of Cell Division

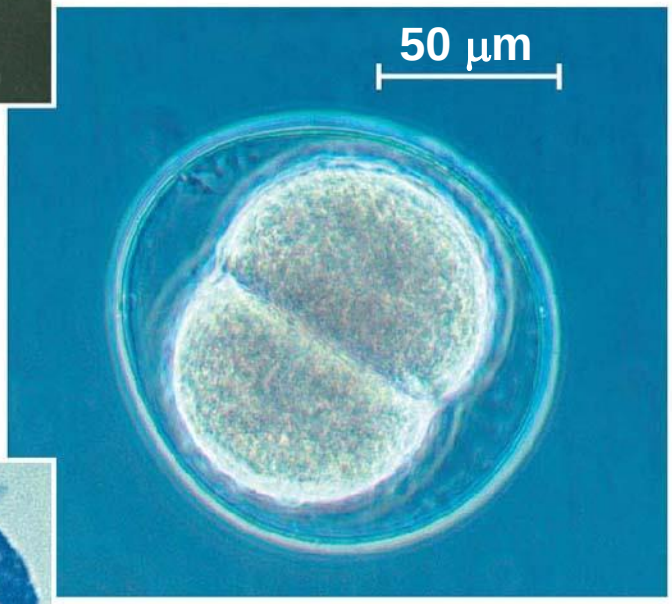
- The ability of organisms to produce more of their own kind best distinguishes living things from nonliving matter
- The continuity of life is based on the reproduction of cells, or **cell division**

- In unicellular organisms, division of one cell reproduces the entire organism
- Cell division enables multicellular eukaryotes to develop from a single cell and, once fully grown, to renew, repair, or replace cells as needed
- Cell division is an integral part of the **cell cycle**, the life of a cell from its formation to its own division

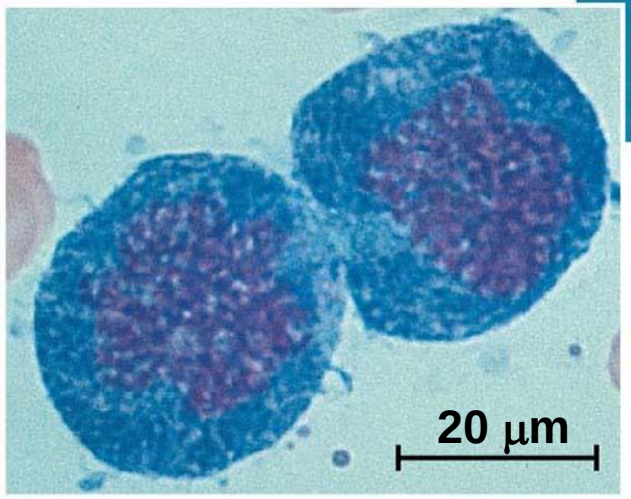
Figure 9.2



◄ (a) Reproduction



► (b) Growth and development



◄ (c) Tissue renewal

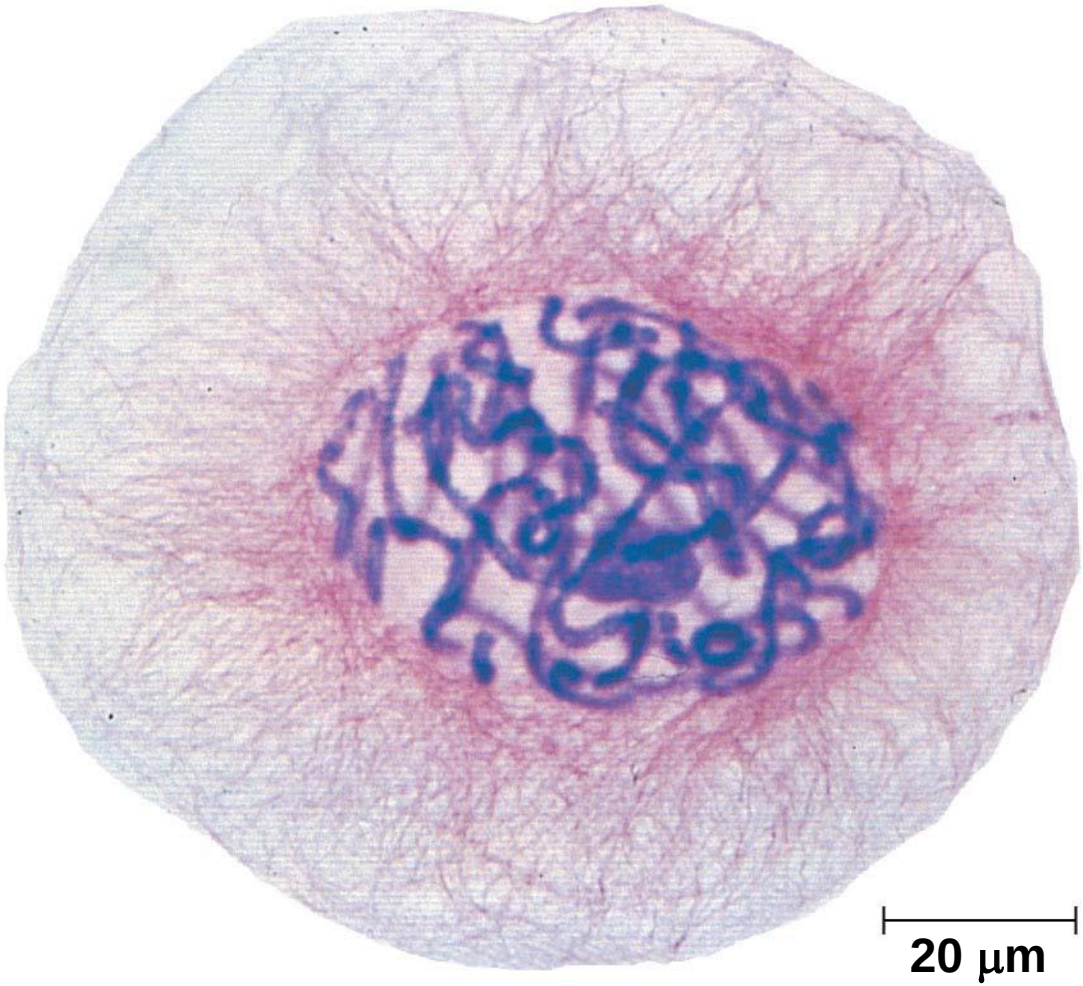
Concept 9.1: Most cell division results in genetically identical daughter cells

- Most cell division results in the distribution of identical genetic material—DNA—to two daughter cells
- DNA is passed from one generation of cells to the next with remarkable fidelity

Cellular Organization of the Genetic Material

- 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 9.3

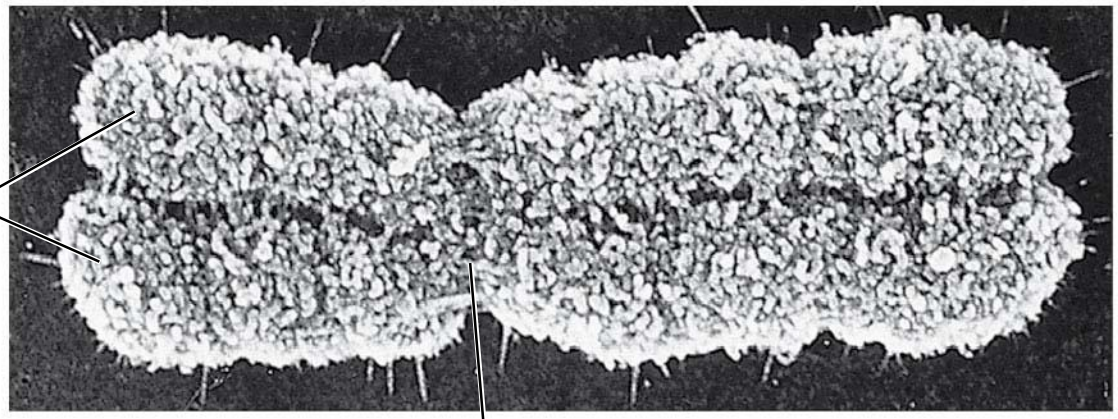


- Eukaryotic chromosomes consist of **chromatin**, a complex of DNA and protein
- Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus
- **Somatic cells** (nonreproductive cells) have two sets of chromosomes
- **Gametes** (reproductive cells: sperm and eggs) have one set of chromosomes

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 identical copies of the original chromosome
- The **centromere** is where the two chromatids are most closely attached

Figure 9.4



- 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 9.5-s1

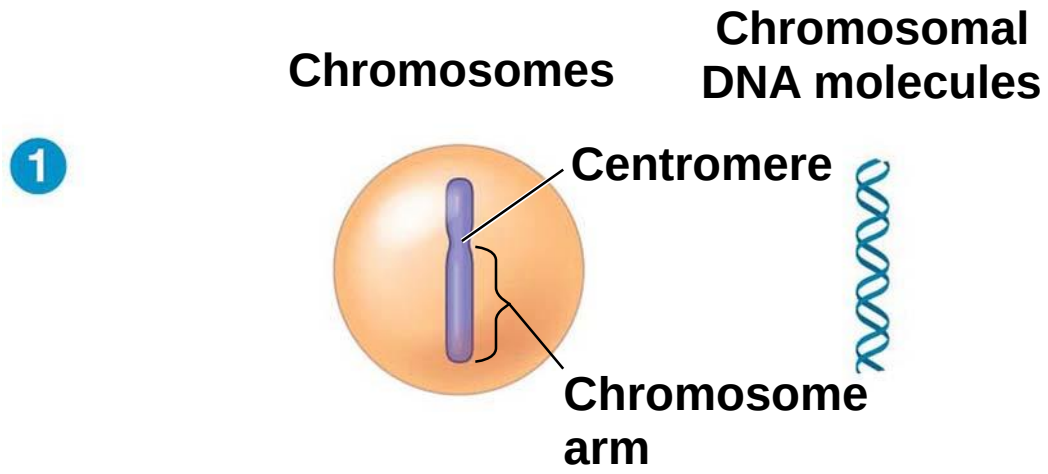


Figure 9.5-s2

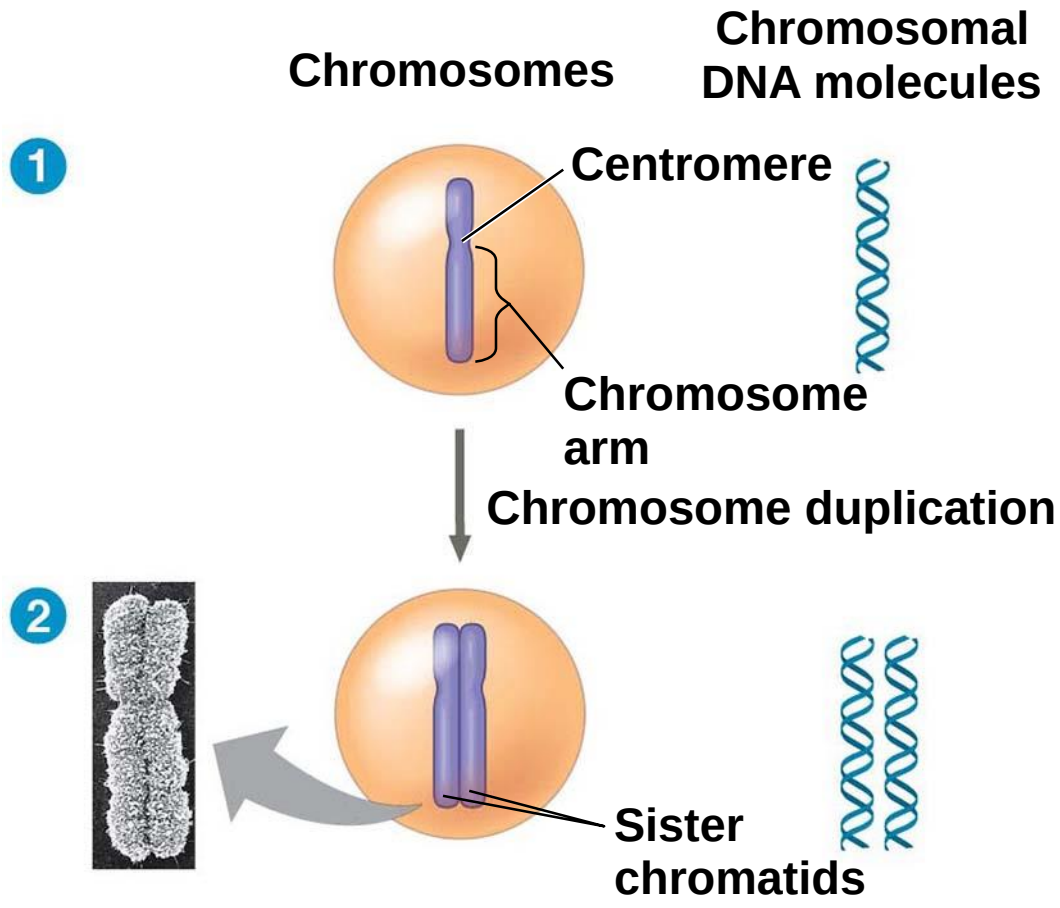
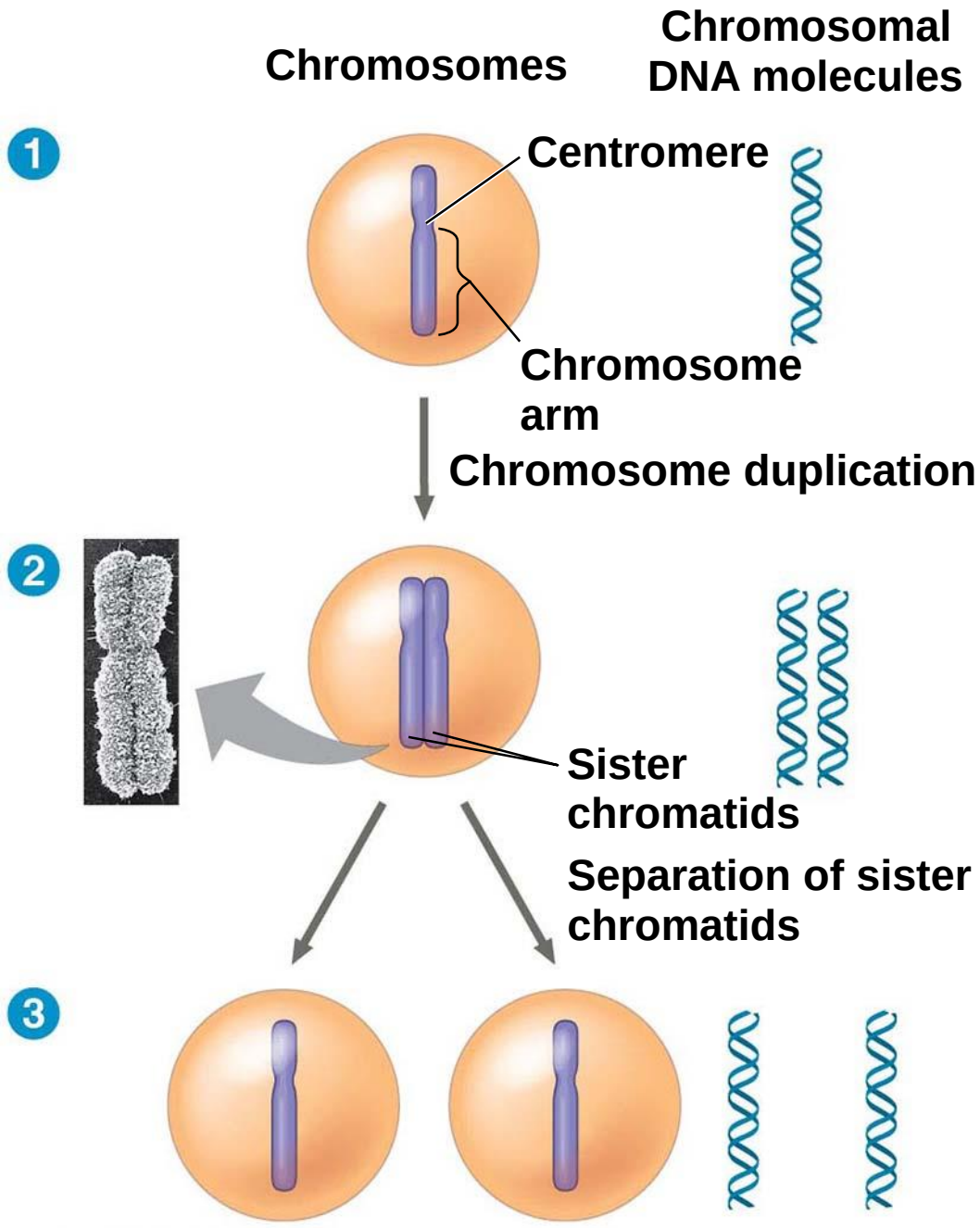


Figure 9.5-s3



- 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 9.2: The mitotic phase alternates with interphase in the cell cycle

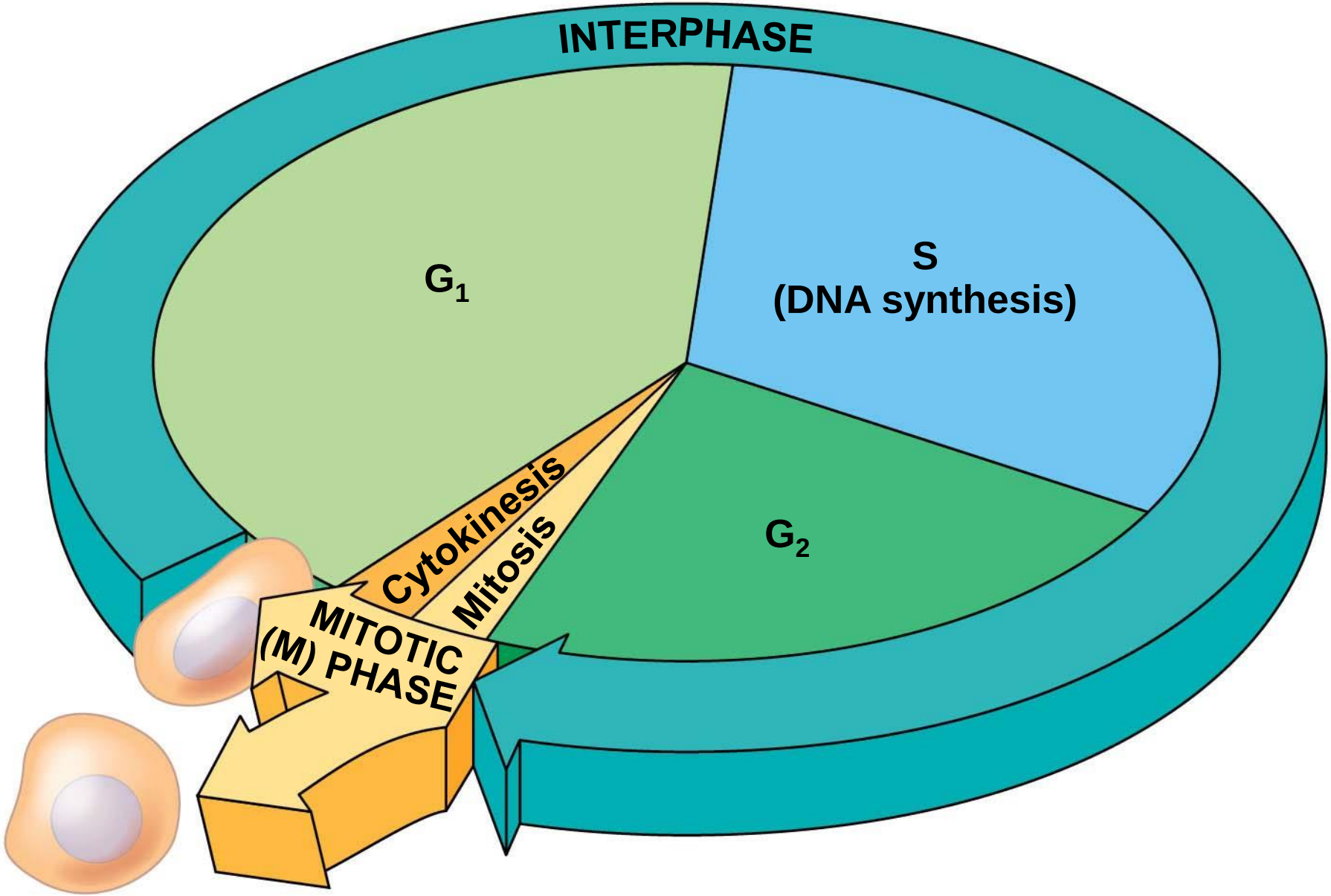
- In 1882, the German anatomist Walther Flemming developed dyes to observe chromosomes during mitosis and cytokinesis

Phases of the Cell Cycle

- The cell cycle consists of
  - **Mitotic** (**M**) **phase**, including mitosis and cytokinesis
  - **Interphase**, including 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 9.6



- Mitosis is conventionally divided into five phases
  - **Prophase**
  - **Prometaphase**
  - **Metaphase**
  - **Anaphase**
  - **Telophase**
- Cytokinesis overlaps the latter stages of mitosis

Figure 9.7-1

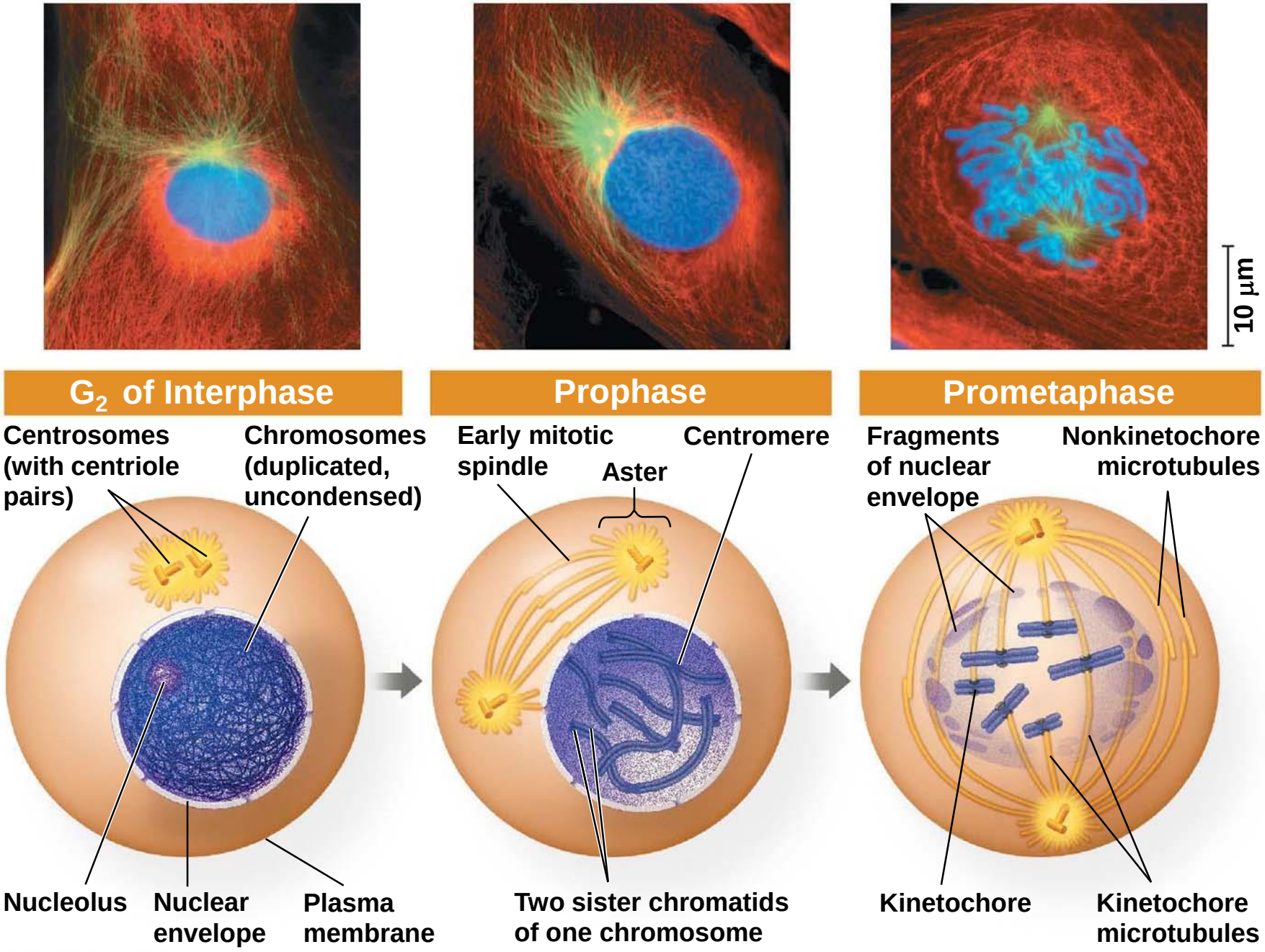


Figure 9.7-2

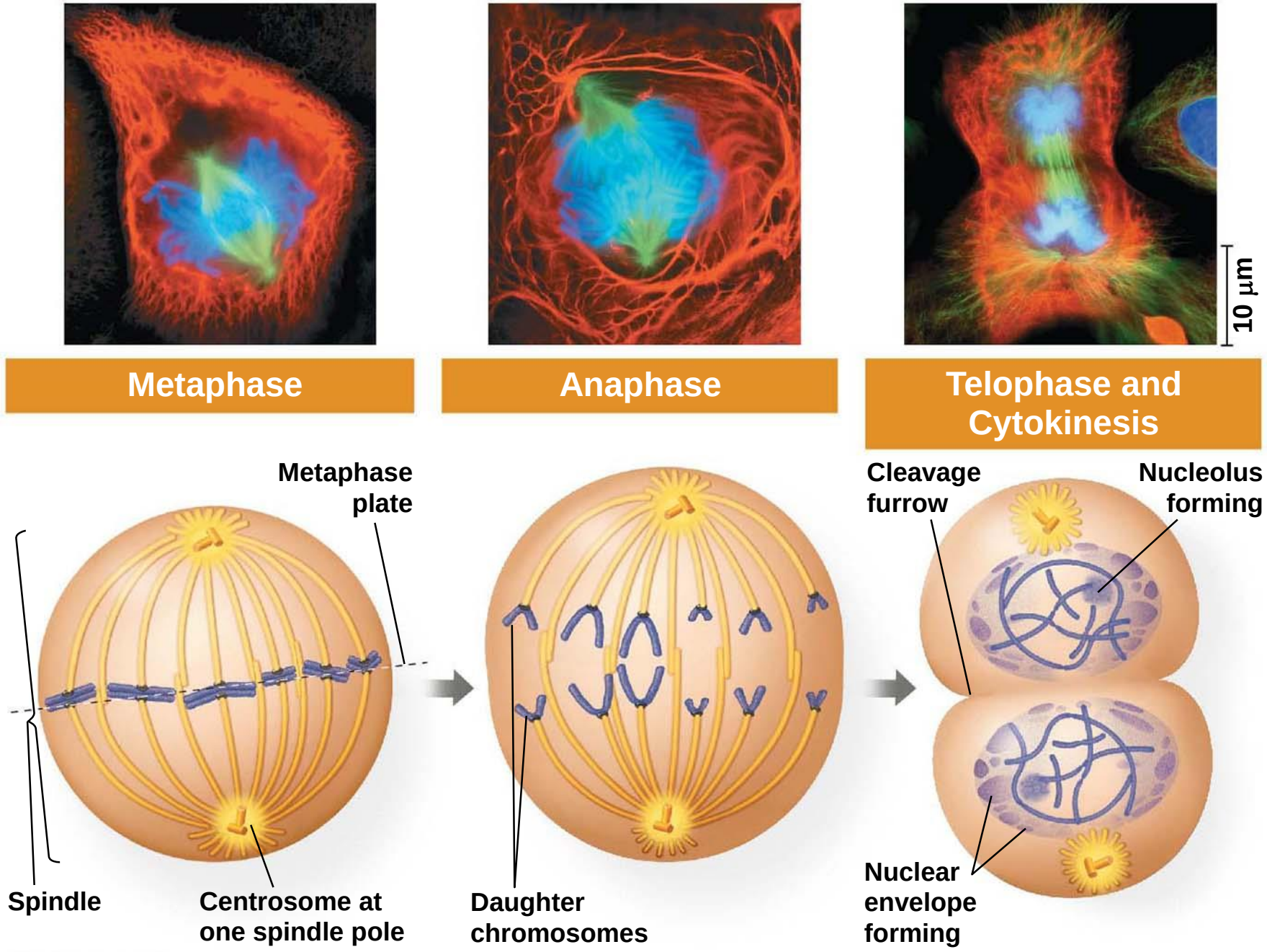


Figure 9.7-3

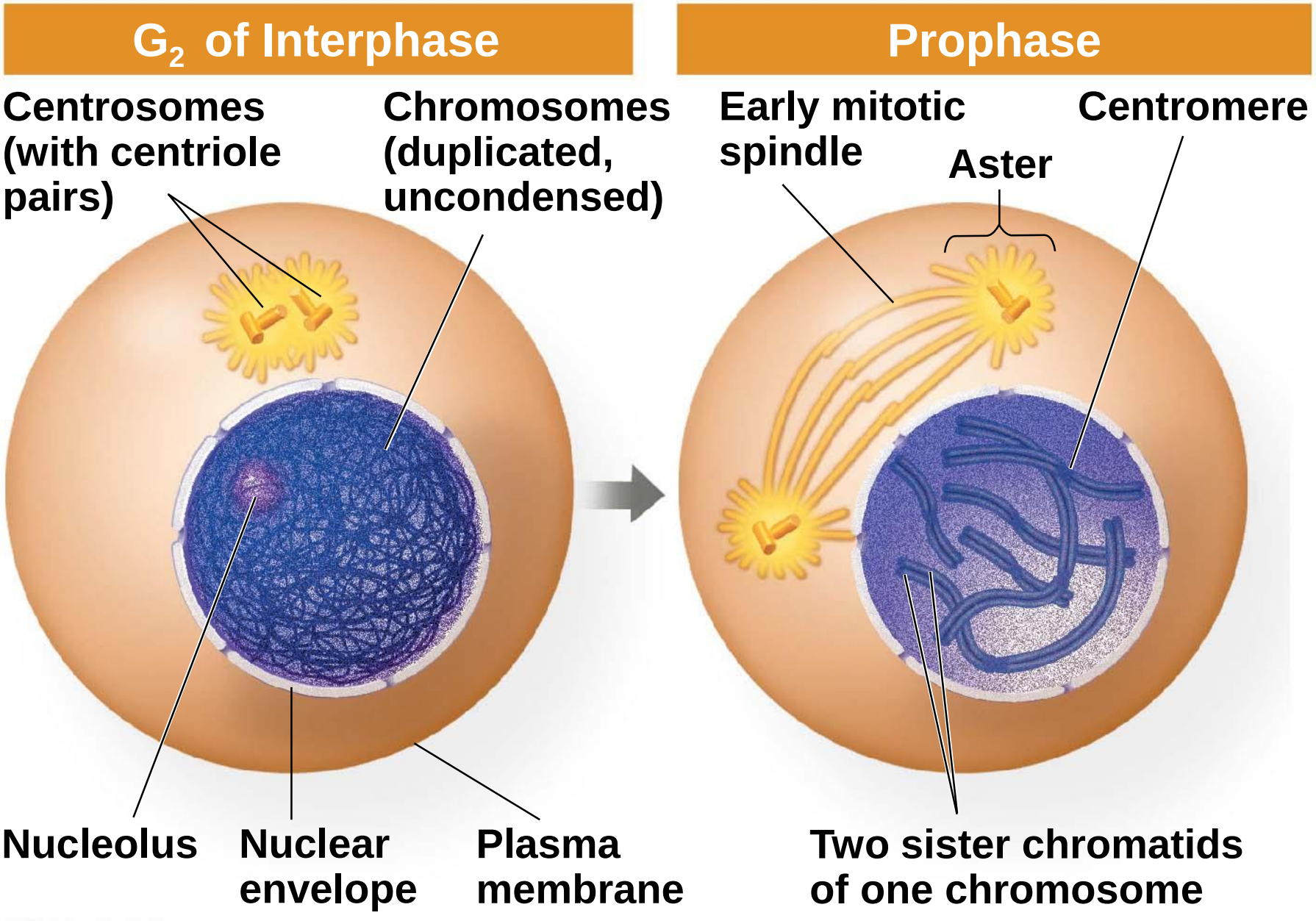


Figure 9.7-4

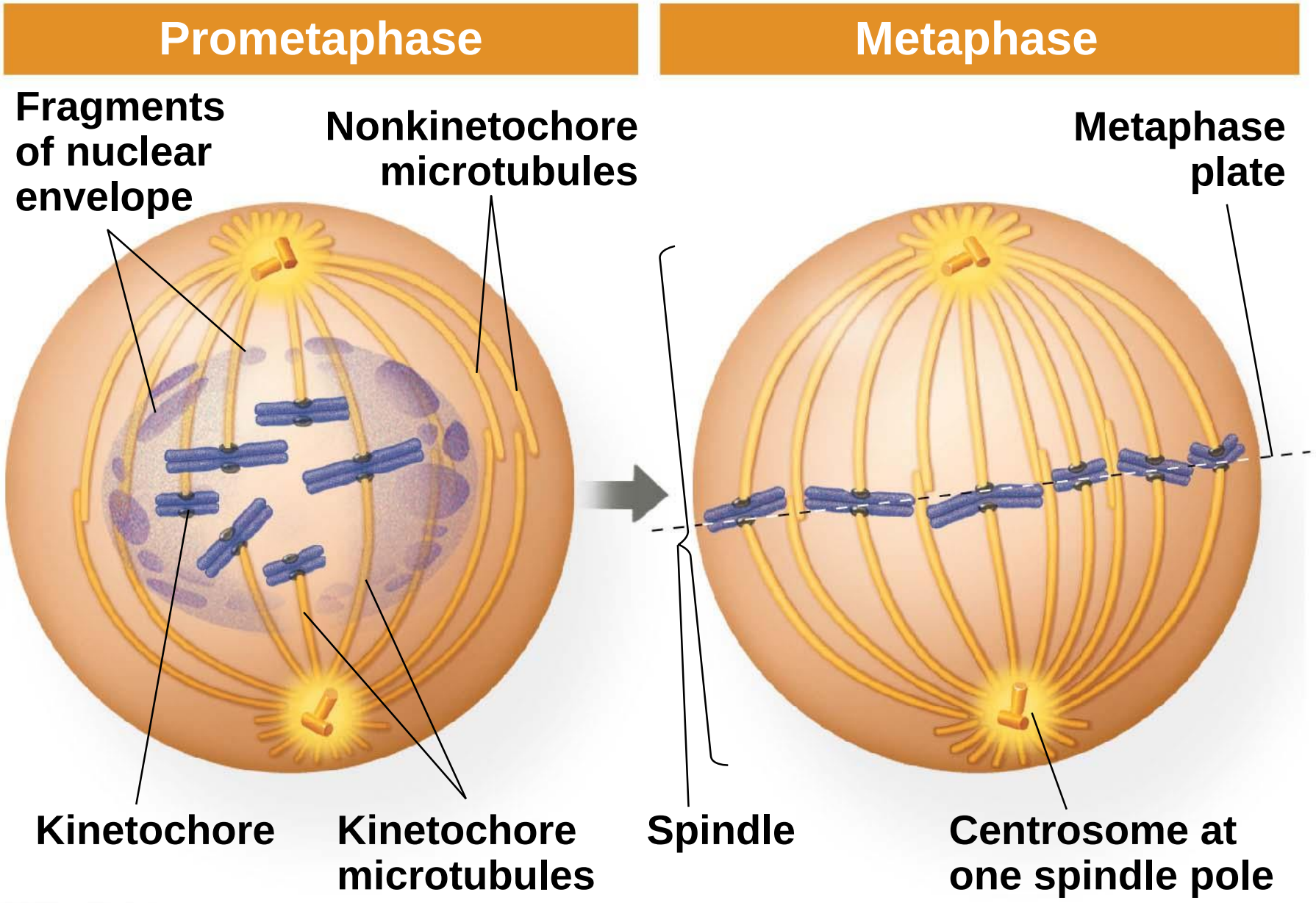


Figure 9.7-5

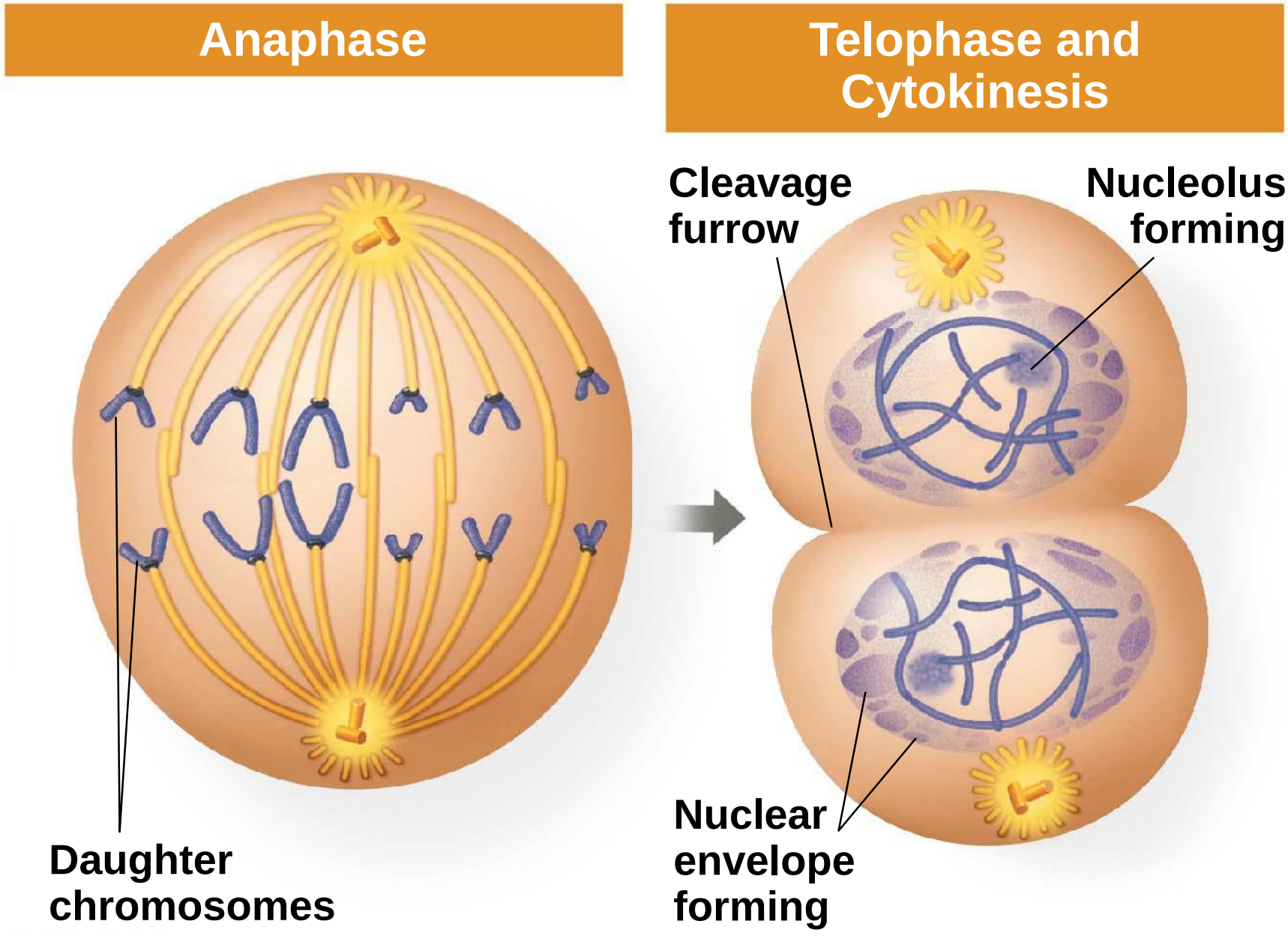
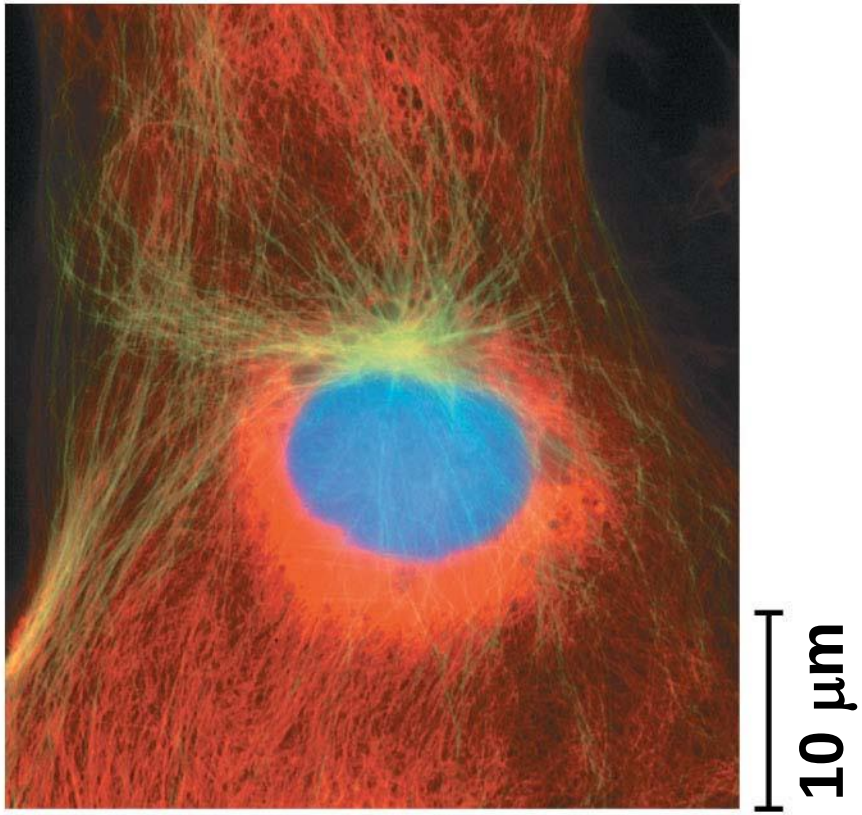
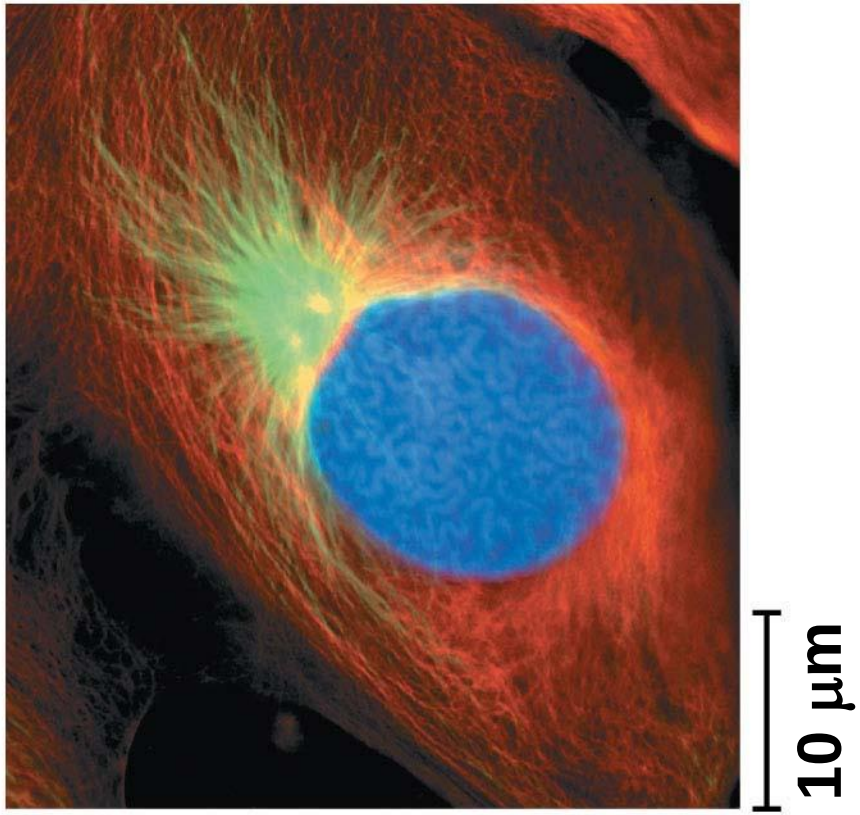


Figure 9.7-6



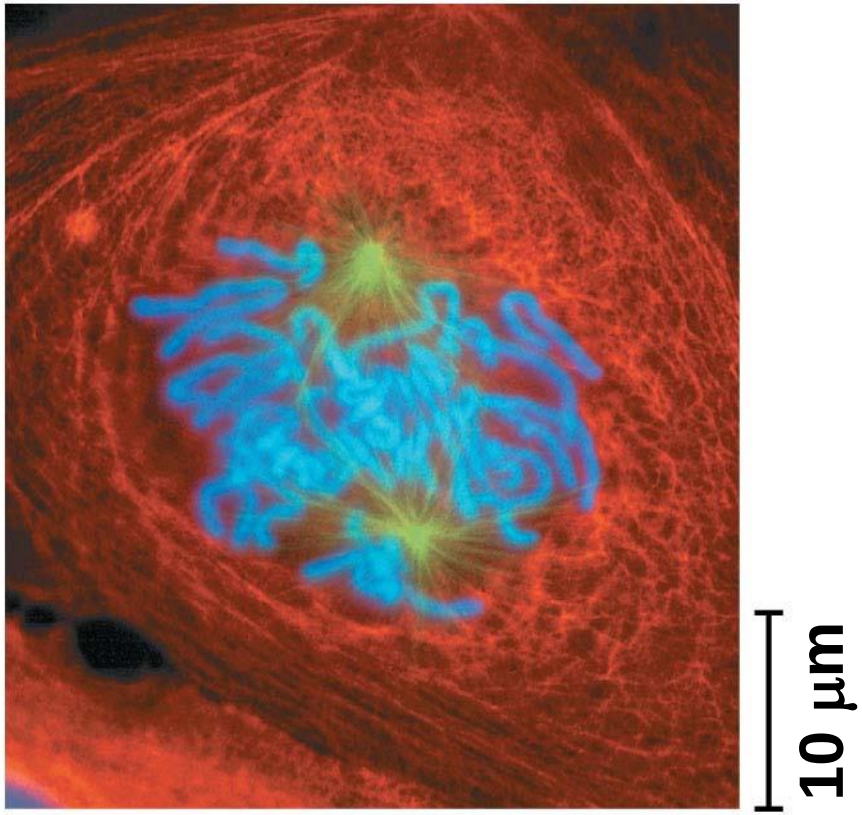
G_2 of Interphase

Figure 9.7-7



Prophase

Figure 9.7-8



Prometaphase

Figure 9.7-9

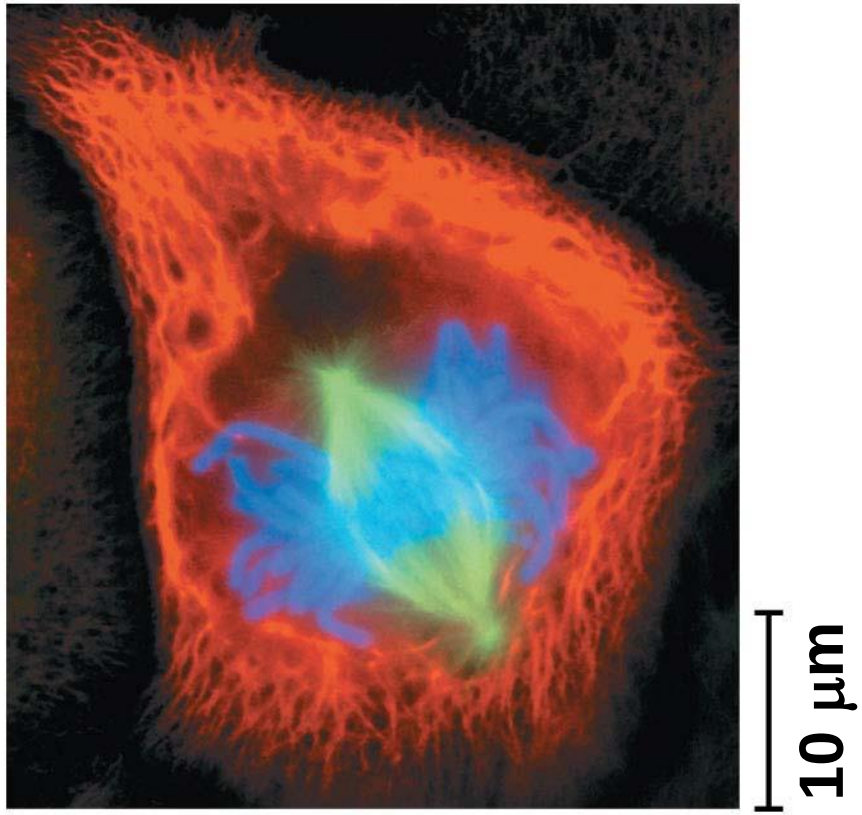
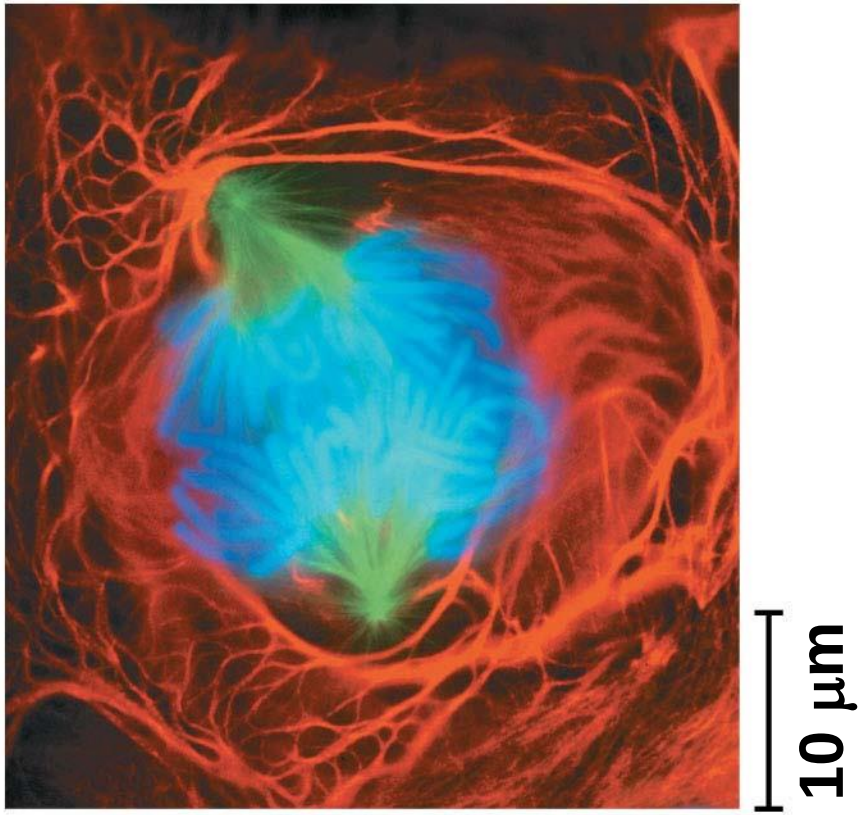
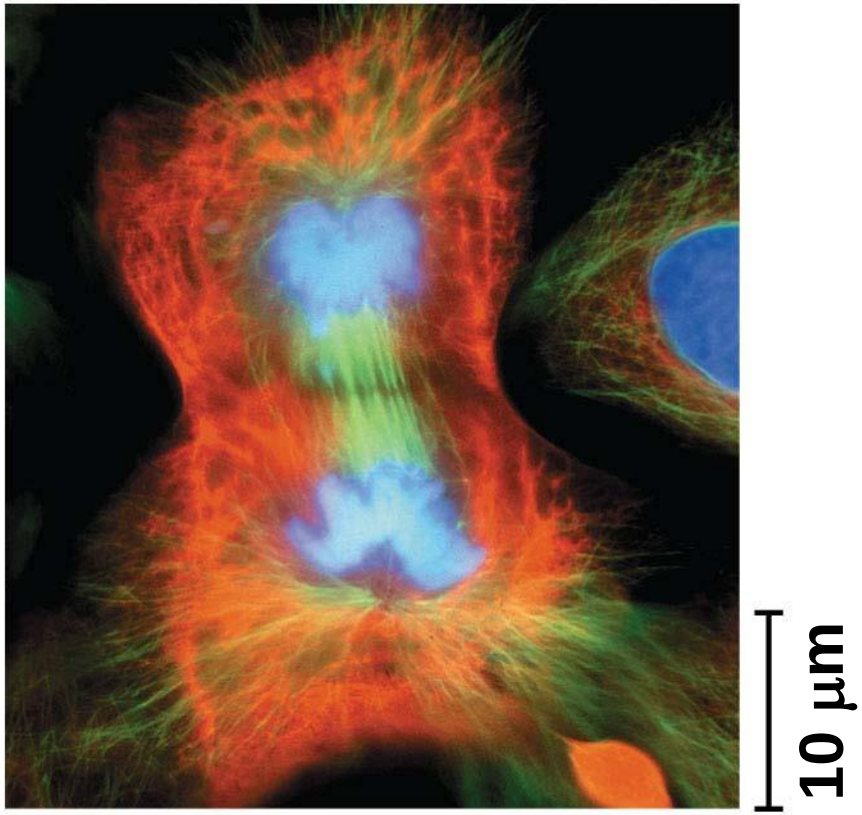


Figure 9.7-10



Anaphase

Figure 9.7-11



Telophase and Cytokinesis

The Mitotic Spindle: *A Closer Look*

- The **mitotic spindle** is a structure made of microtubules and associated proteins
- It controls chromosome movement during mitosis
- In animal cells, assembly of spindle microtubules begins in the **centrosome**, a type of 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** (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 that assemble on sections of DNA at centromeres
- At metaphase, the centromeres of all the chromosomes are at the **metaphase plate**, an imaginary structure at the midway point between the spindle's two poles

Video: Mitosis Spindle

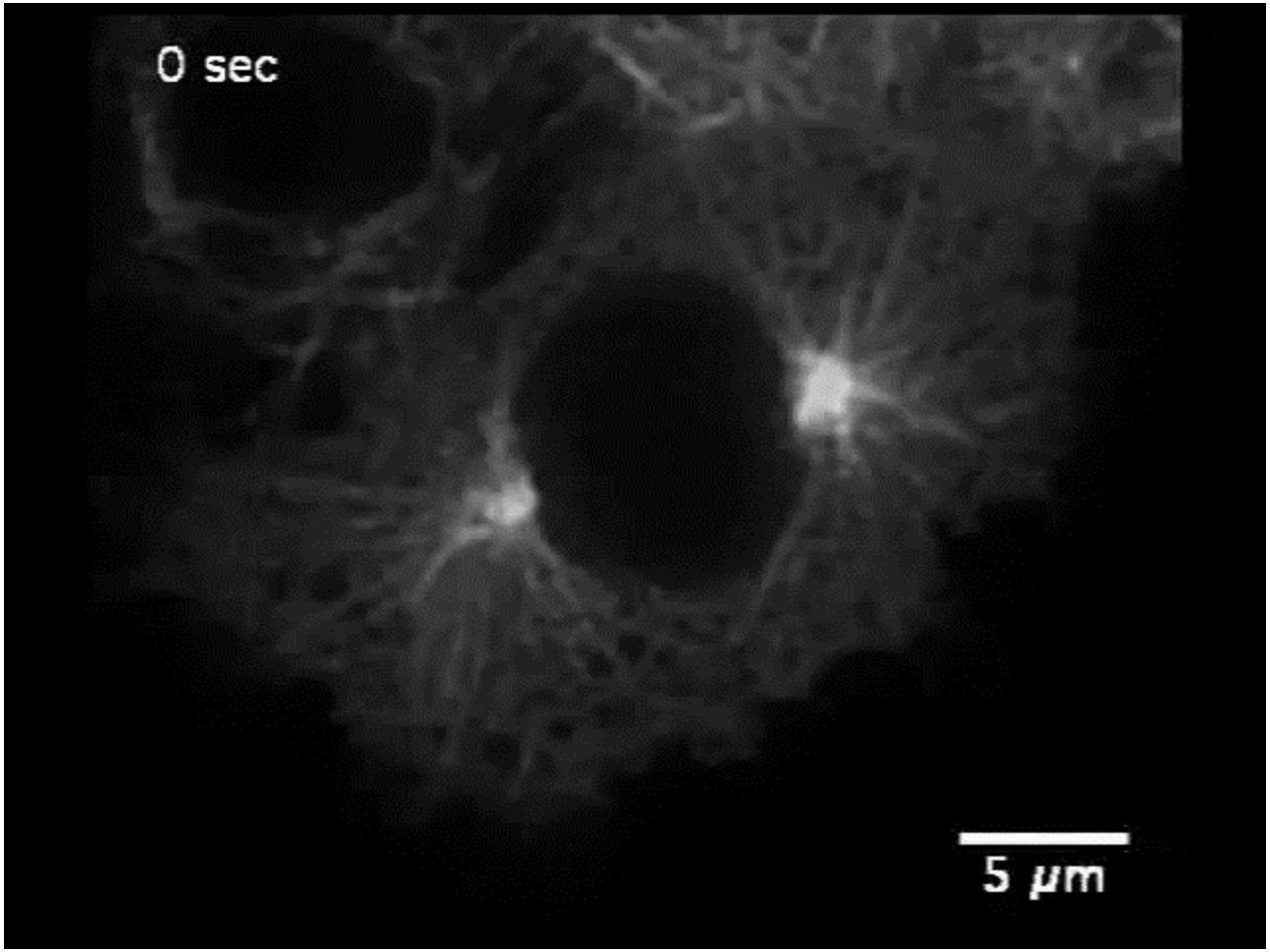


Figure 9.8

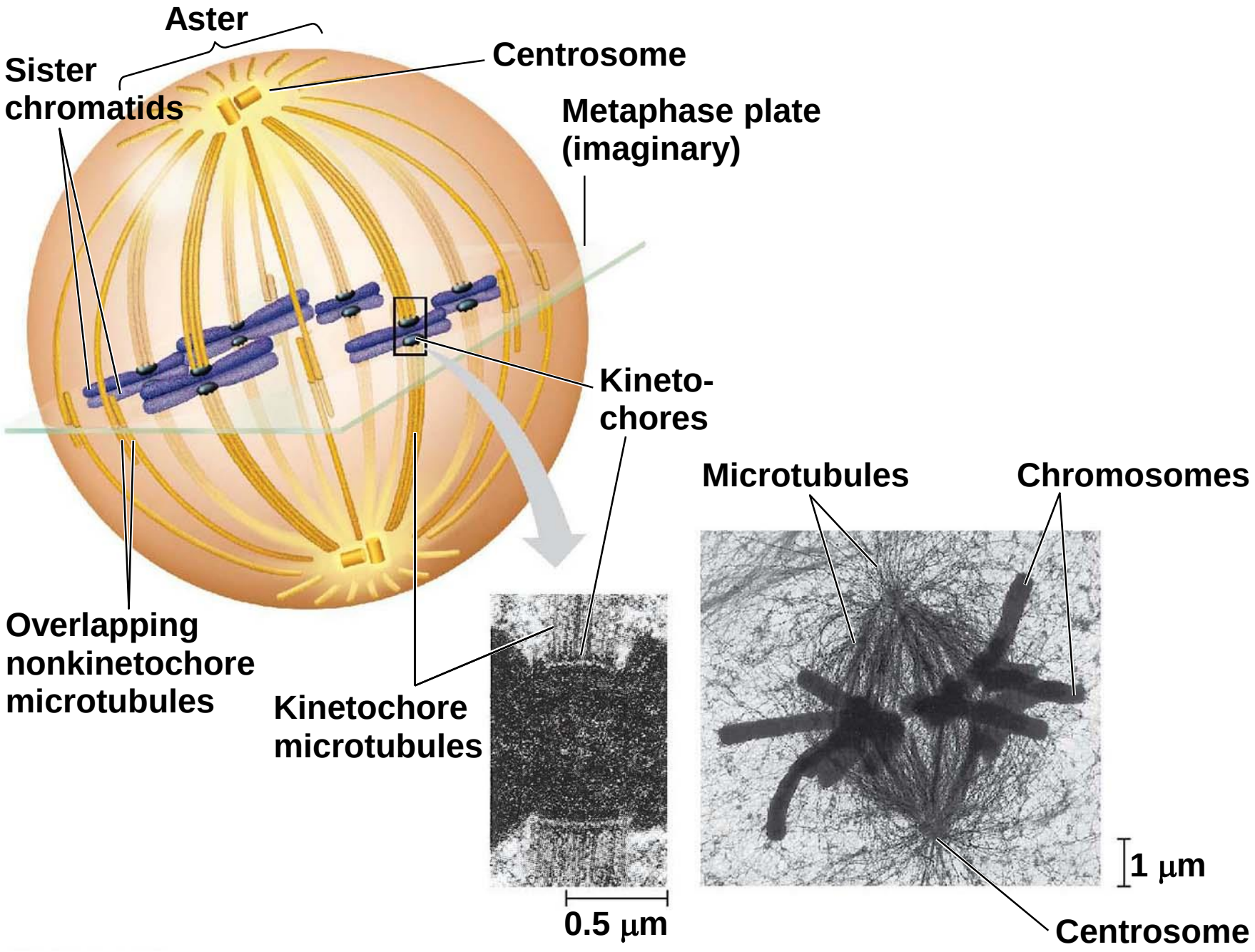


Figure 9.8-1

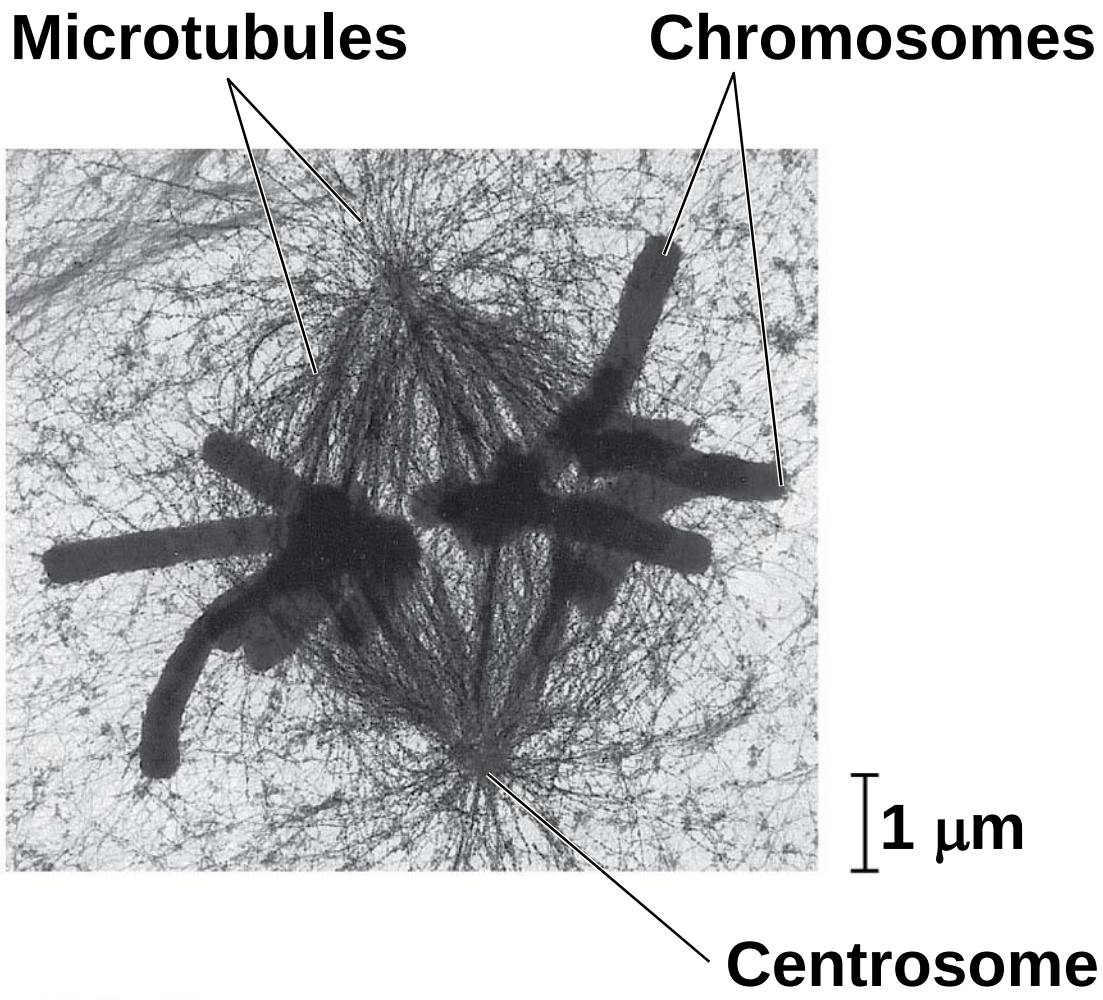
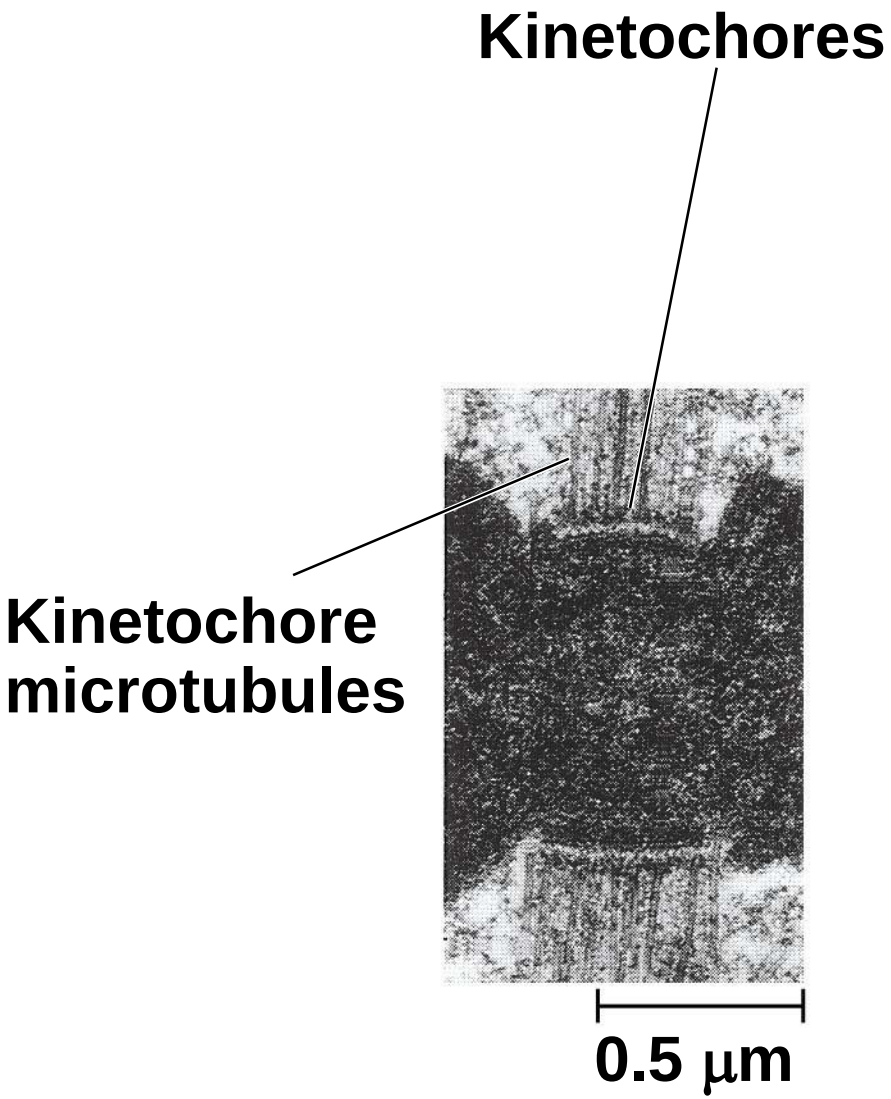


Figure 9.8-2



- 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
- Chromosomes are also “reeled in” by motor proteins at spindle poles, and microtubules depolymerize after they pass by the motor proteins

Figure 9.9

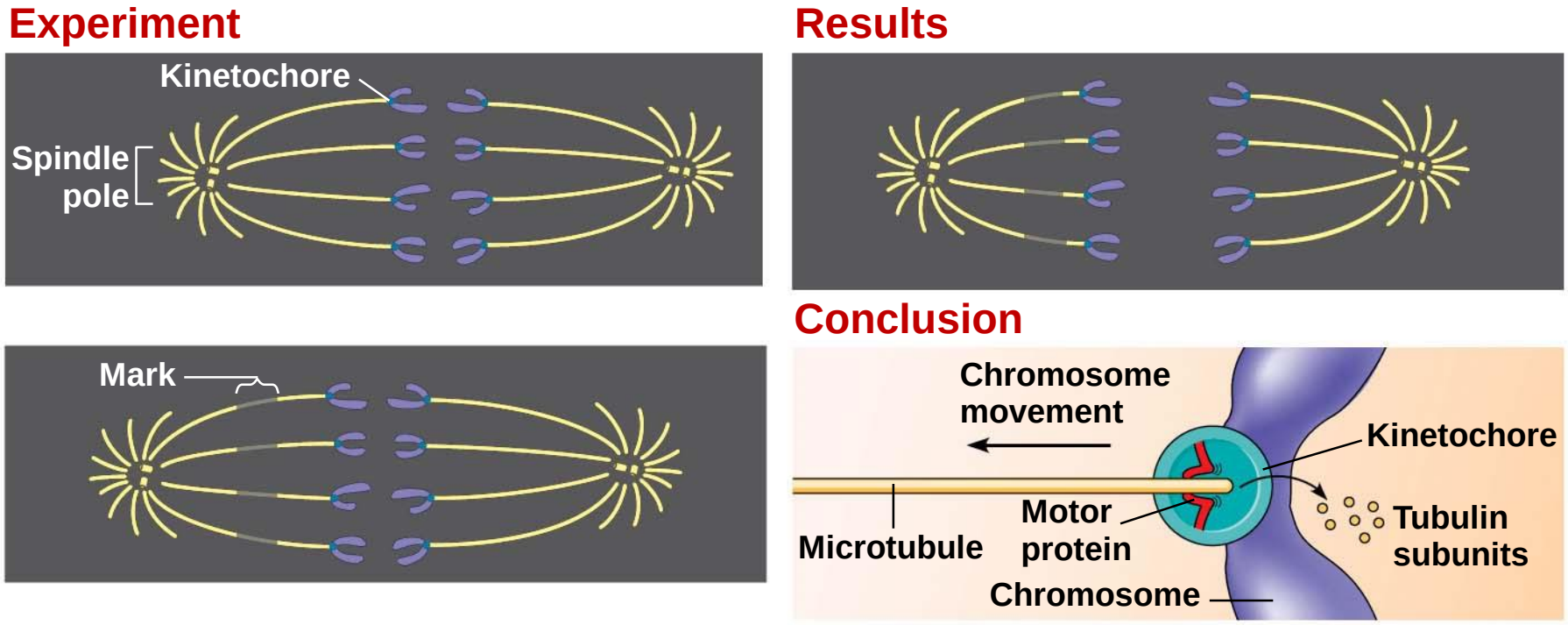


Figure 9.9-1

Experiment

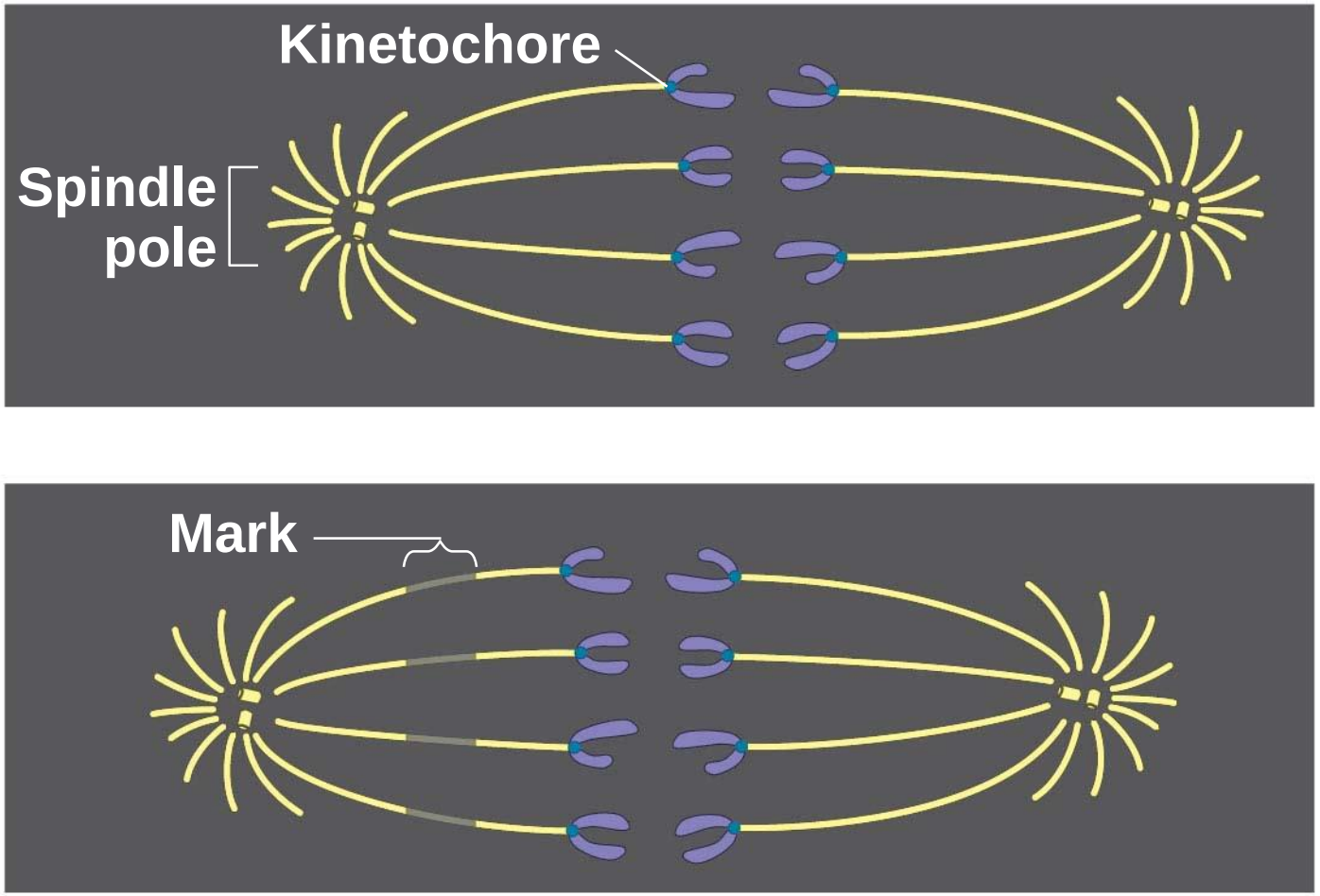
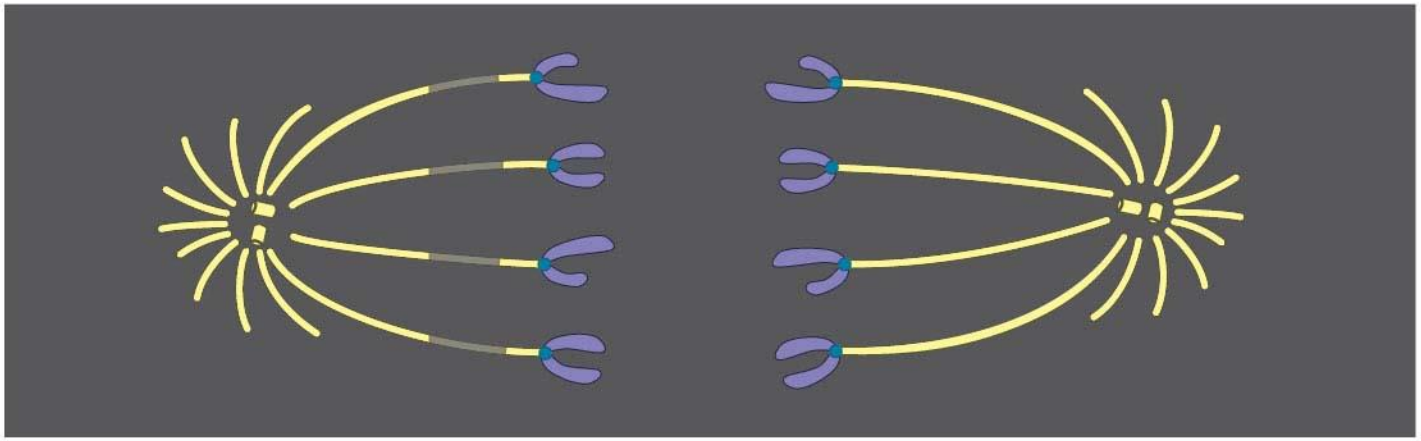
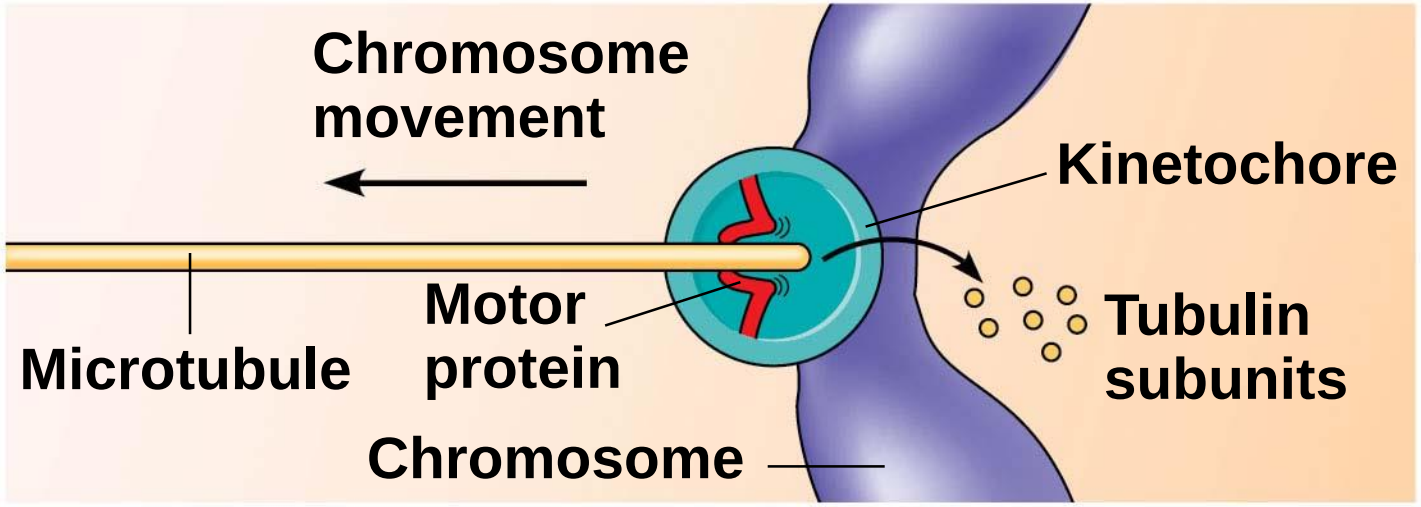


Figure 9.9-2

Results



Conclusion

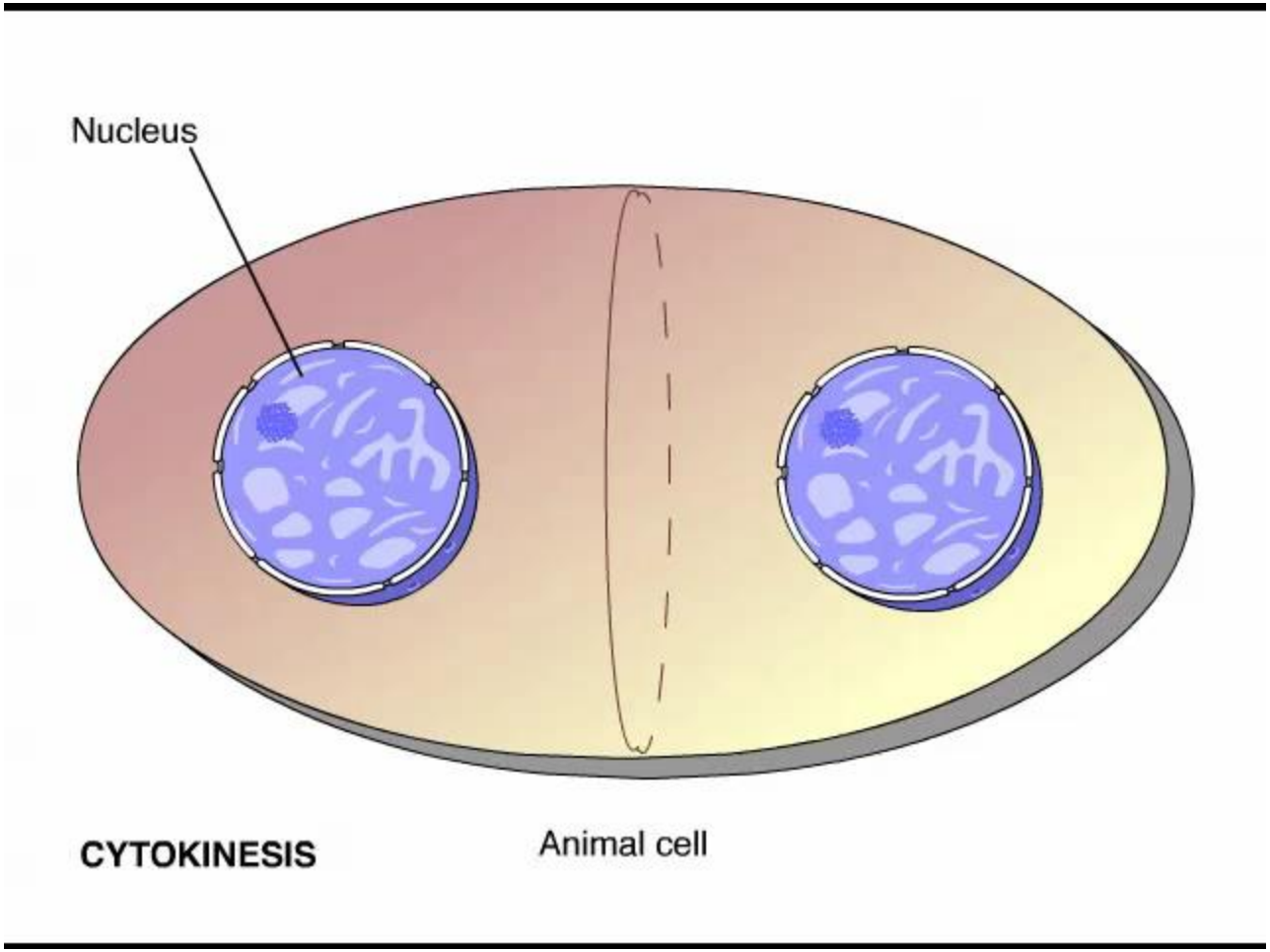


- Nonkinetochore microtubules from opposite poles overlap and push against each other, elongating the cell
- At the end of anaphase, duplicate groups of chromosomes have arrived at opposite ends of the elongated parent cell
- Cytokinesis begins during anaphase or telophase, and the spindle eventually disassembles

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

Animation: Cytokinesis



Video: Cytokinesis and Myosin

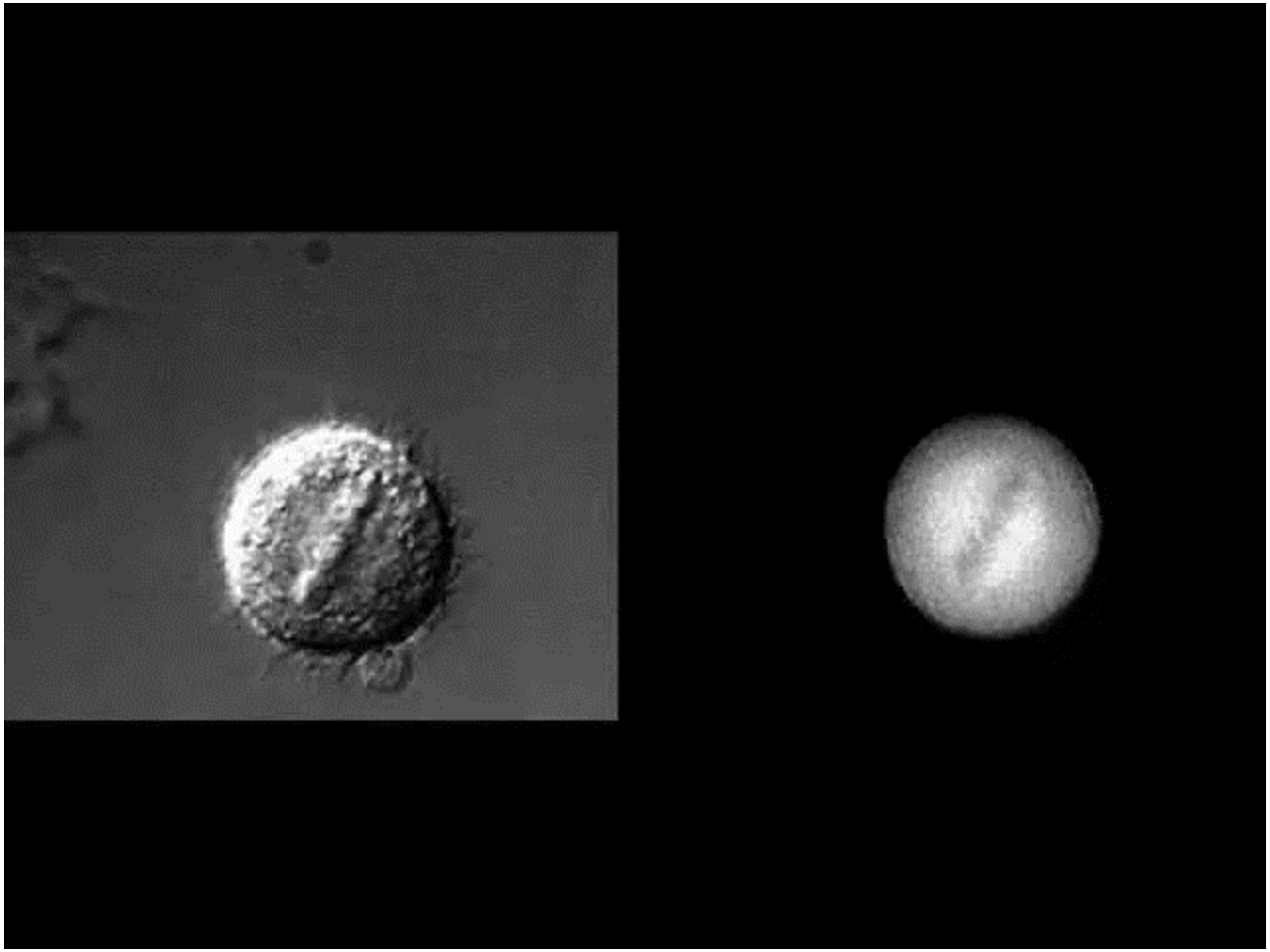


Figure 9.10

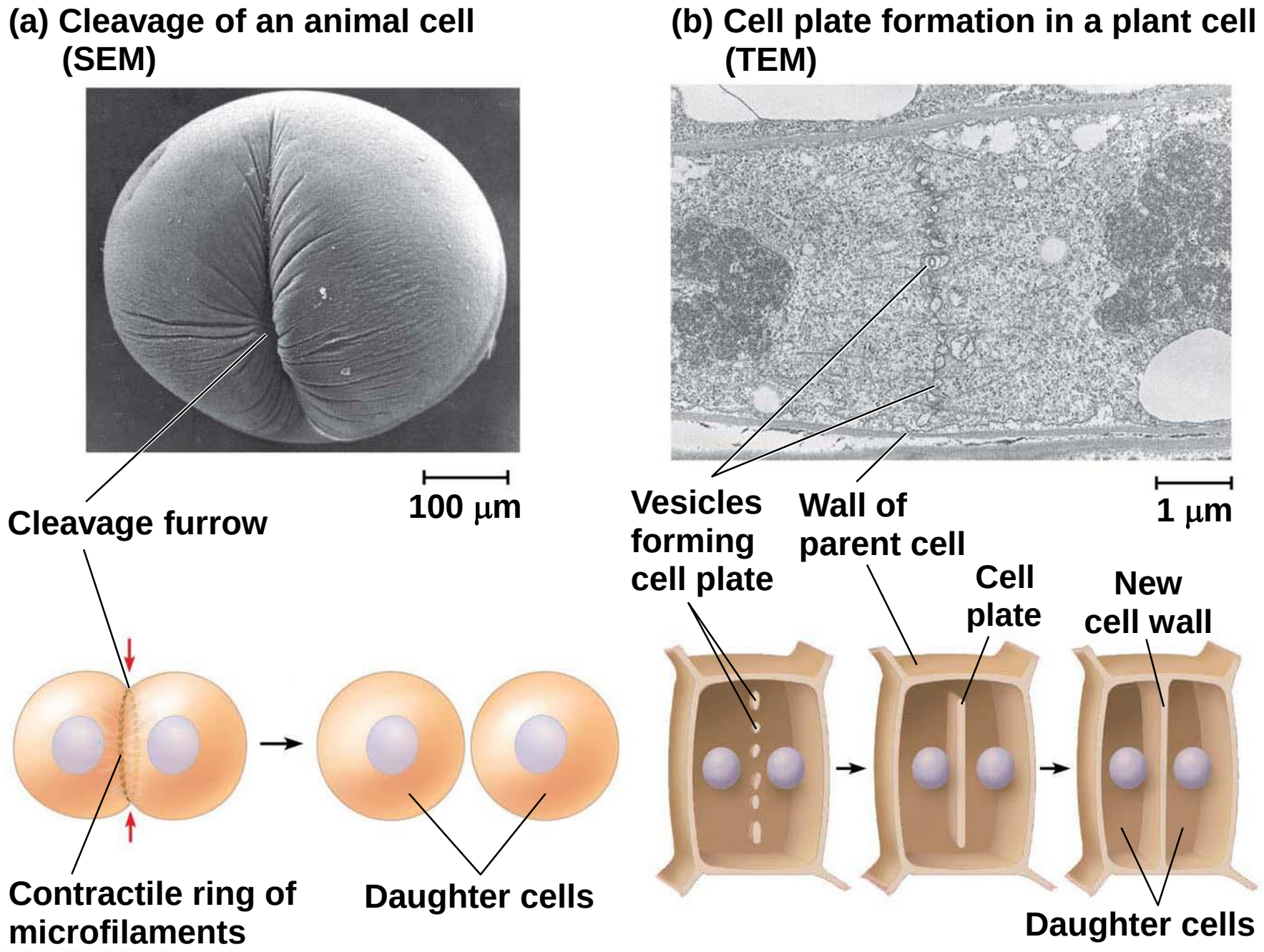


Figure 9.10-1

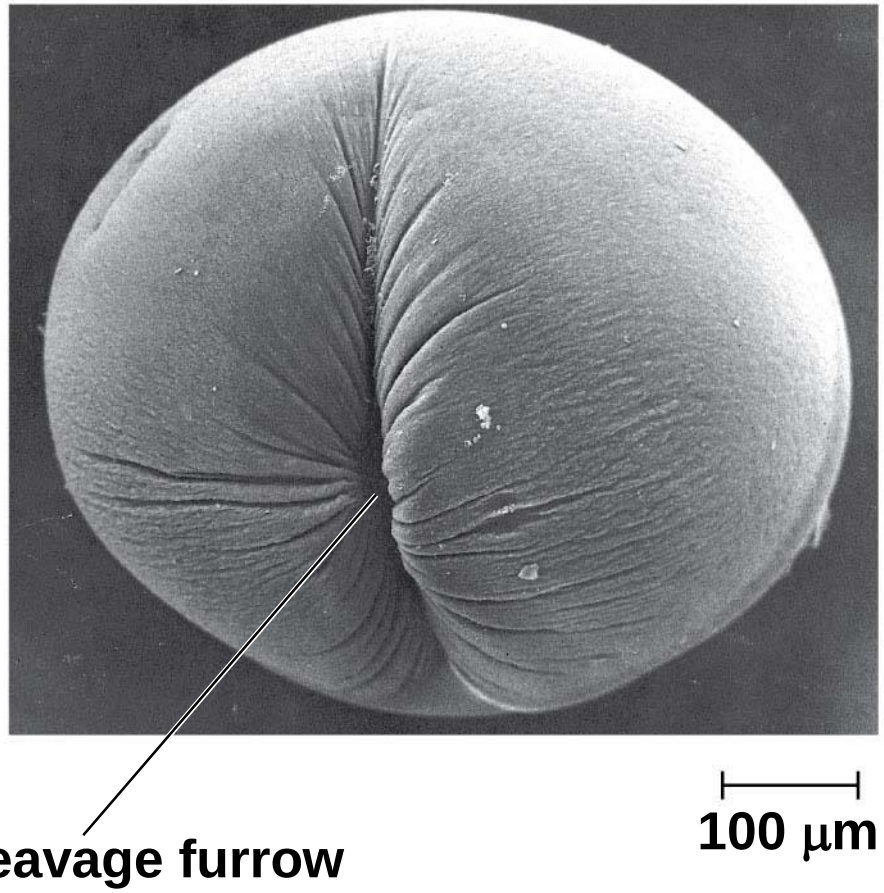


Figure 9.10-2

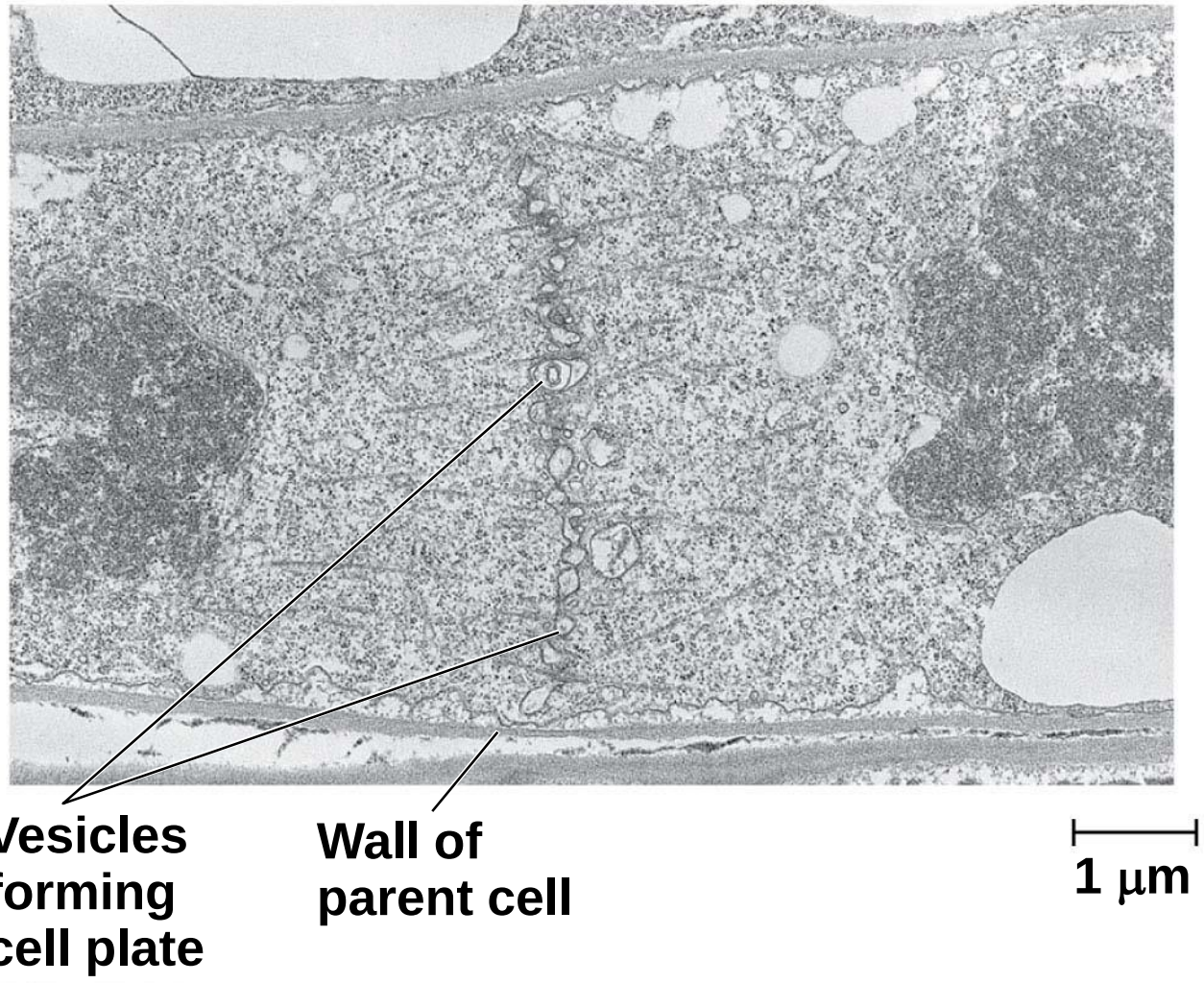


Figure 9.11

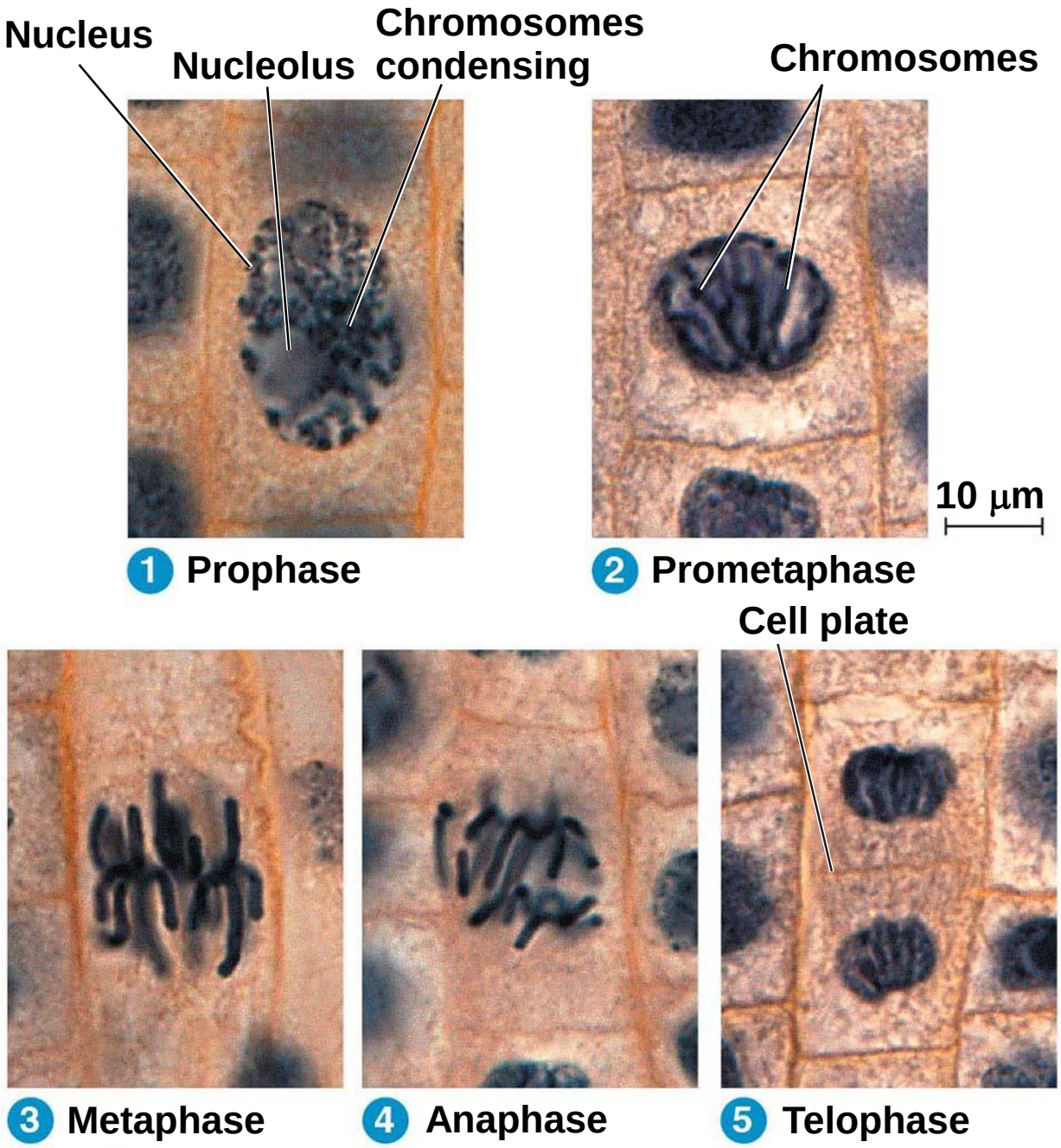


Figure 9.11-1

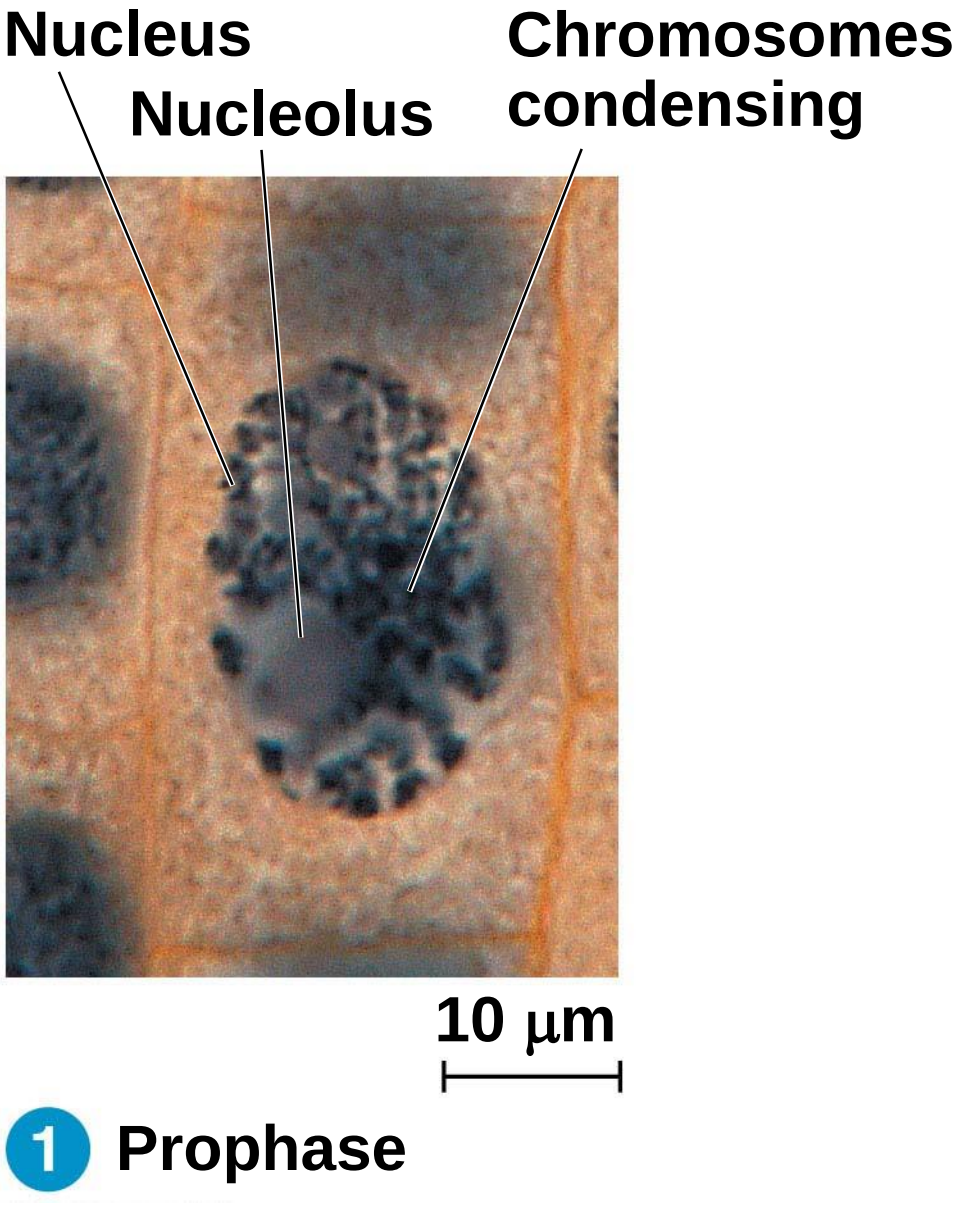


Figure 9.11-2

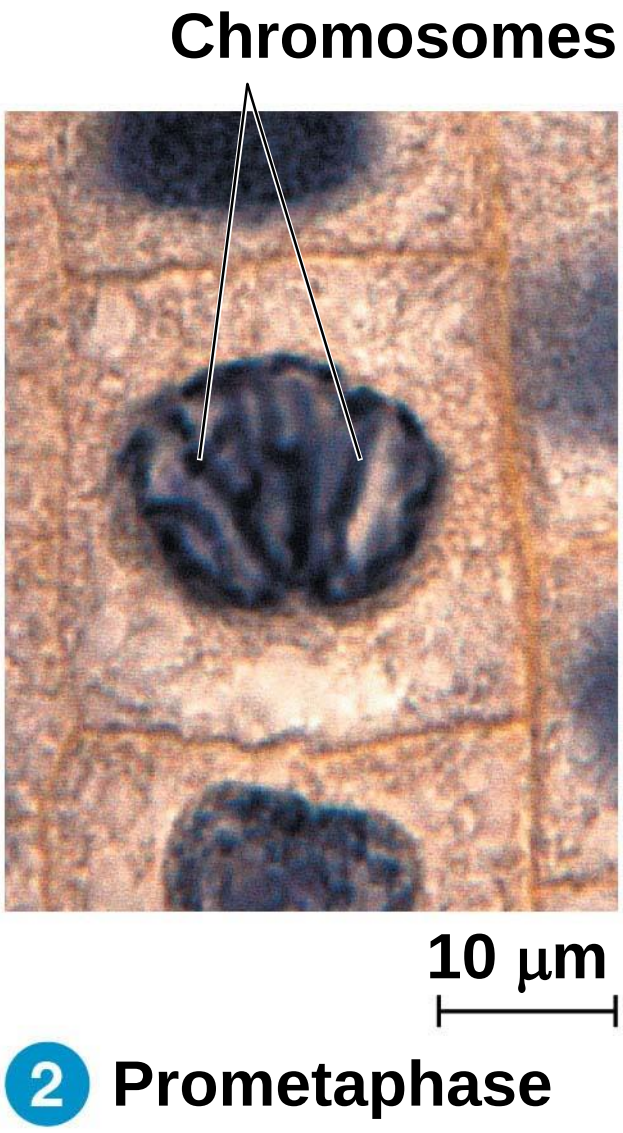
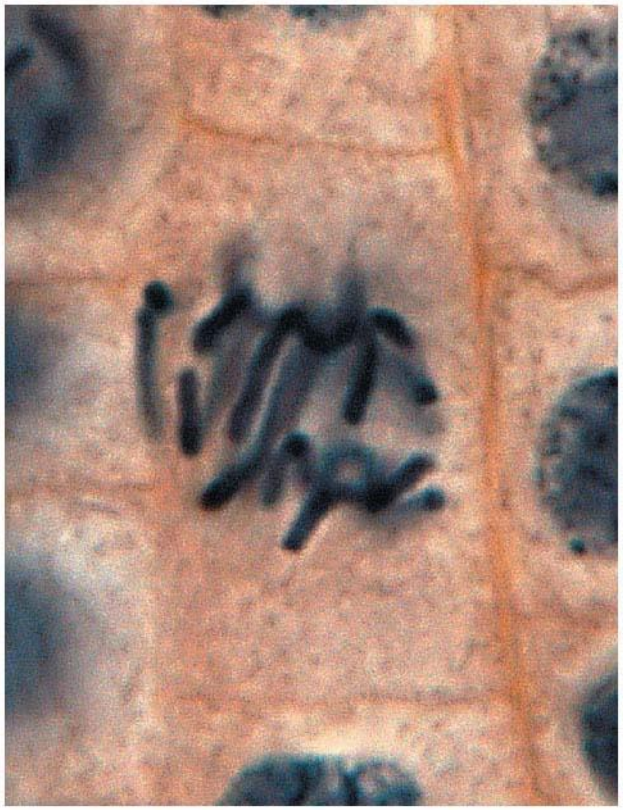


Figure 9.11-3

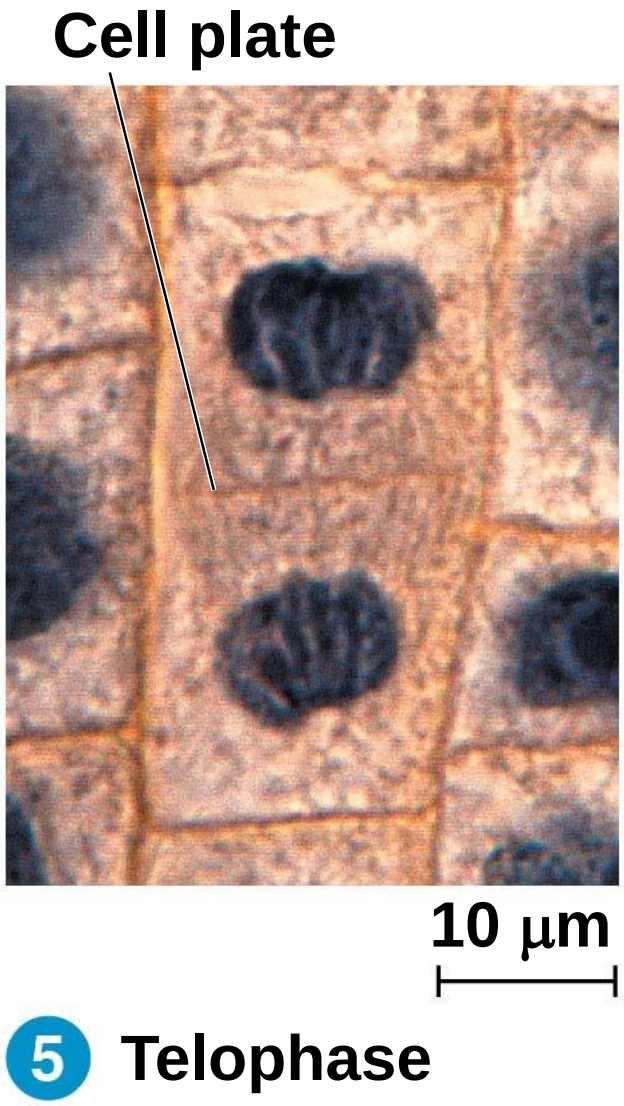
Figure 9.11-4



10 μm

4 Anaphase

Figure 9.11-5



Binary Fission in Bacteria

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

Figure 9.12-s1

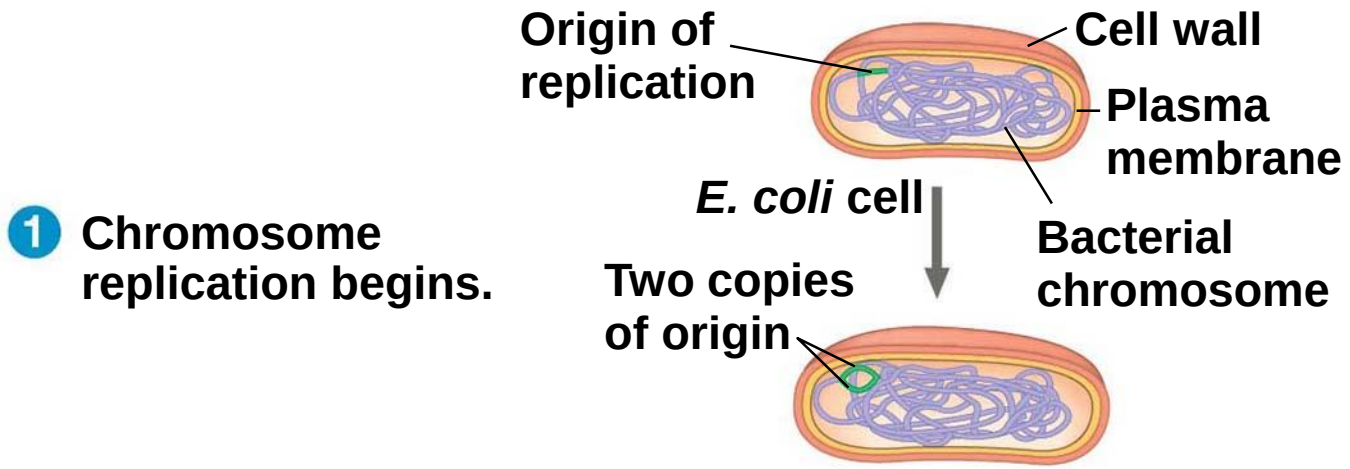


Figure 9.12-s2

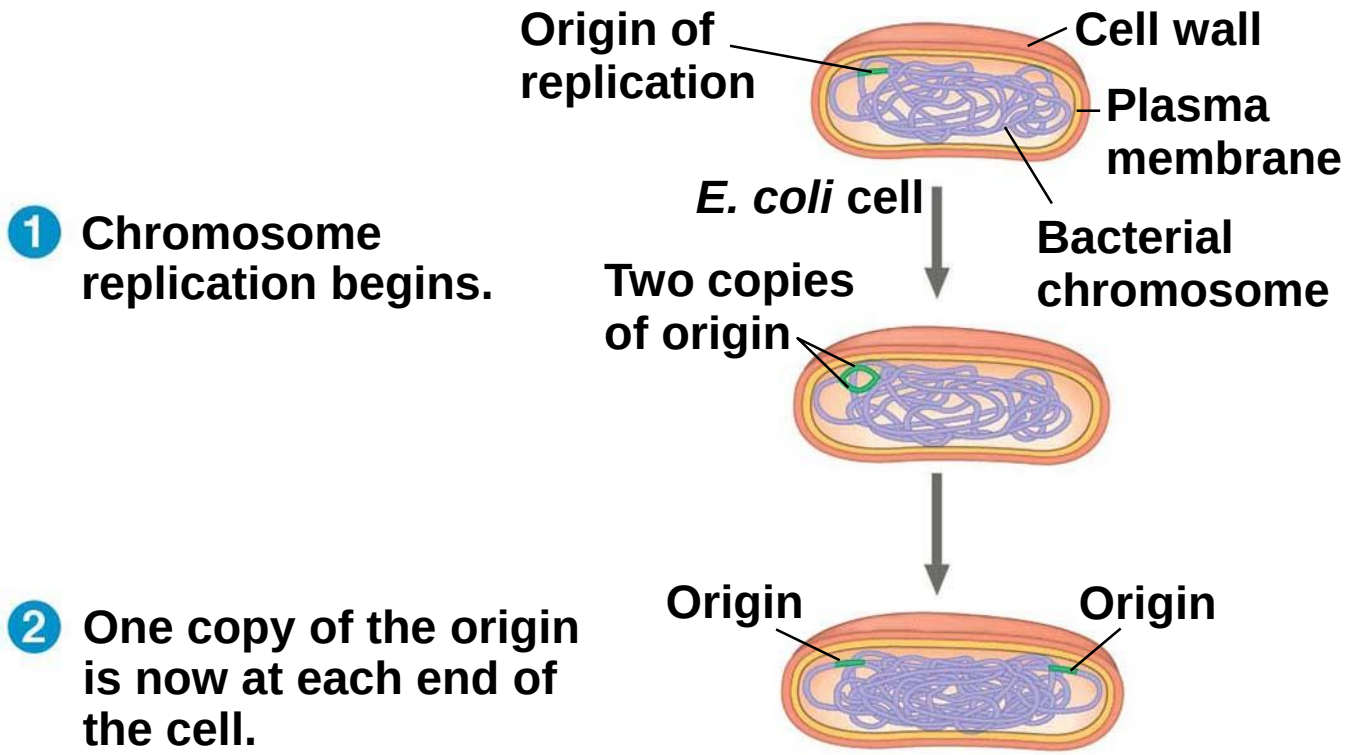
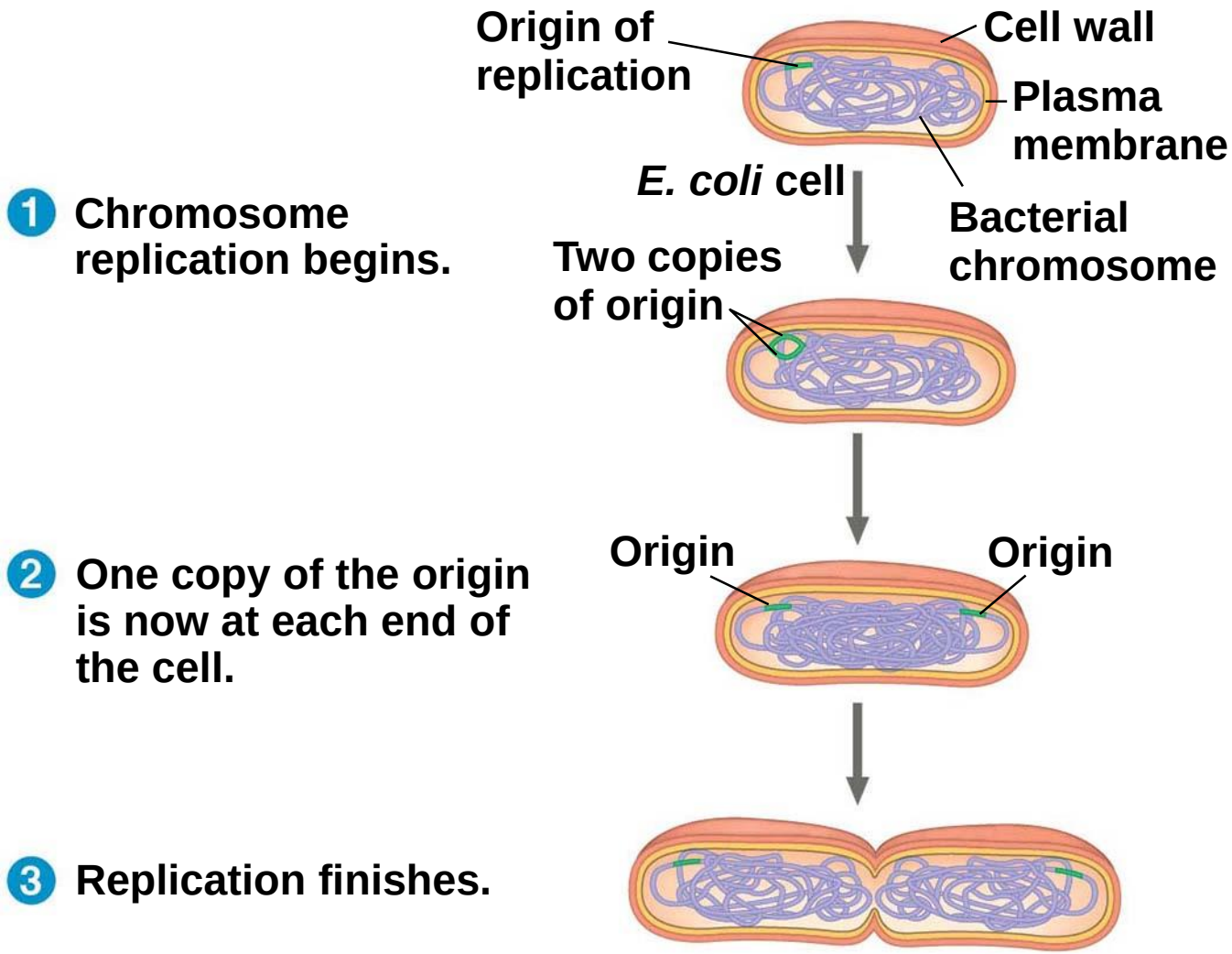


Figure 9.12-s3



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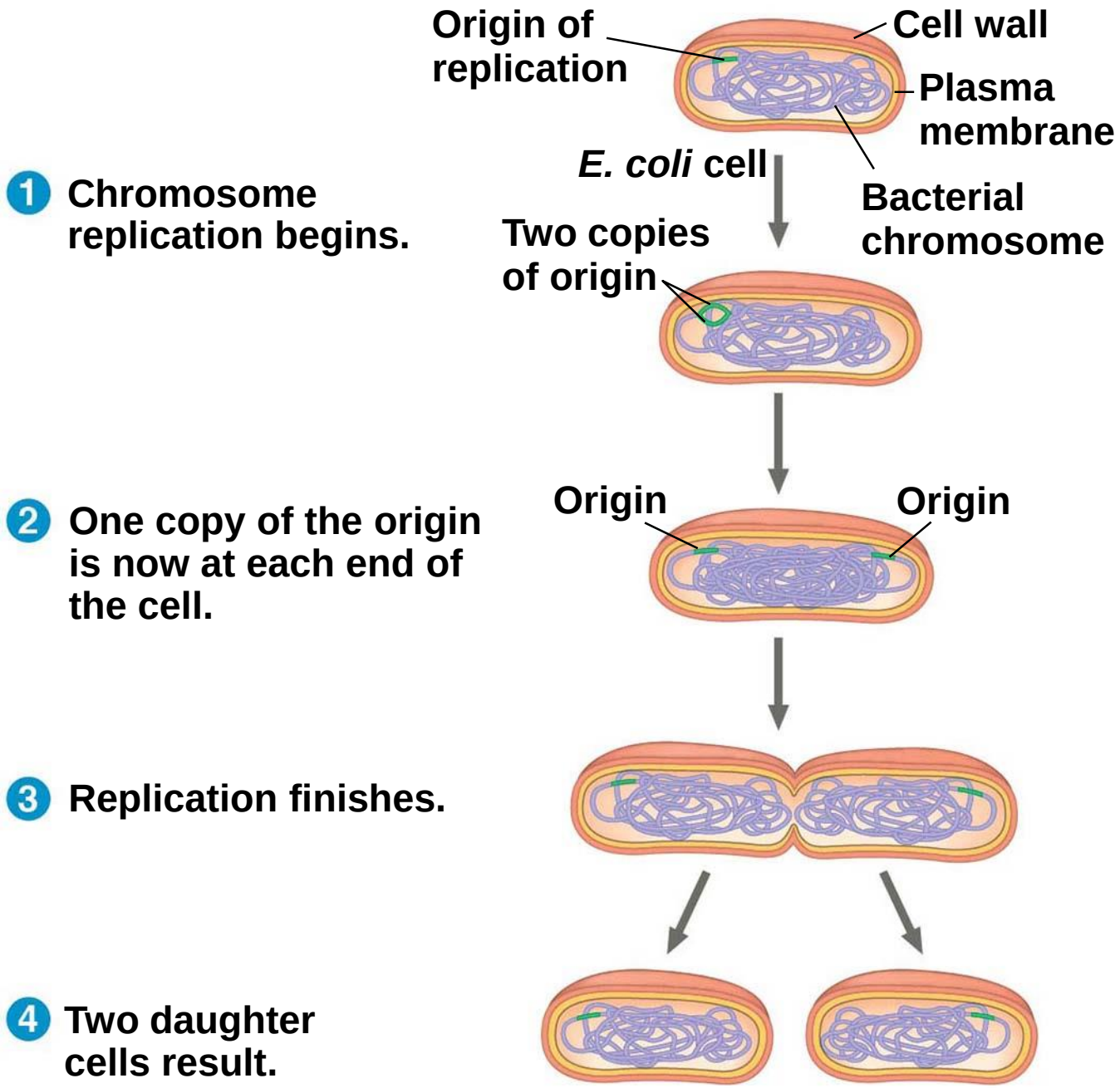
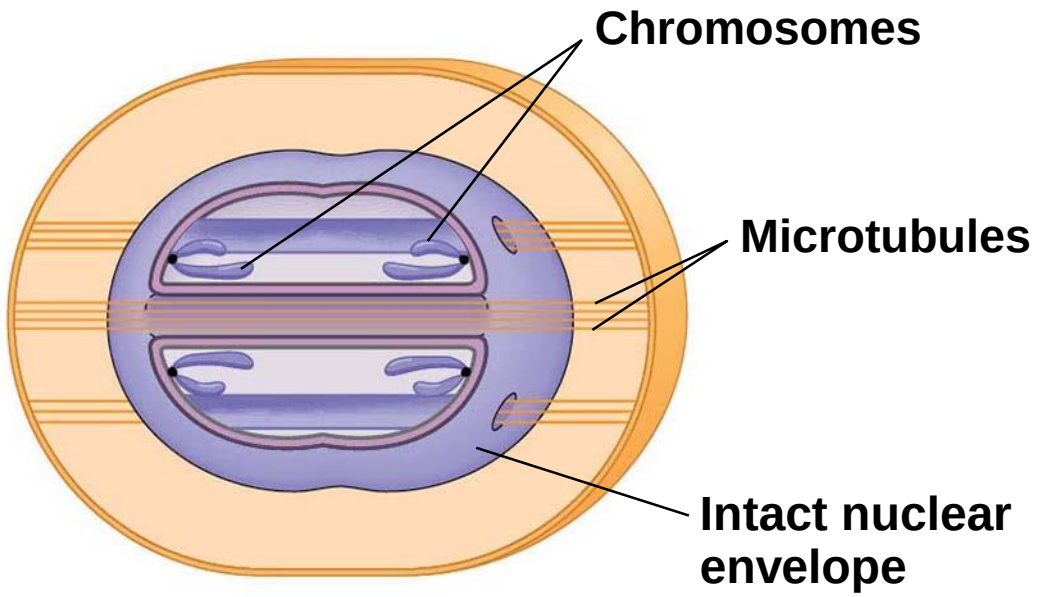


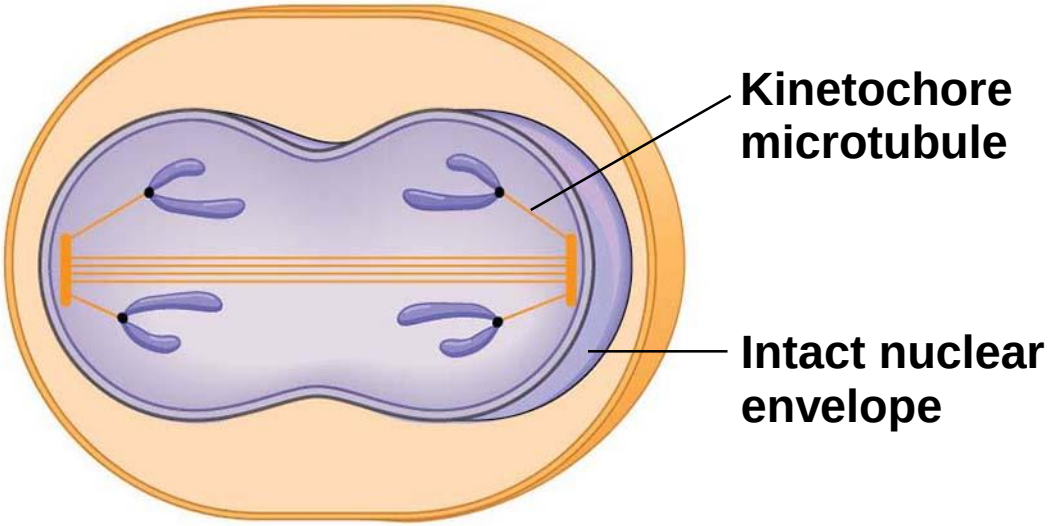
The Evolution of Mitosis

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

Figure 9.13



(a) Dinoflagellates



(b) Diatoms and some yeasts

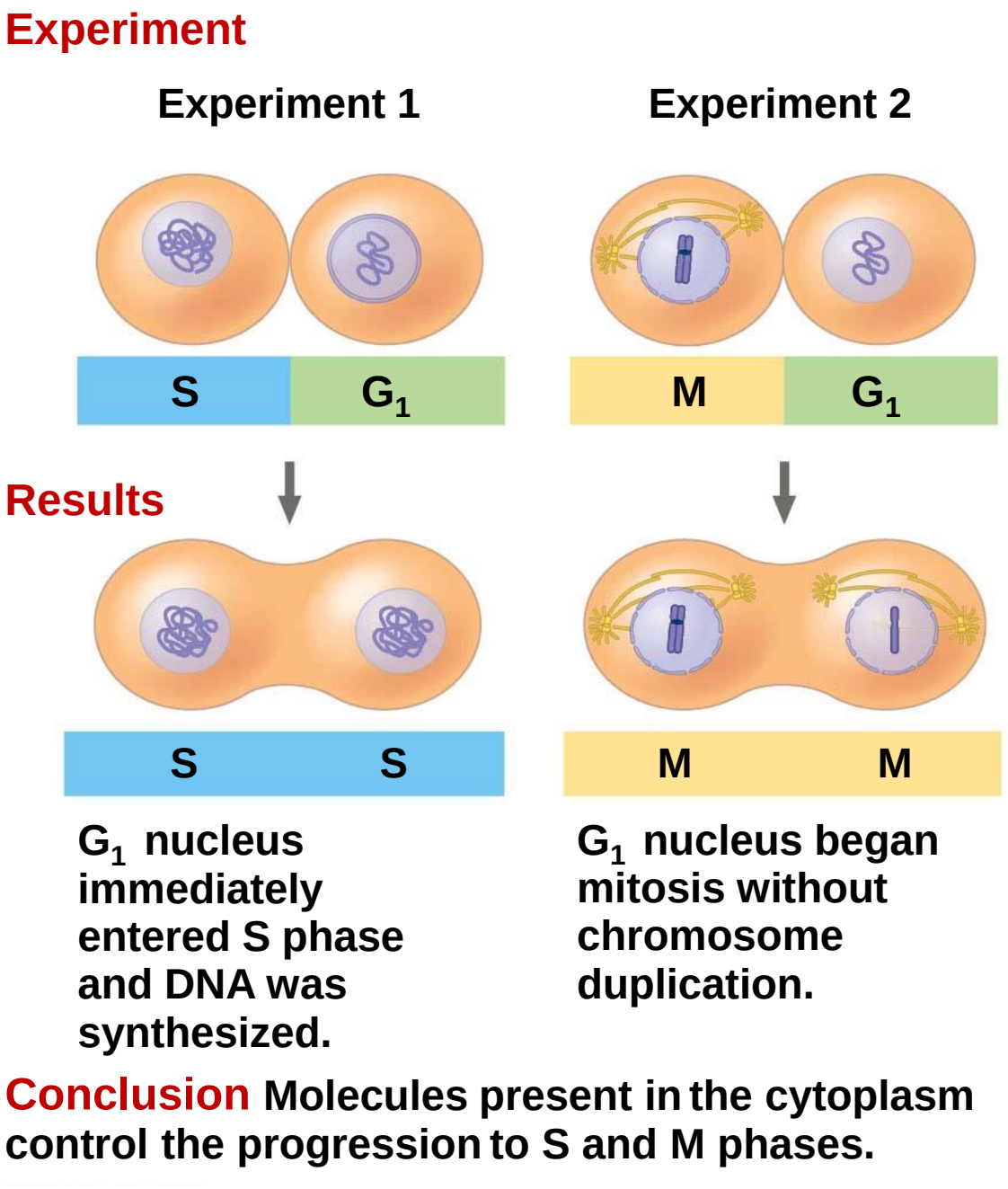
Concept 9.3: The eukaryotic cell cycle is regulated by a molecular control system

- 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 is driven by specific signaling molecules present in the cytoplasm
- Some evidence for this hypothesis comes from experiments with cultured mammalian cells
- Cells at different phases of the cell cycle were fused to form a single cell with two nuclei at different stages
- Cytoplasmic signals from one of the cells could cause the nucleus from the second cell to enter the "wrong" stage of the cell cycle

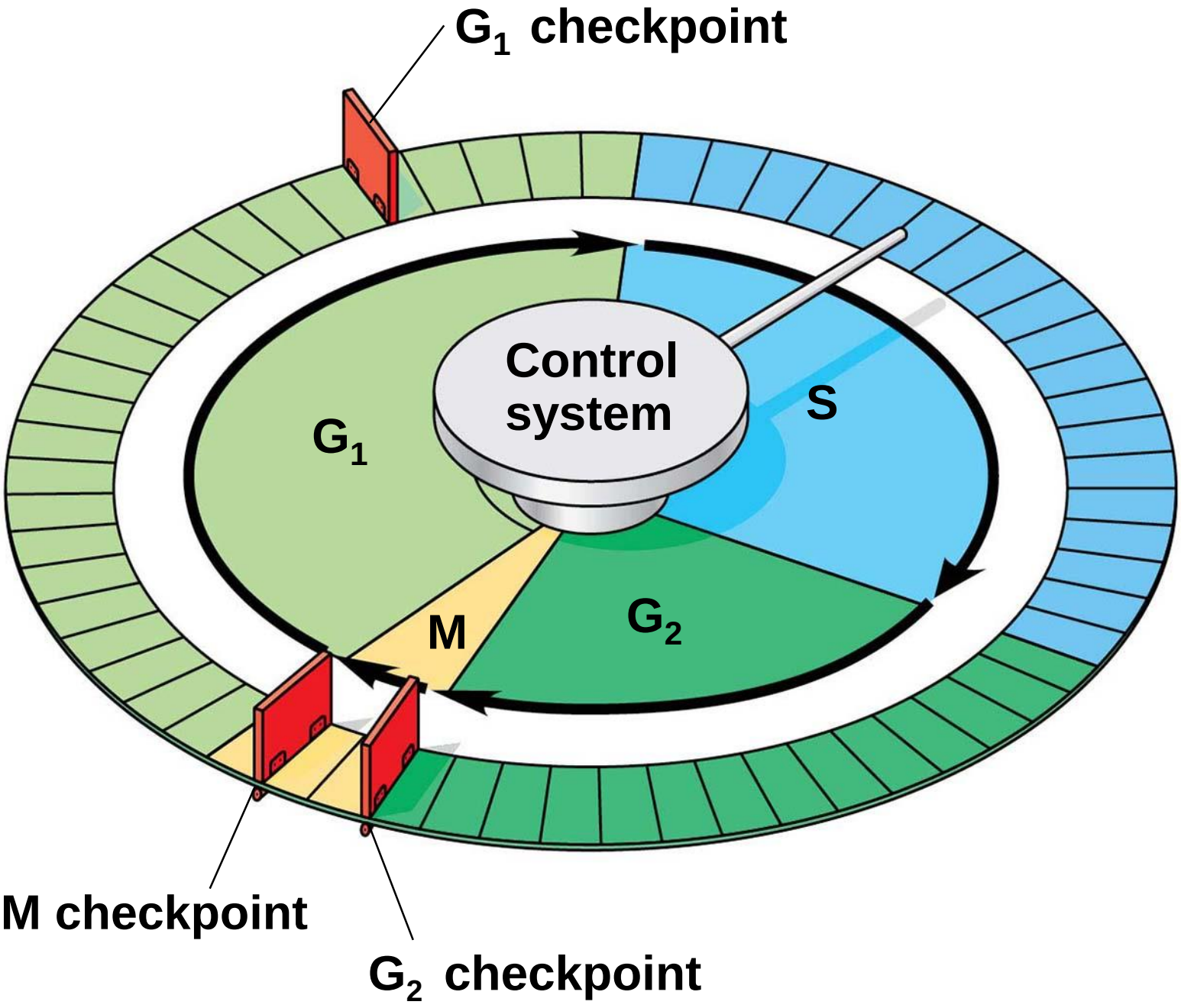
Figure 9.14



Checkpoints of 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 timing device of a washing machine
- 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 9.15



- For many cells, the G_1 checkpoint seems to be the most important
- 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 9.16

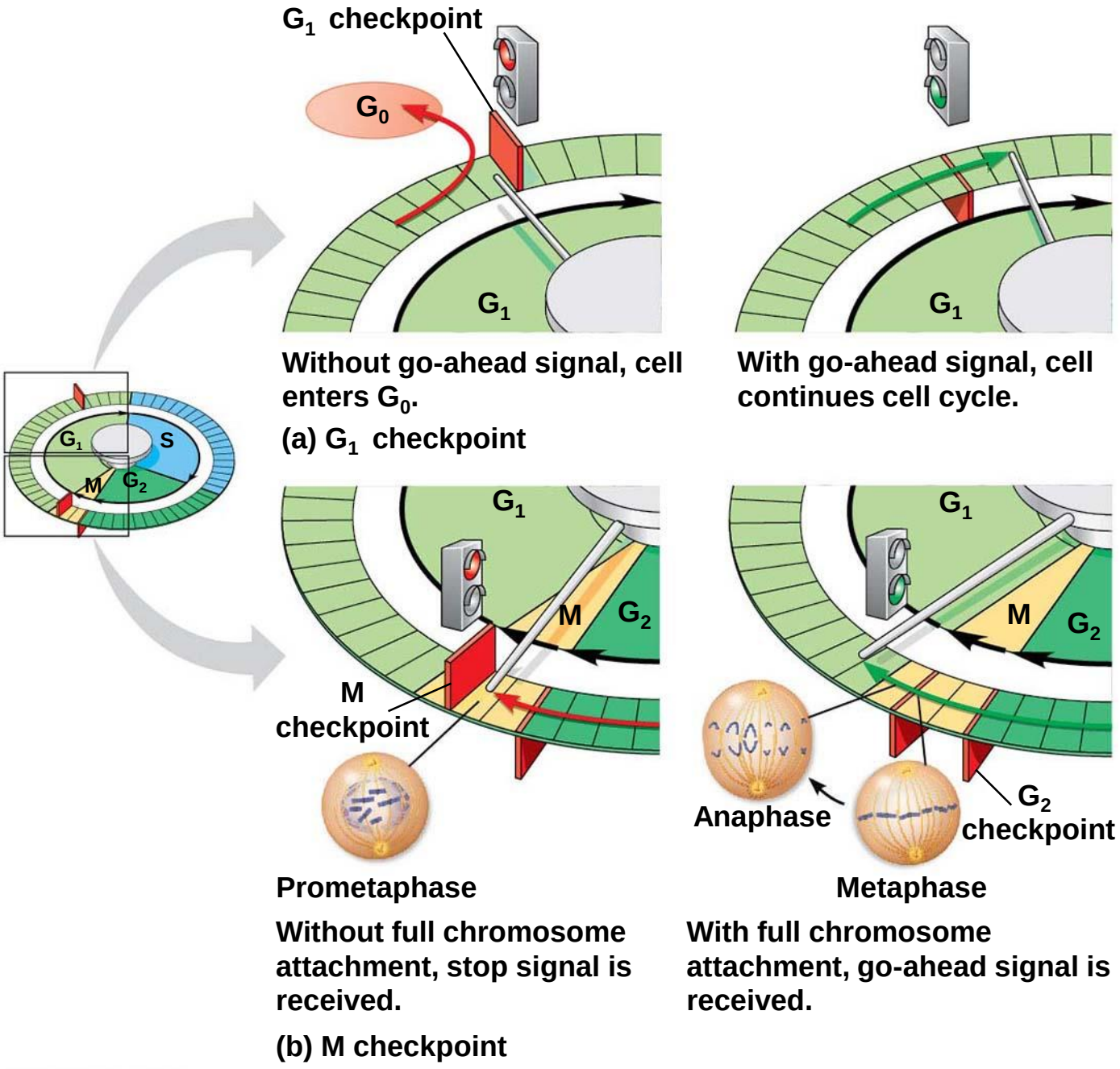
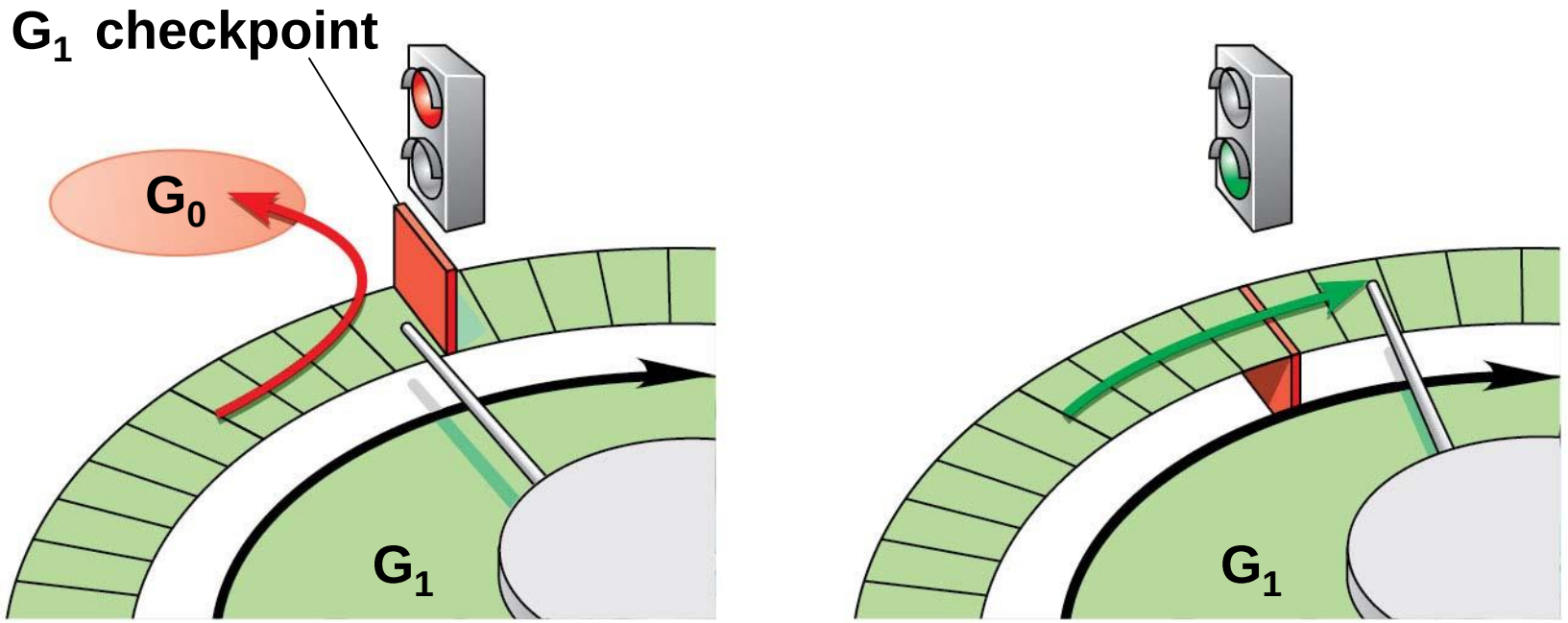


Figure 9.16-1

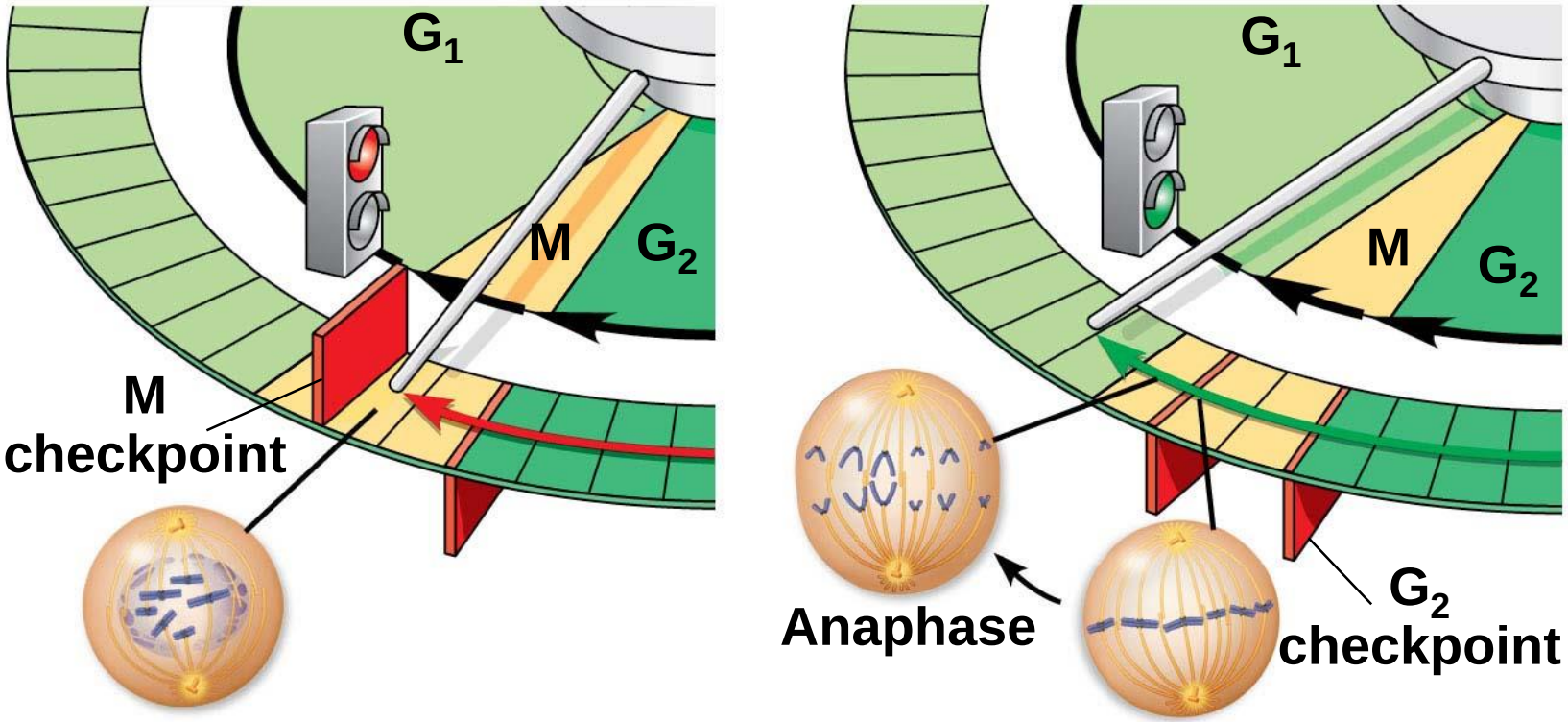


Without go-ahead signal, cell enters G_0.

With go-ahead signal, cell continues cell cycle.

(a) G_1 checkpoint

Figure 9.16-2



Prometaphase

Without full chromosome attachment, stop signal is received.

Metaphase

With full chromosome attachment, go-ahead signal is received.

(b) M checkpoint

- The cell cycle is regulated by a set of regulatory proteins and protein complexes including kinases and proteins called cyclins

- An example of an internal signal occurs at the M phase checkpoint
- In this case, anaphase does not begin if any kinetochores remain unattached to spindle microtubules
- Attachment of all of the kinetochores activates a regulatory complex, which then activates the enzyme separase
- Separase allows sister chromatids to separate, triggering the onset of 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 9.17-s1

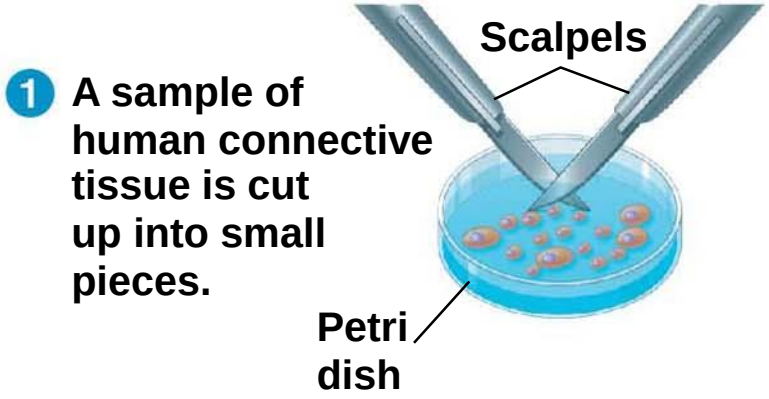


Figure 9.17-s2

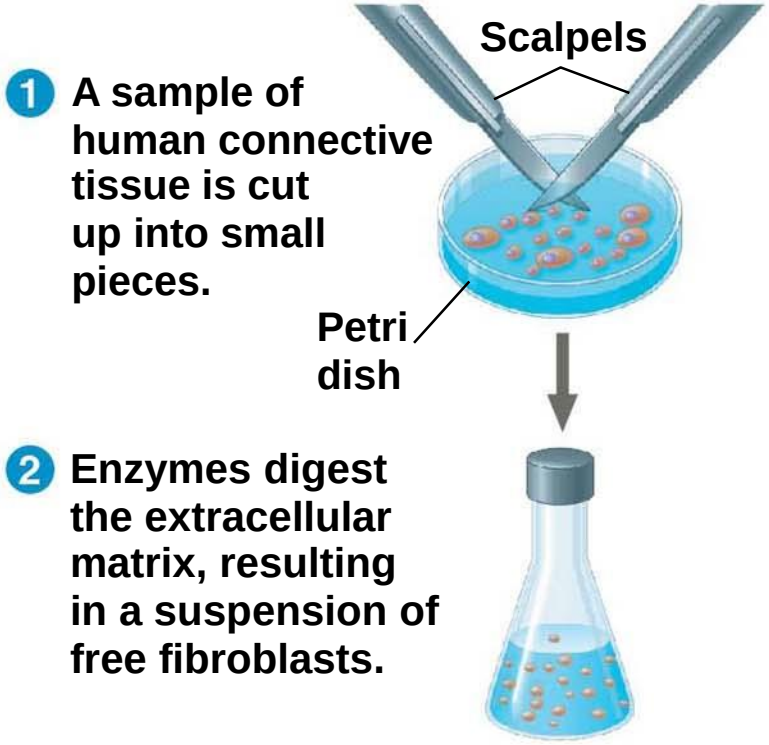


Figure 9.17-s3

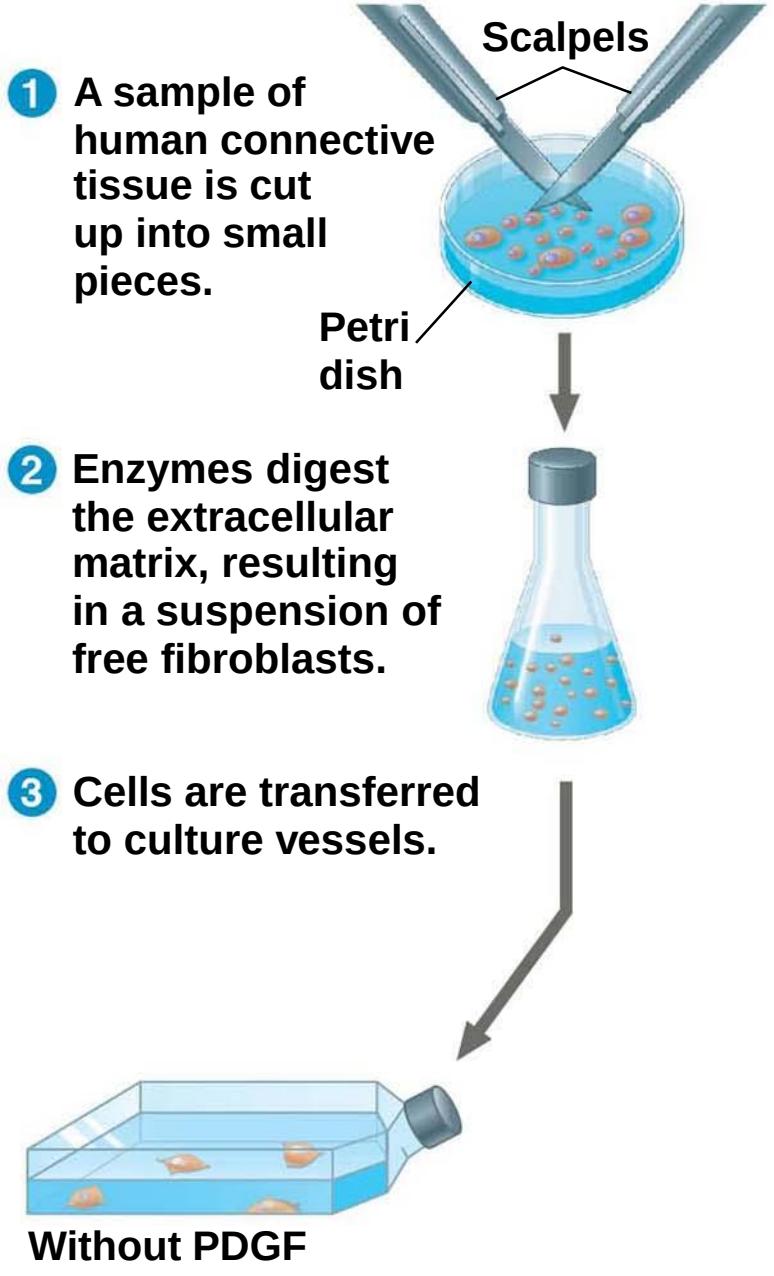


Figure 9.17-s4

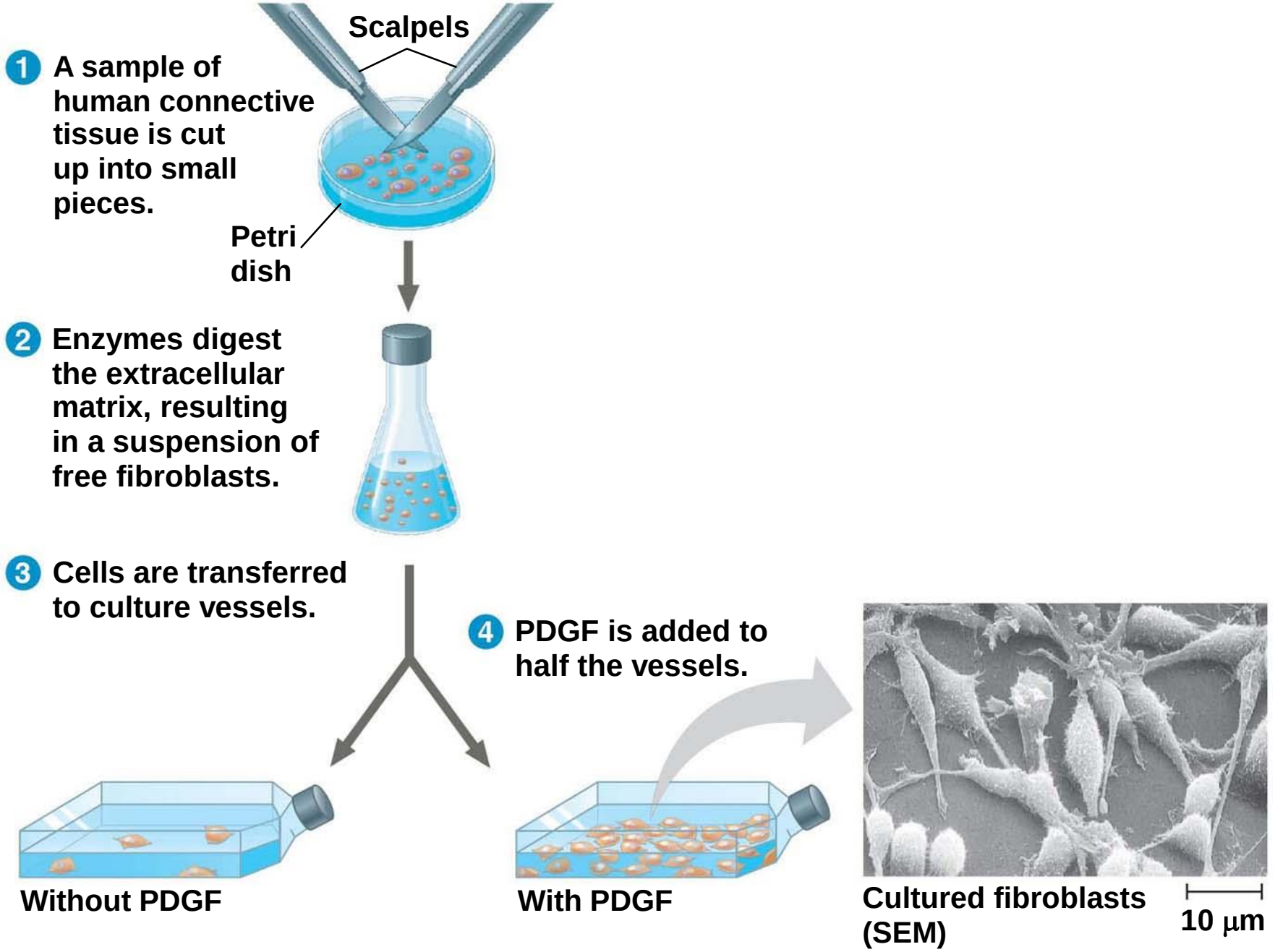
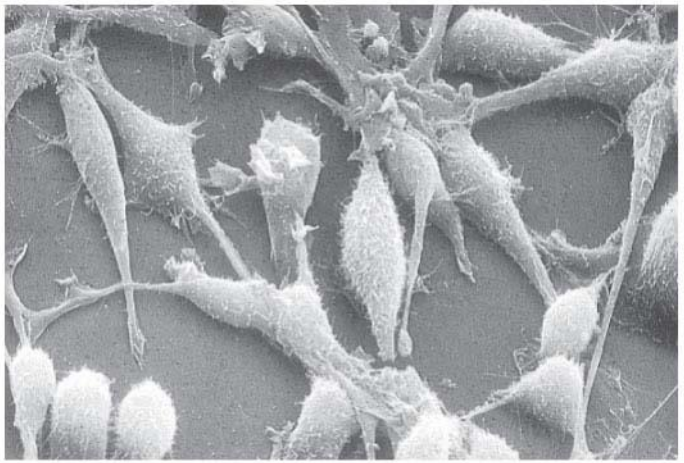


Figure 9.17-1



Cultured fibroblasts (SEM)

10 μm

- Another 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 9.18

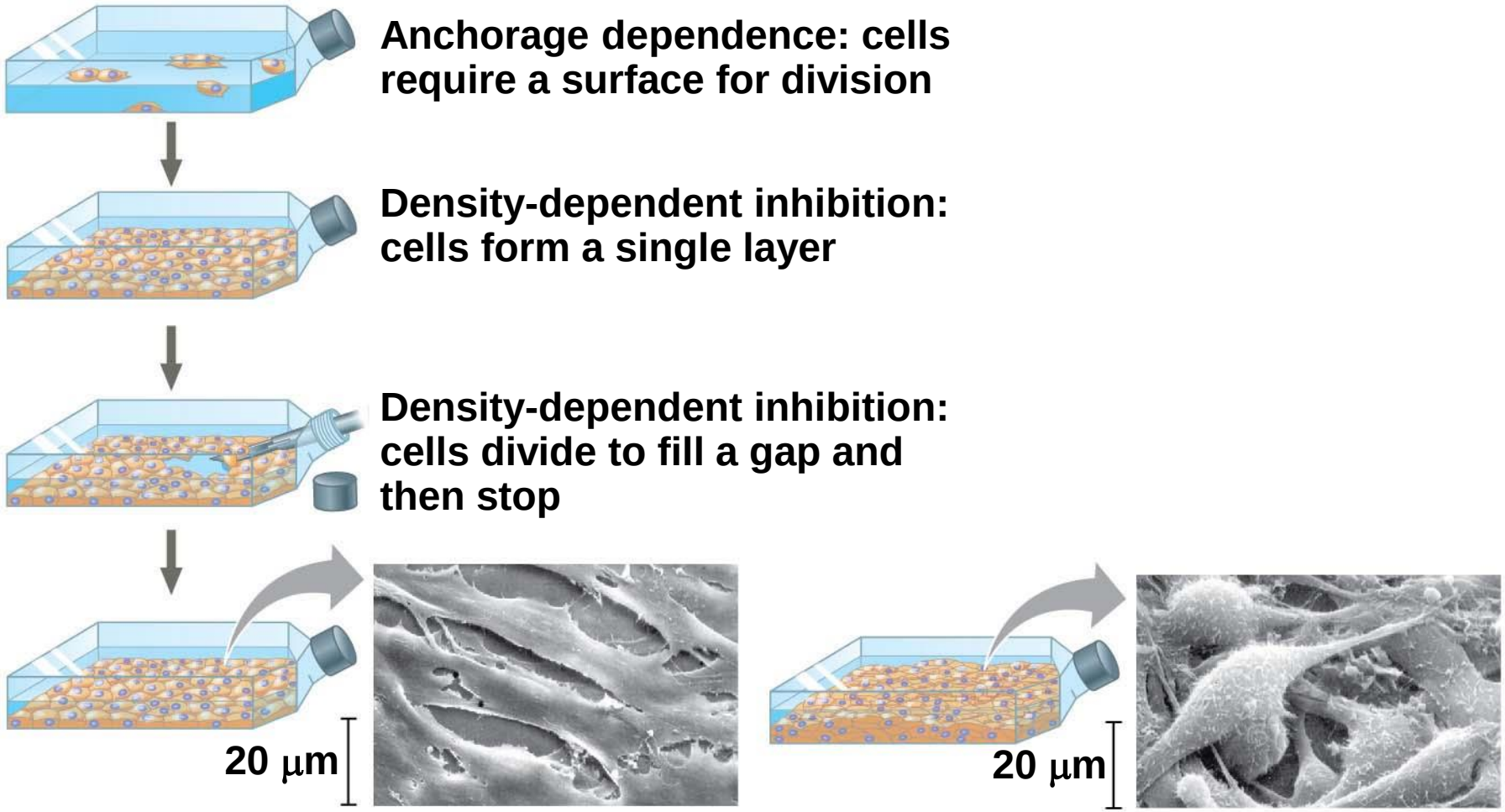
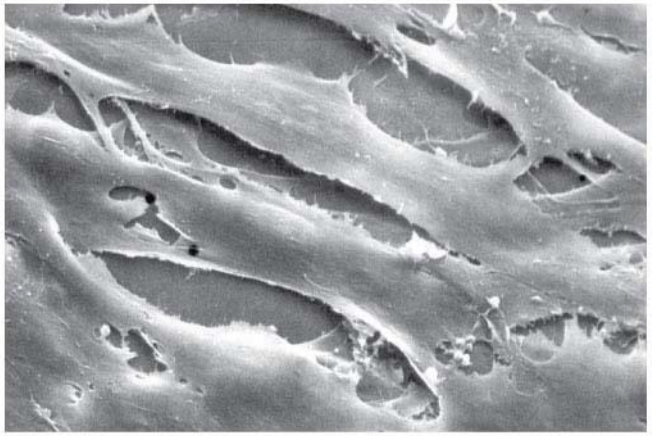
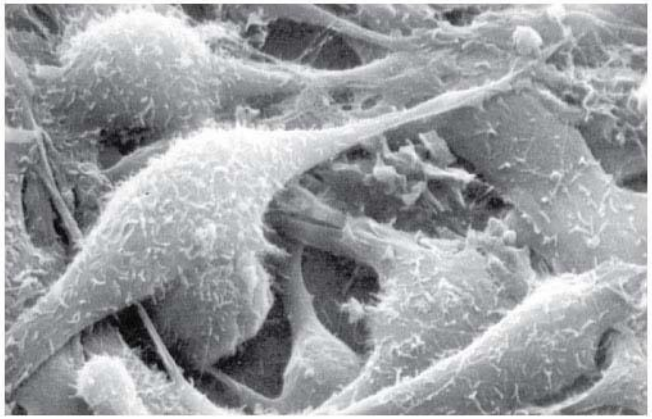


Figure 9.18-1



(a) Normal mammalian cells

Figure 9.18-2



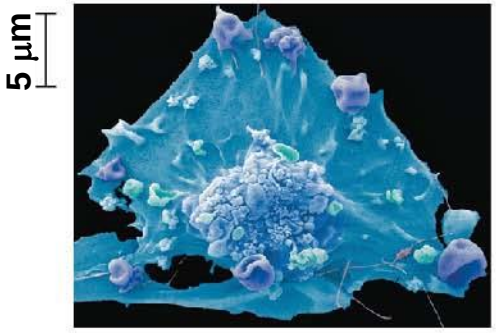
(b) Cancer cells

Loss of Cell Cycle Controls in Cancer Cells

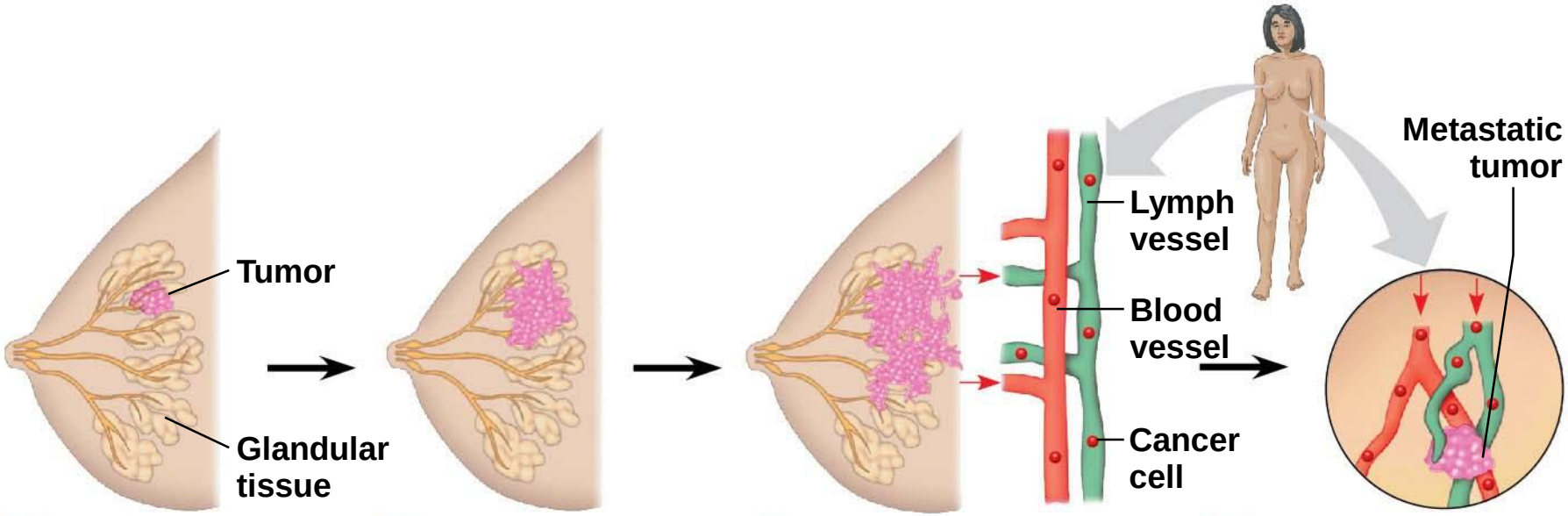
- Cancer cells do not respond to signals that normally regulate the cell cycle
- Cancer cells do not need growth factors to grow and divide
  - They may make their own growth factor
  - They may convey a growth factor's signal without the presence of the growth factor
  - They may have an abnormal cell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

- 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 undergo **metastasis**, exporting cancer cells to other parts of the body, where they may form additional tumors

Figure 9.19



Breast cancer cell
(colorized SEM)



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. A small percentage of cancer cells may metastasize to another part of the body.

Figure 9.19-1

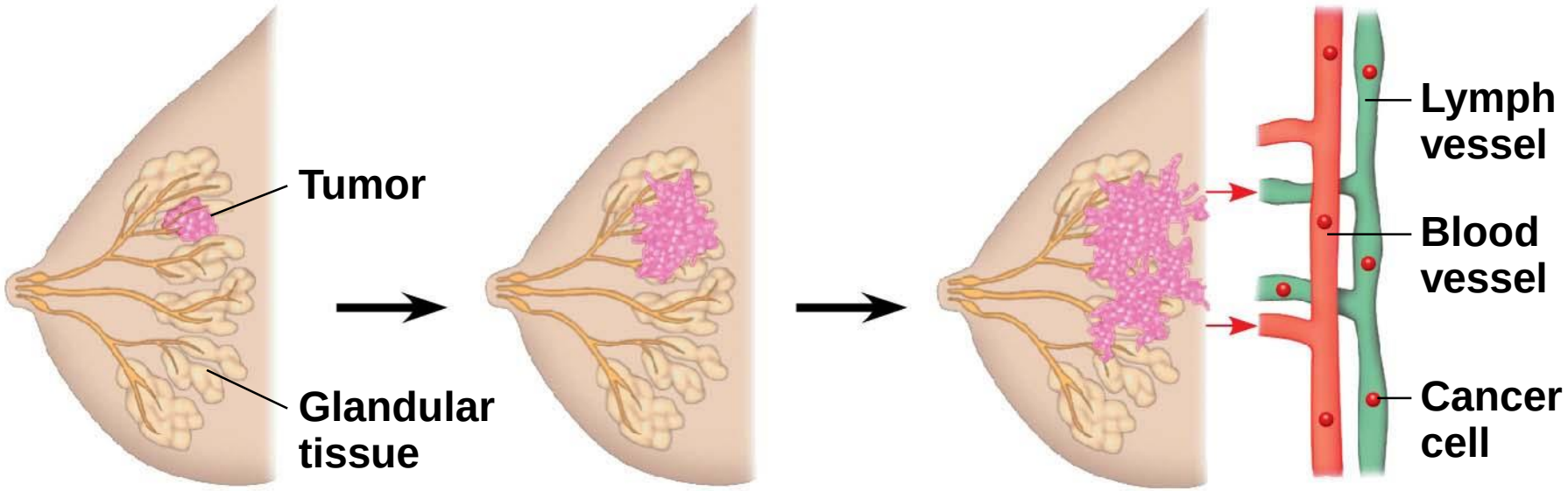
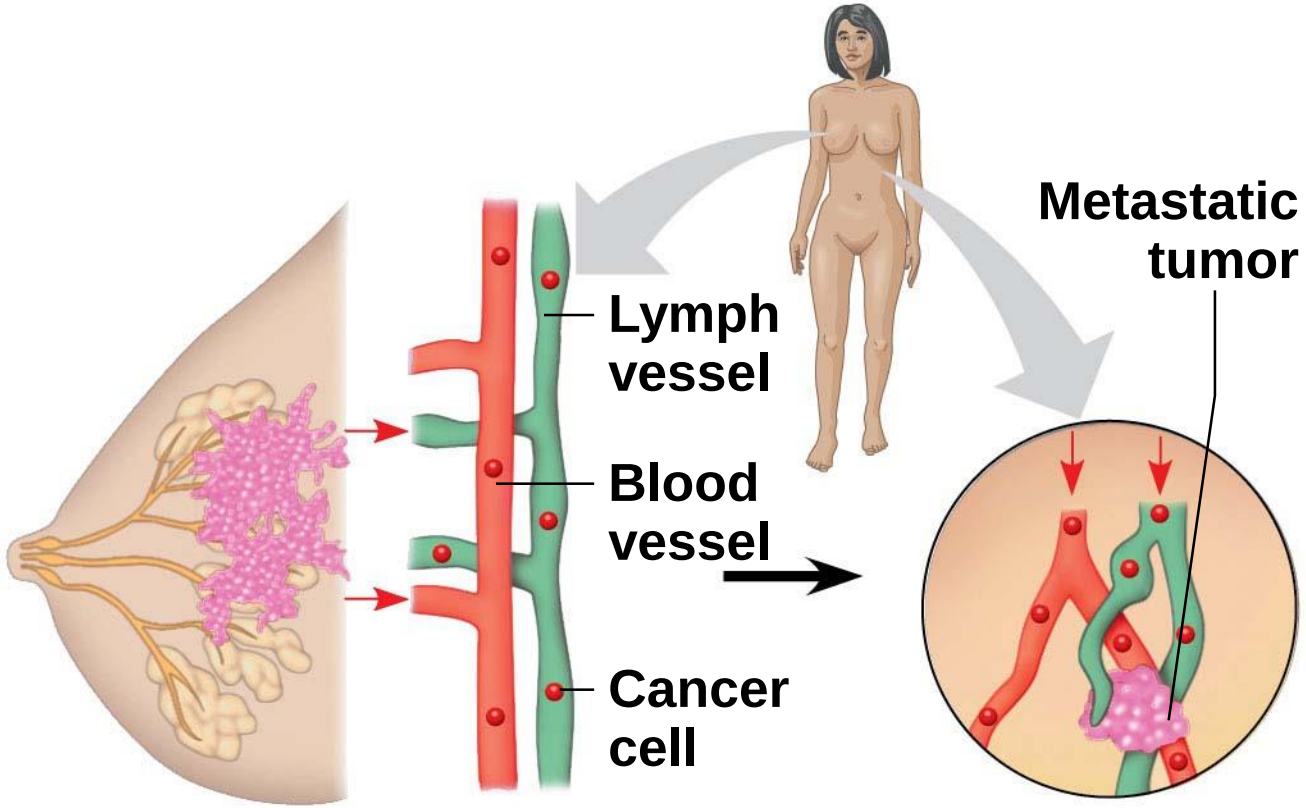


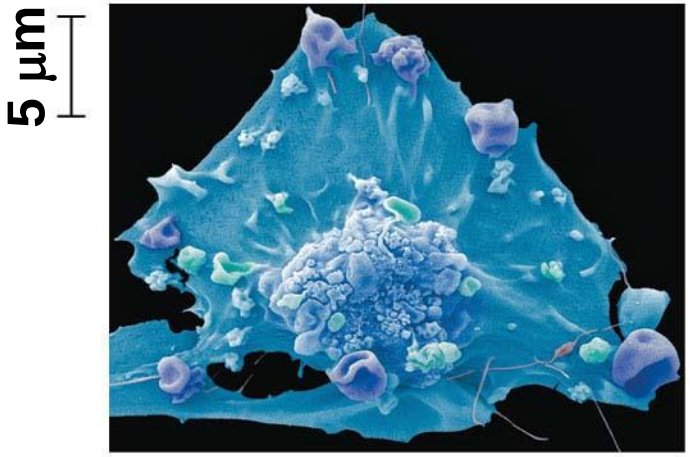
Figure 9.19-2



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

4 A small percentage of cancer cells may metastasize to another part of the body.

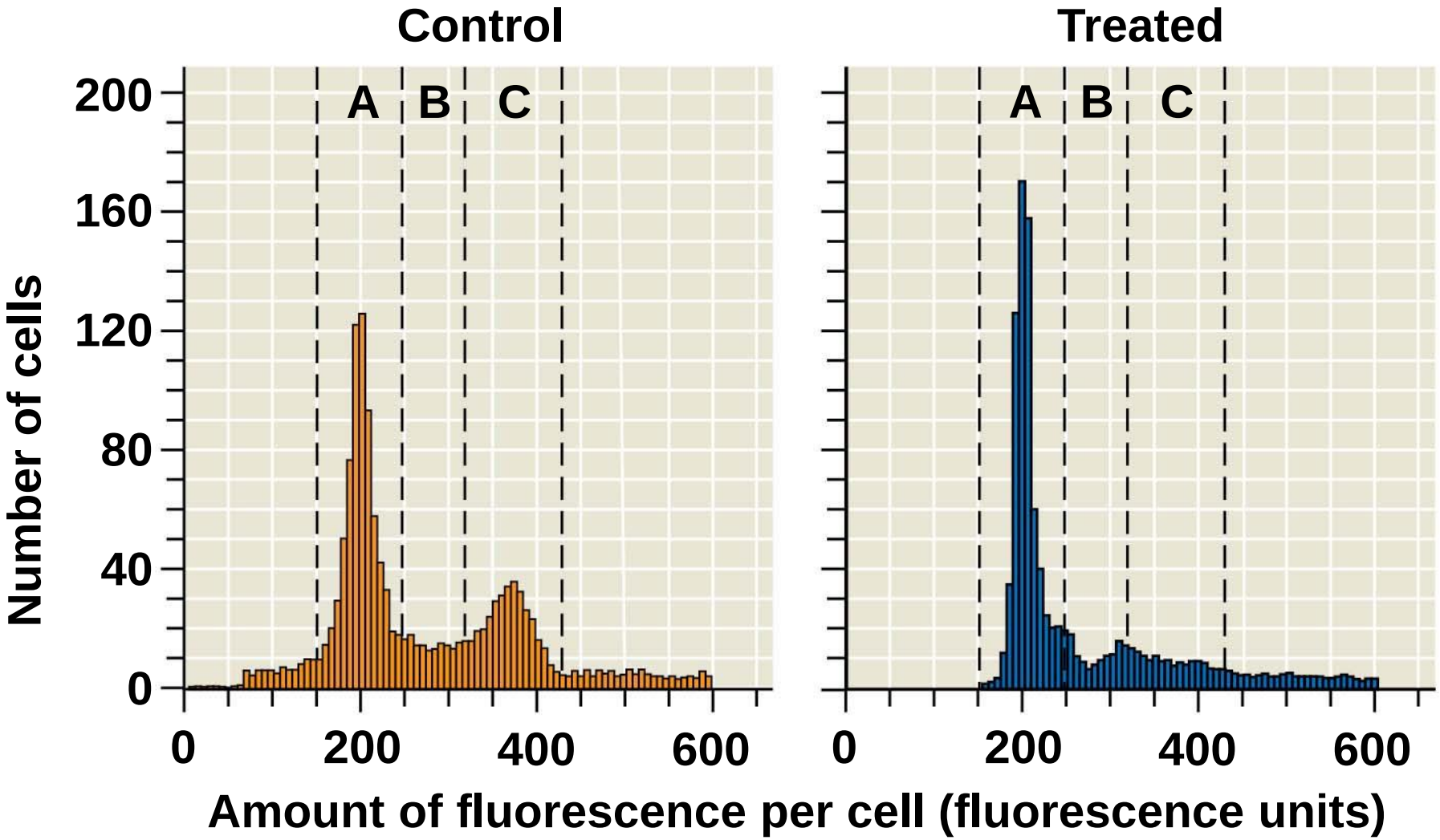
Figure 9.19-3



Breast cancer cell (colorized SEM)

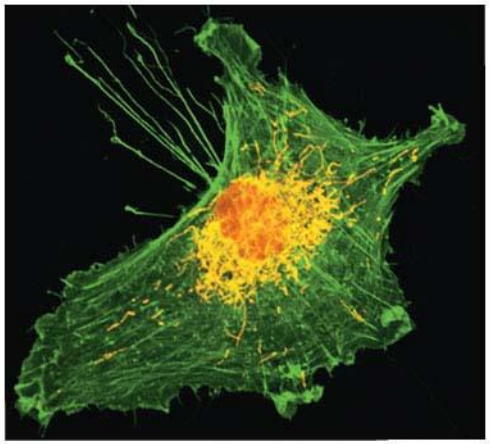
- Recent advances in understanding the cell cycle and cell cycle signaling have led to advances in cancer treatment
- Medical treatments for cancer are becoming more “personalized” to an individual patient’s tumor

Figure 9.UN01-1



Data from K. K. Velpula et al., Regulation of glioblastoma progression by cord blood stem cells is mediated by downregulation of cyclin D1, *PLoS ONE* 6(3): e18017 (2011). doi:10.1371/journal.pone.0018017

Figure 9.UN01-2



▲ **Human glioblastoma cell**

Figure 9.UN02

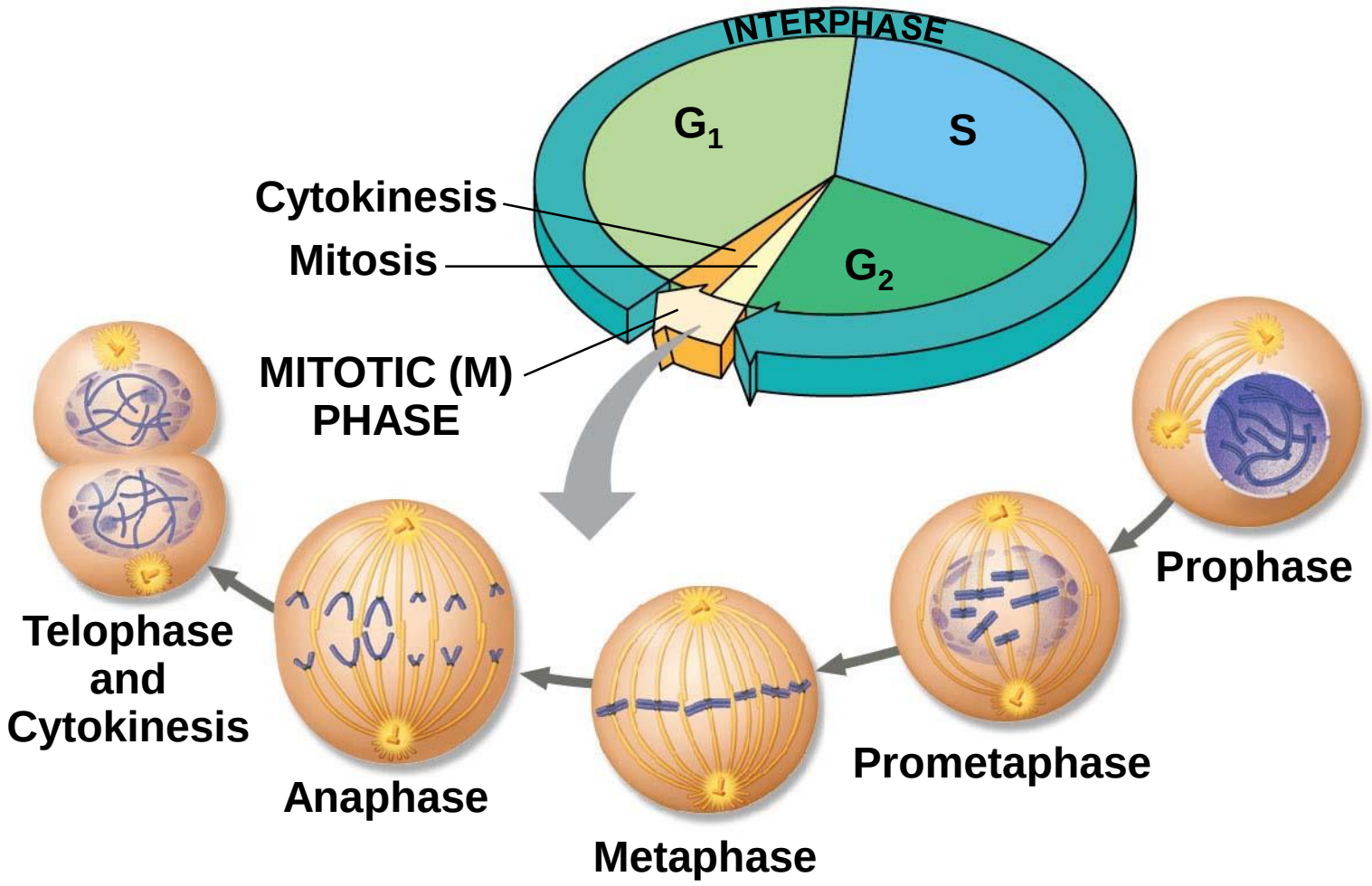


Figure 9.UN03

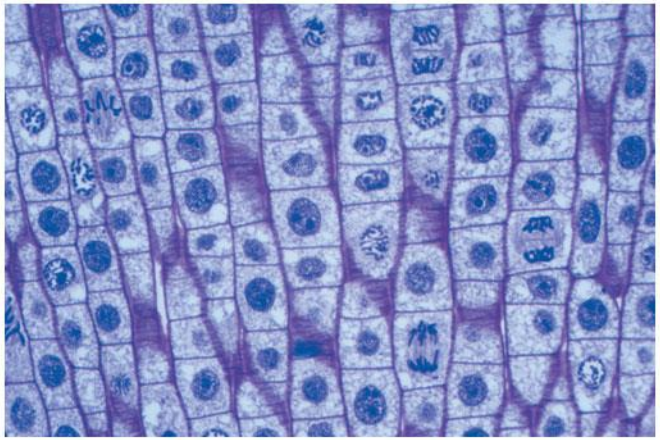


Figure 9.UN04