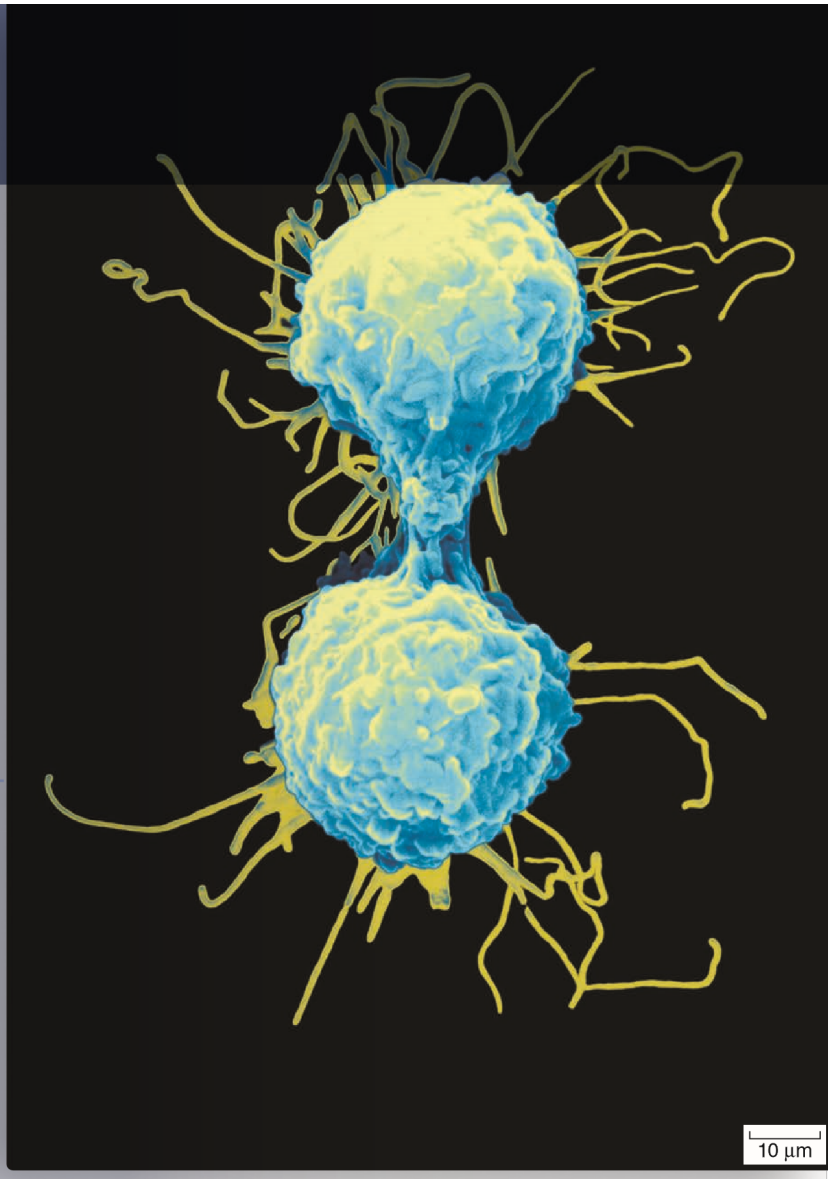
CHAPTER 10

How Cells Divide



Chapter Contents

Introduction

All species of organisms—bacteria, alligators, the weeds in a lawn—grow and reproduce. From the smallest creature to the largest, all species produce offspring like themselves and pass on the hereditary information that makes them what they are. In this chapter, we examine how cells, like the white blood cell shown in the figure, divide and reproduce. Cell division is necessary for the growth of organisms, for wound healing, and to replace cells that are lost regularly, such as those in your skin and in the lining of your gut. The mechanism of cell reproduction and its biological consequences have changed significantly during the evolution of life on Earth. The process is complex in eukaryotes, involving both the replication of chromosomes and their separation into daughter cells. Much of what we are learning about the causes of cancer relates to how cells control this process, and in particular their tendency to divide, a mechanism that in broad outline remains the same in all eukaryotes.

10.1 Bacterial Cell Division

Learning Outcome

1. *Describe the process of binary fission.*

Bacteria divide as a way of reproducing themselves. Although bacteria exchange DNA, they do not have a sexual cycle like eukaryotes. Thus all growth in a bacterial population is due to division to produce new cells. The reproduction of bacteria is clonal—that is, each cell produced by cell division is an identical copy of the original cell.

Binary fission is a simple form of cell division

Cell division in both bacterial and eukaryotic cells produces two new cells with the same genetic information as the original. Despite the differences in these cell types, the essentials of the process are the same: duplication and segregation of genetic information into daughter cells, and division of cellular contents. We begin by looking at the simpler process, **binary fission,** which occurs in bacteria.

Most bacteria have a genome made up of a single, circular DNA molecule. In spite of its apparent simplicity, the DNA molecule of the bacterium *Escherichia coli* is actually on the order of 500 times longer than the cell itself! Thus, this "simple" structure is actually packaged very tightly to fit into the cell. Although not found in a nucleus, the DNA is located in a region called the *nucleoid* that is distinct from the cytoplasm around it.

The compaction and organization of the nucleoid involves a class of proteins called structural maintenance of chromosome, or SMC, proteins. These are ancient proteins that have diversified over evolutionary time to fulfill a variety of roles related to DNA organization in different lineages. In eukaryotes the cohesin and condensin proteins discussed throughout this chapter are SMC proteins.

During binary fission, the chromosome is replicated, and the two products are partitioned to each end of the cell prior to the actual division of the cell. One key feature of bacterial cell division is that replication and partitioning of the chromosome occur as a concerted process. In contrast, DNA replication in eukaryotic cells occurs early in division, and chromosome separation occurs much later.

Bacterial cells control chromosome separation and septum formation

Binary fission begins with the replication of the bacterial DNA at a specific site—the origin of replication (see chapter 14)—and proceeds both directions around the circular DNA to a specific site of termination (figure 10.1). The cell grows by elongation, and division occurs roughly at midcell. For many years, it was thought that newly replicated *E. coli* DNA molecules were passively segregated by attachment to and growth of the membrane as the cell elongated. Experiments that follow the movement of the origin of replication show that it is at midcell prior to replication, then the

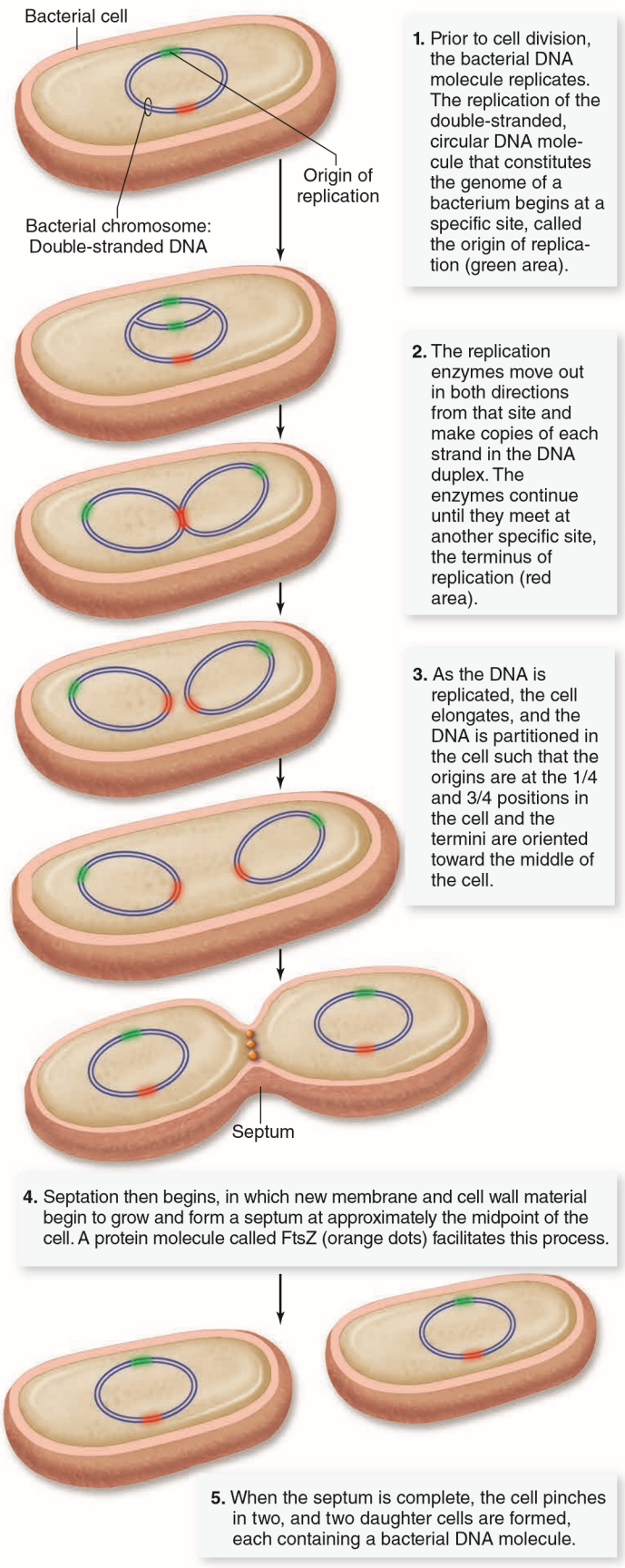


Figure 10.1 **Binary fission.**

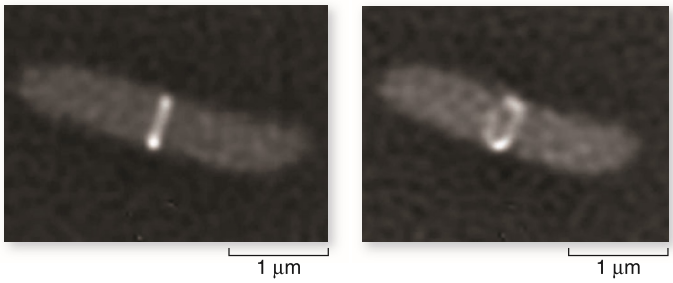


Figure 10.2 The FtsZ protein. In these dividing *E. coli* bacteria, the FtsZ protein is labeled with fluorescent dye to show its location during binary fission. The protein assembles into a ring at approximately the midpoint of the cell, where it facilitates septation and cell division. Bacteria carrying mutations in the *FtsZ* gene are unable to divide.

newly replicated origins move toward opposite ends of the cell. This movement is faster than the rate of elongation, showing that growth alone is not enough. The origins appear to be captured at the one quarter and three quarter positions relative to the length of the cell, which will be midcell of the resulting daughter cells.

Although the actual mechanism of chromosome segregation is unclear, the order of events is not. During replication, first the origin, then the rest of the newly replicated chromosomes are moved to opposite ends of the cell as two new nucleoids are assembled. The final event of replication is decatenation (untangling) of the final replication products. After replication and segregation, the midcell region is cleared of daughter nucleoids, and division occurs. The force behind chromosome segregation has been attributed to DNA replication itself, transcription, and the polymerization of actinlike molecules. At this point, no single model appears to explain the process, and it may involve more than one.

The cell's other components are partitioned by the growth of new membrane and production of the **septum** (figure 10.1). This process, termed **septation,** usually occurs at the midpoint of the cell. It begins with the formation of a ring composed of many copies of the protein FtsZ (figure 10.2). Next, accumulation of a number of other proteins occurs, including ones embedded in the membrane. This structure contracts inward radially until the cell pinches off into two new cells. The midcell location of the FtsZ ring is caused by an oscillation between the two poles of an inhibitor of FtsZ formation.

The FtsZ protein is found in most prokaryotes, including archaea. It can form filaments and rings, and three-dimensional crystals show a high degree of similarity to eukaryotic tubulin. However, its role in bacterial division is quite different from the role of tubulin in mitosis in eukaryotes.

The evolution of eukaryotic cells included much more complex genomes composed of multiple linear chromosomes housed in a membrane-bounded nucleus. These complex genomes may be possible due to the evolution of mechanisms that delay chromosome separation after replication. Although it is unclear how this ability to keep chromosomes together evolved, it does seem more closely related to binary fission than we once thought (figure 10.3).

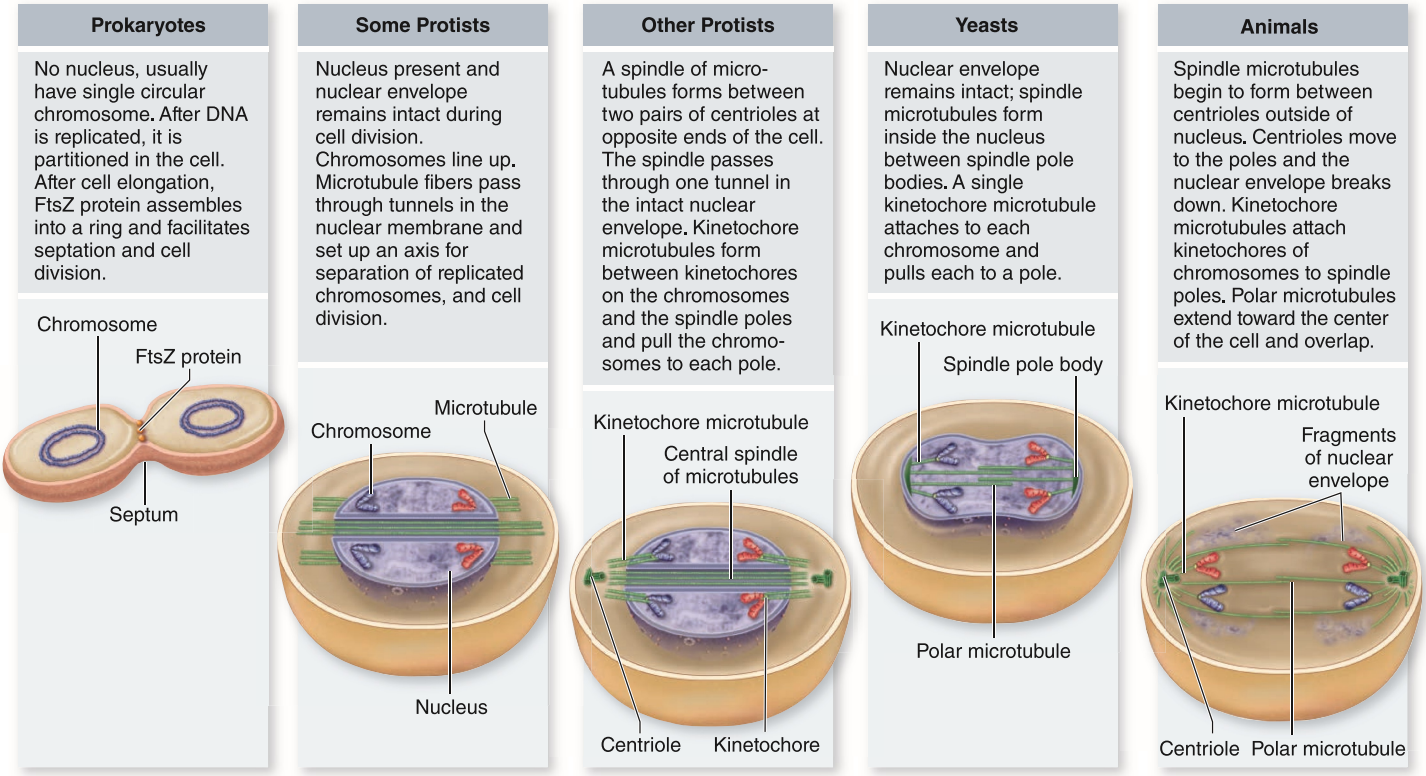


Figure 10.3 A comparison of protein assemblies during cell division among different organisms. The prokaryotic protein FtsZ has a structure that is similar to that of the eukaryotic protein tubulin. Tubulin is the protein component of microtubules, which are fibers that eukaryotic cells use to construct the spindle apparatus that is used to separate chromosomes.

Learning Outcome Review 10.1

Most bacteria divide by binary fission, a form of cell division in which DNA replication and segregation occur simultaneously. This process involves active partitioning of the single bacterial chromosome and positioning of the site of septation.

- *Would binary fission work as well if bacteria had many chromosomes?*

10.2 Eukaryotic Chromosomes

Learning Outcomes

1. *Describe the structure of eukaryotic chromosomes.*
2. *Distinguish between homologues and sister chromatids.*
3. *Contrast replicated and nonreplicated chromosomes.*

TABLE 10.1 Chromosome Number in Selected Eukaryotes

Group	Total Number of Chromosomes
FUNGI	
Neurospora (haploid)	7
Saccharomyces (a yeast)	16
INSECTS	
Mosquito	6
Drosophila	8
Honeybee	diploid females 32, haploid males 16
Silkworm	56
PLANTS	
Haplopappus gracilis	2
Garden pea	14
Corn	20
Bread wheat	42
Sugarcane	80
Horsetail	216
Adder's tongue fern	1262
VERTEBRATES	
Opossum	22
Frog	26
Mouse	40
Human	46
Chimpanzee	48
Horse	64
Chicken	78
Dog	78

Chromosomes were first observed by the German embryologist Walther Flemming (1843–1905) in 1879, while he was examining the rapidly dividing cells of salamander larvae. When Flemming looked at the cells through what would now be a rather primitive light microscope, he saw minute threads within their nuclei that appeared to be dividing lengthwise. Flemming called their division **mitosis,** based on the Greek word *mitos,* meaning "thread."

Chromosome number varies among species

Since their initial discovery, chromosomes have been found in the cells of all eukaryotes examined. Their number may vary enormously from one species to another. A few kinds of organisms have only a single pair of chromosomes, whereas some ferns have more than 500 pairs (table 10.1). Most eukaryotes have between 10 and 50 chromosomes in their body cells.

Human cells each have 46 chromosomes, consisting of 23 nearly identical pairs (figure 10.4). Each of these 46 chromosomes contains hundreds or thousands of genes that play important roles in determining how a person's body develops and functions. Human embryos missing even one chromosome, a condition called *monosomy,* do not survive in most cases. Having an extra copy of any one chromosome, a condition called *trisomy,* is usually fatal except where the smallest chromosomes are involved. (You'll learn more about human chromosome abnormalities in chapter 13.)

Eukaryotic chromosomes exhibit complex structure

Researchers have learned a great deal about chromosome structure and composition in the more than 135 years since their discovery. But despite intense research, the exact structure of eukaryotic chromosomes during the cell cycle remains unclear. The structures described in this chapter represent the currently accepted model.

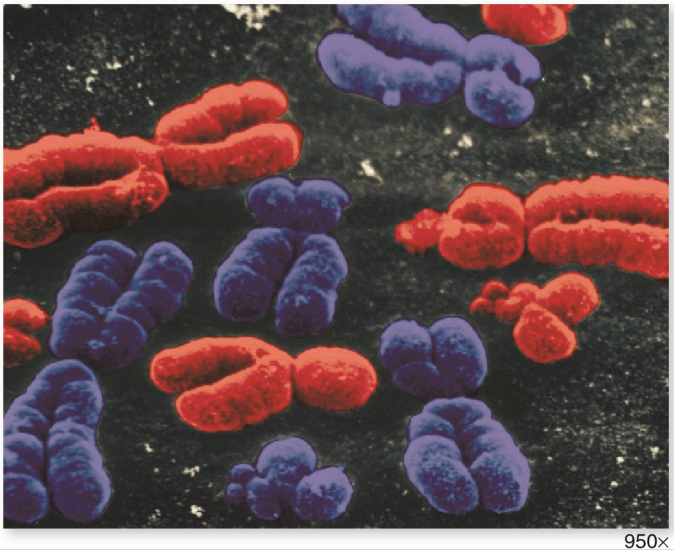


Figure 10.4 Human chromosomes. This scanning electron micrograph shows human chromosomes as they appear immediately before nuclear division. Each DNA molecule has already replicated, forming identical copies held together at a visible constriction called the centromere. False color has been added to the chromosomes.

Composition of chromatin

Chromosomes are composed of **chromatin,** a complex of DNA and protein; most chromosomes are about 40% DNA and 60% protein. A significant amount of RNA is also associated with chromosomes because chromosomes are the sites of RNA synthesis.

Each chromosome contains a single DNA molecule that runs uninterrupted through the chromosome's entire length. A typical human chromosome contains about 140 million (1.4×10^8) nucleotides in its DNA. If we think of each nucleotide as a "word," then the amount of information an average chromosome contains would fill about 280 printed books of 1000 pages each, with 500 "words" per page.

If we could lay out the strand of DNA from a single chromosome in a straight line, it would be about 5 cm (2 in.) long. Fitting such a strand into a cell nucleus is like cramming a string the length of a football field into a baseball—and that's only 1 of 46 chromosomes! In the cell, however, the DNA is compacted, allowing it to fit into a much smaller space than would otherwise be possible.

The organization of chromatin in the nondividing nucleus is not well understood, but geneticists have recognized for years that some domains of chromatin, called **heterochromatin,** are not expressed, and other domains of chromatin, called **euchromatin,** are expressed. This genetically measurable state is also related to the physical state of chromatin, although researchers are just beginning to see the details.

Chromosome structure

If we gently disrupt a eukaryotic nucleus and examine the DNA with an electron microscope, we find that it resembles a string of beads (figure 10.5). Every 200 nucleotides (nt), the DNA duplex (double strand) is coiled around a core of eight **histone proteins.** Unlike most proteins, which have an overall negative charge, histones are positively charged because of an abundance of the basic amino acids arginine and lysine. Thus, they are strongly attracted to the negatively charged phosphate groups of the DNA, and the histone cores act as "magnetic forms" that promote and guide the coiling of the DNA. The complex of DNA and histone proteins is termed a **nucleosome.**

The DNA wrapped in nucleosomes is further coiled into an even more compact structure called the *solenoid.* The precise path of this higher order folding of chromatin is still a subject of debate, but it leads to a fiber with a diameter of 30 nm and thus is called the 30-nm fiber. This 30-nm fiber is the usual state of interphase (nondividing) chromatin.

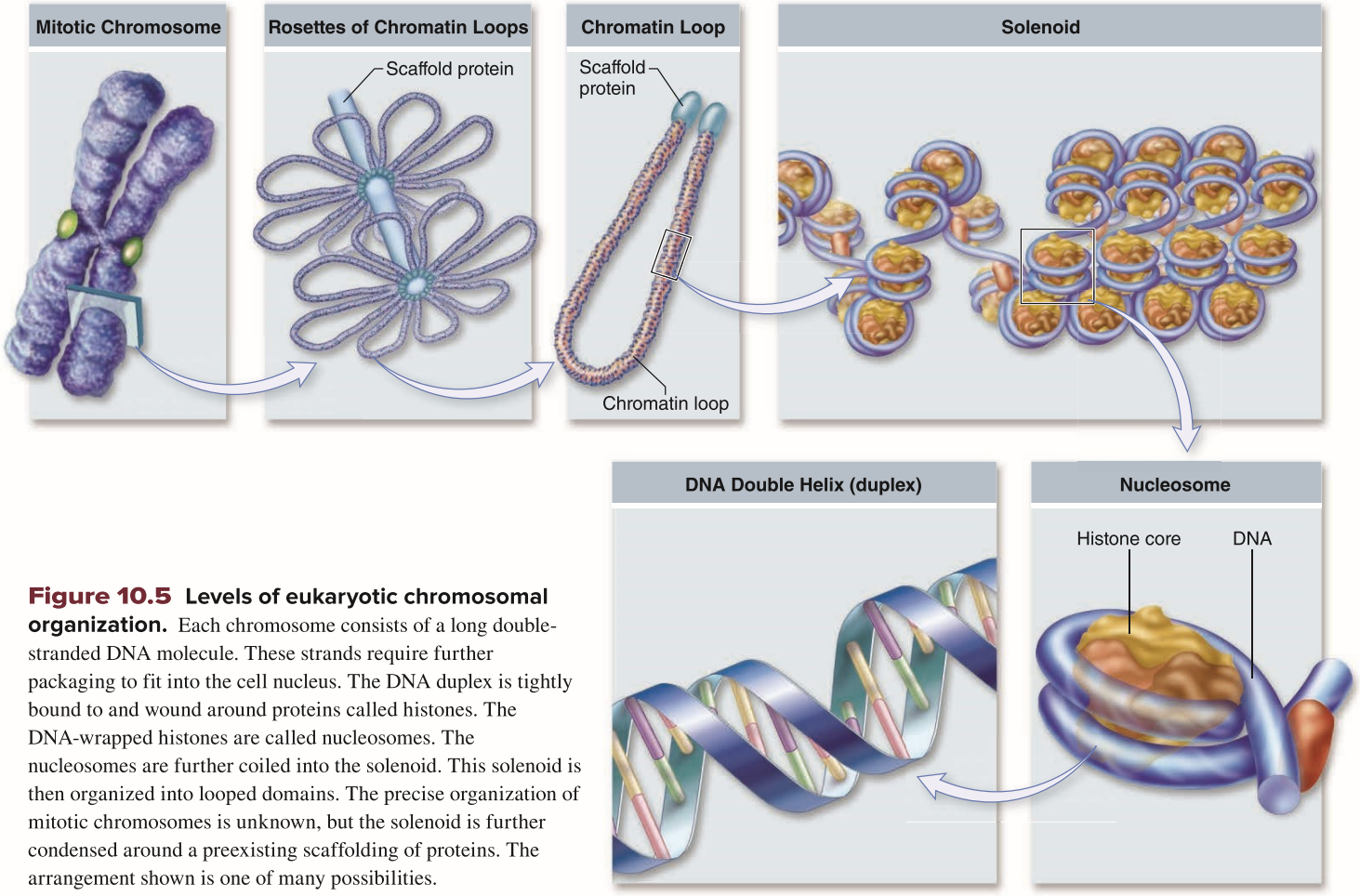


Figure 10.5 Levels of eukaryotic chromosomal organization. Each chromosome consists of a long double-stranded DNA molecule. These strands require further packaging to fit into the cell nucleus. The DNA duplex is tightly bound to and wound around proteins called histones. The DNA-wrapped histones are called nucleosomes. The nucleosomes are further coiled into the solenoid. This solenoid is then organized into looped domains. The precise organization of mitotic chromosomes is unknown, but the solenoid is further condensed around a preexisting scaffolding of proteins. The arrangement shown is one of many possibilities.

During mitosis, proteins are assembled into a scaffold that provides a framework for the final level of compaction. This gives chromosomes their familiar X-shaped structure, and facilitates separation by the mitotic machinery described later. The exact nature of the compaction is unknown, but one longstanding model involves looping of chromatin fibers from the scaffold like the fibers on a wire brush. A complex of proteins called condensin, which are evolutionarily related to bacterial SMC proteins, are necessary for compaction.

Chromosome karyotypes

Chromosomes vary in size, staining properties, the location of the centromere (a constriction found on all chromosomes, described shortly), the relative length of the two arms on either side of the centromere, and the positions of constricted regions along the arms. The particular array of chromosomes an individual organism possesses is called its **karyotype.** The karyotype in figure 10.6 shows the set of chromosomes from a normal human cell.

When defining the number of different chromosomes in a species, geneticists count the **haploid** ***(n)*** number of chromosomes. This refers to one complete set of chromosomes necessary to define an organism. For humans and many other species, the total number of chromosomes in a cell is called the **diploid** ***(2n)*** number, which is twice the haploid number. For humans, the haploid number is 23 and the diploid number is 46. Diploid chromosomes reflect the equal genetic contribution that each parent makes to offspring. We refer to the maternal and paternal chromosomes as being **homologous,** and each one of the pair is termed a **homologue.**

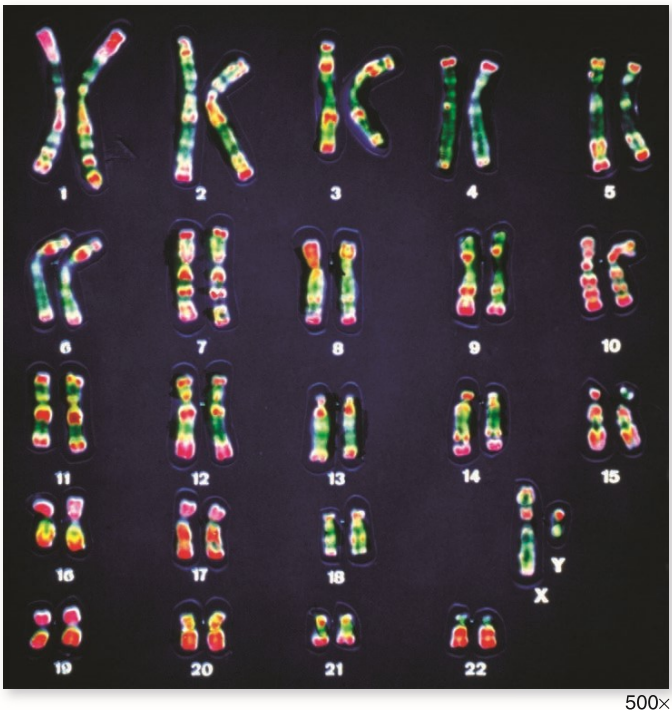


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Figure 10.6 A human karyotype. The individual chromosomes that make up the 23 pairs differ widely in size and in centromere position. In this preparation of a male karyotype, the chromosomes have been specifically stained to indicate differences in their composition and to distinguish them clearly from one another. Notice that members of a chromosome pair are very similar but not identical.

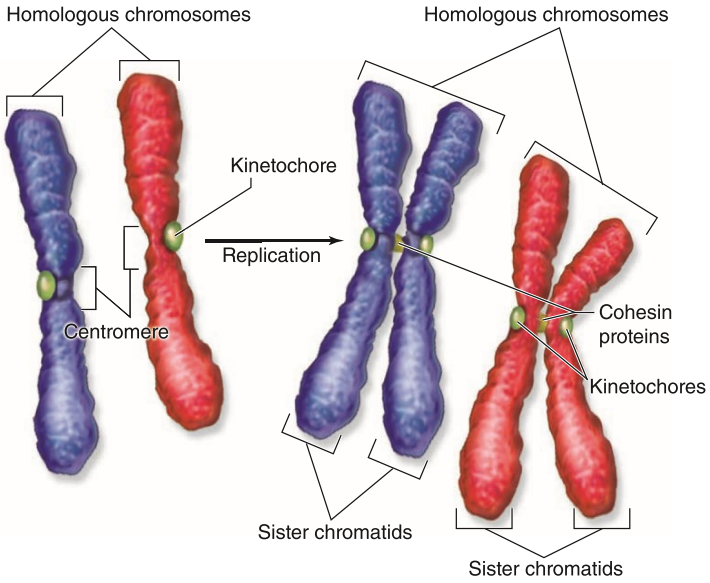

Figure 10.7 The difference between homologous chromosomes and sister chromatids. Homologous chromosomes are the maternal and paternal copies of the same chromosome—say, chromosome number 16. Sister chromatids are the two replicas of a single chromosome held together at their centromeres by cohesin proteins after DNA replication. The kinetochore (described later in section 10.4) is composed of proteins found at the centromere that attach to microtubules during mitosis.

Chromosome replication

Chromosomes as seen in a karyotype are only present for a brief period during cell division. Prior to replicating, each chromosome is composed of a single DNA molecule that is arranged into the 30-nm fiber described earlier in this section. After replication, each chromosome is composed of two identical DNA molecules held together by a complex of proteins called **cohesins.** As the chromosomes become more condensed and arranged about the protein scaffold, they become visible as two strands that are held together at the centromere. At this point, we still call this one chromosome, but it is composed of two **sister chromatids** (figure 10.7).

The fact that the products of replication are held together is critical to the division process. One problem that a cell must solve is how to ensure that each new cell receives a complete set of chromosomes. If we were designing a system, we might use some kind of label to identify each chromosome, much like most of us use when we duplicate files on a computer. Instead of labeling chromosomes, the cell glues replication products together at the centromere. The process of mitosis then separates all of these copies at the same time, ensuring that each daughter cell gets one copy of each chromosome.