2 Chromosomes and Cellular Reproduction

This is Chapter 2 Opener photo legend. (Art Wolfe/Photo Researchers.)

The Diversity of Life

More than by any other feature, life is characterized by diversity: 1.4 million species of plants, animals, and microorganisms have already been described, but this number vastly underestimates the total number of species on Earth. Consider the arthropods—insects, spiders, crustaceans, and related animals with hard exoskeletons. About 875,000 arthropods have been described by scientists worldwide. The results of recent studies, however, suggest that as many as 5 million to 30 million species of arthropods may be living in tropical rain forests *alone*. Furthermore, many species contain numerous genetically distinct populations, and each population contains genetically unique individuals.

Despite their tremendous diversity, living organisms have an important feature in common: all use the same genetic system. A complete set of genetic instructions for any organism is its **genome,** and all genomes are encoded in nucleic acids, either DNA or RNA. The coding system for genomic information also is common to all life—genetic instructions are in the same format and, with rare exceptions, the code words are identical. Likewise, the process by which genetic information is copied and decoded is remarkably similar for all forms of life. This universal genetic system is a consequence of the common origin of living organisms; all life on Earth evolved from the same primordial ancestor that arose between 3.5 billion and 4 billion years ago. Biologist Richard Dawkins describes life as a river of DNA that runs through time, connecting all organisms past and present.

That all organisms have a common genetic system means that the study of one organism's genes reveals principles that apply to other organisms. Investigations of how bacterial DNA is copied (replicated), for example, provides information that applies to the replication of human DNA. It also means that genes will function in foreign cells, which makes genetic engineering possible. Unfortunately, this common genetic system is also the basis for diseases such as AIDS (acquired immune deficiency syndrome), in which viral genes are able to function—sometimes with alarming efficiency—in human cells.

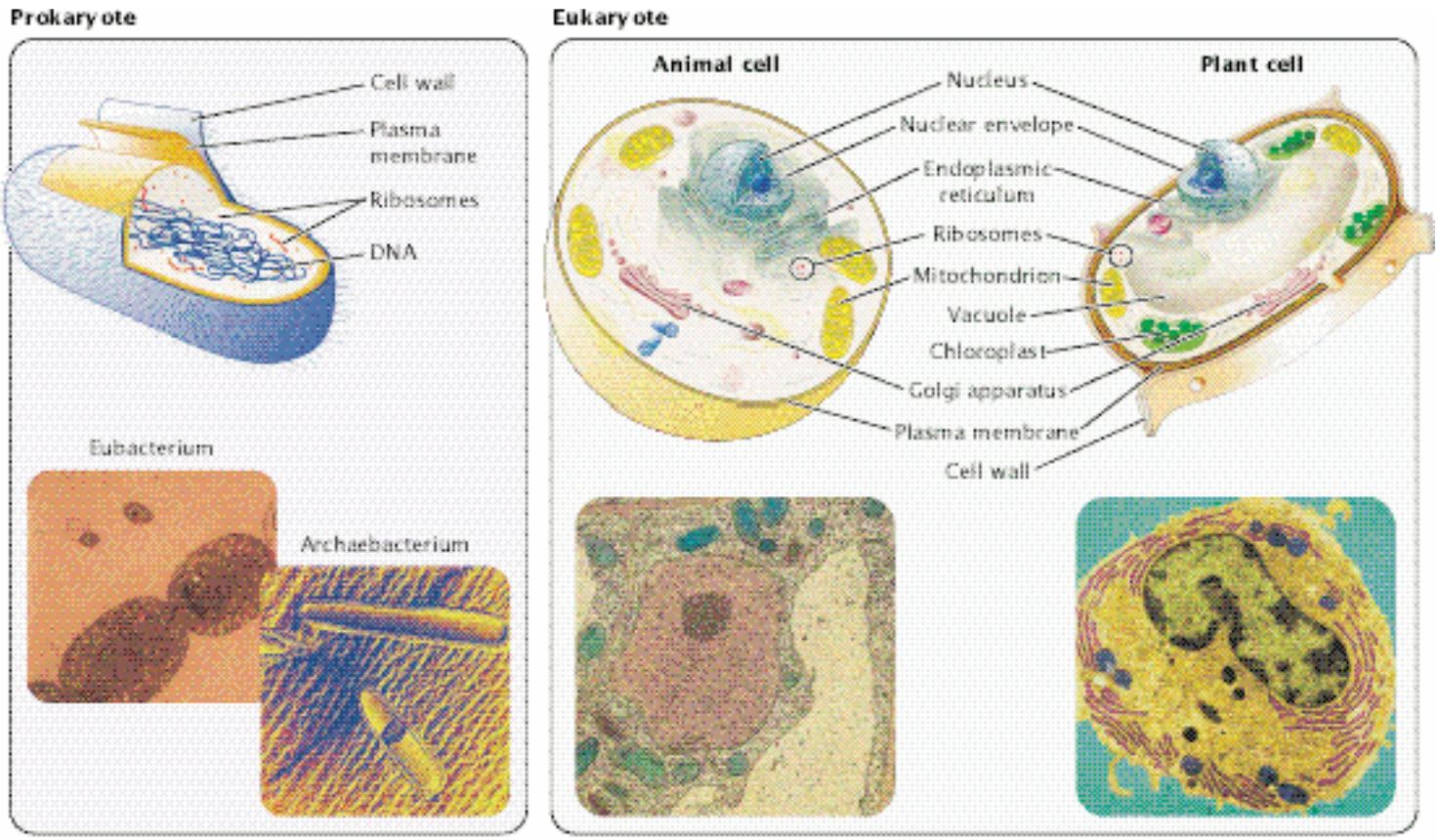
This chapter explores cell reproduction and how genetic information is transmitted to new cells. In prokaryotic cells, cell division is relatively simple because a prokaryotic

cell usually possesses only a single chromosome. In eukaryotic cells, multiple chromosomes must be copied and distributed to each of the new cells. Cell division in eukaryotes takes place through mitosis and meiosis, processes that serve as the foundation for much of genetics; so it is essential to understand them well.

Grasping mitosis and meiosis requires more than simply memorizing the sequences of events that take place in each stage, although these events are important. The key is to understand how genetic information is apportioned during cell reproduction through a dynamic interplay of DNA synthesis, chromosome movement, and cell division. These processes bring about the transmission of genetic information and are the bases of similarities and differences between parents and progeny.

Basic Cell Types: Structure and Evolutionary Relationships

Biologists traditionally classify all living organisms into two major groups, the *prokaryotes* and the *eukaryotes.* A **prokaryote** is a unicellular organism with a relatively simple cell structure (FIGURE 2.1). A **eukaryote** has a compartmentalized cell structure divided by intracellular membranes; eukaryotes may be unicellular or multicellular.



Characteristic	Prokaryotic cells	Eukaryotic cells
Nucleus:	Absent	Present
Cell diameter:	Relatively small, from 1 to 10 μm	Relatively large, from 10 to 100 μm
Genome:	Usually one circular DNA molecule	Multiple linear DNA molecules
DNA:	Not complexed with histones in eubacteria; some histones in archaea	Complexed with histones
Amount of DNA:	Relatively small	Relatively large
Membrane-bounded organelles:	Absent	Present
Cytoskeleton:	Absent	Present

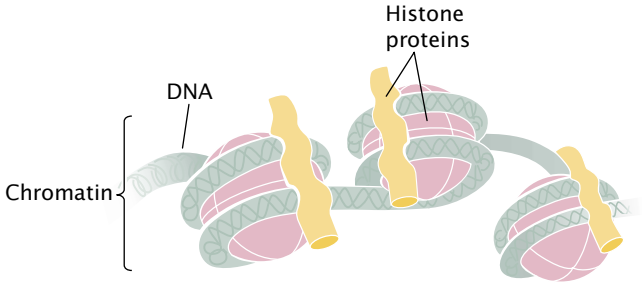
2.1 Prokaryotic and eukaryotic cells differ in structure. (Left to right: T.J. Beveridge/Visuals Unlimited; W. Baumeister/Science Photo/Library/Photo Researchers; Biophoto Associates/Photo Researchers; G. Murti/Phototake.)

Research indicates that dividing life into two major groups, the prokaryotes and eukaryotes, is incorrect. Although similar in cell structure, prokaryotes include at least two fundamentally distinct types of bacteria. These distantly related groups are termed **eubacteria** (the true bacteria) and **archaea** (ancient bacteria). An examination of equivalent DNA sequences reveals that eubacteria and archaea are as distantly related to one another as they are to the eukaryotes. Although eubacteria and archaea are similar in cell structure, some genetic processes in archaea (such as transcription) are more similar to those in eukaryotes, and the archaea may actually be evolutionarily closer to eukaryotes than to eubacteria. Thus, from an evolutionary perspective, there are three major groups of organisms: eubacteria, archaea, and eukaryotes. In this book, the prokaryotic–eukaryotic distinction will be used frequently, but important eubacterial–archaeal differences also will be noted.

From the perspective of genetics, a major difference between prokaryotic and eukaryotic cells is that a eukaryote has a *nuclear envelope*, which surrounds the genetic material to form a **nucleus** and separates the DNA from the other cellular contents. In prokaryotic cells, the genetic material is in close contact with other components of the cell—a property that has important consequences for the way in which genes are controlled.

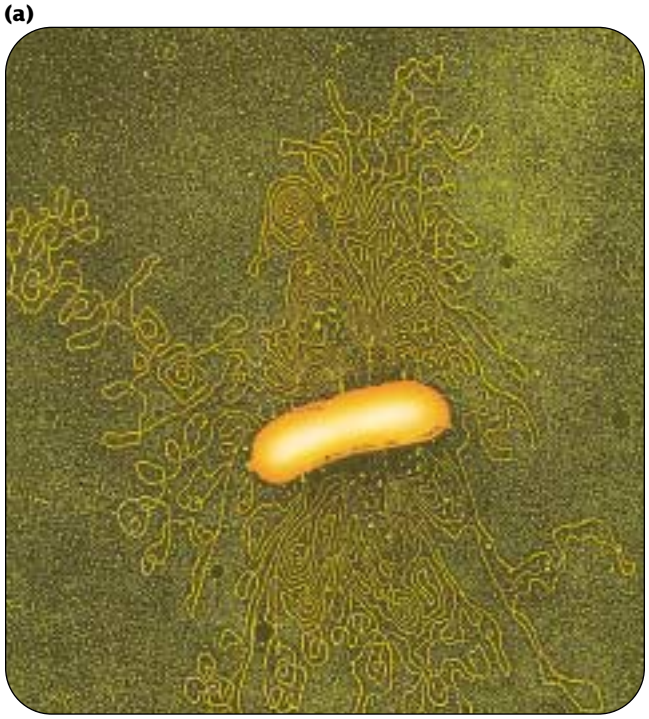
Another fundamental difference between prokaryotes and eukaryotes lies in the packaging of their DNA. In eukaryotes, DNA is closely associated with a special class of proteins, the **histones,** to form tightly packed chromosomes. This complex of DNA and histone proteins is termed **chromatin,** which is the stuff of eukaryotic chromosomes (FIGURE 2.2). Histone proteins limit the accessibility of enzymes and other proteins that copy and read the DNA but they enable the DNA to fit into the nucleus. Eukaryotic DNA must separate from the histones before the genetic information in the DNA can be accessed. Archaea also have some histone proteins that complex with DNA, but the structure of their chromatin is different from that found in eukaryotes. However, eubacteria do not possess histones, so their DNA does not exist in the highly ordered, tightly packed arrangement found in eukaryotic cells (FIGURE 2.3). The copying and reading of DNA are therefore simpler processes in eubacteria.

Genes of prokaryotic cells are generally on a single, circular molecule of DNA, the chromosome of the prokaryotic cell. In eukaryotic cells, genes are located on multiple, usually linear DNA molecules (multiple chromosomes). Eukaryotic cells therefore require mechanisms that ensure that a copy of each chromosome is faithfully transmitted to each new cell. This generalization—a single, circular chromosome in prokaryotes and multiple, linear chromosomes in eukaryotes—is not always true. A few bacteria have more than one chromosome, and important bacterial genes are frequently found on other DNA molecules called plasmids. Furthermore, in some eukaryotes, a few genes are located on circular DNA molecules found outside the nucleus (see Chapter 20).

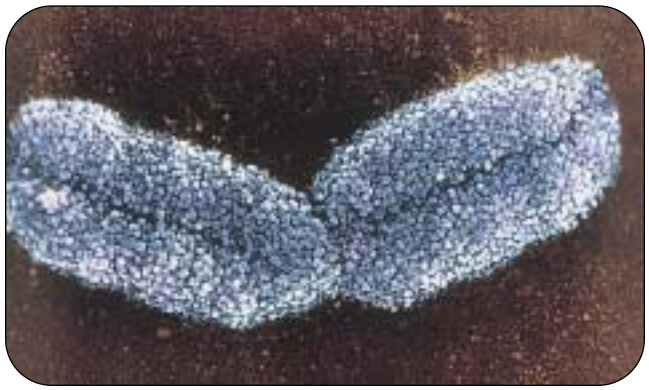


2.2 **In eukaryotic cells, DNA is complexed to histone proteins to form chromatin.**

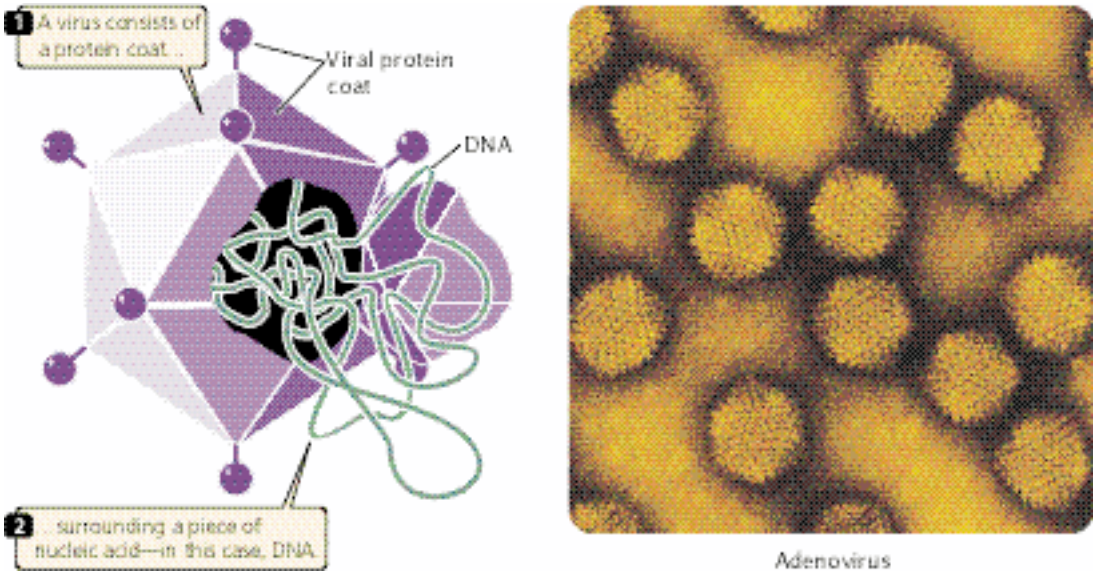
(a)



(b)



2.3 **Prokaryotic DNA (a) is not surrounded by a nuclear membrane nor is the DNA complexed with histone proteins; eukaryotic DNA (b) is complexed to histone proteins to form chromosomes that are located in the nucleus.**
(Part a, Dr. G. Murti/Science Photo Library/Photo Researchers; Part b, *Biophoto Associates/Photo Researchers*.)



2.4 A virus consists of DNA or RNA surrounded by a protein coat. (Hans Gelderblam/Visuals Unlimited.)

Concepts

Organisms are classified as prokaryotes or eukaryotes, and prokaryotes comprise archaea and eubacteria. A prokaryote is a unicellular organism that lacks a nucleus, its DNA is not complexed to histone proteins, and its genome is usually a single chromosome. Eukaryotes are either unicellular or multicellular, their cells possess a nucleus, their DNA is complexed to histone proteins, and their genomes consist of multiple chromosomes.

Viruses are relatively simple structures composed of an outer protein coat surrounding nucleic acid (either DNA or RNA; **Figure 2.4**). Viruses are neither cells nor primitive forms of life: they can reproduce only within host cells, which means that they must have evolved after, rather than before, cells. In addition, viruses are not an evolutionarily distinct group but are most closely related to their hosts—the genes of a plant virus are more similar to those in a plant cell than to those in animal viruses, which suggests that viruses evolved from their hosts, rather than from other viruses. The close relationship between the genes of virus and host makes viruses useful for studying the genetics of host organisms.

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Cell Reproduction

For any cell to reproduce successfully, three fundamental events must take place: (1) its genetic information must be copied, (2) the copies of genetic information must be separated from one another, and (3) the cell must divide. All cellular reproduction includes these three events, but the processes that lead to these events differ in prokaryotic and eukaryotic cells.

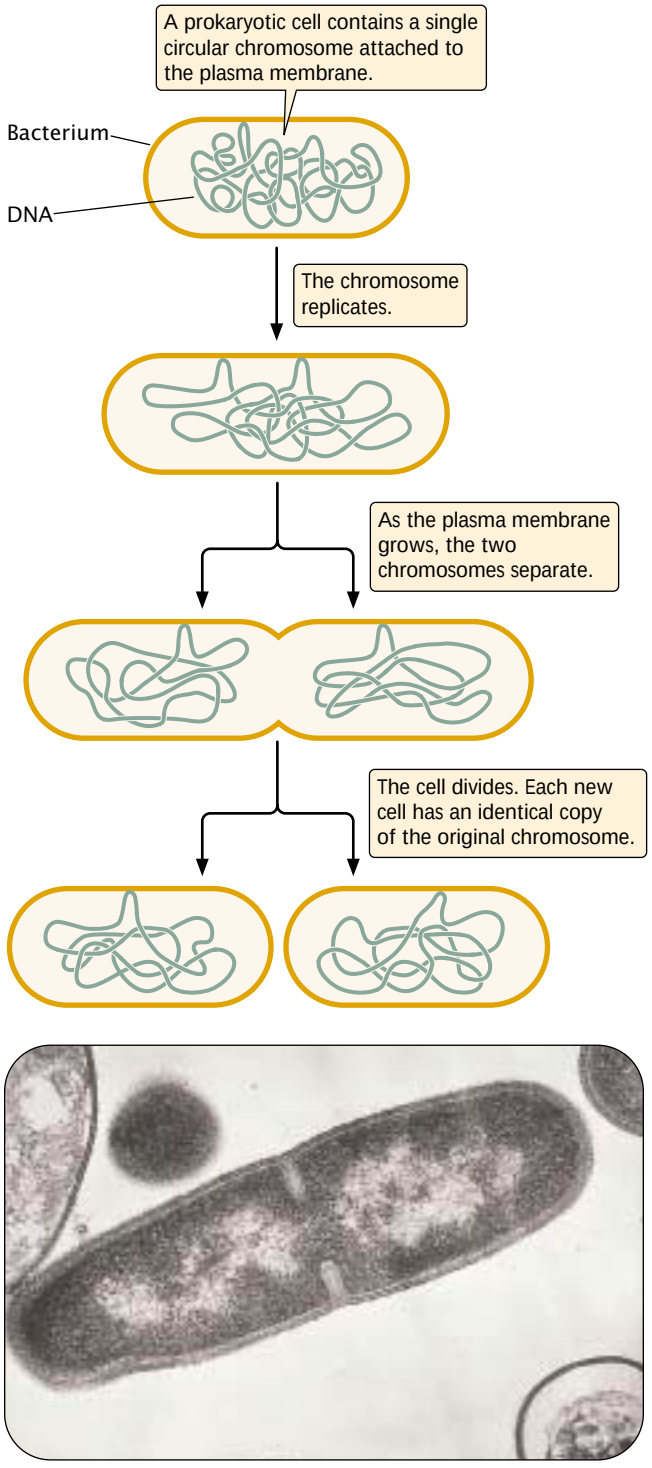
Prokaryotic Cell Reproduction

When prokaryotic cells reproduce, the circular chromosome of the bacterium is replicated (**Figure 2.5**). The two resulting identical copies are attached to the plasma membrane, which grows and gradually separates the two chromosomes. Finally, a new cell wall forms between the two chromosomes, producing two cells, each with an identical copy of the chromosome. Under optimal conditions, some bacterial cells divide every 20 minutes. At this rate, a single bacterial cell could produce a billion descendants in a mere 10 hours.

Eukaryotic Cell Reproduction

Like prokaryotic cell reproduction, eukaryotic cell reproduction requires the processes of DNA replication, copy separation, and division of the cytoplasm. However, the presence of multiple DNA molecules requires a more complex mechanism to ensure that one copy of each molecule ends up in each of the new cells.

Eukaryotic chromosomes are separated from the cytoplasm by the nuclear envelope. The nucleus was once thought to be a fluid-filled bag in which the chromosomes



2.5 Prokaryotic cells reproduce by simple division. (Micrograph Lee D, Simon/Photo Researchs.)

floated, but we now know that the nucleus has a highly organized internal scaffolding called the *nuclear matrix*. This matrix consists of a network of protein fibers that maintains precise spatial relations among the nuclear components and takes part in DNA replication, the expression of genes, and the modification of gene products before they leave the nucleus. We will now take a closer look at the structure of eukaryotic chromosomes.

Eukaryotic chromosomes

Each eukaryotic species has a characteristic number of chromosomes per cell: potatoes have 48 chromosomes, fruit flies have 8, and humans have 46. There appears to be no special significance between the complexity of an organism and its number of chromosomes per cell.

In most eukaryotic cells, there are two *sets* of chromosomes. The presence of two sets is a consequence of sexual reproduction; one set is inherited from the male parent and the other from the female parent. Each chromosome in one set has a corresponding chromosome in the other set, together constituting a **homologous pair** (FIGURE 2.6). Human cells, for example, have 46 chromosomes, comprising 23 homologous pairs.

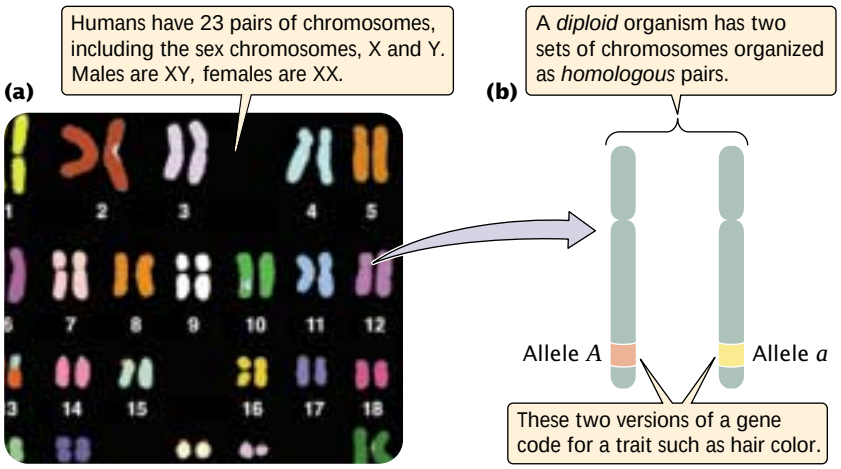
The two chromosomes of a homologous pair are usually alike in structure and size, and each carries genetic information for the same set of hereditary characteristics. (An exception is the sex chromosomes, which will be discussed in Chapter 4.) For example, if a gene on a particular chromosome encodes a characteristic such as hair color, another gene (called an allele) at the same position on that chromosome's homolog *also* encodes hair color. However, these two alleles need not be identical: one might produce red hair and the other might produce blond hair. Thus, most cells carry two sets of genetic information; these cells are **diploid.** But not all eukaryotic cells are diploid: reproductive cells (such as eggs, sperm, and spores) and even nonreproductive cells in some organisms may contain a single set of chromosomes. Cells with a single set of chromosomes are **haploid.** Haploid cells have only one copy of each gene.

Concepts

Cells reproduce by copying and separating their genetic information and then dividing. Because eukaryotes possess multiple chromosomes, mechanisms exist to ensure that each new cell receives one copy of each chromosome. Most eukaryotic cells are diploid, and their two chromosomes sets can be arranged in homologous pairs. Haploid cells contain a single set of chromosomes.

Chromosome structure

The chromosomes of eukaryotic cells are larger and more complex than those found in prokaryotes, but each unreplicated chromosome nevertheless consists of a single molecule of DNA. Although linear, the DNA molecules in eukaryotic chromosomes are highly folded and condensed; if stretched out, some human chromosomes



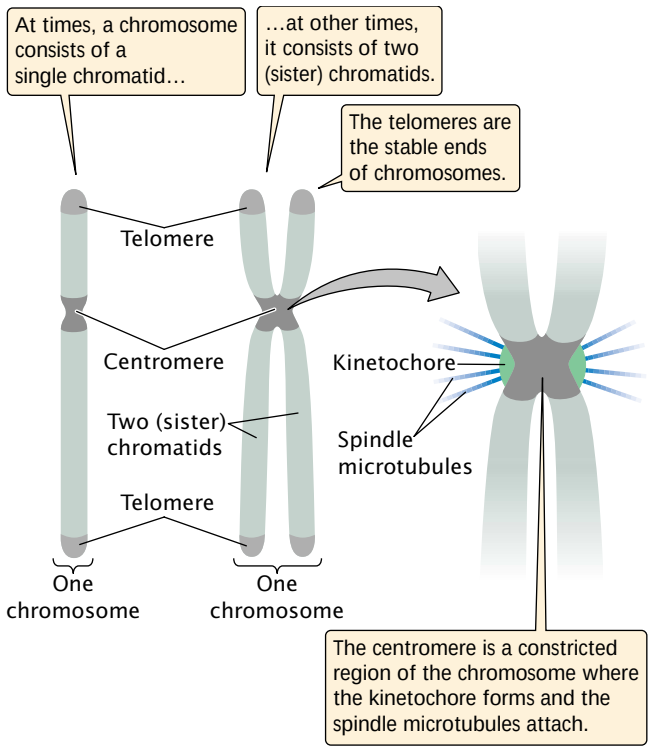
2.6 Diploid eukaryotic cells have two sets of chromosomes.
(a) A set of chromosomes from a human cell.
(b) The chromosomes are present in homologous pairs, which consist of chromosomes that are alike in size and structure and carry information for the same characteristics. (Courtesy of Dr. Thomas Ried and Dr. Evelin Schrock.)

would be several centimeters long—thousands of times longer than the span of a typical nucleus. To package such a tremendous length of DNA into this small volume, each DNA molecule is coiled again and again and tightly packed around histone proteins, forming the rod-shaped chromosomes. Most of the time the chromosomes are thin and difficult to observe but, before cell division, they condense further into thick, readily observed structures; it is at this stage that chromosomes are usually studied (FIGURE 2.7).

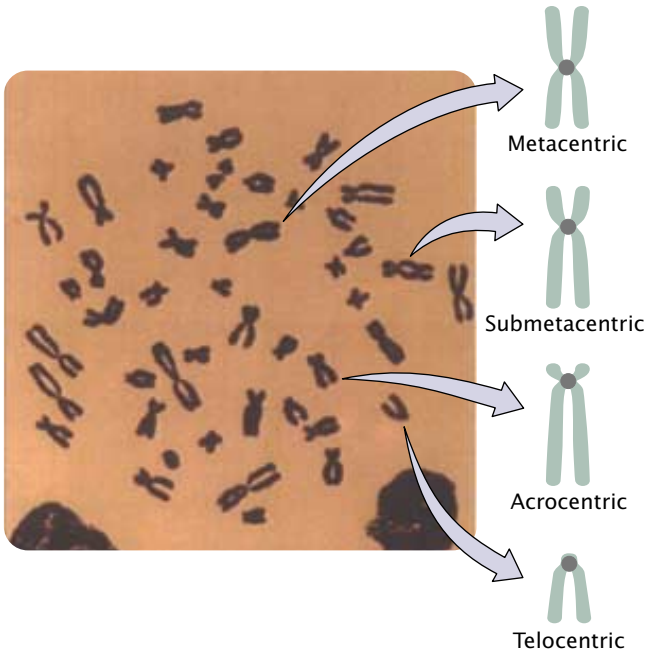
A functional chromosome has three essential elements: a centromere, a pair of telomeres, and origins of replication. The *centromere* is the attachment point for *spindle microtubules*, which are the filaments responsible for moving chromosomes during cell division. The centromere appears as a constricted region that often stains less strongly than does the rest of the chromosome. Before cell division, a protein complex called the *kinetochore* assembles on the centromere, to which spindle microtubules later attach. Chromosomes without a centromere cannot be drawn into the newly formed nuclei; these chromosomes are lost, often with catastrophic consequences to the cell. On the basis of the location of the centromere, chromosomes are classified into four types: metacentric, submetacentric, acrocentric, and telocentric (FIGURE 2.8). One of the two arms of a chromosome (the short arm of a submetacentric or acrocentric chromosome) is designated by the letter p and the other arm is designated by q.

Telomeres are the natural ends, the tips, of a linear chromosome (see Figure 2.7); they serve to stabilize the chromosome ends. If a chromosome breaks, producing new ends, these ends have a tendency to stick together, and the chromosome is degraded at the newly broken ends. Telomeres provide chromosome stability. The results of research (discussed in Chapter 12) suggest that telomeres also participate in limiting cell division and may play important roles in aging and cancer.

Origins of replication are the sites where DNA synthesis begins; they are not easily observed by microscopy. Their structure and function will be discussed in more detail in Chapters 11 and 12. In preparation for cell division, each



2.7 Structure of a eukaryotic chromosome.



2.8 Eukaryotic chromosomes exist in four major types. (L. Lisco, D. W. Fawcett/Visuals Unlimited.)

chromosome replicates, making a copy of itself. These two initially identical copies, called **sister chromatids,** are held together at the centromere (see Figure 2.7). Each sister chromatid consists of a single molecule of DNA.

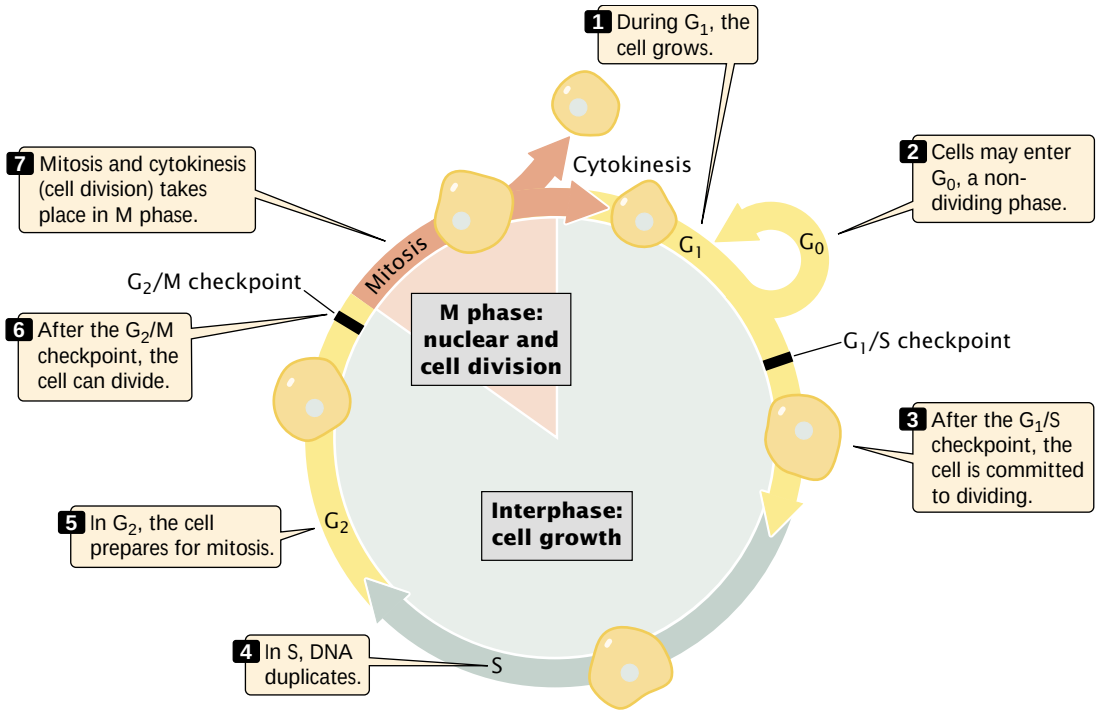
Concepts

Sister chromatids are copies of a chromosome held together at the centromere. Functional chromosomes contain centromeres, telomeres, and origins of replication. The kinetochore is the point of attachment for the spindle microtubules; telomeres are the stabilizing ends of a chromosome; origins of replication are sites where DNA synthesis begins.

The Cell Cycle and Mitosis

The **cell cycle** is the life story of a cell, the stages through which it passes from one division to the next (**Figure 2.9**). This process is critical to genetics because, through the cell cycle, the genetic instructions for all characteristics are passed from parent to daughter cells. A new cycle begins after a cell has divided and produced two new cells. A new cell metabolizes, grows, and develops. At the end of its cycle, the cell divides to produce two cells, which can then undergo additional cell cycles.

The cell cycle consists of two major phases. The first is **interphase,** the period between cell divisions, in which the cell grows, develops, and prepares for cell division. The second is **M phase** (mitotic phase), the period of active cell division. M phase includes **mitosis,** the process of nuclear division, and **cytokinesis,** or cytoplasmic division. Let's take a closer look at the details of interphase and M phase.



2.9 The cell cycle consists of interphase (a period of cell growth) and M phase (the period of nuclear and cell division).

Interphase Interphase is the extended period of growth and development between cell divisions. Although little activity can be observed with a light microscope, the cell is quite busy: DNA is being synthesized, RNA and proteins are being produced, and hundreds of biochemical reactions are taking place.

By convention, interphase is divided into three phases: G_1, S, and G_2 (see Figure 2.9). Interphase begins with G_1 (for gap 1). In G_1, the cell grows, and proteins necessary for cell division are synthesized; this phase typically lasts several hours. There is a critical point in the cell cycle, termed the *G_1/S checkpoint*, in G_1; after this checkpoint has been passed, the cell is committed to divide.

Before reaching the G_1/S checkpoint, cells may exit from the active cell cycle in response to regulatory signals and pass into a nondividing phase called G_0 (see Figure 2.9), which is a stable state during which cells usually maintain a constant size. They can remain in G_0 for an extended period of time, even indefinitely, or they can reenter G_1 and the active cell cycle. Many cells never enter G_0; rather, they cycle continuously.

After G_1, the cell enters the *S* phase (for DNA synthesis), in which each chromosome duplicates. Although the cell is committed to divide after the G_1/S checkpoint has been passed, DNA synthesis must take place before the cell can proceed to mitosis. If DNA synthesis is blocked (with drugs or by a mutation), the cell will not be able to undergo mitosis. Before *S* phase, each chromosome is composed of one chromatid; following *S* phase, each chromosome is composed of two chromatids.

After the S phase, the cell enters G_2 (gap 2). In this phase, several additional biochemical events necessary for cell division take place. The important *G_2/M checkpoint* is reached in G_2; after this checkpoint has been passed, the cell is ready to divide and enters M phase. Although the length of interphase varies from cell type to cell type, a typical dividing mammalian cell spends about 10 hours in G_1, 9 hours in S, and 4 hours in G_2 (see Figure 2.9).

Throughout interphase, the chromosomes are in a relatively relaxed, but by no means uncoiled, state, and individual chromosomes cannot be seen with the use of a microscope. This condition changes dramatically when interphase draws to a close and the cell enters M phase.

Mphase M phase is the part of the cell cycle in which the copies of the cell's chromosomes (sister chromatids) are separated and the cell undergoes division. A critical process in M phase is the separation of sister chromatids to provide a complete set of genetic information for each of the resulting cells. Biologists usually divide M phase into six stages: the five stages of mitosis (prophase, prometaphase, metaphase, anaphase, and telophase) and cytokinesis (**Figure 2.10**). It's important to keep in mind that M phase is a continuous process, and its separation into these six stages is somewhat artificial.

During interphase, the chromosomes are relaxed and are visible only as diffuse chromatin, but they condense during **prophase**, becoming visible under a light microscope. Each chromosome possesses two chromatids because the chromosome was duplicated in the preceding S phase. The *mitotic spindle*, an organized array of microtubules that move the chromosomes in mitosis, forms. In animal cells, the spindle grows out from a pair of *centrosomes* that migrate to opposite sides of the cell. Within each centrosome is a special organelle, the *centriole*, which is also composed of microtubules. (Higher plant cells do not have centrosomes or centrioles, but they do have mitotic spindles).

Disintegration of the nuclear membrane marks the start of **prometaphase**. Spindle microtubules, which until now have been outside the nucleus, enter the nuclear region. The ends of certain microtubules make contact with the chromosome and anchor to the kinetochore of *one* of the sister chromatids; a microtubule from the opposite centrosome then attaches to the *other* sister chromatid, and so each chromosome is anchored to both of the centrosomes. The microtubules lengthen and shorten, pushing and pulling the chromosomes about. Some microtubules extend from each centrosome toward the center of the spindle but do not attach to a chromosome.

During **metaphase**, the chromosomes arrange themselves in a single plane, the *metaphase plate*, between the two centrosomes. The centrosomes, now at opposite ends of the cell with microtubules radiating outward and meeting in the middle of the cell, center at the spindle pole. **Anaphase** begins when the sister chromatids separate and move toward opposite spindle poles. After the chromatids have separated, each is considered a separate chromosome. **Telophase** is marked by the arrival of the chromosomes at the spindle poles. The nuclear membrane re-forms around each set of chromosomes, producing two separate nuclei within the cell. The chromosomes relax and lengthen, once again disappearing from view. In many cells, division of the cytoplasm (cytokinesis) is simultaneous with telophase. The major features of the cell cycle are summarized in Table 2.1.

Concepts

The active cell-cycle phases are interphase and M phase. Interphase consists of G_1, S, and G_2. In G_1, the cell grows and prepares for cell division; in the S phase, DNA synthesis takes place; in G_2, other biochemical events necessary for cell division take place. Some cells enter a quiescent phase called G_0. M phase includes mitosis and cytokinesis and is divided into prophase, prometaphase, metaphase, anaphase, and telophase.

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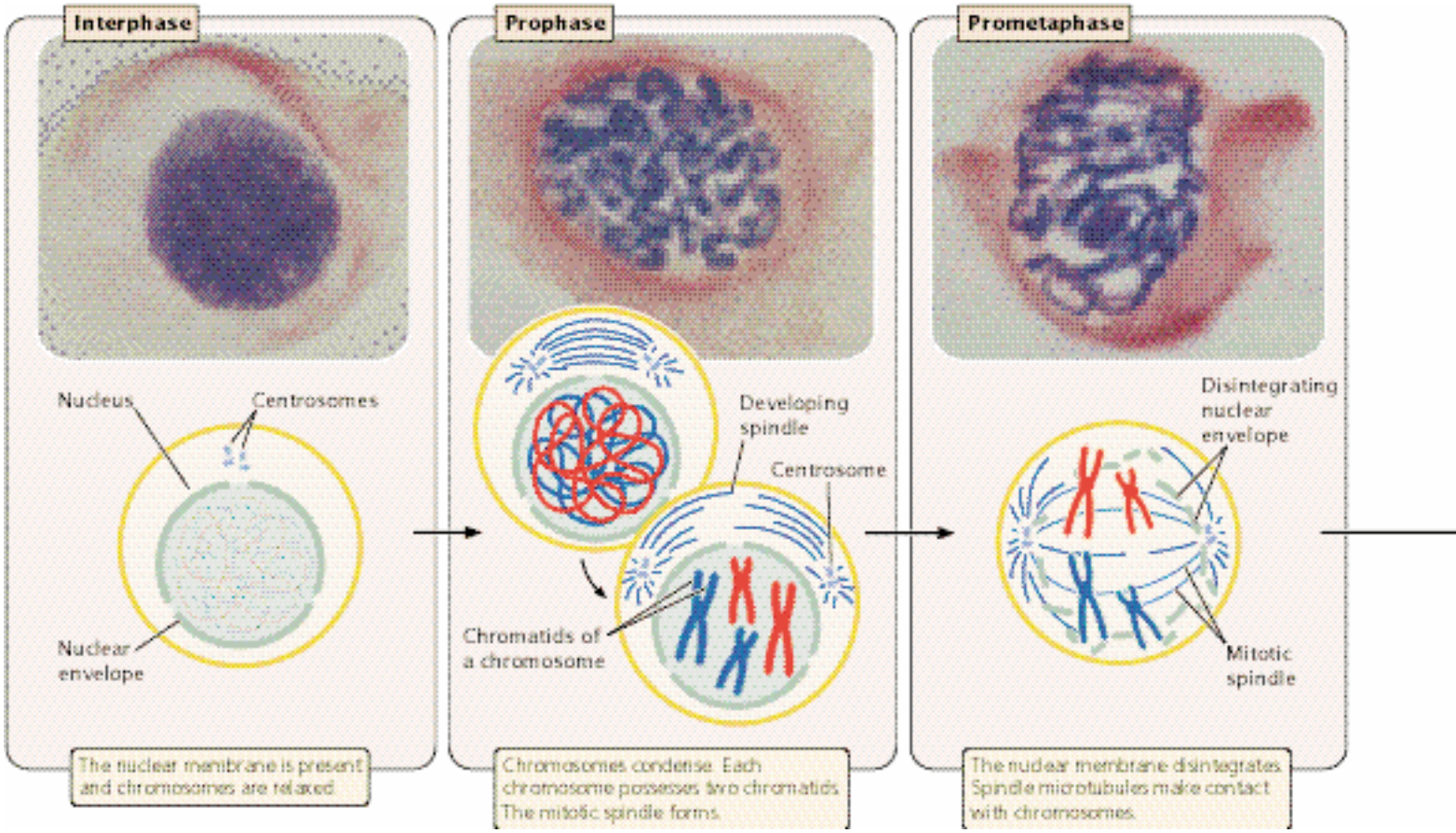
Movement of Chromosomes in Mitosis

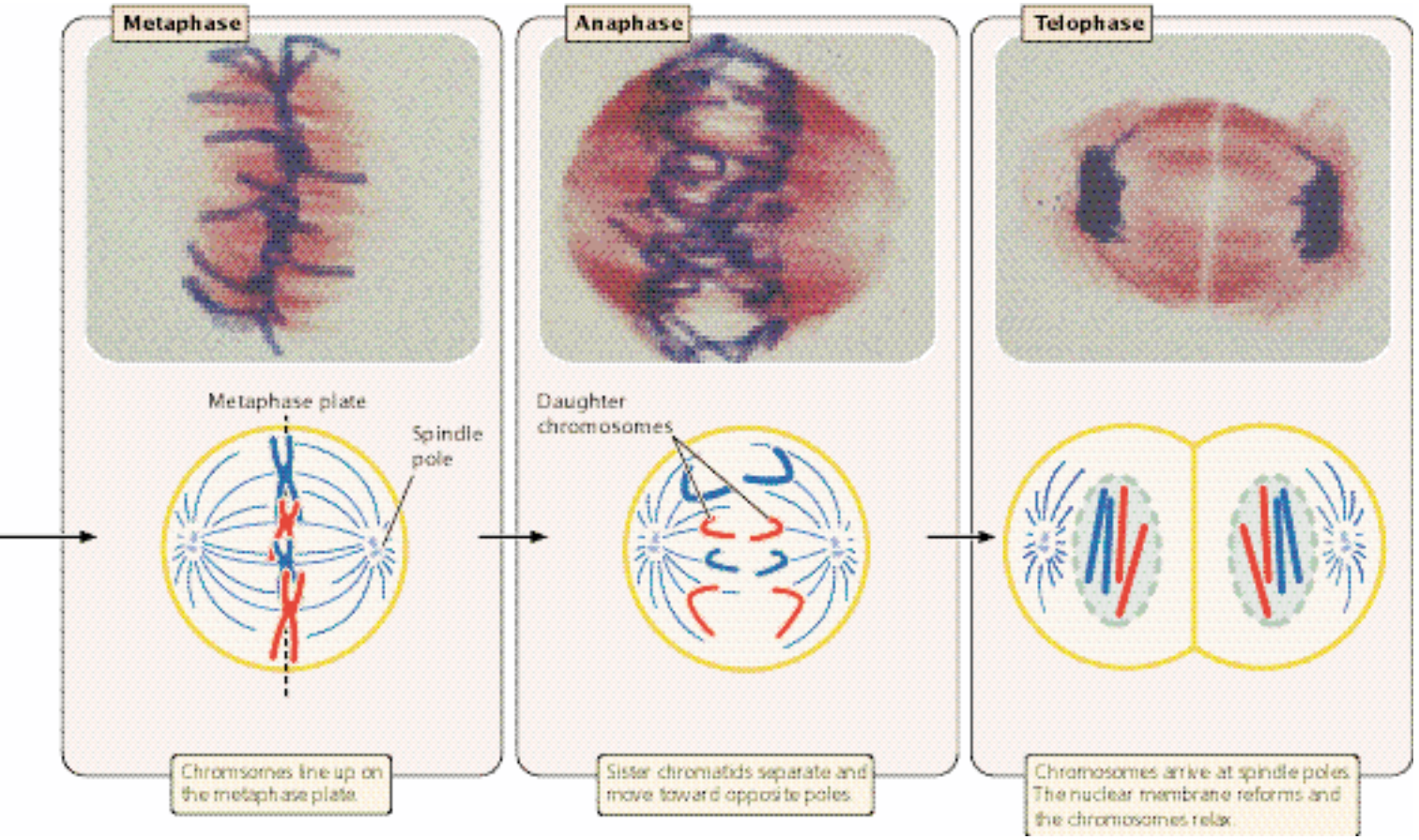
Each microtubule of the spindle is composed of subunits of a protein called tubulin, and each microtubule has direction



2.10 **The cell cycle is divided into stages.** (Photos © Andrew S. Bajer, University of Oregon.)

Table 2.1 Features of the cell cycle

Stage	Major Features
G_0 phase	Stable, nondividing period of variable length
Interphase	
G_1 phase	Growth and development of the cell; G_1/S checkpoint
S phase	Synthesis of DNA
G_2 phase	Preparation for division; G_2/S checkpoint
M phase	
Prophase	Chromosomes condense and mitotic spindle forms
Prometaphase	Nuclear envelope disintegrates, spindle microtubules anchor to kinetochores
Metaphase	Chromosomes align on the metaphase plate
Anaphase	Sister chromatids separate, becoming individual chromosomes that migrate toward spindle poles
Telophase	Chromosomes arrive at spindle poles, the nuclear envelope re-forms, and the condensed chromosomes relax
Cytokinesis	Cytoplasm divides; cell wall forms in plant cells



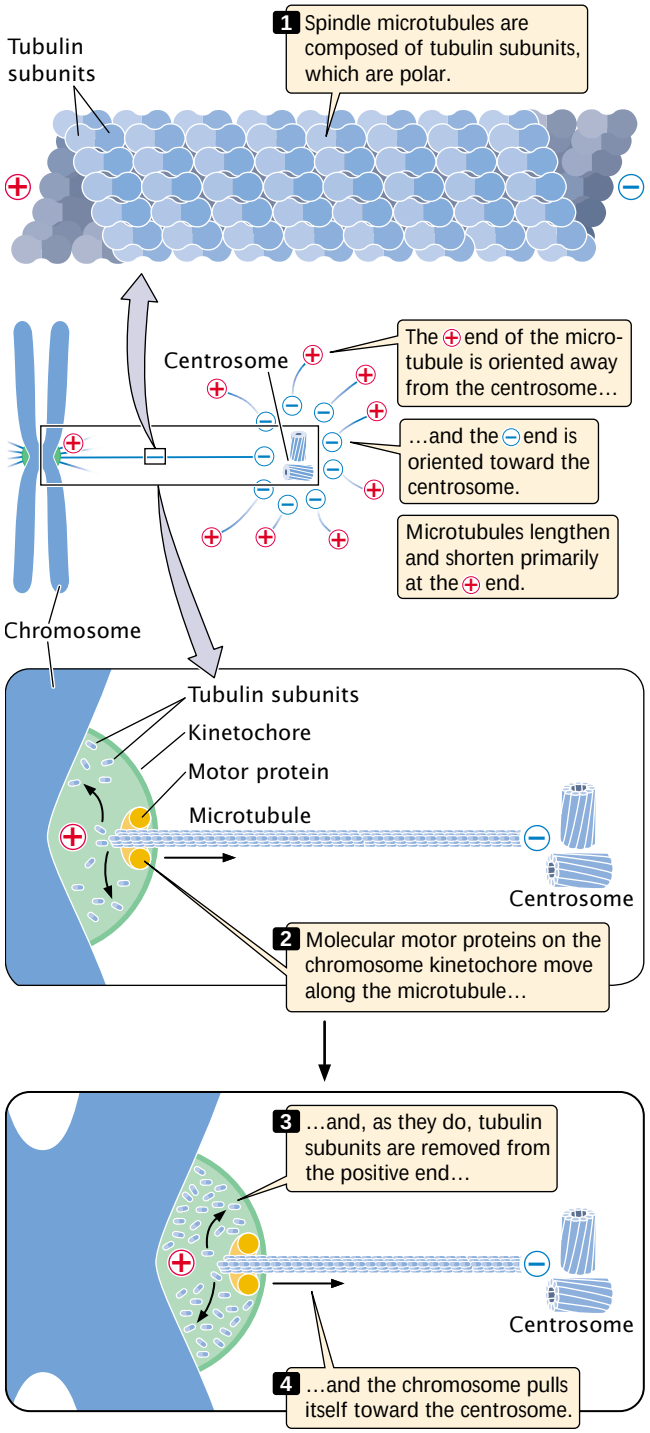
or polarity. Like a flashlight battery, one end is referred to as plus (+) and the other end as minus (−). The "−" end is always oriented toward the centrosome, and the "+" end is always oriented away from the centrosome; microtubules lengthen and shorten by the addition and removal of subunits primarily at the "+" end.

At one time, chromosomes were viewed as passive carriers of genetic information that were pushed about by the active spindle microtubules. Research findings now indicate that chromosomes actively control and generate the forces responsible for their movement in the course of mitosis and meiosis. Chromosome movement is accomplished through complex interactions between the kinetochore of the chromosome and the microtubules of the spindle apparatus.

The forces responsible for the poleward movement of chromosomes during anaphase are generated at the kinetochore itself but are not completely understood. Located within each kinetochore are specialized proteins called *molecular motors*, which may help pull a chromosome toward the spindle pole (◖ FIGURE 2.11). The poleward force is created by the removal of the tubulin primarily at the "+" end of the microtubule.

In mitosis, deploymerization of tubulin and perhaps also molecular motors pull the chromosome toward the pole, but this force is initially counterbalanced by the attachment of the two chromatids. Throughout prophase, prometaphase, and metaphase, the sister chromatids are held together by a gluelike material called cohesion. The cohesion material breaks down at the onset of anaphase, allowing the two chromatids to separate and the resulting newly formed chromosomes to move toward the spindle pole. While the chromosomal microtubules shorten, other microtubules elongate, pushing the two spindle poles farther apart. As the chromosomes near the spindle poles, they contract to form a compact mass. In spite of much study, the precise role of the poles, kinetochores, and microtubules in the formation and function of the spindle apparatus is still incompletely understood.

Genetic consequences of the cell cycle What are the genetically important results of the cell cycle? From a single cell, the cell cycle produces two cells that contain the same genetic instructions. These two cells are identical with each other and with the cell that gave rise to them. They are identical because DNA synthesis in S phase creates an exact copy of each DNA molecule, giving rise to two genetically



2.11 Removal of the tublin subunits from microtubules at the kinetochore and perhaps molecular motors, are responsible for the poleward movement of chromosomes during anaphase.

identical sister chromatids. Mitosis then ensures that one chromatid from each replicated chromosome passes into each new cell.

Another genetically important result of the cell cycle is that each of the cells produced contains a full complement of chromosomes—there is no net reduction or increase in chromosome number. Each cell also contains approximately half the cytoplasm and organelle content of the original parental cell, but no precise mechanism analogous to mitosis ensures that organelles are evenly divided. Consequently, not all cells resulting from the cell cycle are identical in their cytoplasmic content.

Control of the cell cycle For many years, the biochemical events that controlled the progression of cells through the cell cycle were completely unknown, but research has now revealed many of the details of this process. Progression of the cell cycle is regulated at several checkpoints, which ensure that all cellular components are present and in good working order before the cell proceeds to the next stage. The checkpoints are necessary to prevent cells with damaged or missing chromosomes from proliferating.

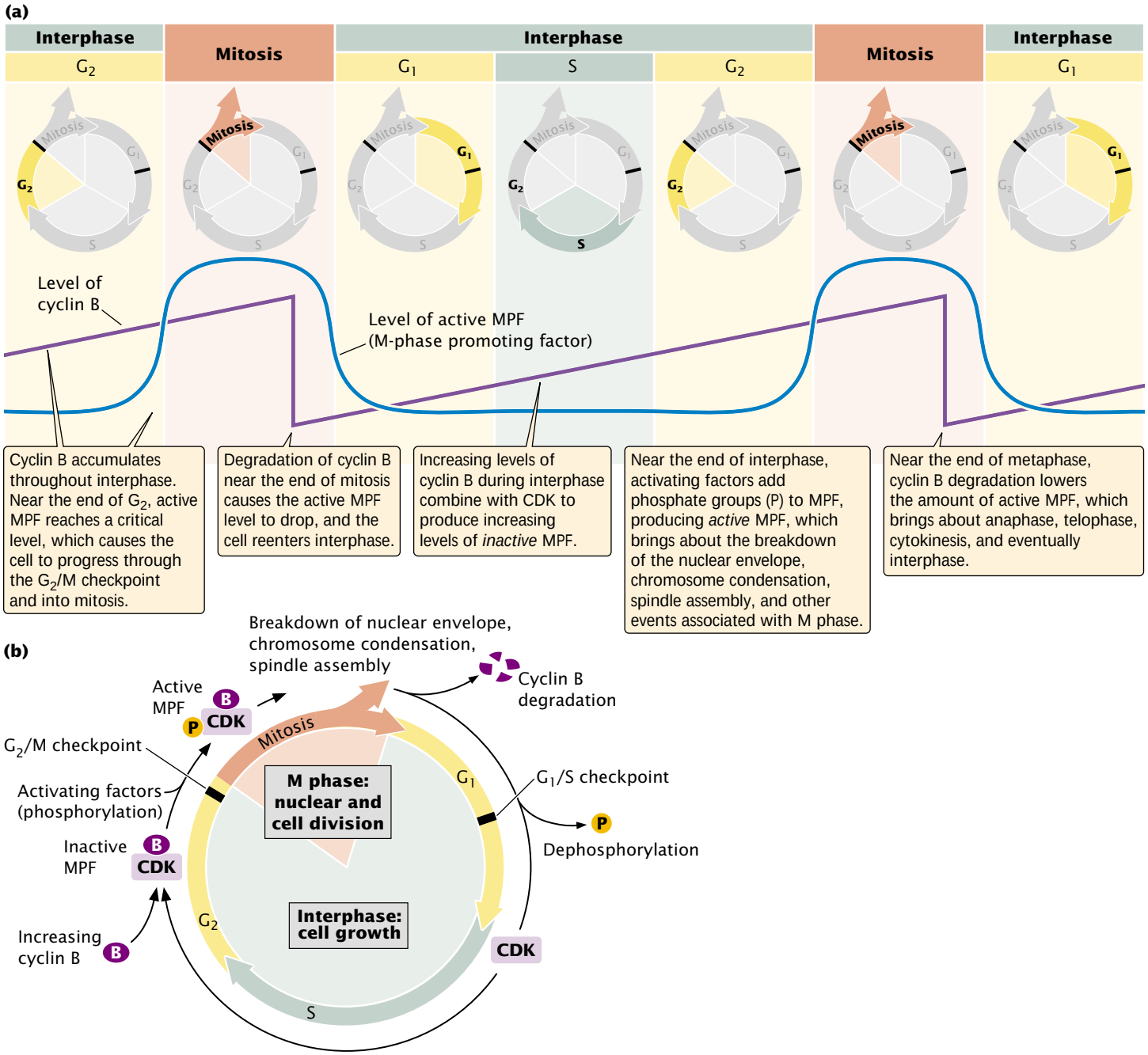
One important checkpoint mentioned earlier, the G_1/S checkpoint, comes just before the cell enters into S phase and replicates its DNA. When this point has been passed, DNA replicates and the cell is committed to divide. A second critical checkpoint, called the G_2/M checkpoint, is at the end of G_2, before the cell enters mitosis.

Both the G_1/S and the G_2/M checkpoints are regulated by a mechanism in which two proteins interact. The concentration of the first protein, *cyclin*, oscillates during the cell cycle (◖ FIGURE 2.12a). The second protein, *cyclin-dependent kinase* (CDK), cannot function unless it is bound to cyclin. Cyclins and CDKs are called by different names in different organisms, but here we will use the terms applied to these molecules in yeast.

Let's begin by looking at the G_2/M checkpoint. This checkpoint is regulated by cyclin B, which combines with CDK to form *M-phase promoting factor* (MPF). After MPF is formed, it must be activated by the addition of a phosphate group to one of the amino acids of CDK (◖ FIGURE 2.12b).

Whereas the amount of cyclin B changes throughout the cell cycle, the amount of CDK remains constant. During G_1, cyclin B levels are low; so the amount of MPF also is low (see Figure 2.12a). As more cyclin B is produced, it combines with CDK to form increasing amounts of MPF. Near the end of G_2, the amount of active MPF reaches a critical level, which commits the cell to divide. The MPF concentration continues to increase, reaching a peak in mitosis (see Figure 2.12a).

The active form of MPF is a protein kinase, an enzyme that adds phosphate groups to certain other proteins. Active MPF brings about many of the events associated with mitosis, such as nuclear-membrane breakdown, spindle formation, and chromosome condensation. At the end of metaphase, cyclin is abruptly degraded, which lowers the amount of MPF and, initiating anaphase, sets in motion a chain of events that ultimately brings mitosis to a close



2.12 Progression through the cell cycle is regulated by cyclins and CDKs. Shown here is regulation of the G_2/M checkpoint in yeast.

(see Figure 2.12b). Ironically, active MPF brings about its own demise by destroying cyclin. In brief, high levels of active MPF stimulate mitosis, and low levels of MPF bring a return to interphase conditions.

A number of factors stimulate the synthesis of cyclin B and the activation of MPF, whereas other factors inhibit MPF. Together these factors determine whether the cell passes through the G_2/M checkpoint and ensure that mitosis is not initiated until conditions are appropriate for cell division. For example, DNA damage inhibits the activation of MPF; the cell is arrested in G_2 and does not undergo division.

The G_1/S checkpoint is regulated in a similar manner. In fission yeast *(Shizosaccharomyces pombe)*, the same CDK is used, but it combines with G_1 cyclins. Again, the level of CDK remains relatively constant, whereas the level of G_1 cyclins increases throughout G_1. When the activated CDK–G_1–cyclin complex reaches a critical concentration, proteins necessary for replication are activated and the cell enters S phase.

Many cancers are caused by defects in the cell cycle's regulatory machinery. For example, mutation in the gene that encodes cyclin D, which has a role in the human G_1/S checkpoint, contributes to the rise of B-cell lymphoma. The overexpression of this gene is associated with both breast and esophageal cancer. Likewise, the tumor-suppressor gene *p53*, which is mutated in about 75% of all colon cancers, regulates a potent inhibitor of CDK activity.

Concepts

The cell cycle produces two genetically identical cells, with no net change in chromosome number. Progression through the cell cycle is controlled at checkpoints, which are regulated by interactions between cyclins and cyclin-dependent kinases.

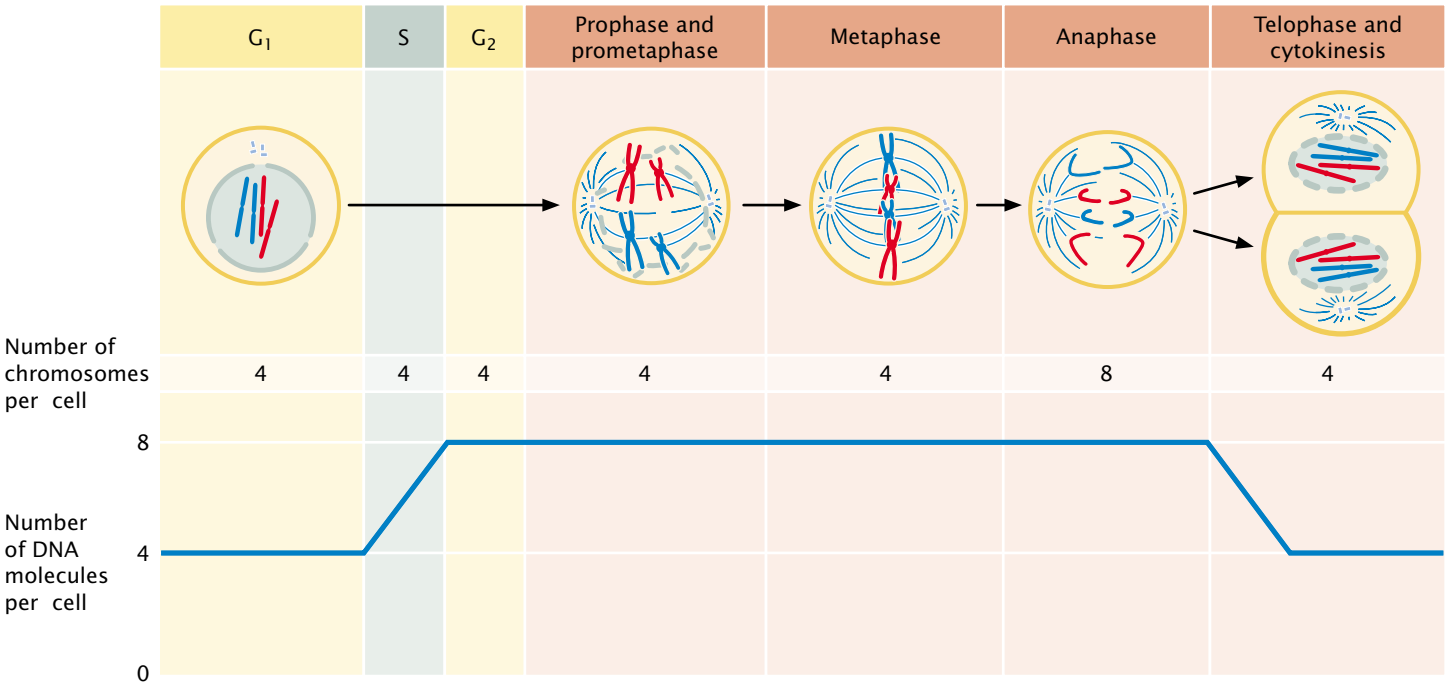
Connecting Concepts

Counting Chromosomes and DNA Molecules

The relations among chromosomes, chromatids, and DNA molecules frequently cause confusion. At certain times, chromosomes are unreplicated; at other times, each possesses two chromatids (see Figure 2.7b). Chromosomes sometimes consist of a single DNA molecule; at other times, they consist of two DNA molecules. How can we keep track of the number of these structures in the cell cycle?

There are two simple rules for counting chromosomes and DNA molecules: (1) to determine the number of chromosomes, count the number of functional centromeres; (2) to determine the number of DNA molecules, count the number of chromatids. Let's examine a hypothetical cell as it passes through the cell cycle (**Figure 2.13**). At the beginning of G_1, this diploid cell has a complete set of four chromosomes, inherited from its parent cell. Each chromosome consists of a single chromatid—a single DNA molecule—so there are four DNA molecules in the cell during G_1. In S phase, each DNA molecule is copied. The two resulting DNA molecules combine with histones and other proteins to form sister chromatids. Although the amount of DNA doubles during S phase, the number of chromosomes remains the same, because the two sister chromatids share a single functional centromere. At the end of S phase, this cell still contains four chromosomes, each with two chromatids; so there are eight DNA molecules present.

Through prophase, prometaphase, and metaphase, the cell has four chromosomes and eight DNA molecules. At anaphase, however, the sister chromatids separate. Each now has its own functional centromere, and so each is considered a separate chromosome. Until cytokinesis, each cell contains eight chromosomes, each consisting of a single chromatid;



2.13 The number of chromosomes and DNA molecules changes in the course of the cell cycle. The number of chromosomes per cell equals the number of functional centromeres, and the number of DNA molecules per cell equals the number of chromatids.

thus, there are still eight DNA molecules present. After cytokinesis, the eight chromosomes (eight DNA molecules) are distributed equally between two cells; so each new cell contains four chromosomes and four DNA molecules, the number present at the beginning of the cell cycle.

Sexual Reproduction and Genetic Variation

If all reproduction were accomplished through the cell cycle, life would be quite dull, because mitosis produces only genetically identical progeny. With only mitosis, you, your children, your parents, your brothers and sisters, your cousins, and many people you didn't even know would be clones—copies of one another. Only the occasional mutation would introduce any genetic variability. This is how all organisms reproduced for the first 2 billion years of Earth's existence (and the way in which some organisms still reproduce today). Then, some 1.5 billion to 2 billion years ago, something remarkable evolved: cells that produce genetically variable offspring through sexual reproduction.

The evolution of sexual reproduction is one of the most significant events in the history of life. As will be discussed in Chapters 22 and 23, the pace of evolution depends on the amount of genetic variation present. By shuffling the genetic information from two parents, sexual reproduction greatly increases the amount of genetic variation and allows for accelerated evolution. Most of the tremendous diversity of life on Earth is a direct result of sexual reproduction.

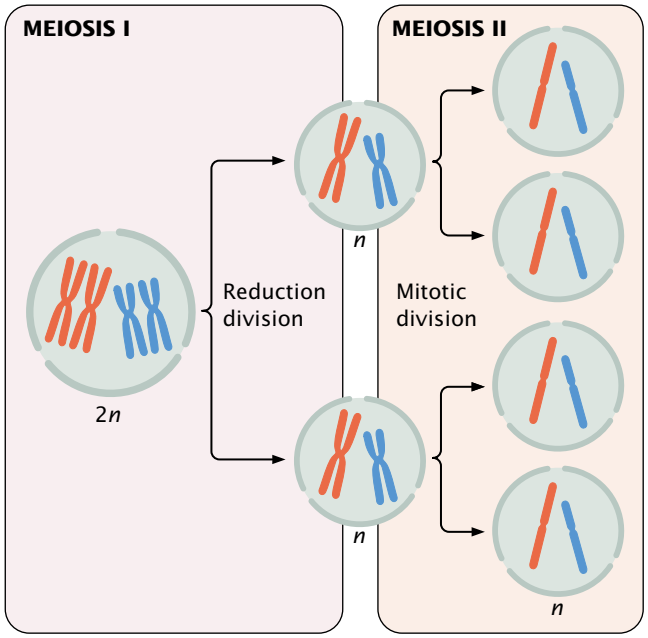
Sexual reproduction consists of two processes. The first is **meiosis,** which leads to gametes in which chromosome number is reduced by half. The second process is **fertilization,** in which two haploid gametes fuse and restore chromosome number to its original diploid value.

Meiosis

The words mitosis and meiosis are sometimes confused. They sound a bit alike, and both include chromosome division and cytokinesis. Don't let this deceive you. The outcomes of mitosis and meiosis are radically different, and several unique events that have important genetic consequences take place only in meiosis.

How is meiosis different from mitosis? Mitosis consists of a single nuclear division and is usually accompanied by a single cell division. Meiosis, on the other hand, consists of two divisions. After mitosis, chromosome number in newly formed cells is the same as that in the original cell, whereas meiosis causes chromosome number in the newly formed cells to be reduced by half. Finally, mitosis produces genetically identical cells, whereas meiosis produces genetically variable cells. Let's see how these differences arise.

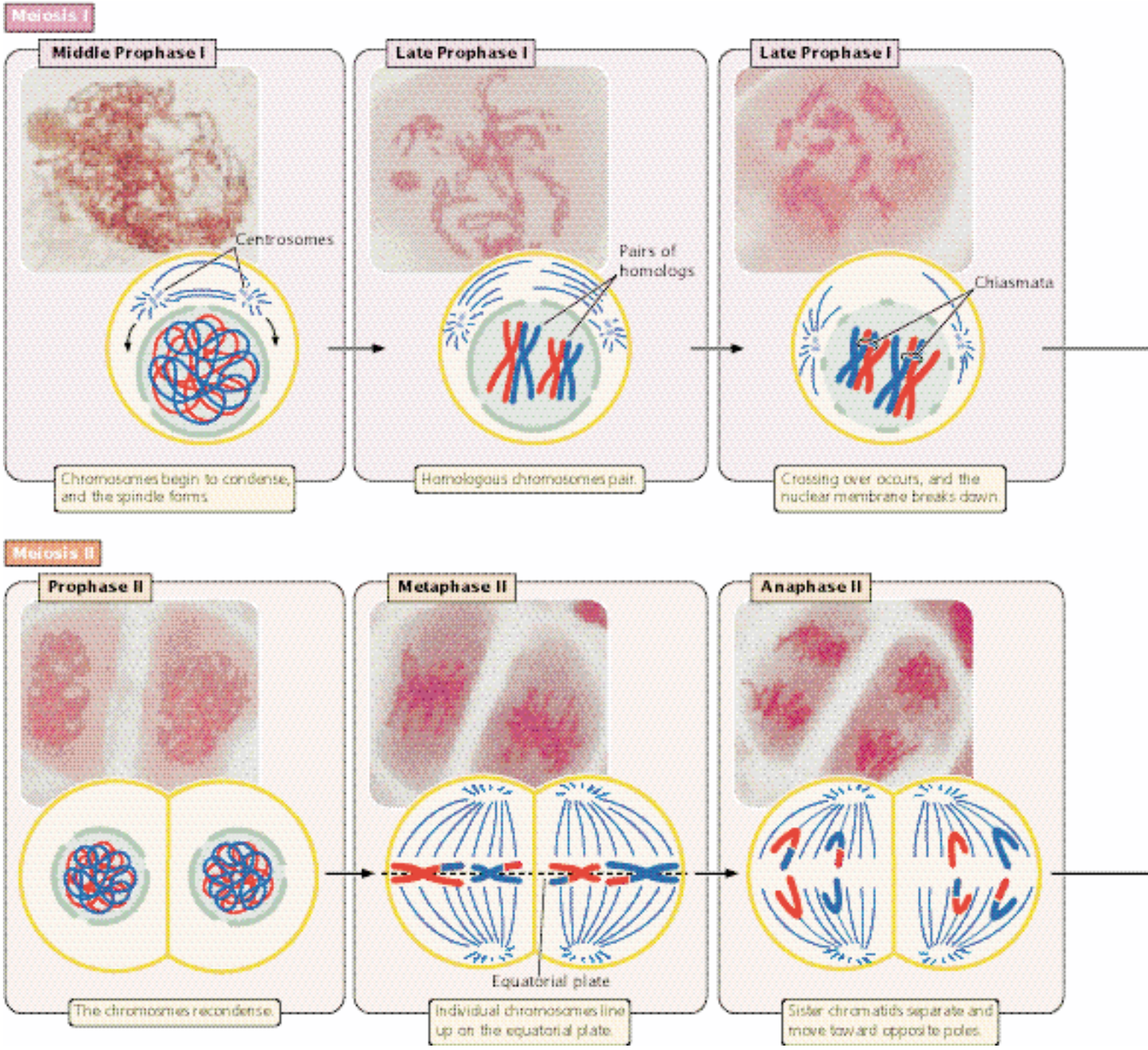
Like mitosis, meiosis is preceded by an interphase stage that includes G_1, S, and G_2 phases. Meiosis consists of two distinct phases: *meiosis I* and *meiosis II,* each of which



2.14 Meiosis includes two cell divisions. In this figure, the original cell is 2n=4. After two meiotic divisions each resulting cell 1n=2.

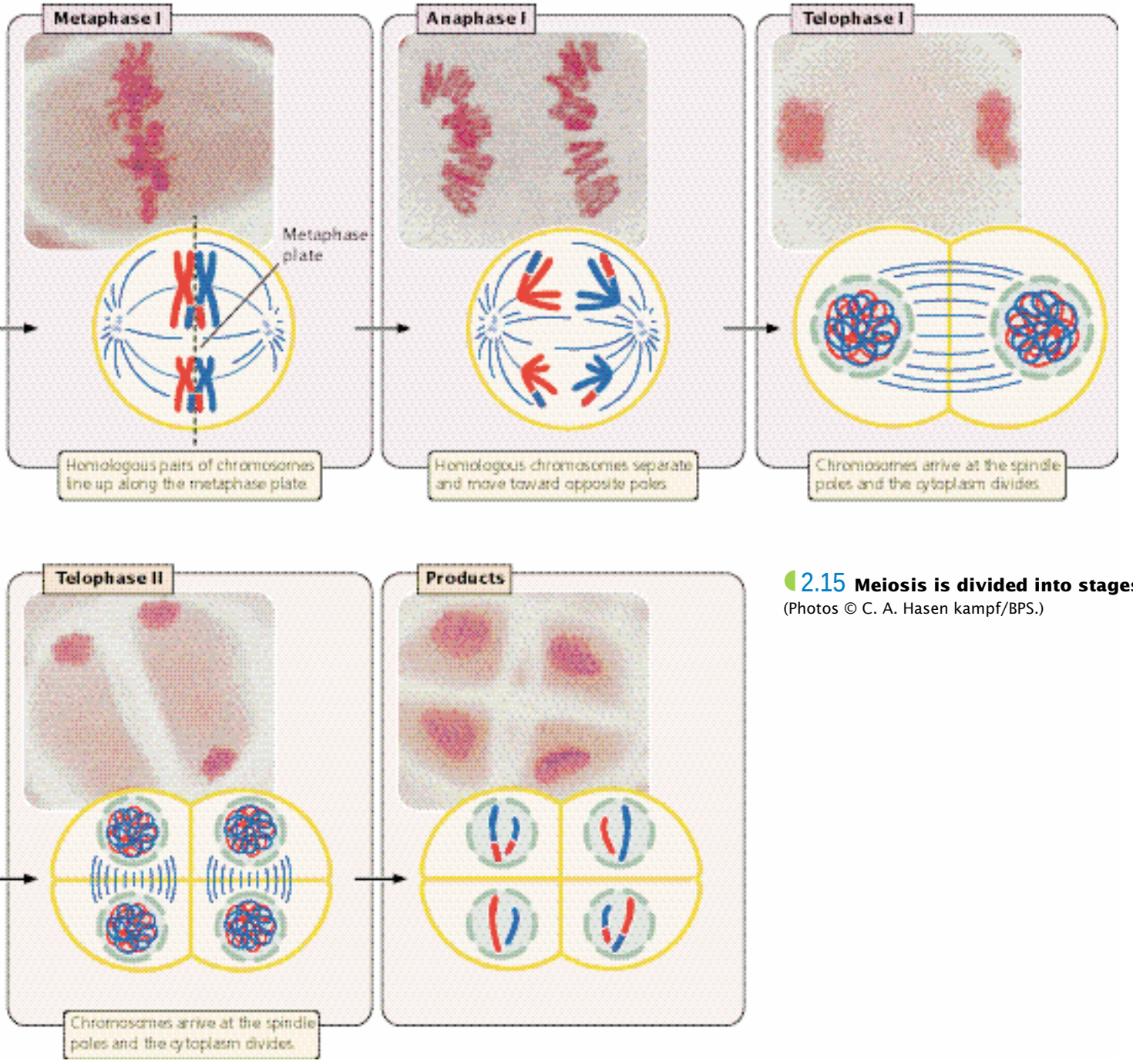
includes a cell division. The first division is termed the reduction division because the number of chromosomes per cell is reduced by half (FIGURE 2.14). The second division is sometimes termed the equational division because the events in this phase are similar to those of mitosis. However, meiosis II differs from mitosis in that chromosome number has already been halved in meiosis I, and the cell does not begin with the same number of chromosomes as it does in mitosis (see Figure 2.14).

The stages of meiosis are outlined in FIGURE 2.15. During interphase, the chromosomes are relaxed and visible as diffuse chromatin. **Prophase I** is a lengthy stage, divided into five substages (FIGURE 2.16). In *leptotene*, the chromosomes contract and become visible. In *zygotene*, the chromosomes continue to condense; homologous chromosomes begin to pair up and begin **synapsis,** a very close pairing association. Each homologous pair of synapsed chromosomes consists of four chromatids called a **bivalent** or **tetrad.** In *pachytene*, the chromosomes become shorter and thicker, and a three-part *synaptonemal complex* develops between homologous chromosomes. **Crossing over** takes place, in which homologous chromosomes exchange genetic information. The centromeres of the paired chromosomes move apart during *diplotene;* the two homologs remain attached at each *chiasma* (plural, chiasmata), which is the result of crossing over. In *diakinesis*, chromosome condensation continues, and the chiasmata move toward the ends of the chromosomes as the strands slip apart; so the homologs remained paired only at the tips. Near the end of prophase I, the nuclear membrane breaks down and the spindle forms.



Metaphase I is initiated when homologous pairs of chromosomes align along the metaphase plate (see Figure 2.15). A microtubule from one pole attaches to one chromosome of a homologous pair, and a microtubule from the other pole attaches to the other member of the pair. **Anaphase I** is marked by the separation of homologous chromosomes. The two chromosomes of a homologous pair are pulled toward opposite poles. Although the homologous chromosomes separate, the sister chromatids remain attached and travel together. In **telophase I,** the chromosomes arrive at the spindle poles and the cytoplasm divides.

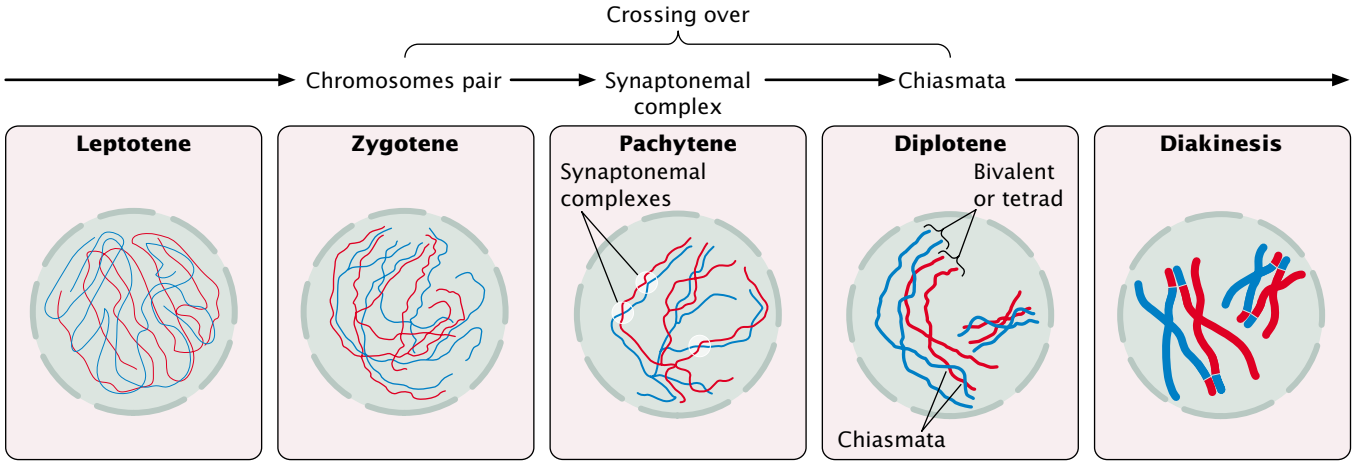
The period between meiosis I and meiosis II is **interkinesis,** in which the nuclear membrane re-forms around the chromosomes clustered at each pole, the spindle breaks down, and the chromosomes relax. These cells then pass through **Prophase II,** in which these events are reversed: the



2.15 **Meiosis is divided into stages.**
(Photos © C. A. Hasen kampf/BPS.)

chromosomes recondense, the spindle re-forms, and the nuclear envelope once again breaks down. In interkinesis in some types of cells, the chromosomes remain condensed, and the spindle does not break down. These cells move directly from cytokinesis into **metaphase II,** which is similar to metaphase of mitosis: the individual chromosomes line up on the metaphase plate, with the sister chromatids facing opposite poles.

In **anaphase II,** the kinetochores of the sister chromatids separate and the chromatids are pulled to opposite poles. Each chromatid is now a distinct chromosome. In **telophase II,** the chromosomes arrive at the spindle poles, a nuclear envelope re-forms around the chromosomes, and the cytoplasm divides. The chromosomes relax and are no longer visible. The major events of meiosis are summarized in Table 2.2.



2.16 **Crossing over takes place in prophase I.** In yeast, rough pairing of chromosomes begins in leptotene and continues in zygotene. The synaptonemal complex forms in pachytene. Crossing over is initiated in zygotene, before the synaptonemal complex develops, and is not completed until near the end of prophase I.

Table 2.2 Major events in each stage of meiosis

Stage	Major Events
Meiosis I	
Prophase I	Chromosomes condense, homologous pairs of chromosomes synapse, crossing over takes place, nuclear envelope breaks down, and mitotic spindle forms
Metaphase I	Homologous pairs of chromosomes line up on the metaphase plate
Anaphase I	The two chromosomes (each with two chromatids) of each homologous pair separate and move toward opposite poles
Telophase I	Chromosomes arrive at the spindle poles
Cytokinesis	The cytoplasm divides to produce two cells, each having half the original number of chromosomes
Interkinesis	In some cells the spindle breaks down, chromosomes relax, and a nuclear envelope re-forms, but no DNA synthesis takes place
Meiosis II	
Prophase II*	Chromosomes condense, the spindle forms, and the nuclear envelope disintegrates
Metaphase II	Individual chromosomes line up on the metaphase plate
Anaphase II	Sister chromatids separate and migrate as individual chromosomes toward the spindle poles
Telophase II	Chromosomes arrive at the spindle poles; the spindle breaks down and a nuclear envelope re-forms
Cytokinesis	The cytoplasm divides

*Only in cells in which the spindle has broken down, chromosomes have relaxed, and the nuclear envelope has re-formed in telophase I. Other types of cells skip directly to metaphase II after cytokinesis.

Consequences of Meiosis

What are the overall consequences of meiosis? First, meiosis comprises two divisions; so each original cell produces four cells (there are exceptions to this generalization, as, for example, in many female animals; see Figure 2.22b). Second, chromosome number is reduced by half; so cells produced by meiosis are haploid. Third, cells produced by meiosis are genetically different from one another and from the parental cell.

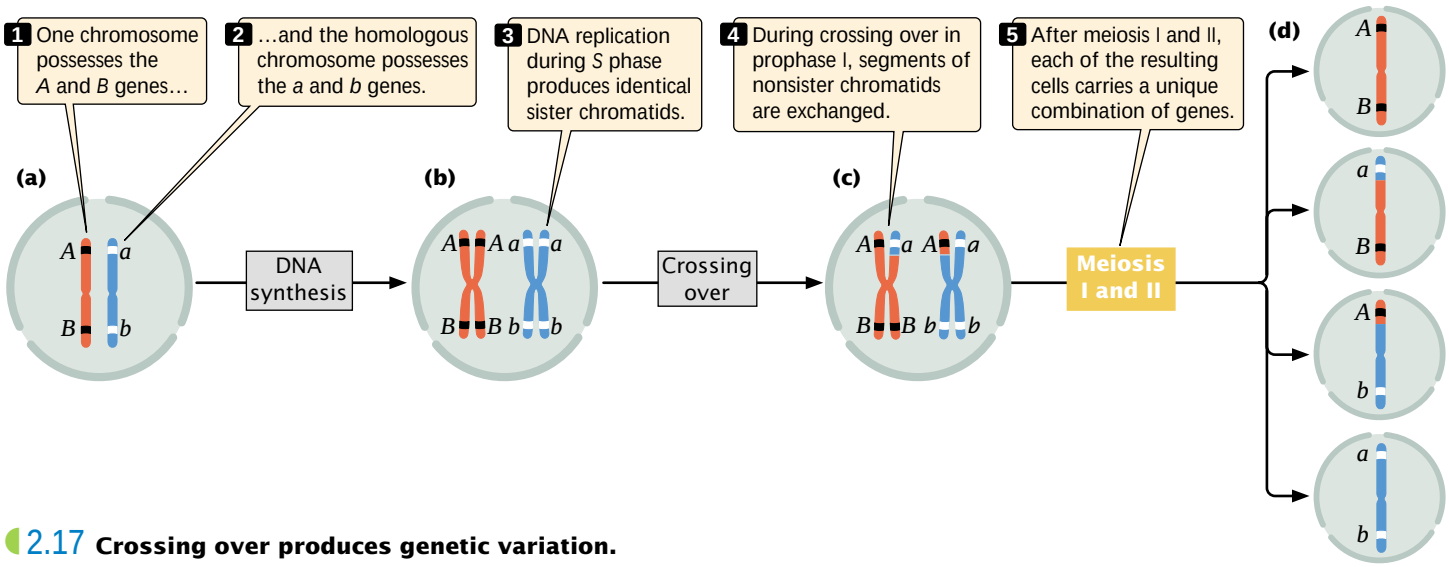
Genetic differences among cells result from two processes that are unique to meiosis. The first is crossing over, which takes place in prophase I. Crossing over refers to the exchange of genes between nonsister chromatids (chromatids from different homologous chromosomes). At one time, this process was thought to take place in pachytene (Figure 2.15b), and the synaptonemal complex was believed to be a requirement for crossing over. However, recent evidence from yeast suggests that the situation is more complex, as shown in Figure 2.16. Crossing over is initiated in zygotene, before the synaptonemal complex develops, and is not completed until near the end of prophase I.

After crossing over has taken place, the sister chromatids may no longer be identical. Crossing over is the basis for intrachromosomal **recombination,** creating new combinations of alleles on a chromatid. To see how crossing over produces genetic variation, consider two pairs of alleles, which we will abbreviate *Aa* and *Bb*. Assume that one chromosome possesses the *A* and *B* alleles and its homolog possesses the *a* and *b* alleles (Figure 2.17a). When DNA is replicated in the S stage, each chromosome duplicates, and so the resulting sister chromatids are identical (Figure 2.17b).

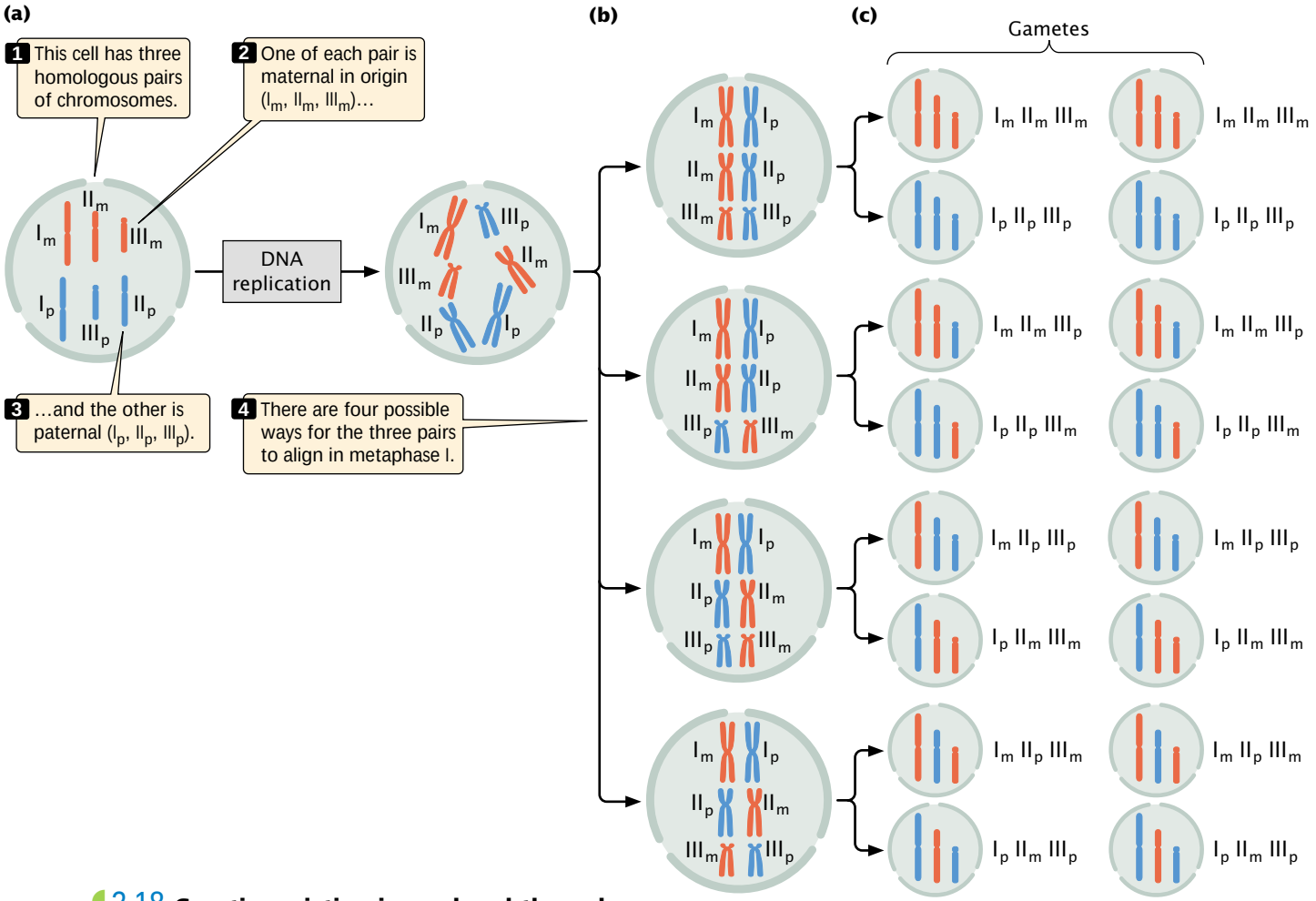
In the process of crossing over, breaks occur in the DNA strands and the breaks are repaired in such a way that segments of nonsister chromatids are exchanged (Figure 2.17c). The molecular basis of this process will be described in more detail in Chapter 12; the important thing here is that, after crossing over has taken place, the two sister chromatids are no longer identical—one chromatid has alleles *A* and *B*, whereas its sister chromatid (the chromatid that underwent crossing over) has alleles *a* and *B*. Likewise, one chromatid of the other chromosome has alleles *a* and *b*, and the other has alleles *A* and *b*. Each of the four chromatids now carries a unique combination of alleles: *A B*, *a B*, *A b*, and *a b*. Eventually, the two homologous chromosomes separate, each going into a different cell. In meiosis II, the two chromatids of each chromosome separate, and thus each of the four cells resulting from meiosis carries a different combination of alleles (Figure 2.17d).

The second process of meiosis that contributes to genetic variation is the random distribution of chromosomes in anaphase I of meiosis following their random alignment during metaphase I. To illustrate this process, consider a cell with three pairs of chromosomes I, II, and III (Figure 2.18a). One chromosome of each pair is maternal in origin (I_m, II_m, and III_m); the other is paternal in origin (I_p, II_p, and III_p). The chromosome pairs line up in the center of the cell in metaphase I and, in anaphase I, the chromosomes of each homologous pair separate.

How each pair of homologs aligns and separates is random and independent of how other pairs of chromosomes align and separate (Figure 2.18b). By chance, all the maternal chromosomes might migrate to one side, with all the paternal chromosomes migrating to the other. After division, one cell would contain chromosomes I_m, II_m, and III_m, and the other, I_p, II_p, and III_p. Alternatively, the I_m, II_m, and III_p chromosomes might move to one side, and the I_p, II_p, and III_m chromosomes to the other. The different migrations would produce different combinations of chromosomes in the resulting cells (Figure 2.18c). There are four ways in which a diploid cell with three pairs of chromosomes can divide, producing a total of eight different



2.17 **Crossing over produces genetic variation.**



2.18 Genetic variation is produced through the random distribution of chromosomes in meiosis. In this example, the cell shown possesses three homologous pairs of chromosomes.

combinations of chromosomes in the gametes. In general, the number of possible combinations is 2^n, where n equals the number of homologous pairs. As the number of chromosome pairs increases, the number of combinations quickly becomes very large. In humans, who have 23 pairs of chromosomes, there are 8,388,608 different combinations of chromosomes possible from the random separation of homologous chromosomes. Through the random distribution of chromosomes in anaphase I, alleles located on different chromosomes are sorted into different combinations. The genetic consequences of this process, termed independent assortment, will be explored in more detail in Chapter 3.

In summary, crossing over shuffles alleles on the *same* homologous chromosomes into new combinations, whereas the random distribution of maternal and paternal chromosomes shuffles alleles on *different* chromosomes into new combinations. Together, these two processes are capable of producing tremendous amounts of genetic variation among the cells resulting from meiosis.

Concepts

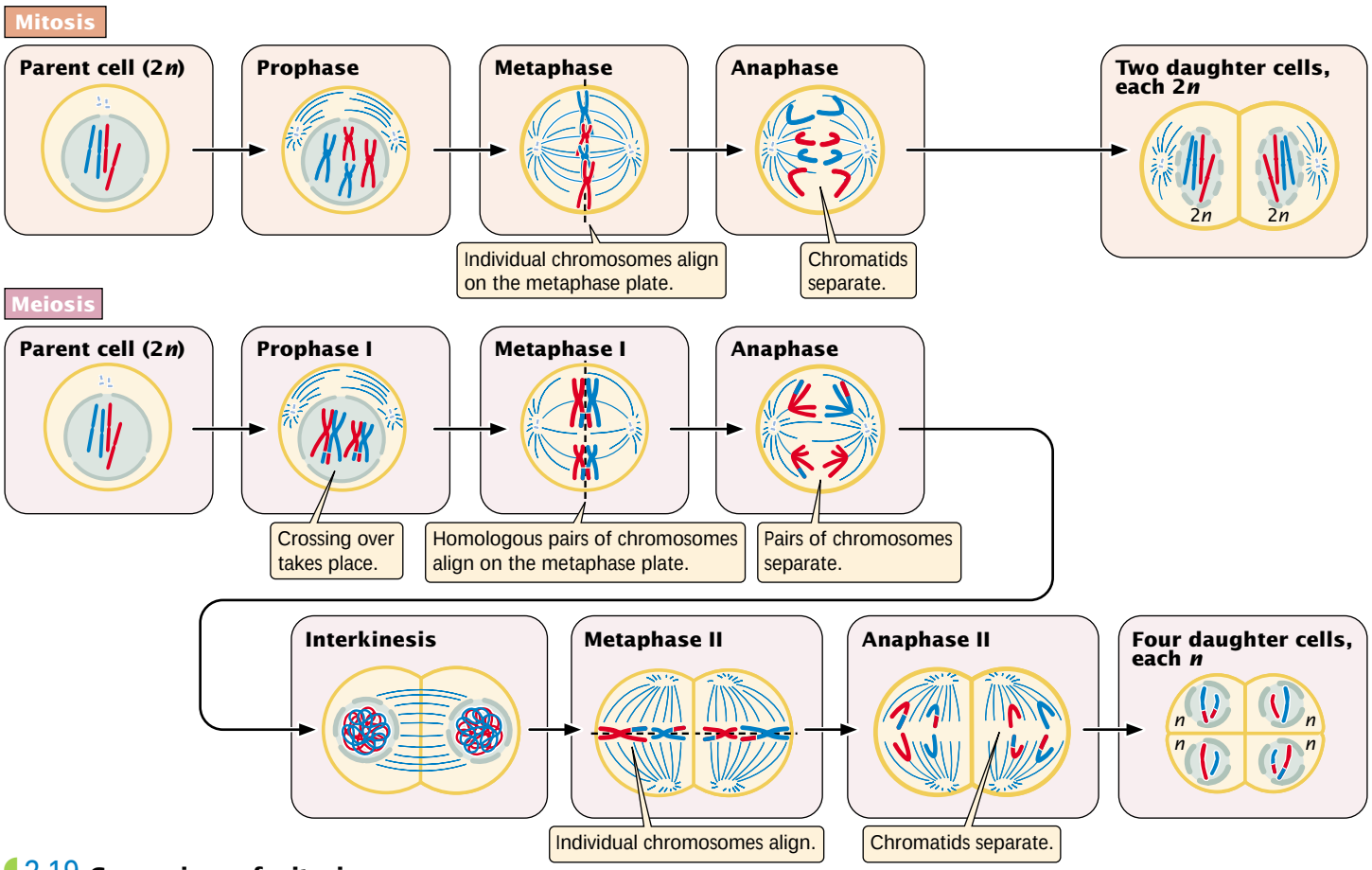
Meiosis consists of two distinct divisions: meiosis I and meiosis II. Meiosis (usually) produces four haploid cells that are genetically variable. The two processes responsible for genetic variation are crossing over and the random distribution of maternal and paternal chromosomes.

www.whfreeman.com/pierce A tutorial and animations of meiosis

Connecting Concepts

Comparison of Mitosis and Meiosis

Now that we have examined the details of mitosis and meiosis, let's compare the two processes (Figure 2.19). In both mitosis and meiosis, the chromosomes contract and



2.19 Comparison of mitosis and meiosis (female, ♀; male, ♂).

become visible; both processes include the movement of chromosomes toward the spindle poles, and both are accompanied by cell division. Beyond these similarities, the processes are quite different.

Mitosis entails a single cell division and usually produces two daughter cells. Meiosis, in contrast, comprises two cell divisions and usually produces four cells. In diploid cells, homologous chromosomes are present before both meiosis and mitosis, but the pairing of homologs takes place only in meiosis.

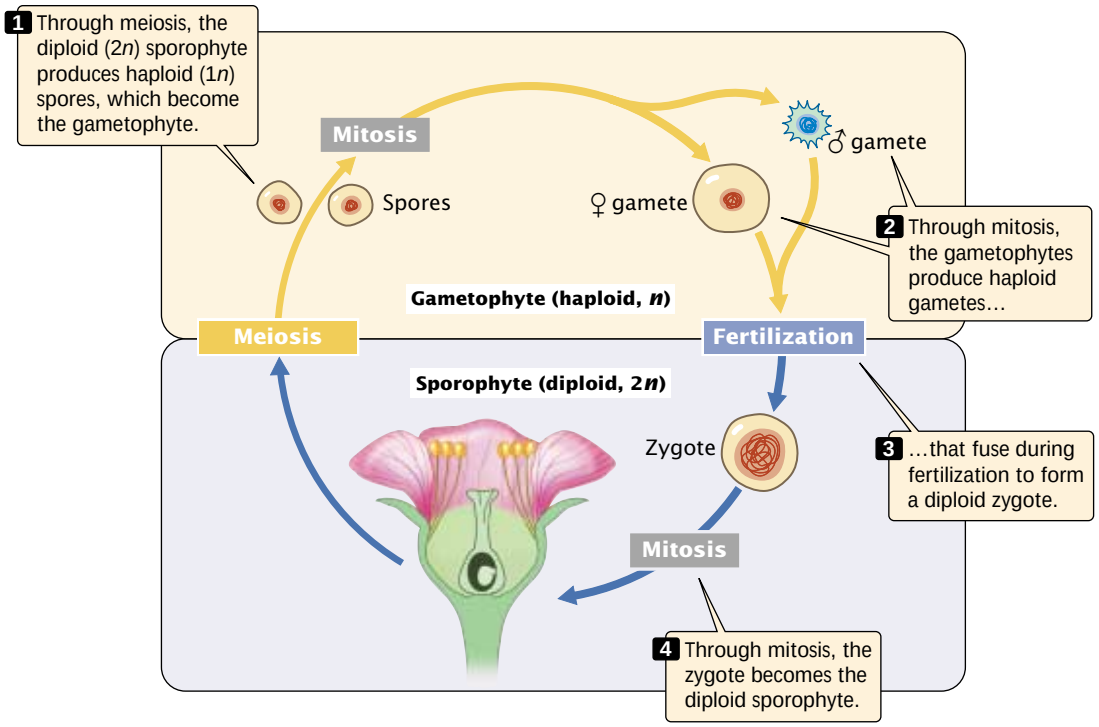
Another difference is that, in meiosis, chromosome number is reduced by half in anaphase I, but no chromosome reduction takes place in mitosis. Furthermore, meiosis is characterized by two processes that produce genetic variation: crossing over (in prophase I) and the random distribution of maternal and paternal chromosomes (in anaphase I). There are normally no equivalent processes in mitosis.

Mitosis and meiosis also differ in the behavior of chromosomes in metaphase and anaphase. In metaphase I of meiosis, *homologous pairs* of chromosomes line up on the metaphase plate, whereas *individual chromosomes* line up on the metaphase plate in metaphase of mitosis (and metaphase II of meiosis). In anaphase I of meiosis, *paired chromosomes* separate, and each of the chromosomes that migrate toward a pole possesses two chromatids attached at the centromere. In contrast, in anaphase of mitosis (and anaphase II of meiosis), *chromatids* separate, and each chromosome that moves toward a spindle pole consists of a single chromatid.

Meiosis in the Life Cycle of Plants and Animals

The overall result of meiosis is four haploid cells that are genetically variable. Let's now see where meiosis fits into the life cycle of a multicellular plant and a multicellular animal.

Sexual reproduction in plants Most plants have a complex life cycle that includes two distinct generations (stages): the diploid *sporophyte* and the haploid *gametophyte*. These two stages alternate; the sporophyte produces haploid spores through meiosis, and the gametophyte produces haploid gametes through mitosis (**Figure 2.20**). This type of life cycle is sometimes called *alternation of generations*. In this cycle, the immediate products of meiosis



2.20 Plants alternate between diploid and haploid life stages.

are called spores, not gametes; the spores undergo one or more mitotic divisions to produce gametes. Although the terms used for this process are somewhat different from those commonly used in regard to animals (and from some of those employed so far in this chapter), the processes in plants and animals are basically the same: in both, meiosis leads to a reduction in chromosome number, producing haploid cells.

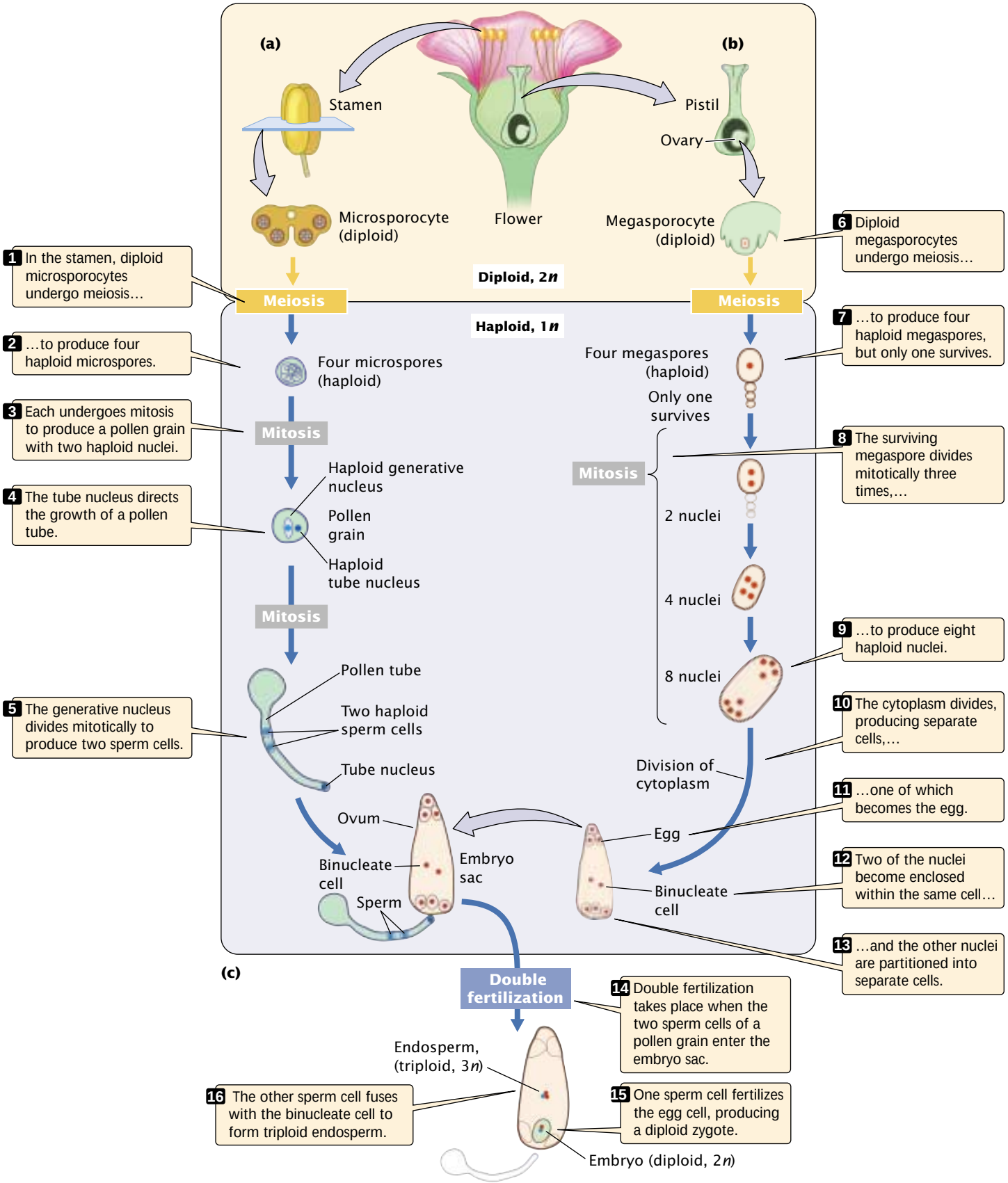
In flowering plants, the sporophyte is the obvious, vegetative part of the plant; the gametophyte consists of only a few haploid cells within the sporophyte. The flower, which is part of the sporophyte, contains the reproductive structures. In some plants, both male and female reproductive structures are found in the same flower; in other plants, they exist in different flowers. In either case, the male part of the flower, the stamen, contains diploid reproductive cells called **microsporocytes,** each of which undergoes meiosis to produce four haploid **microspores** (FIGURE 2.21a). Each microspore divides mitotically, producing an immature pollen grain consisting of two haploid nuclei. One of these nuclei, called the tube nucleus, directs the growth of a pollen tube. The other, termed the generative nucleus, divides mitotically to produce two sperm cells. The pollen grain, with its two haploid nuclei, is the male gametophyte.

The female part of the flower, the ovary, contains diploid cells called **megasporocytes,** each of which undergoes meiosis to produce four haploid **megaspores** (FIGURE 2.21b), only one of which survives. The nucleus of the surviving megaspore divides mitotically three times, producing a total of eight haploid nuclei that make up the female gametophyte, the embryo sac. Division of the cytoplasm then produces separate cells, one of which becomes the *egg.*

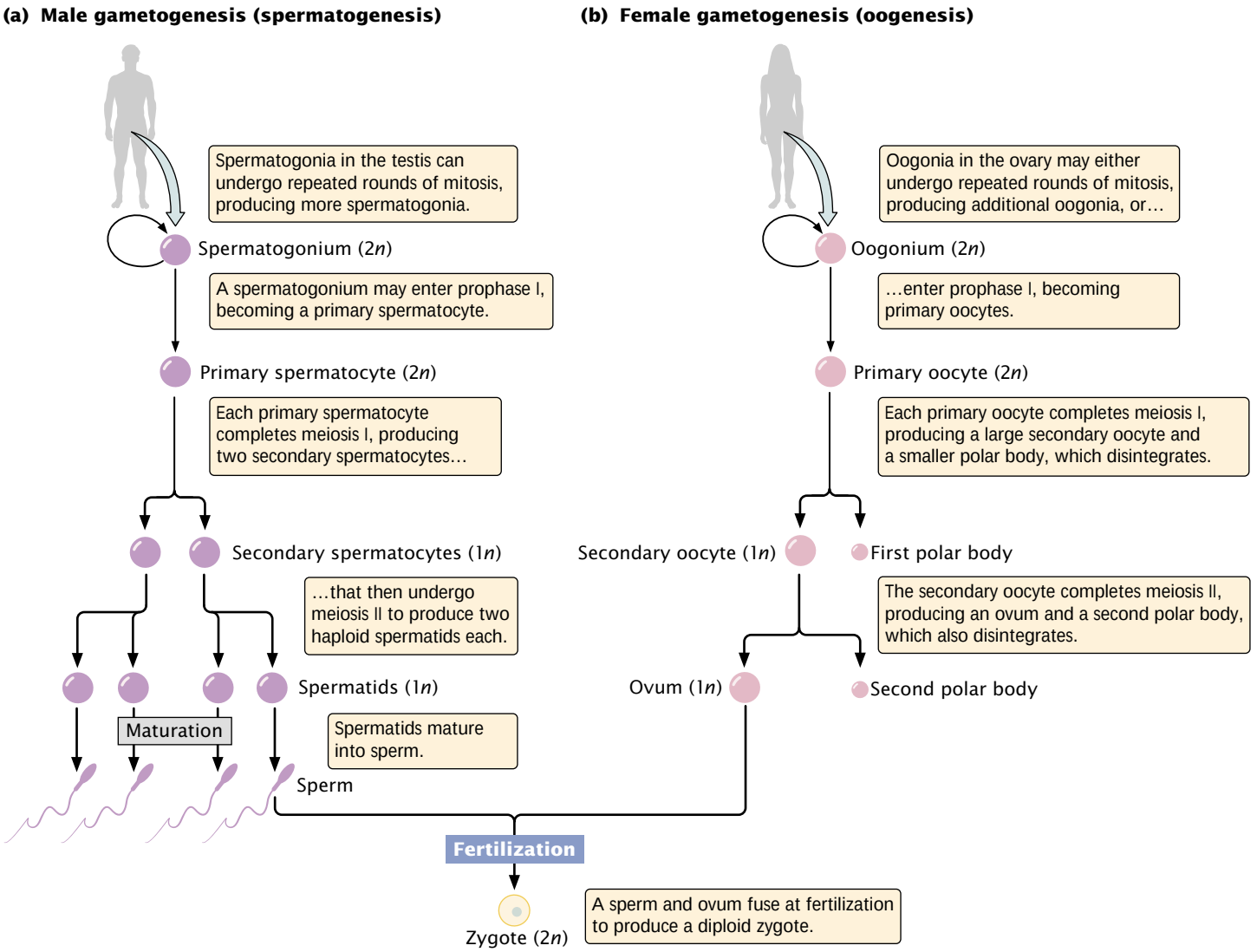
When the plant flowers, the stamens open and release pollen grains. Pollen lands on a flower's stigma—a sticky platform that sits on top of a long stalk called the style. At the base of the style is the ovary. If a pollen grain germinates, it grows a tube down the style into the ovary. The two sperm cells pass down this tube and enter the embryo sac (FIGURE 2.21c). One of the sperm cells fertilizes the egg cell, producing a diploid zygote, which develops into an embryo. The other sperm cell fuses with two nuclei enclosed in a single cell, giving rise to a 3*n* (triploid) endosperm, which stores food that will be used later by the embryonic plant. These two fertilization events are termed *double fertilization.*

Concepts

In the stamen of a flowering plant, meiosis produces haploid microspores that divide mitotically to produce haploid sperm in a pollen grain. Within the ovary, meiosis produces four haploid megaspores, only one of which divides mitotically three times to produce eight haploid nuclei. During pollination, one sperm fertilizes the egg cell, producing a diploid zygote; the other fuses with two nuclei to form the endosperm.



2.21 Sexual reproduction in flowering plants.



2.22 Gamete formation in animals.

Meiosis in animals The production of gametes in a male animal **(spermatogenesis)** takes place in the testes. There, diploid primordial germ cells divide mitotically to produce diploid cells called **spermatogonia** (Figure 2.22a). Each spermatogonium can undergo repeated rounds of mitosis, giving rise to numerous additional spermatogonia. Alternatively, a spermatogonium can initiate meiosis and enter into prophase I. Now called a **primary spermatocyte,** the cell is still diploid because the homologous chromosomes have not yet separated. Each primary spermatocyte completes meiosis I, giving rise to two haploid **secondary spermatocytes** that then undergo meiosis II, with each producing two haploid **spermatids.** Thus, each primary spermatocyte produces a total of four haploid spermatids, which mature and develop into sperm.

The production of gametes in the female **(oogenesis)** begins much like spermatogenesis. Diploid primordial germ cells within the ovary divide mitotically to produce **oogonia** (Figure 2.22b). Like spermatogonia, oogonia can undergo repeated rounds of mitosis or they can enter into meiosis. Once in prophase I, these still-diploid cells are called **primary oocytes.** Each primary oocyte completes meiosis I and divides.

Here the process of oogenesis begins to differ from that of spermatogenesis. In oogenesis, cytokinesis is unequal: most of the cytoplasm is allocated to one of the two haploid cells, the **secondary oocyte.** The smaller cell, which contains half of the chromosomes but only a small part of the cytoplasm, is called the **first polar body;** it may or may not divide further. The secondary oocyte completes meiosis II, and again cytokinesis is unequal—most of the cytoplasm passes into one of the cells. The larger cell, which acquires most of the cytoplasm, is the **ovum,** the mature female gamete. The smaller cell is the **second polar body.** Only the ovum is capable of being fertilized, and the polar bodies usually disintegrate. Oogenesis, then, produces a single mature gamete from each primary oocyte.

We have now examined the place of meiosis in the sexual cycle of two organisms, a flowering plant and a typical multicellular animal. These cycles are just two of the many variations found among eukaryotic organisms. Although the cellular events that produce reproductive cells in plants and animals differ in the number of cell divisions, the number of haploid gametes produced, and the relative size of the final products, the overall result is the same: meiosis gives rise to haploid, genetically variable cells that then fuse during fertilization to produce diploid progeny.

Concepts

In the testes, a diploid spermatogonium undergoes meiosis, producing a total of four haploid sperm cells. In the ovary, a diploid oogonium undergoes meiosis to produce a single large ovum and smaller polar bodies that normally disintegrate.

Connecting Concepts Across Chapters

This chapter focused on the processes that bring about cell reproduction, the starting point of all genetics. We have examined four major concepts: (1) the differences that exist in the organization and packaging of genetic material in prokaryotic and eukaryotic cells; (2) the cell cycle and its genetic results; (3) meiosis, its genetic results, and how it differs from mitosis of the cell cycle; and (4) how meiosis fits into the reproductive cycles of plants and animals.

Several of the concepts presented in this chapter serve as an important foundation for topics in other chapters of this book. The fundamental differences in the organization of genetic material of prokaryotes and eukaryotes are important to keep in mind as we explore the molecular functioning of DNA. The presence of histone proteins in eukaryotes affects the way that DNA is copied (Chapter 12) and read (Chapter 13). The direct contact between DNA and cytoplasmic organelles in prokaryotes and the separation of DNA by the nuclear envelope in eukaryotes have important implications for gene regulation (Chapter 16) and the way that gene products are modified before they are translated into proteins (Chapter 14). The smaller amount of DNA per cell in prokaryotes also affects the organization of genes on chromosomes (Chapter 11).

A critical concept in this chapter is meiosis, which serves as the cellular basis of genetic crosses in most eukaryotic organisms. It is the basis for the rules of inheritance presented in Chapters 3 through 6 and provides a foundation for almost all of the remaining chapters of this book.

CONCEPTS SUMMARY

- A prokaryotic cell possesses a simple structure, with no nuclear envelope and usually a single, circular chromosome. A eukaryotic cell possesses a more complex structure, with a nucleus and multiple linear chromosomes consisting of DNA complexed to histone proteins.
- Cell reproduction requires the copying of the genetic material, separation of the copies, and cell division.
- In a prokaryotic cell, the single chromosome replicates, and each copy attaches to the plasma membrane; growth of the plasma membrane separates the two copies, which is followed by cell division.
- In eukaryotic cells, reproduction is more complex than in prokaryotic cells, requiring mitosis and meiosis to ensure that a complete set of genetic information is transferred to each new cell.
- In eukaryotic cells, chromosomes are typically found in homologous pairs.
- Each functional chromosome consists of a centromere, a telomere, and multiple origins of replication. Centromeres are the points at which kinetochores assemble and to which microtubules attach. Telomeres are the stable ends of chromosomes. After a chromosome is copied, the two copies remain attached at the centromere, forming sister chromatids.
- The cell cycle consists of the stages through which a eukaryotic cell passes between cell divisions. It consists of: (1) interphase, in which the cell grows and prepares for division and (2) M phase, in which nuclear and cell division take place. M phase consists of mitosis, the process of nuclear division, and cytokinesis, the division of the cytoplasm.
- Interphase begins with G_1, in which the cell grows and synthesizes proteins necessary for cell division, followed by S phase, during which the cell's DNA is replicated. The cell then enters G_2, in which additional biochemical events necessary for cell division take place. Some cells exit G_1 and enter a nondividing state called G_0.
- M phase consists of prophase, prometaphase, metaphase, anaphase, telophase, and cytokinesis. In these stages, the chromosomes contract, the nuclear membrane breaks down, and the spindle forms. The chromosomes line up in the center of the cell. Sister chromatids separate and become independent chromosomes, which then migrate to opposite ends of the cell. The nuclear membrane reforms around chromosomes at each end of the cell, and the cytoplasm divides.
- The usual result of mitosis is the production of two genetically identical cells.

- Progression through the cell cycle is controlled by interactions between cyclins and cyclin-dependent kinases.
- Sexual reproduction produces genetically variable progeny and allows for accelerated evolution. It includes meiosis, in which haploid sex cells are produced, and fertilization, the fusion of sex cells. Meiosis includes two cell divisions. In meiosis I, crossing over occurs and homologous chromosomes separate. In meiosis II, chromatids separate.
- The usual result of meiosis is the production of four haploid cells that are genetically variable.
- Genetic variation in meiosis is produced by crossing over and by the random distribution of maternal and paternal chromosomes.
- In plants, diploid microsporocytes in the stamens undergo meiosis, each microsporocyte producing four haploid microspores. Each microspore divides mitotically to produce two haploid sperm cells. In the ovary, diploid megasporocytes undergo meiosis, each megasporocyte producing four haploid macrospores, only one of which survives. The surviving megaspore divides mitotically three times to produce eight haploid nuclei, one of which forms the egg. During pollination, one sperm fertilizes the egg cell and the other fuses with two haploid nuclei to form a 3*n* endosperm.
- In animals, diploid spermatogonia initiate meiosis and become diploid primary spermatocytes, which then complete meiosis I, producing two haploid secondary spermatocytes. Each secondary spermatocyte undergoes meiosis II, producing a total of four haploid sperm cells from each primary spermatocyte. Diploid oogonia in the ovary enter meiosis and become diploid primary oocytes, each of which then completes meiosis I, producing one large haploid secondary oocyte and one small haploid polar body. The secondary oocyte completes meiosis II to produce a large haploid ovum and a smaller second polar body.

IMPORTANT TERMS

genome (p. 16)
prokaryote (p. 17)
eukaryote (p. 17)
eubacteria (p. 18)
archaea (p. 18)
nucleus (p. 18)
histone (p. 18)
chromatin (p. 18)
homologous pair (p. 20)
diploid (p. 20)
haploid (p. 20)
telomere (p. 21)
origin of replication (p. 21)
sister chromatid (p. 22)
cell cycle (p. 22)
interphase (p. 22)
M phase (p. 22)
mitosis (p. 22)
cytokinesis (p. 22)
prophase (p. 23)
prometaphase (p. 23)
metaphase (p. 23)
anaphase (p. 23)
telophase (p. 23)
meiosis (p. 29)
fertilization (p. 29)
prophase I (p. 29)
synapsis (p. 29)
bivalent (p. 29)
tetrad (p. 29)
crossing over (p. 29)
metaphase I (p. 30)
anaphase I (p. 30)
telophase I (p. 30)
interkinesis (p. 30)
prophase II (p. 30)
metaphase II (p. 31)
anaphase II (p. 31)
telophase II (p. 31)
recombination (p. 33)
microsporocyte (p. 36)
microspore (p. 36)
megasporocyte (p. 36)
megaspore (p. 36)
spermatogenesis (p. 38)
spermatogonium (p. 38)
primary spermatocyte (p. 38)
secondary spermatocyte (p. 38)
spermatid (p. 38)
oogenesis (p. 38)
oogonium (p. 38)
primary oocyte (p. 38)
secondary oocyte (p. 38)
first polar body (p. 38)
ovum (p. 38)
second polar body (p. 38)

Worked Problems

1. A student examines a thin section of an onion root tip and records the number of cells that are in each stage of the cell cycle. She observes 94 cells in interphase, 14 cells in prophase, 3 cells in prometaphase, 3 cells in metaphase, 5 cells in anaphase, and 1 cell in telophase. If the complete cell cycle in an onion root tip requires 22 hours, what is the average duration of each stage in the cycle? Assume that all cells are in active cell cycle (not G_0).

• Solution

This problem is solved in two steps. First, we calculate the proportions of cells in each stage of the cell cycle, which correspond to the amount of time that an average cell spends in each stage. For example, if cells spend 90% of their time in interphase, then, at any given moment, 90% of the cells will be in interphase. The second step is to convert the proportions into lengths of time, which is done by multiplying the proportions by the total time of the cell cycle (22 hours).

Step 1. Calculate the proportion of cells at each stage. The proportion of cells at each stage is equal to the number of cells found in that stage divided by the total number of cells examined:

Interphase	$^{94}/_{120} = 0.783$
Prophase	$^{14}/_{120} = 0.117$
Prometaphase	$^{3}/_{120} = 0.025$
Metaphase	$^{3}/_{120} = 0.025$
Anaphase	$^{5}/_{120} = 0.042$
Telophase	$^{1}/_{120} = 0.008$

We can check our calculations by making sure that the proportions sum to 1.0, which they do.

Step 2. Determine the average duration of each stage. To determine the average duration of each stage, multiply the proportion of cells in each stage by the time required for the entire cell cycle:

Interphase	0.783×22 hours $= 17.23$ hours
Prophase	0.117×22 hours $=$ 2.57 hours
Prometaphase	0.025×22 hours $=$ 0.55 hour
Metaphase	0.025×22 hours $=$ 0.55 hour
Anaphase	0.042×22 hours $=$ 0.92 hour
Telophase	0.008×22 hours $=$ 0.18 hour

2. A cell in G_1 of interphase has 8 chromosomes. How many chromosomes and how many DNA molecules will be found per cell as this cell progresses through the following stages: G_2, metaphase of mitosis, anaphase of mitosis, after cytokinesis in mitosis, metaphase I of meiosis, metaphase II of meiosis, and after cytokinesis of meiosis II?

• Solution

Remember the rules that we learned about counting chromosomes and DNA molecules: (1) to determine the number of chromosomes, count the functional centromeres; and (2) to determine the number of DNA molecules, count the chromatids. Think carefully about when and how the numbers of chromosomes and DNA molecules change in the course of mitosis and meiosis.

The number of DNA molecules increases only in S phase, when DNA replicates; the number of DNA molecules decreases only when the cell divides. Chromosome number increases only when sister chromatids separate in anaphase of mitosis and anaphase II of meiosis (homologous chromosomes, not chromatids, separate in anaphase I of meiosis). Chromosome number, like the number of DNA molecules, is reduced only by cell division.

Let us now apply these principles to the problem. A cell in G_1 has 8 chromosomes, each consisting of a single chromatid; so 8 DNA molecules are present in G_1. DNA replicates in S stage; so, in G_2, 16 DNA molecules are present per cell. However, the two copies of each DNA molecule remain attached at the centromere; so there are still only 8 chromosomes present. As the cell passes through prophase and metaphase of the cell cycle, the number of chromosomes and DNA molecules remains the same; so, at metaphase, there are 16 DNA molecules and 8 chromosomes. In anaphase, the chromatids separate and each becomes an independent chromosome; at this point, the number of chromosomes increases from 8 to 16. This increase is temporary, lasting only until the cell divides in telophase or subsequent to it. The number of DNA molecules remains at 16 in anaphase. The number of DNA molecules and chromosomes per cell is reduced by cytokinesis after telophase, because the 16 chromosomes and DNA molecules are now distributed between two cells. Therefore, after cytokinesis, each cell has 8 DNA molecules and 8 chromosomes, the same numbers that were present at the beginning of the cell cycle.

Now, let's trace the numbers of DNA molecules and chromosomes through meiosis. At G_1, there are 8 chromosomes and 8 DNA molecules. The number of DNA molecules increases to 16 in S stage, but the number of chromosomes remains at 8 (each chromosome has two chromatids). The cell therefore enters metaphase I with 16 DNA molecules and 8 chromosomes. In anaphase I of meiosis, homologous chromosomes separate, but the number of chromosomes remains at 8. After cytokinesis, the original 8 chromosomes are distributed between two cells; so the number of chromosomes per cell falls to 4 (each with two chromatids). The original 16 DNA molecules also are distributed between two cells; so the number of DNA molecules per cell is 8. There is no DNA synthesis during interkinesis, and each cell still maintains 4 chromosomes and 8 DNA molecules through metaphase II. In anaphase II, the two chromatids of each chromosome separate, temporarily raising the number of chromosomes per cell to 8, whereas the number of DNA molecules per cell remains at 8. After cytokinesis, the chromosomes and DNA molecules are again distributed between two cells, providing 4 chromosomes and 4 DNA molecules per cell. These results are summarized in the following table:

Stage	Number of chromosomes per cell	Number of DNA molecules per cell
G_1	8	8
G_2	8	16
Metaphase of mitosis	8	16
Anaphase of mitosis	16	16
After cytokinesis of mitosis	8	8
Metaphase I of meiosis	8	16
Metaphase II of meiosis	4	8
After cytokinesis of meiosis II	4	4

COMPREHENSION QUESTIONS

1. All organisms have the same universal genetic system. What are the implications of this universal genetic system?
2. Why are the viruses that infect mammalian cells useful for studying the genetics of mammals?
* 3. List three fundamental events that must take place in cell reproduction.
4. Outline the process by which prokaryotic cells reproduce.
5. Name three essential structural elements of a functional eukaryotic chromosome and describe their functions.
* 6. Sketch and label four different types of chromosomes based on the position of the centromere.
7. List the stages of interphase and the major events that take place in each stage.
* 8. List the stages of mitosis and the major events that take place in each stage.

* 9. What are the genetically important results of the cell cycle?

10. Why are the two cells produced by the cell cycle genetically identical?

11. What are checkpoints? What two general classes of compounds regulate progression through the cell cycles?

12. What are the stages of meiosis and what major events take place in each stage?

*13. What are the major results of meiosis?

14. What two processes unique to meiosis are responsible for genetic variation? At what point in meiosis do these processes take place?

*15. List similarities and differences between mitosis and meiosis. Which differences do you think are most important and why?

16. Outline the process by which male gametes are produced in plants. Outline the process of female gamete formation in plants.

17. Outline the process of spermatogenesis in animals. Outline the process of oogenesis in animals.

APPLICATION QUESTIONS AND PROBLEMS

18. A certain species has three pairs of chromosomes: an acrocentric pair, a metacentric pair, and a submetacentric pair. Draw a cell of this species as it would appear in metaphase of mitosis.

19. A biologist examines a series of cells and counts 160 cells in interphase, 20 cells in prophase, 6 cells in prometaphase, 2 cells in metaphase, 7 cells in anaphase, and 5 cells in telophase. If the complete cell cycle requires 24 hours, what is the average duration of M phase in these cells? Of metaphase?

*20. A cell in G1 of interphase has 12 chromosomes. How many chromosomes and DNA molecules will be found per cell when this original cell progresses to the following stages?

(a) G_2 of interphase

(b) Metaphase I of meiosis

(c) Prophase of mitosis

(d) Anaphase I of meiosis

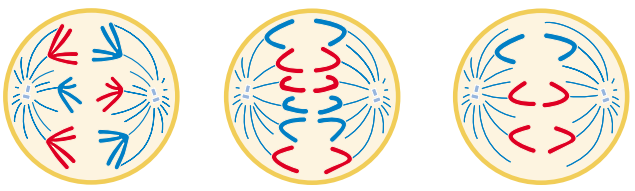
(e) Anaphase II of meiosis

(f) Prophase II of meiosis

(g) After cytokinesis following mitosis

(h) After cytokinesis following meiosis II

*21. All of the following cells, shown in various stages of mitosis and meiosis, come from the same rare species of plant. What is the diploid number of chromosomes in this plant? Give the names of each stage of mitosis or meiosis shown.



22. A cell has 1*x* amount of DNA in G_1 of interphase. How much DNA (in multiples or fractions of *x*) will be present per cell at the following stages?

(a) G_2

(b) Anaphase of mitosis

(c) Prophase II of meiosis

(d) After cytokinesis associated with meiosis II

23. A cell in prophase II of meiosis contains 12 chromosomes. How many chromosomes would be present in a cell from the same organism if it were in prophase of mitosis? Prophase I of meiosis?

*24. The fruit fly *Drosophila melanogaster* has four pairs of chromosomes, whereas the house fly *Musca domestica* has six pairs of chromosomes. Other things being equal, in which species would you expect to see more genetic variation among the progeny of a cross? Explain your answer.

*25. A cell has two pairs of submetacentric chromosomes, which we will call chromosomes I_a, I_b, II_a, and II_b (chromosomes I_a and I_b are homologs, and chromosomes II_a and II_b are homologs). Allele *M* is located on the long arm of chromosome I_a, and allele *m* is located at the same position on chromosome I_b. Allele *P* is located on the short arm of chromosome I_a, and allele *p* is located at the same position on chromosome I_b. Allele *R* is located on chromosome II_a and allele *r* is located at the same position on chromosome II_b.

(a) Draw these chromosomes, labeling genes *M*, *m*, *P*, *p*, *R*, and *r*, as they might appear in metaphase I of meiosis. Assume that there is no crossing over.

(b) Considering the random separation of chromosomes in anaphase I, draw the chromosomes (with labeled genes) present in all possible types of gametes that might result from this cell going through meiosis. Assume that there is no crossing over.

26. A horse has 64 chromosomes and a donkey has 62 chromosomes. A cross between a female horse and a male donkey produces a mule, which is usually sterile. How many chromosomes does a mule have? Can you think of any reasons for the fact that most mules are sterile?

CHALLENGE QUESTIONS

27. Suppose that life exists elsewhere in the universe. All life must contain some type of genetic information, but alien genomes might not consist of nucleic acids and have the same features as those found in the genomes of life on Earth. What do you think might be the common features of all genomes, no matter where they exist?

28. On average, what proportion of the genome in the following pairs of humans would be exactly the same if no crossing over occurred? (For the purposes of this question only, we will ignore the special case of the X and Y sex chromosomes and assume that all genes are located on nonsex chromosomes.)

    (a) Father and child

    (b) Mother and child

    (c) Two full siblings (offspring that have the same two biological parents)

    (d) Half siblings (offspring that have only one biological parent in common)

    (e) Uncle and niece

    (f) Grandparent and grandchild

29. Females bees are diploid and male bees are haploid. The haploid males produce sperm and can successfully mate with diploid females. Fertilized eggs develop into females and unfertilized eggs develop into males. How do you think the process of sperm production in male bees differs from sperm production in other animals?

30. Rec8 is a protein that is found in yeast chromosome arms and centromeres. Rec8 persists throughout meiosis I but breaks down at anaphase II. When the gene that encodes Rec8 is deleted, sister chromatids separate in anaphase I.

    (a) From these observations, propose a mechanism for the role of Rec8 in meiosis that helps to explain why sister chromatids normally separate in anaphase II but not anaphase I.

    (b) Make a prediction about the presence or absence of Rec8 during the various stages of mitosis.

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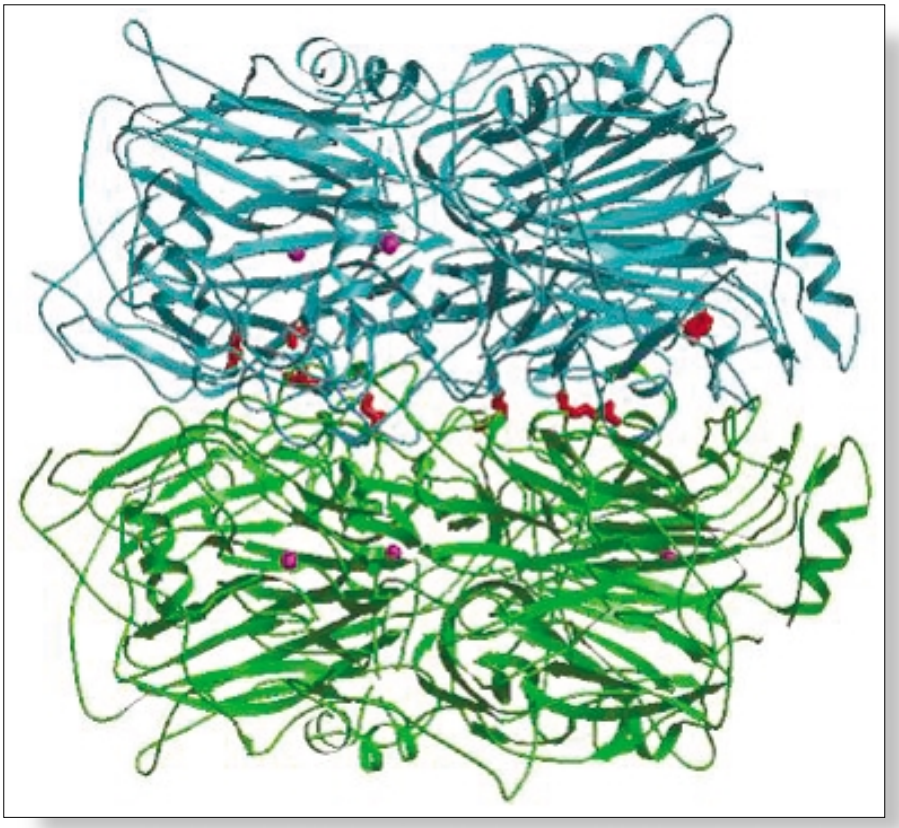
3 Basic Principles of Heredity



Alkaptonuria results from impaired function of homogentisate dioxygenase (shown here), an enzyme required for catabolism of the amino acids phenylalanine and tyrosine. (Courtesy of David E. Timm, Department of Molecular Biology, Indiana School of Medicine, and Miguel Penalva, Centro de Investigaciones. Biológicas CSIC, Madrid, Spain.)

Black Urine and First Cousins

Voiding black urine is a rare and peculiar trait. In 1902, Archibald Garrod discovered the hereditary basis of black urine and, in the process, contributed to our understanding of the nature of genes.

Garrod was an English physician who was more interested in chemical explanations of disease than in the practice of medicine. He became intrigued by several of his patients who produced black urine, a condition known as alkaptonuria. The urine of alkaptonurics contains homogentisic acid, a compound that, on exposure to air, oxidizes and turns the urine black. Garrod observed that alkaptonuria appears at birth and remains for life. He noted that often several children in the same family were affected: of the 32 cases that he knew about, 19 appeared in only seven families. Furthermore, the parents of these alkaptonurics were frequently first cousins. With the assistance of geneticist William Bateson, Garrod recognized that this pattern of inheritance is precisely the pattern produced by the transmission of a rare, recessive gene.

Garrod later proposed that several other human disorders, including albinism and cystinuria, are inherited in the same way as alkaptonuria. He concluded that each gene