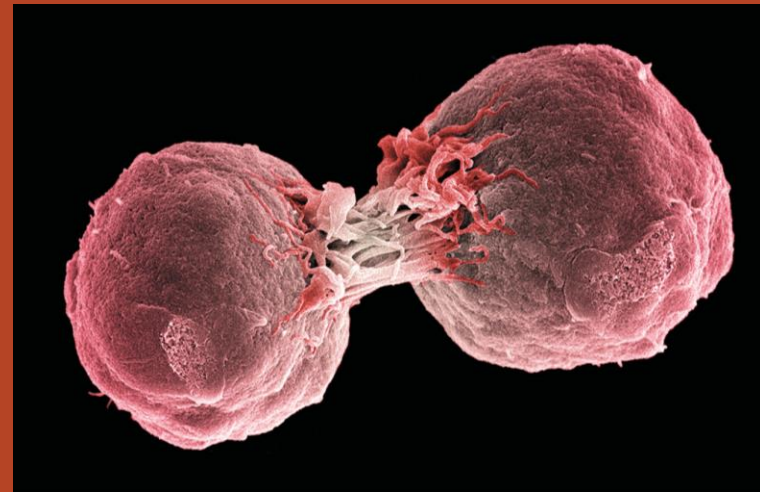
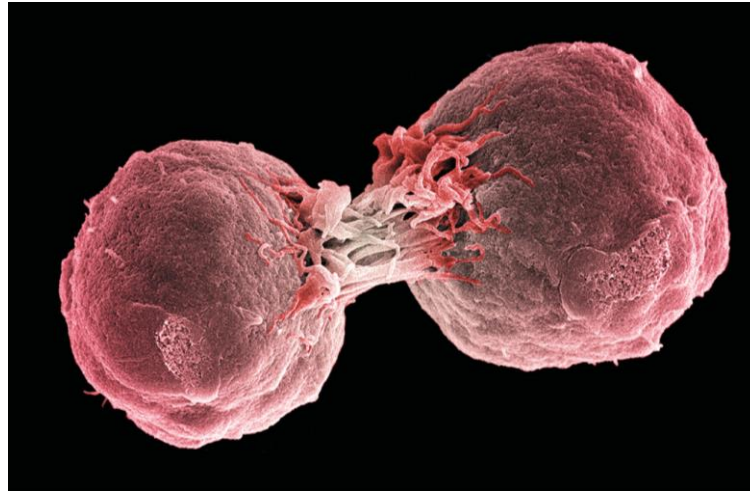


# 11

## *The Cell Cycle and Cell Division*



**Cells divide because?**



**DNA/cell**

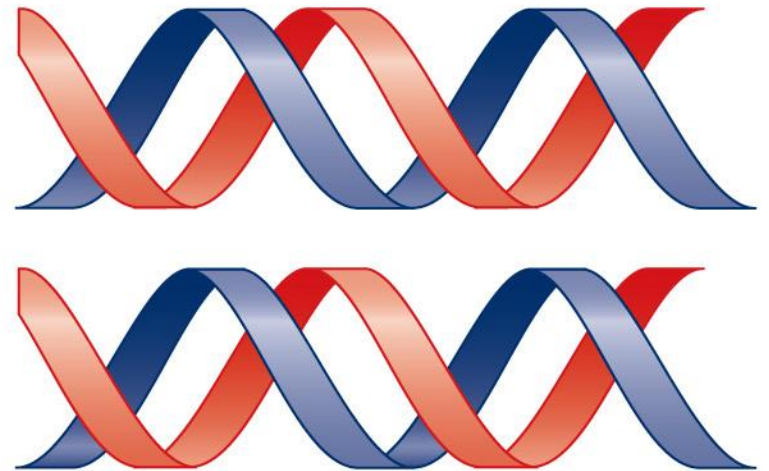
# DNA Replication

**(A)**

**Original DNA**



**After one round  
of replication**



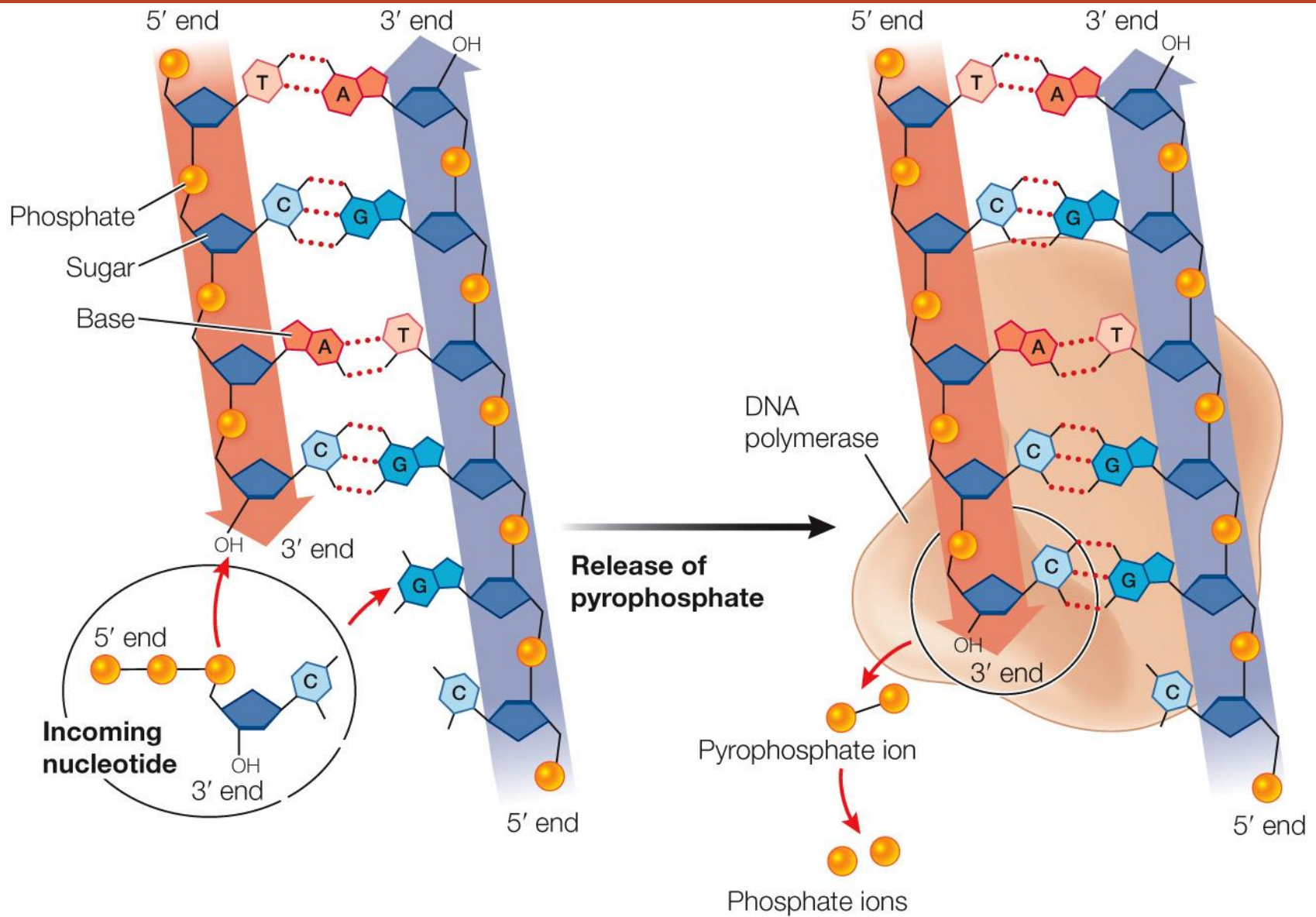
# DNA Replication

- DNA replication requires deoxyribonucleoside triphosphates, DNA polymerase, and a DNA template.

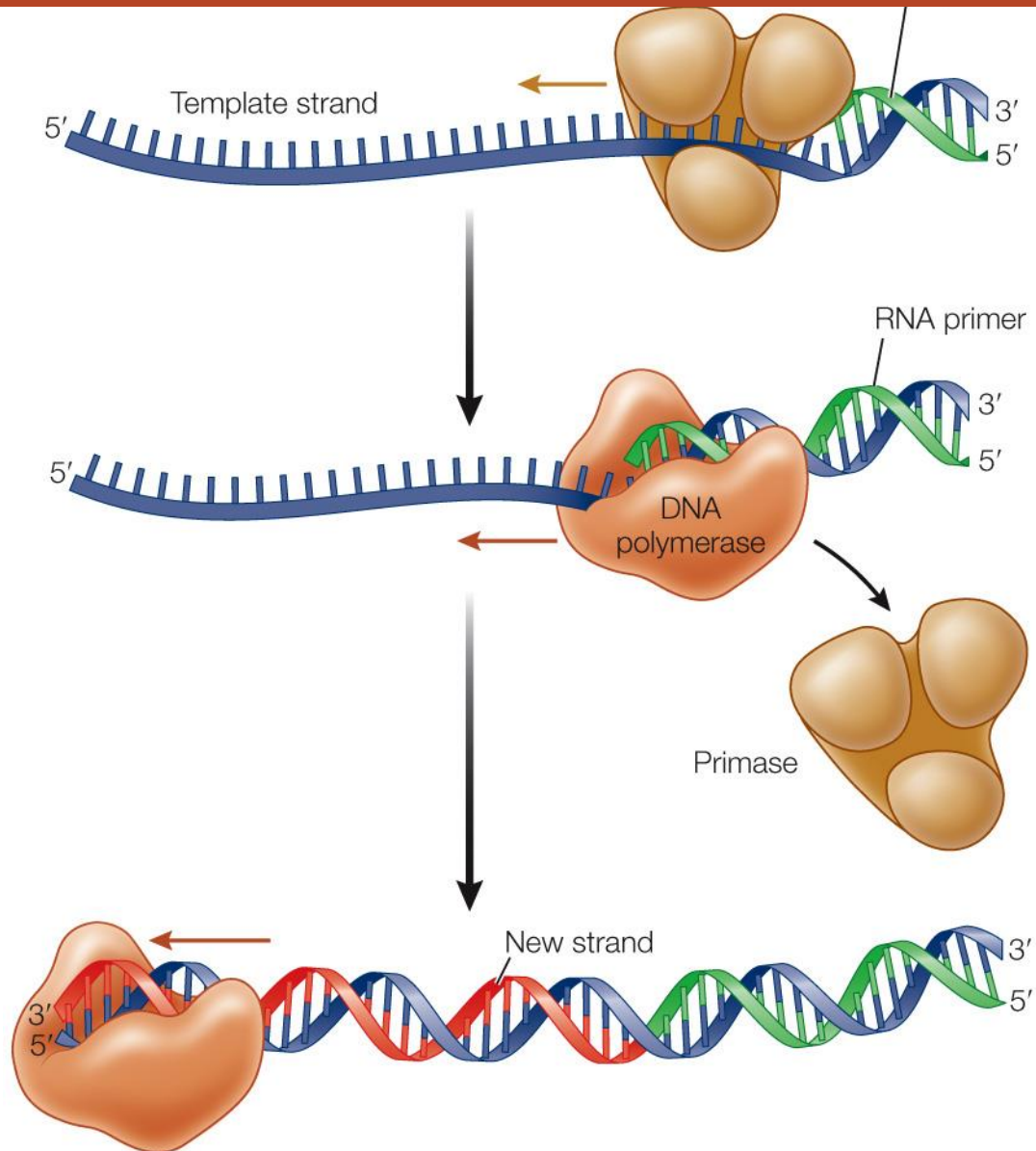
## Key Concept 13.3 Focus Your Learning

- DNA helicases, single-stranded binding proteins, DNA primases, and DNA ligases assist in DNA replication.
- Telomerases provide an important function to maintain the integrity of DNA in an organism.
- DNA replication proceeds bidirectionally from multiple replication starting points.

# Figure 13.9 Each New DNA Strand Grows from Its 5' End to Its 3' End

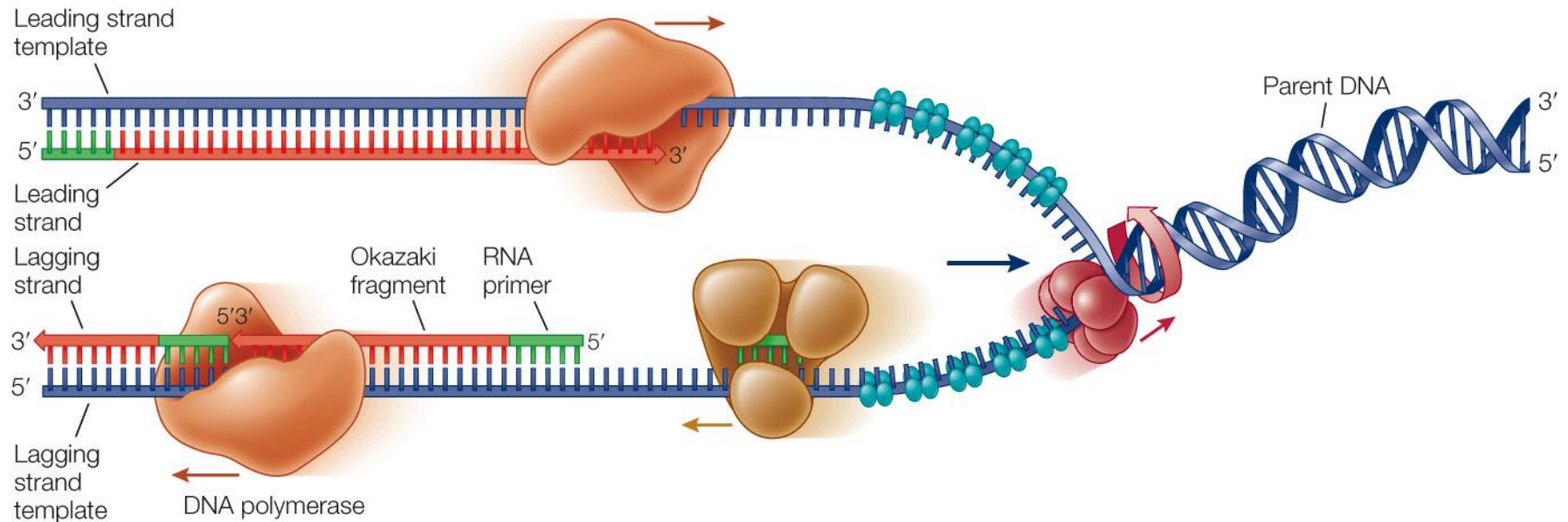


# Figure 13.11 DNA Forms with a Primer





# Figure 13.13 Many Proteins Collaborate in the Replication Complex

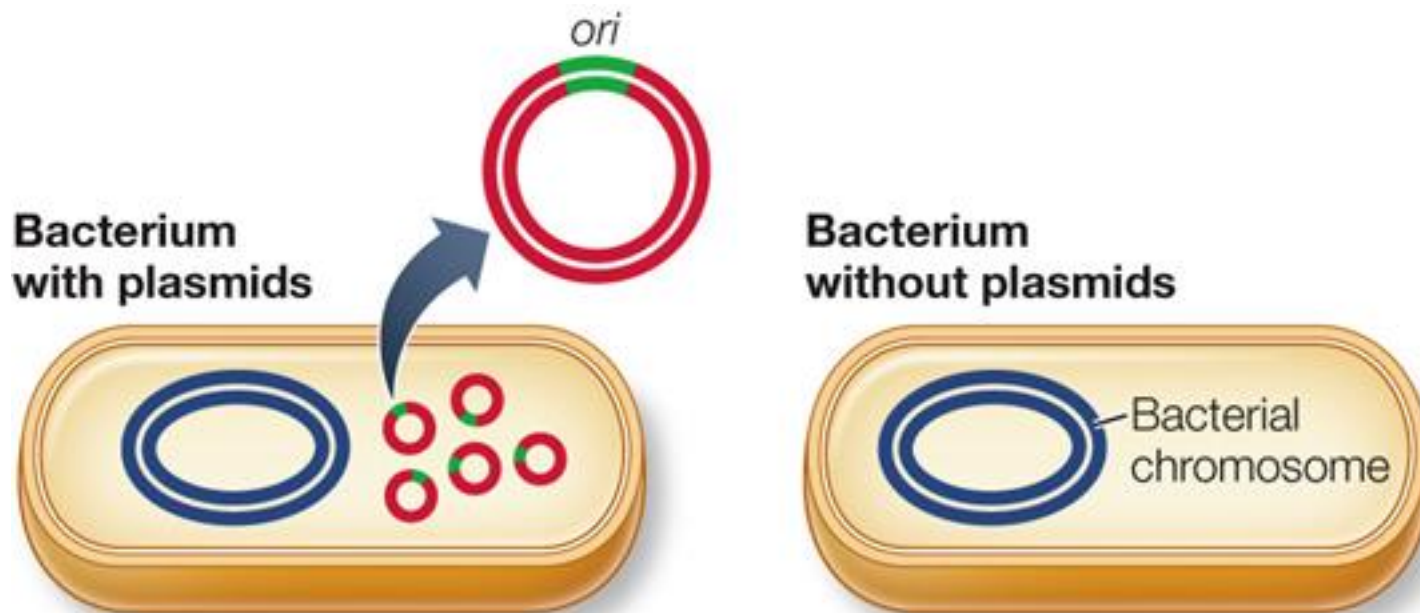


*LIFE: THE SCIENCE OF BIOLOGY 11e*, Figure 13.13

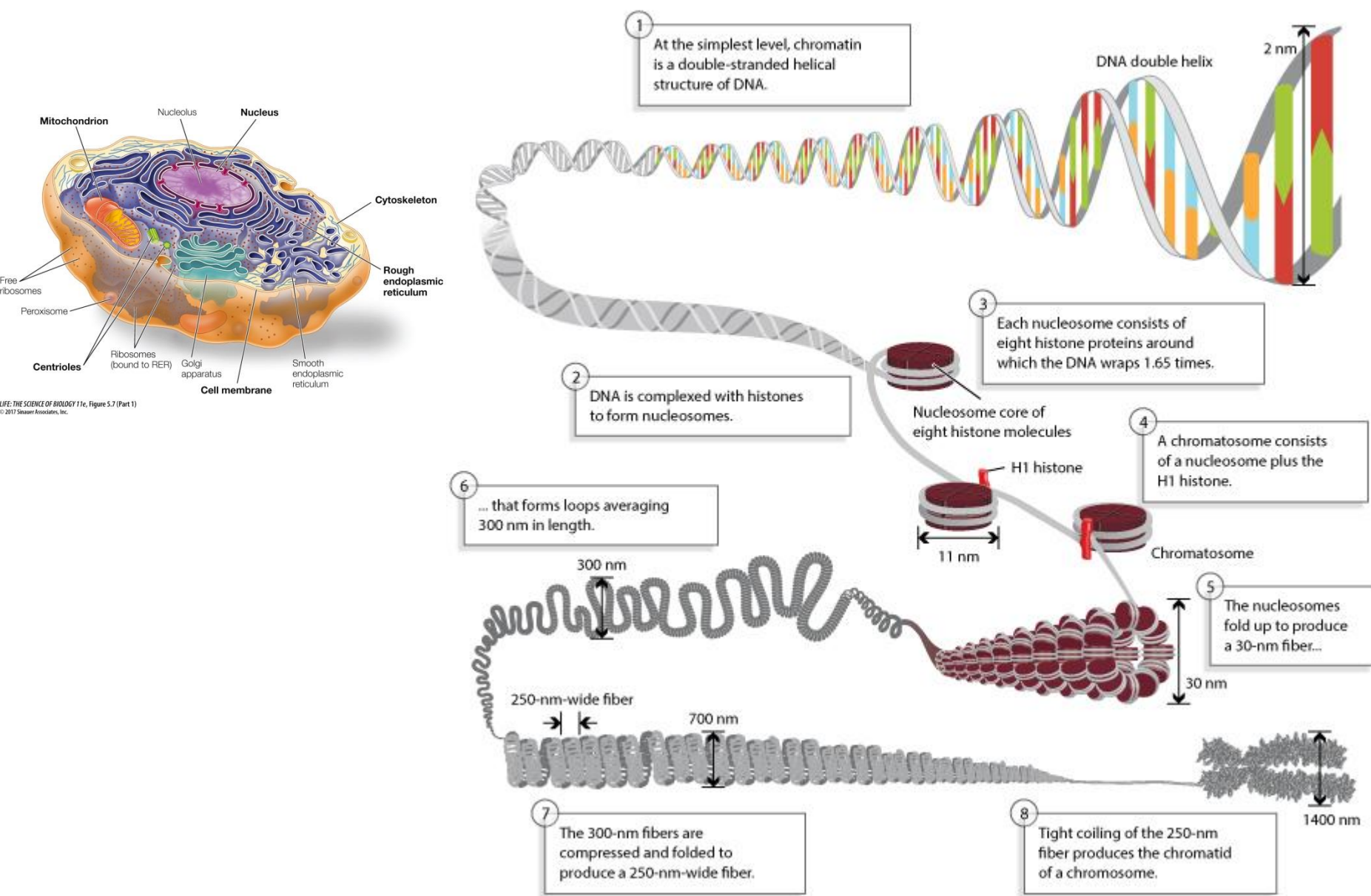
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# Prokaryotic chromosome

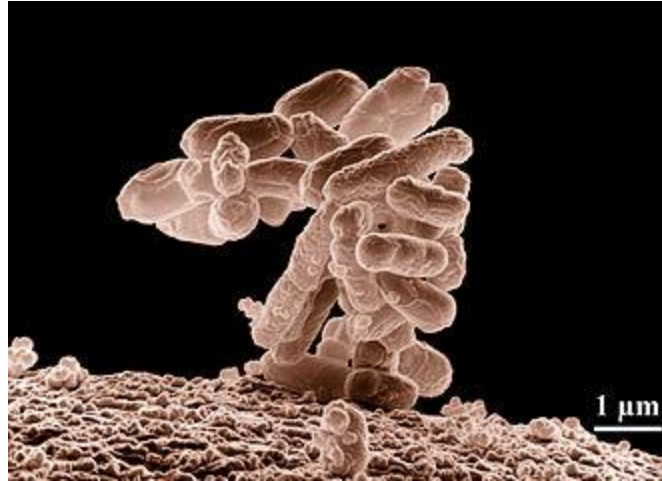


# Eukaryotic chromosome



# Chromosome

**Prokaryote (haploid;  $n=1$ )**  
**4.6 million base pairs**



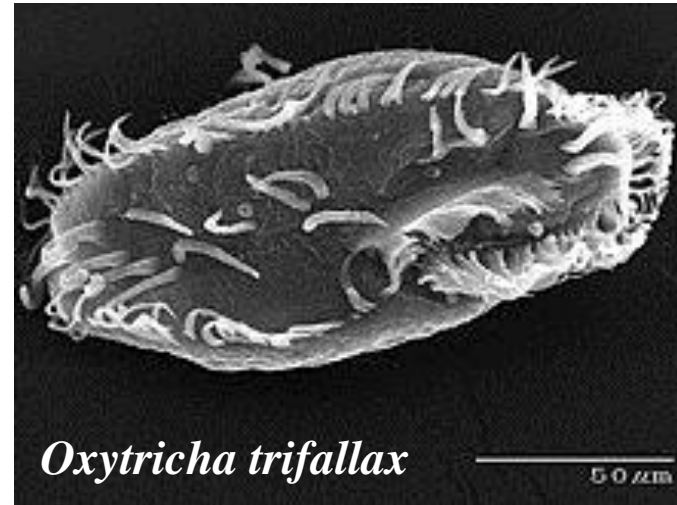
**Human (diploid;  $2n=46$ )**  
**3 billion base pairs**



**Ant (haploid;  $n=1$ )**



**Ciliate (polyploid; 2000x16000)**



# Chapter 11 Key Concepts

11.1 All Cells Derive from Other Cells

11.2 The Eukaryotic Cell Division Cycle Is Regulated

11.3 Eukaryotic Cells Divide by Mitosis

11.4 Cell Division Plays Important Roles in the Sexual Life Cycle

11.5 Meiosis Leads to the Formation of Gametes

11.6 Cell Death Is Important in Living Organisms

11.7 Unregulated Cell Division Can Lead to Cancer

## Key Concept 11.1 Focus Your Learning

- All cell division processes involve four main events: initiation, DNA replication, DNA segregation, and cytokinesis.
- Cell division in prokaryotes is rapid, occurs in response to environmental signals, and results in new individual cells, which are often the entire organism.
- Cell division in eukaryotes is complex, occurs in response to internal signals, and may reproduce the entire organism for single-celled eukaryotes, or result in more cells within a multicellular organism.

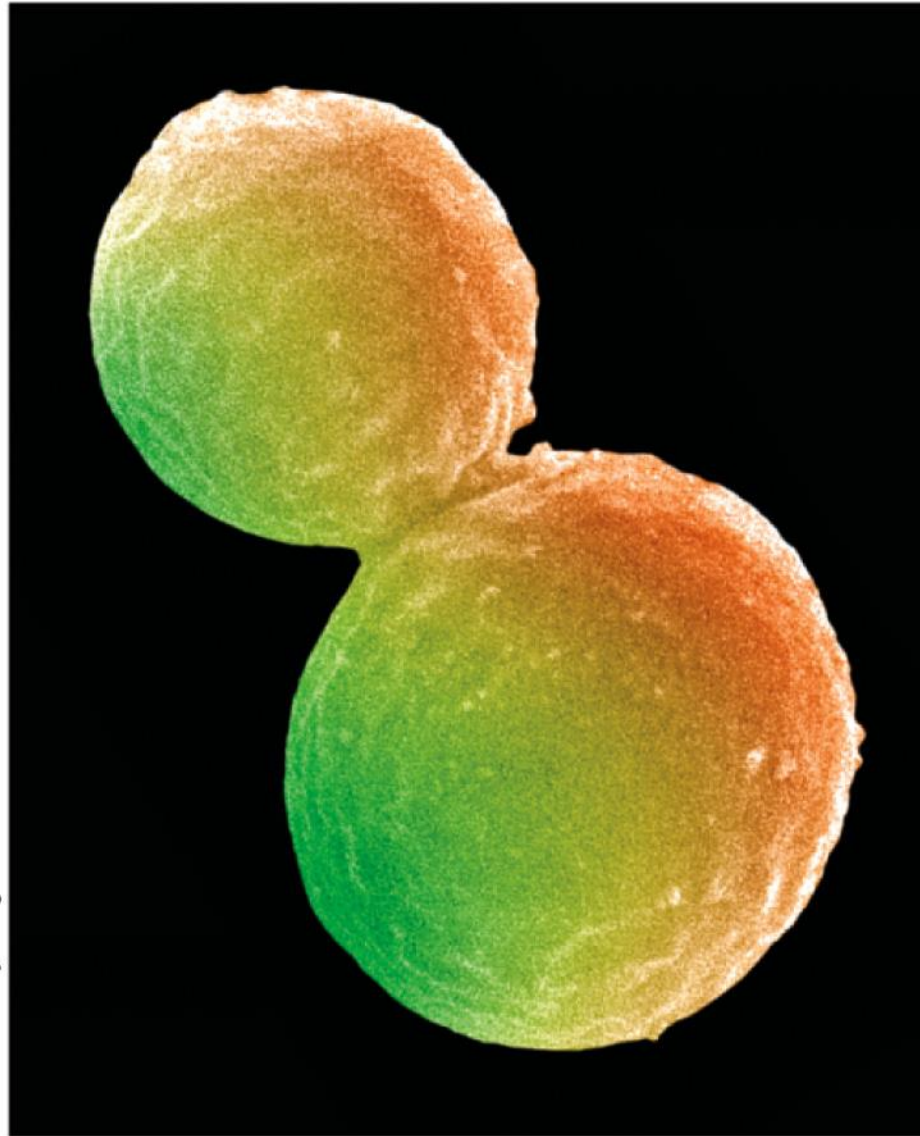
## 11.1 All Cells Derive from Other Cells

The life cycle of an organism is closely linked to cell division.

Cell division is important in development, growth and repair of tissues, and reproduction of all organisms.



## (A) Reproduction



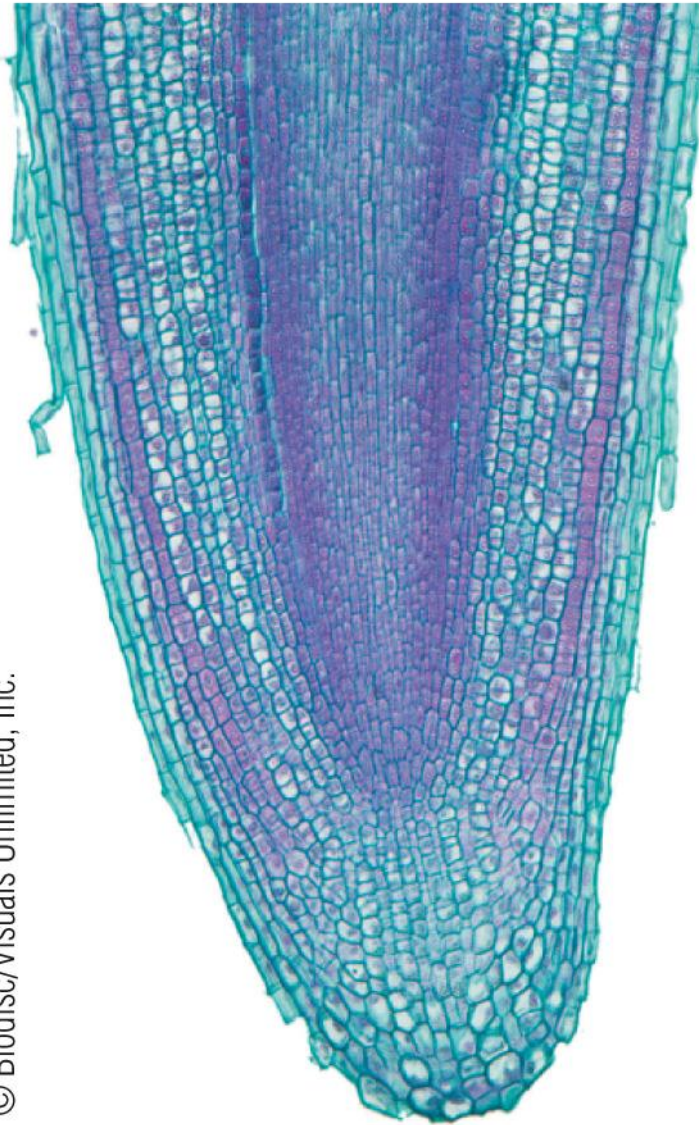
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## (B) Growth



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## (C) Regeneration

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## 11.1 All Cells Derive from Other Cells

### Events in cell division

- A **reproductive signal** initiates cell division
- **Replication** of DNA
- **Segregation**—distribution of DNA into two new cells
- **Cytokinesis**—separation of cellular material into the two new cells

## 11.1 All Cells Derive from Other Cells

In prokaryotes, binary fission results in two new single-celled organisms.

External factors such as nutrient concentration and environmental conditions are the reproductive signals.

For many bacteria, abundant food supplies speed up the division cycle.

## 11.1 All Cells Derive from Other Cells

Most prokaryotes have one chromosome, a single molecule of DNA. Often circular, but folded.

Two important regions

- *ori*—where replication starts (origin)
- *ter*—where replication ends (terminus)

## 11.1 All Cells Derive from Other Cells

Replication occurs as the DNA moves through a “replication complex” of proteins.

In rapidly dividing prokaryotes, DNA replication occupies the entire time between cell divisions.

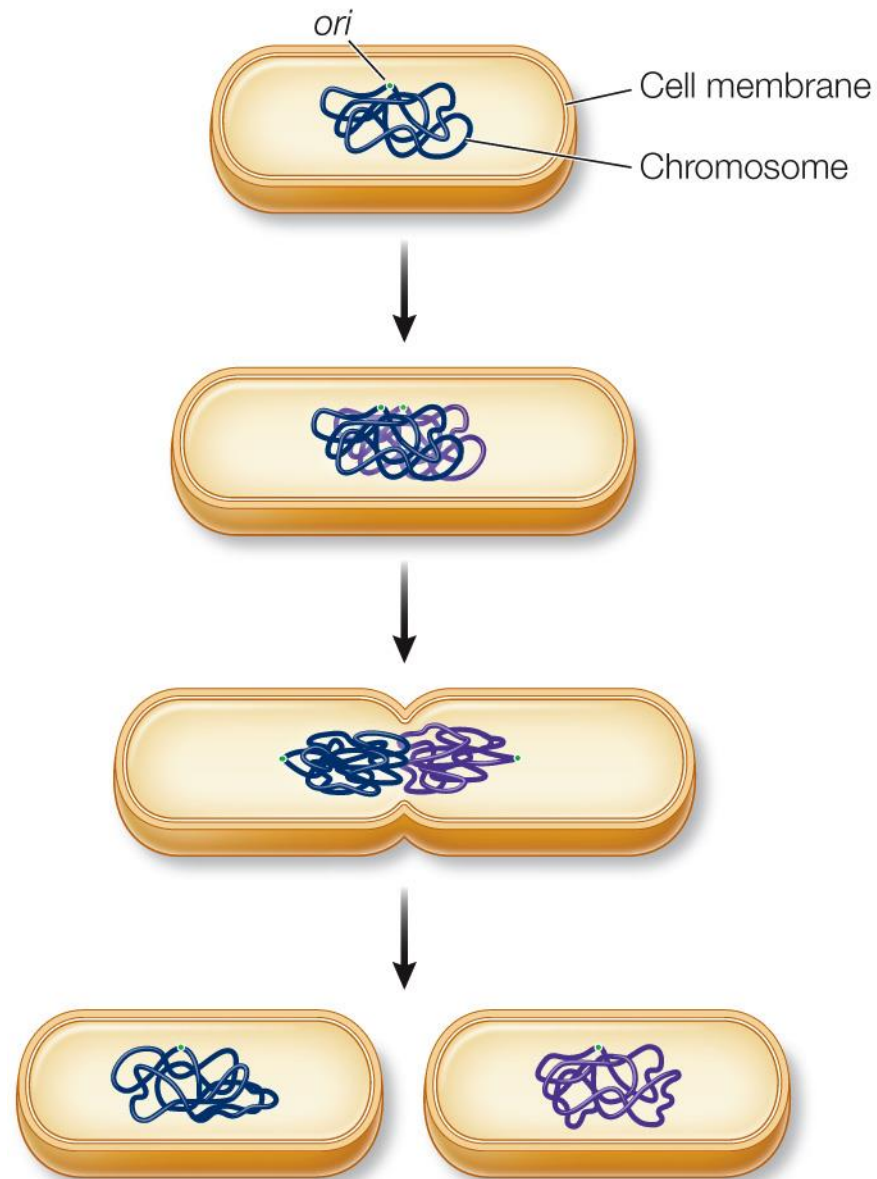
When replication is complete, the *ori* regions move toward opposite ends of the cell, segregating the daughter DNA molecules.

Cytokinesis: The cell membrane pinches in; protein fibers form a ring.

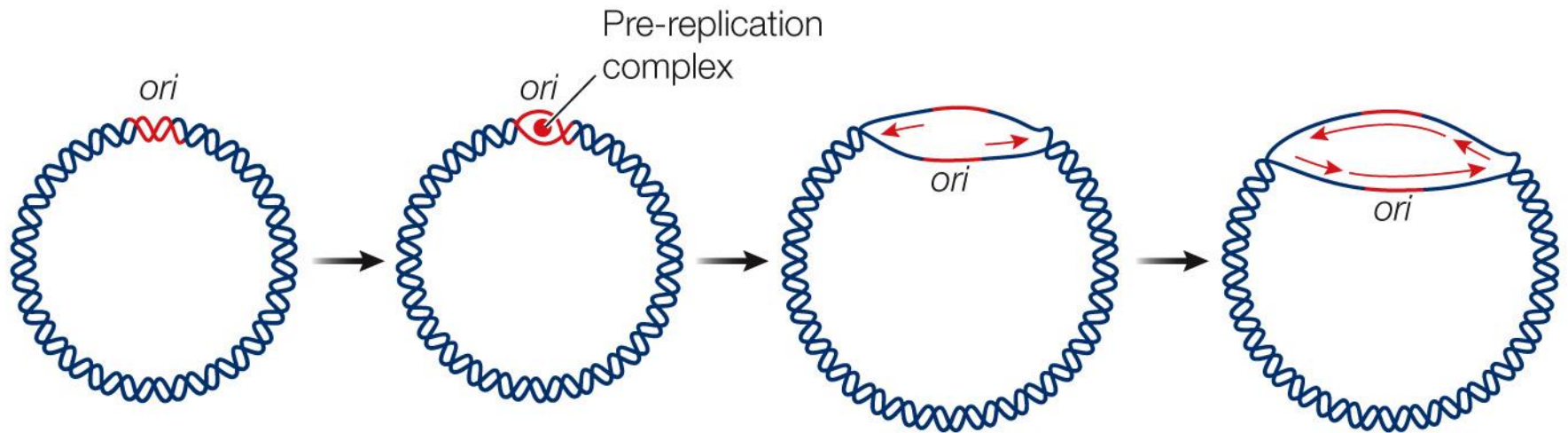
- New cell wall materials are synthesized, resulting in separation of the two cells.



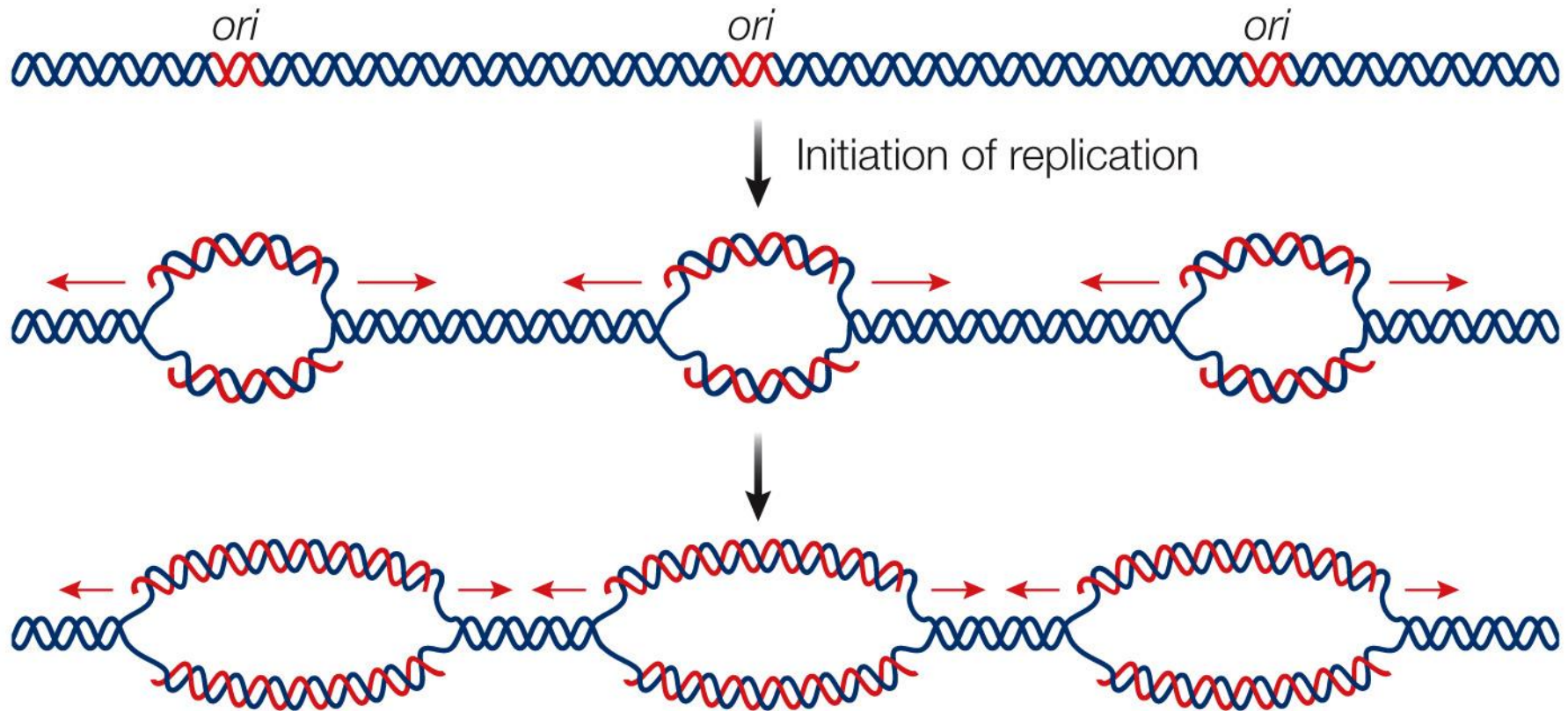
**(A) Binary fission in a bacterium**

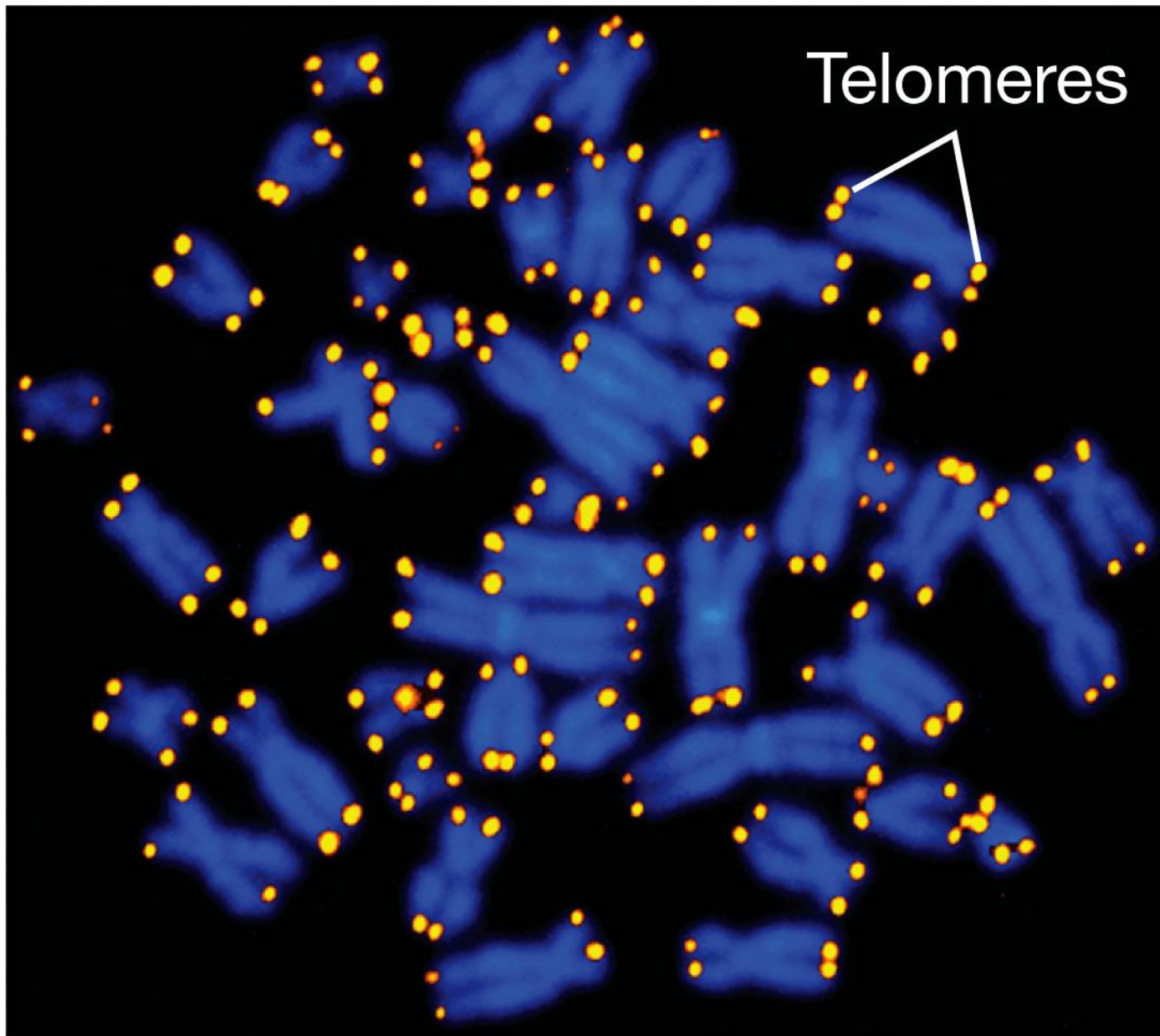


**(A) A single *ori* in a prokaryotic chromosome**



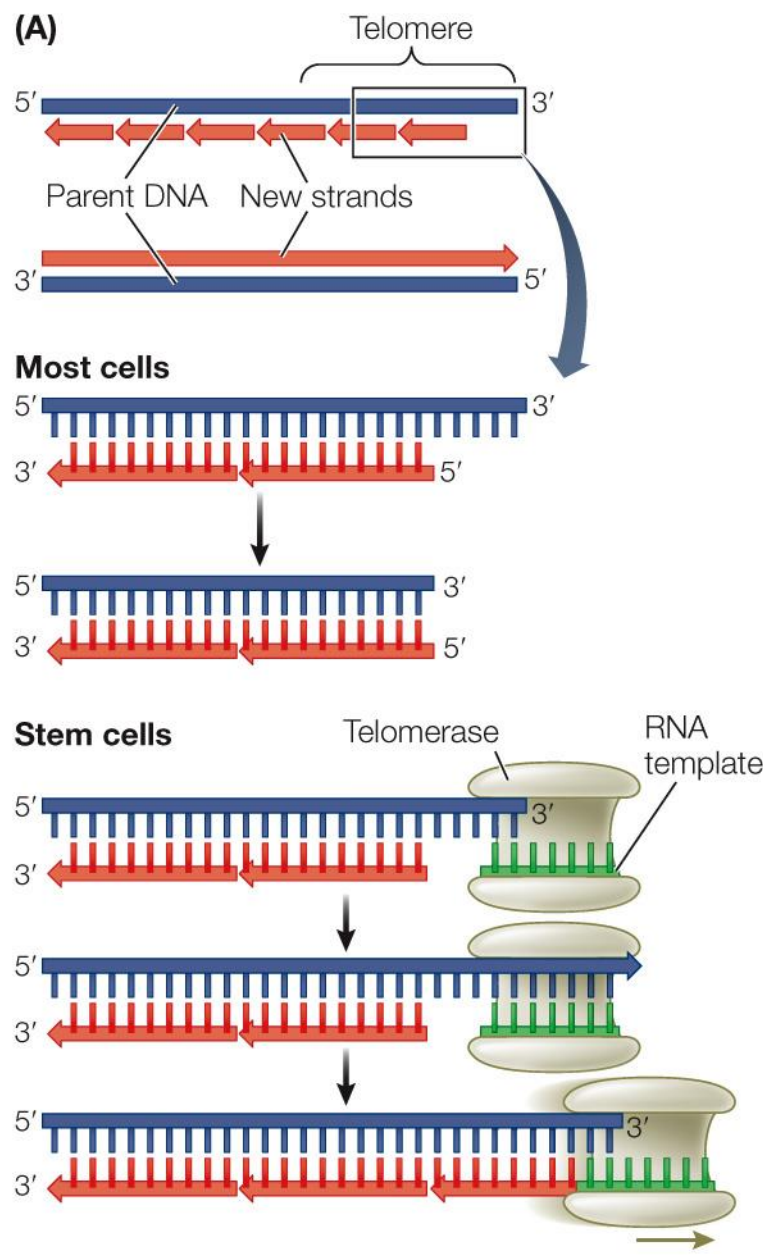
**(B) Multiple *ori* in a eukaryotic chromosome**





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Figure 13.17 Telomeres and Telomerase (Part 1)





Continuously dividing cells, such as bone marrow stem cells, have **telomerase**, which catalyzes addition of lost telomeres.

Telomerase is expressed in most cancer cells and is important in their ability to keep dividing.

- It is a target for anti-cancer drugs.

Principles of DNA replication were used to develop the **polymerase chain reaction (PCR)** technique.

An automated process makes multiple copies of short DNA sequences for genetic manipulation and research (DNA amplification).



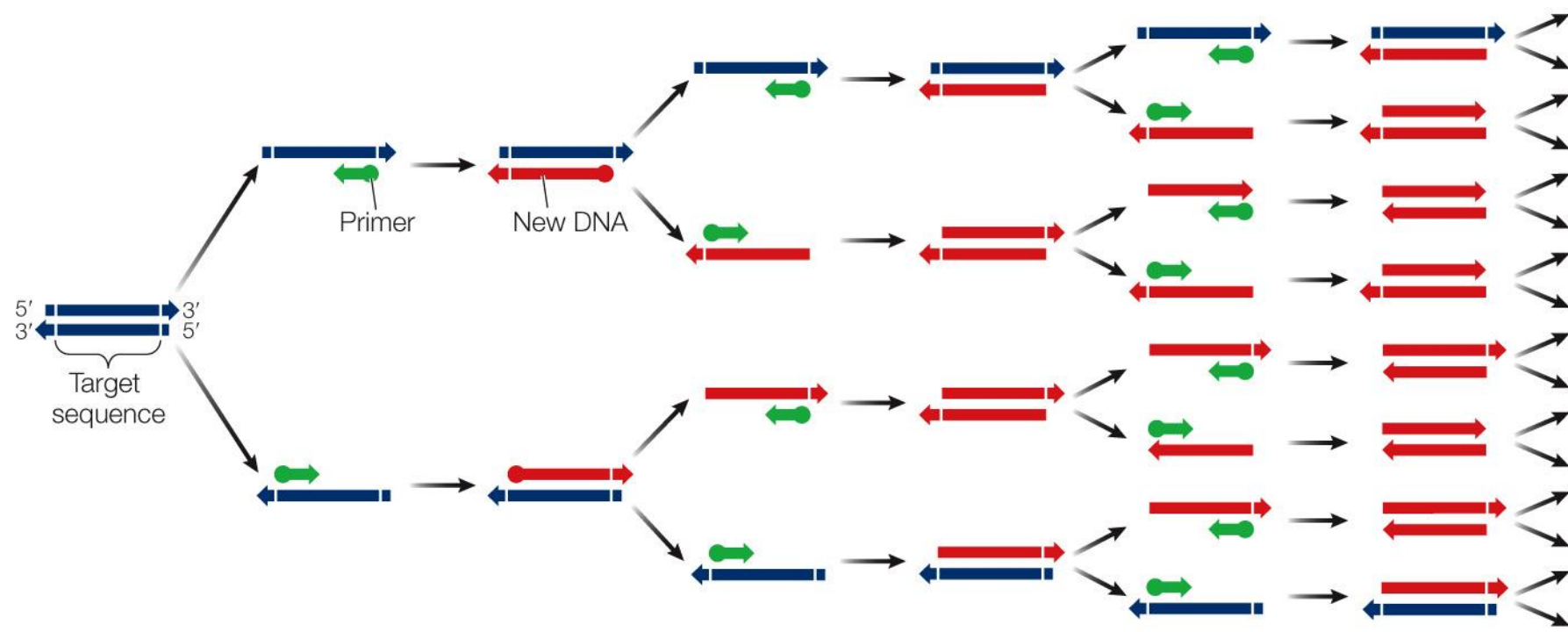
A PCR mixture contains:

- A sample of double-stranded DNA (the template)
- Two artificially synthesized primers
- The four dNTPs
- DNA polymerase that can tolerate high temperatures
- Salts and pH buffer

### PCR amplification

- DNA strands are separated (denatured) by heating
- Reaction is cooled to allow primers to bind (anneal) to template strands
- Reaction is warmed; DNA polymerase catalyzes new strands
- The sequence is repeated many times

Figure 13.19 The Polymerase Chain Reaction



*LIFE: THE SCIENCE OF BIOLOGY 11e*, Figure 13.19  
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Base sequences at the 3' ends of the DNA strands must be known, so that primers can be made.

The specificity of the primers is a key to the power of PCR.

An initial problem with PCR: the temperature needed to denature the DNA destroyed most DNA polymerases.

A DNA polymerase that does not denature at high temperatures (90°C) was taken from a hot springs bacterium, *Thermus aquaticus*.

## 11.1 All Cells Derive from Other Cells

In eukaryotes, reproductive signals are related to the needs of the entire organism.

Many cells in multicellular organisms become specialized and seldom divide.

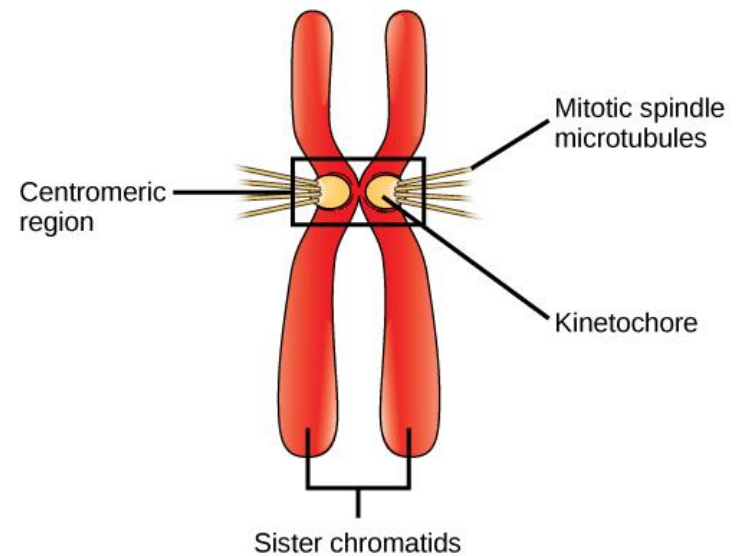
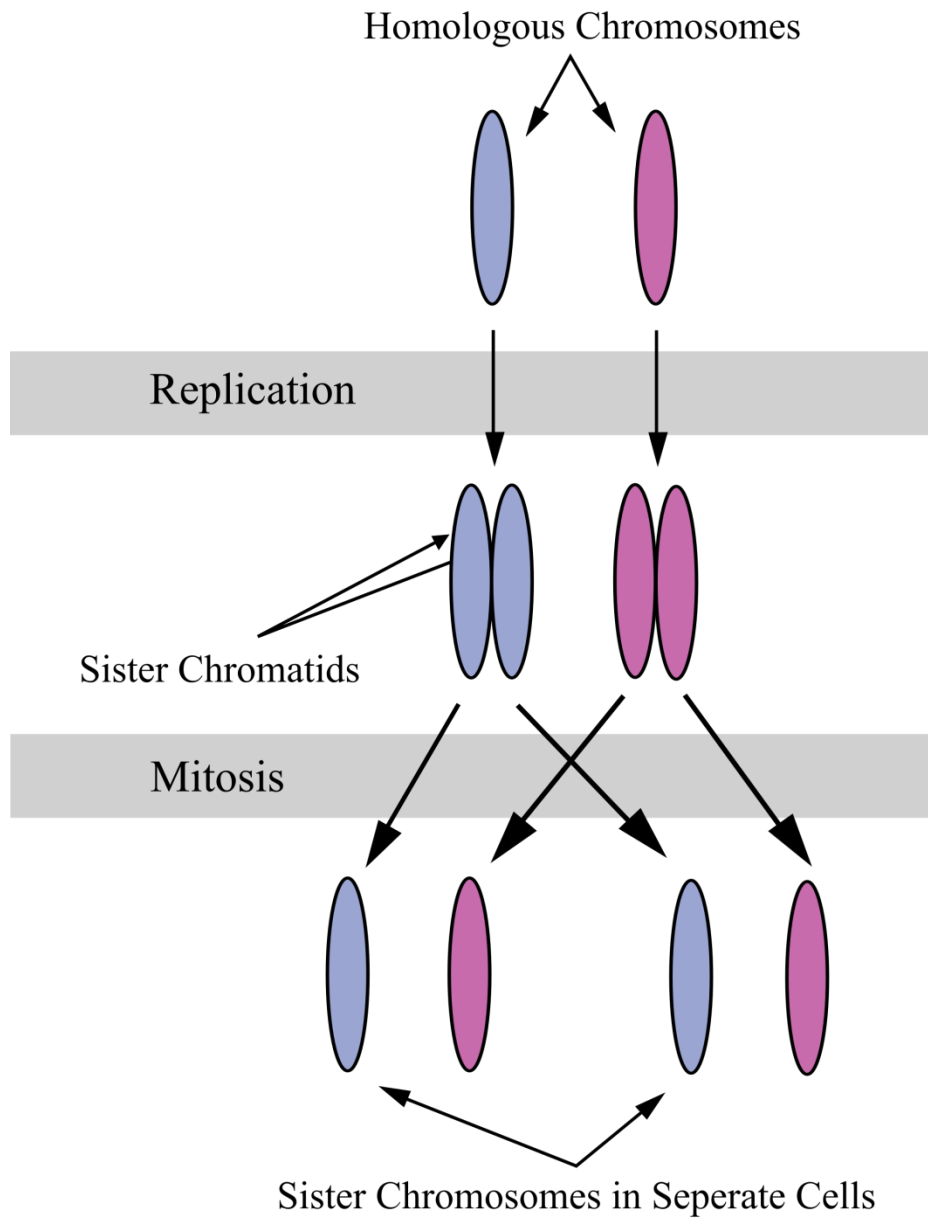
## 11.1 All Cells Derive from Other Cells

Newly replicated chromosomes are closely associated (**sister chromatids**).

**Mitosis** separates them into two new nuclei.

Cytokinesis proceeds differently in animal and plant cells (plants have cell walls).





## Key Concept 11.2 Focus Your Learning

- Dividing eukaryotic cells undergo an orderly sequence of events that together make up the cell cycle.
- Events of the eukaryotic cell cycle are internally regulated.
- External factors stimulate eukaryotic cells in the G0 state to begin dividing.

## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

**Cell cycle:** Period from one cell division to the next.

**Interphase:** Nucleus is visible and cell functions occur.

- Duration of interphase is highly variable.

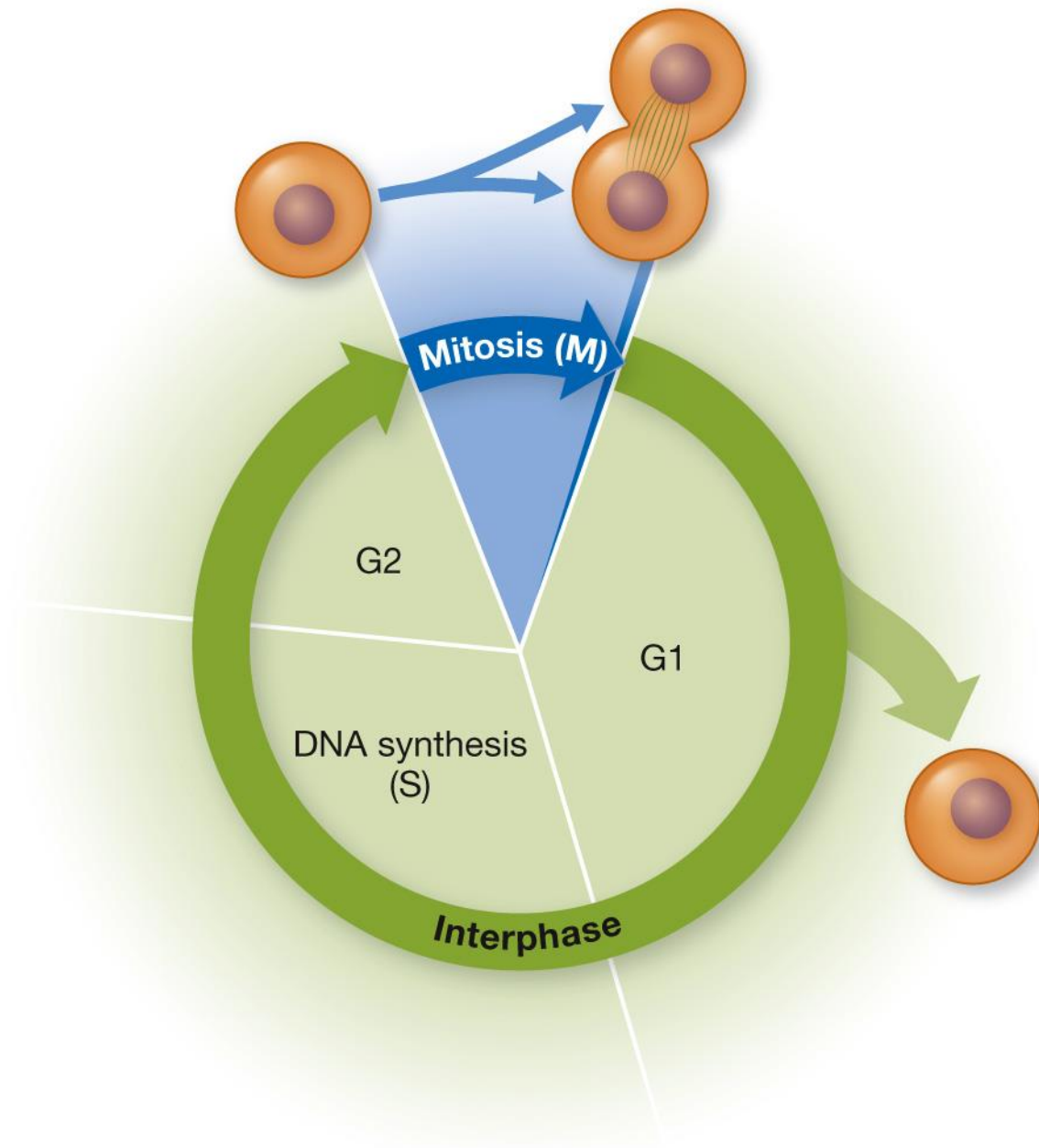
## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

Interphase has 3 subphases: G1, S, G2.

**G1:** Between cytokinesis and S phase; chromosomes are single.

- Duration of G1 is variable, from minutes to years. Some cells enter a resting phase (G0).

Figure 11.3 The Eukaryotic Cell Cycle



## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

**Restriction (R) point:** G1-to-S transition—*commitment* to DNA replication and subsequent cell division.

**S phase:** DNA replicates; sister chromatids remain together.

**G2:** Cell prepares for mitosis.

## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

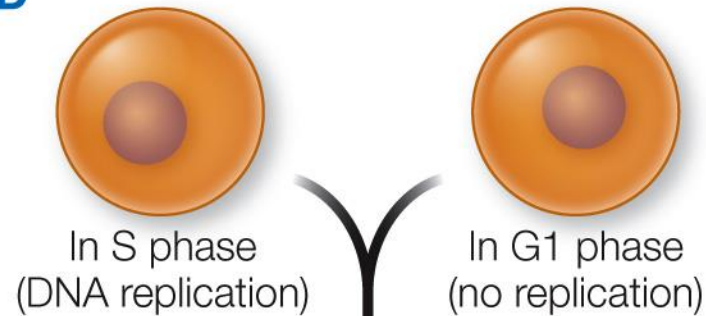
Specific signals trigger the transition from one phase to another.

Identification of these signals came from cell fusion experiments.

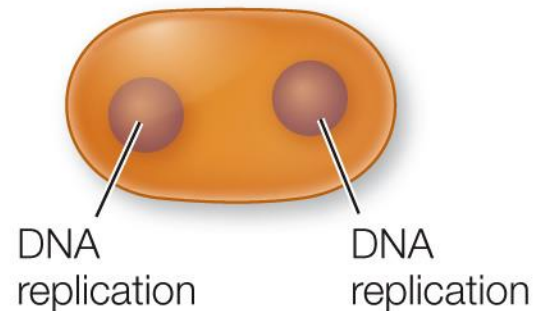
Hypothesis: A cell in S phase contains an activator of DNA replication.

**HYPOTHESIS** ► A cell in S phase contains an activator of DNA replication.

**METHOD**



**RESULTS**



**CONCLUSION** ► The S phase cell contains a substance that diffuses to the G1 nucleus and activates DNA replication.



## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

Progress through the cell cycle is controlled by **cyclin-dependent kinases (Cdk's)**.

Protein kinases catalyze transfer of a phosphate group from ATP to a protein (phosphorylation).

- This changes the shape and function of the protein.

## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

Cdk is activated by binding to **cyclin** (allosteric regulation); this alters its shape and exposes the active site.

There are many different cyclin–cdk complexes acting at different stages of the cell cycle.

Figure 11.4 Cyclin Binding Activates Cdk

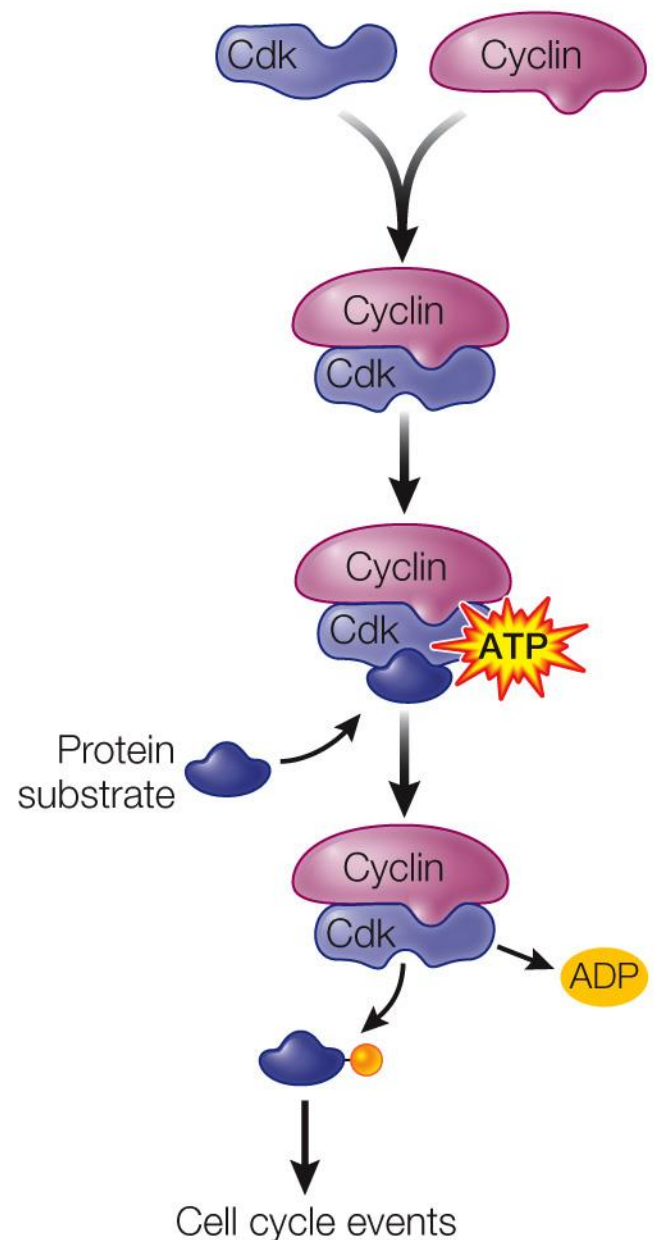
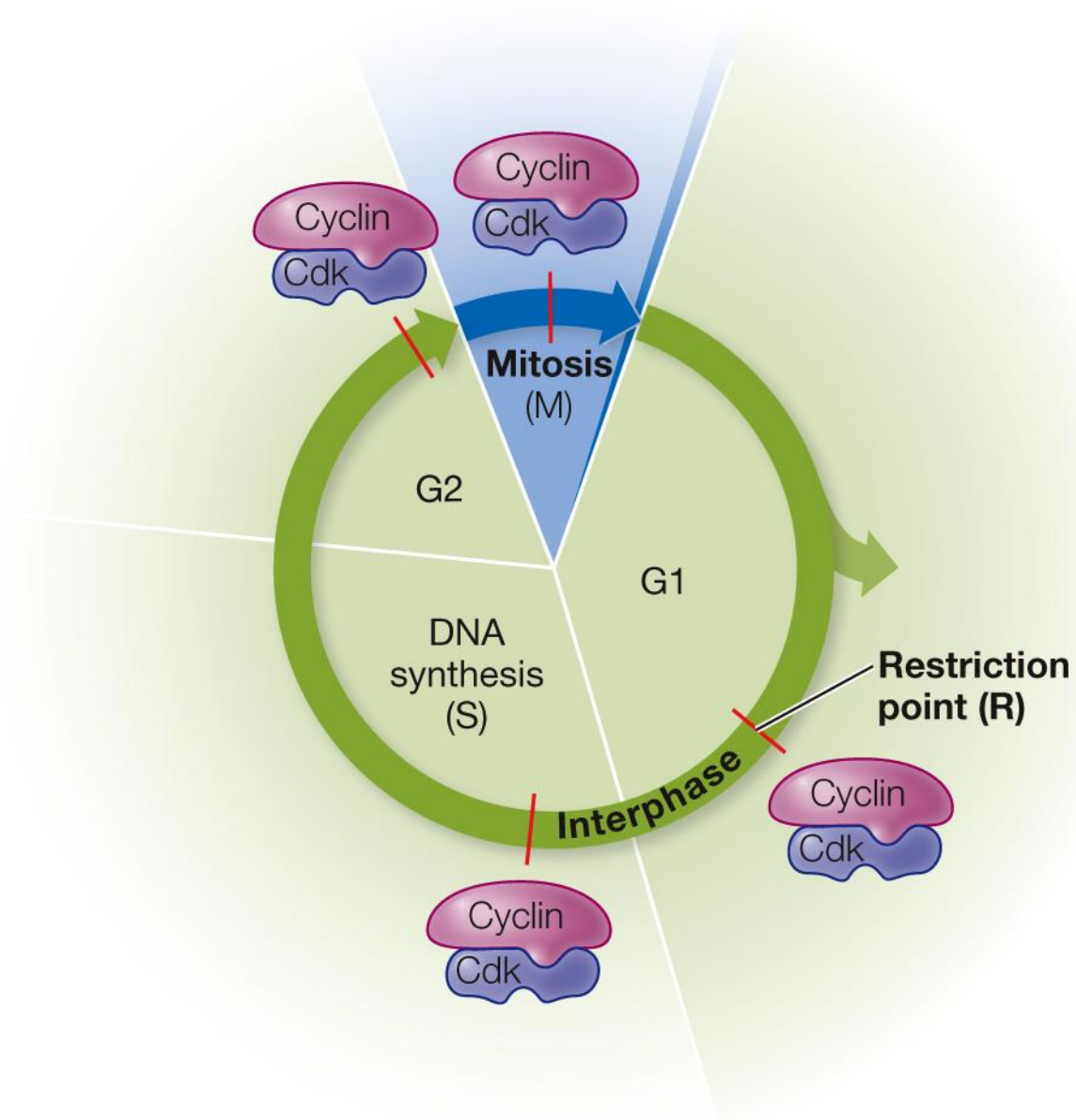


Figure 11.5 Cyclin-Dependent Kinases Regulate Progress through the Cell Cycle



## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

Progress past the restriction point depends on retinoblastoma protein (RB).

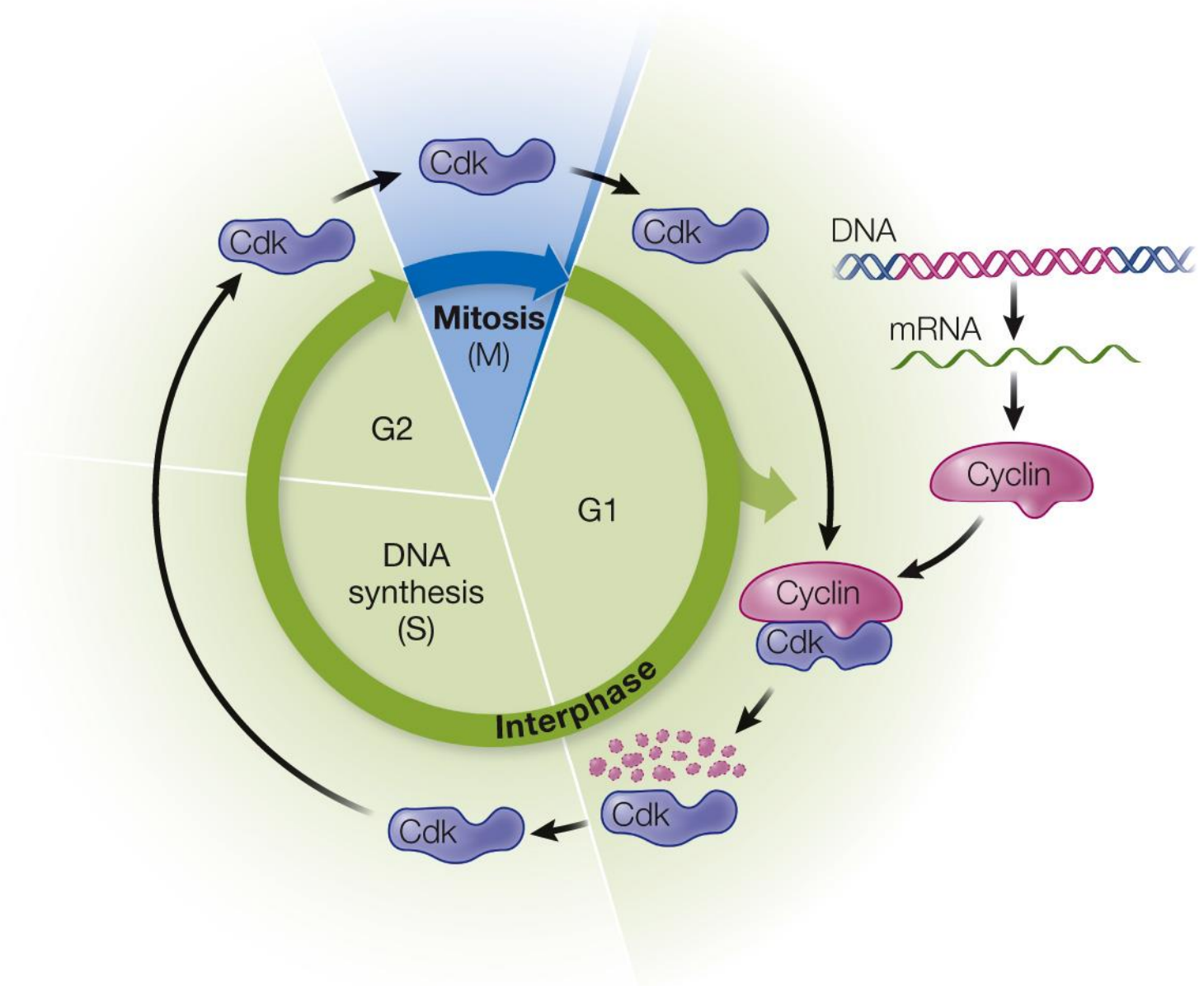
RB normally inhibits the cell cycle, but when phosphorylated by cyclin-Cdk, RB becomes inactive and no longer blocks the cell cycle.

## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

Progress through the cell cycle depends on Cdk activity, so regulating Cdk is a key to regulating cell division.

Cdk's can be regulated by the presence or absence of cyclins.

Figure 11.6 Cyclins Are Transient in the Cell Cycle



## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

Cyclin–Cdk's act at **cell cycle checkpoints** to regulate progress.

- Example: At checkpoint R, if DNA is damaged, p21 protein is made.
  - p21 binds to G1 Cdk's, preventing their activation.
  - The cell cycle pauses while DNA is repaired.



**table 11.1 Cell Cycle Checkpoints**

| Cell Cycle Phase | Checkpoint Trigger                   |
|------------------|--------------------------------------|
| G1               | DNA damage                           |
| S                | Incomplete replication or DNA damage |
| G2               | DNA damage                           |
| M                | Chromosome unattached to spindle     |

## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

The cell cycle is also influenced by external signals.

Some cells divide infrequently or go into G<sub>0</sub>. They must be stimulated by **growth factors** to divide.

- Platelet-derived growth factor: From platelets that initiate blood clotting; stimulates skin cells to divide and heal wounds.

## 11.2 The Eukaryotic Cell Division Cycle Is Regulated

- Interleukins and erythropoietin are growth factors that stimulate division and specialization of blood cells.

Growth factors activate signal transduction pathways that end with cyclin synthesis, thereby activating Cdk's and the cell cycle.

## Key Concept 11.3 Focus Your Learning

- Mitosis ensures that each daughter cell receives a complete copy of the parent cell's DNA.
- Mitosis involves ordered events within the dividing cell nucleus.
- Cytokinesis is the process by which a cell's cytoplasm divides. It occurs once mitosis is complete.

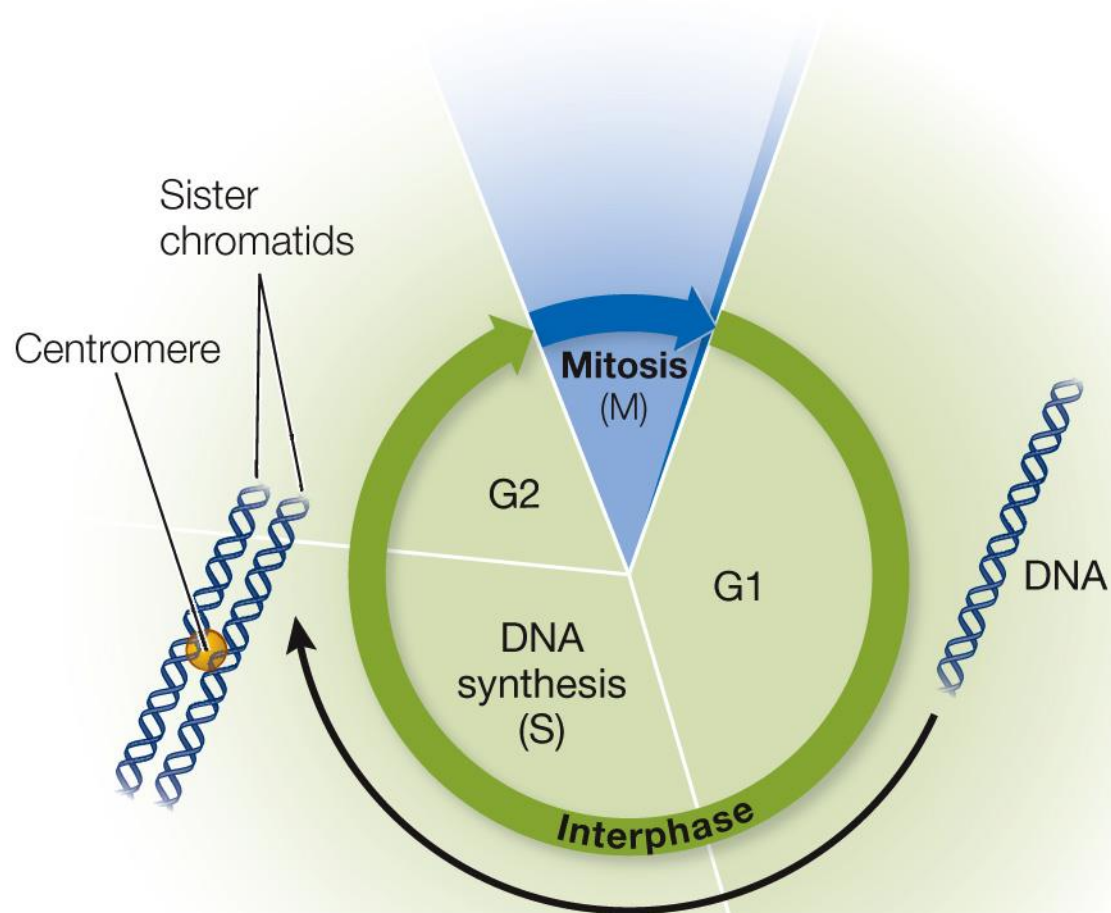
## 11.3 Eukaryotic Cells Divide by Mitosis

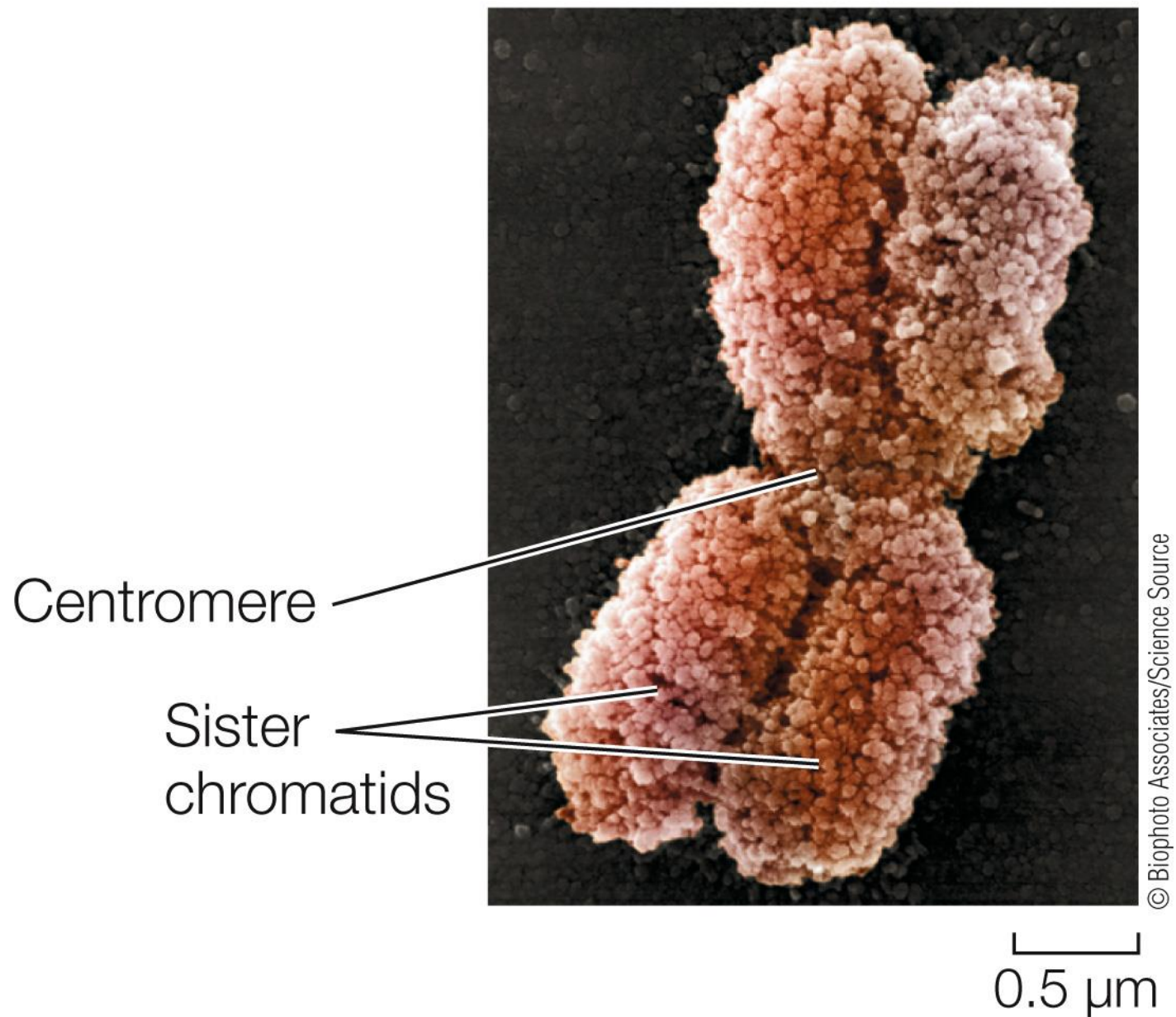
DNA molecules are bound to proteins to form **chromatin**.

After replication, sister chromatids are held together during G2 by proteins called cohesins.

At mitosis cohesin is removed, except at the **centromere**. Condensins coat the DNA molecules and make them more compact.

Figure 11.7 Chromosomes, Chromatids, and Chromatin (Part 1)





## 11.3 Eukaryotic Cells Divide by Mitosis

Eukaryotic DNA molecules are “packed” and organized by histones—proteins with positive charges that attract the negative phosphate groups of DNA.

Interactions result in the formation of beadlike units, or **nucleosomes**.



Figure 11.8 DNA Is Packed into a Mitotic Chromosome (Part 1)

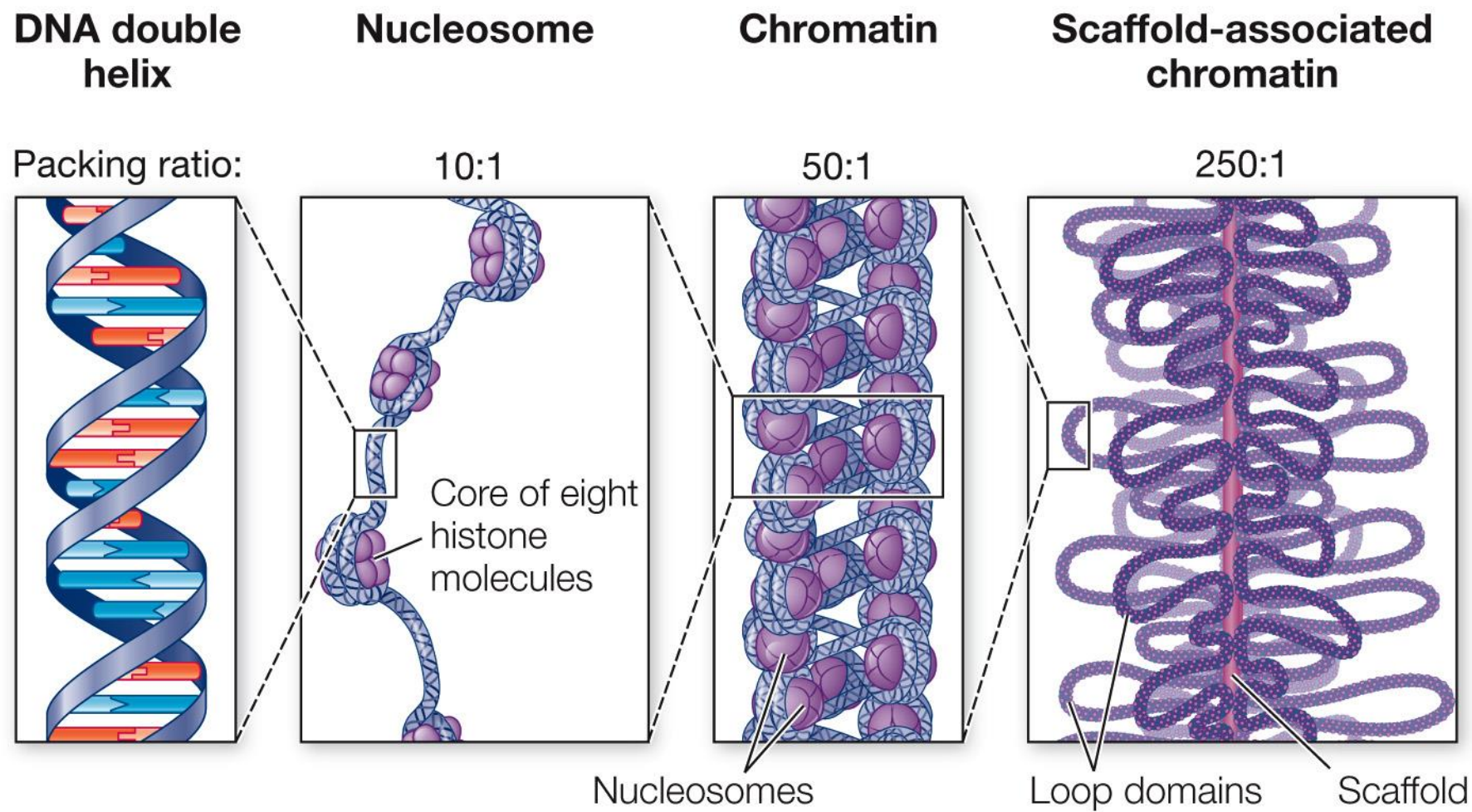
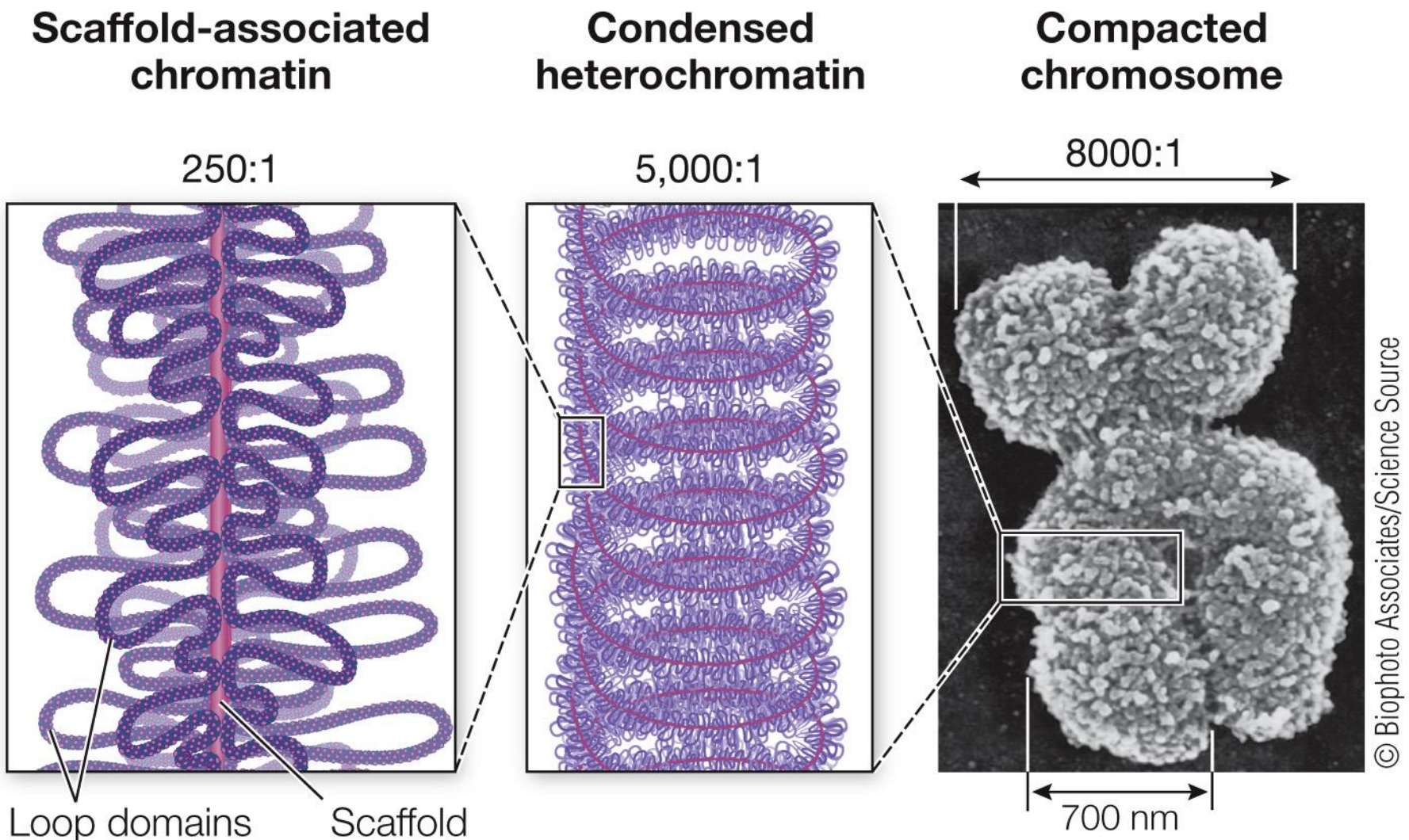


Figure 11.8 DNA Is Packed into a Mitotic Chromosome (Part 2)





**table 11.2** Summary of Cell Cycle Events

| Phase              | Events   |
|--------------------|--|
| <b>Interphase:</b> |  |
| G1                 | Growth; restriction point at end                             |
| S                  | DNA replication  |
| G2                 | Spindle synthesis begins; preparation for mitosis            |
| <b>Mitosis:</b>    |  |
| Prophase           | Condensation of chromosomes; spindle assembly                |
| Prometaphase       | Nuclear envelope breakdown; chromosome attachment to spindle |
| Metaphase          | Alignment of chromosomes at equatorial plate                 |
| Anaphase           | Separation of chromatids; migration to poles                 |
| Telophase          | Chromosomes decondense; nuclear envelope re-forms            |
| Cytokinesis        | Cell separation; cell membrane and/or wall formation         |

### The **spindle apparatus**

- Moves sister chromatids apart
- Made of microtubules
- Orientation is determined by the **centrosome**, an organelle near the nucleus

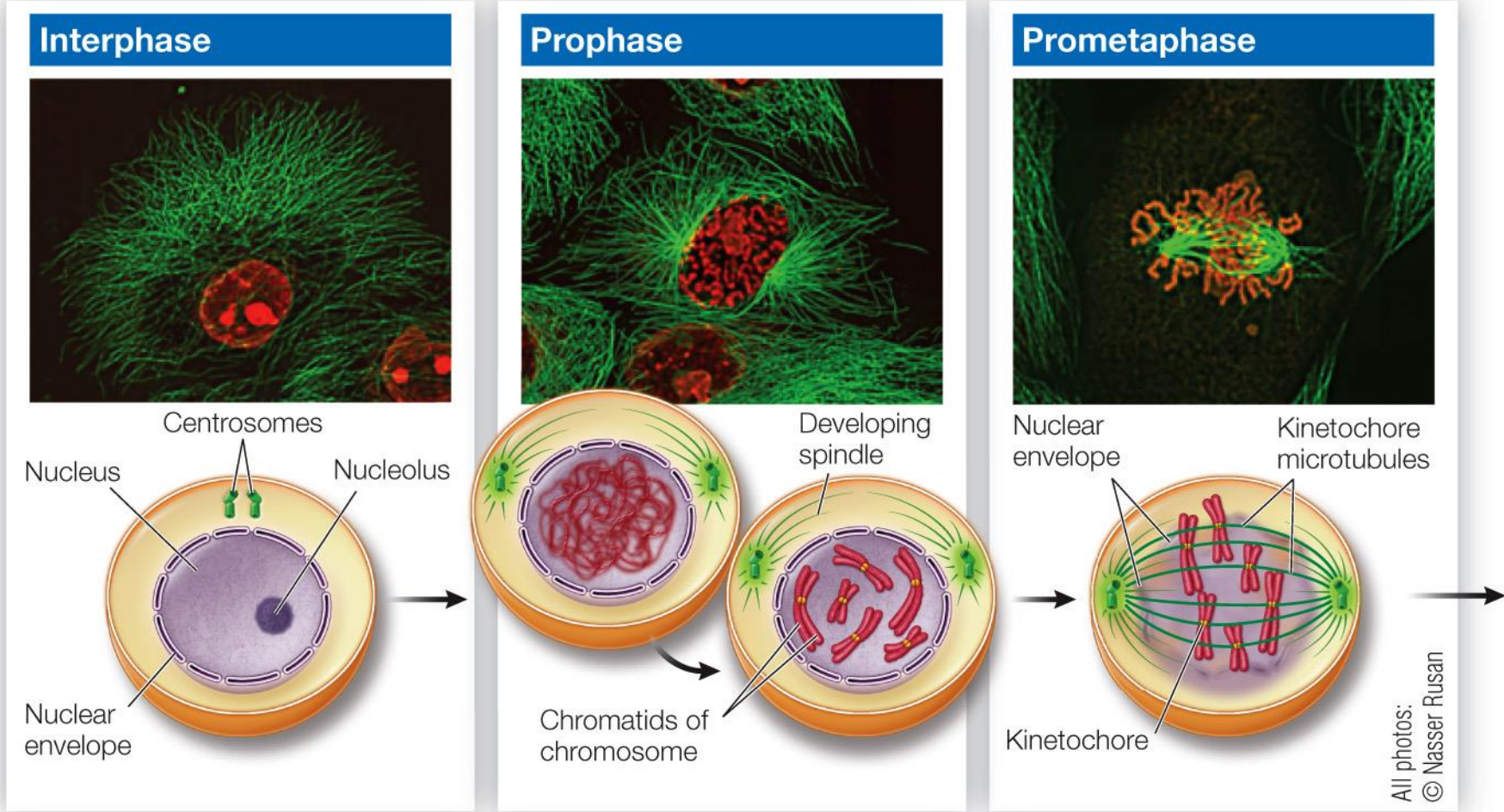
## 11.3 Eukaryotic Cells Divide by Mitosis

Centrosomes replicate during S phase; during prophase, they move to opposite ends of the nuclear envelope.

- They identify the “poles” toward which the chromosomes move.

Late in prophase, **kinetochores** develop on each chromatid.

Figure 11.9 The Phases of Mitosis in an Animal Cell (Part 1)

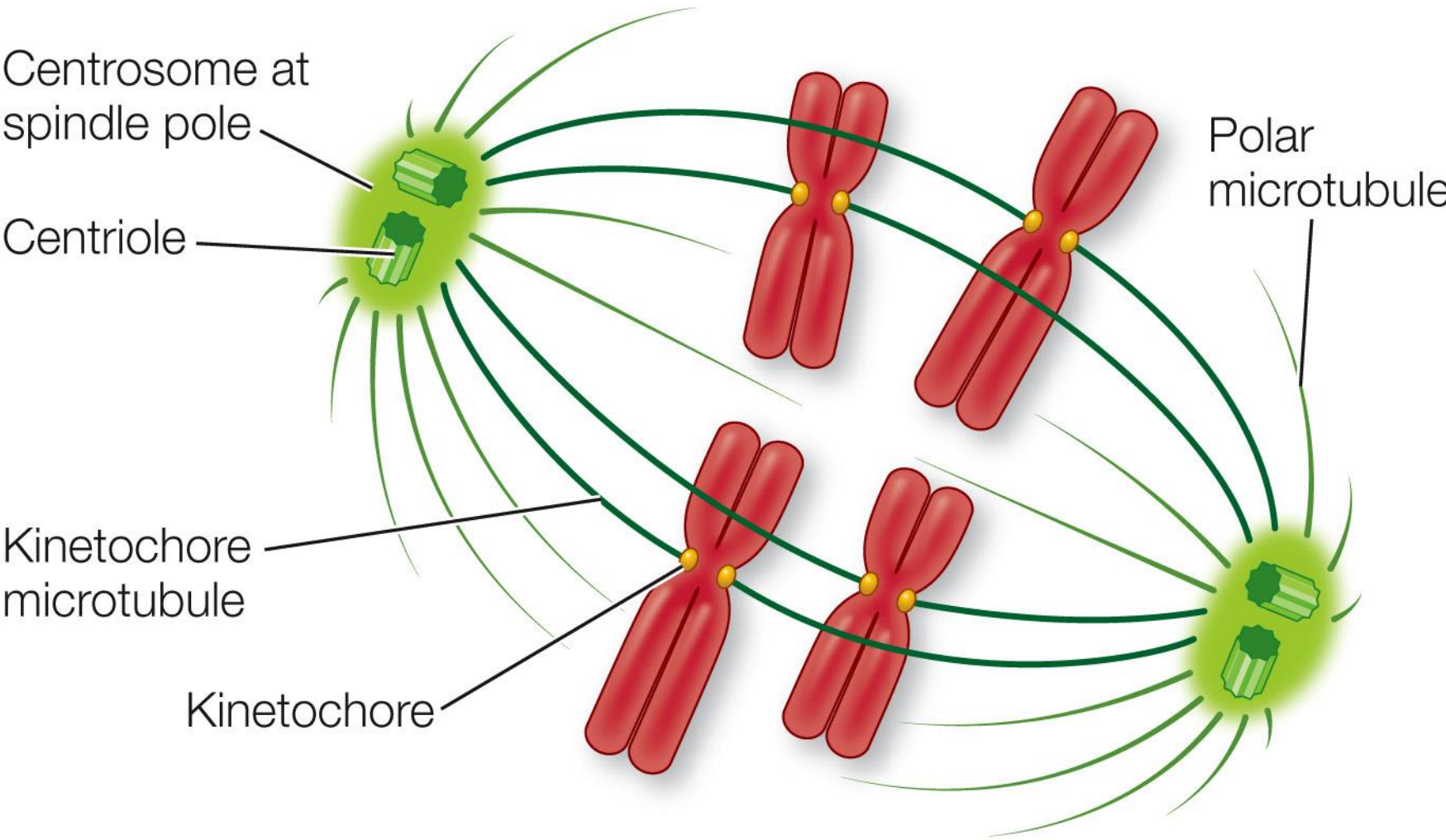


## 11.3 Eukaryotic Cells Divide by Mitosis

Two types of microtubules in the spindle:

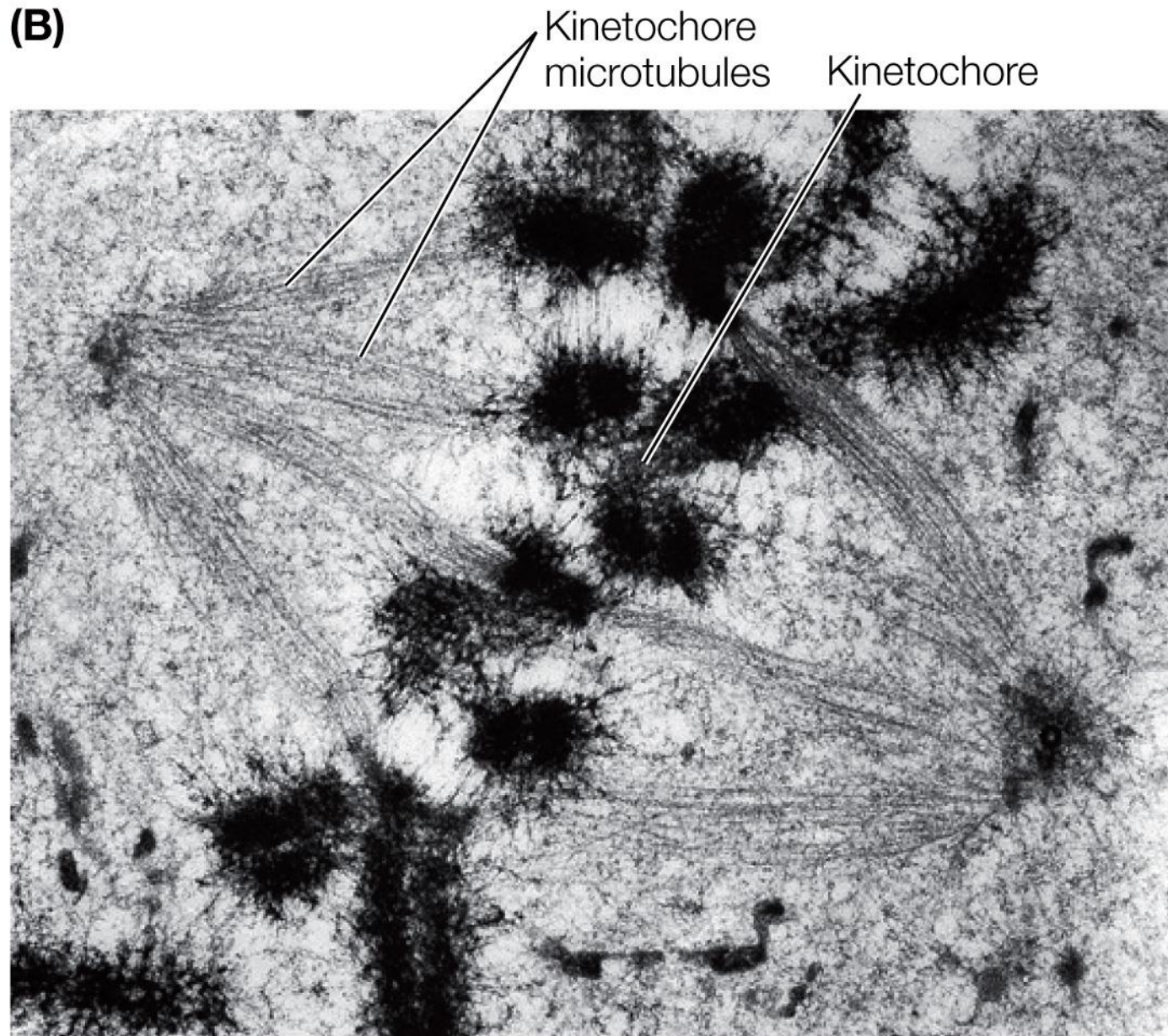
- Polar microtubules form spindle framework
- Kinetochore microtubules attach to kinetochores and to microtubules in opposite halves of the spindle.

(A)





**(B)**



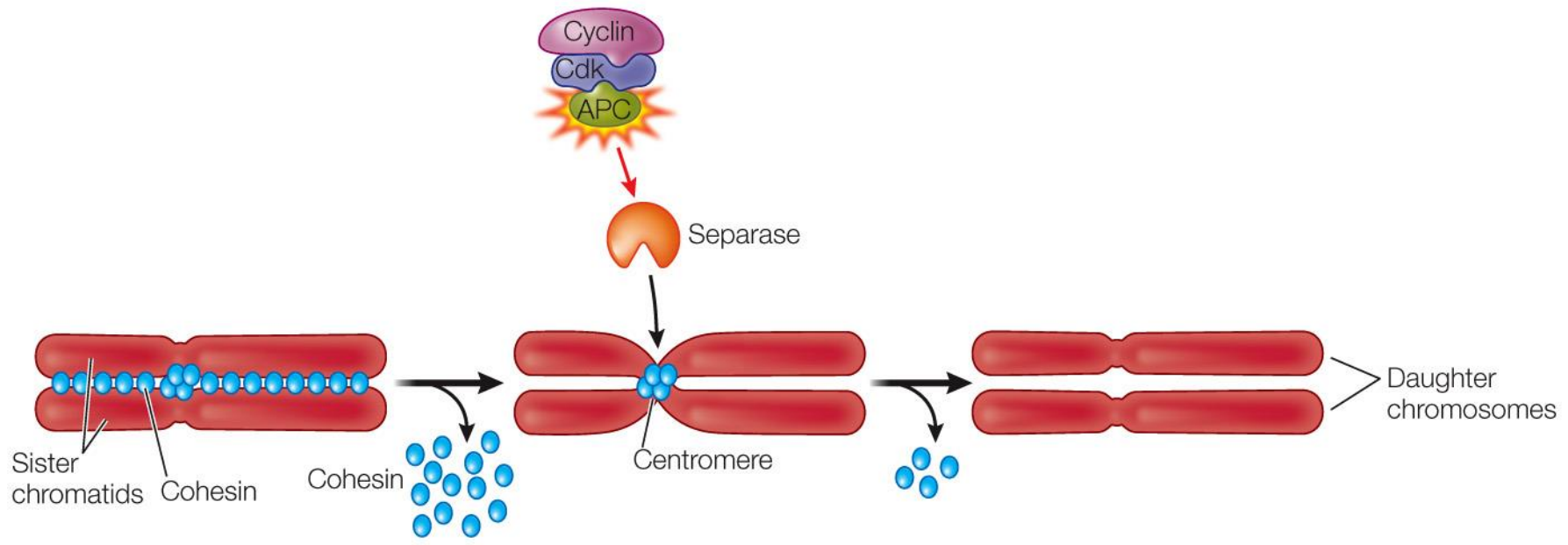
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## 11.3 Eukaryotic Cells Divide by Mitosis

During anaphase, separation of sister chromatids is controlled by M phase cyclin–Cdk; it activates anaphase-promoting complex (APC).

Cohesin that holds the chromatids together is hydrolyzed by separase.

Figure 11.11 Chromatid Attachment and Separation



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## 11.3 Eukaryotic Cells Divide by Mitosis

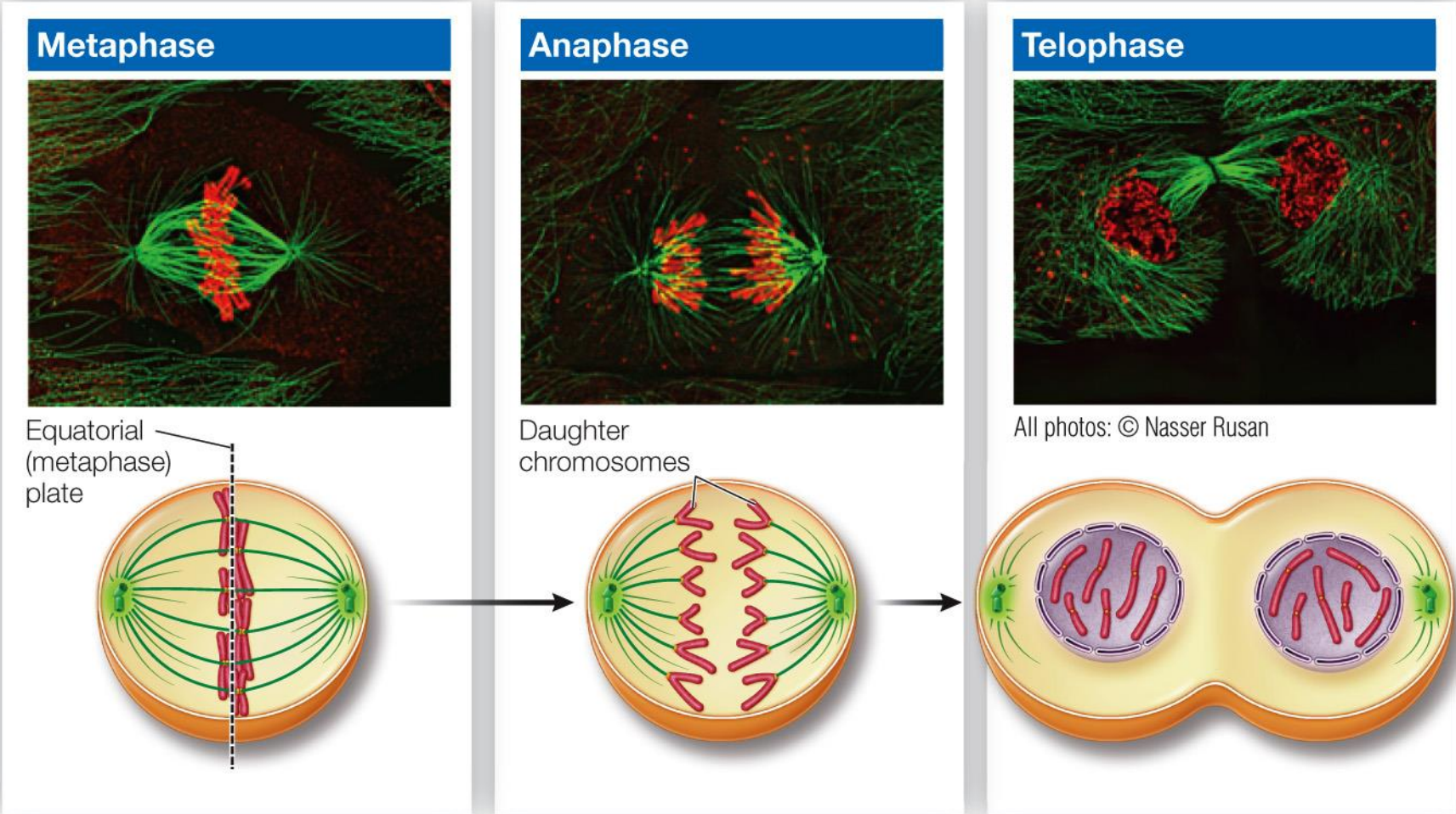
A spindle assembly checkpoint occurs at the end of metaphase.

It inhibits APC if a chromosome is not attached properly to the spindle.

When all are attached, APC is activated and the chromatids separate.



Figure 11.9 The Phases of Mitosis in an Animal Cell (Part 2)



## 11.3 Eukaryotic Cells Divide by Mitosis

After separation, the chromatids are called **daughter chromosomes**.

- Chromatids share a centromere.
- Chromosomes have their own centromere.

# the centrosome cycle

## 1 Centriole disengagement

The tight link between mother and daughter centrioles is severed. The centrioles are still connected by a loose fibrous structure.

## 2 Centrosome duplication

The mother and daughter centrioles duplicate themselves—new centrioles form near their proximal ends. This takes place during S-phase, at the same time as when the cell duplicates its DNA.

## 3 Centriole engagement

The newly formed centrioles reach full length. Meanwhile, the original daughter centriole becomes a mother centriole, and the link between the two is severed.

## 4 Centrosome maturation

The two centriole pairs, now centrosomes, collect additional pericentriolar material.

## 5 Centrosome separation

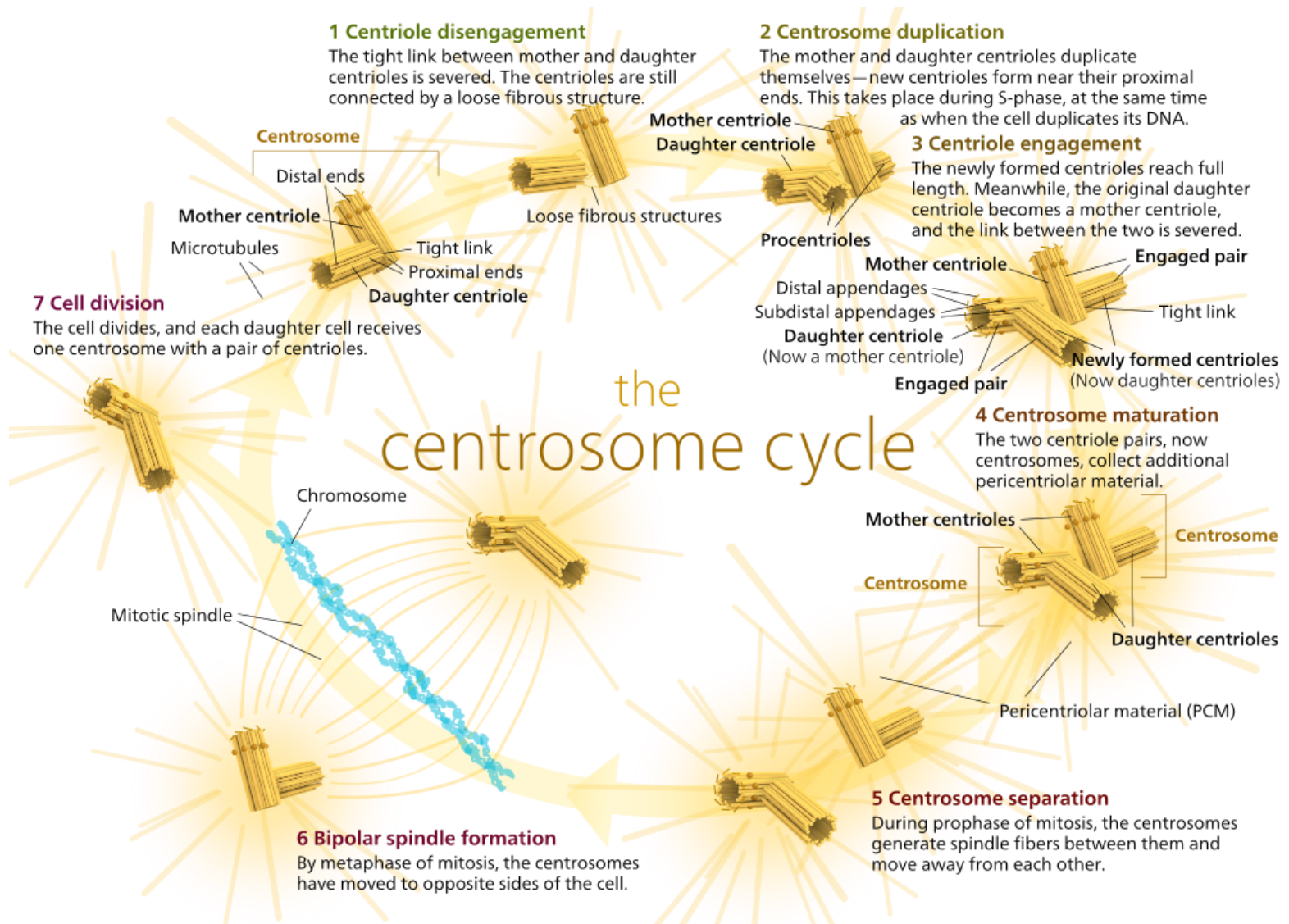
During prophase of mitosis, the centrosomes generate spindle fibers between them and move away from each other.

## 6 Bipolar spindle formation

By metaphase of mitosis, the centrosomes have moved to opposite sides of the cell.

## 7 Cell division

The cell divides, and each daughter cell receives one centrosome with a pair of centrioles.

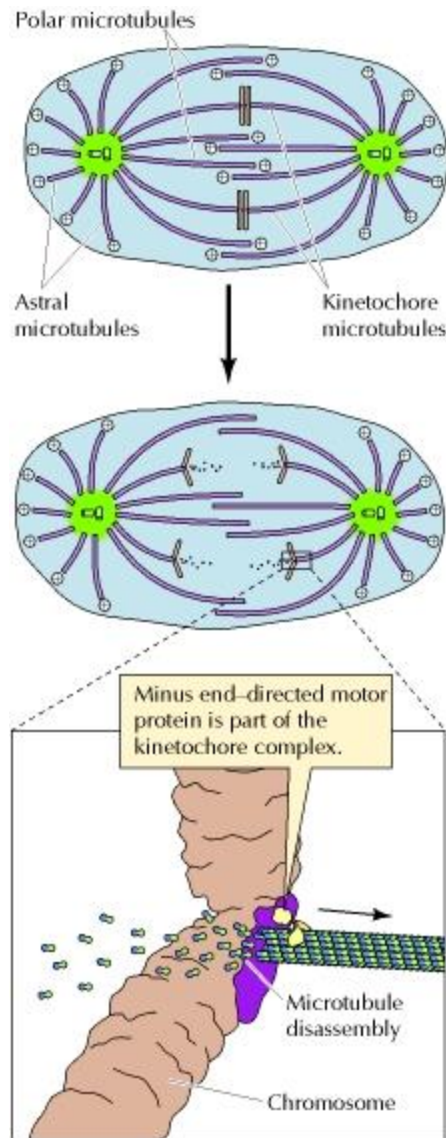


## 11.3 Eukaryotic Cells Divide by Mitosis

Three mechanisms move the chromosomes:

- Kinetochores have motor proteins—kinesins and cytoplasmic dynein.
- Kinetochore microtubules also shorten, drawing chromosomes toward poles.
- The centrosomes move apart, aiding in separation.

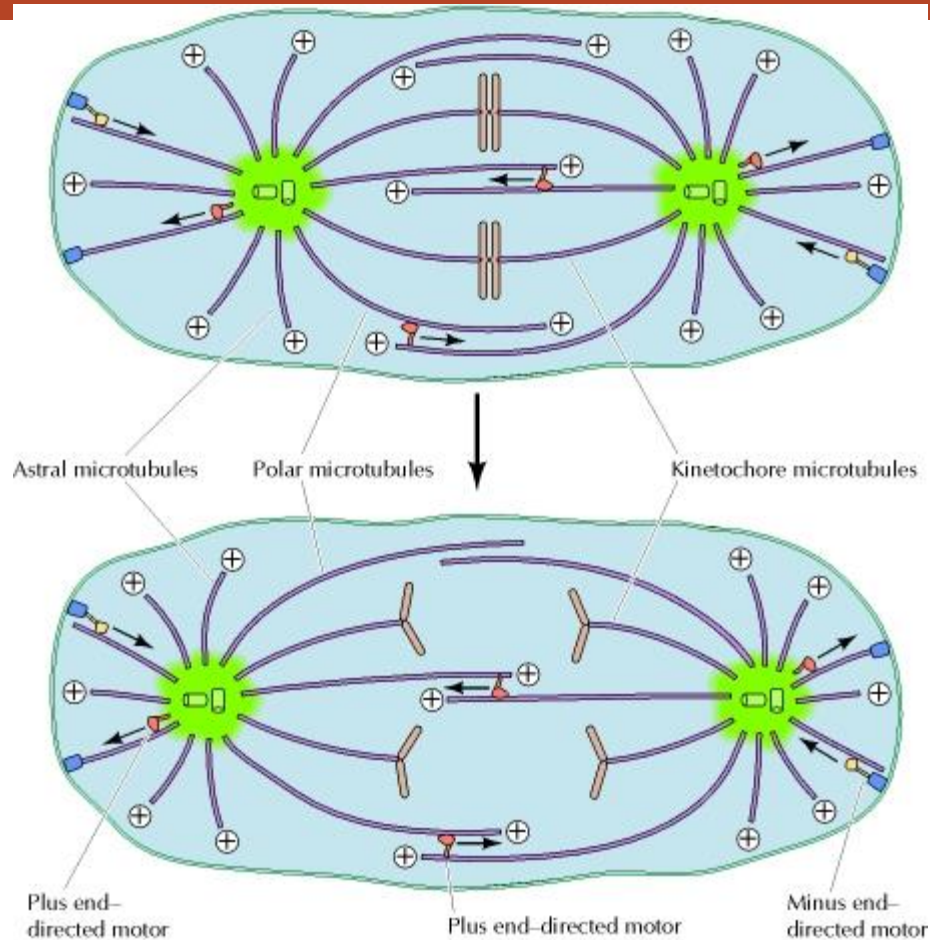




## Anaphase A chromosome movement

Chromosomes move toward the spindle poles along the [kinetochore microtubules](#).

Chromosome movement is thought to be driven by minus end-directed motor [proteins](#) associated with the kinetochore. The action of these motor proteins is coupled to disassembly and shortening of the kinetochore microtubules.



## Spindle pole separation in anaphase B

The separation of spindle poles results from two types of movement. First, overlapping [polar microtubules](#) slide past each other to push the spindle poles apart, probably as a result of the action of plus end-directed motor [proteins](#). Second, the spindle poles are pulled apart by the [astral microtubules](#). The driving force could be either a minus end-directed motor anchored to a cytoplasmic structure, such as the [cell cortex](#), or a plus end-directed motor associated with the spindle pole.

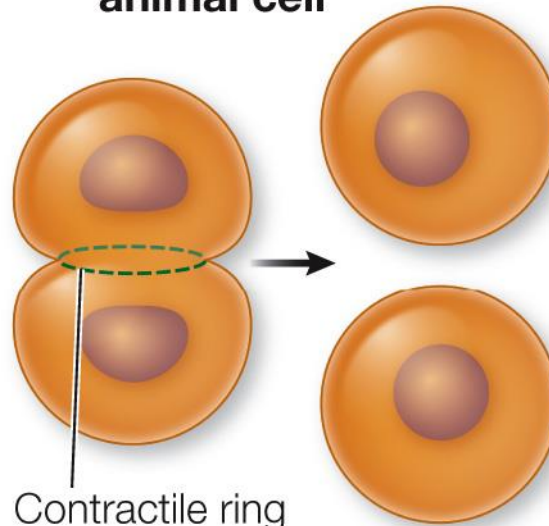
## 11.3 Eukaryotic Cells Divide by Mitosis

Cytokinesis: Division of the cytoplasm.

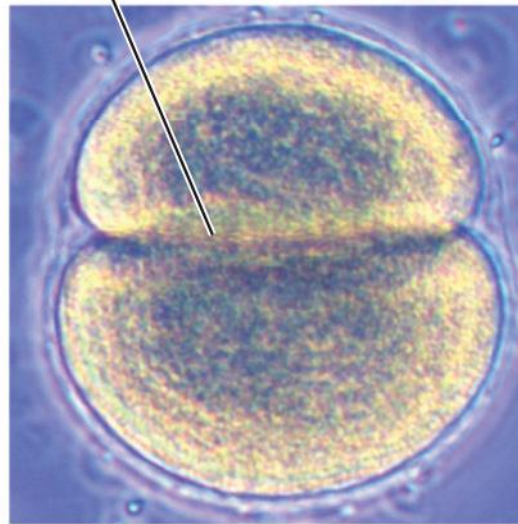
In animal cells the plasma membrane pinches in between the nuclei.

- A contractile ring of microfilaments of actin and myosin forms; the proteins interact to contract and pinch the cell in two.

**(A) Cytokinesis of an animal cell**

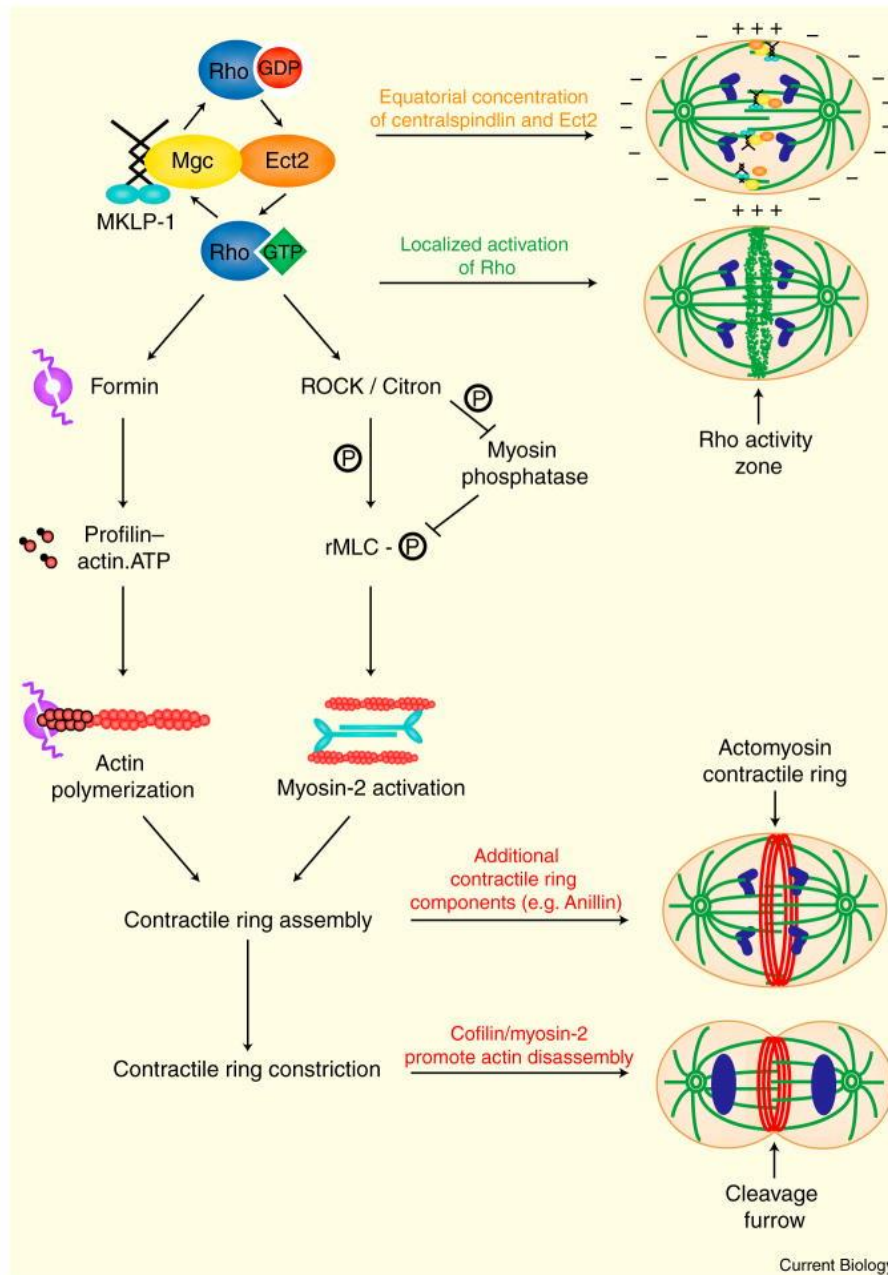


Contractile ring



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50  $\mu\text{m}$





## Key Concept 11.4 Focus Your Learning

- Asexual reproduction occurs via mitosis whereas sexual reproduction occurs via meiosis and mitosis.
- All sexual life cycles involve haploid and diploid phases.

## 11.4 Cell Division Plays Important Roles in the Sexual Life Cycle

**Sexual reproduction:** Offspring are not identical to the parents.

**Gametes** are created by meiosis; each parent contributes one gamete to an offspring.

Gametes and offspring differ genetically from each other and from the parents. Meiosis generates genetic diversity that is the raw material of evolution.



## 11.4 Cell Division Plays Important Roles in the Sexual Life Cycle

**Somatic cells:** Body cells *not* specialized for reproduction.

- Each somatic cell has **homologous pairs** of chromosomes with corresponding genes.
- Each parent contributes one **homolog** to an offspring.

## 11.4 Cell Division Plays Important Roles in the Sexual Life Cycle

Gametes contain only one set of chromosomes—one homolog of each pair.

- Chromosome number is **haploid** ( $n$ ).

**Fertilization:** 2 haploid gametes fuse to form a **diploid zygote**.

- Chromosome number =  $2n$ .

## 11.4 Cell Division Plays Important Roles in the Sexual Life Cycle

Evolution has generated many different versions of the sexual life cycle, but

- All involve meiosis to produce haploid cells
- Fertilization and meiosis alternate
- Haploid ( $n$ ) cells or organisms alternate with diploid ( $2n$ ) cells or organisms

Figure 11.14 Fertilization and Meiosis Alternate in Sexual Reproduction (Part 1)

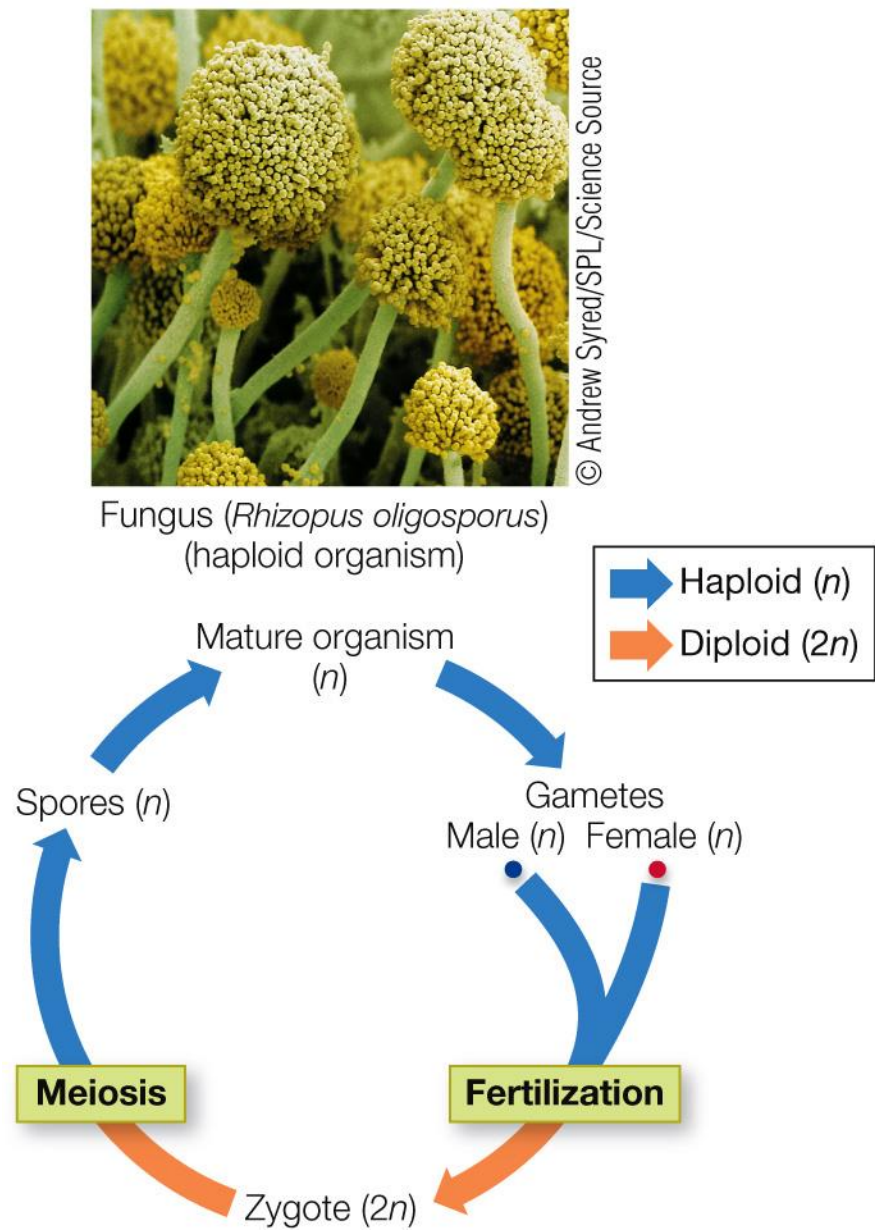
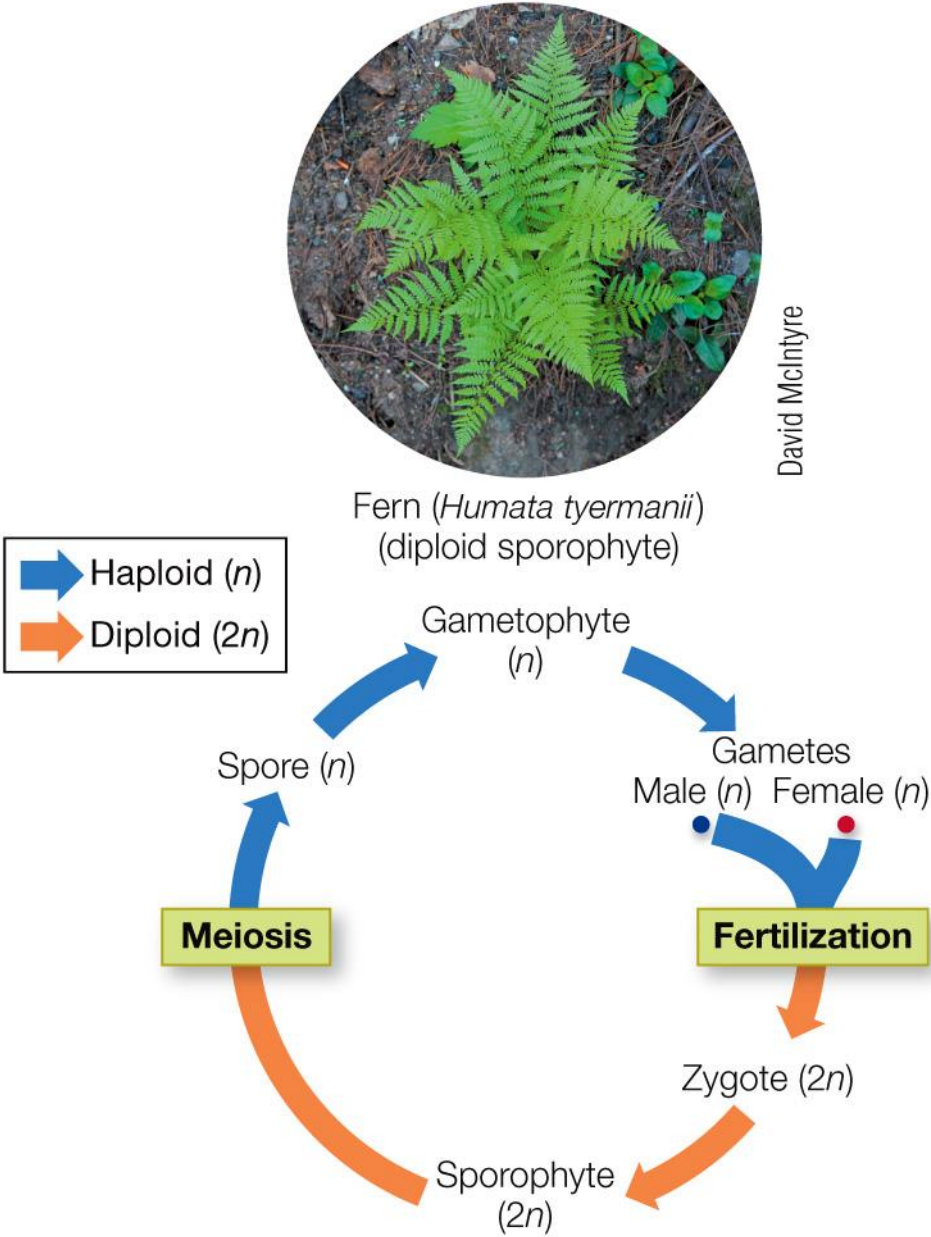
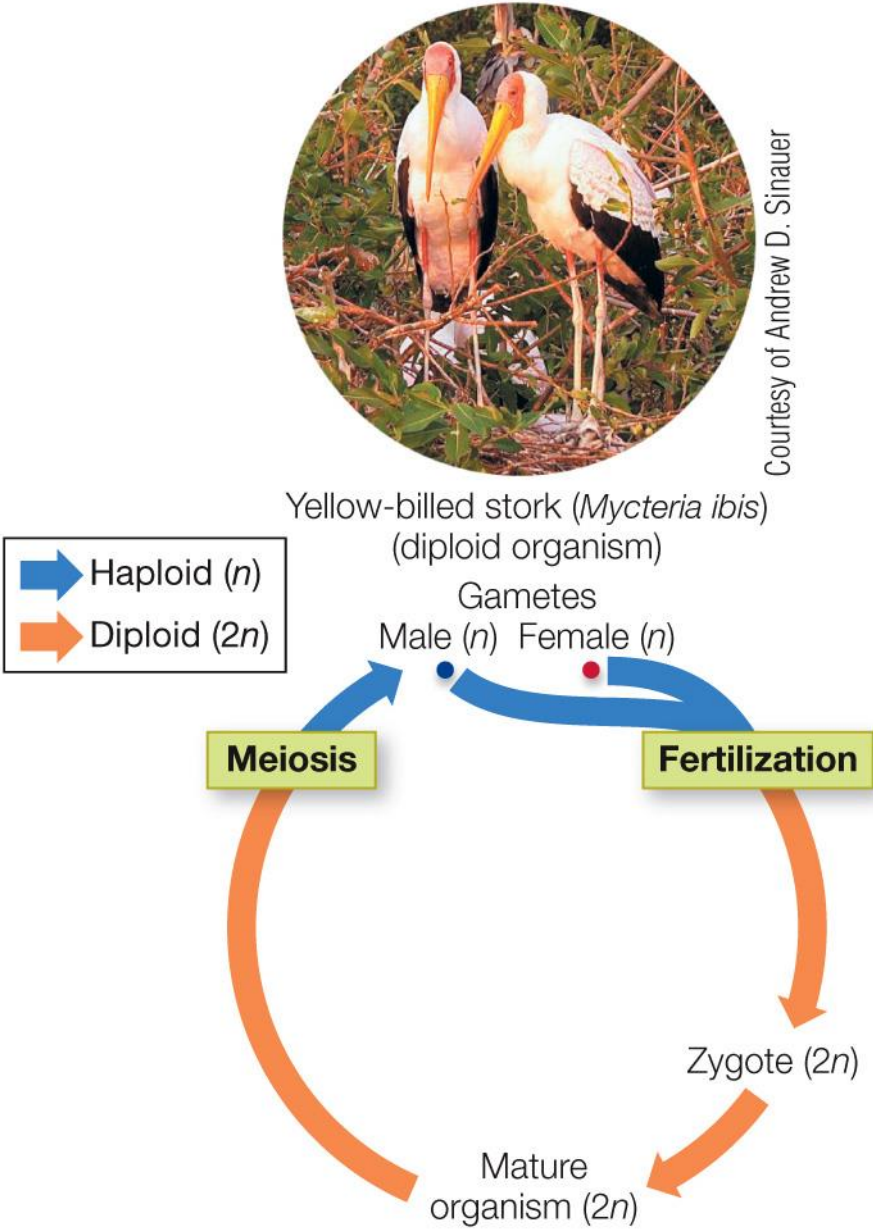


Figure 11.14 Fertilization and Meiosis Alternate in Sexual Reproduction (Part 2)



David McIntyre

Figure 11.14 Fertilization and Meiosis Alternate in Sexual Reproduction (Part 3)



## Key Concept 11.5 Focus Your Learning

- Gametes, the products of meiosis, are genetically different from each other and from the parent cell.
- Recombination events during meiosis increase genetic variability in gametes.
- Random gene combinations in gametes result from events during meiosis.
- Meiotic errors and other events introduce additional genetic variation in gametes.

## 11.5 Meiosis Leads to the Formation of Gametes

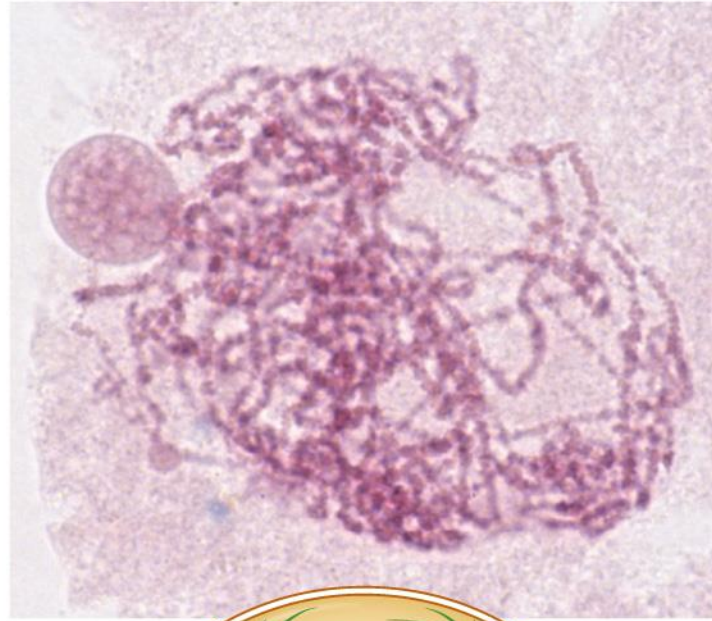
**Meiosis:** Two nuclear divisions, but DNA is replicated only once.

### **Meiosis I:**

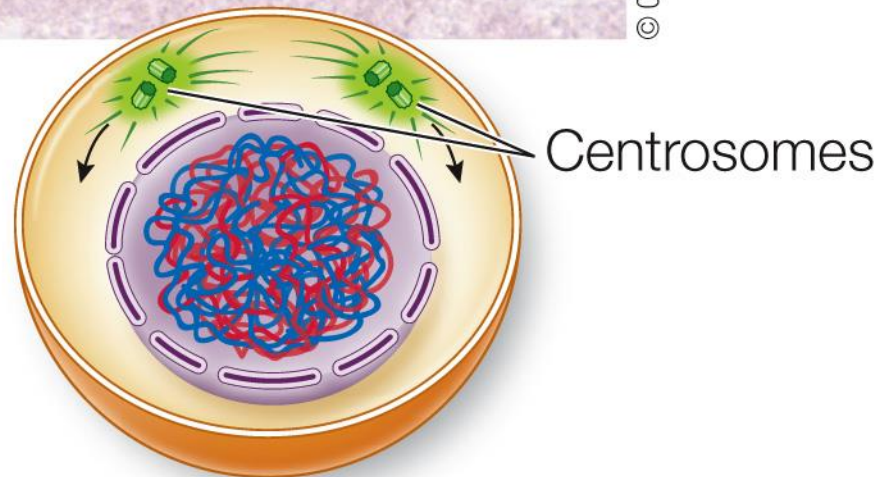
- Preceded by DNA replication in S phase.
- Homologous chromosome pairs separate, but the individual chromosomes (sister chromatids), stay together.



## Early prophase I



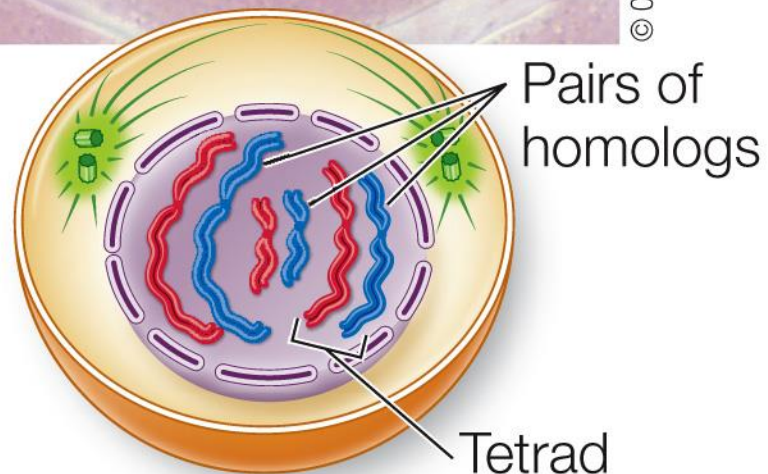
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## Mid-prophase I



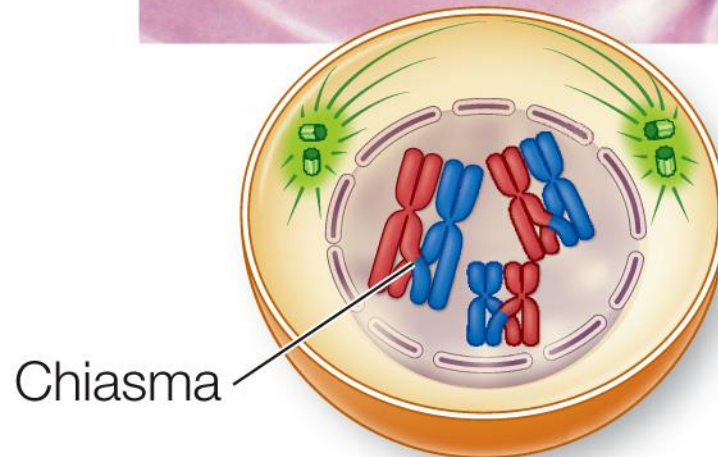
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## Late prophase I– Prometaphase



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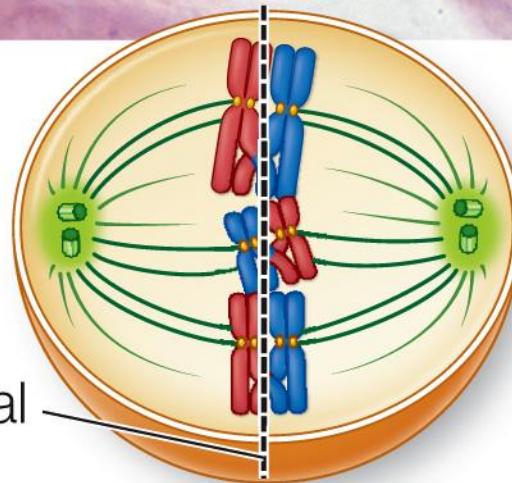


Chiasma

## Metaphase 1



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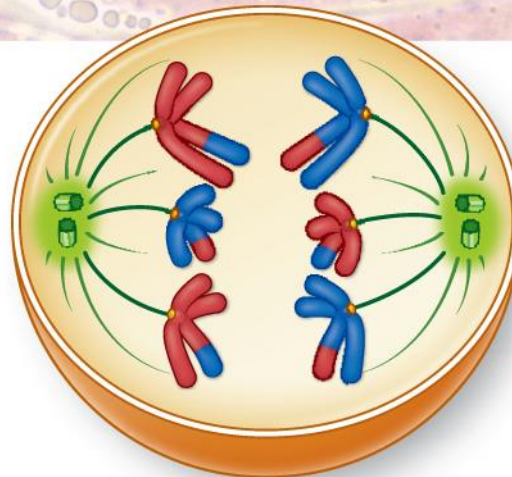
Equatorial  
plate



## Anaphase I



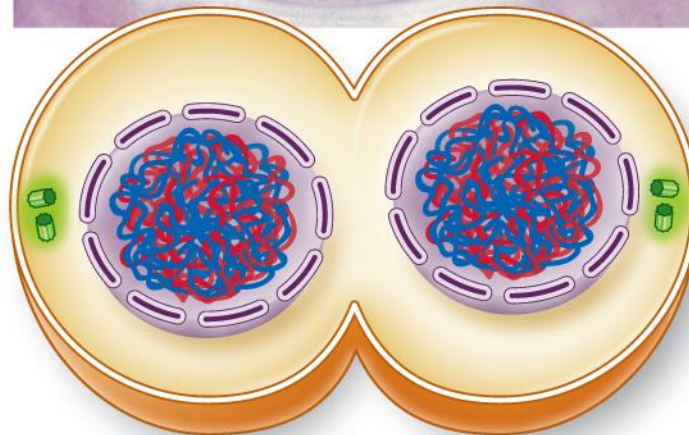
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## Telophase I



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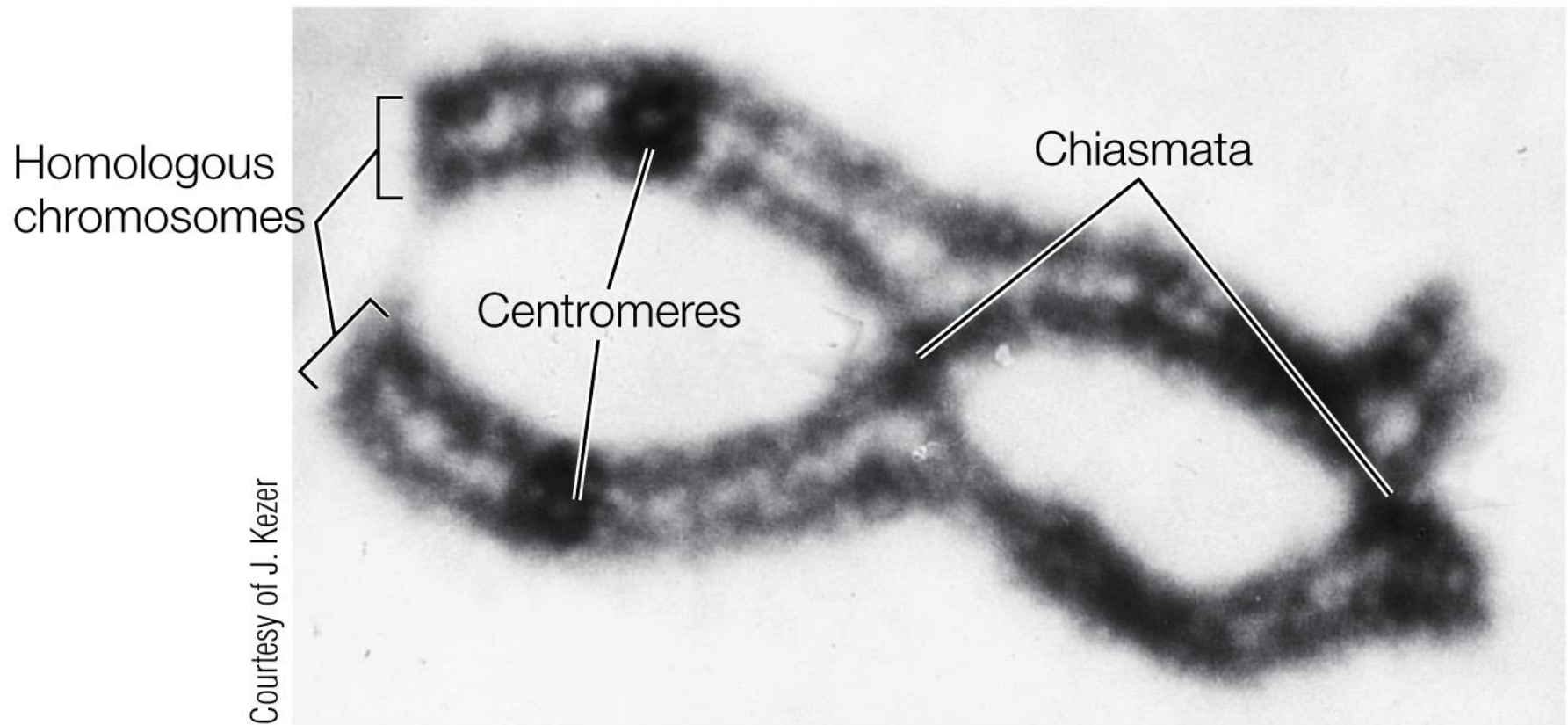


## 11.5 Meiosis Leads to the Formation of Gametes

Prophase I: Homologous chromosomes pair by adhering along their lengths: **synapsis**.

The 4 chromatids of each homologous pair form a **tetrad**.

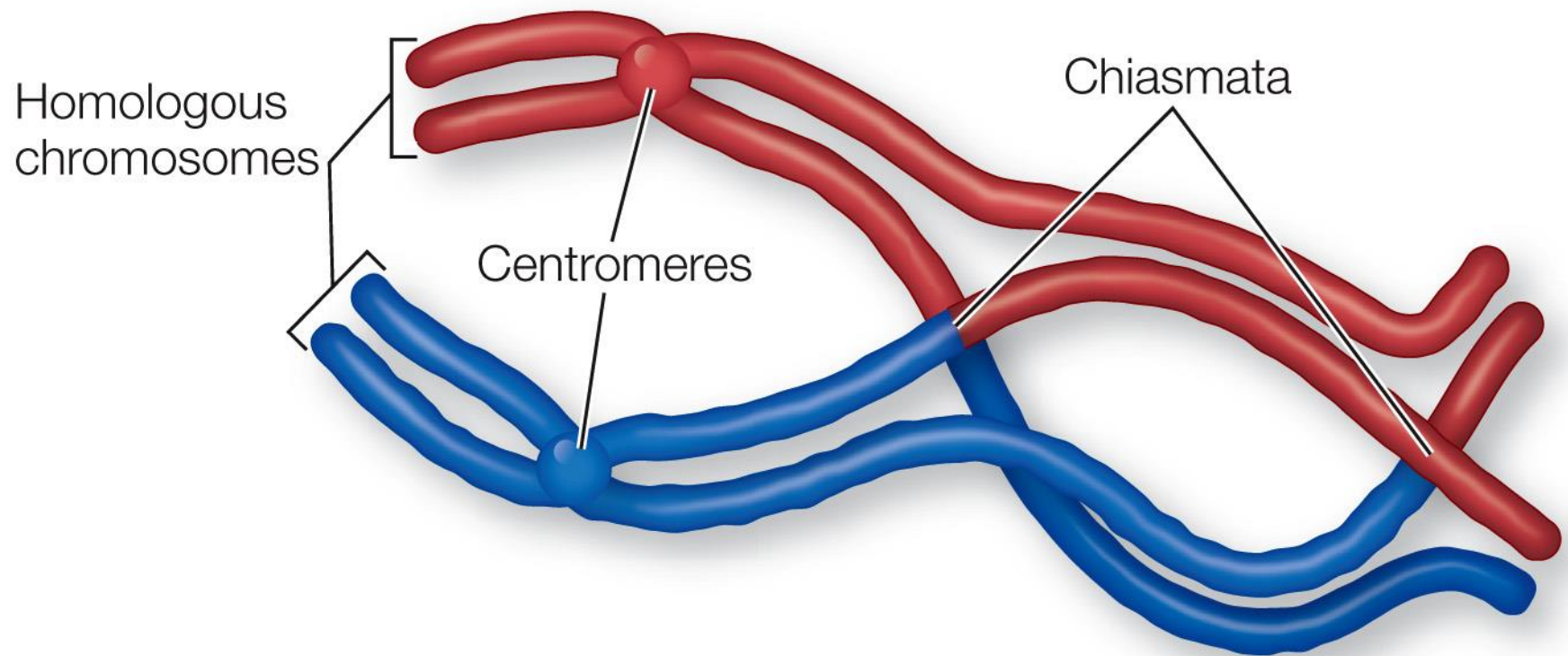
**Chiasmata:** Regions of attachment that form between nonsister chromatids.



*LIFE: THE SCIENCE OF BIOLOGY 11e*, Figure 11.16 (Part 1)

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*LIFE: THE SCIENCE OF BIOLOGY 11e*, Figure 11.16 (Part 2)  
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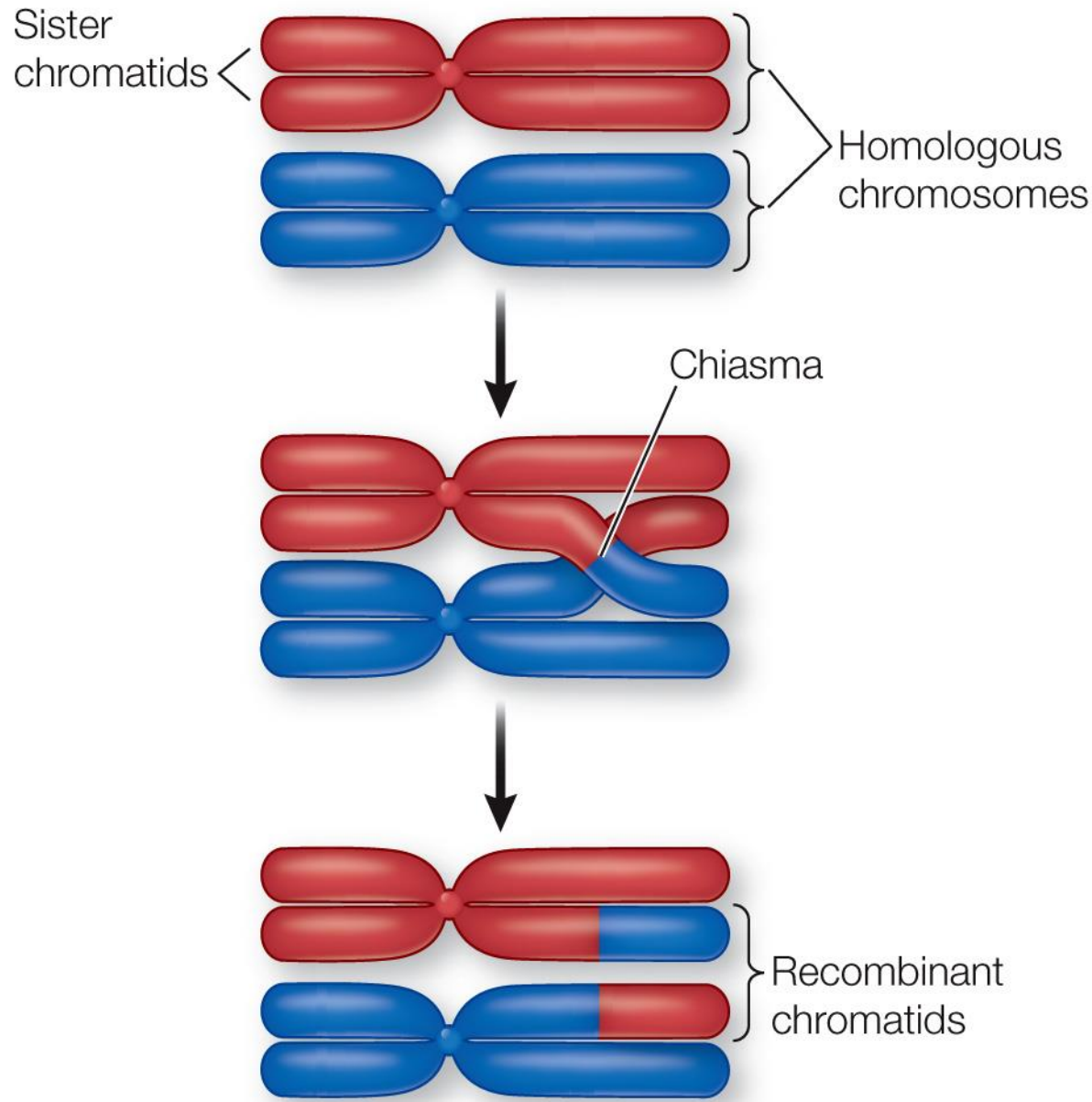
Singular: chiasma

## 11.5 Meiosis Leads to the Formation of Gametes

**Crossing over:** Exchange of genetic material between nonsister chromatids at the chiasmata.

Crossing over results in **recombinant chromatids** and increases genetic variability of the products.

Figure 11.17 Crossing Over Forms Genetically Diverse Chromosomes



## 11.5 Meiosis Leads to the Formation of Gametes

Crossing over is one reason for genetic diversity in meiosis I products.

**Independent assortment** also allows for chance combinations.

- It is a matter of chance how the homologous chromosomes line up in anaphase I and which ones go to which daughter cell.

Figure 11.18 Mitosis and Meiosis: A Comparison (Part 1)

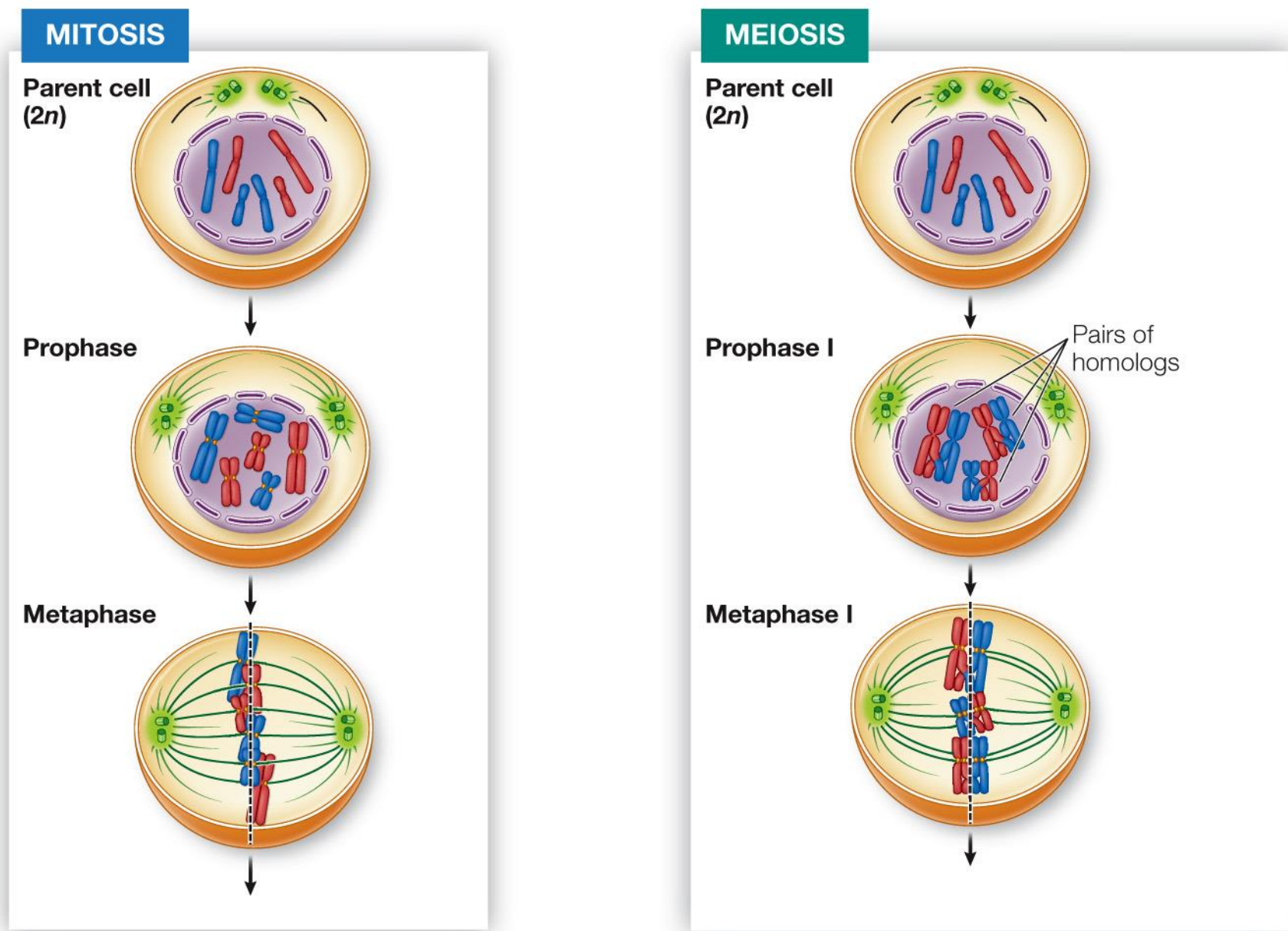
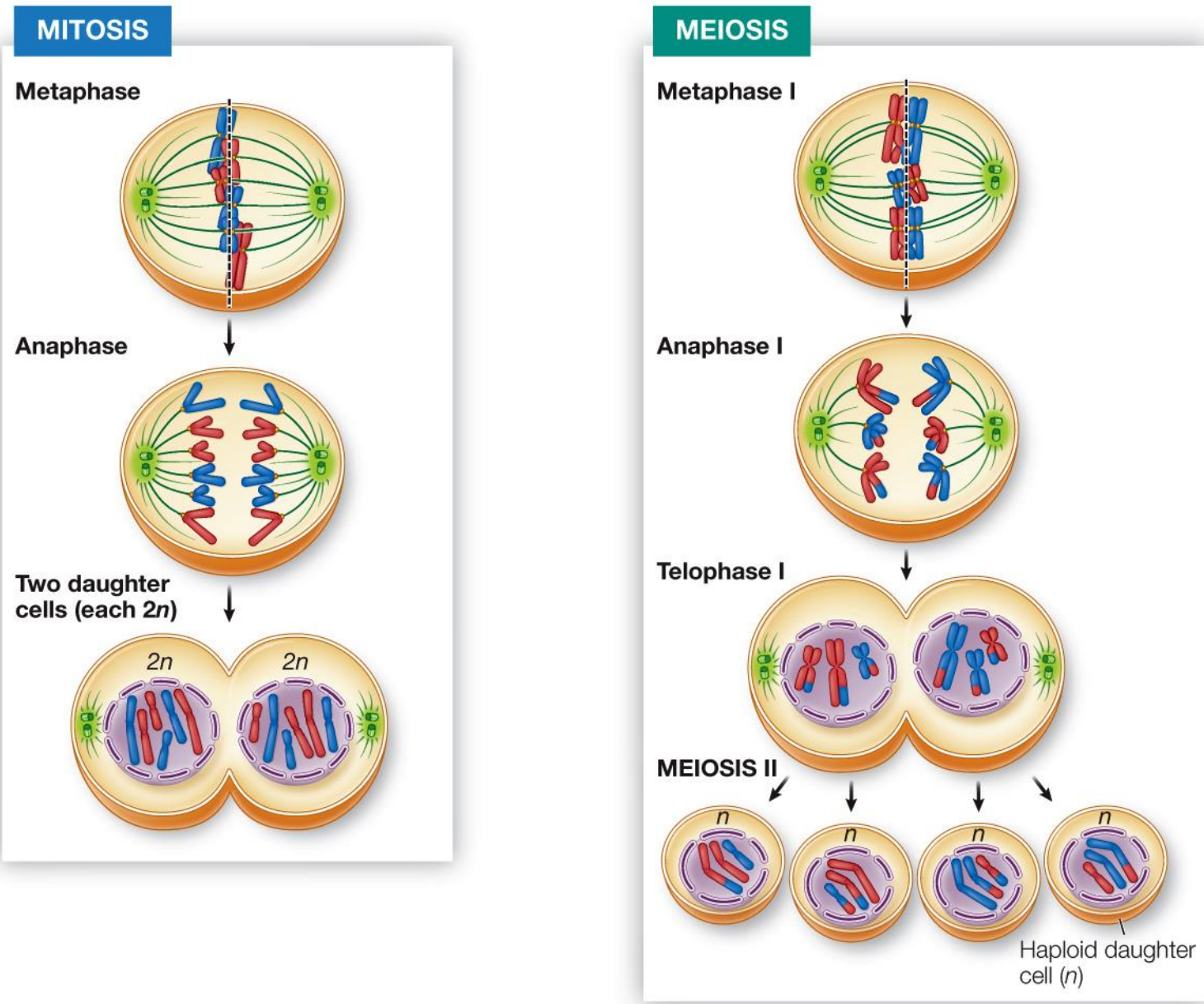
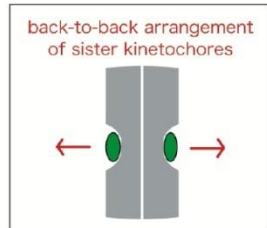




Figure 11.18 Mitosis and Meiosis: A Comparison (Part 2)



## MITOSIS



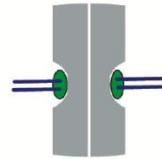
### attachment:

kinetochores in  
relation to spindle poles

### orientation:

chromosome in  
relation to spindle poles

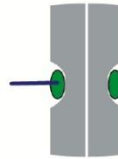
sister kinetochores  
attached to  
opposite poles



amphitelic

bi-orientation

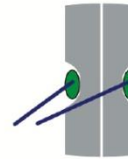
only one of the  
sister kinetochores  
attached to one pole



monotelic

(monotelic)  
mono-orientation

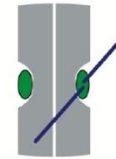
both sister kinetochores  
attached to  
the same pole



syntelic

(syntelic)  
mono-orientation

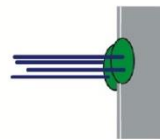
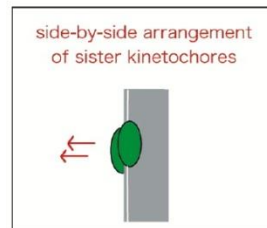
one of the  
sister kinetochores  
attached to both poles



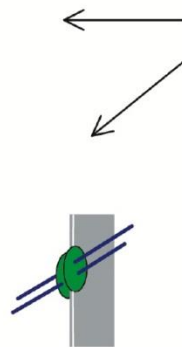
merotelic

(merotelic)  
bi-orientation

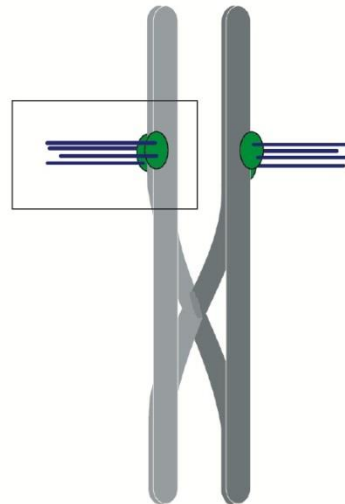
## MEIOSIS I



mono-orientation of  
sister kinetochores



bi-orientation of  
sister kinetochores  
(side-by-side arrangement  
can be preserved or not)



bi-orientation of  
bivalent



mono-orientation  
of bivalent

### **Meiosis II:**

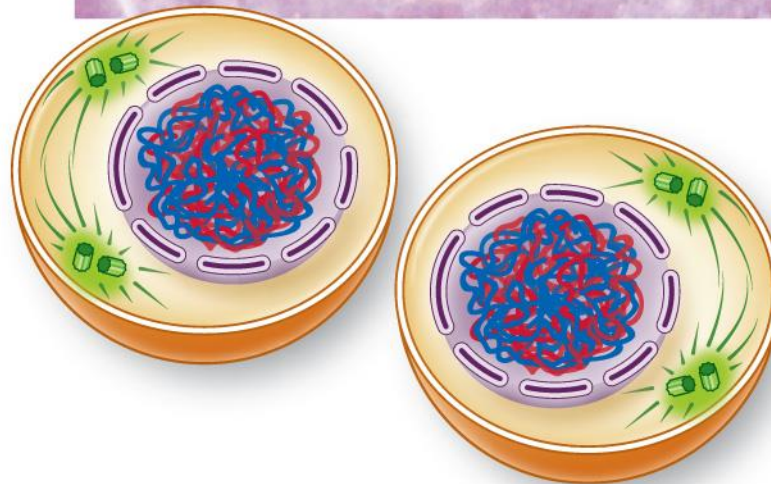
- Not preceded by DNA replication
- Sister chromatids are separated
- Chance assortment of the chromatids contributes to genetic diversity
- Final products are four haploid daughter cells ( $n$ )



## Prophase II



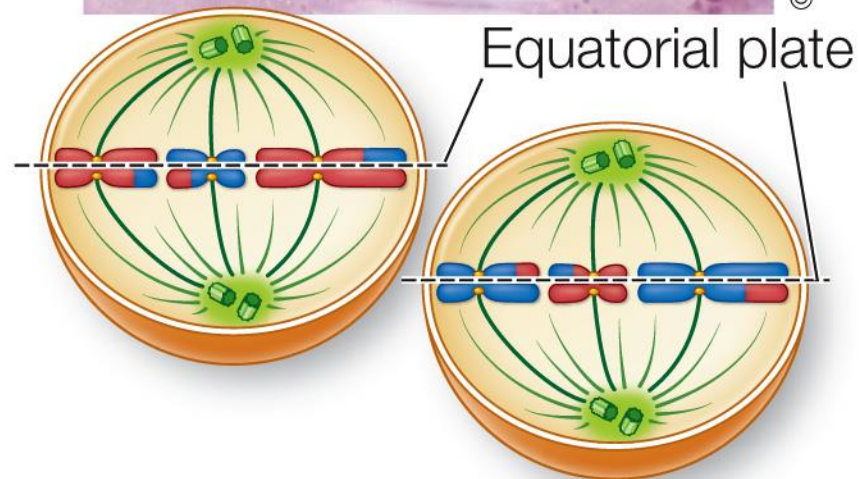
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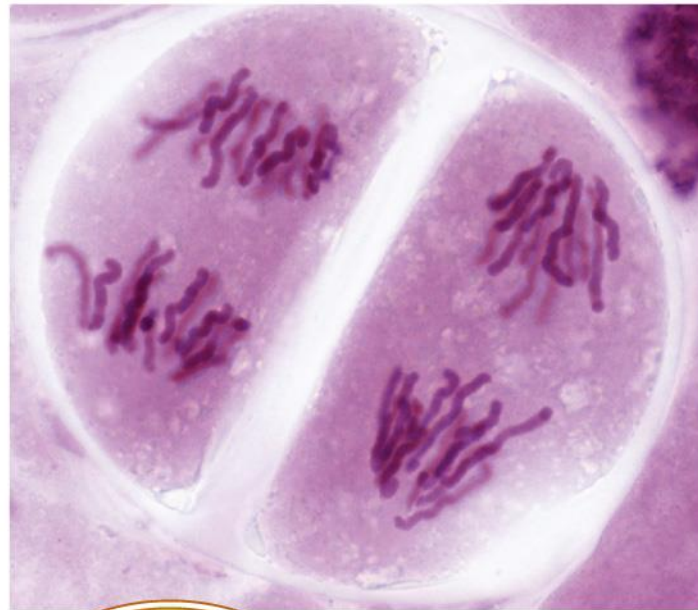
## Metaphase II



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## Anaphase II



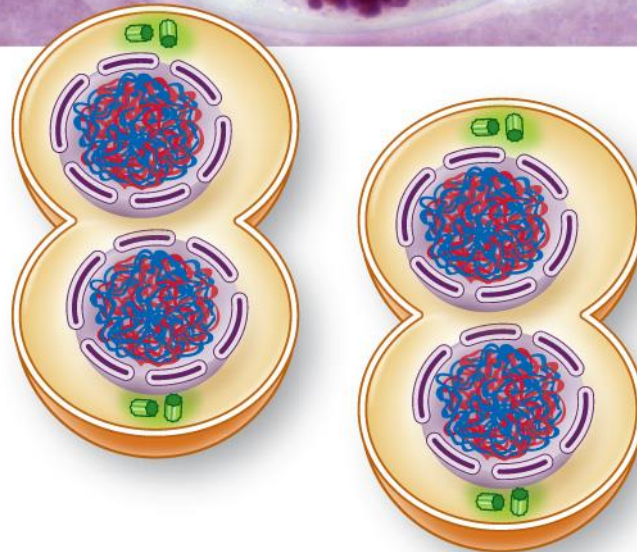
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## Telophase II

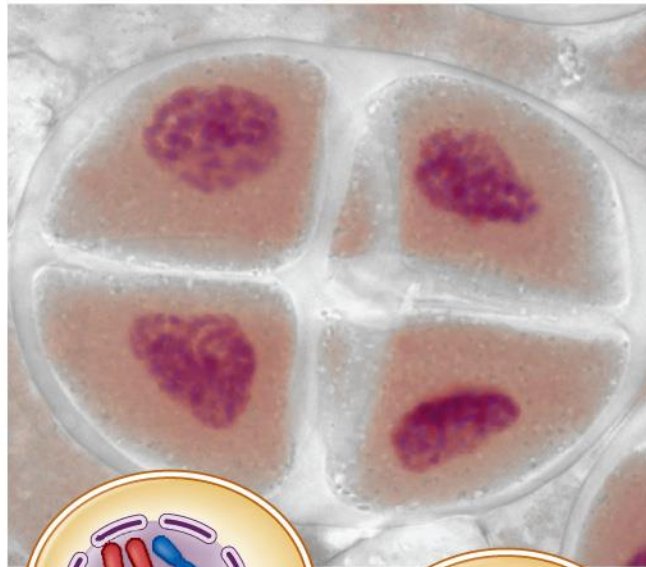


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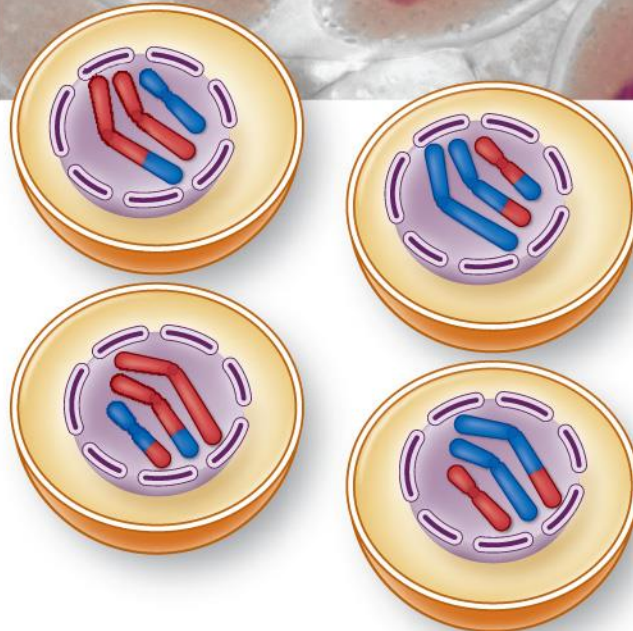


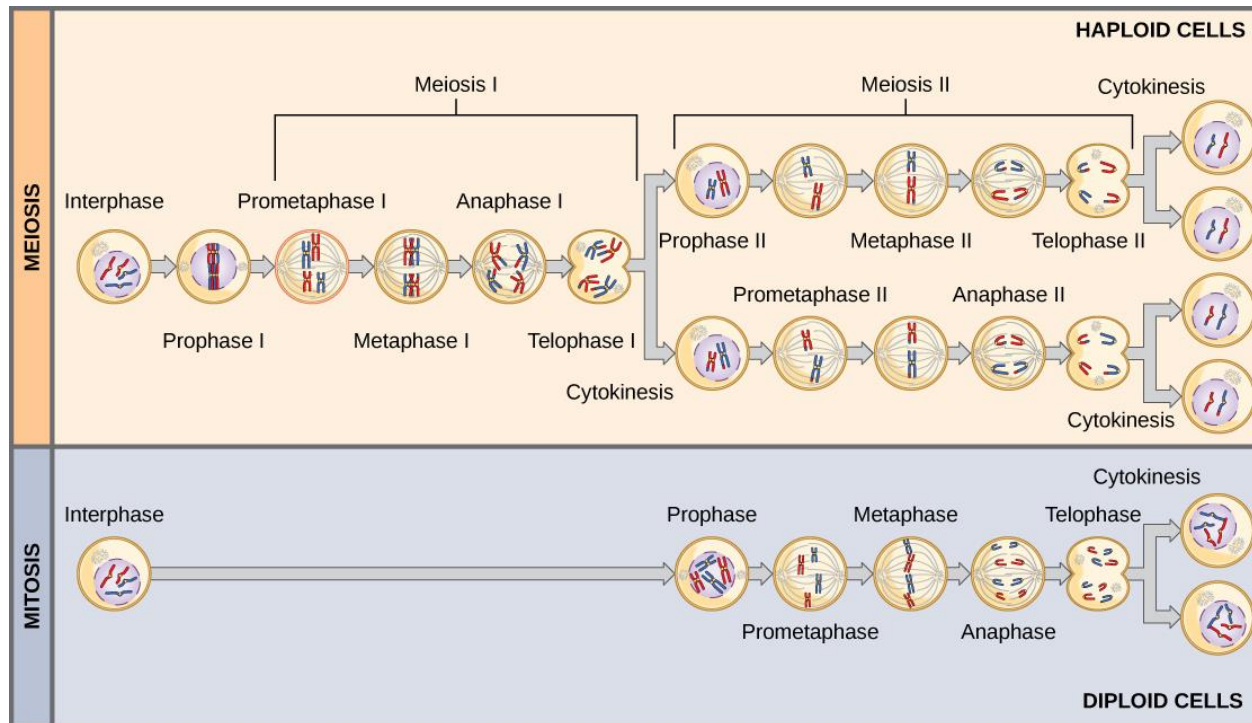


## Products



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|         |                                 |                                    |                           |   |  | OUTCOME  |
|---------|---------------------------------|------------------------------------|---------------------------|---|--|--|
| PROCESS | DNA synthesis                   | Synapsis of homologous chromosomes | Crossover                 | Homologous chromosomes line up at metaphase plate | Sister chromatids line up at metaphase plate | Number and genetic composition of daughter cells |
| MEIOSIS | Occurs in S phase of interphase | During prophase I                  | During prophase I         | During metaphase I                                | During metaphase II                          | Four haploid cells at the end of meiosis II      |
| MITOSIS | Occurs in S phase of interphase | Does not occur in mitosis          | Does not occur in mitosis | Does not occur in mitosis                         | During metaphase                             | Two diploid cells at the end of mitosis          |

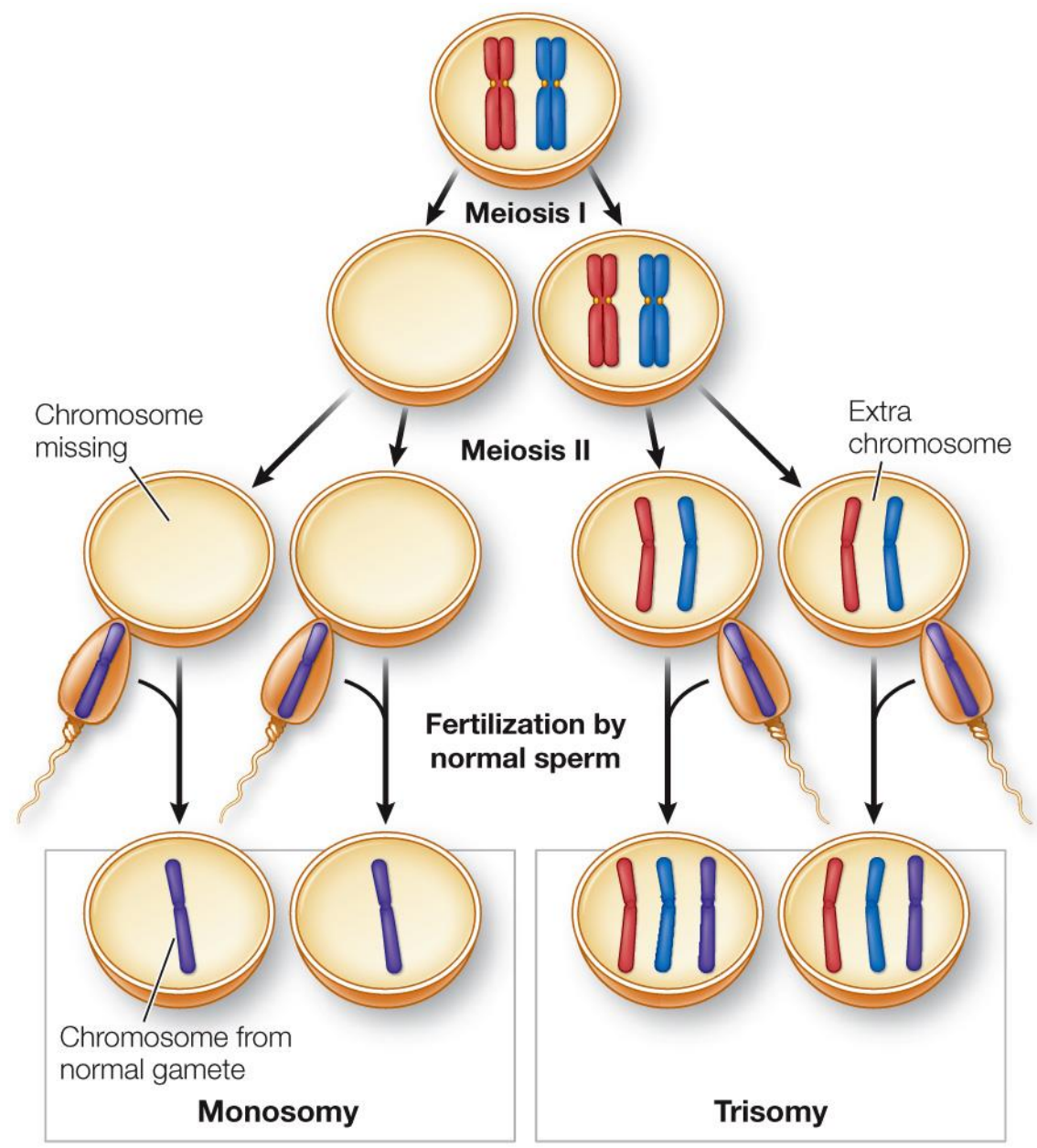
## 11.5 Meiosis Leads to the Formation of Gametes

There can be errors in meiosis.

- **Nondisjunction**

- Homologous pairs may fail to separate at anaphase I
- In meiosis II, sister chromatids may fail to separate
- Results in **aneuploidy**—chromosomes are either lacking or present in excess

Figure 11.19 Nondisjunction Leads to Aneuploidy





## 11.5 Meiosis Leads to the Formation of Gametes

Aneuploidy may be caused by lack of cohesins that hold the homologous pairs together.

Without cohesins both homologs may go to the same pole.

The resulting gametes will have two of the same chromosome or none.

## 11.5 Meiosis Leads to the Formation of Gametes

In humans, Down syndrome results from a gamete with two copies of chromosome 21. After fertilization, there are three copies (**trisomic**).

A fertilized egg that did not receive a copy of chromosome 21 will be **monosomic**, which is lethal.

## 11.5 Meiosis Leads to the Formation of Gametes

**Translocation:** A piece of chromosome may break away and attach to another chromosome.

An individual with a translocated piece of chromosome 21 plus two normal copies will have Down syndrome.

## 11.5 Meiosis Leads to the Formation of Gametes

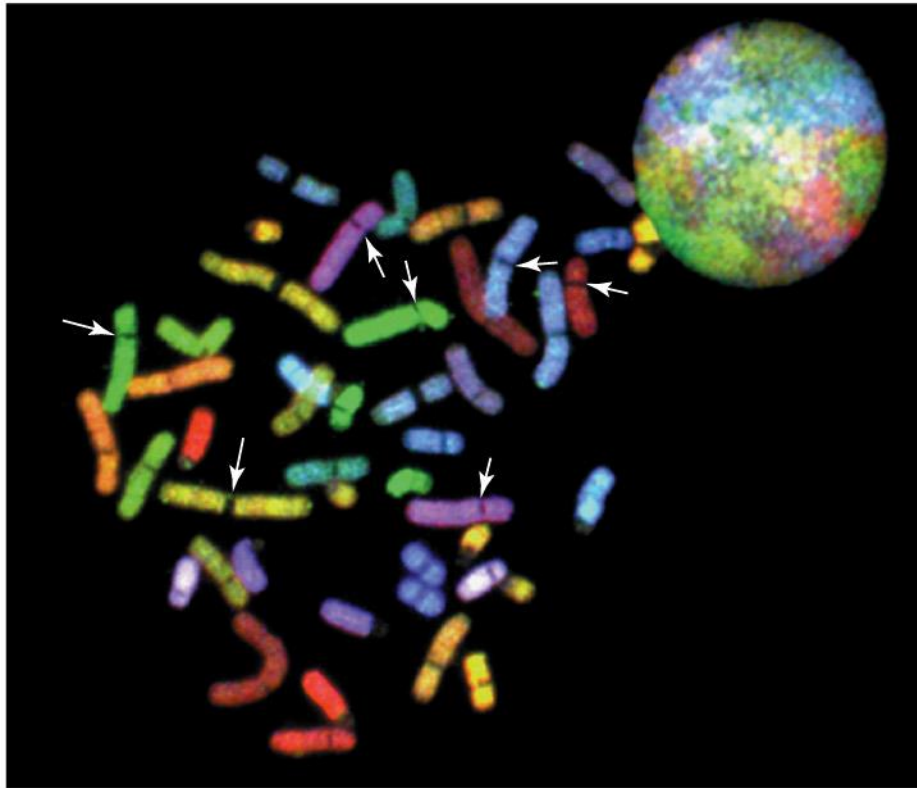
When cells are in metaphase of mitosis, the chromosomes can be counted.

The **karyotype** is the number, shapes, and sizes of all chromosomes of a cell.

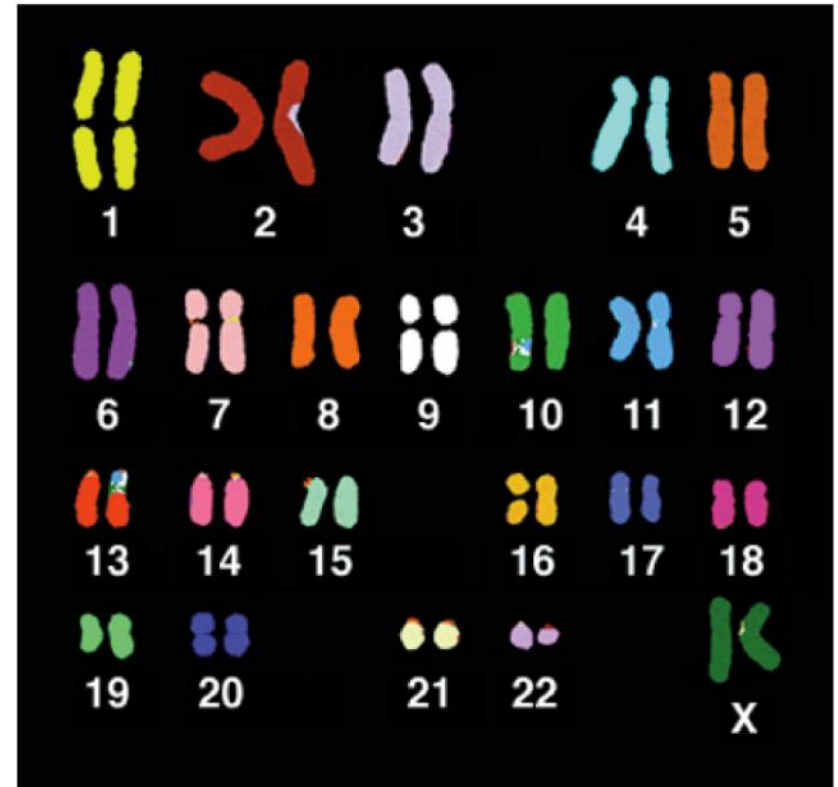
Karyotypes can be used to diagnose abnormalities such as trisomies, a branch of medicine called cytogenetics.

# Figure 11.20 The Human Karyotype

(A)



(B)



Courtesy of Dr. Thomas Ried and Dr. Evelin Schröck, NIH

*LIFE: THE SCIENCE OF BIOLOGY 11e*, Figure 11.20

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## 11.6 Cell Death Is Important in Living Organisms

Cell death occurs in two ways:

- **Necrosis:** Cell is damaged or starved of oxygen or nutrients.
  - The cell swells and bursts.
  - Cell contents are released to the extracellular environment and can cause inflammation.

## 11.6 Cell Death Is Important in Living Organisms

- **Apoptosis:** Programmed cell death.
  - Cells may no longer be needed (e.g., connective tissue between the fingers of a fetus).
  - Old cells are prone to genetic damage that can lead to cancer (e.g., epithelial cells may be exposed to radiation and toxins; they live only days or weeks).



## 11.6 Cell Death Is Important in Living Organisms

### Events of apoptosis:

- Cell detaches from its neighbors
- Chromatin is digested by enzymes that cut DNA between nucleosomes
- The cell forms membranous lobes called “blebs” that break into fragments
- Surrounding, living cells ingest remains of the dead cell and recycle the contents

## 11.6 Cell Death Is Important in Living Organisms

Signals that initiate apoptosis: hormones, growth factors, viral infections, toxins, extensive DNA damage.

The signals act through signal transduction pathways.

Some pathways affect mitochondria, increasing membrane permeability. ATP production stops and the cell dies.

## 11.6 Cell Death Is Important in Living Organisms

Proteases called **caspases** may be activated in apoptosis.

Caspases hydrolyze membrane proteins in nuclear and cell membranes and nucleosomes.

## Key Concept 11.7 Focus Your Learning

- Improperly controlled cell division and the ability to migrate are two characteristics that distinguish cancer cells from normal cells.
- Cell cycle abnormalities play an important role in the development of cancer.
- Cancer therapies are targeted to events in the cell cycle.

## 11.7 Unregulated Cell Division Can Lead to Cancer

Cancer cells lose control over cell division.

Normal cells divide in response to extracellular signals such as growth factors.

Cancer cells divide almost continuously, forming **tumors** (large masses of cells).

## 11.7 Unregulated Cell Division Can Lead to Cancer

**Benign** tumors grow slowly, resemble the tissue they grow from, and remain localized.

They are not cancerous but must be removed if they obstruct an organ or its function.

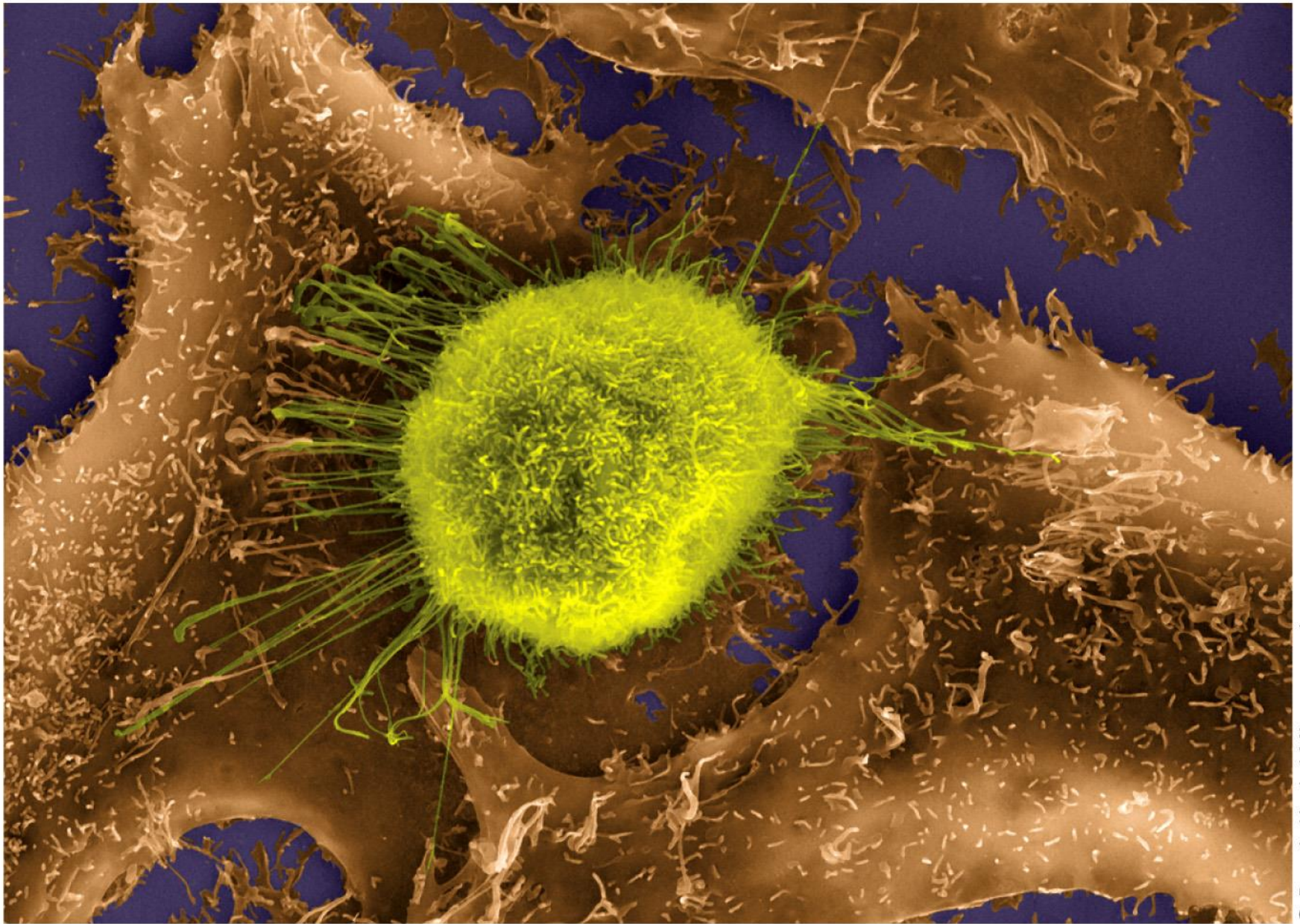
## 11.7 Unregulated Cell Division Can Lead to Cancer

**Malignant** tumors do not resemble the parent tissue.

The cells often have irregular structures that can be used to identify the cells as malignant.



Figure 11.22 A Cancer Cell with its Normal Neighbors



© Dennis Kunkel Microscopy, Inc.

### **Metastasis**

- Cancer cells invade surrounding tissue and travel through bloodstream or lymph system.
- Wherever the cancer cells lodge, they continue dividing and form new tumors.

## 11.7 Unregulated Cell Division Can Lead to Cancer

In normal cells, the cell cycle is regulated.

- Positive regulators such as growth factors stimulate cell division.
- Negative regulators such as retinoblastoma protein (RB) inhibit the cell cycle.

The two regulatory systems ensure that the cells divide only when needed.

**Oncogene** proteins: Positive regulators in cancer cells.

- Normal regulators are mutated to be overactive or present in excess.
  - Example: DNA changes that increase production of the growth factor receptor HER2 in breast tissue may result in rapid cell proliferation.

**Tumor suppressors:** Negative regulators such as RB, which are inactive in cancer cells.

- Some viruses inactivate tumor suppressors.
  - Human papillomavirus produces a protein that blocks RB.

## 11.7 Unregulated Cell Division Can Lead to Cancer

- p53 is a transcription factor involved in cell cycle checkpoints.
  - More than 50% of human tumors have mutations in the gene that encodes p53.



## 11.7 Unregulated Cell Division Can Lead to Cancer

There may be several oncogenes and tumor suppressor genes involved in a single tumor.

- Example: Two important oncogenes in mouse cells
  - *Myc*—stimulates the cell cycle and prevents apoptosis
  - *Ras*—a signaling molecule