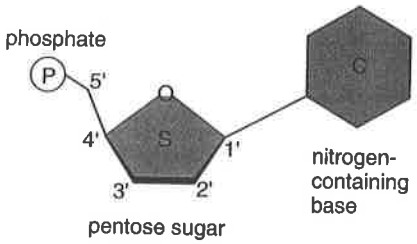
2.8 Nucleic Acids

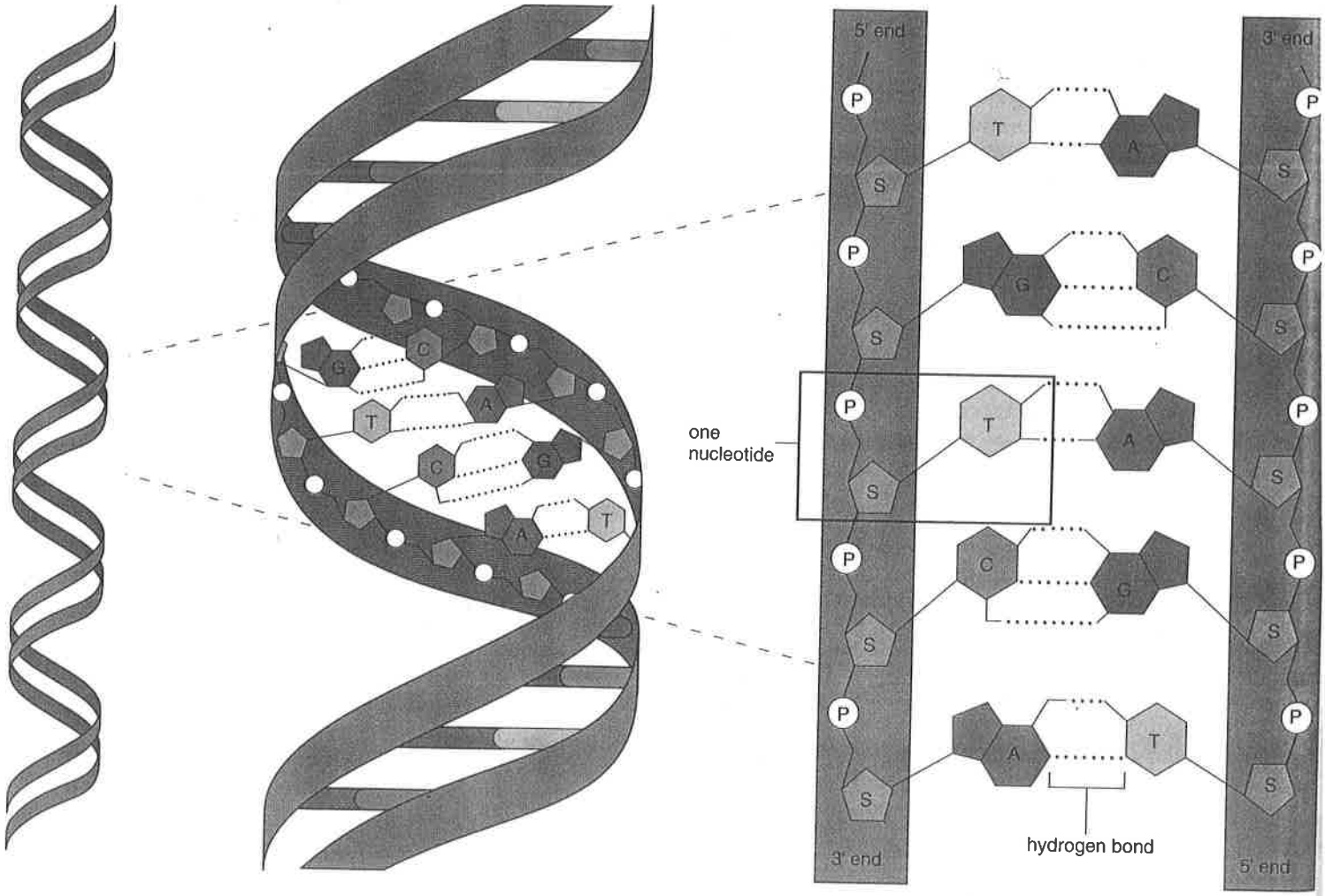
Nucleic acids, such as **DNA (deoxyribonucleic acid)** and **RNA (ribonucleic acid),** are huge polymers of nucleotides. Every **nucleotide** is a molecular complex of three types of subunit molecules: phosphate (phosphoric acid), a pentose sugar, and a nitrogen-containing base:



DNA makes up the genes and stores information regardi its own replication and the order in which amino acids are be joined to form a protein. RNA is an intermediary in t process of protein synthesis, conveying information frc DNA regarding the amino acid sequence in a protein.

The nucleotides in DNA contain the sugar deoxyribos and in RNA they contain the sugar ribose; this difference a counts for their respective names (Table 2.3). As indicated Figure 2.28, there are four different types of bases in DN. A = **adenine,** T = **thymine,** G = **guanine,** and C = **cytosin** The base can have two rings (adenine or guanine), or or ring (thymine or cytosine) These structures are called bas because their presence raises the pH of a solution. In RN the base **uracil** replaces the base thymine.

Although the sequence can vary between molecule any particular DNA or RNA has a definite sequence. The nu cleotides form a linear molecule called a strand i



a. **DNA double helix** b. **Complementary base pairing** c. **Ladder configuration**

Figure 2.28 Overview of DNA structure.
a. Double helix. **b.** Complementary base pairing between strands. **c.** Ladder configuration. Notice that the uprights are composed of phosphate and sugar molecules and that the rungs are complementary paired bases.

Replication of DNA

Exact copies of DNA are produced during the replication process. The double-stranded structure of DNA aids replication because each strand can serve as a template for the formation of a complementary strand. A **template** is most often a mold used to produce a shape opposite to itself. In this case, each old (parental) strand is a template for each new (daughter) strand.

Replication has the following steps (Fig. 25.3):

1. *Unwinding.* The two strands that make up DNA unwind and "unzip" (i.e., the weak hydrogen bonds between the paired bases break). A special enzyme called helicase causes the molecule to unwind.
2. *Complementary base pairing.* New complementary nucleotides, always present in the nucleus, fit into place by the process of complementary base pairing.
3. *Joining.* The complementary nucleotides join to form new strands. This step is carried out by an enzyme called DNA **polymerase.**

Because each old strand has produced a new strand through complementary base pairing, there are now two DNA helices identical to each other and to the original molecule. DNA replication is termed *semiconservative* because each new double helix has one old strand and one new strand. In other words, one of the parental strands is conserved, or present, in each new double helix.

DNA replication must occur before a cell can divide. Cancer, which is characterized by rapidly dividing cells, is treated with chemotherapeutic drugs that stop replication and therefore cell division. Some chemotherapeutic drugs are analogs that have a similar, but not identical, structure to the four nucleotides in DNA. When these are mistakenly used by the cancer cells to synthesize DNA, replication stops and the cells die off.

During DNA replication, DNA unwinds and unzips, and new strands that are complementary to the original strands form.

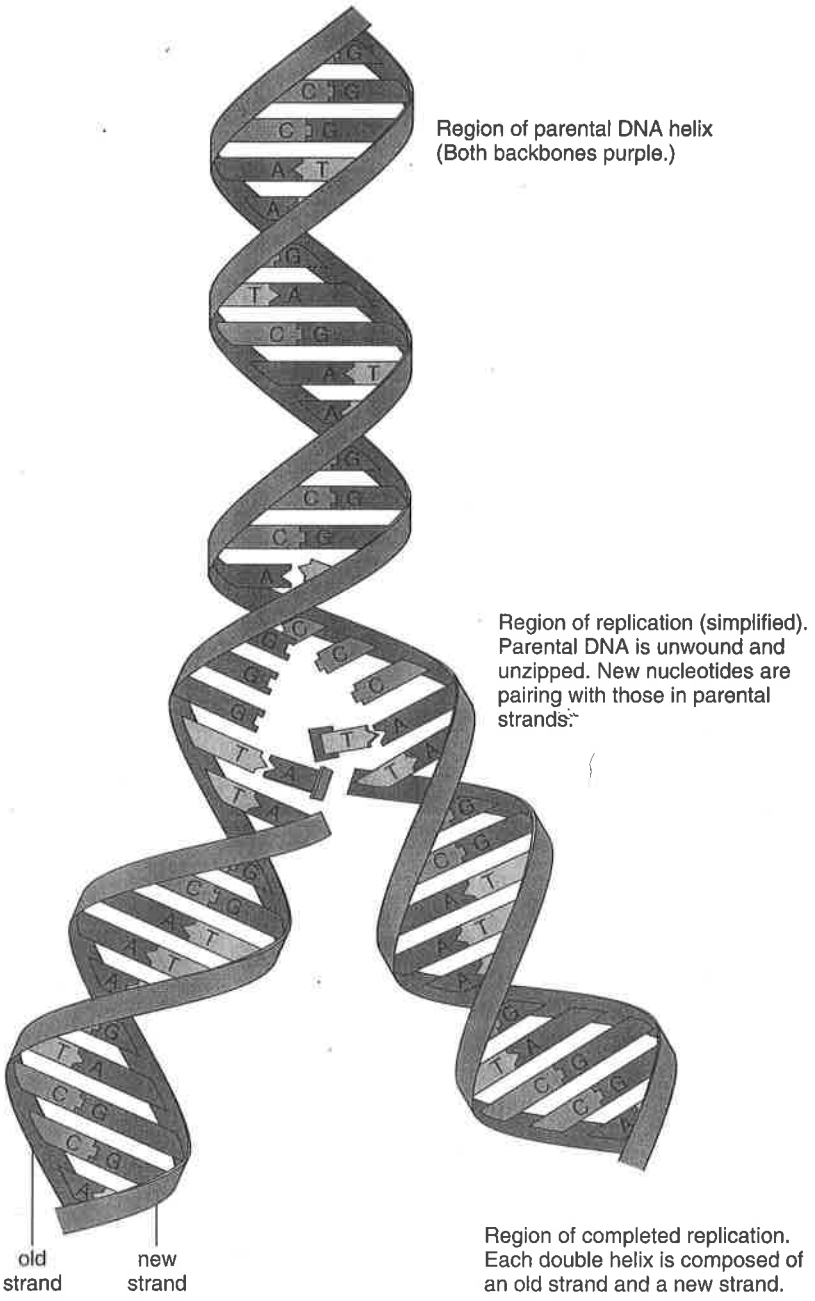


Figure 25.3 DNA replication.
After the DNA molecule unwinds, each old strand serves as a template for the formation of the new strand. Complementary nucleotides available in the cell pair with those of the old strand and then are joined together to form a daughter strand. After replication is complete, there are two daughter strands. Replication is called semiconservative because each new double helix is composed of an old (parental) strand and a new (daughter) strand. Each molecule has the same sequence of base pairs as the parent molecule had before unwinding occurred.

Transcription

During transcription, a segment of the DNA helix unwinds and unzips, and complementary RNA nucleotides from an RNA nucleotide pool in the nucleus pair with the DNA nucleotides of one strand. The RNA nucleotides are joined by an enzyme called **RNA polymerase,** and an mRNA molecule results (Fig. 25.7). Therefore, when mRNA forms, it has a sequence of bases complementary to DNA; wherever A, T, G, or C is present in the DNA template, U, A, C, or G is incorporated into the mRNA molecule. In this way, the code is transcribed, or copied. Now mRNA has a sequence of codons, three bases that are complementary to the DNA triplet code.

Following transcription, mRNA has a sequence of bases complementary to one of the DNA strands. Now, mRNA contains codons which are complementary to the DNA triplet code.

Processing of mRNA

Most genes in humans are interrupted by segments of DNA that are not part of the gene. These portions are called *introns* because they are intragene segments. The other portions of the gene are called *exons* because they are ultimately expressed. They result in a protein product.

When DNA is transcribed, the mRNA contains bases that are complementary to both exons and introns, but before the mRNA exits the nucleus, it is *processed.* During processing, the nucleotides complementary to the introns are spliced out by ribozymes. **Ribozymes** are organic catalysts composed of RNA and not protein. There has been much speculation about the role of introns. It is possible that they allow crossing-over within a gene during meiosis. It is also possible that introns divide a gene into domains that can be joined in different combinations to give novel genes and protein products, facilitating the evolution of new species.

Processing occurs in the nucleus. The newly formed mRNA is called the primary mRNA molecule, and the processed mRNA is called the mature mRNA molecule. The mature mRNA molecule passes from the cell nucleus into the cytoplasm. There it becomes associated with ribosomes.

In humans, the primary mRNA molecule is processed; introns are removed, so that the mature mRNA molecule contains only exons. Mature RNA leaves the nucleus and becomes associated with ribosomes.

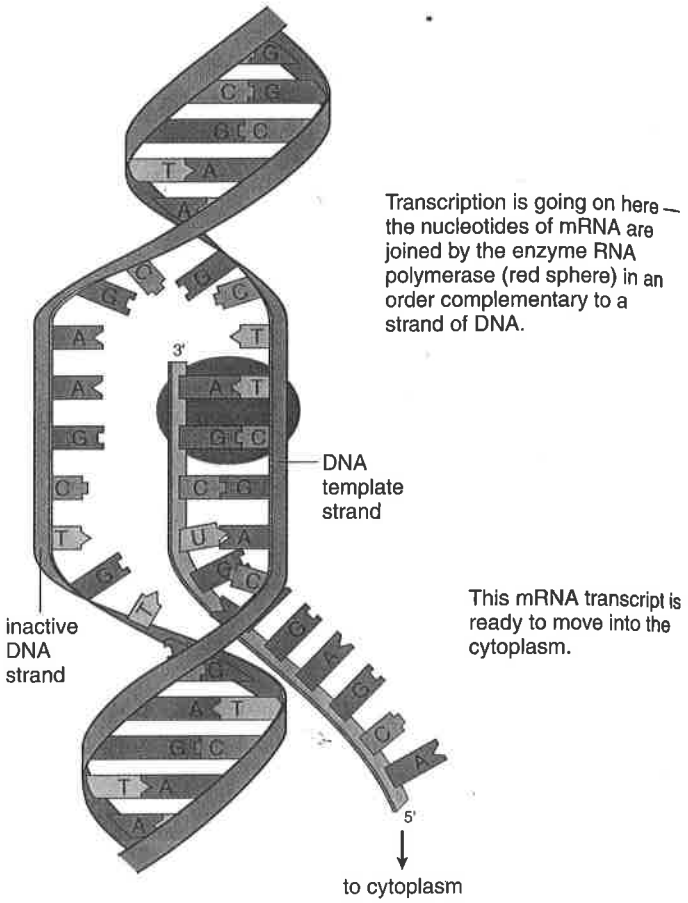


Figure 25.7 Transcription.
During transcription, complementary RNA is made from a DNA template. A portion of DNA unwinds and unzips at the point of attachment of RNA polymerase. A strand of mRNA is produced when complementary bases join in the order dictated by the sequence of bases in DNA. Transcription occurs in the nucleus and the mRNA passes out of the nucleus to enter the cytoplasm.

Translation

Translation, which takes place in the cytoplasm of eukaryotic cells, is the second step by which gene expression leads to protein synthesis. During translation, the sequence of codons in mRNA specifies the order of amino acids in a polypeptide. This is called translation because the sequence of DNA and then RNA bases is translated into a sequence of amino acids. Translation requires several enzymes and two other types of RNA: transfer RNA and ribosomal RNA.

From DNA to RNA to Protein

DNA not only serves as a template for its own replication, it is also a template for RNA formation. **Transcription** is making an RNA molecule that is complementary to a portion of DNA. Following transcription, RNA moves into the cytoplasm. There are micrographs showing radioactively labeled RNA moving through a nuclear pore to the cytoplasm, where protein synthesis occurs. *Messenger RNA* (*m*RNA) carries information for the synthesis of a polypeptide. During **translation,** this information is used to sequence the amino acids of a polypeptide (Fig. 25.5).

In ordinary speech, transcription means making a close copy of a document, and translation means putting the document in an entirely different language. In genetics, transcription is making a strand of RNA with the same base sequence as DNA; translation is going from a sequence of nucleotides (bases) to a sequence of amino acids.

The Genetic Code

DNA has a particular sequence of bases, and a polypeptide has a particular sequence of amino acids. This suggests that DNA contains coded information. Can four bases provide enough combinations to code for 20 amino acids? If the code were a doublet (any two bases stand for one amino acid), it would not be possible to code for 20 amino acids, but if the code were a triplet, then the four bases could supply 64 different triplets, far more than needed to code for 20 different amino acids. It should come as no surprise, then, to learn that the code is a **triplet code.**

To crack the code, a cell-free experiment was done: artificial RNA was added to a medium containing bacterial ribosomes and a mixture of amino acids. Comparison of the bases in the RNA with the resulting polypeptide allowed investigators to decipher the code. Each three-letter unit of an mRNA molecule is called a **codon.** All 64 mRNA codons have been determined (Fig. 25.6). Sixty-one triplets correspond to a particular amino acid; the remaining three are stop codons, which signal polypeptide termination. The one codon that stands for the amino acid methionine is also a start codon signaling polypeptide initiation.

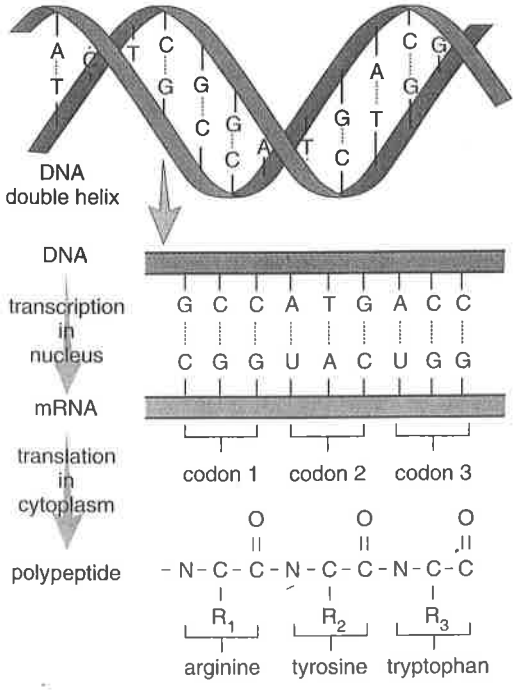
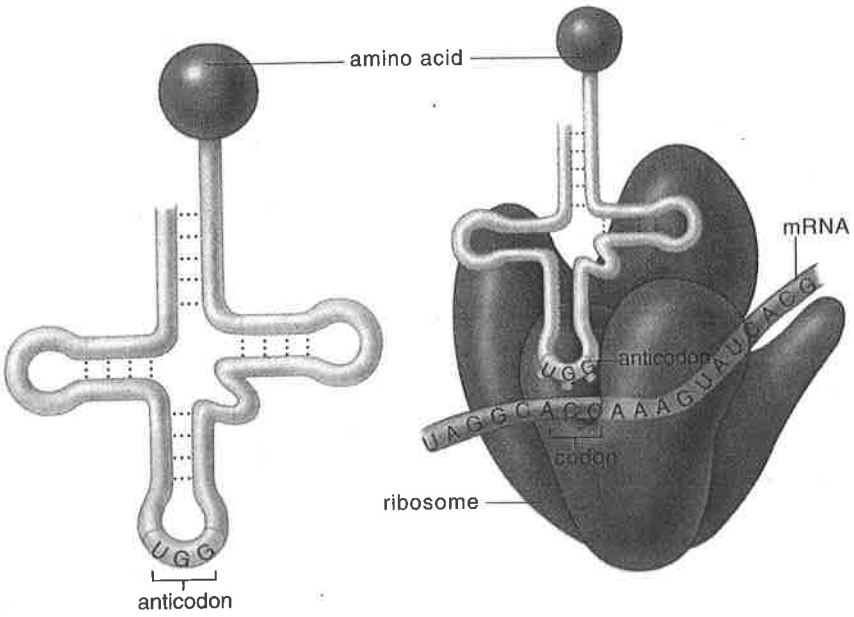


Figure 25.5 Overview of gene expression.
Transcription occurs in the nucleus when DNA acts as a template for mRNA synthesis. Translation occurs in the cytoplasm when the sequence of the mRNA codons determines the sequence of the amino acids in a polypeptide.

First Base	Second Base				Third Base
	U	C	A	G	
U	UUU phenylalanine	UCU serine	UAU tyrosine	UGU cysteine	U
	UUC phenylalanine	UCC serine	UAC tyrosine	UGC cysteine	C
	UUA leucine	UCA serine	UAA *stop*	UGA *stop*	A
	UUG leucine	UCG serine	UAG *stop*	UGG tryptophan	G
C	CUU leucine	CCU proline	CAU histidine	CGU arginine	U
	CUC leucine	CCC proline	CAC histidine	CGC arginine	C
	CUA leucine	CCA proline	CAA glutamine	CGA arginine	A
	CUG leucine	CCG proline	CAG glutamine	CGG arginine	G
A	AUU isoleucine	ACU threonine	AAU asparagine	AGU serine	U
	AUC isoleucine	ACC threonine	AAC asparagine	AGC serine	C
	AUA isoleucine	ACA threonine	AAA lysine	AGA arginine	A
	AUG (*start*) methionine	ACG threonine	AAG lysine	AGG arginine	G
G	GUU valine	GCU alanine	GAU aspartate	GGU glycine	U
	GUC valine	GCC alanine	GAC aspartate	GGC glycine	C
	GUA valine	GCA alanine	GAA glutamate	GGA glycine	A
	GUG valine	GCG alanine	GAG glutamate	GGG glycine	G

Figure 25.6 Messenger RNA codons.
Notice that in this chart, each of the codons (blue squares) is composed of three letters representing the first base, second base, and third base. For example, find the blue square where C for the first base and A for the second base intersect. You will see that U, C, A, or G can be the third base. The three bases CAU and CAC are codons for histidine; the three bases CAA and CAG are codons for glutamine.



a. tRNA–amino acid b. tRNA–amino acid at ribosome

Figure 25.8 Anticodon-codon base pairing.
a. tRNA molecules have an amino acid attached to one end and an anticodon at the other end. **b.** The anticodon of a tRNA molecule is complementary to a codon. The pairing between codon and anticodon ensures that the sequence of amino acids in a polypeptide is that directed originally by DNA. If the codon is ACC, the anticodon is UGG, and the amino acid is threonine.

Transfer RNA

Transfer RNA (tRNA) molecules bring amino acids to the ribosomes. Each is a single-stranded nucleic acid that doubles back on itself to create regions where complementary bases are hydrogen bonded to one another. There is at least one tRNA molecule for each of the twenty amino acids found in proteins. The amino acid binds to one end of the molecule (Fig. 25.8*a*). Attachment requires ATP energy, and the resulting bond is a high-energy bond represented by a wavy line. The entire complex is designated as tRNA–amino acid. One area of active research is to determine how the correct amino acid becomes attached to the correct tRNA molecule. Somehow an enzyme called *tRNA synthetase* recognizes which amino acid should be joined to which tRNA molecule.

At the other end of each tRNA molecule, there is a specific **anticodon,** a group of three bases that is complementary to an mRNA codon (Fig. 25.8*b*). A tRNA molecule comes to the ribosome, where its anticodon pairs with an mRNA codon. Let us consider an example: If the codon is ACC, what is the anticodon, and what amino acid will be attached to the tRNA molecule? Inspection of Figure 25.8 allows us to determine this:

Codon	Anticodon	Amino Acid
ACC	UGG	Threonine

The order of the codons of the mRNA determines the order that tRNA–amino acids come to a ribosome, and therefore the final sequence of amino acids in a polypeptide.

Ribosomal RNA

Ribosomal RNA (rRNA) is called structural RNA because it is found in the **ribosomes,** small structural bodies. Ribosomal RNA is produced in a nucleolus within the nucleus. There it joins with proteins manufactured in the cytoplasm. Ribosomal subunits then migrate to the cytoplasm, where they join just as protein synthesis begins. The small subunit contains one rRNA molecule and many different types of proteins, and the large subunit contains two rRNA molecules and also many different types of proteins. Among these proteins is the enzyme that joins amino acids together by means of a peptide bond.

During translation, the sequence of bases in mRNA determines the order that tRNA amino acids come to a ribosome and therefore the order of amino acids in a particular polypeptide.

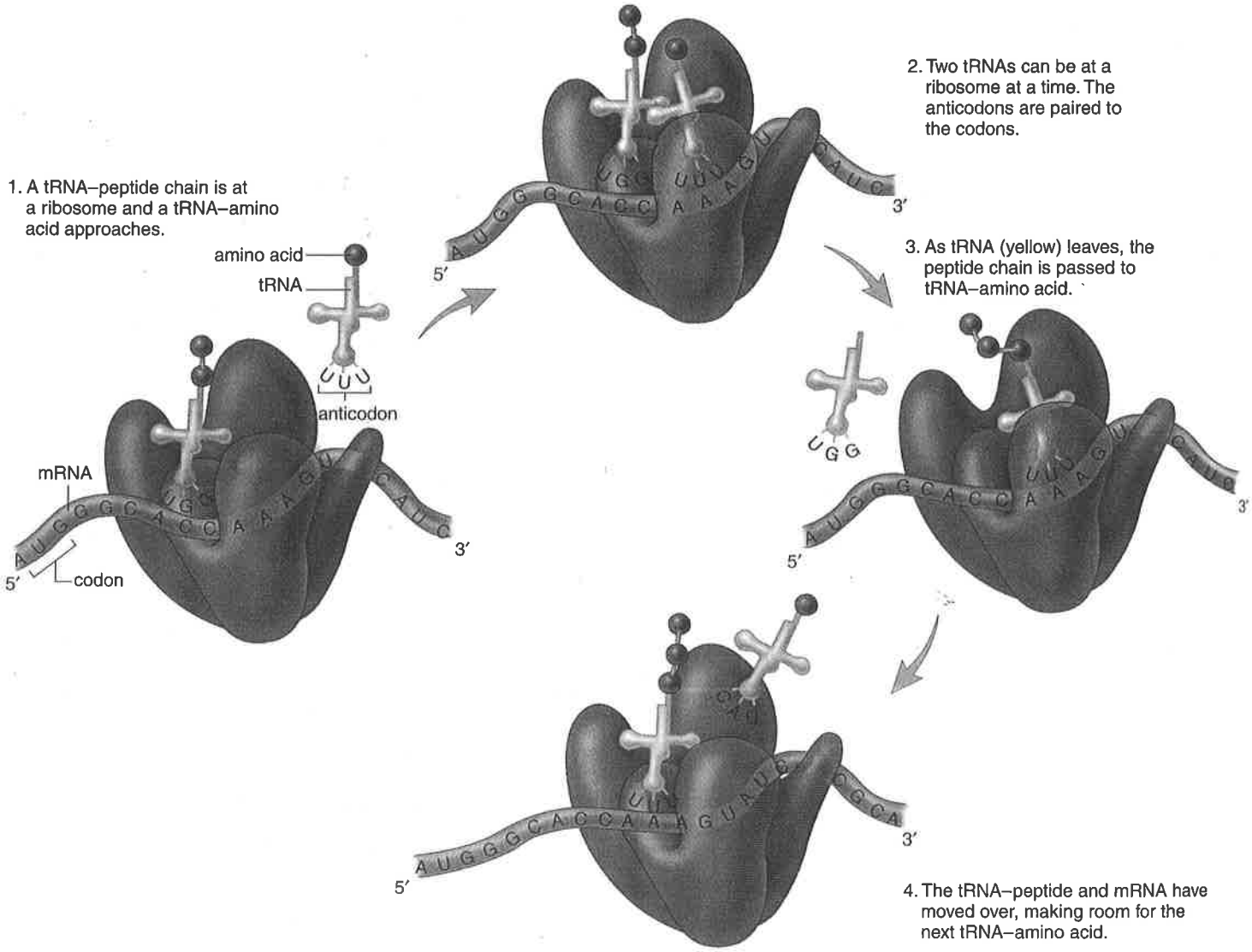


Figure 25.9 Translation.
Transfer RNA (tRNA)–amino acid molecules arrive at the ribosome, and the sequence of messenger RNA (mRNA) codons dictates the order in which amino acids become incorporated into a polypeptide.

Steps of Translation

Polypeptide synthesis requires three steps: initiation, elongation, and termination.

1. During *initiation*, a small ribosomal subunit attaches to the mRNA in the vicinity of the start codon (AUG). The first, or initiator, tRNA pairs with this codon. Then a large ribosomal subunit joins to the small subunit.
2. During *elongation*, the polypeptide lengthens one amino acid at a time (Fig. 25.9). A ribosome is large enough to accommodate two tRNA molecules: the incoming tRNA molecule and the outgoing tRNA molecule. The incoming tRNA–amino acid complex receives the peptide from the outgoing tRNA. The ribosome then moves laterally so that the next mRNA codon is available to receive an incoming tRNA–amino acid complex. In this manner, the peptide grows and the primary structure of a polypeptide comes about. (The secondary and tertiary structures of a polypeptide appear after termination, as the amino acids interact with one another. Some proteins consist of one polypeptide and some have more than one polypeptide chain.)
3. Then *termination* of synthesis occurs at a stop codon on the mRNA. The release factor which binds to this site enzymatically cleaves the polypeptide from the last tRNA. The ribosome dissociates into its two subunits and falls off the mRNA molecule.

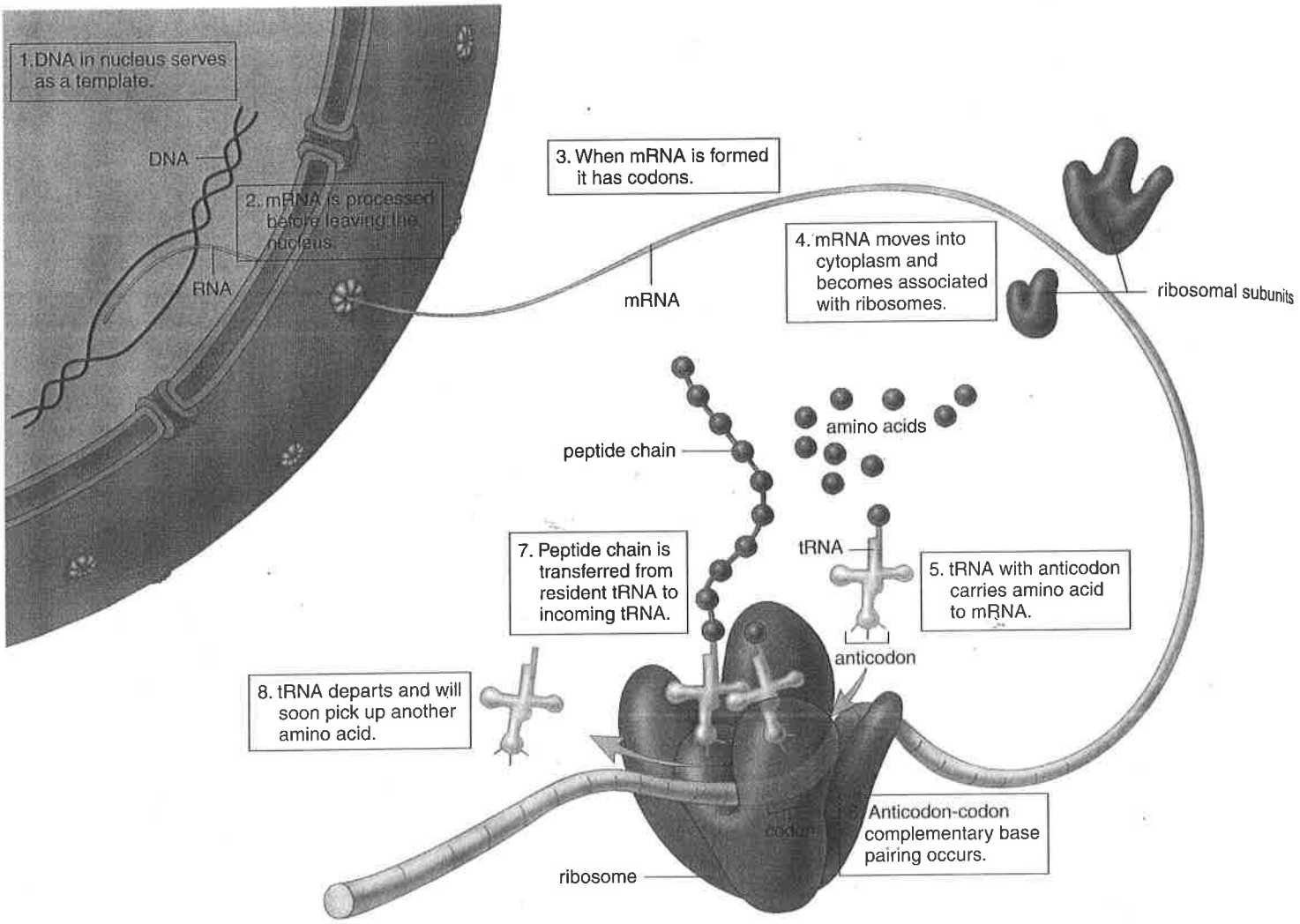


Figure 25.11 Gene expression.
Gene expression leads to the formation of a product, most often a protein. The two steps required for gene expression are transcription, which occurs in the nucleus, and translation, which occurs in the cytoplasm at the ribosomes.

Review of Gene Expression

DNA in the nucleus contains a *triplet code.* Each group of three bases stands for a specific amino acid (Figure 25.11 and Table 25.2). During transcription, a segment of a DNA strand serves as a template for the formation of messenger RNA (mRNA). The bases in mRNA are complementary to those in DNA; every three bases is a *codon* for a certain amino acid. mRNA is processed before it leaves the nucleus, during which time the introns are removed. mRNA carries a sequence of codons to the *ribosomes,* which are composed of rRNA and proteins. A transfer RNA (tRNA) bond to a particular amino acid, has an *anticodon* that pairs complementarily to a codon in mRNA. During translation, tRNAs and their attached amino acids arrive at the ribosomes, where the linear sequence of codons of mRNA determines the order amino acids become incorporated into a protein.

Name of Molecule	Special Significance	Definition
DNA	Genetic information	Sequence of DNA bases
mRNA	Codons	Sequence of three RNA bases complementary to DNA
tRNA	Anticodon	Sequence of three RNA bases complementary to codon
rRNA	Ribosome	Site of protein synthesis
Amino acid	Building block for protein	Transported to ribosome by tRNA
Protein	Enzyme, structural protein, or secretory product	Amino acids joined in a predetermined order