CHAPTER 17

Molecular Genetics

Reflecting Questions

- How did the discovery of the role of DNA in heredity change our understanding of genetics?
- How does the structure of DNA contribute to its function as the material of heredity?
- How does the information stored in an organism's DNA guide its development?
- How can changes in an organism's environment affect the expression of its genetic information?

The chicks of this white-crowned sparrow will learn the song of their species only if they hear it at least a few times within the first month of their lives. They will not learn the song of any other bird, however, no matter how often they hear it.

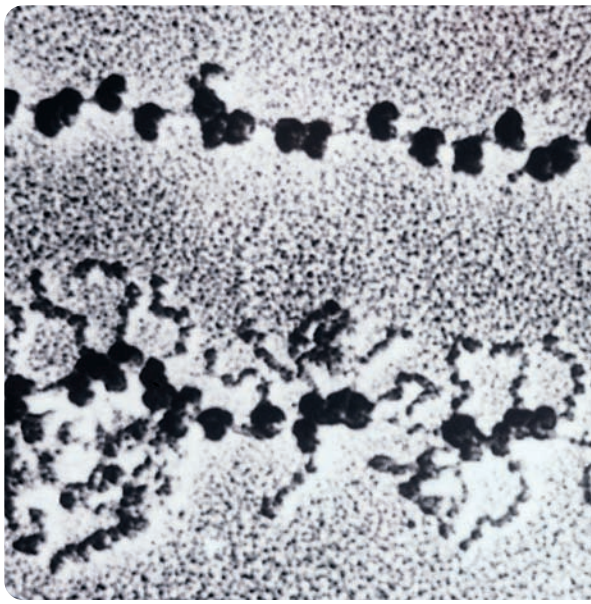
What genetic mechanisms are at work here? Clearly there is a song-learning skill programmed into the cells of the chicks. There is also an element of timing, since this skill is only activated during a specific stage of the chicks' lives. Finally, there is an environmental component, since the chicks' innate ability to learn the song can be fulfilled only if they hear the correct song.

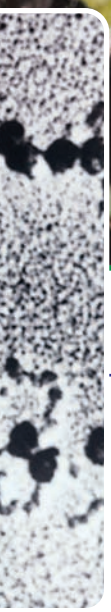
All these components can be traced to the expression of stored hereditary information through proteins created by specialized cellular structures like the ones shown below. The genetic information inherited by each chick defines which proteins will be created in each of its cells throughout its life.

This means that every aspect of the chick's development, from the enzymes in its digestive tract to its ability to sing, is determined by its DNA. But how can the information leading to a specific singing pattern be stored in and transmitted by molecules? And how do these processes interact with the outside world?

The task of molecular genetics is to examine how genetic information is expressed. In this chapter, you will find out how DNA came to be identified as the material of heredity, and how the properties of this molecule enable it to encode simple chemical information that shapes all of Earth's living organisms. You will study how nucleic acids direct the synthesis of the proteins that give each cell its particular properties. Lastly, you will see how the external environment can affect the expression of hereditary information, and how mutations can alter the genetic information carried by a cell.

Specialized structures use the information encoded in hereditary material to construct proteins.





Chapter Contents

17.1 Isolating the Material of Heredity

OUTCOMES

- **Describe the main scientific discoveries that led to the identification of DNA as the material of heredity.**
- **Describe the molecular components of nucleic acids.**
- **Describe the scientific evidence that led to the modern concept of the gene.**

As you saw in the previous chapter, Gregor Mendel's research on patterns of inheritance in garden peas set the groundwork for the study of genetics. Mendel first presented his findings to the Natural Science Society in Brunn, Austria, in 1865. Only four years later, and less than 300 km away, the young Swiss physician and scientist Friedrich Miescher isolated a substance he called "nuclein" from the nuclei of white blood cells. Miescher, shown in Figure 17.1, determined that nuclein was made up of an acidic portion (which he termed "nucleic acid") and an alkaline portion (which was later shown to be protein).

Figure 17.1 Friedrich Miescher was 25 years old when he isolated nucleic acids from the nuclei of white blood cells in 1869. He was working in a hospital treating wounded soldiers, and he was able to collect white blood cells from their bandages.

After this discovery, Miescher did not pursue the study of nucleic acids. Not until almost a century later did scientists establish the connection between the nucleic acid isolated by Miescher and Mendel's factors of inheritance.

The Components of Nucleic Acids

Following the work of Miescher, other research showed that nuclein was made up of a series of strand-like complexes of nucleic acids and proteins tightly bound together. These strands came to be called chromosomes. Little else was known about nuclein until the early 1900s, when Phoebus Levene made several important discoveries about the properties of nucleic acids.

Levene isolated two types of nucleic acids that could be distinguished by the different sugars involved in their composition. One acid contained the five-carbon sugar ribose, so Levene called it "**ribose nucleic acid**" (**ribonucleic acid** or **RNA**). The other acid contained a previously unknown five-carbon sugar molecule. Since this sugar was similar in structure to ribose but lacked one oxygen molecule, Levene called it deoxyribose. He went on to call the nucleic acid containing this sugar "**deoxyribose nucleic acid**" (**deoxyribonucleic acid** or **DNA**). Figure 17.2 shows the structures of ribose and deoxyribose sugars.

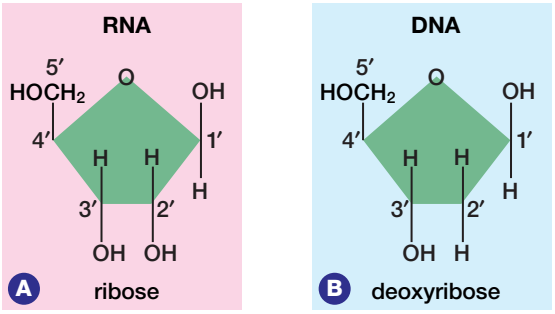


Figure 17.2 The structure of (A) ribose, found in RNA, and (B) deoxyribose, found in DNA. In ribose, the 2′ carbon is bonded to a hydroxyl group. In deoxyribose, this carbon is bonded to a single hydrogen molecule.

Levene showed that nucleic acids are made up of long chains of individual units he termed **nucleotides**. Both DNA and RNA contain a combination of four different nucleotides. As shown in Figure 17.4, each nucleotide is composed

of a five-carbon sugar, a phosphate group, and one of four nitrogen-containing (**nitrogenous**) bases. The bases found in DNA nucleotides are **adenine** (A), **guanine** (G), **cytosine** (C), and **thymine** (T). In RNA, the base **uracil** (U) is found instead of thymine. The only difference between the nucleotides in each nucleic acid is in their bases. As a result, scientists studying nucleic acids soon began to identify the nucleotides simply by their bases or, more commonly, by their initials: A, G, C, T, and U.

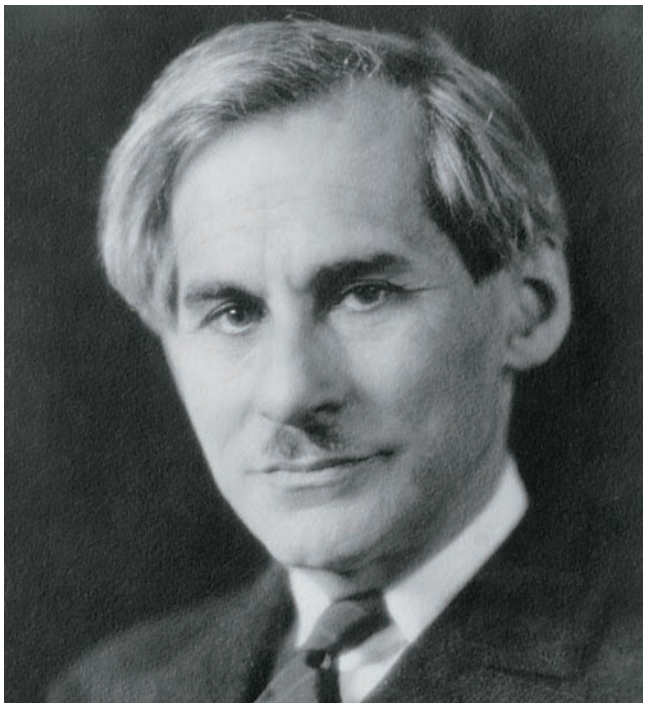


Figure 17.3 Phoebus Levene made some important discoveries about the properties of nucleic acids but also drew an inaccurate conclusion from his research.

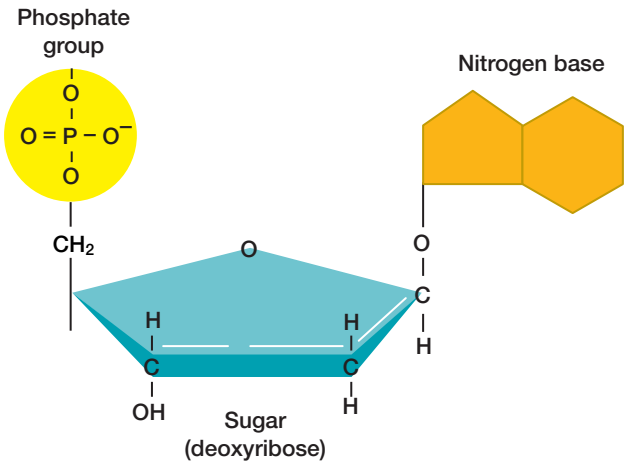


Figure 17.4 The general structure of a DNA nucleotide. In DNA the nitrogenous base is one of the following: adenine (A), guanine (G), cytosine (C), or thymine (T). In RNA, the sugar is ribose and the nitrogenous base uracil (U) appears instead of thymine.

Nucleotides are joined together to form long chains, much like beads on a necklace. The phosphate group of one nucleotide is bonded to the deoxyribose sugar of an adjacent nucleotide, as shown in Figure 17.5. The phosphate groups and deoxyribose molecules form the backbone of the chain, and the nitrogenous bases stick out like the teeth on a zipper.

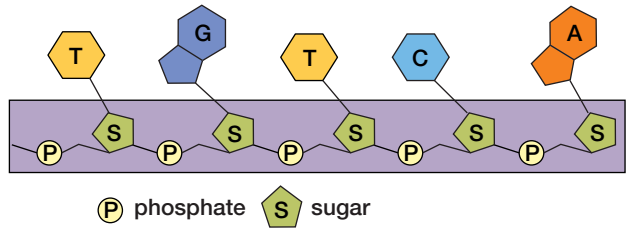


Figure 17.5 Nucleotides are joined together in a long chain.

At this point, the results of Levene's work led him to conclude incorrectly that nucleic acids contained equal amounts of each of these nucleotides. Based on this finding, he suggested that DNA and RNA were made up of long chains in which the nucleotides appeared over and over again in the same order; for example, ACTGACTG ACTG and so on. This, in turn, caused most scientists to conclude that DNA could not be the material of heredity because it was not complex enough to account for the tremendous variation in inherited traits. Instead, they believed that the primary instructions for inherited traits must lie in the proteins that are also found in chromosomes. Several decades passed before Levene's conclusion was finally corrected.

Mounting Evidence for the Role of DNA in Heredity

In 1928, English medical officer Fred Griffith was studying the bacteria responsible for a pneumonia epidemic in London. Griffith set up an experiment using dead streptococcal bacteria as a control. When he ran his experiment, he discovered to his surprise that the dead pathogenic (disease-causing) bacteria had somehow passed on their pathogenic properties to live non-pathogenic bacteria. Griffith called this phenomenon the **transforming principle**. His experiments are summarized in Figure 17.6.

Griffith was killed during World War II, before he could discover what caused the transformation. The team of Oswald Avery, Colin MacLeod, and Maclyn McCarty took up the challenge. They

undertook a series of experiments to isolate the agent behind the transforming principle, with the following results:

- When they treated the pathogenic bacteria with a protein-destroying enzyme, transformation still took place.
- When they treated the pathogenic bacteria with a DNA-destroying enzyme, transformation did not occur.
- When they treated the bacteria with an enzyme that destroyed RNA but not DNA, the transformation occurred.

These results demonstrated that the substance responsible for the transformation of the non-pathogenic bacteria into a pathogenic strain was DNA. Even so, many scientists refused to believe that the apparently simple DNA molecule could be an agent of heredity.

Over the next few years, other experimental evidence of the role of DNA in heredity began to accumulate. In the late 1940s, Erwin Chargaff revisited Levene's experiments on the nucleotide composition of DNA. Chargaff's work overturned one of Levene's main conclusions. Chargaff discovered that the four nucleotides were not present in equal quantities, but rather were found in varying but characteristic proportions:

- the nucleotide composition of DNA (that is, the proportion of A, C, G, and T nucleotides) varies from one species to another;
- the nucleotide composition of DNA specimens taken from different animals of the same species is constant;
- in any sample of DNA, the amount of adenine is always equal to the amount of thymine, and the amount of cytosine is always equal to the amount

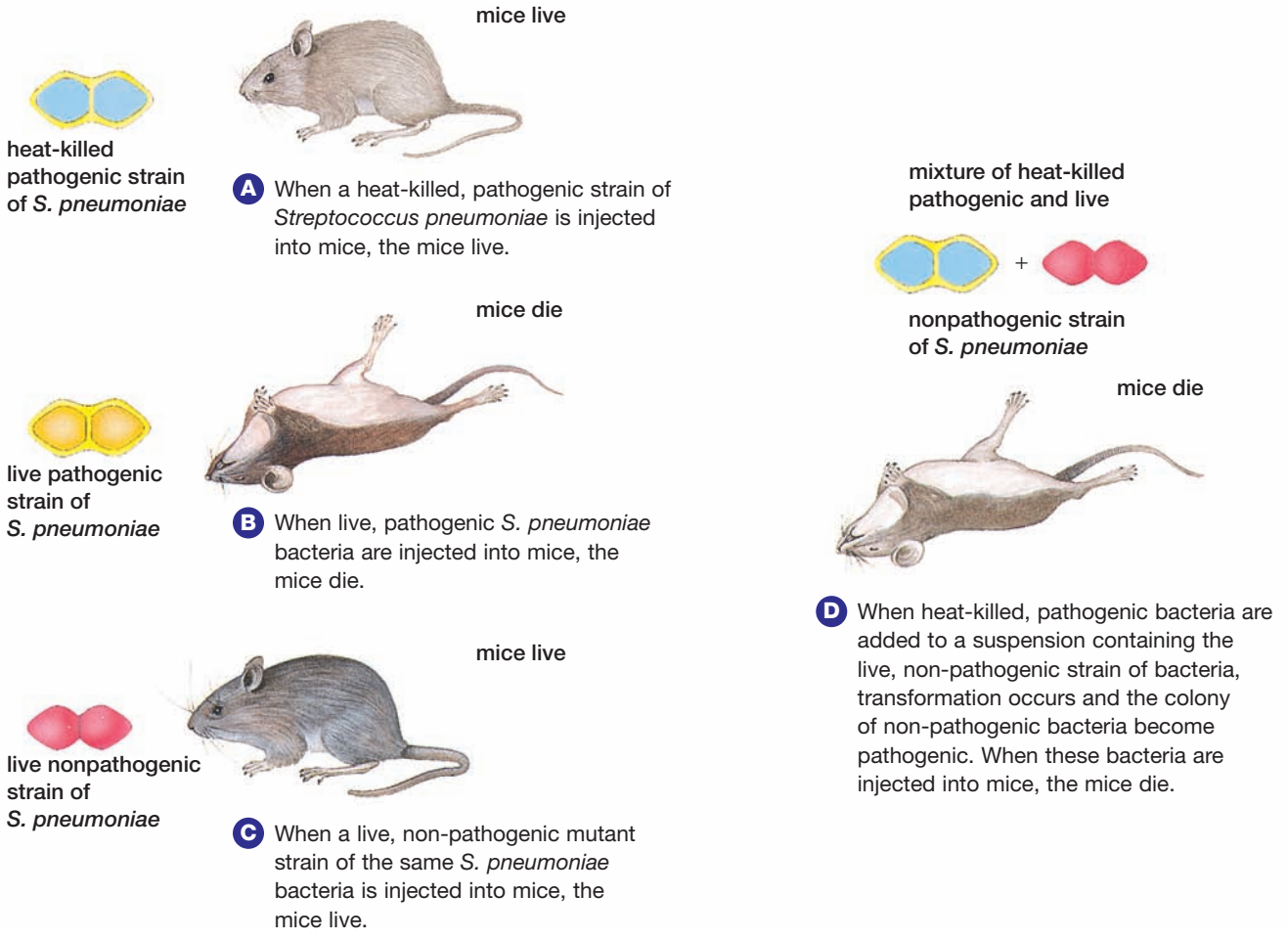


Figure 17.6 Griffith's discovery of the "transforming principle" in 1928 was accidental. He employed heat-killed, pathogenic bacteria as a control in an experiment on infection, but did not treat the cells at a high enough temperature to denature their DNA. In so doing, he discovered that the dead cells' pathogenic properties could be passed on to living bacterial cells. Griffith died of injuries suffered in an air raid during World War II before he could discover what caused this transformation. In 1944, Avery and his team were the first to demonstrate that the transforming principle was DNA.

of guanine. This constant relationship is known as **Chargaff's rule**.

The experiment that provided final proof that DNA, not protein, carried genetic information took place in 1952. American researchers Alfred Hershey and Martha Chase used radioactive labelling techniques in an experiment with a virus, or **phage**, that infects bacterial cells. As shown in Figure 17.7, the phage first attaches to the bacterium and then injects its own DNA into the cell. The bacterial cell soon begins to manufacture new viruses and then bursts, releasing the viruses, which go on to attack other cells.

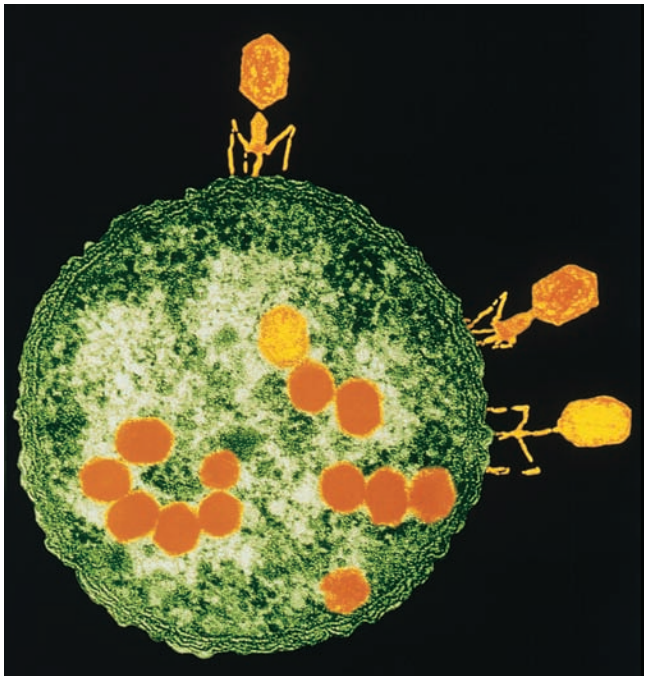
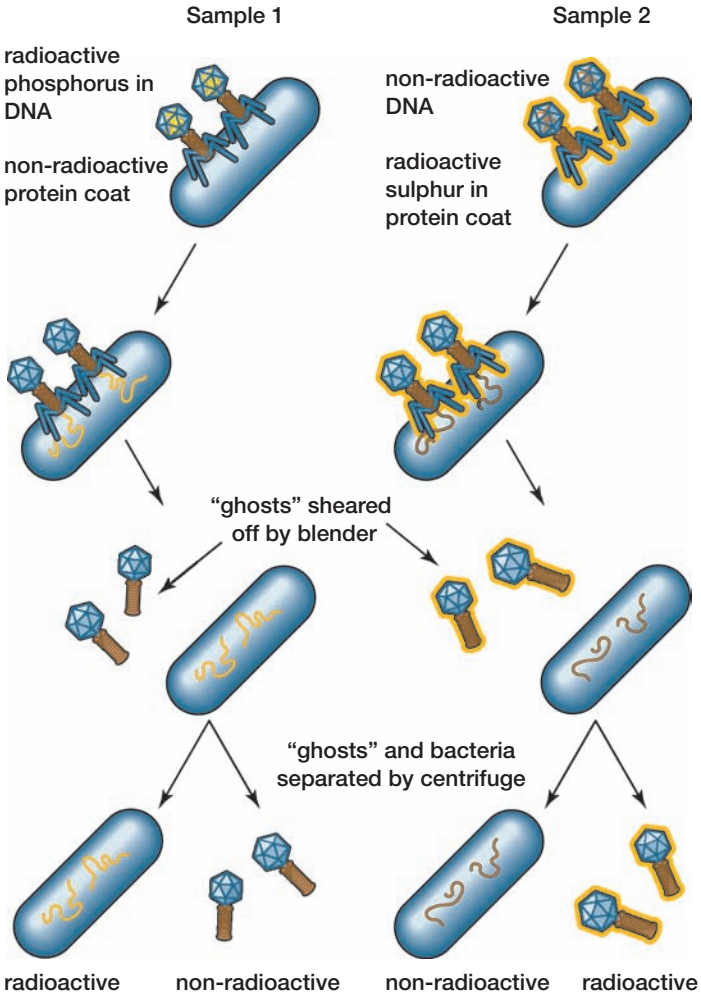


Figure 17.7 Looking somewhat like space capsules, these T2 phages use leg-like structures to bind to the cell wall of a bacterium.



A Two batches of phages are cultured. One has radioactively tagged DNA, while the other has a radioactively tagged protein coat. A sample of each type of virus is added to a separate suspension of non-radioactive *E. coli*.

B The viruses inject their DNA into the bacteria.

C Each suspension is shaken in a blender to separate the virus heads or "ghosts" from the outside of the cell walls of the infected bacteria.

D The bacterial cells infected by the virus with radioactive DNA are found to be radioactive, indicating that the viral DNA entered the host cell. In contrast, the bacterial cells infected by the virus with radioactive protein are found to be non-radioactive, indicating that no viral protein entered the host cell.

Figure 17.8 The experiments conducted by Hershey and Chase demonstrated that when a virus infects a bacterium, only the DNA of the virus enters the host cell.

Figure 17.8 illustrates the Hershey-Chase experiment. They prepared two different samples of the T2 virus, one tagged with radioactive phosphorus (which "tagged" the phage DNA) and the other tagged with radioactive sulfur (which "tagged" the phage protein coat). Each sample was then added to a separate suspension of non-radioactive *E. coli*.

In both cases, the bacteria became infected by the phage. In the first sample, in which the viral DNA was radioactive, the infected bacteria were found to be radioactive while the fluid containing the separated viral protein coats was not. In the second sample, in which only the virus protein coat was labelled, the reverse occurred — the fluid containing the protein coats was radioactive while the infected bacteria were not. Hershey and Chase concluded that only the DNA from the virus entered the bacterial cell; the protein coat remained outside the cell wall. Therefore, the transmission of genetic information from the virus to the bacterium could only take place as a result of the injection of DNA into the bacterium.

Through the 1940s and into the early 1950s, convincing evidence mounted to support the central role of DNA in the mechanisms of heredity. Scientists from a variety of fields began to devote more and more attention to the problem of determining the structure of DNA. The race that ensued crossed the boundaries of scientific disciplines as individuals and teams from different nations competed with one another. The race finally ended in 1953 with the publication of a landmark paper describing the molecular structure of DNA. You will study this structure in more detail in the next section.

SECTION REVIEW

1. What is the relationship between nuclein and a chromosome?

2. Identify the five different nucleotides. Which one is only found in RNA?

3. Draw the general structure of a DNA nucleotide and label each of its components.

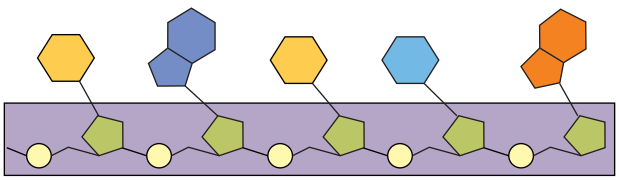
4. Define Chargaff's rule and explain its significance.

5. Explain why researchers believed for many years that DNA was too simple a molecule to serve as the material of heredity. Whose research conclusion lent support to this belief?

6. The diagram below illustrates the structure of a chain of nucleotides.

(a) Copy this diagram and label each of the components.

(b) Prepare a short caption that explains how the chain of nucleotides is held together.



7. You are given an enzyme that replaces the 2′ hydroxyl group of a sugar molecule with a methyl ($-CH_3$) group. The enzyme has no other effect. If you treat a suspension of heat-killed, pathogenic bacteria with this enzyme and then add a culture of live, non-pathogenic bacteria, will transformation occur? Explain your reasoning.

8. Several researchers besides Mendel made outstanding contributions that eventually helped to pinpoint DNA as the molecule of heredity. Develop a flowchart that summarizes the work of the following scientists and shows how their discoveries contributed to the discoveries that followed.

(a) Miescher

(b) Levene

(c) Griffith

(d) Avery, MacLeod, and McCarty

9. You have learned about several milestones in the development of the science of genetics. In your opinion, what technologies or cultural issues might have influenced the timing of these milestones and other discoveries in genetics?

10. Historians debate the degree to which key people actually change the course of history. Do you think the individual scientists discussed in this section influenced the actual progress of knowledge? Why or why not?

17.2 The Structure of Nucleic Acids

OUTCOMES

- Describe the double helix model of DNA.
- Compare and contrast the structure of DNA and RNA.
- Describe the arrangement of DNA within living cells.

By the late 1940s, it was known that DNA was made up of a strand of nucleotides, and that each nucleotide was made up of a sugar, a phosphate group, and a particular nitrogenous base. Exactly how the strand was arranged, however, remained a mystery. The methodical work undertaken by British scientists Rosalind Franklin, pictured in Figure 17.9, and Maurice Wilkins to photograph and analyze X-ray diffraction images of DNA molecules added a number of new observations that helped other scientists to finally deduce the molecule's structure.

Figure 17.9 Rosalind Franklin's work was a major factor in the effort to determine the structure of DNA. Her contribution was not widely recognized at the time, in part because of prevailing attitudes toward women in science in the 1950s. Franklin died of cancer at age 38, shortly before the Nobel prize was awarded to Watson and Crick. Her many years of work with X rays may have contributed to her illness.

The pattern of shaded areas in the image shown in Figure 17.10, for example, indicated that DNA had a helical structure. From the nature of these X-ray "shadows," Franklin was able to identify two distinct but regularly repeating patterns in the structure — one pattern recurring at intervals of 0.34 nm, and another at intervals of 3.4 nm. As she prepared her samples for photographing, Franklin also observed how DNA reacted to water. From this evidence she deduced that the hydrophobic nitrogenous bases must be located on the inside of the helical structure, and that the hydrophilic sugar-phosphate backbone must be located on the outside, facing toward the watery nucleus of the cell. Her observations proved to be important keys to understanding the structure of DNA.

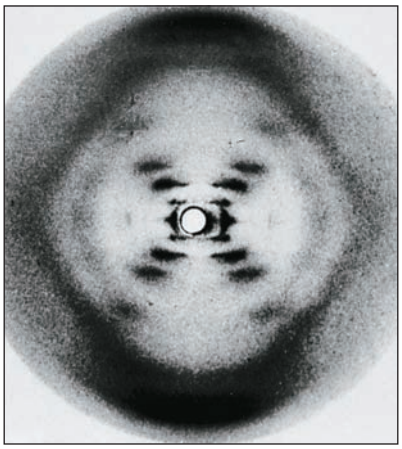


Figure 17.10 The shaded areas in this deceptively simple image indicate the pattern formed by X rays as they diffract through crystallized DNA. This photograph was made by Rosalind Franklin in 1953, and provided a number of important clues about DNA's molecular structure.

The partnership between the American geneticist James Watson and the British physicist Francis Crick was the first to produce a structural model of DNA that could account for all the experimental evidence at hand. Watson and Crick worked with physical models, as shown in Figure 17.11 on the next page, trying different arrangements until they decided on the double-helix model that soon became established as the definitive structure for DNA. They published their results in a two-page paper in *Nature* magazine in 1953.

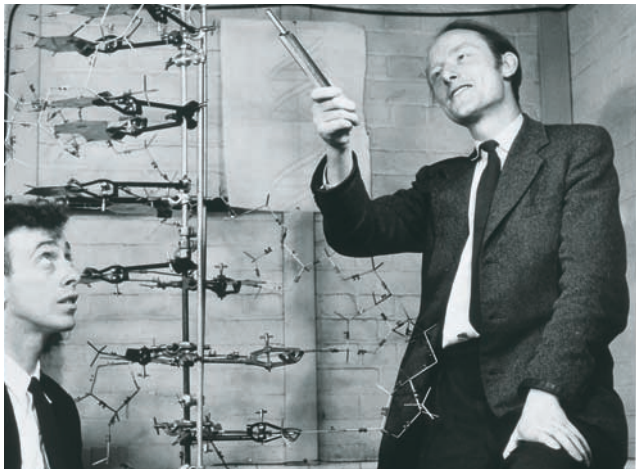


Figure 17.11 James Watson (left) and Francis Crick in 1953 with their model of a DNA molecule.

The Double Helix

DNA is a thread-like molecule made up of two long strands of nucleotides bound together in the shape of a double helix. If the helix were unwound, the molecule would look something like a ladder, as shown in Figure 17.12. The sugar-phosphate "handrails" form the two sides, while the paired nitrogenous bases form the rungs.

One of the challenges facing Watson and Crick was to determine how the bases could be arranged in such a way that the distance between the two handrails remained constant. They knew that the four bases fell into two different categories. Adenine and guanine are derived from the family of nitrogenous compounds known as **purines**,

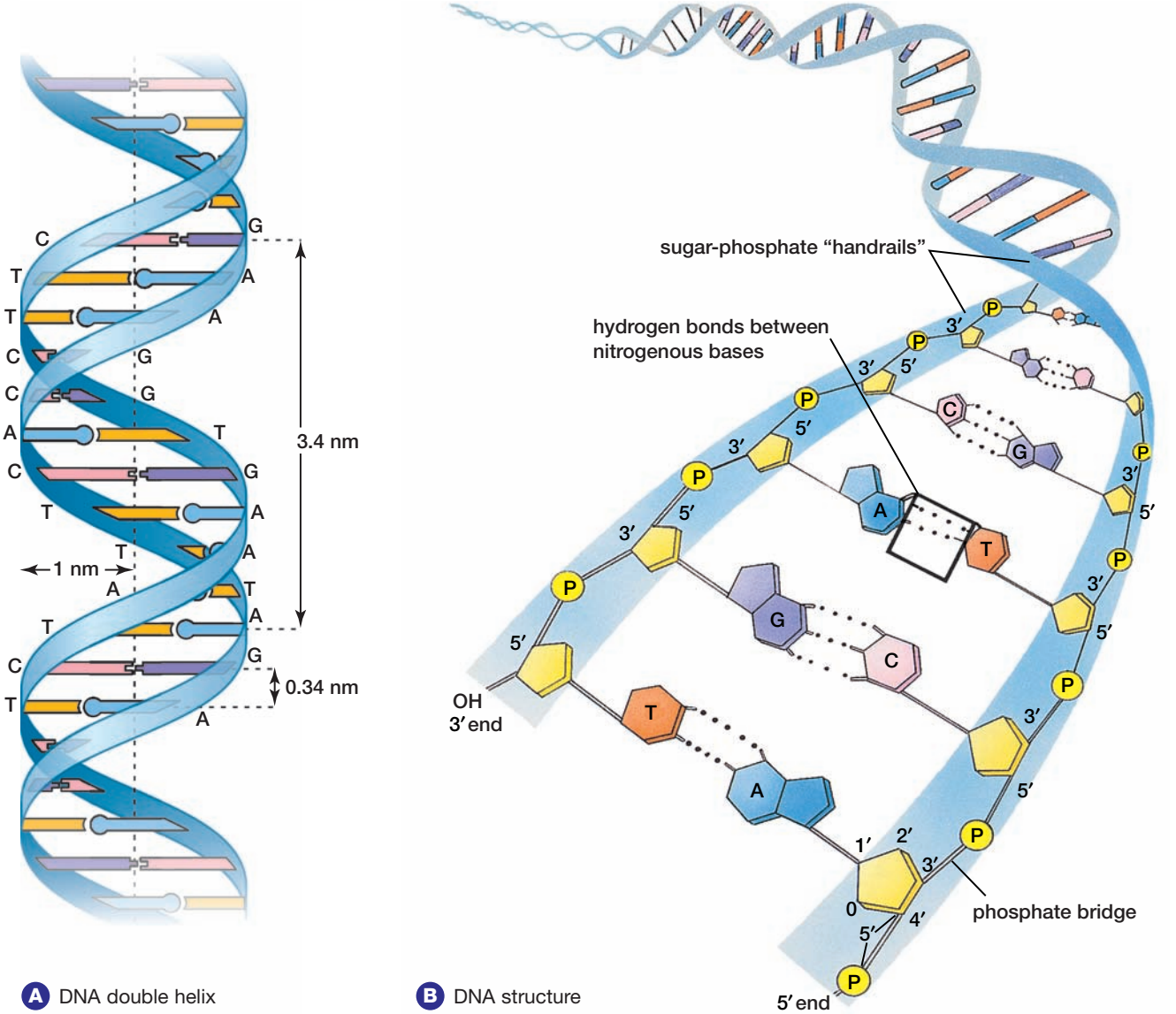


Figure 17.12 The DNA molecule is made up of two chains of nucleotides wound around each other. The "handrails" of the molecule are made up of alternating sugar and phosphate groups, with the phosphate groups serving as bridges between nucleotides. The nitrogenous bases protrude at regular intervals into the interior of the molecule.

which have a double ring structure. Thymine and cytosine are derived from **pyrimidines**, which have a single ring structure. Watson and Crick hit upon the idea that if a purine always bonded with a pyrimidine, the base pairs would have a constant total width of three rings.

The structure of the bases allows only certain **complementary base pairings**: Adenine (A) can only form a stable bond with thymine (T), and cytosine (C) with guanine (G). These pairings provided for the constant width of the molecule and, equally importantly, also supported Chargaff's rule. Wherever an A nucleotide appears on one DNA strand, a T must appear opposite it on the other, and wherever a C nucleotide appears on one strand, the other strand will have a G nucleotide. Figure 17.3 shows how the base pairs are held together by hydrogen bonds. C-G pairs form three hydrogen bonds, while A-T pairs form two hydrogen bonds.

As illustrated in Figure 17.13, the two strands of DNA that make up each double helix are not identical but rather complementary to each other. The strands are also **antiparallel** — that is, the phosphate bridges run in opposite directions in each strand. This means that the end of each double-stranded DNA molecule contains the 5′ end of one strand and the 3′ end of the other. These two properties have important implications for DNA replication and protein synthesis, as you will see later.

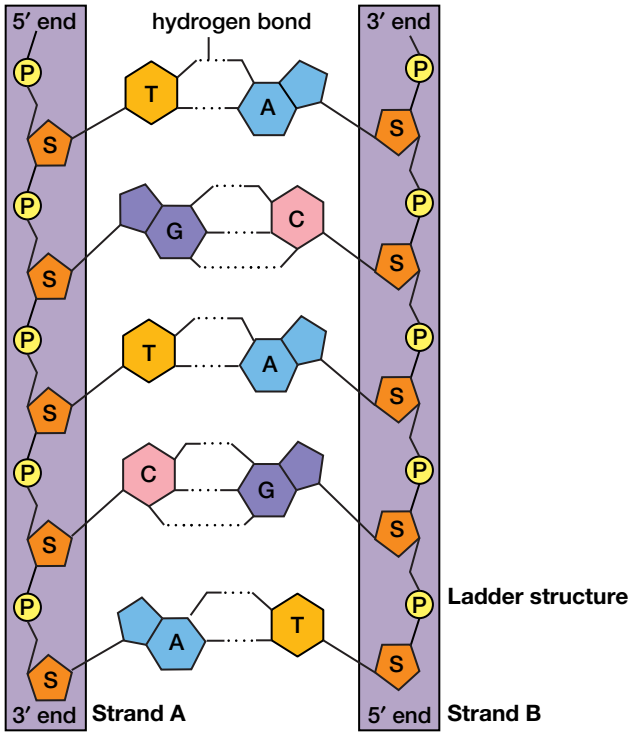


Figure 17.13 The two complementary DNA strands are antiparallel. That is, the 5′–3′ orientation runs in the opposite direction on each strand.

BIO FACT

If you could arrange all the DNA strands contained in your body end to end, their total length would stretch 2×10^{10} km. This is well over 100 times the distance between Earth and the Sun.

THINKING LAB

DNA Deductions

Background

Erwin Chargaff discovered that although the nucleotide composition of DNA varies from one species to another, that composition always follows certain rules.

Imagine you are working with a research team sampling the ocean floor near a hot vent that releases a steady stream of hot water.

Nucleotide	Presence in DNA of bacterial sample 1 (percent)	Presence in DNA of bacterial sample 2 (percent)
adenine	31	18
cytosine		
guanine		
thymine		

Your team collects two samples of bacteria — one from the mouth of the hot vent, and one from the ocean floor about 20 m away. When you return to the lab, you isolate the DNA from these bacteria to determine their nucleotide composition. The table shows the results of your test for the adenine content of the DNA.

You Try It

Apply what you have learned about Chargaff's findings and DNA composition to solve the following problems.

1. Complete the table to determine the amounts of the other nucleotides found in each DNA sample.
2. For each DNA sample, draw a linear stretch of DNA about 15 nucleotides long, with a nucleotide composition that corresponds to its data set. With a dotted line, illustrate the hydrogen bonds between complementary base pairs.

RNA

Along with DNA, RNA is the other main nucleic acid. Both DNA and RNA are found in most bacteria and in eukaryotic cell nuclei. The molecular structure of RNA is similar to that of DNA, with three key differences.

- As Levene observed, the sugar component of RNA is ribose rather than deoxyribose.
- As noted previously, the nucleotide thymine is not found in RNA; in its place is the nucleotide uracil.
- RNA remains single stranded, although at times this single strand can fold back on itself to produce regions of complementary base pairs.

The different structures that may be assumed by the RNA molecule result in several different types of RNA, each serving a particular function. The specific structures and roles of these different molecules are described in more detail later in this chapter.

Organization of Genetic Material

So far, you have examined the primary structure of DNA — that is, the way in which nucleotides are joined together to form a chain. You have also looked at its secondary structure, in which the chain of nucleotides forms a stable double helix. How is this material organized in three-dimensional space within a cell?

Genetic Material in Prokaryotes

Most prokaryotes have a single, double-stranded DNA molecule. One of the characteristic features of prokaryotes is that they have no nucleus. Therefore, there is no nuclear membrane to keep the DNA strand contained in a particular location within the cell.

Instead, an arrangement of proteins helps to coil the DNA molecule tightly into a specific region known as the **nucleoid**, or nuclear zone, of the cell. In addition to the relatively large DNA molecule

Investigation 17 • A

SKILL FOCUS

- Predicting
- Performing and recording
- Communicating results
- Conducting research

DNA Extraction

DNA is always pictured as a double helix. It takes a very high-powered microscope to actually see the double helix, however. In this investigation, you will extract DNA from animal tissue to find out what DNA looks like with the unaided eye.

Pre-lab Question

What two safety precautions must be considered when working with NaCl and ethanol?

Problem

How can DNA be extracted from animal tissue?

Prediction

Predict what must occur to a cell before its DNA can be removed.

CAUTION: When using NaCl, ethanol, and animal tissues, avoid contact with eyes or skin. If contact does occur, rinse thoroughly with water and inform your teacher. Wash your hands thoroughly with soap and water after you have completed this investigation.

Materials

mortar and pestle
250 mL beaker
glass stirring rod
cheesecloth
50 mL beaker (2)
graduated cylinder
small piece of fish muscle tissue (approximately 1 cm^3)
0.9% NaCl (0.9 g of NaCl in 100 mL distilled water)
10% dishwashing detergent (10 mL in 90 mL water)
95% ethanol (ice cold)

Procedure

1. Place the sample of fish tissue in the mortar.
2. Add 10 mL of 0.9% NaCl and grind thoroughly with the pestle for 2 to 5 min.
3. Strain the solution through three layers of cheesecloth and collect the liquid in the 250 mL beaker.
4. Pour the liquid into one 50 mL beaker and add 1.5 mL of 10% dishwashing detergent.
5. Estimate the volume of the extract in the beaker. Then measure approximately twice as much ice-cold 95% ethanol into the other 50 mL beaker.

found in the nucleoid, prokaryotes often have one or more small circular double-stranded DNA molecules floating free in the cytoplasm of the cell. These additional DNA molecules are called **plasmids**. Although plasmids are not physically part of the nucleoid DNA, these small strands of genetic material can contribute to the cell metabolism and hereditary mechanism. For example, the genes that confer resistance to antibiotics may be found on plasmids rather than within the nucleoid DNA. Plasmids can be copied and transmitted between cells, or they may be incorporated into the cell's nucleoid DNA and reproduced during cell division. The result is that the hereditary information contained on a plasmid can spread within bacterial colonies.

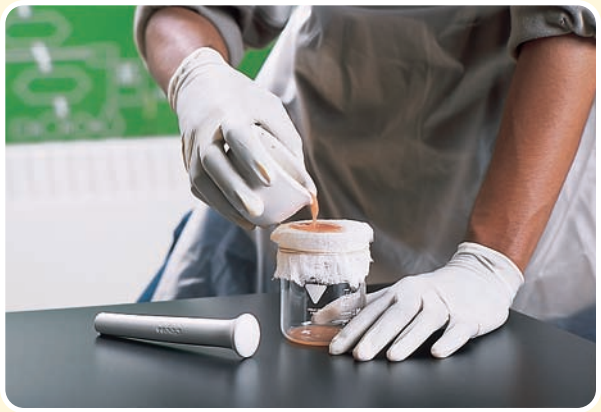
Plasmids have proven to be a valuable tool in genetic engineering techniques. You will learn more about the use of plasmids in DNA sequencing processes and in other applications later in this unit.

Genetic Material in Eukaryotes

Each human cell nucleus contains about 2 m of DNA, or 6 billion base pairs. This is roughly the equivalent of packing 400 km of spaghetti into a bathtub — yet these DNA fibres never become entangled. A highly structured arrangement of proteins and DNA helps to compact and organize this material within the cell.

The nuclei of both plant and animal cells contain double-stranded DNA. This DNA is organized into a number of separate chromosomes. Each chromosome contains one linear double-stranded DNA molecule together with different types of the protein **histone**. Overall, the composition of a chromosome is about 60 percent protein, 35 percent DNA and 5 percent RNA. These components are organized into the long fibres that Miescher called "nuclein," and which are now known as **chromatin**.

Figure 17.14 shows the arrangement of genetic material in a eukaryotic cell. The DNA molecule



6. Slightly tilt the beaker holding the fish extract and gently add the ethanol to the suspension by pouring ethanol down the inside of the beaker.
7. Use the glass stirring rod to gently stir the mixture. When you see a precipitate form at the boundary of the two liquids, twirl the rod to spool the DNA sample onto the glass rod.

Post-lab Questions

1. Qualitatively describe DNA.
2. List the components that make up DNA.

Conclude and Apply

3. Draw a labelled diagram of a DNA molecule.
4. Why did you use detergent in step 4? Think about what you normally use detergent for. (Hint: Cell membranes are made of proteins and lipids.)

Exploring Further

5. How is DNA extracted from tissue on a larger scale? Conduct research to find out, and describe the process in a paragraph or flowchart.

wraps tightly around groups of histone molecules in a regular pattern to produce bead-like structural units called **nucleosomes**. Each nucleosome bead is a short segment of DNA wrapped twice around a cluster of eight histone molecules. The attraction between the acidic DNA and the highly alkaline histone molecules helps to keep the arrangement in place.

A short stretch of DNA extends between each nucleosome. This short segment of DNA is bound to a single molecule of histone. The interaction among the histone molecules helps to draw the arrangement into a tight, regular array.

In turn, this array (which has a total thickness of about 30 nm) undergoes another level of compacting. It forms loops that attach to a supporting structure of non-histone proteins. As the cell prepares to reproduce, the protein structure folds back on itself to condense the chromatin even further. The result is the short, thick chromosomes you have seen in typical karyotypes.

Genes and the Genome

How much do you have in common with a small, spiny fish like that shown in Figure 17.15? Studies of DNA from such diverse organisms as pufferfish, fruit flies, yeast, and humans demonstrate a number of shared patterns in the way hereditary information is organized at the molecular level. For instance, there are similarities in how individual **genes** — specific sequences of DNA that have the potential to be expressed to guide an organism's development — are organized. There are also similarities in the organization of that organism's **genome** — the sum of all the DNA carried in its cells.

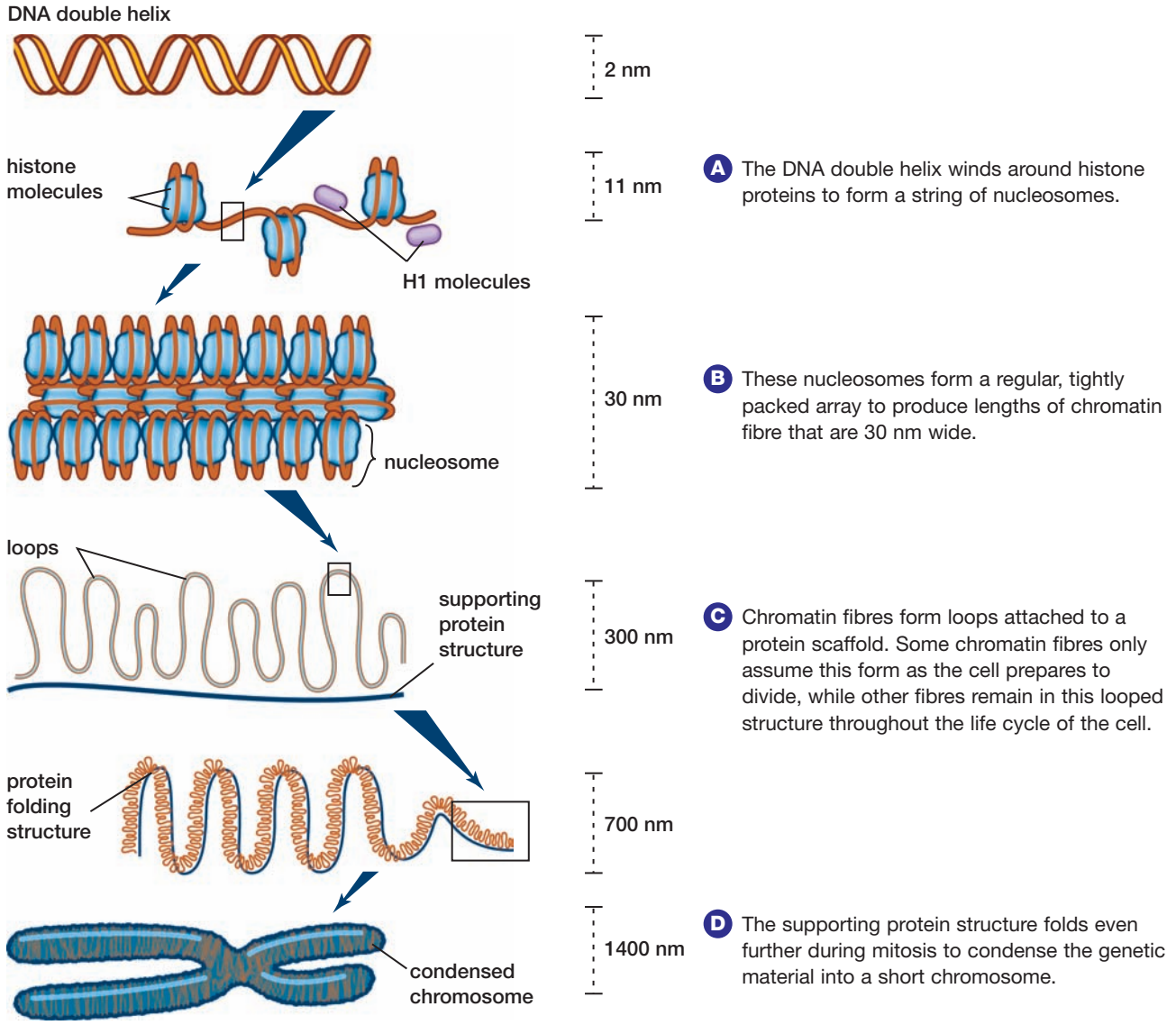


Figure 17.14 The successive ordering of genetic material within a eukaryotic cell.

Figure 17.15 Although pufferfish are separated from humans by millions of years of evolution, their DNA contain thousands of genes that are nearly identical to genes found in humans.

Genes

The gene is the major functional sub-unit of DNA. Each chromosome in any living cell carries a particular set of genes. The specific number, type, and arrangement of genes are unique to each species, but even organisms that are only distantly related may carry very similar genes. The pufferfish genome, for example, includes genes that are almost identical to the human genes associated with Huntington's disease and Alzheimer's disease.

Although Mendel was unaware of the existence of DNA or chromosomes, his factors of inheritance underlie the traditional definition of a gene. According to this definition, a gene is the portion of inherited information that defines one particular trait of an organism's physical characteristics. The more precise functional definition of a gene has evolved since then, keeping pace with researchers' growing understanding of the role of DNA in directing development.

In the 1940s, after DNA had been identified as the material of heredity but before its structure had been discovered, George Beadle and Edward Tatum studied patterns of development in a particular species of *Neurospora* bread mould. They identified a number of different strains of this mould that had different nutritional needs. The wild variety of *Neurospora* could be grown on an agar medium containing minimal nutrients. Various mutant strains would grow only on a medium that contained additional nutrients such as particular sugars or amino acids.

Beadle and Tatum hypothesized that while the wild variety of *Neurospora* can synthesize all the amino acids it requires from the minimal medium, different mutations disrupt the metabolic pathways by which the mould synthesizes the proteins it requires for development. With further research, they were able (in many cases) to identify the specific stage in a metabolic pathway that was blocked by a particular mutation. This work, illustrated in Figure 17.16, led them to conclude that each mutant variety of the mould had one defective gene that caused the mould to be deficient in one enzyme that catalyzed a particular step in a given metabolic pathway. Their hypothesis became known as the one gene-one enzyme theory of gene function.

WEB LINK

www.mcgrawhill.ca/links/atlbiology

Comparative genomics is the study of the similarities and differences among the genomes of different organisms. Use the Internet to compare human DNA with that of another organism. Go to the web site above, and click on **Web Links**. What percentage of the genes in the human genome are found in the genome of your comparison organism, and vice versa? What do these numbers indicate? What are some of the practical applications of studying the DNA of the comparison organism?

In the years that followed, this functional definition was broadened to one gene-one protein, since some genes were found to code for proteins other than enzymes. (Examples include structural proteins such as collagen and the silk of spider webs.) This definition was later modified to one gene-one polypeptide when scientists found that the different polypeptides in a single protein complex may be coded for by entirely separate genes. An example of this is hemoglobin — different genes code for each of the two types of polypeptide sub-units that make up one hemoglobin molecule.

In short, the precise functional definition of a gene has become more complex as scientists have learned more about how genes work. The one gene-one polypeptide theory still does not account for all aspects of gene function. In eukaryotes, a single gene can code for several different polypeptide

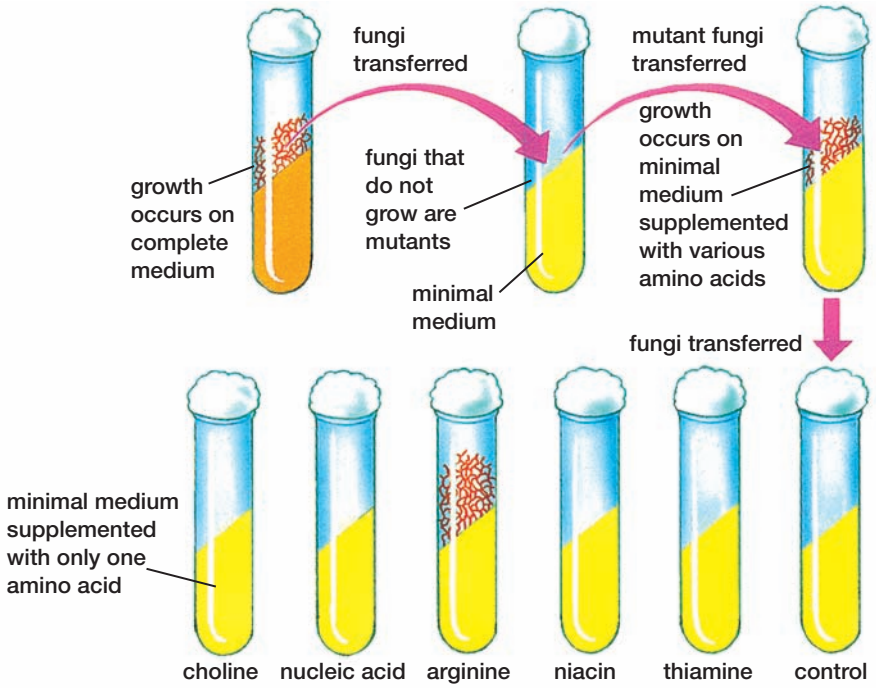


Figure 17.16 Beadle and Tatum isolated mutant strains of the mould that could grow on a complete medium but not on a minimal medium. By gradually adding one nutrient at a time to the minimal medium, they were able to isolate different mutant strains. Here, the mutant strain isolated lacks the ability to produce arginine, and so will grow only on a medium in which this nutrient has been added.

products. Other genes code for the synthesis of non-polypeptide products, such as the various types of RNA molecules that play a role in protein synthesis and other cellular processes.

Arrangement of the Genome

Genes are not spaced regularly along chromosomes. In any eukaryotic organism, the density of genes varies from one chromosome to another. In humans, for example, chromosome 4 is close to 1300 million bases long and has about 200 genes, while chromosome 19 is only 72 million bases long and has about 1450 genes. This makes chromosome 19 approximately three times richer in genes than chromosome 4.

Similarly, there is no set relationship between the number of genes in an organism and the total size of its genome. The single-celled protozoan *Amoeba dubia* has an enormous genome of over 650 billion base pairs, but fewer than 7000 genes. The human genome, in contrast, contains about three billion base pairs and an estimated 35 000 genes. A roundworm has 30 times less DNA than a human, but over half as many genes. This means that the genomes of different organisms contain varying quantities of DNA that do not serve as genes or regulatory sequences.

BIO FACT

In the human genome, genes make up just over one percent of the total length of DNA.

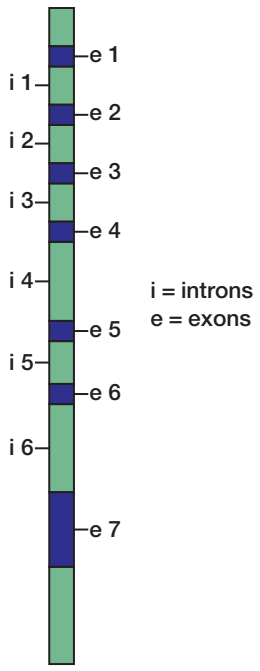


Figure 17.17 The gene for ovalbumin, the protein found in egg whites, is divided into seven exons. The total length of the exons (the expressed portions of the gene) is much smaller than the total length of the six introns. Some eukaryote genes have many more introns. The human gene for the muscle protein titin, for example, contains almost 180 introns.

In eukaryotes, each gene is composed of one or more coding regions known as expressed regions, or **exons**. These coding regions are interspersed with a number of intervening non-coding nucleotide sequences, or **introns**. As shown in Figure 17.17, introns can make up well over half of the total length of a gene.

In general, the frequency and length of introns is loosely related to the developmental complexity of the organism. The bacterial genome has no introns. Only about five percent of yeast genes contain introns, and it is rare for any one yeast gene to

contain more than one intron. Vertebrates, on the other hand, have introns in about 95 percent of their genes, and it is not uncommon for a single gene to have dozens of introns. Human introns typically contain about 100 base pairs, although some can be tens of thousands of base pairs long.

Along with introns, the vertebrate genome contains many other types of non-coding DNA. These include repetitive sequences — in which the same sequence of nucleotides is repeated hundreds or thousands of times — and pseudogenes, which are non-coding duplicates of functional genes. Both repetitive sequences and pseudogenes can result from the random copying of genetic material within the genome.

When non-coding DNA was first discovered in the 1970s, it was often referred to as "junk DNA" because it had no known function. These sequences do, however, serve a variety of developmental and regulatory functions. For example, a repetitive sequence occurs on chromosomes where the centromere forms, suggesting that this sequence helps in the attachment of spindle fibres during cell division (see Chapter 14). Later in this chapter you will see how another form of "junk" DNA plays a key role in regulating the life span of a cell.

So far you have examined the molecular structure of the DNA molecule and how it is arranged within living cells. But how is genetic information passed on from parents to their offspring? Each time a cell reproduces, its entire genome is copied. In the next section, you will study the processes involved in DNA replication. These processes ensure that hereditary material is transmitted accurately from one generation to the next.

SECTION REVIEW

1. Describe the observations made by Franklin that proved to be keys to understanding the molecular structure of DNA.
2. Describe the evidence that led Watson and Crick to their particular model of DNA.
3. The DNA molecule is a double helix, resembling a twisted ladder. Describe the component molecules that make up the ladder uprights and the pattern of their arrangement.
4. Create a chart that compares and contrasts the similarities and differences in the structure of DNA and RNA.
5. Describe the organization of genetic material in prokaryotic organisms.
6. Describe the organization of DNA in eukaryotic organisms. What is the reason for the compact nature of chromosomes?
7. Should scientists be compelled to share information out of a spirit of fairness? Linus Pauling was one of the favoured competitors in the race to discover the molecular structure of DNA, due to his superior knowledge of organic chemistry. However, Watson and Crick, who had access to Franklin and Wilkins' X-ray pictures and knowledge of Pauling's theories from his son, claimed the victory. Based on your independent review of the history of this event, how do you think the race might have ended differently?
8. Make a sketch showing the structure of a double-stranded DNA molecule.
9. Explain what is meant by the phrase "complementary base pairing." What are the complementary base pairs in DNA?
10. Explain what is meant by the phrase "the two strands of a DNA molecule are antiparallel."
11. One strand of a DNA molecule contains the following sequence of nucleotides: 5′ – AGTTGCA – 3′. How would the sequence of its complementary strand be written, according to convention?
12. The best DNA extractions come from cells that are dividing rapidly. If you were planning to extract DNA from cells other than fish muscle cells (which were used in Investigation 17-A on page 000), what cells might you use? Explain your answer.
13. Discuss how the definition of a gene has changed since Mendel conducted his experiments. What evidence contributed to this change?
14. If a gene has three introns, how many exons does it contain? Draw a labeled diagram showing how the introns and exons are arranged along a stretch of DNA.

17.3 DNA Replication

OUTCOMES

- **Describe the current model of DNA replication and methods of repair following an error.**
- **Demonstrate an understanding of the roles played by the key enzymes involved in the process of replication.**
- **Explain how differences between the molecular structure of DNA in prokaryote cells and eukaryote cells affect the process of replication.**

The eight cells in the human blastula shown in Figure 17.18 arose from the single-celled zygote formed by the merging of sperm and egg. During the 240-day gestation period, the cells of the blastula will divide over and over again to produce about one hundred trillion more cells. These trillions of cells will differentiate into the hundreds of different structures and tissues that make up a human baby, yet each cell will have exactly the same genetic complement as the original zygote. The success of this process of development depends on two factors — the genome must be copied relatively quickly, and it must be copied accurately.

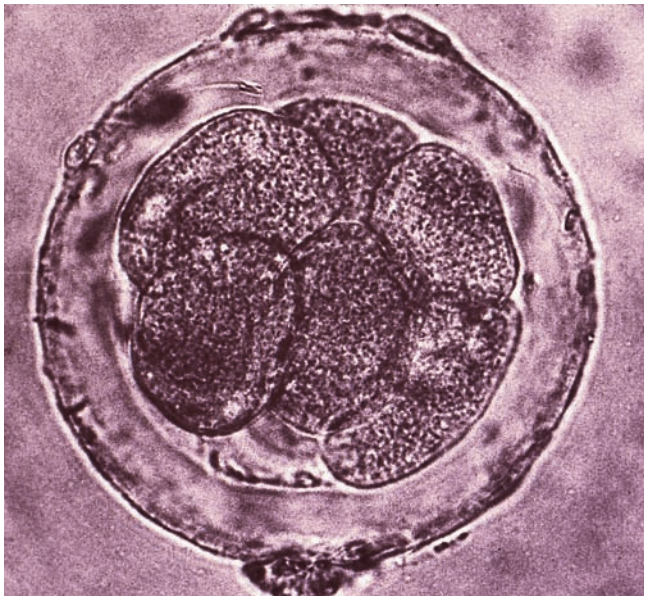


Figure 17.18 The process of DNA replication balances the need for speed and the need for accuracy.

Imagine you are asked to type out one-letter codes for each of the six billion base pairs in the genome of a single human cell. If you type at a rate equivalent to 60 words per minute and work without a break, it will take you over 30 years to complete the sequence. The cell, on the other hand, needs only a few hours to copy the same material. The error rate of the cell's replication process is about one per billion nucleotide pairs, which is the equivalent of you making a one-letter error once in every five years of steady typing. The remarkable speed and accuracy of the replication process relies on both the structural features of DNA and the action of a set of enzymes.

The Process of Replication

During DNA replication, two molecules of DNA are made from one. As shown in Figure 17.18, the replication follows a **semi-conservative** model. This means that when a molecule of DNA is copied, each new molecule contains one strand of parental DNA and one strand of new DNA, as shown in Figure 17.19.

The following pages describe the three main stages of replication: initiation, when a portion of the double helix is unwound; elongation, when two new strands of DNA are assembled; and termination, when the new DNA molecules re-form into helices. In reality, all of these activities may take place simultaneously on the same molecule of DNA.

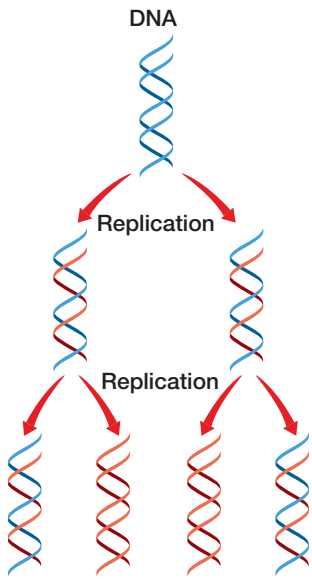


Figure 17.19 DNA replication results in the formation of two DNA molecules from one. Each new molecule contains one original strand of DNA and one newly formed strand, which is shown in red.

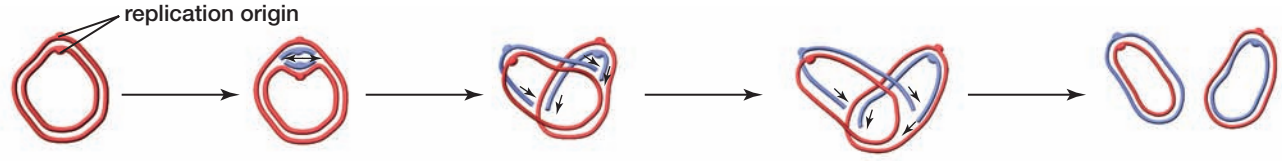


Figure 17.20 The movement of the replication forks around the circular chromosome in a prokaryote. Note that one replication bubble incorporates two replication forks, and that replication proceeds in both directions around the circular chromosome.

Initiation

In bacteria, the circular DNA strand includes a specific nucleotide sequence of about 100 to 200 base pairs known as the **replication origin**. This nucleotide sequence is recognized by a group of enzymes that bind to the DNA at the origin and separate the two strands to open a replication bubble. After a replication bubble has been opened, molecules of an enzyme called **DNA polymerase** insert themselves into the space between the two strands. Using the parent strands as a template, the polymerase molecules begin to add nucleotides one at a time to create a new strand that is complementary to the existing template strand.

For most of the life cycle of the cell, DNA is a tightly bound and stable structure. Because the bases face into the interior of the molecule, the helix must be unwound for the individual chains of nucleotides to serve as templates for the formation of new strands. The points at which the DNA helix is unwound and new strands develop are called **replication forks**. One replication fork is found at each end of a replication bubble, as shown in Figure 17.20.

A set of enzymes known as **helicases** cleave and unravel short segments of DNA just ahead of the replicating fork. As the helicases work their way along the DNA, the replication forks move around the circular DNA molecule until they meet at the other side. At this point the two daughter DNA molecules separate from each another.

Figure 17.21 shows the pattern of replication along a linear strand of eukaryotic DNA. Replication is initiated at hundreds or even thousands of replication origins at any one time. Replication continues until all the replication bubbles have met and the two new DNA molecules separate from each other.

BIO FACT

In the bacteria *E. coli*, unwinding DNA spins at a rate of over 4500 r/min — almost twice as fast as the engine speed of an average car cruising on an expressway — and the replicating fork moves at a rate of over 650 nucleotides per second.

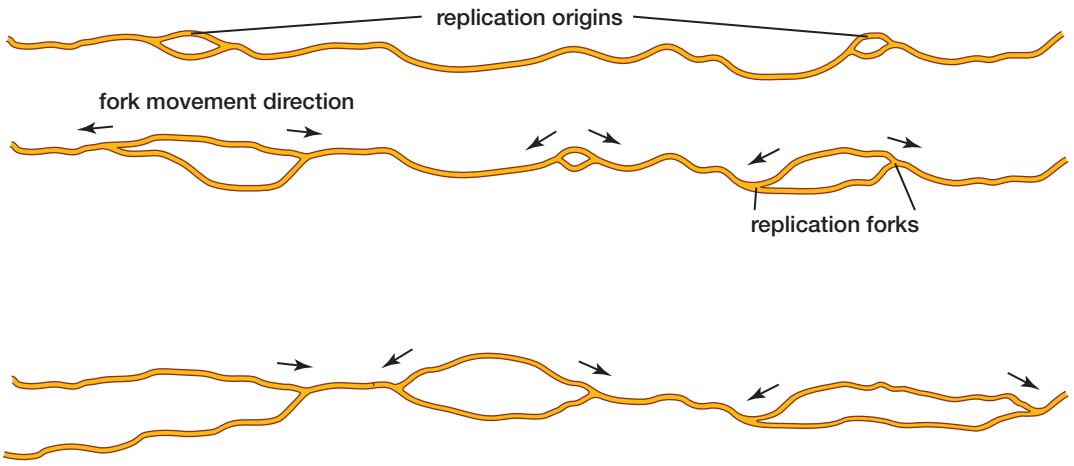


Figure 17.21 Replication bubbles open simultaneously at many sites along a linear DNA strand. As replication proceeds along the strand, the bubbles grow until they meet and the daughter strands separate from each other.

Elongation

Recall that the formation of a new DNA strand relies on the action of DNA polymerase. This enzyme has a very specific role in catalyzing the elongation of DNA molecules — it attaches new nucleotides only to the free 3′ hydroxyl end of a pre-existing chain of nucleotides. This imposes two conditions on the elongation process. First, replication can only take place in the 5′ to 3′ direction. Second, a short strand of ribonucleic acid known as a **primer** must be available to serve as a starting point for the attachment of new nucleotides. Each of these conditions helps shape the process of building new DNA strands.

The fact that polymerase can only catalyze elongation in the 5′ to 3′ direction appears to conflict with the observations that both DNA strands are replicated simultaneously and replication proceeds in both directions simultaneously along the template strand. This puzzle was solved with the discovery that, during replication, much of the newly formed DNA could be found in short fragments of one to two thousand nucleotides in prokaryotes (and a few hundred nucleotides in eukaryotes). These are known as **Okazaki fragments** after Japanese scientist Reiji Okazaki, who first observed the fragments and deduced their role in replication in the late 1960s. Okazaki fragments occur during the elongation of the daughter DNA strand that must be built in the 3′ to 5′ direction.

As illustrated in Figure 17.22, replication takes place in a slightly different way along each strand of the parent DNA. One strand is replicated continuously in the 5′ to 3′ direction, with the steady addition of nucleotides along the daughter strand. On this strand, elongation proceeds in the same direction as the movement of the replication fork. This strand is called the **leading strand**. In the other strand, which is first made in short pieces, nucleotides are still added by DNA polymerase to the 3′ hydroxyl group. However, elongation takes place here in the opposite direction to the movement of the replicating fork. DNA polymerase builds Okazaki fragments in the 5′ to 3′ direction. The fragments are then spliced together by an enzyme called **DNA ligase**, which catalyzes the formation of phosphate bonds between nucleotides. This strand is called the **lagging strand**, because it is manufactured more slowly than the leading strand.

Remember that DNA polymerase is unable to synthesize new DNA fragments — it can only attach nucleotides to an existing nucleotide chain. This means that a separate mechanism is required to establish an initial chain of nucleotides that can serve as a starting point for the elongation of a daughter DNA strand. In fact, a short strand of RNA that is made up of a few nucleotides with a base sequence complementary to the DNA template serves as a primer for DNA synthesis. The formation of this primer requires the action of an enzyme called primase. Once the primer has been constructed, DNA polymerase extends the fragment by adding DNA nucleotides. Then DNA polymerase removes the RNA molecules starting at the 5′ end of the molecule and working in a 5′ to 3′ direction.

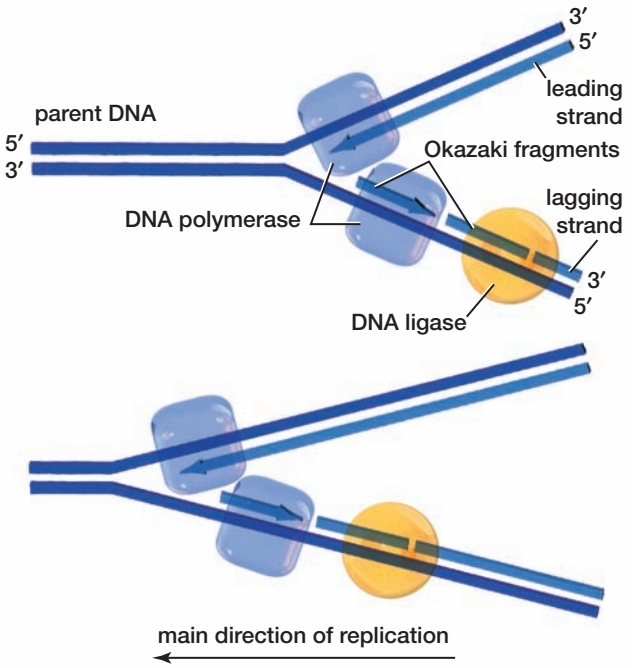


Figure 17.22 During DNA synthesis the overall direction of elongation is the same for both daughter strands, but different along each of the parent DNA strands. Along the lagging strand, DNA polymerase moves in a 5′ to 3′ direction, while DNA ligase moves in the 3′ to 5′ direction to connect the Okazaki fragments into one daughter strand.

On the leading strand, only one primer has to be constructed. On the lagging strand, however, a new primer has to be made for each Okazaki fragment. Once these primers have been constructed, DNA polymerase adds a stretch of DNA nucleotides to the 3′ end of the strand. Then another molecule of DNA polymerase attaches to the 5′ end of the fragment and removes each RNA nucleotide individually from the primer stretch. At the same time, this DNA polymerase extends the preceding Okazaki fragment, working in the 5′ to 3′ direction to replace the excised RNA nucleotides with DNA

nucleotides. Finally, the two fragments are joined together by the action of DNA ligase. This process is illustrated in detail in Figure 17.23.

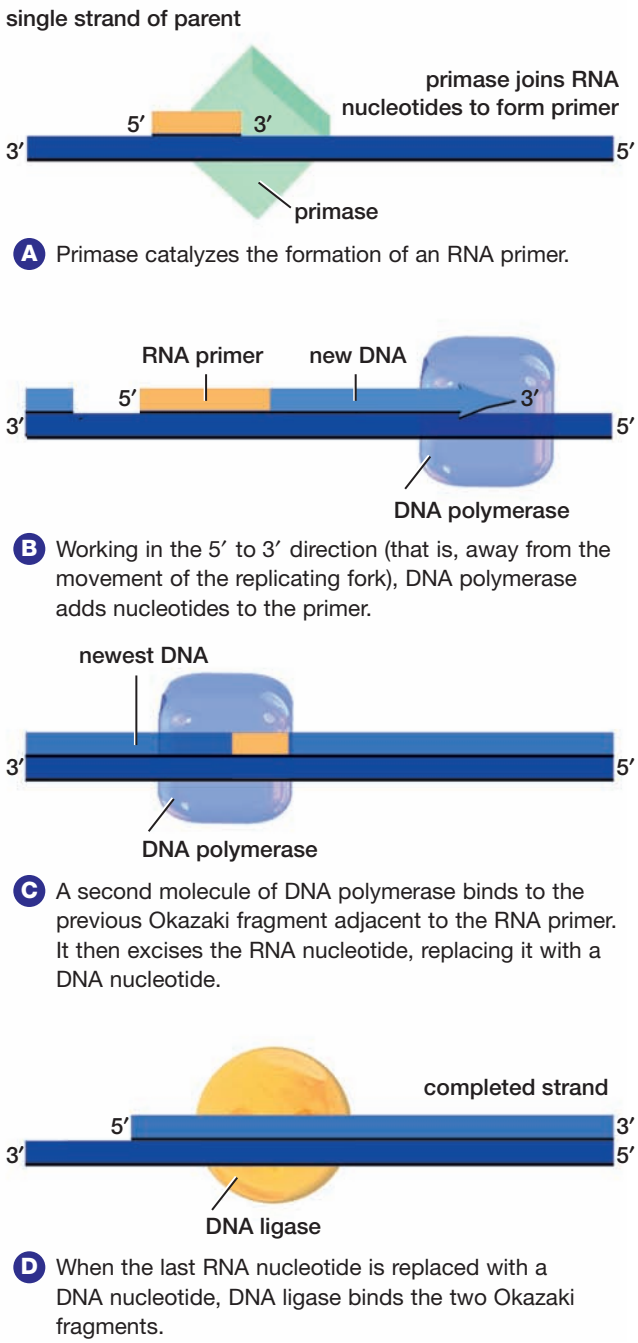


Figure 17.23 Elongation of the lagging strand

WEB LINK

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To view an animation of DNA replication, go to the web site above, and click on **Electronic Learning Partner**.

Termination

Once the newly formed strands are complete, the daughter DNA molecules rewind automatically in order to regain their chemically stable helical structure. This rewinding process does not require any enzyme activity. However, the synthesis of daughter DNA molecules creates a new problem at each end of a linear chromosome.

As you saw earlier, each time DNA polymerase excises an RNA primer from an Okazaki fragment, the resulting gap is normally filled by the addition of nucleotides to the 3′ end of the adjacent Okazaki fragment. But what happens once the RNA primer has been dismantled from the 5′ end of each daughter DNA molecule? There is no adjacent nucleotide chain with a 3′ end that can be extended to fill in the gap, and the cell has no enzyme that can work back in the 3′ to 5′ direction to complete the 5′ end of the DNA strand. Furthermore, the nucleotides on the complementary strand are left unpaired, and they eventually break off from the new strand. As shown in Figure 17.24, the result is that each daughter DNA molecule is slightly shorter than its parent template. With each replication, more DNA is lost. Human cells lose about 100 base pairs from the ends of each chromosome with each replication. Prokaryotes, which have circular DNA, do not have the same problem.

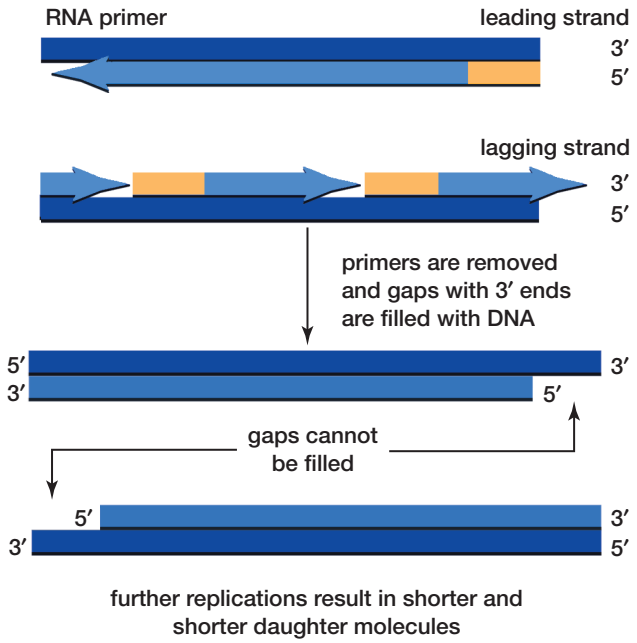


Figure 17.24 Each end of a linear chromosome presents a problem for the DNA replication process. Once the RNA primer has been removed from the 5′ end of each daughter strand, there is no adjacent fragment onto which new DNA nucleotides can be added to fill the gap. Therefore, each replication results in a slightly shorter daughter chromosome.

The loss of genetic material with each cell division could prove disastrous for a cell, since this lost material might code for activities that are important for cell functions. Special regions at the end of each chromosome in eukaryotes help to guard against this problem. These regions, called telomeres, serve as a form of buffer zone. **Telomeres** are stretches of highly repetitive nucleotide sequences that are typically rich in G nucleotides. In human cells, telomeres are composed of the sequence TTAGGG repeated several thousand times. These regions do not direct cell development. Instead, their erosion with each cell division helps to protect against the loss of other genetic material.

As you might expect, the erosion of the telomeres is related to the death of the cell. Conversely, the extension of telomeres is linked to a longer life span for the cell. Studies published in 2001 by a Canadian-led team of scientists working at the University of British Columbia found that the activity of a gene that codes for telomerase (an enzyme that extends telomeres) is directly linked to longevity in organisms such as worms and fruit flies. Cancer cells, which continue to divide well beyond the normal life span of a somatic cell, also contain telomerase. This finding has led scientists to explore the possibility of controlling cancer by pinpointing the trigger for the production of this enzyme.

Proofreading and Correction

The illustrations shown in this chapter present DNA replication as an orderly, step by step process. In reality, the setting at a molecular level is nothing short of chaotic. Imagine a sea of small and large molecules — nucleotides, free phosphate groups, dozens of different enzymes, Okazaki fragments, DNA helices, proteins, and more — all involved in a complex series of molecular collisions and chemical reactions. In this dynamic environment, it is hardly surprising that the wrong base is occasionally inserted into a lengthening strand of DNA. Studies suggest that if the replication process relied only on the accuracy of the base pairing function of DNA polymerase, errors would occur with a frequency of about one in every 10 000 to

Investigation 17 • B

SKILL FOCUS

- Performing and recording
- Analyzing and interpreting
- Conducting research

DNA Structure and Replication

James Watson and Francis Crick did not conduct any experiments in their efforts to discover the structure of DNA. Instead, they worked with physical models, trying to build a structure that could account for all the available evidence. In this investigation, you will design and build a DNA model and use this model to simulate the process of DNA replication.

Pre-lab Questions

- What happens during DNA replication?
- How does the structure of DNA contribute to the accurate transmission of hereditary material?

Problem

How can you use physical models to simulate molecular interactions?

Prediction

Predict how closely your model will resemble the one constructed by Watson and Crick.

Materials

DNA model-building supplies
sketching supplies
notebook

Procedure

1. Working with a partner, make a list of all the facts that were known about DNA when Watson and Crick began their work.

100 000 nucleotides. In fact, the accuracy of the process is up to 10 000 times better. An additional process must therefore be involved in ensuring the accuracy of replication. This function is also performed by DNA polymerase.

After each nucleotide is added to a new DNA strand, DNA polymerase can recognize whether or not hydrogen bonding is taking place between base pairs. The absence of hydrogen bonding indicates a mismatch between the bases. When this occurs, the polymerase excises the incorrect base from the new strand and then adds the correct nucleotide using the parent strand as a template. This double check brings the accuracy of the replication process to a factor of about one error per billion base pairs.

In total, the process of DNA replication involves the action of dozens of different enzymes and other proteins. These substances work closely together in a complex known as a **replication machine**. Figure 17.25 on the following page shows a simplified version of a replication machine, while Table 17.1 summarizes the roles of the key enzymes.

Table 17.1
Key enzymes in DNA replication

Enzyme group	Function
helicase	cleaves and unwinds short sections of DNA ahead of the replication fork
DNA polymerase	three different functions: – adds new nucleotides to 3′ end of elongating strand – dismantles RNA primer – proofreads base pairing
DNA ligase	catalyzes the formation of phosphate bridges between nucleotides to join Okazaki fragments
primase	synthesizes an RNA primer to begin the elongation process

In this section, you saw how DNA can be replicated quickly and accurately through the action of enzymes in the cell. In the next section, you will examine the process of protein synthesis to see how hereditary information is carried on DNA and how this information is expressed.

2. Use the materials available to construct a short strand of DNA. Make a note of how each fact on your list is supported by your model.
3. Write down the nucleotide sequences for each strand of DNA in your molecule, using the correct conventions.
4. Now use your model to simulate the process of DNA replication. Keeping in mind the specific action of the enzyme DNA polymerase, use your model to demonstrate:
   (a) replication along the leading strand;
   (b) replication along the lagging strand; and
   (c) the problem created at the ends of linear chromosomes.

Post-lab Questions

1. Which base pairs in a DNA molecule will be least resistant to heat? Why?
2. Are there any aspects of DNA replication that your model cannot illustrate? Explain.

Conclude and Apply

3. Make a list of the key replication enzymes in the order in which they are involved. For each enzyme, write a brief description of what would happen if that enzyme were not present in the replication medium. (For the purpose of this exercise, assume that the absence of any one enzyme does not affect the activity of others.) Compare your findings with those of another group.
4. Draw a flowchart or concept map relating events at the molecular level to the observed changes in chromosomes during cell division. You may wish to refer to Chapter 00 for a review of cell division.
5. In one of the early models tested by Watson and Crick, the sugar-phosphate handrails were located on the inside of the helix while the nitrogenous bases protruded outward. In what ways is this model inconsistent with experimental evidence about the structure of nucleic acids?

Exploring Further

6. In the late 1940s and early 1950s, before the publication of Watson and Crick's paper, other researchers proposed different structures for the DNA molecule. Conduct research on one of these early models. Prepare a short written report that compares this model with Watson and Crick's. How did Watson and Crick's model fit better with the scientific evidence?

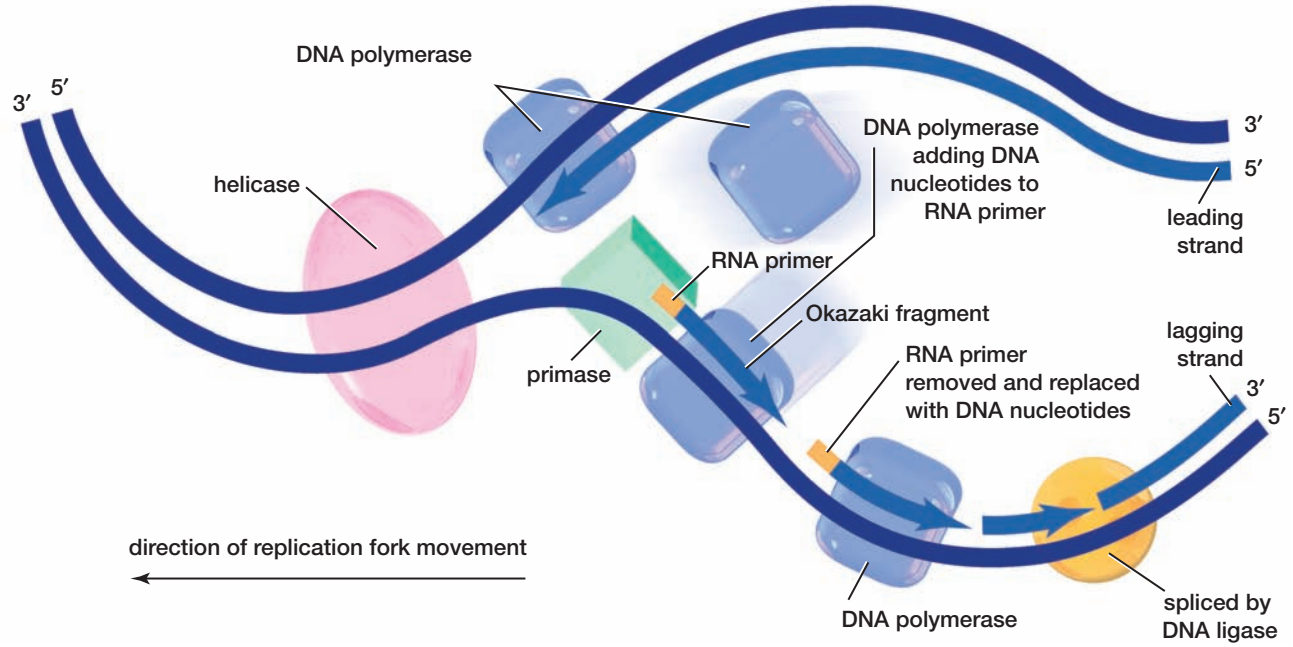


Figure 17.25 As this illustration of the replication machine indicates, only a very short region of either the parent or daughter DNA strand is ever left in a non-base-paired form as the replication fork progresses.

SECTION REVIEW

1. In a series of sketches, briefly outline the three phases of DNA replication.

2. Explain the role of the following enzymes in DNA replication.

(a) helicase **(b)** DNA polymerase

(c) DNA ligase **(d)** DNA primase

3. What is the purpose of the Okazaki fragments? What happens to them during replication?

4. Explain how replication errors are corrected.

5. Some scientists studying telomeres hope their research will eventually lead to a way of treating cancer. Give two examples of additional applications that could arise from a better understanding of these structures.

6. Suppose mammalian cells are cultured in a medium containing radioactive thymine. They grow and divide many times, until eventually every chromosome contains radioactive thymine. The cells are then removed and allowed to replicate several more times in a culture medium containing normal thymine. Daughter chromosomes are tested with each successive generation to determine whether they carry the radioactive thymine.

(a) Predict the radioactive status of the daughter chromosomes after one, two, and three rounds of division in the normal medium.

(b) Explain how your predictions are consistent with semi-conservative DNA replication.

7. Lacking knowledge of Franklin's X-ray analysis of the DNA molecule, Linus Pauling proposed a DNA structure in which the phosphate groups were tightly packed on the inside of the molecule, thus leaving the nitrogenous bases sticking outward. If DNA replication occurred in this structure, how do you think it would differ from what you know is the actual process?

8. Could you use what you have learned about the replication of DNA to develop a drug that kills bacteria but not eukaryotic cells? Explain your answer.

9. Describe what is meant by "semi-conservative replication."

10. Using diagrams, show the pattern of replication

(a) along a bacterial chromosome;

(b) along a eukaryotic chromosome.

11. When Watson and Crick first published their landmark paper on the structure of DNA in 1953, they included the comment that the complementarity of DNA strands pointed to a means of accurate replication of DNA molecules. What do you think they meant by this? In what way does the current model of DNA replication support or refute this comment?

17.4 Protein Synthesis and Gene Expression

OUTCOMES

- **Explain the roles of DNA and RNA in protein synthesis.**
- **Discuss the influence of external factors on gene expression.**
- **Distinguish among different types of mutations and predict their effects on protein synthesis and heredity.**

Like the Morse code, DNA stores information in a type of code — the **genetic code**. The order of base pairs in a DNA molecule makes up the genetic code of an organism. Before you can decipher the genetic code, however, it is important to understand the type of information that the code carries. For example, what instructions does DNA give to a cell? To answer this, you need to understand the relationship between genes and proteins.

As you saw in Chapter 2, proteins are made of 20 kinds of amino acids linked together in a certain order in each protein. Linked amino acids form long chains called **polypeptides**, and two or more polypeptides are joined to make a particular protein. A protein may be made of hundreds or thousands of amino acids. Each different type of protein contains different numbers of the 20 amino acids, arranged in a specific order.

All organisms contain and make proteins. Proteins are important structural components of your cells, and of your body as a whole. Certain types of cells are largely made up of protein. For example, your hair and fingernails are made mostly of a protein called keratin. The hemoglobin found in your red blood cells is a protein, as is insulin and other hormones. Other proteins produced by cells, called enzymes, control virtually all of the chemical reactions going on in your body; it is these chemical reactions that provide your body with energy. All of your actions, including running, eating, and even thinking, depend on enzymes. Some enzymes drive the cell cycles of growth and division, while others stop cell cycles.

DNA determines how amino acids are strung together and how proteins are made. The sequence of amino acids is determined by the sequence of nucleotides in the DNA. In other words, the DNA is a code that specifies how to put amino acids in a particular order. A gene is the segment of DNA that controls the production of a protein. The order of nucleotides in a gene is a type of message — written in genetic code — that provides the information necessary to build a protein.

Figure 17.26 summarizes the path of **gene expression**, the term used to describe the transfer of genetic information from DNA to protein. First, the information in DNA is copied onto an RNA molecule in a process called **transcription**. In a eukaryotic cell, this process takes place in the cell nucleus. Then the RNA molecule moves to the cytoplasm of the cell, where the RNA nucleotide sequence directs the synthesis of a polypeptide. This second step is called **translation**. The theory that genetic information flows from DNA to RNA to protein is often referred to as the "central dogma" of gene expression. In the next few pages you will examine the genetic code and the process of gene expression in more detail.

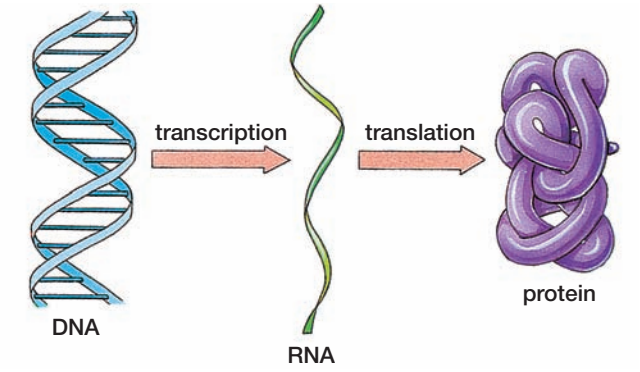


Figure 17.26 Crick's "central dogma" proposes a two-step process of gene expression. In this process, genetic information is first transcribed from DNA to RNA, and then translated from RNA to protein.

The Genetic Code

How is the genetic code written? Recall that there are 20 amino acids but that DNA contains only four kinds of bases. If you tried to use nucleotides one at a time to code for amino acids, you would only be able to code for four different amino acids. If you took the nucleotides two at a time (for example, using AU or CG to code for a single amino acid),

you still would not be able to come up with enough different combinations to code for all 20 amino acids. It takes combinations of three nucleotides in order to have enough different "code words" to represent 20 amino acids. Using three base sequences at a time (for example, ACU, AAC, CAG), there are 64 possible combinations of the four different nucleotides. This is far more than is needed to code for 20 different amino acids. Each set of three bases is known as a **codon**. Since there are 64 possible codons and only 20 amino acids, in some cases two or more codons code for the same amino acids. In other words, there are codon synonyms.

Table 17.2
The genetic code. Since genetic information is passed from DNA to RNA, codons are always written in the form of the RNA transcript from the DNA molecule.

First letter	Second letter				Third letter
	U	C	A	G	
U	phenylalanine	serine	tyrosine	cysteine	U
	phenylalanine	serine	tyrosine	cysteine	C
	leucine	serine	**stop**	**stop**	A
	leucine	serine	**stop**	tryptophan	G
C	leucine	proline	histidine	arginine	U
	leucine	proline	histidine	arginine	C
	leucine	proline	glutamine	arginine	A
	leucine	proline	glutamine	arginine	G
A	isoleucine	threonine	asparagine	serine	U
	isoleucine	threonine	asparagine	serine	C
	isoleucine	threonine	lysine	arginine	A
	start/ methionine	threonine	lysine	arginine	G
G	valine	alanine	aspartate	glycine	U
	valine	alanine	aspartate	glycine	C
	valine	alanine	glutamate	glycine	A
	valine	alanine	glutamate	glycine	G

Table 17.2 shows the full set of RNA codons and their corresponding amino acids. As you can see, there are one or more codons for each of the 20 amino acids. There are also codons for "stop" and "start."

By convention, the genetic code is always presented in terms of the RNA codon rather than the nucleotide sequence of the original DNA strand. The RNA codons are written in the 5′ to 3′ direction. To read the table, find the first letter of the RNA codon in the column titled "First letter." Then read across the rows in the column titled "Second letter" to find the second letter of the codon. This will take you to a set of four possible amino acids. Finally, read down the column titled "Third letter" to find the last letter of the codon. This will indicate the amino acid that corresponds to that codon. For example, the RNA codon GAG codes for glutamate. What amino acid corresponds to the codon CAU?

Characteristics of the Genetic Code

The genetic code has a number of important characteristics. As you saw above, it is *redundant* — that is, more than one codon can code for the same amino acid. Only three codons code for no amino acid. As you will see later, these codons serve as "stop" signals that end protein synthesis. Second, as shown in Figure 17.27, the genetic code is *continuous*. That is, the code reads as a series of three-letter codons without spaces, punctuation, or overlap. Knowing exactly where to start and stop transcription is therefore essential. A shift of one or two nucleotides in either direction will alter the **reading frame**, or codon groupings, and result in an incorrect amino acid sequence. Finally, the genetic code is *universal*. The genetic code shown in Table 17.2 is the same in almost all living organisms. This has important implications for gene technology, since a gene that is taken from one kind of organism and inserted into another can still produce the same protein. For example, a bacterium can express a human gene. Later in this unit, you will learn how this principle is applied in genetic technologies.

BIO FACT

Mitochondria contain their own DNA in the form of a closed, circular molecule like the one found in bacteria. This DNA has a slightly different genetic code than the DNA in most living cells, including the cells in which the mitochondria are located.

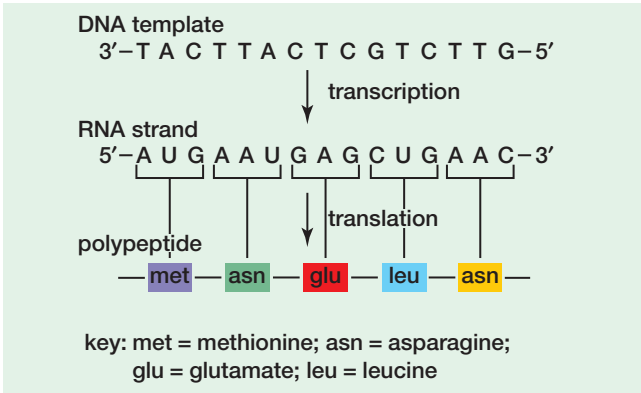


Figure 17.27 Two characteristics of the genetic code are continuity and redundancy. Here, a portion of a DNA molecule serves as a template for the synthesis of a strand of RNA. The genetic code is made up of three-letter codons along the RNA strand. Each codon correlates with one amino acid. Note that the codons are read as an unbroken series of non-overlapping words (continuity). Note also that two different codons can code for the same amino acid (redundancy).

Transcription

The objective of transcription is to make an accurate copy of a small piece of an organism's genome. The information in DNA is copied onto a particular type of RNA molecule called **messenger RNA**. Messenger RNA, or **mRNA**, is a linear strand of RNA that carries information from DNA in the nucleus to the protein synthesis machinery of the cell. What advantages does this copying process provide to a cell? Recall that in a eukaryotic cell, transcription occurs in the nucleus while translation takes place in the cytoplasm. Transcription onto mRNA keeps the DNA safely in the nucleus. This copying process also means that only a relatively small RNA molecule containing the nucleotide sequence of a specific gene has to be transported, so the cell saves energy.

The main enzyme that catalyzes the synthesis of RNA is **RNA polymerase**. A particular sequence of nucleotides on the DNA molecule tells RNA polymerase where to bind. For each gene, only one strand of the double-stranded DNA molecule will be transcribed. This strand is called the **template (anti-sense)** strand. The other strand, which is not transcribed, is called the **coding (sense strand)** because it has the same sequence of bases that the RNA will have. Once RNA polymerase has bound to the sense strand of the DNA molecule, it opens a section of the double helix. The enzyme then works its way along the template strand and synthesizes a strand of RNA that is complementary to the DNA.

The elongation of an mRNA transcript works in much the same way as the elongation of a new DNA strand during the process of DNA replication (which was discussed in Chapter 16). Like DNA polymerase, RNA polymerase works in the to direction, adding each new nucleotide to the -OH group of the previous nucleotide. RNA transcribes only one strand of the DNA template, however. There is therefore no need for Okazaki fragments. The process of elongation is illustrated in Figure 17.28.

RNA polymerase moves along the double helix, opening it one section at a time. As the polymerase molecule passes, the DNA helix re-forms and the mRNA strand separates from its template DNA strand. As soon as this RNA polymerase begins tracking along the DNA molecule after leaving the promoter region, a new RNA polymerase can bind there to begin a new transcript. This means that dozens or even hundreds of copies of the same gene can be made in a very short time.

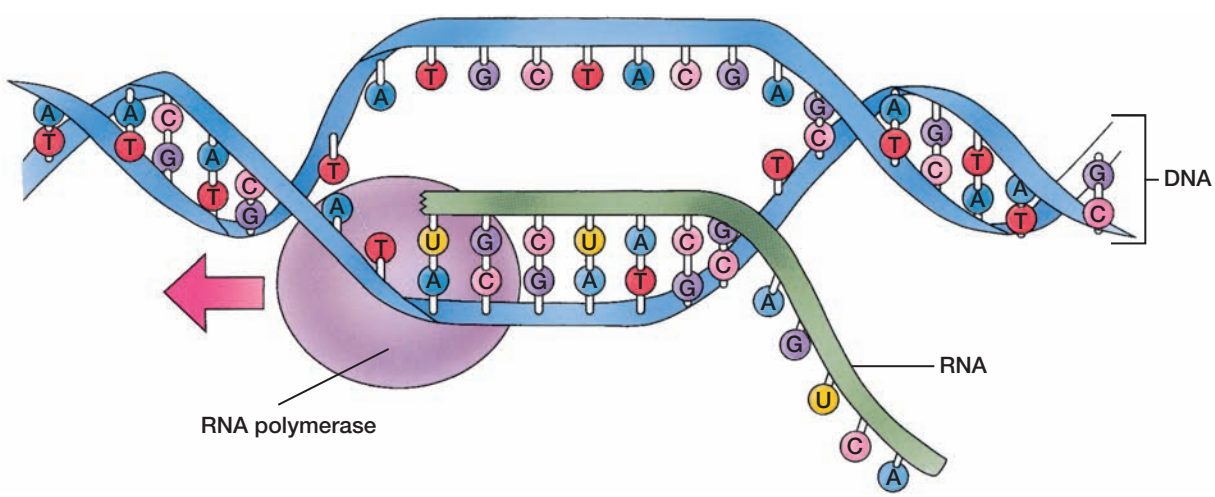


Figure 17.28 During elongation, RNA polymerase tracks along the template strand of DNA, synthesizing a strand of mRNA by adding nucleotides in the to direction. Only a short strand of the DNA helix is opened at any one time. As the helix re-forms, the elongating mRNA strand separates and trails out behind the RNA polymerase.

mRNA Processing

The RNA polymerase continues along the DNA molecule until it encounters a signal that ends transcription. The polymerase and the mRNA molecule separate from the DNA molecule. In prokaryotes, the mRNA molecule is now ready to begin directing protein synthesis. (In fact, since both transcription and translation take place in the cytoplasm of prokaryotes, the free end of an mRNA molecule can begin translation even before transcription is complete.) In eukaryotes, however, the mRNA molecule undergoes additional processing before it leaves the nucleus.

A special sequence of nucleotides is added to both the and ends of the mRNA molecule. In addition, some sections of the RNA molecule are removed. As you saw in the previous chapter, most eukaryote genes contain both expressed nucleotide sequences or exons (which form part of the instructions for protein synthesis) and intervening non-coding nucleotide sequences or introns. The RNA polymerase does not distinguish between introns and exons as it transcribes a gene. The initial mRNA transcript therefore contains long stretches of nucleotides that must be removed before the transcript is used to construct a polypeptide.

A complex of enzymes and nucleic acids splices out the introns and joins the ends of the exons.

WEB LINK

www.mcgrawhill.ca/links/atlbiology

To view animation clips on DNA transcription, go to the web site above and click on **Electronic Learning Partner**.

After the processing is complete, the finished mRNA molecule is transported from the nucleus to the cytoplasm, where translation begins.

Translation

In the process of translation, a number of elements work together to read the genetic code carried on the mRNA and to assemble protein products. The following are two key elements of this process.

Transfer RNA (tRNA) Different **transfer RNA**, or **tRNA**, molecules link each codon on the mRNA with its specific amino acid. The tRNA molecules have a characteristic cloverleaf shape like that shown in Figure 17.29. At the end of one lobe is the **anticodon**. The anticodon is a nucleotide triplet with a sequence that is complementary to the codon of the mRNA molecule. At the end of the tRNA is an amino acid attachment site. Special enzymes bind each tRNA molecule to its corresponding amino acid. For example, a tRNA with the anticodon sequence GGU will bind to the amino acid proline, and will carry this amino acid to the mRNA codon CCA.

Ribosomes **Ribosomes** are specialized structures in the cell that bring together the mRNA strand, tRNA molecules carrying amino acids, and the enzymes involved in building polypeptides. A ribosome contains different kinds of proteins together with a third kind of RNA known as **ribosomal RNA**, or **rRNA**. Ribosomal RNA is a linear strand of RNA that always stays bound to proteins within ribosomes. Each ribosome has two sub-units, one large and one small, that fit together to produce one active ribosome.

THINKING LAB

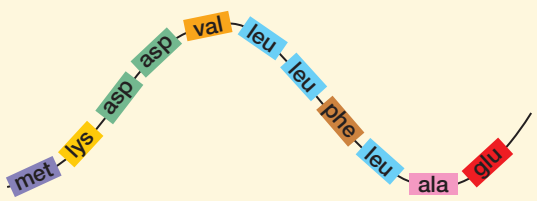
Transcription in Reverse

Background

The nucleotide sequence of DNA guides the process of protein synthesis. In this activity, you will work backwards from a polypeptide chain to construct a stretch of DNA that might code for this product.

You Try It

1. The illustration at right shows an imaginary polypeptide produced by a bacterial cell. Using Table 17.1 (on page 000) and the information given about its amino acid sequence, draw one possible nucleotide sequence of the DNA molecule containing the gene for this polypeptide.
2. Label the DNA sense strand and anti-sense strand.
3. Write a paragraph or prepare a table contrasting the process of DNA replication with that of mRNA transcription.
4. Could DNA work as a messenger molecule instead of mRNA? What would be the effect on transcription? Write down some ideas and discuss them with a partner.



The Translation Cycle

Translation is initiated when an mRNA molecule binds to an active ribosome. The mRNA is bound is such a way that two adjacent codons are exposed. The first tRNA molecule carrying an amino acid base-pairs with the first exposed mRNA codon. Once these pieces are in place, translation follows a cycle of three steps:

1. A second loaded tRNA molecule arrives at the codon adjacent to the first tRNA.
2. Enzymes then catalyze the formation of a peptide bond that joins the amino acid carried by the first tRNA to that carried by the second tRNA. At the same time, the polypeptide chain is transferred from the first tRNA to the second.
3. The ribosome moves a distance of one codon along the mRNA strand. The first tRNA molecule detaches from the mRNA and then picks up another amino acid. The second tRNA now holds a growing polypeptide chain. A third tRNA molecule arrives at the exposed codon next to the second tRNA, and the cycle repeats.

The translation cycle continues until a "stop" codon is reached. At this point, the completed amino acid is released and the ribosome assembly comes apart. Figure 17.29 summarizes the steps in translation, while Table 17.3 on page 594 compares and contrasts the structure and function of the different nucleic acids involved.

WEB LINK

www.mcgrawhill.ca/links/atlbiology
To view an animation clip on tRNA and translation, go to the web site above and click on **Electronic Learning Partner**.

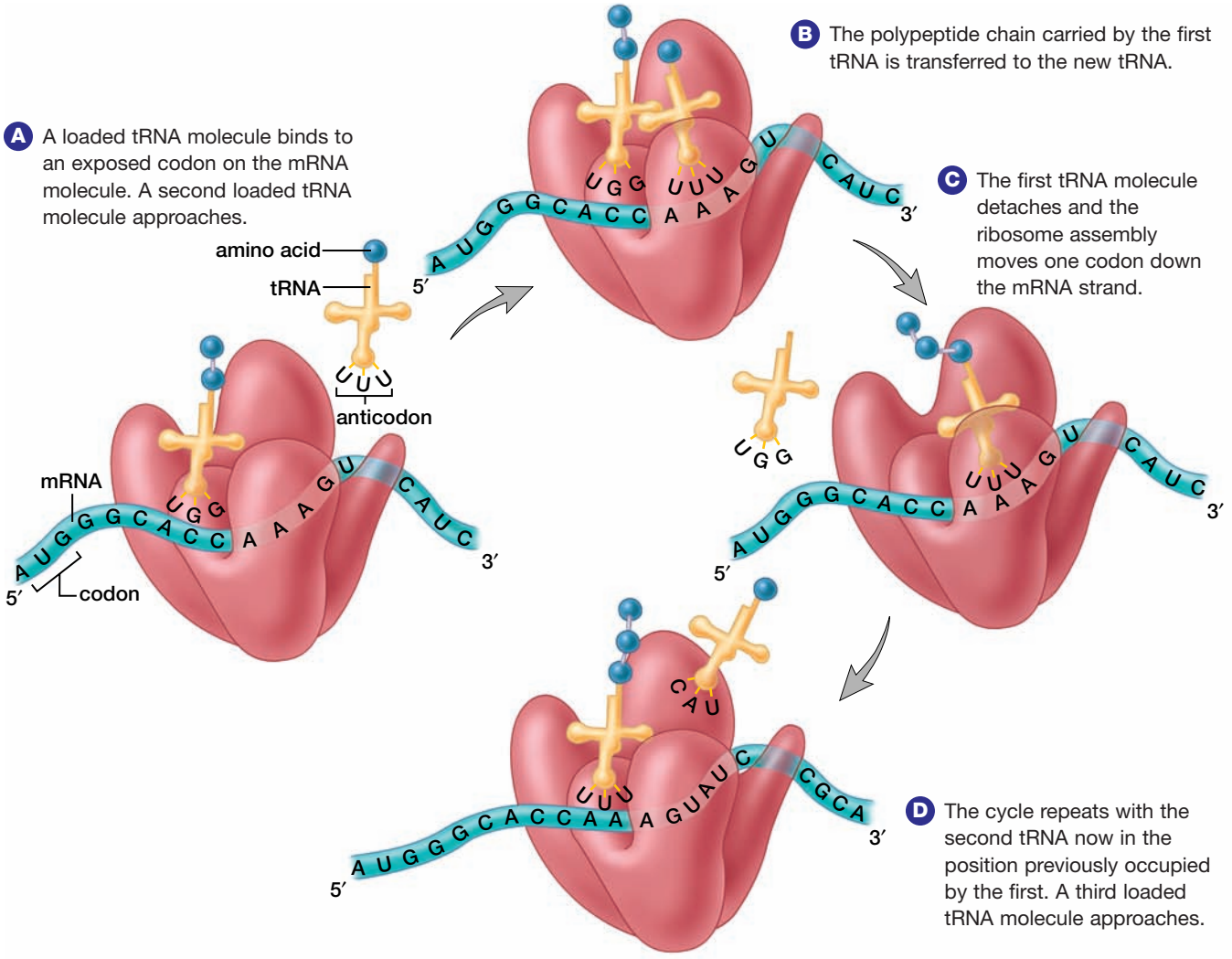


Figure 17.29 Translation follows a three-step cycle. Note the characteristic three-lobed shape of the tRNA molecules.

Table 17.3
The main nucleic acids involved in transcription and translation

Nucleic Acid	Structure	Function
DNA	double helix	DNA stores genetic information.
messenger RNA (mRNA)	linear single strand	Messenger RNA carries genetic information from DNA to the protein assembly line. In eukaryotes, mRNA must be processed before it moves to the cytoplasm for translation.
transfer RNA (tRNA)	three-lobed "cloverleaf"	Transfer RNA carries a particular amino acid associated with a specific mRNA codon to the correct binding site in the protein assembly line.
ribosomal RNA (rRNA)	linear single strand	Ribosomal RNA combines with a complex of proteins to form a ribosome, the main structure in the protein assembly line.

Regulating Gene Expression

Every living cell has the ability to respond to its environment by changing the kinds and amounts of polypeptides it produces. All polypeptides originate from the same processes of transcription and translation that you have studied so far in this chapter. By exercising control over these processes, a cell can regulate its gene expression.

For example, the white colour of arctic foxes (*Alopex lagopus*) in winter, helps to conceal the foxes from both prey and predators. As the temperature warms and the snow melts, the ground will take on the browns of the arctic tundra. The warmer temperature triggers the synthesis of polypeptides that act as pigments in the fur. As a result, the foxes will turn brown. Some animals show even more dramatic changes in gene expression during their lifetimes. For example, if a male slipper limpet (*Crepidola fornicata*) is surrounded by other males, as shown in Figure 17.30, it will turn into a female.

Investigation 17 • C

SKILL FOCUS

- Predicitng
- Planning and initiating
- Performing and recording
- Communicating results
- Conducting research

Simulating Protein Synthesis

Throughout the 1950s and 1960s, scientists developed a number of models to explain the steps in protein synthesis even though they were not able to see most of the processes taking place at the cellular level. Today's researchers can now use electron microscopy to help them see and analyze molecular processes, but large-scale models are still an important tool in scientific research. In this investigation, you will work with a team to develop and present a simulation of protein synthesis.

Problem

How can you use materials available in your home or classroom to simulate the process of transcription and translation?

Prediction

Predict which aspects of protein synthesis will be relatively easy to simulate in the classroom, and which will be more difficult.

Materials

Select your own materials as determined by your experimental plan.

Experimental Plan

1. Working in a group, make a list of the steps involved in transcription and translation. Prepare a second list that includes the main structures, molecules, and processes involved at each step.
2. Discuss with your group how you might simulate the processes of transcription and translation in the classroom. Some possibilities include
   - assigning different locations in the classroom to different cellular structures, and the actions of different molecules to various students to role play; or
   - developing models using paper cutouts or other materials.

Figure 17.30 Slipper limpets live in stacked colonies. If no female limpets are present, some males will turn into females.

Many factors can affect the rate of transcription and translation in living cells, including:

- **Changes in temperature or light** Various organisms respond to temperature changes. Many animals, for example, change colour or grow thicker fur coats in the winter. Warm temperatures can cause plants to germinate, while cool temperatures may trigger a period of dormancy. Bright lights activate the production of proteins associated with particular behaviours (such as wakefulness) in many animals, and the proteins involved in photosynthesis in plants.
- **The presence or absence of nutrients in the environment** *E. coli* bacteria respond to the presence of lactose in their environment by increasing the rate of production of enzymes involved in synthesizing lactose. Similarly, they react to the presence of the amino acid tryptophan by reducing their production of the enzymes that synthesize tryptophan.
- **The presence of hormones in the body** Hormones are a particular kind of protein that trigger protein synthesis mechanisms in other cells.

The development of living organisms is governed by the regulation of gene expression. From the moment of conception, each of your cells contains exactly the same genetic information as every other cell of your body. Certain genes, known as *homeobox genes*, or *hox genes*, control which

3. Decide on one plan and assign responsibilities to each member of your group.
4. Assemble the materials you will need and prepare your presentation.

Checking the Plan

1. Check your plan against your initial list of the structures, molecules, and processes involved in protein synthesis. Have you included all the important steps?
2. Do the materials you are using help to explain the processes involved at each step?
3. Has your teacher approved your plan?

Data and Observations

Present your simulation of protein synthesis to the class. Make a note of any comments you receive from other groups. Identify which parts of your presentation seemed to be the most effective at simulating protein synthesis. Do these results match your initial hypothesis?

Analyze

1. Among the different approaches used by the groups in the class, which do you think was the most effective? Explain.
2. Now that you have seen how other groups approached the problem, how would you revise your own presentation?

Conclude and Apply

3. Identify three ways in which the two-step process of protein synthesis helps living cells conserve energy or reduce the risk of damage from mutations.
4. What are the adaptive advantages and disadvantages of the presence of introns in eukaryotic cells?

Exploring Further

5. Almost all living organisms on Earth use the same 20 amino acids. However, molecular biologists have been able to develop a number of artificial amino acids, which can be used to develop synthetic proteins that have many potential applications. In response, some research teams are exploring the possibility of expanding the genetic code to include new nucleotides that could be used to code for artificial amino acids. Use your library or the Internet to find out more about this research. Write a brief report explaining some of the hurdles that will have to be overcome as scientists try to expand the genetic code. What are some of the scientific and social implications of this research?

parts of the genome are activated in different cells of a developing embryo. In turn, this process ensures that each body cell develops the properties of only one particular tissue or organ.

Mutations

Much of what you have learned about genetics so far depicts hereditary information as relatively stable. You have learned, for example, that brown eyes are dominant and blue eyes are recessive, and that these traits are passed from parents to their offspring in a statistically predictable way — but you have probably also seen a dog or cat that has one blue eye and one brown eye. How can this be? In fact, the genome of any organism is far from stable. In the dynamic environment of the cell, the structure of DNA is constantly changing.

The changes that take place at the molecular level within genes are an important source of genetic variation. A permanent change in the genetic material of an organism is called a **mutation** (see Figure 17.31). All mutations are heritable in that they will be copied during DNA replication. Not all mutations will be passed on to future generations, however. Only changes that affect the genetic information contained in the reproductive cells of an organism, called **germ cell mutations**, will be passed on to offspring. Mutations that arise in the other cells of an organism during its lifetime are called **somatic cell mutations**. Somatic mutations are not inherited by future generations, but they are passed on to daughter cells within the body of that organism during the process of mitotic cell division.

Figure 17.31 This three-legged northern leopard frog (*Rana pipiens*) is deformed as the result of mutations in its DNA.

Types of Mutations

Mutations happen constantly in the DNA of any living organism. More than one trillion mutations occurred in your own DNA in the time it took you to read this sentence. Most of these are changes at the level of individual nucleotides, but mutations can also involve larger-scale re-organizations of genetic material.

Many mutations involve small changes in the nucleotide sequence within individual genes. A chemical change that affects just one or a few nucleotides is called a **point mutation**. Point mutations may involve the substitution of one nucleotide for another, or the insertion or deletion of one or more nucleotides.

A nucleotide substitution is the replacement of one nucleotide by another — a change from the DNA sequence CATCAT to CATTAT, for example. Such substitutions may have a relatively minor effect on the metabolism of the cell. One reason for this minimal effect is the redundancy of the genetic code. This redundancy means that a change in the coding sequence of a gene does not always result in a change to the polypeptide product of that gene. For example, a change in the DNA sense strand sequence from CCT to CCC will not alter the polypeptide product, since the associated mRNA codons both code for the amino acid serine.

Even in a case where the point mutation results in the substitution of one amino acid for another, this substitution may not have a significant effect on the final structure or function of the protein product. A mutation that has no effect on the cell's metabolism is called a **silent mutation**. This kind of mutation, along with others that may result from nucleotide substitutions, is illustrated in Figure 17.32.

In other cases, a substitution may lead to a slightly altered but still functional protein product. Mutations that result in such altered proteins are known as **mis-sense mutations**. Mis-sense mutations can be harmful; for example, a change in a single amino acid in one of the proteins that makes up hemoglobin is responsible for the genetic blood disorder known as sickle cell disease. On the other hand, mis-sense mutations may help organisms develop new forms of proteins that can meet different requirements. For example, researchers have evidence that mis-sense mutations play an important role in generating the enormous variety of antibodies that your body requires to fight infections.

Some substitutions can have severe consequences for a cell. A change in a gene's coding sequence that erases a "start" signal or that results in a premature "stop" signal can mean that the gene is unable to produce a functional protein. In the same

way, a nucleotide substitution that affects a regulatory sequence may result in the cell being unable to respond properly to metabolic signals. A mutation that renders the gene unable to code for any functional polypeptide product is called a **nonsense mutation**.

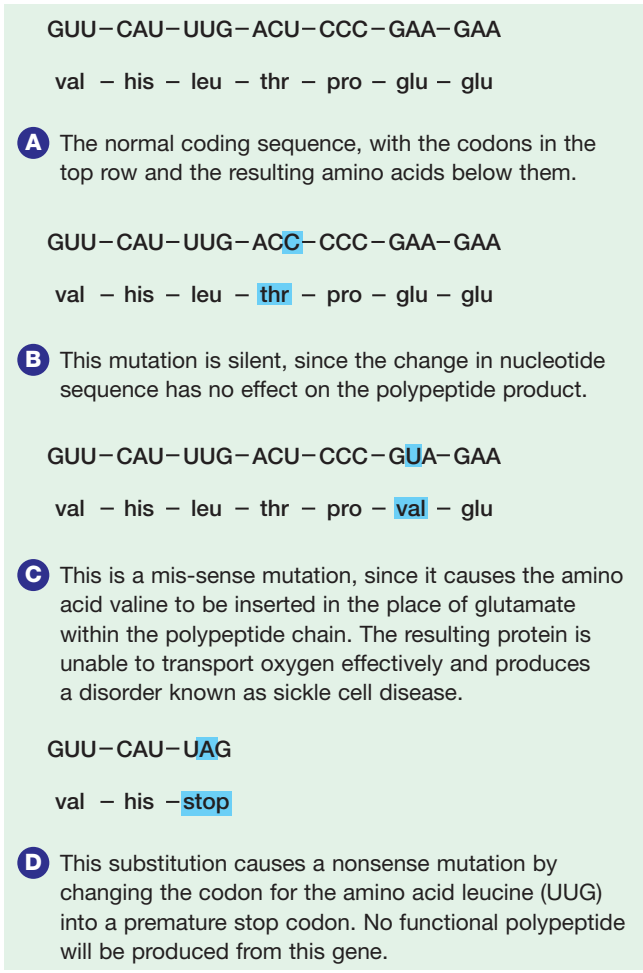


Figure 17.32 A nucleotide substitution can result in different types of mutations, as shown here on a portion of the gene that codes for human beta-globulin, one of two polypeptides in the blood protein hemoglobin.

Nucleotide Insertions or Deletions

The insertion or deletion of one or two nucleotides within a sequence of codons produces a second type of point mutation known as a **frameshift mutation**. Unlike nucleotide substitutions (which do not affect neighbouring codons of DNA), nucleotide insertions or deletions cause the entire reading frame of the gene to be altered, as illustrated in Figure 17.33. It is possible for two frameshift mutations to cancel each other out — that is, the addition of one nucleotide at one location on a gene can be compensated for by the deletion of another nucleotide further along the coding sequence. In such a case, the result may be a mis-sense mutation. In most cases, however, a frame shift will result in a nonsense mutation.

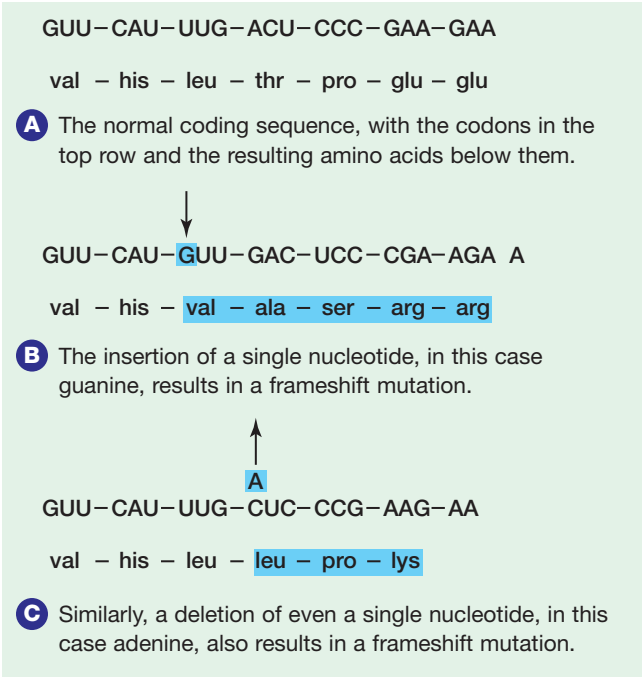


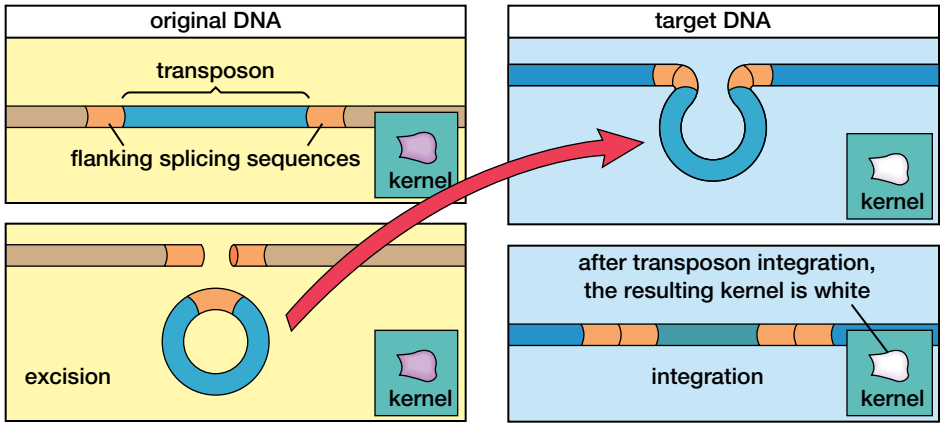
Figure 17.33 Frameshift mutations usually result in nonsense mutations.

Chromosomal Mutations

Substitutions and frameshift mutations typically affect only a single gene. Other mutations may involve rearrangements of genetic material that affect multiple genes, including genes located on separate chromosomes. One example of such a mutation is the exchange of portions of chromosomes that may take place between sister chromatids during the process of meiosis. (For a review of the somatic cell cycle, see Chapter 14.) Portions of chromosomes can also become lost or duplicated during DNA replication; this can result in changes to structural or regulatory DNA sequences.

Another factor that can rearrange genetic material is the activity of transposable elements, also known as jumping genes or **transposons**. These are short strands of DNA capable of moving from one location to another within a cell's genetic material. A transposon is located between nucleotide sequences that are recognized by an enzyme called transposase. Transposase excises the transposon out of one location and splices it into another. One effect of transposons is illustrated in Figure 17.34.

Transposons were first discovered by American researcher Barbara McClintock in 1957. McClintock found that the random pattern of colours in the



A When a transposon is located within a strand of DNA that does not code for kernel colour (top), the default kernel colour will be purple.

B When the transposon is excised and re-inserted into a gene that codes for kernel colour (top), it can disrupt the coding sequence and block the action of that gene.

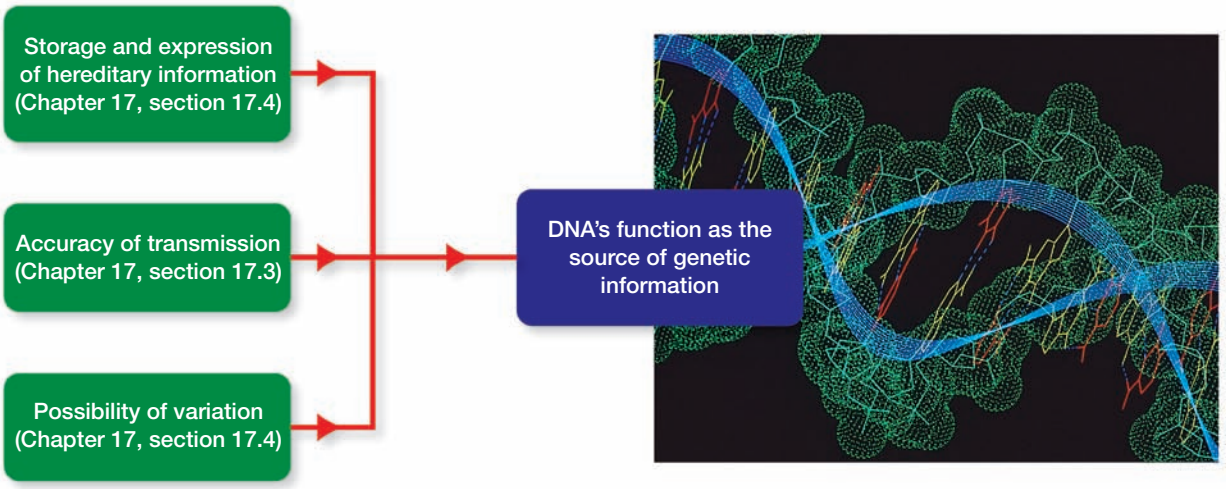
Figure 17.34 The action of a transposon. Transposons are also known as "jumping genes" because of the way they can move from one location in the genome to another.

kernels of Indian corn could be explained by the movement of short strands of DNA from one position within a cell's chromosomes to another. In 1983, McClintock was awarded a Nobel prize for her work. Mutations of this nature help to explain some of the rapid genetic changes that may lead to the development of new species of organisms. As Figure 17.35 indicates, stability and the variability that can result from mutations are both important features of the material of heredity.

Causes of Mutations

Many mutations arise as a result of the molecular interactions that take place naturally within the cell. These mutations are known as **spontaneous mutations**. One source of spontaneous mutations is incorrect base pairing by DNA polymerase during the process of DNA replication. The rate of spontaneous mutations varies among organisms and even among different genes within a single cell.

CONCEPT ORGANIZER **The Material of Heredity**



Several factors combine to make it possible for DNA to function as the material of heredity. The molecular structure of DNA stores the information needed to synthesize polypeptides. As this information is expressed, the enzymes and other proteins that cells need to survive and develop are produced. The high level of accuracy in DNA replication ensures that the structure and function of cells and organisms are maintained through countless generations. At the same time, the possibility that DNA can be modified through mutations provides an important source of genetic variation that contributes to the emergence of new types of organisms.

Figure 17.35 Three key factors make it possible for DNA to function as the material of heredity.

While every cell undergoes spontaneous mutations, exposure to certain factors in the environment can increase the rate of mutation. Mutations that are caused by agents outside the cell are said to be **induced**. A substance or event that increases the rate of mutation in an organism is called a **mutagen**. Mutagens fall into two general categories, as described below.

BIO FACT

In mammals, spontaneous mutations are more than twice as likely to arise in the DNA of males than in females.

Physical Mutagens

Over a period of more than 20 years in the early 1900s, American researcher Thomas Morgan observed about 400 visible mutations in the tens of millions of fruit flies with which he worked. In 1926, one of Morgan's students (American Herman Muller) bombarded a population of fruit flies with X rays and produced several hundred mutants in a single day. Muller went on to study the mutagenic properties of X-ray radiation, and was awarded the Nobel prize in 1946.

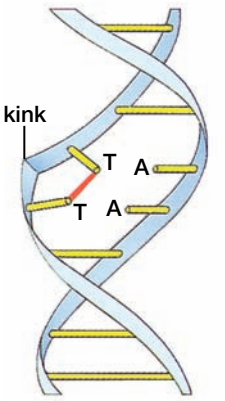


Figure 17.36 Exposure to UV radiation can cause a new bond to form between adjacent thymine bases. The resulting dimer distorts the DNA double helix and interferes with replication.

High-energy radiation, like that from X rays and gamma rays, is known as a **physical mutagen** because it literally tears through a DNA strand, causing random changes in nucleotide sequences. It may break one or both strands of the DNA molecule, causing mutations ranging from the deletion of just a few nucleotides to the loss of large portions of chromosomes. High-energy radiation is the most damaging form of mutagen known.

Ultraviolet (UV) radiation, which is present in ordinary sunshine, has a lower energy level range than X rays but is still a powerful mutagen. It is most likely to affect the pyrimidine bases (C and T) within the DNA molecule. Where two pyrimidines are adjacent to each other, UV radiation can cause a chemical change in the bases that bonds them covalently to form a larger molecule called a dimer. Figure 17.36 shows how the resulting dimer distorts the DNA molecule. The distortion then interferes with DNA replication. UV radiation damage as a result of exposure to the Sun is one of the most common causes of cancer (specifically melanoma, a form of skin cancer) among light-skinned people. The skin pigment melanin helps to absorb UV radiation and offers some protection to the DNA within skin cells. For this reason, people with dark skin have a lower risk of developing cancer as a result of exposure.

BIO FACT

For light-skinned people, a single sunburn can double their risk of developing skin cancer.

A **chemical mutagen** is a molecule that can enter the cell nucleus and induce mutations by reacting chemically with DNA. Chemical mutagens may act by inserting themselves into the DNA molecule in a manner that causes a frameshift mutation. Other chemical mutagens have a structure similar to that of ordinary nucleotides, but with different base-pairing properties. When these molecules are incorporated into a DNA strand, they can cause incorrect nucleotides to be inserted during DNA replication.

Even without exposure to mutagens, each of your genes undergoes thousands of mutations during your lifetime. If these mutations all remained intact, the cumulative effect on your body would be disastrous. Fortunately, the cells of your body produce hundreds of types of enzymes that constantly work to repair damage to your DNA.

Even so, a series of mutations — some spontaneous, some induced by exposure to mutagens — builds up over the life of a cell. While a single mutation often has little effect on a living cell, the accumulation of mutations can result in damage that is more serious. Most cancers are the result of combinations of mutations. Some of these mutations may be inherited, while others may arise because of exposure to mutagens in the environment (many mutagens are **carcinogenic**, or cancer-causing). The fact that mutations accumulate within a cell helps explain why exposure to chemicals that are known to be carcinogenic does not always result in cancer, and why cancer can occur without exposure to any known carcinogens.

In the natural world, mutations occur randomly and are typically harmful to a cell. In the laboratory however, scientists have developed a number of techniques to alter the genetic make-up of living organisms in specific and predictable ways. You will learn about these processes, and about their potential benefits and risks, in the next chapter.

WEB LINK

www.mcgrawhill.ca/links/atlbiology
To view an interactive exploration on mutations, go to the web site above and click on **Electronic Learning Partner**.

SECTION REVIEW

1. Use Table 17.1 on page 587 to answer the following questions.

(a) What amino acids are coded for by each of the following codons?

(i) UUC

(ii) ACU

(iii) GCG

(iv) UAA

(b) What codons could code for the amino acid serine? for the amino acid aspartate?

(c) Write all the possible codon sequences that code for the polypeptide serine-methionine-glutamate

2. Use analogies from another field (such as music or sports) to describe the following features of the genetic code:

(a) redundancy

(b) universality

(c) continuity

3. Complete the following table.

Nucleic Acid	Structure	Function
DNA		
	three-lobed "cloverleaf"	
ribosomal RNA (rRNA)		
		Carries genetic information from DNA to the cell's protein synthesis machinery

4. List the main steps in the transcription process in a eukaryotic cell.

5. A portion of an mRNA molecule has the sequence CCUAGGCUA. What is the sequence of the anti-sense strand of the corresponding DNA molecule?

6. Given that gene expression involves transcribing information from only one strand of the DNA molecule, what might be some biological advantages of double-stranded DNA?

7. Unlike DNA polymerase, RNA polymerase has no proofreading function. Is base-pairing accuracy in transcription as important as in DNA replication? Explain.

8. Arrange the following events in the order in which they occur during protein synthesis:

- binding between two amino acids
- binding of tRNA to mRNA
- binding of tRNA to an amino acid
- binding of mRNA and ribosome

9. Describe the difference between a substitution mutation and a frameshift mutation. Which is likely to cause the greatest damage to a cell?

10. Explain how the action of a transposon can affect the expression of two different genes at once, even when these genes are located on different chromosomes.

11. Older people are usually at a higher risk of developing cancer than young people. Why is this?

12. Many substances known to be mutagenic are, nevertheless, used in manufacturing and in food processing. In a small group, brainstorm some of the social and ethical issues that are associated with the deliberate use of mutagens. Write a short report that explains the circumstances under which you believe the risks of exposure to mutagens can be outweighed by the benefits of using these substances.

Chapter Summary

Briefly explain each of the following points.

- For many years, scientists believed that proteins rather than DNA were the material of heredity. (17.1)
- The bonding of nucleotide base pairs proposed by Watson and Crick accounts both for Chargaff's rule and for the observed structure of the DNA molecule. (17.1)
- The two strands in a DNA molecule are complementary and antiparallel. (17.2)
- The mammalian genome contains a great deal of DNA other than that contained in genes. (17.2)
- The base pairing properties of DNA provide a way to replicate the molecule accurately. (17.2)
- DNA can only be synthesized in one direction, but replication of DNA strands proceeds in two directions at once. (17.2)
- The four different nucleotides found in DNA make up the genetic "words" that code for all 20 different amino acids. (17.3)
- The genetic code is redundant but not ambiguous. (17.3)
- Gene expression involves transcription from DNA to RNA, and translation from RNA to protein. (17.4)
- Three different types of RNA are involved in the main steps of protein synthesis. (17.4)
- All mutations are heritable from one cell to its daughter cells, but only germ cell mutations will be passed from an organism to its offspring. (17.4)
- A number of factors contribute to the severity of a mutation. (17.4)

Language of Biology

Write a sentence using each of the following words or terms. Use any six terms in a concept map to show your understanding of how they are related.

- ribose nucleic acid (ribonucleic acid or RNA)
- deoxyribose nucleic acid (deoxyribonucleic acid or DNA)
- nucleotide
- nitrogenous
- adenine
- guanine
- cytosine
- thymine
- uracil
- transforming principle
- Chargaff's rule
- phage
- directionality
- purine
- pyrimidine
- complementary
- antiparallel
- nucleoid
- plasmid
- histone
- chromatin
- nucleosome
- semi-conservative
- replication origin
- DNA polymerase
- replication forks
- helicases
- primer
- Okazaki fragments
- leading strand
- DNA ligase
- lagging strand
- primase
- telomere
- replication machine
- gene
- genome
- exon
- intron
- genetic code
- gene expression
- transcription
- translation
- codon
- reading frame
- messenger RNA (mRNA)
- RNA polymerase
- sense strand
- anti-sense strand
- transfer RNA (tRNA)
- anticodon
- ribosome
- ribosomal RNA (rRNA)
- mutation
- germ cell mutation
- somatic cell mutation
- silent mutation
- mis-sense mutation
- nonsense mutation
- frameshift mutation
- transposon
- spontaneous mutation
- induced mutation
- mutagen
- physical mutagen
- chemical mutagen

UNDERSTANDING CONCEPTS

1. Identify and describe three experiments that helped pave the way to the discovery of DNA as the hereditary material.
2. What are the components of a single nucleotide?
3. What is Chargaff's rule? Explain how this rule contributed to the discovery of the structure of DNA.
4. Using symbols to represent the four nitrogenous bases, illustrate the molecular structure of both strands of a portion of a DNA molecule. Use each base at least twice.
5. What is the base sequence of the DNA strand that is complementary to a strand with the sequence ACGTTGCTA?
6. Do all your body tissues contain the same amount of DNA? Explain.

7. The replication of DNA is said to be semi-conservative. What does this mean?
8. What is the function of primase in DNA replication?
9. Briefly compare the roles played by the following:
   (a) leading strand and lagging strand
   (b) pyrimidine and purine
   (c) DNA polymerase and DNA ligase
10. Refer to Chapter 14 to review the cell life cycle. Does DNA replication occur during mitosis or meiosis, or both?
11. Fill in the following table to show the molecules and enzymes involved in DNA replication.

Molecule or enzyme	Function	Involved in leading strand or lagging strand synthesis, or both
primer		
DNA ligase		
DNA polymerase		
Okazaki fragments		
helicase		

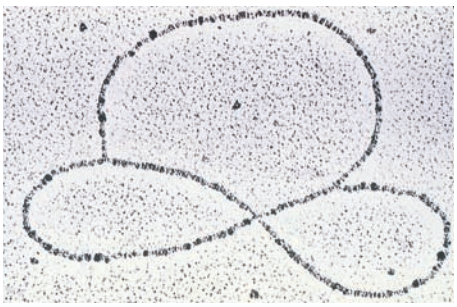
12. In what ways is the one gene-one enzyme definition of a gene inaccurate?
13. During the process of cell division in a human cell, the chromosomes are visible under a microscope as short, thick strands. Describe how a single molecule of DNA is organized within one of these chromosomes.
14. A gene coding for the same enzyme is found in both earthworms and rats. Which gene is likely to have a greater total length? Explain.
15. How is it possible for information on DNA that is confined to the nucleus of a eukaryotic cell to be expressed as protein products outside the nucleus?
16. Use the genetic code table on page 000 to identify the amino acids coded for by the following codons: AGC, GUU, UAU, AUG.
17. Name three features of the genetic code and explain why they are important.
18. Define the term "sense strand." What is its counterpart called, and why?
19. Draw a diagram that illustrates the main steps in the elongation cycle of translation. Label and describe the role of each of the following nucleic acids:
   (a) rRNA
   (b) tRNA
   (c) mRNA
20. Distinguish between somatic cell mutations and germ cell mutations.
21. Distinguish between a substitution mutation and an insertion mutation. Which is likely to cause greater damage?

INQUIRY

22. Provide evidence to support the conclusion that DNA is, in fact, the genetic material.
23. As part of your research you isolate the DNA from a particular strain of virus. Your analysis indicates the following base composition:

base	A	C	G	T
concentration (%)	36	24	18	22

   (a) What can you conclude about the DNA of this virus?
24. A biochemist develops a chemical that interferes with histone-histone bonding. What effect would you expect this chemical to have on the following:
   (a) the organization of DNA within a prokaryotic cell?
   (b) the organization of DNA within a eukaryotic cell?
25. Examine the photograph at right, taken by an electron microscope.
   (a) What events and processes are taking place in this image?
   (b) Make an illustration showing what you would expect to see if a second photograph were taken a short time after this one.



26. Carbon is found both in DNA and in the protein coat of a virus. Could Hershey and Chase have used radioactively labeled carbon in their experiments to determine the material of heredity? Explain.

27. A substance is capable of entering the nucleus of a cell and inserting an additional C nucleotide at random places in a DNA strand.

(a) Would this substance be considered a chemical mutagen or a physical mutagen?

(b) What kind of mutation would result?

(c) Under what circumstances would this mutation **not** have any effect on the functioning of the cell?

COMMUNICATING

28. Create a table that contrasts the structure and function of DNA and RNA.

29. Develop a flowchart that illustrates how the discoveries of the following researchers contributed to an understanding of the role of DNA in heredity: Hershey and Chase; Chargaff; Franklin; Watson and Crick; Meselson and Stahl.

30. DNA is sometimes said to be like a language. In a short essay, explain the ways in which this comparison is valid.

31. Create a set of flash cards that could be used to help others study the various types of RNA and their roles in transcription and translation.

32. Illustrate the basic structure of a tRNA molecule and label it. Write a caption to go with your illustration that explains the function of tRNA.

33. Gene regulation is an important part of the growth and development of living organisms. Explain this statement in a short essay.

34. In a short essay, explain what is meant by the statement "the genome of any organism is far from stable." What evidence can you offer to support this statement? What evidence can you offer to refute it?

35. Your cousin tells you that "whether or not you get cancer from smoking is just a matter of luck." List a series of points you would make in response. Will your cousin be able to identify any weak points in your argument?

MAKING CONNECTIONS

36. How do Mendel's factors relate to today's definition of a gene?

37. Only a small portion of the mammalian genome is made up of genes. The rest was originally referred to as "junk DNA." How do popular terms such as this help or hinder society's understanding of the need for scientific procedures and ongoing research? What are some of the potential advantages and disadvantages to an organism of having large quantities of non-gene DNA?

38. A certain planarian has a genome 6000 times larger than that of a particular yeast cell.

(a) What conclusions, if any, could you draw about the relative complexities of the two organisms?

(b) What practical applications could there be from a study that compared the genomes of the two organisms?

39. A molecular biologist creates a form of RNA polymerase that has the same proofreading capability as DNA polymerase. Describe what you think some of the advantages and disadvantages of this form of RNA polymerase could be

(a) for researchers in a laboratory setting

(b) for living organisms

40. The study of the structure of genomes, including the nucleotide sequence of individual genes, is often referred to as "genomics." Many researchers claim that genomics is not nearly as significant as "proteomics," which is the study of protein structure and function. Based on the information in this chapter, which field would you argue holds the greatest promise for advances in medicine and in understanding human development?