Molecular

Genetics

- **DNA The Genetic Material**
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DNA; The Genetic Material

Twentieth-century biologists realized that a molecule that serves as the genetic material must have certain characteristics to explain the proper-ties of life: First, the genetic material must be able to code for the sequence of amino acids in proteins and control protein synthesis. Second, it must be able to replicate itself prior to cell division. Third, the genetic material must be in the nucleus of eukaryotic cells. Fourth, it must be able to change over time to account for evolutionary change. Only one molecule, DNA (de-oxyribonucleic acid), fulfills all of these requirements.

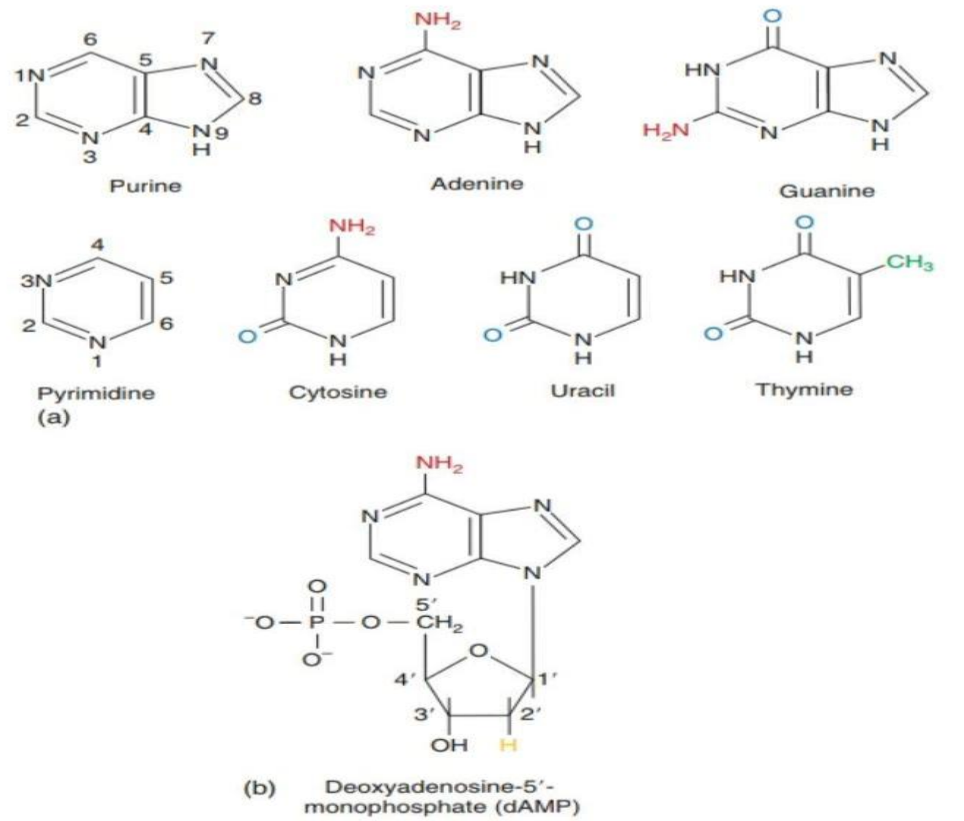


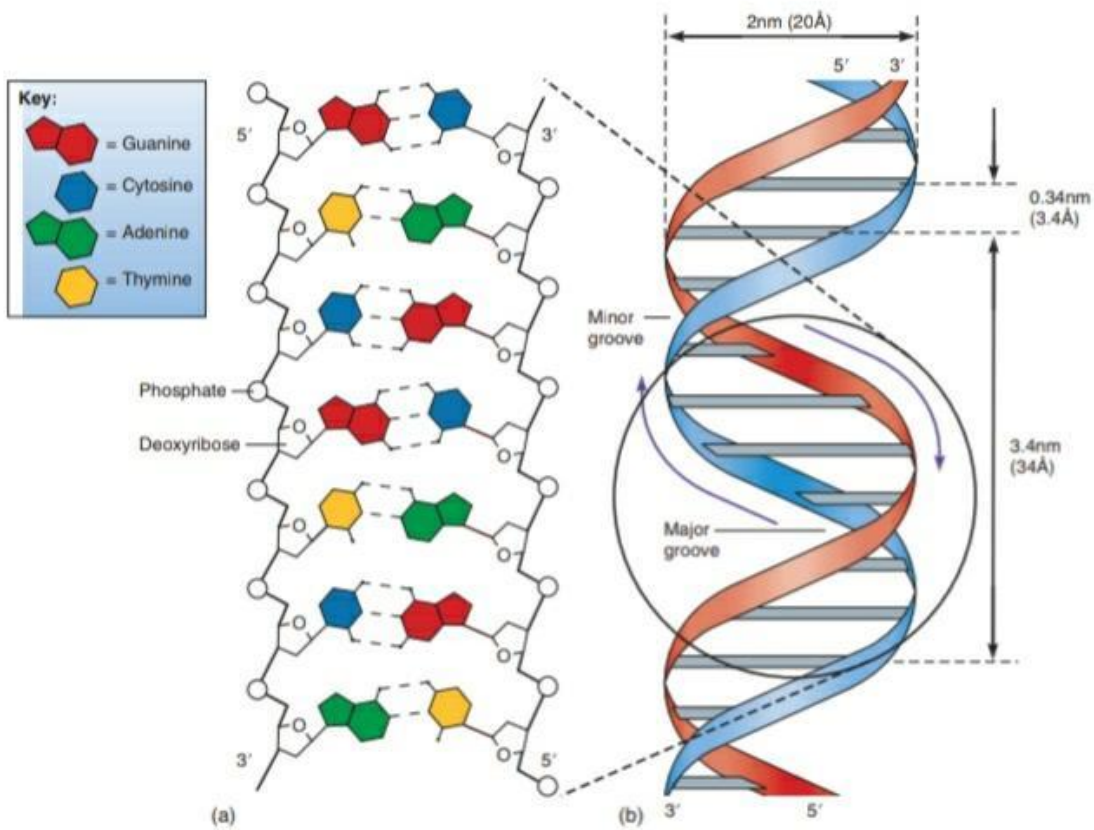
FIGURE 3.8

Components of Nucleic Acids. (*a*) The nitrogenous bases in DNA and RNA. (*b*) Nucleotides form by attaching a nitrogenous base to the 1' carbon of a pentose sugar and attaching a phosphoric acid to the 5' carbon of the sugar. (Carbons of the sugar are numbered with primes to distinguish them from the carbons of the nitrogenous base.) The sugar in DNA is deoxyribose, and the sugar in RNA is ribose. In ribose, a hydroxyl group (−OH) would replace the hydrogen shaded yellow.

<u>The Double Helix Model of DNA:</u>

Two kinds of molecules participate in protein synthesis. Both are based on a similar building block, the nucleotide, giving them their name—nucleic acids. One of these molecules, deoxyribonucleic acid or DNA, is the genetic material, and the other, ribonucleic acid or RNA, is produced in the nucleus and moves to the cytoplasm, where it participates in protein synthesis. The study of how the information stored in DNA codes for RNA and protein is molecular genetics.

DNA and RNA are large molecules made up of sub-units called nucleotides (figure 3.8). A nucleotide consists of a nitrogen-containing organic base, either in the form of a double ring (purine) or a single ring (pyrimidine). Nucleotides also contain a pentose (five-carbon) sugar and a phosphate (-PO4)group.



Figuure 3.9:Structure of DNA. (a) Nucleotides of one strand of nucleic acid join by linking the phosphate of one nucleotide to the 3' carbon of an adjacent nucleotide. Dashed lines between the nitrogenous bases indicate hydrogen bonds. Three hydrogen bonds are between cytosine and guanine, and two are between thymine and adenine. The antiparallel orientation of the two strands is indicated by using the 3' and 5' carbons at the ends of each strand. (b) Three-dimensional representation of DNA. The antiparallel nature of the strands is indicated by the curved arrows.

DNA and RNA molecules, however, differ in several ways. Both DNA and RNA contain the purine bases adenine and guanine, and the pyrimidine base cytosine. The second pyrimidine in DNA, however, is thymine, whereas in RNA it is uracil. A second difference between DNA and RNA involves the sugar present in the nucleotides. The pentose of DNA is deoxyribose, and in RNA it is ribose. A third important difference between DNA and RNA is that DNA is a double-stranded molecule and RNA is single stranded, although it may fold back on itself and coil.

The key to understanding the function of DNA is knowing how nucleotides link into a three-dimensional structure. The DNA molecule is ladder like, with the rails of the ladder consisting of alternating sugar-phosphate groups (figure 3.9a). The phosphate of a nucleotide attaches at the fifth (5') carbon of deoxyribose. Adjacent nucleotides attach to one another by a covalent bond between the phosphate of one nucleotide and the third (3')carbon of deoxyribose. The pairing of nitrogenous bases between strands holds the two strands together. Adenine (a purine) is hydrogen bonded to its complement, thymine (a pyrimidine), and guanine (a purine) is hydrogen bonded to its complement, cytosine (a pyrimidine) (figure 3.9a). Each strand of DNA is oriented such that the 3' carbons of deoxyribose in one strand are oriented in the opposite directions from the 3' carbons in the other strand.The strands’ terminal phosphates are, therefore, at opposite ends,and the DNA molecule is thus said to be antiparallel (Gr. anti,against +para, beside+ allelon, of one another). The entire molecule is twisted into a right-handed helix, with one complete spiral every 10 base pairs (figure 3.9b).

DNA Replication In Eukaryotes

During DNA replication, each DNA strand is a template for a new strand. The pairing requirements between purine and pyrimidine bases dictate the positioning of nucleotides in a new strand(figure 3.10). Thus, each new DNA molecule contains one strand from the old DNA molecule and one newly synthesized strand.Because half of the old molecule is conserved in the new molecule, DNA replication is said to be semiconservative.

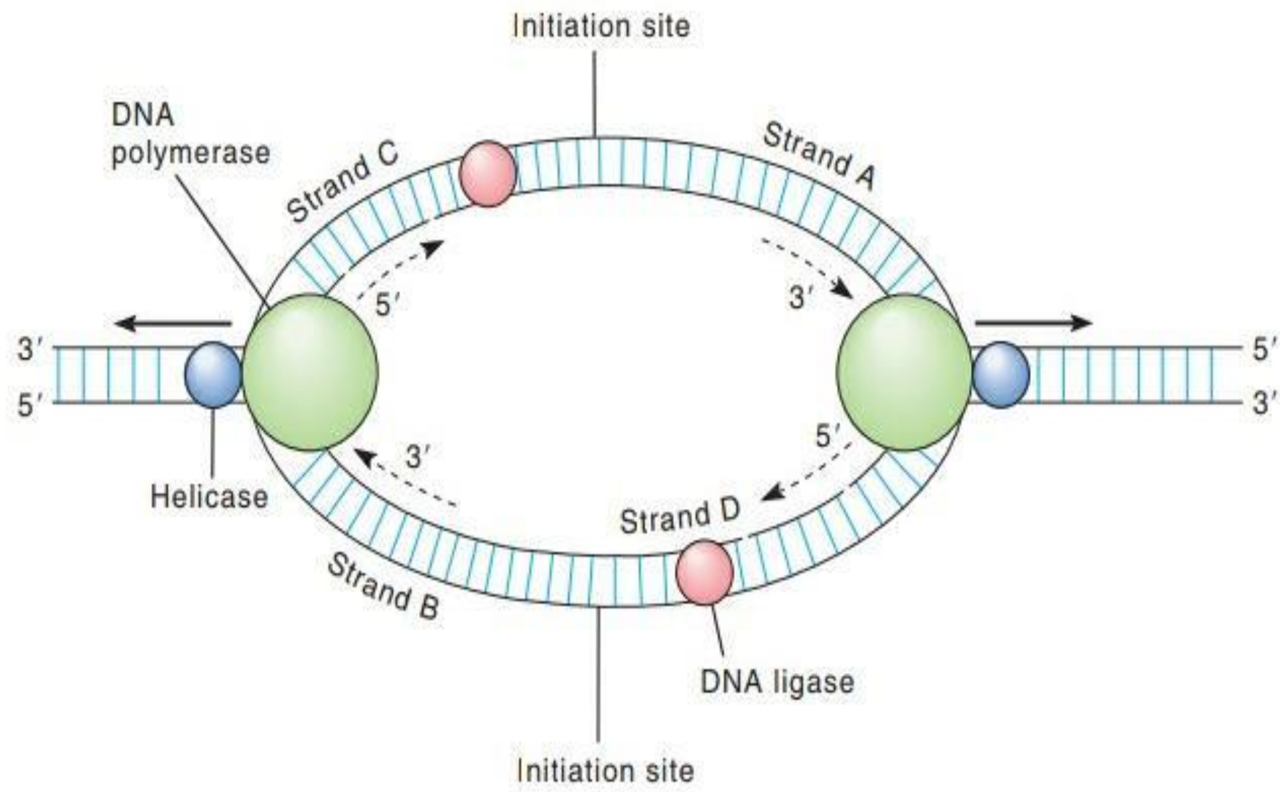


Figure 3.10

DNA Replication. Replication begins simultaneously at many initiation sites along the length of a chromosome. Notice that synthesis of strands A and B is continuous from the initiation site, and that synthesis of strands C and D is discontinuous from the initiation site. Strands C and D are produced in fragments because DNA polymerase can only produce new DNA strands in the 5' to 3' direction. Helicase enzymes aid in the untwisting of the double helix during replication, and DNA ligase enzymes join DNA fragments produced during replication. Replication is bidirectional from the initiation site. Dashed arrows indicate the direction of DNA elongation. Solid arrows indicate the bidirectional progress of replication.

Genes In Action

A gene can be defined as a sequence of bases in DNA that codes for the synthesis of one polypeptide, and genes must somehow transmit their information from the nucleus to the cytoplasm, where protein synthesis occurs. The synthesis of an RNA molecule from DNA is called transcription (L. trans, across + scriba, to write),and the formation of a protein from RNA at the ribosome is called translation (L. trans, to transfer + latere, to remain hidden).

Three Major Kinds of RNA

Each of the three major kinds of RNA has a specific role in protein synthesis and is produced in the nucleus from DNA. Messenger RNA (mRNA) is a linear strand that carries a set of genetic instructions for synthesizing proteins to the cytoplasm. Transfe RNA (tRNA) picks up amino acids in the cytoplasm, carries them to ribosomes, and helps position them for incorporation into a polypeptide. Ribosomal RNA (rRNA), along with proteins,makes up ribosomes.

The Genetic Code:

DNA must code for the 20 different amino acids found in all organisms. The information-carrying capabilities of DNA reside in the sequence of nitrogenous bases. The genetic code is a sequence of three bases—a triplet code. Figure 3.11 shows the genetic cod as reflected in the mRNA that will be produced from DNA. Each three-base combination is a codon.More

Second position

First position	U	C	A	G	Third position
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA STOP	UGA STOP	A
	UUG Leu	UCG Ser	UAG STOP	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gin	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gin	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

Ala	= Alanine	Leu	= Leucine
Arg	= Arginine	Lys	= Lysine
Asn	= Aparagine	Met	= Methionine
Asp	= Aspartic acid	Phe	= Phenylalanine
Cys	= Cysteine	Pro	= Proline
Gin	= Glutamine	Ser	= Serine
Glu	= Glutamic acid	Thr	= Threonine
Gly	= Glycine	Trp	= Tryptophan
His	= Histidine	Tyr	= Tyrosine
Ile	= Isoleucine	Val	= Valine

FIGURE 3.11
Genetic Code. Sixty-four messenger RNA codons are shown here. The first base of the triplet is on the left side of the figure, the second base is at the top, and the third base is on the right side. The abbreviations for amino acids are also shown. In addition to coding for the amino acid methionine, the AUG codon is the initiator codon. Three codons—UAA, UAG, and UGA—do not code for an amino acid but act as a signal to stop protein synthesis.

than one codon can specify the same amino acid because there are 64 possible codons,but only 20 amino acids. This characteristic of the code is referred to as degeneracy. Note that not all codons code for an amino acid. The base sequences UAA, UAG, and UGA are all stop signals that indicate where polypeptide synthesis should end.The base sequence AUG codes for the amino acid methionine,which is a start signal.

Transcription:

The genetic information in DNA is not translated directly into proteins, but is first transcribed into mRNA. Transcription involves numerous enzymes that unwind a region of a DNA molcule, initiate and end mRNA synthesis, and modify the mRNA after transcription is complete. Unlike DNA replication, only one or a few genes are exposed, and only one of the two DNA strands is transcribed (figure 3.12).

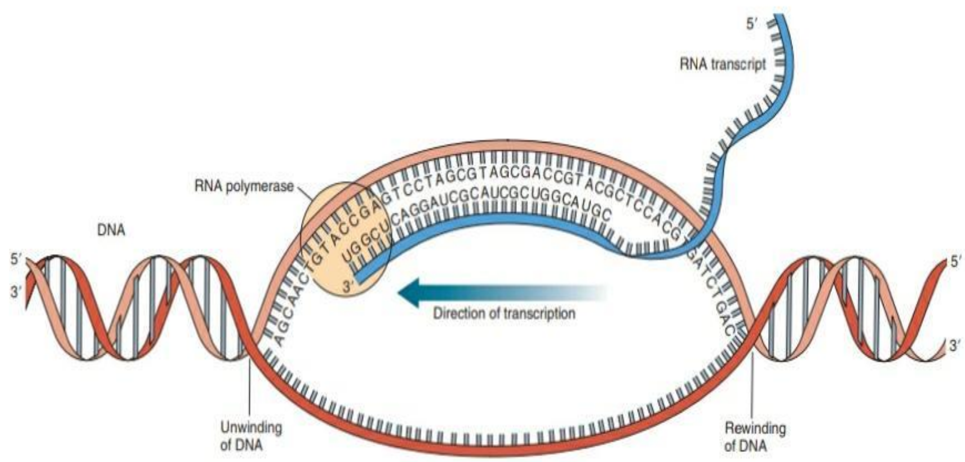


FIGURE 3.12

Transcription. Transcription involves the production of a messenger RNA molecule from the DNA segment. Note that transcription is similar to DNA replication in that the molecule is synthesized in the 5' to 3' direction.

One of the important enzymes of this process is RNA polymerase. After a section of DNA is unwound, RNA polymerase recognizes a specific sequence of DNA nucleotides. RNA polymerase attaches and begins joining ribose nucleotides, which are complementary to the 3' end of the DNA strand. In RNA, the same complementary bases in DNA are paired, except that in RNA, the base uracil replaces the base thymine as a complement to adenine.

Newly transcribed mRNA, called the primary transcript,must be modified before leaving the nucleus to carry out protein synthesis. Some base sequences in newly transcribed mRNA do not code for proteins. RNA splicing involves cutting out noncoding regions so that the mRNA coding region can be read continuously at the ribosome.

Translation:

Translation is protein synthesis at the ribosomes in the cytoplasm,based on the genetic information in the transcribed mRNA. Another type of RNA, called transfer RNA (tRNA), is important in the translation process (figure 3.13). It brings the different amino acids coded for by the mRNA into alignment so that a polypeptide can be made. Complementary pairing of bases across the molecule maintains tRNA's configuration. The presence of some unusual bases

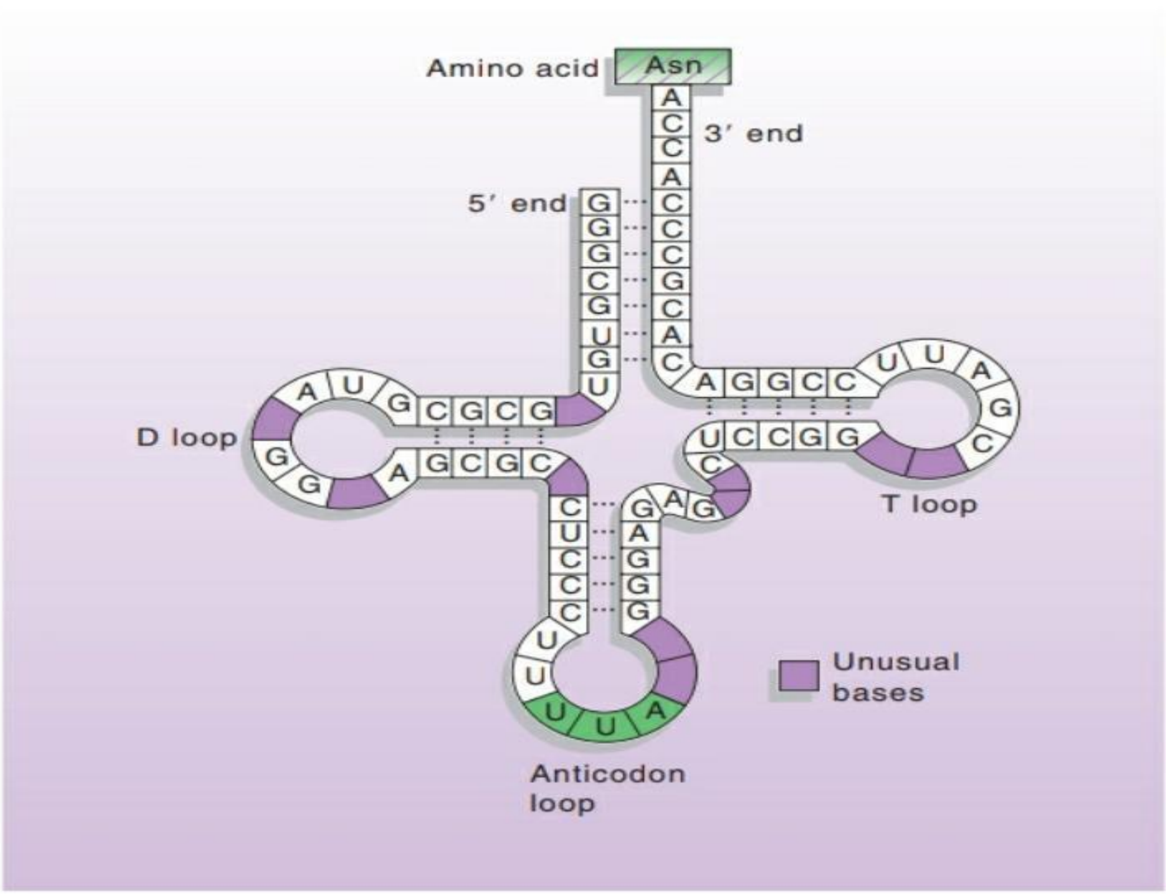


FIGURE 3.13

Structure of Transfer RNA. Diagrammatic representation of the secondary structure of transfer RNA (tRNA). An amino acid attaches to the 3' end of the molecule. The anticodon is the sequence of three bases that pairs with the codon in mRNA, thus positioning the amino acid that tRNA carries. Other aspects of tRNA structure position the tRNA at the ribosome and in the enzyme that attaches the correct amino acid to the tRNA.

(i.e., other than adenine, thymine, cytosine, guanine, or uracil) disrupts the normal base pairing and forms loops in the molecule. The center loop (the “anticodon loop”) has a sequence of three unpaired bases called the anticodon. During translation,pairing of the mRNA codon with its complementary anticodon of tRNA appropriately positions the amino acid that tRNA carries.

Ribosomes, the sites of protein synthesis, consist of large and small subunits that organize the pairing between the codon and the anticodon. Several sites on the ribosome are binding sites for mRNA and tRNA. At the initiation of translation, mRNA binds to a small, separate ribosomal subunit. Attachment of the mRNA requires that the initiation codon (AUG) of mRNA be aligned with the P (peptidyl) site of the ribosome. A tRNA with a complementary anticodon for methionine binds to the mRNA,and a large subunit joins, forming a complete ribosome.

Polypeptide formation can now begin. Another site, the A (aminoacyl) site, is next to the P site. A second tRNA, whose anti-codon is complementary to the codon in the A site, is positioned.Two tRNA molecules with their attached amino acids are now side-by-side in the P and A sites (figure 3.14). This step requires enzyme aid and energy, in the form of guanine triphosphate (GTP).An enzyme (peptidyl transferase), which is actually a part of the larger ribosomal subunit, breaks the bond between the amino acid and tRNA in the P site, and catalyzes the formation of a peptide bond between that amino acid and the amino acid in the A site.

The mRNA strand then moves along the ribosome a distance of one codon. The tRNA with two amino acids attached to it that was in the A site is now in the P site. A third tRNA can now enter the exposed A site. This process continues until the entire mRNA has been translated, and a polypeptide chain has been synthesized. Translation ends when a termination codon (e.g.,UAA) is encountered.

Protein synthesis often occurs on ribosomes on the surface of the rough endoplasmic reticulum. The positioning of ribosomes on the ER allows proteins to move into the ER as the protein is being synthesized. The protein can then be moved to the Golgi apparatus for packaging into a secretory vesicle or a lysosome.

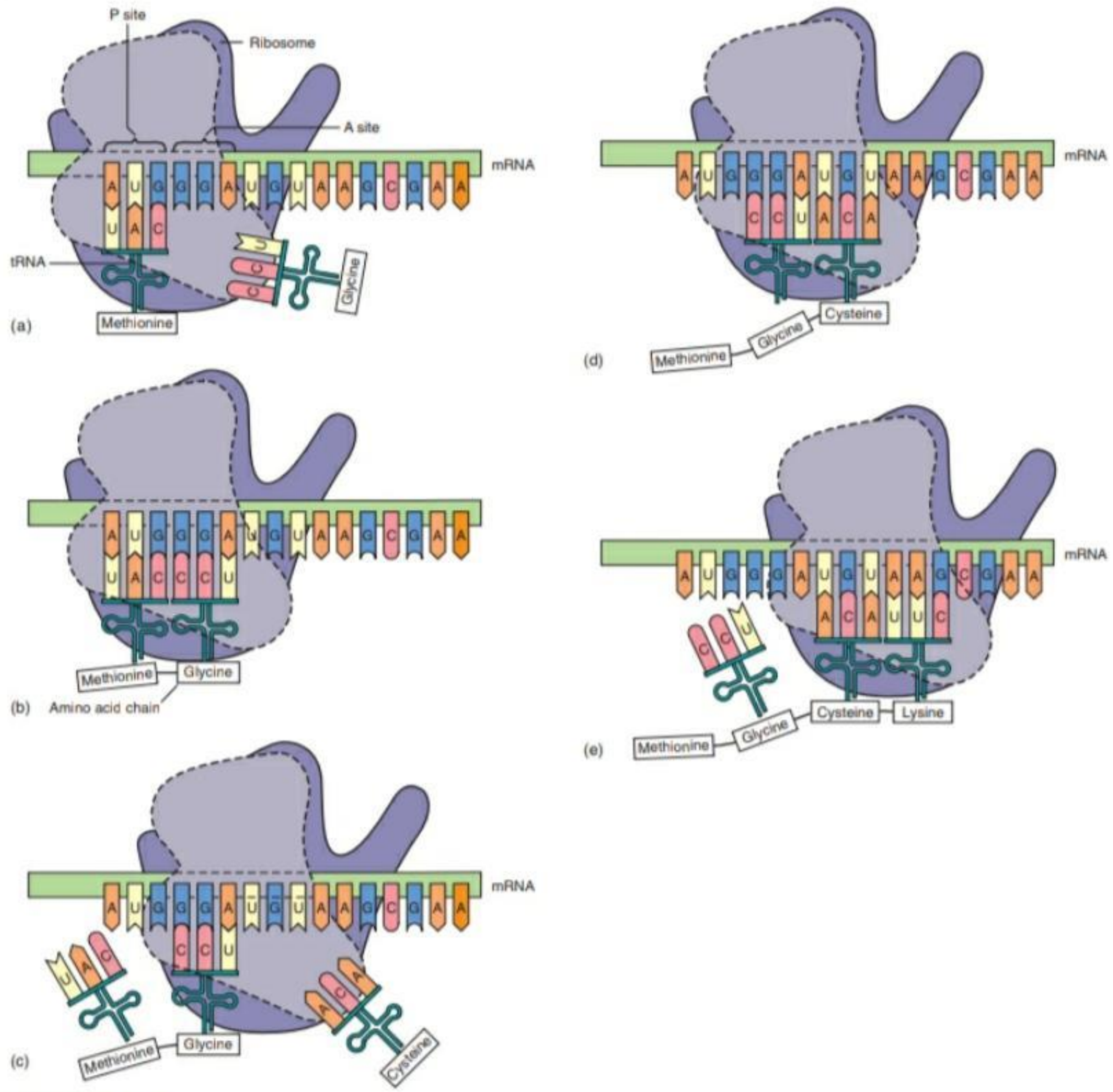


FIGURE 3.14

Events of Translation. (*a*) Translation begins when a methionine tRNA associates with the P site of the smaller ribosomal subunit and the initiation codon of mRNA associated with that subunit. The larger ribosomal subunit attaches to the small subunit/tRNA complex. (*b*) A second tRNA carrying the next amino acid enters the A site. A peptide bond forms between the two amino acids, freeing the first tRNA in the P site. (*c*) The mRNA, along with the second tRNA and its attached dipeptide, moves the distance of one codon. The first tRNA is discharged, leaving its amino acid behind. The second tRNA is now in the P site, and the A site is exposed and ready to receive another tRNA-amino acid. (*d*) A second peptide bond forms. (*e*) This process continues until an mRNA stop signal is encountered.