GLOBAL EDITION

Biology
A Global Approach
ELEVENTH EDITION

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Chapter 17

Expression of Genes

The Flow of Genetic Information

- The information content of genes is in the specific sequences of nucleotides

- The DNA inherited by an organism leads to specific traits by dictating the synthesis of proteins

- Proteins are the links between genotype and phenotype

- **Gene expression**, the process by which DNA directs protein synthesis, includes two stages: transcription and translation

Figure 17.1

Figure 17.1a

An albino raccoon

Concept 17.1: Genes specify proteins via transcription and translation

- How was the fundamental relationship between genes and proteins discovered?

Evidence from the Study of Metabolic Defects

- In 1902, British physician Archibald Garrod first suggested that genes dictate phenotypes through enzymes that catalyze specific chemical reactions

- He thought symptoms of an inherited disease reflect an inability to synthesize a certain enzyme

- Cells synthesize and degrade molecules in a series of steps, a metabolic pathway

Nutritional Mutants in Neurospora: Scientific Inquiry

- George Beadle and Edward Tatum exposed bread mold to X-rays, creating mutants that were unable to survive on minimal media

- Their colleagues Adrian Srb and Norman Horowitz identified three classes of arginine-deficient mutants

- Each lacked a different enzyme necessary for synthesizing arginine

- The results of the experiments provided support for the one gene–one enzyme hypothesis

- The hypothesis states that the function of a gene is to dictate production of a specific enzyme
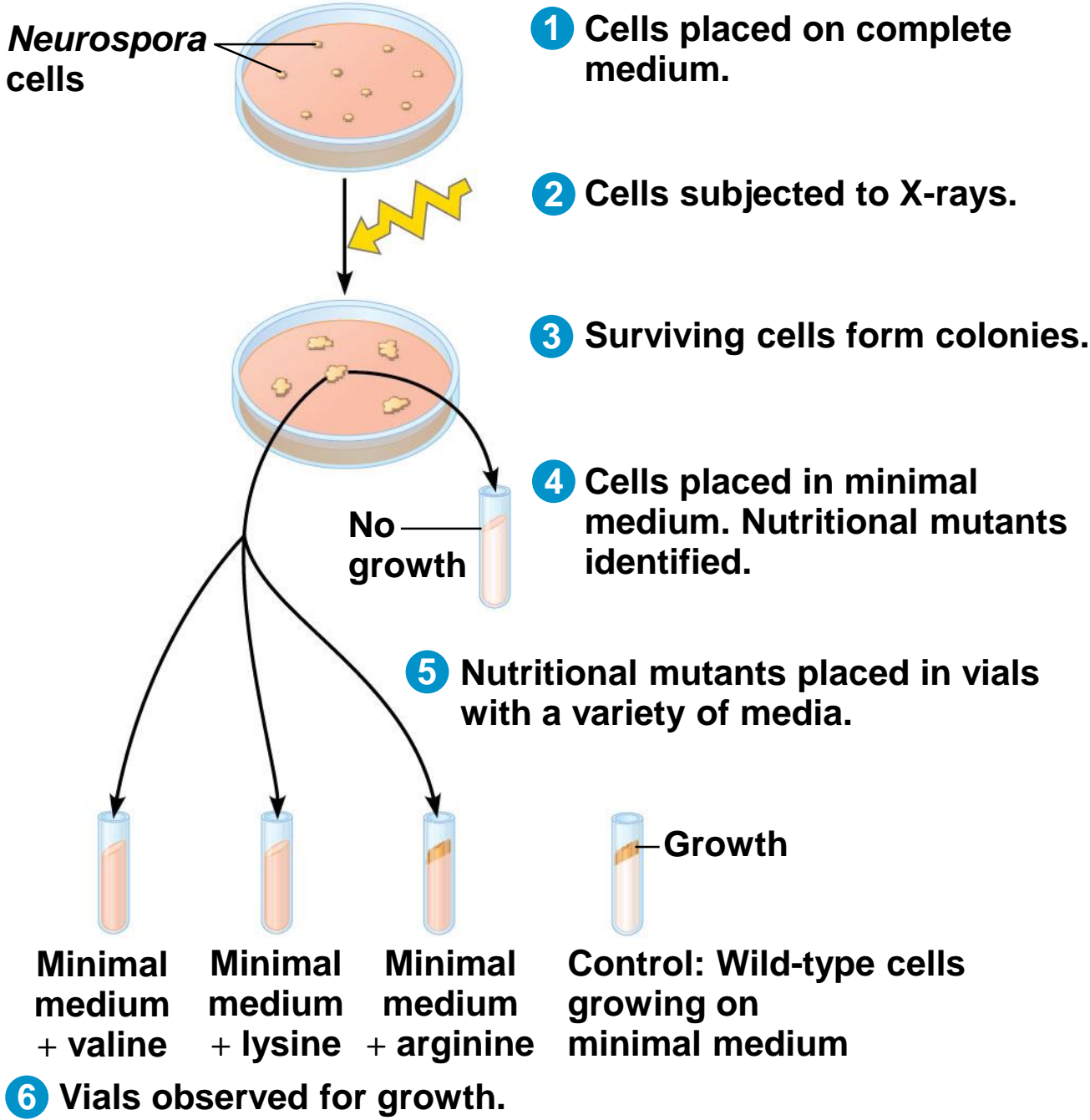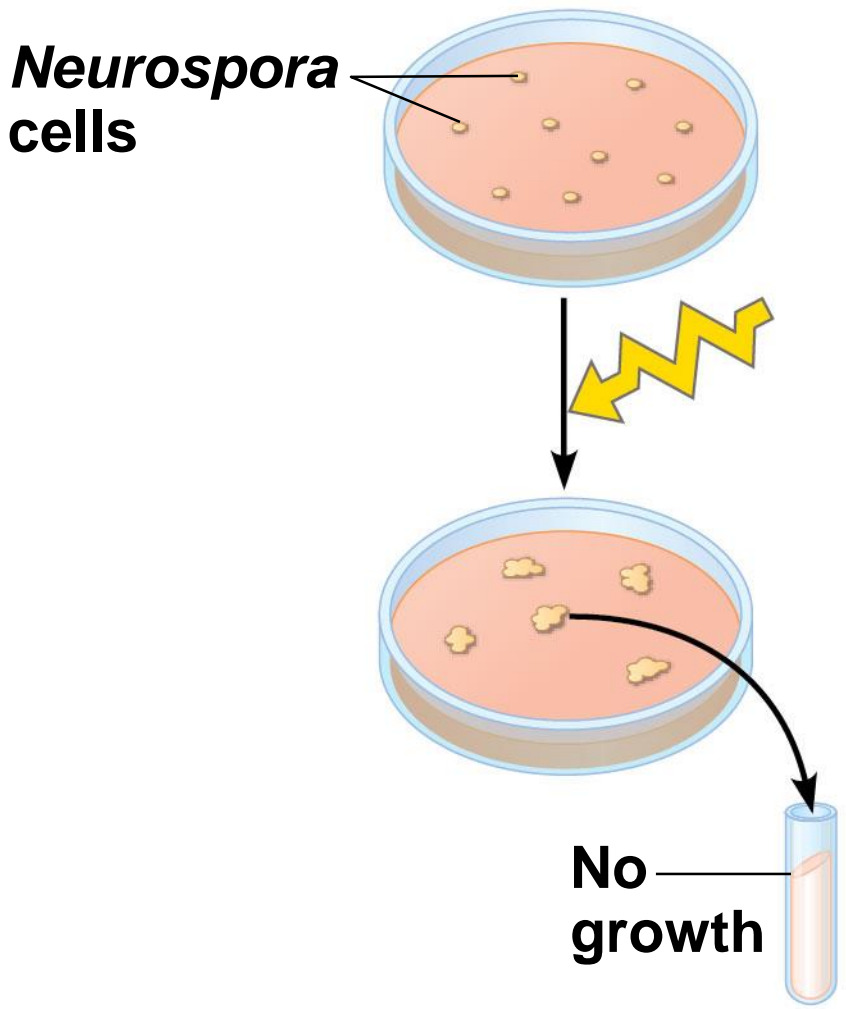
Figure 17.2

Neurospora cells

1 Cells placed on complete medium.

2 Cells subjected to X-rays.

3 Surviving cells form colonies.

4 Cells placed in minimal medium. Nutritional mutants identified.

No growth

5 Nutritional mutants placed in vials with a variety of media.

Growth

Minimal medium + valine

Minimal medium + lysine

Minimal medium + arginine

Control: Wild-type cells growing on minimal medium

6 Vials observed for growth.

Figure 17.2a

Neurospora cells

① Cells placed on complete medium.

② Cells subjected to X-rays.

③ Surviving cells form colonies.

No growth

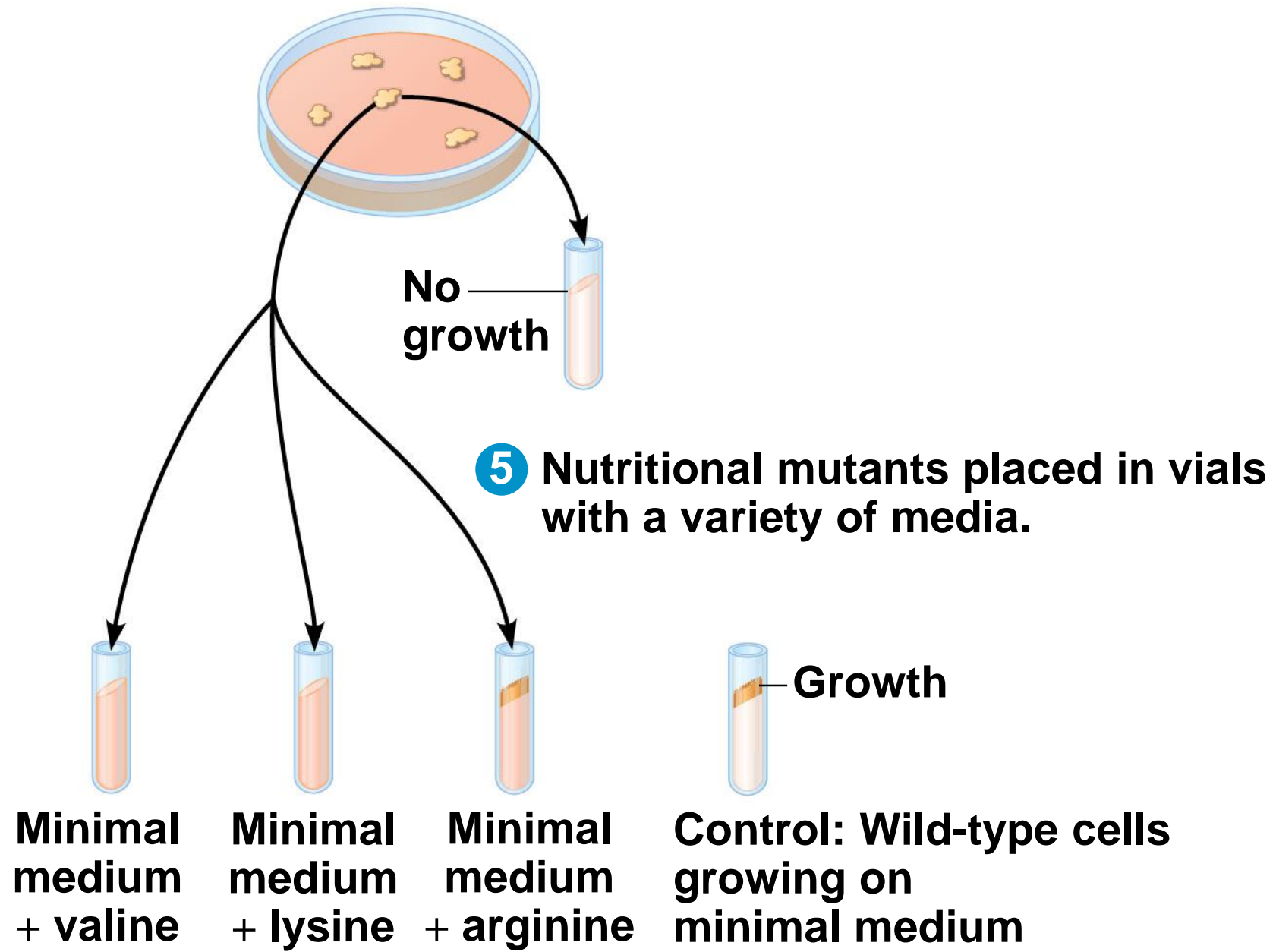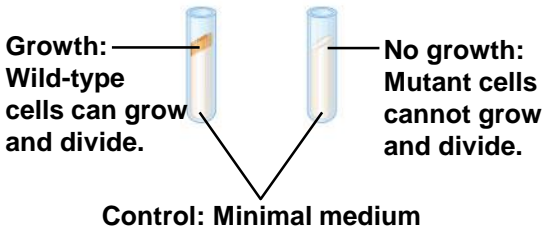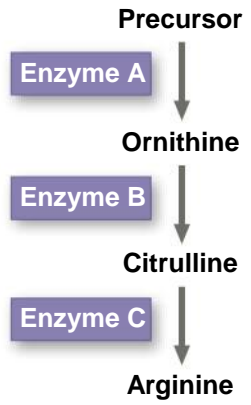④ Cells placed in minimal medium. Nutritional mutants identified.

Figure 17.2b

No growth

5 Nutritional mutants placed in vials with a variety of media.

Growth

Minimal medium + valine

Minimal medium + lysine

Minimal medium + arginine

Control: Wild-type cells growing on minimal medium

6 Vials observed for growth.

Figure 17.3

Precursor
↓ Enzyme A
Ornithine
↓ Enzyme B
Citrulline
↓ Enzyme C
Arginine

Growth: Wild-type cells can grow and divide.

No growth: Mutant cells cannot grow and divide.

Control: Minimal medium

Results Table		Classes of *Neurospora crassa*			
Condition		Wild type	Class I mutants	Class II mutants	Class III mutants
	Minimal medium (MM) (control)				
	MM + ornithine				
	MM + citrulline				
	MM + arginine (control)				
	Summary of results	Can grow with or without any supplements	Can grow on ornithine, citrulline, or arginine	Can grow only on citrulline or arginine	Require arginine to grow

Gene (codes for enzyme)	Wild type	Class I mutants (mutation in gene *A*)	Class II mutants (mutation in gene *B*)	Class III mutants (mutation in gene *C*)
	Precursor	Precursor	Precursor	Precursor
Gene *A* →	Enzyme A	~~Enzyme A~~	Enzyme A	Enzyme A
	Ornithine	Ornithine	Ornithine	Ornithine
Gene *B* →	Enzyme B	Enzyme B	~~Enzyme B~~	Enzyme B
	Citrulline	Citrulline	Citrulline	Citrulline
Gene *C* →	Enzyme C	Enzyme C	Enzyme C	~~Enzyme C~~
	Arginine	Arginine	Arginine	Arginine

Figure 17.3a

Precursor

Enzyme A

Ornithine

Enzyme B

Citrulline

Enzyme C

Arginine

Figure 17.3b

Growth:
Wild-type
cells can grow
and divide.

No growth:
Mutant cells
cannot grow
and divide.

Control: Minimal medium

Figure 17.3c

Results Table	Classes of *Neurospora crassa*			
Condition	**Wild type**	**Class I mutants**	**Class II mutants**	**Class III mutants**
Minimal medium (MM) (control)				
MM + ornithine				
MM + citrulline				
MM + arginine (control)				
Summary of results	Can grow with or without any supplements	Can grow on ornithine, citrulline, or arginine	Can grow only on citrulline or arginine	Require arginine to grow

Data from A. M. Srb and N. H. Horowitz, The ornithine cycle in *Neurospora* and its genetic control,
***Journal of Biological Chemistry* 154:129–139 (1944).**

Figure 17.3d
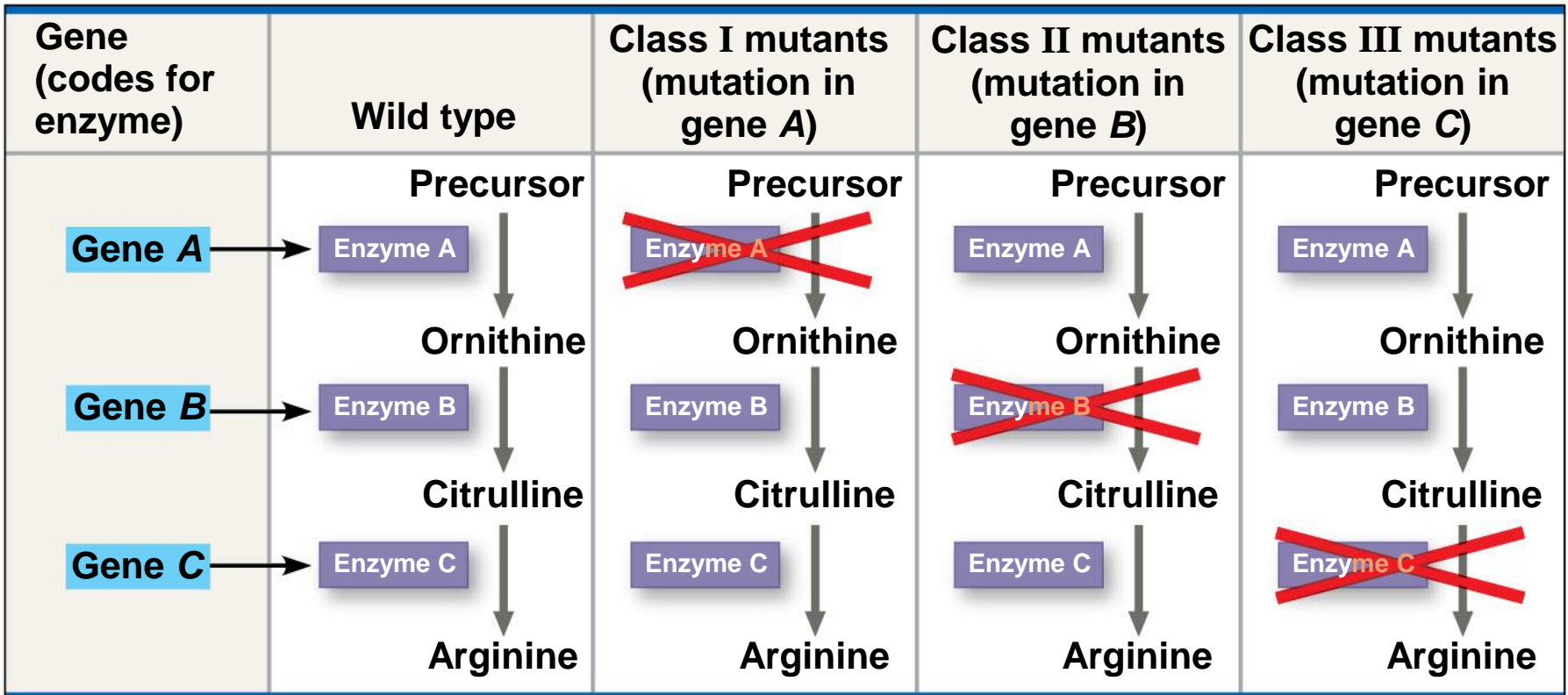
Gene (codes for enzyme)	Wild type	Class I mutants (mutation in gene *A*)	Class II mutants (mutation in gene *B*)	Class III mutants (mutation in gene *C*)
	Precursor	Precursor	Precursor	Precursor
Gene *A* → Enzyme A	Enzyme A ↓	~~Enzyme A~~ ↓	Enzyme A ↓	Enzyme A ↓
	Ornithine	Ornithine	Ornithine	Ornithine
Gene *B* → Enzyme B	Enzyme B ↓	Enzyme B ↓	~~Enzyme B~~ ↓	Enzyme B ↓
	Citrulline	Citrulline	Citrulline	Citrulline
Gene *C* → Enzyme C	Enzyme C ↓	Enzyme C ↓	Enzyme C ↓	~~Enzyme C~~ ↓
	Arginine	Arginine	Arginine	Arginine

Data from A. M. Srb and N. H. Horowitz, The ornithine cycle in *Neurospora* and its genetic control, *Journal of Biological Chemistry* 154:129–139 (1944).

The Products of Gene Expression:
A Developing Story

- Not all proteins are enzymes, so researchers later revised the hypothesis: one gene–one protein

- Many proteins are composed of several polypeptides, each of which has its own gene

- Therefore, Beadle and Tatum's hypothesis is now restated as the one gene–one polypeptide hypothesis

- It is common to refer to gene products as proteins rather than polypeptides

Basic Principles of Transcription and Translation

- RNA is the bridge between genes and the proteins for which they code

- **Transcription** is the synthesis of RNA using information in DNA

- Transcription produces **messenger RNA (mRNA)**

- **Translation** is the synthesis of a polypeptide, using information in the mRNA

- **Ribosomes** are the sites of translation

- In prokaryotes, translation of mRNA can begin before transcription has finished

- In a eukaryotic cell, the nuclear envelope separates transcription from translation

- Eukaryotic RNA transcripts are modified through RNA processing to yield the finished mRNA

Figure 17.4
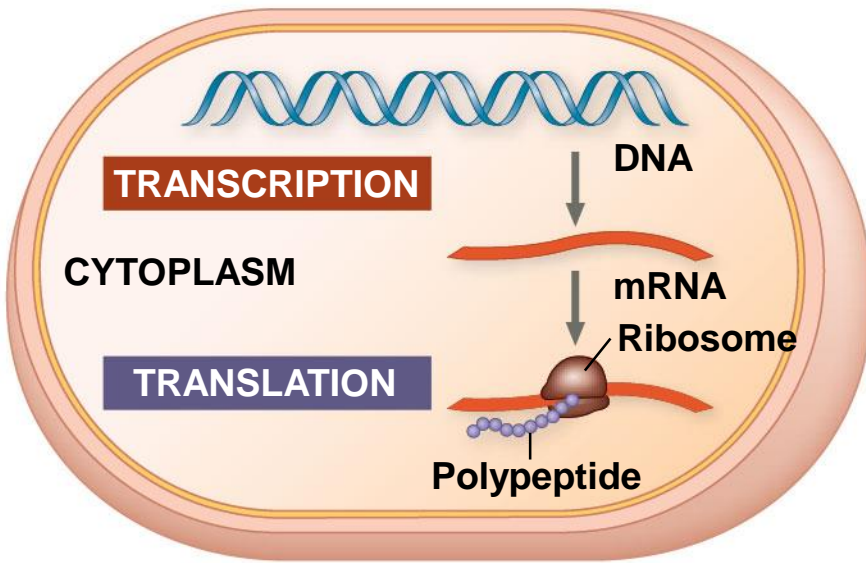
(a) Bacterial cell
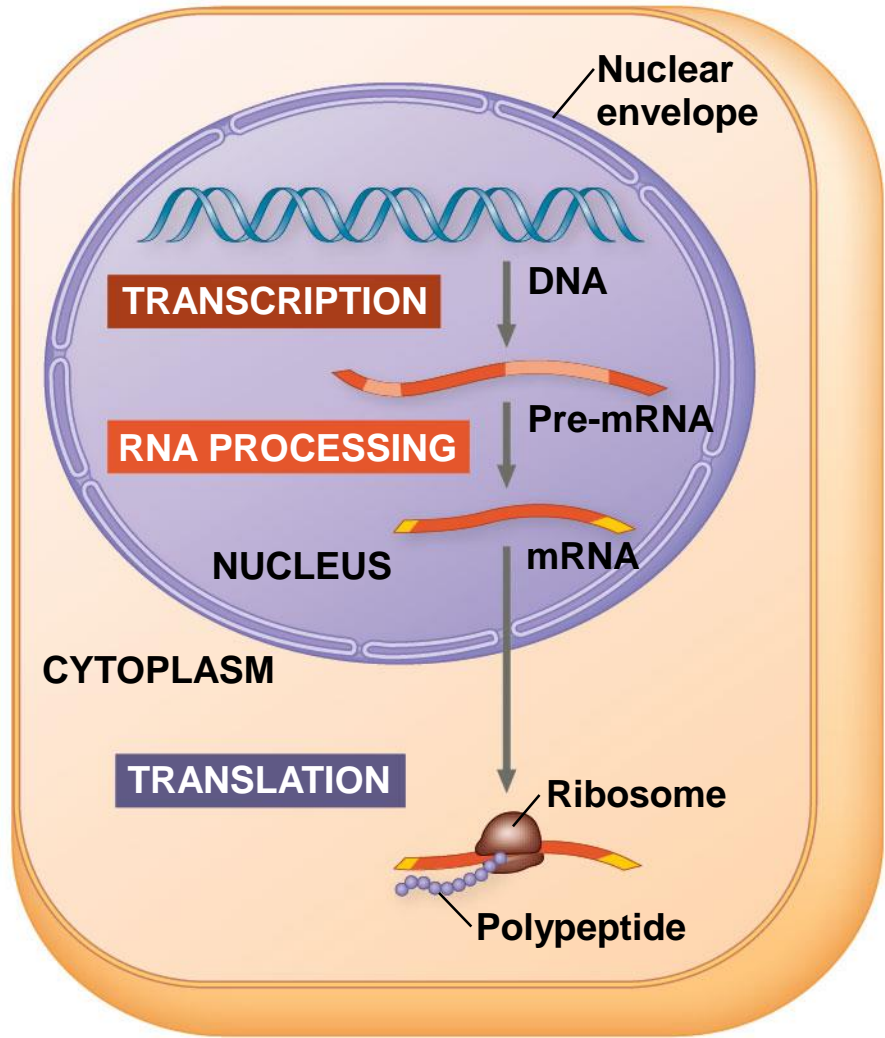
(b) Eukaryotic cell

Figure 17.4a_1
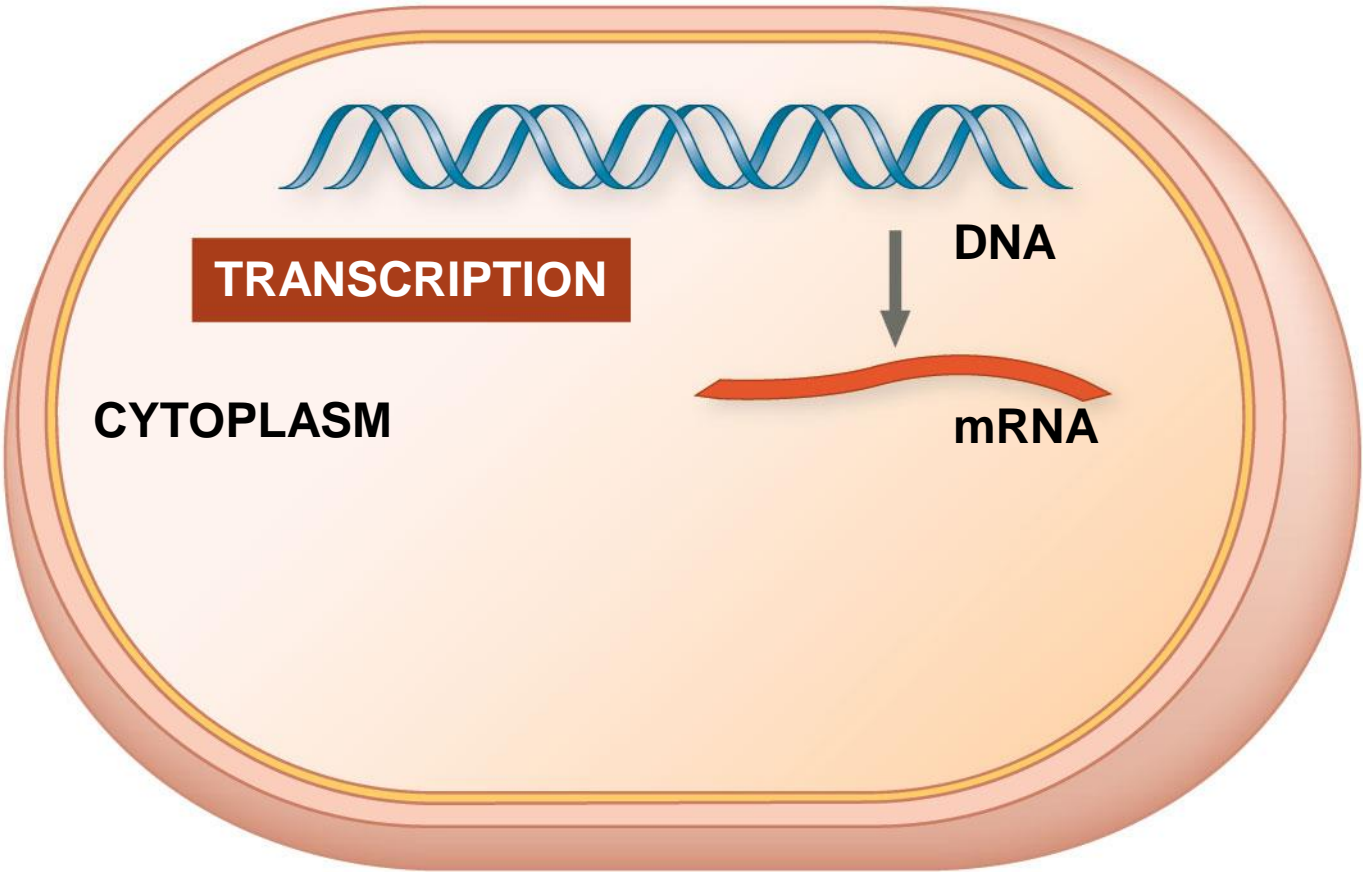
(a) Bacterial cell

Figure 17.4a_2

(a) Bacterial cell

Figure 17.4b_1

Nuclear envelope

TRANSCRIPTION

DNA

Pre-mRNA

NUCLEUS

CYTOPLASM
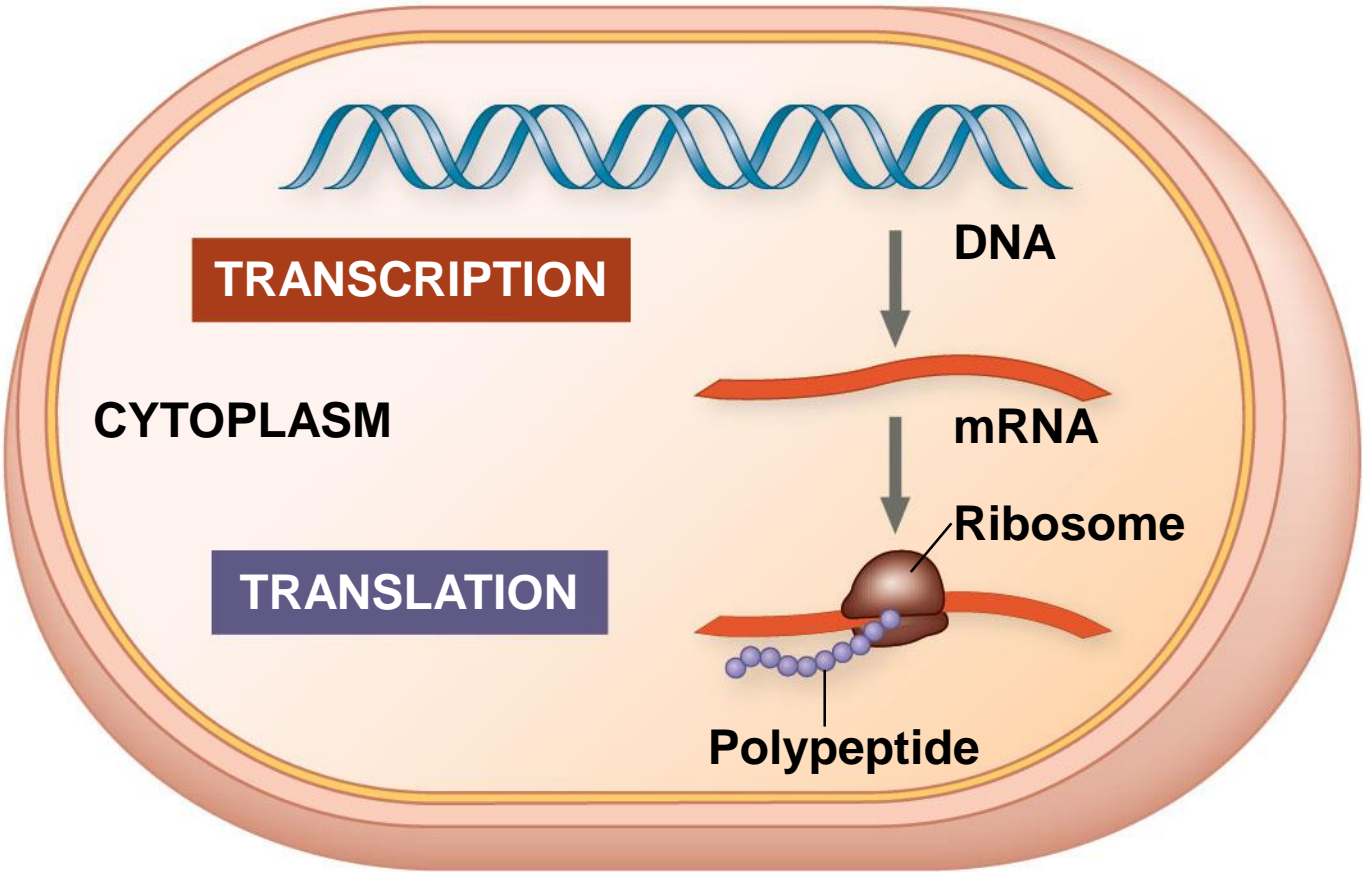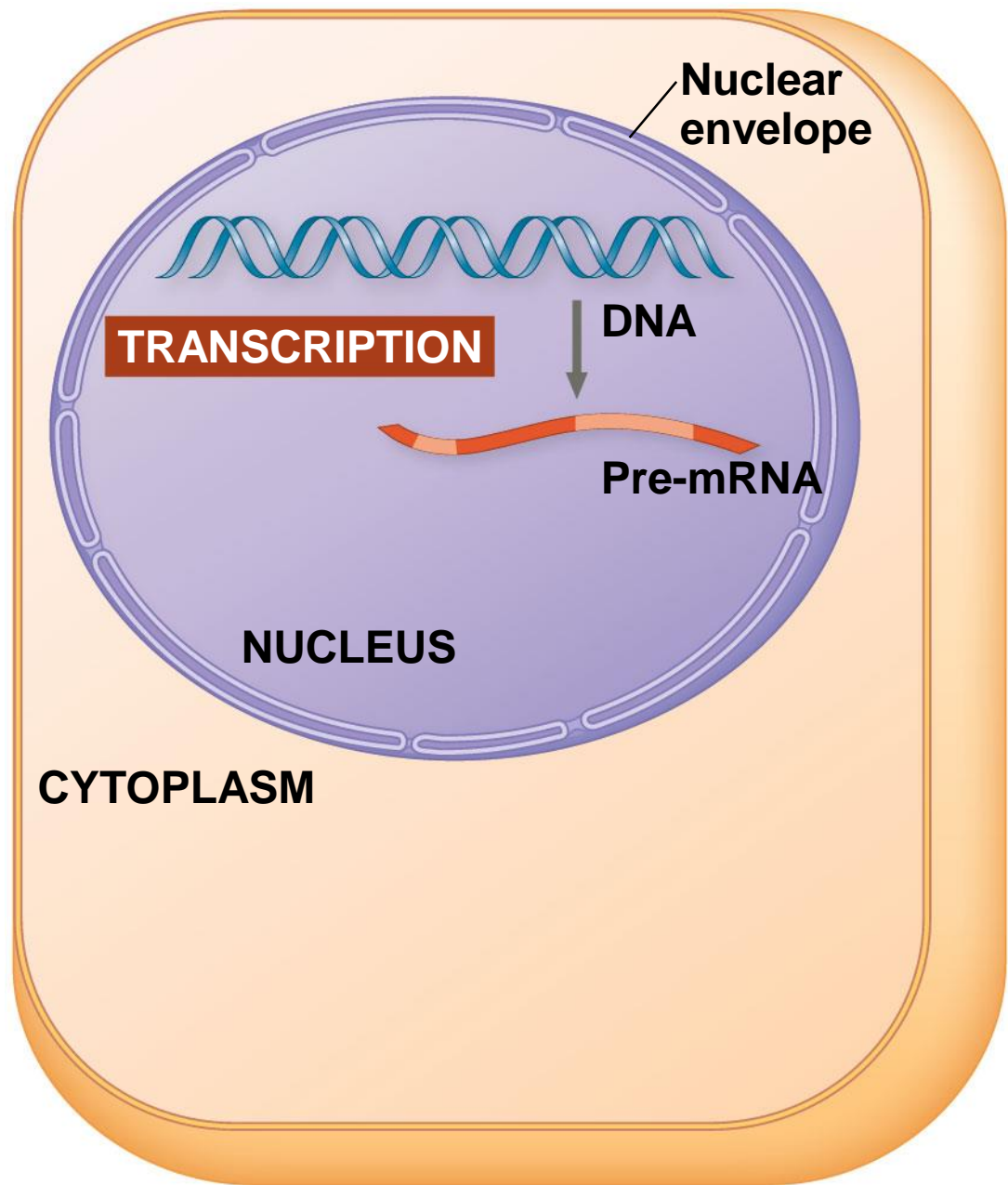
(b) Eukaryotic cell

Figure 17.4b_2

(b) Eukaryotic cell

Figure 17.4b_3

Nuclear envelope

TRANSCRIPTION

DNA

Pre-mRNA

RNA PROCESSING

NUCLEUS

mRNA

CYTOPLASM

TRANSLATION

Ribosome

Polypeptide
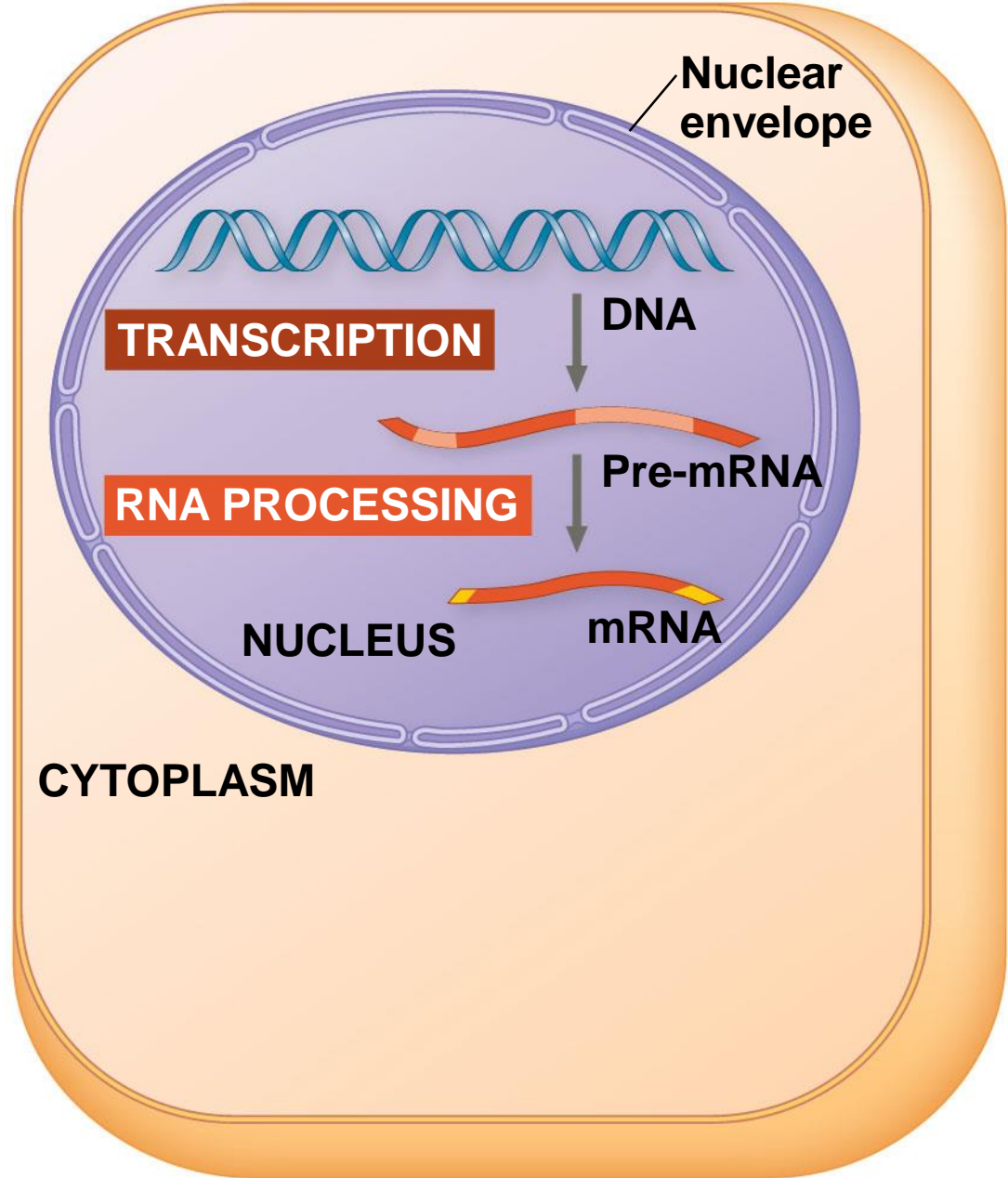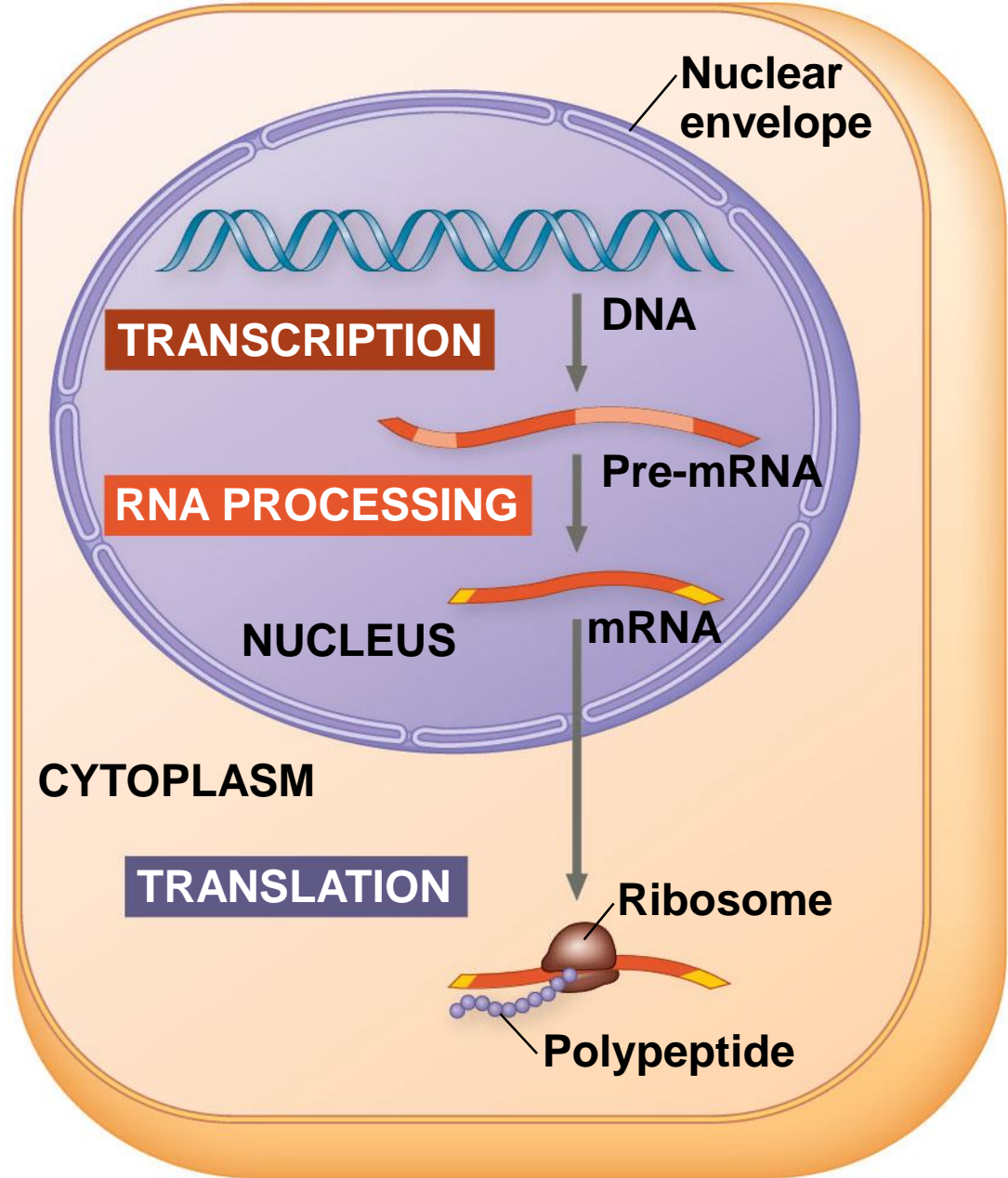
(b) Eukaryotic cell

- A **primary transcript** is the initial RNA transcript from any gene prior to processing

- The central dogma is the concept that cells are governed by a cellular chain of command:
  DNA → RNA → protein

Figure 17.UN01

The Genetic Code

- How are the instructions for assembling amino acids into proteins encoded into DNA?

- There are 20 amino acids, but there are only four nucleotide bases in DNA

- How many nucleotides correspond to an amino acid?

Codons: Triplets of Nucleotides

- The flow of information from gene to protein is based on a **triplet code**: a series of nonoverlapping, three-nucleotide words

- The words of a gene are transcribed into complementary nonoverlapping three-nucleotide words of mRNA

- These words are then translated into a chain of amino acids, forming a polypeptide

Figure 17.5

DNA molecule

Gene 1

Gene 2

Gene 3

DNA template strand

3′ A C C A A A C C G A G T 5′

5′ T G G T T T G G C T C A 3′

TRANSCRIPTION

mRNA 5′ U G G U U U G G C U C A 3′

Codon

TRANSLATION

Protein

Trp   Phe   Gly   Ser

Amino acid

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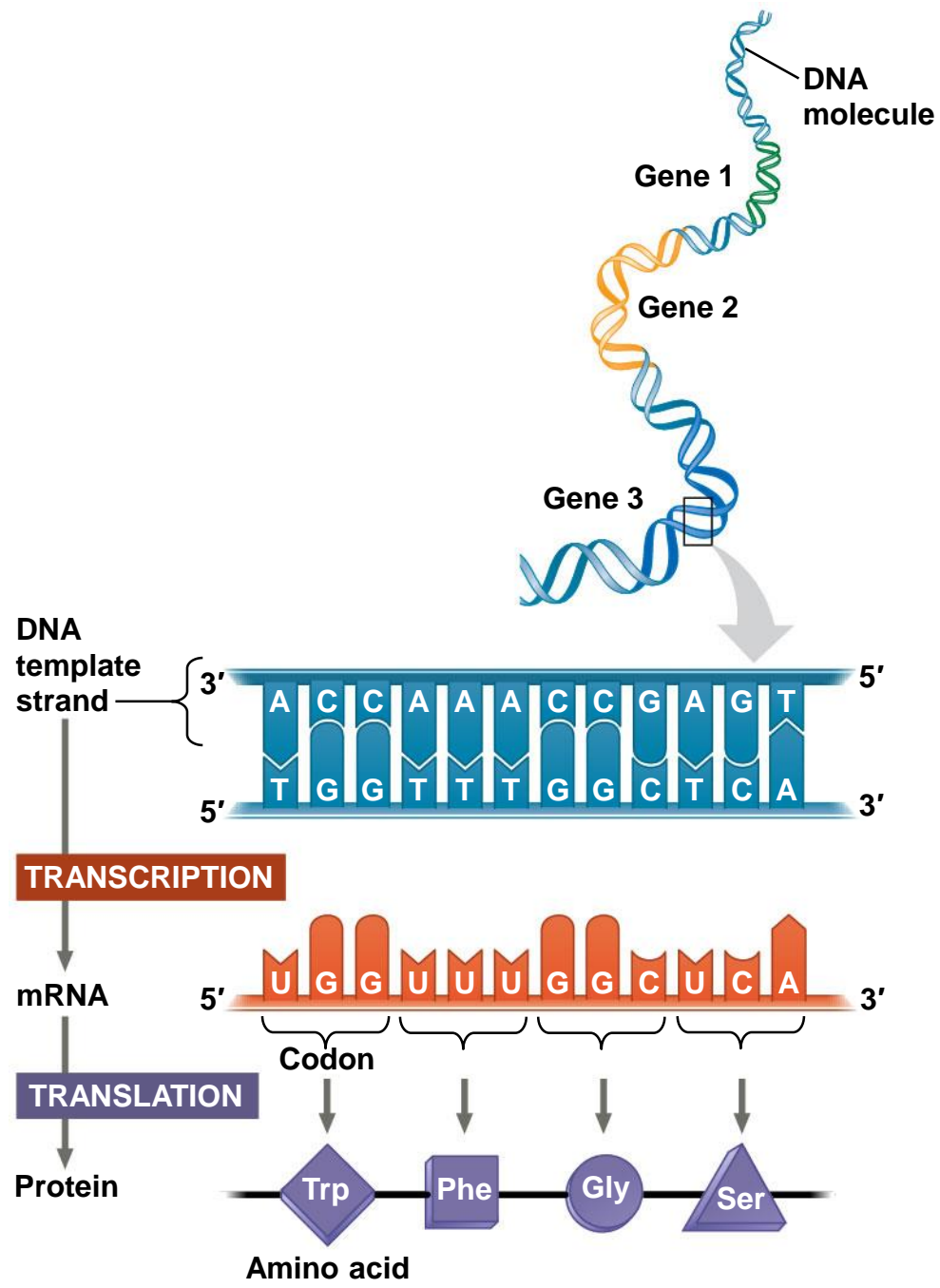
Figure 17.5a

DNA template strand

3′ A C C A A A C C G A G T 5′
5′ T G G T T T G G C T C A 3′

TRANSCRIPTION

mRNA

5′ U G G U U U G G C U C A 3′

Codon

TRANSLATION

Protein

Trp   Phe   Gly   Ser

Amino acid
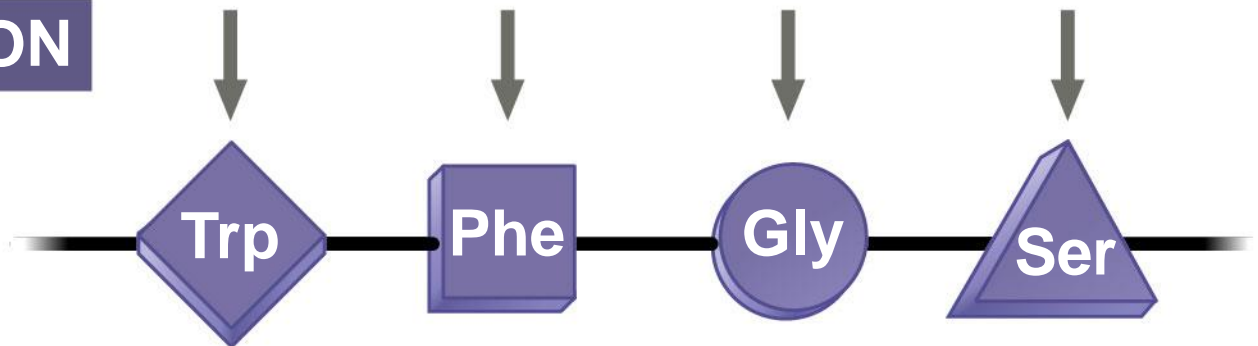
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- One of the two DNA strands, the **template strand**, provides a template for ordering the sequence of complementary nucleotides in an RNA transcript

- The template strand is always the same strand for a given gene

- The strand used as the template is determined by the orientation of the enzyme that transcribes the gene

- This in turn, depends on the DNA sequences associated with the gene

- During translation, the mRNA base triplets, called **codons**, are read in the $5' \rightarrow 3'$ direction

- The nontemplate strand is called the coding strand because the nucleotides of this strand are identical to the codons, except that T is present in the DNA in place of U in the RNA

- Each codon specifies the amino acid (one of 20) to be placed at the corresponding position along a polypeptide

Cracking the Code

- All 64 codons were deciphered in the early 1960s

- Of the 64 triplets, 61 code for amino acids; 3 triplets are "stop" signals to end translation

- The genetic code is redundant (more than one codon may specify a particular amino acid) but not ambiguous; no codon specifies more than one amino acid

- Codons must be read in the correct **reading frame** (correct groupings) in order for the specified polypeptide to be produced

Figure 17.6

Second mRNA base

	U	C	A	G	
U	UUU] Phe (F) UUC UUA] Leu (L) UUG	UCU UCC] Ser (S) UCA UCG	UAU] Tyr (Y) UAC UAA Stop UAG Stop	UGU] Cys (C) UGC UGA Stop UGG Trp (W)	U C A G
C	CUU CUC] Leu (L) CUA CUG	CCU CCC] Pro (P) CCA CCG	CAU] His (H) CAC CAA] Gln (Q) CAG	CGU CGC] Arg (R) CGA CGG	U C A G
A	AUU] Ile (I) AUC AUA AUG Met (M) or start	ACU ACC] Thr (T) ACA ACG	AAU] Asn (N) AAC AAA] Lys (K) AAG	AGU] Ser (S) AGC AGA] Arg (R) AGG	U C A G
G	GUU GUC] Val (V) GUA GUG	GCU GCC] Ala (A) GCA GCG	GAU] Asp (D) GAC GAA] Glu (E) GAG	GGU GGC] Gly (G) GGA GGG	U C A G

First mRNA base (5′ end of codon)

Third mRNA base (3′ end of codon)

Evolution of the Genetic Code

- The genetic code is nearly universal, shared by the simplest bacteria and the most complex animals

- Genes can be transcribed and translated after being transplanted from one species to another

Figure 17.7

(a) Tobacco plant expressing a firefly gene

(b) Pig expressing a jellyfish gene

Figure 17.7a

(a) Tobacco plant expressing a firefly gene

Figure 17.7b

(b) Pig expressing a jellyfish gene

Concept 17.2: Transcription is the DNA-directed synthesis of RNA: *a closer look*

- Transcription is the first stage of gene expression

Molecular Components of Transcription

- RNA synthesis is catalyzed by **RNA polymerase**, which pries the DNA strands apart and joins together the RNA nucleotides

- The RNA is complementary to the DNA template strand

- RNA polymerase does not need any primer

- RNA synthesis follows the same base-pairing rules as DNA, except that uracil substitutes for thymine

Figure 17.8_1

Promoter　**Transcription unit**

5′
3′

RNA polymerase　**Start point**　**DNA**

1 **Initiation**

Unwound DNA　**Nontemplate strand of DNA**

5′
3′

RNA transcript　**Template strand of DNA**

Figure 17.8_2

Promoter　　**Transcription unit**

5′
3′

DNA

Start point

RNA polymerase

1 Initiation

Unwound DNA

Nontemplate strand of DNA

5′　　　　　　　　　　　　　　　　　　　　　　　　**3′**
3′　　　　　　　　　　　　　　　　　　　　　　　　**5′**

RNA transcript

Template strand of DNA

2 Elongation

Rewound DNA

5′　　　　　　　　　　　　　　　　　　**3′**　　**3′**
3′　　　　　　　　　　　　　　　　　　　　　　　**5′**

5′

RNA transcript

Direction of transcription ("downstream")

Figure 17.8_3

Promoter **Transcription unit**

5′
3′

Start point **DNA**

RNA polymerase

1 **Initiation**

Unwound DNA **Nontemplate strand of DNA**

5′   3′
3′   5′

RNA transcript **Template strand of DNA**

2 **Elongation**

Rewound DNA

5′   3′
3′   3′   5′

5′

RNA transcript **Direction of transcription ("downstream")**

3 **Termination**

5′   3′
3′   5′

5′   3′

Completed RNA transcript

Animation: Transcription
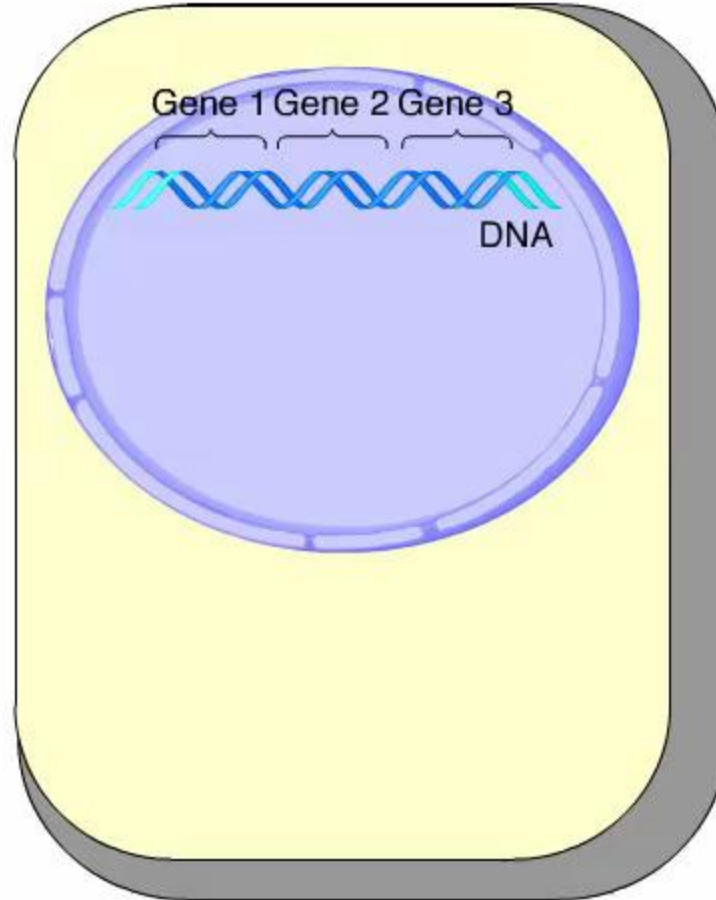
- The DNA sequence where RNA polymerase attaches is called the **promoter**

- In bacteria, the sequence signaling the end of transcription is called the **terminator**

- The stretch of DNA that is transcribed is called a **transcription unit**

Synthesis of an RNA Transcript

- The three stages of transcription:
  - Initiation
  - Elongation
  - Termination

RNA Polymerase Binding and Initiation of Transcription

- Promoters signal the transcription **start point** and usually extend several dozen nucleotide pairs upstream of the start point

- **Transcription factors** mediate the binding of RNA polymerase and the initiation of transcription

- The completed assembly of transcription factors and RNA polymerase II bound to a promoter is called a **transcription initiation complex**

- A promoter called a **TATA box** is crucial in forming the initiation complex in eukaryotes

Figure 17.9

A eukaryotic promoter

DNA

5′ — TATAAAA ——————————————————— 3′
3′ — ATATTTT ——————————————————— 5′

Promoter

Nontemplate strand

TATA box

Start point

Template strand

1 A eukaryotic promoter

Transcription factors

5′ ———————————————————————————— 3′
3′ ———————————————————————————— 5′
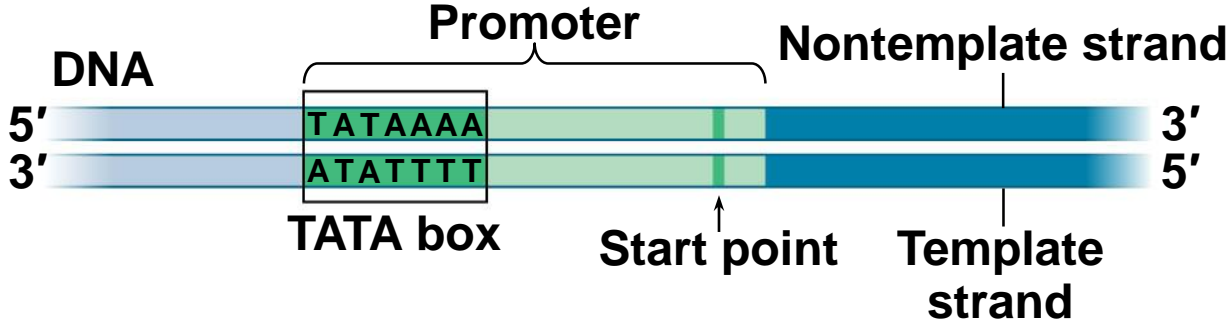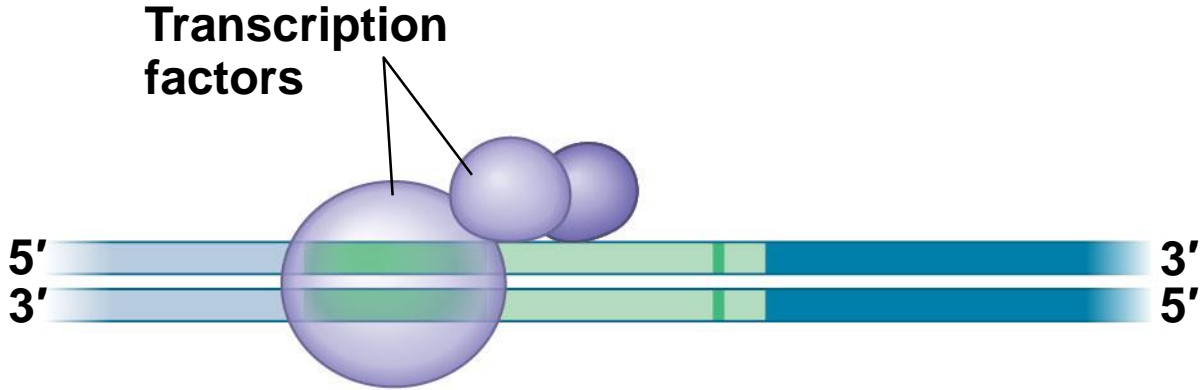
2 Several transcription factors bind to DNA.

RNA polymerase II

Transcription factors

5′ ———————————————————————————— 3′
3′ ———————————————————————————— 5′

5′ 3′
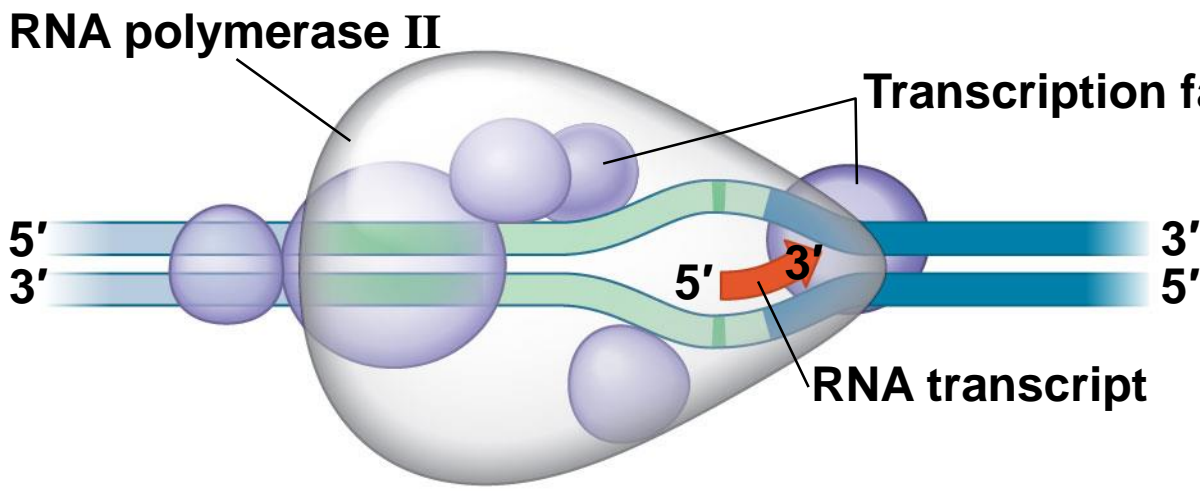
RNA transcript

3 Transcription initiation complex forms.

Elongation of the RNA Strand

- As RNA polymerase moves along the DNA, it untwists the double helix, 10 to 20 bases at a time

- Transcription progresses at a rate of 40 nucleotides per second in eukaryotes

- A gene can be transcribed simultaneously by several RNA polymerases

- Nucleotides are added to the 3′ end of the growing RNA molecule

Figure 17.10

Nontemplate strand of DNA

RNA nucleotides

RNA polymerase

3′

5′

3′ end

5′

T C A T C C A A T T
U
A T C C A A T T G C U
C A U C C A A U C
T A G G T T A A C

5′

3′

Direction of transcription

Template strand of DNA

5′

Newly made RNA

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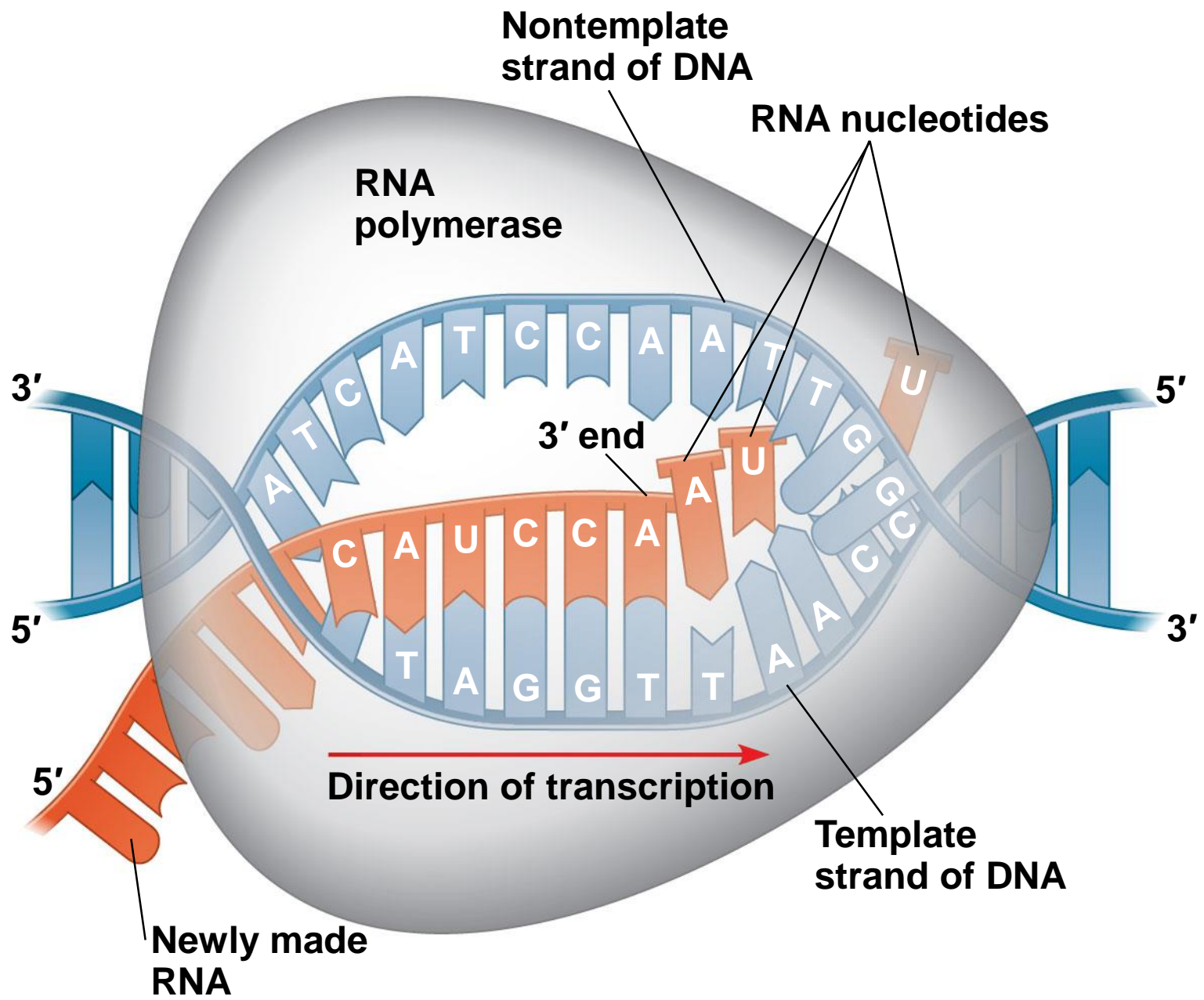
Termination of Transcription

- The mechanisms of termination are different in bacteria and eukaryotes

- In bacteria, the polymerase stops transcription at the end of the terminator and the mRNA can be translated without further modification

- In eukaryotes, RNA polymerase II transcribes the polyadenylation signal sequence; the RNA transcript is released 10–35 nucleotides past this polyadenylation sequence

Concept 17.3: Eukaryotic cells modify RNA after transcription

- Enzymes in the eukaryotic nucleus modify pre-mRNA (**RNA processing**) before the genetic messages are dispatched to the cytoplasm

- During RNA processing, both ends of the primary transcript are altered

- Also, in most cases, certain interior sections of the molecule are cut out and the remaining parts spliced together

Alteration of mRNA Ends

- Each end of a pre-mRNA molecule is modified in a particular way
  - The 5′ end receives a modified nucleotide **5′ cap**
  - The 3′ end gets a **poly-A tail**
- These modifications share several functions
  - They seem to facilitate the export of mRNA to the cytoplasm
  - They protect mRNA from hydrolytic enzymes
  - They help ribosomes attach to the 5′ end

Figure 17.11

A modified guanine nucleotide added to the 5′ end

Region that includes protein-coding segments

Polyadenylation signal

50–250 adenine nucleotides added to the 3′ end

5′

3′

G — P — P — P —   AAUAAA   AAA···AAA

5′ Cap   5′ UTR   Start codon   Stop codon   3′ UTR   Poly-A tail

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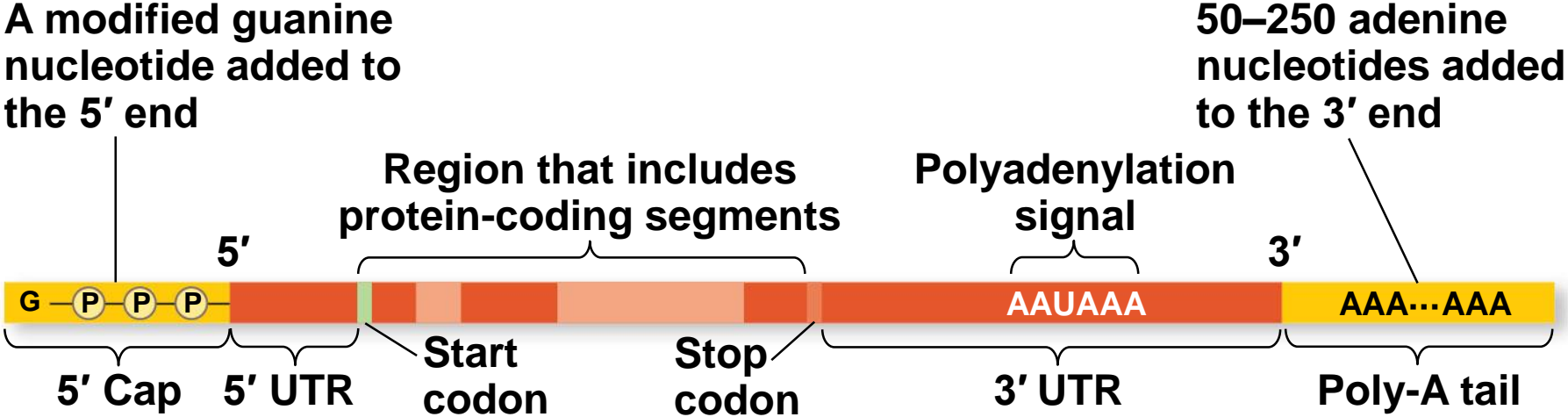
Split Genes and RNA Splicing

- Most eukaryotic genes and their RNA transcripts have long noncoding stretches of nucleotides that lie between coding regions

- These noncoding regions are called intervening sequences, or **introns**

- The other regions are called **exons** because they are eventually expressed, usually translated into amino acid sequences

- **RNA splicing** removes introns and joins exons, creating an mRNA molecule with a continuous coding sequence

Figure 17.12

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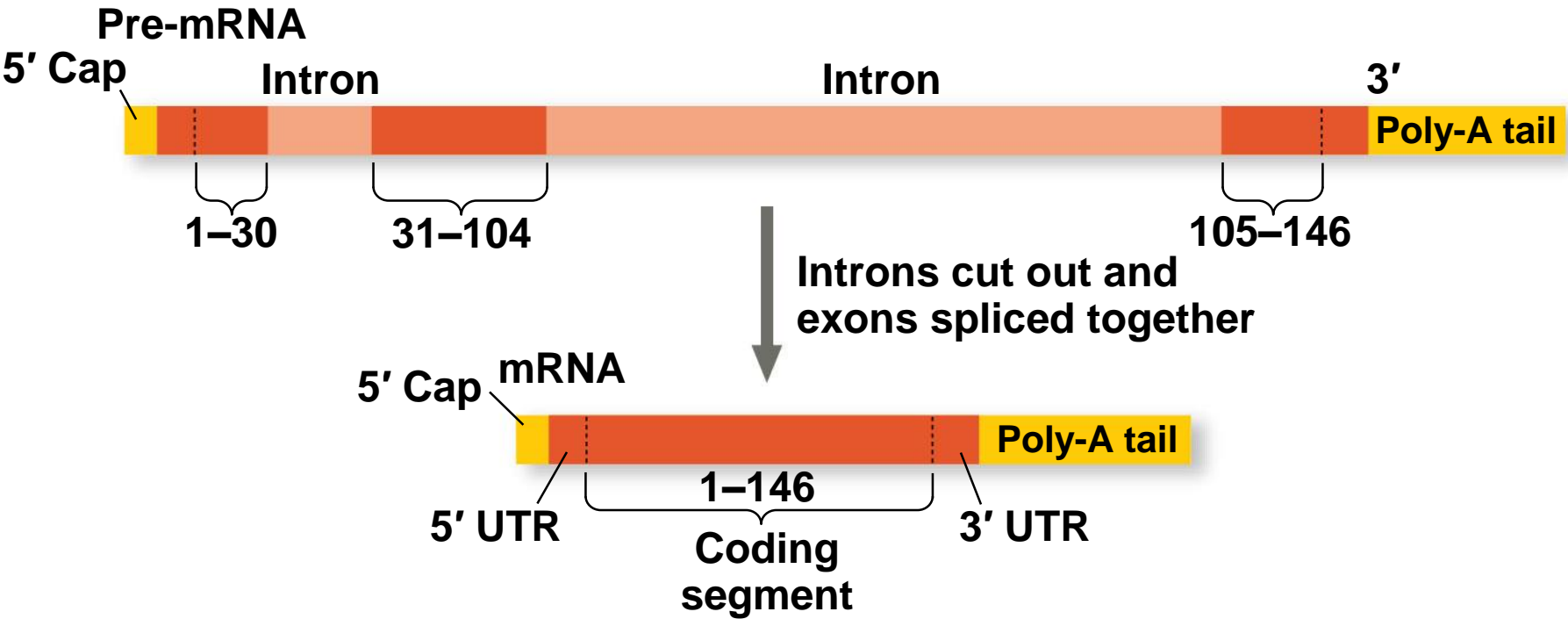
- In some cases, RNA splicing is carried out by spliceosomes

- **Spliceosomes** consist of a variety of proteins and several small RNAs that recognize the splice sites

- The RNAs of the spliceosome also catalyze the splicing reaction

Figure 17.13

Spliceosome

Small RNAs

5′

Pre-mRNA

Exon 1

Intron

Exon 2

Spliceosome
components

mRNA

Cut-out
intron

5′

Exon 1   Exon 2
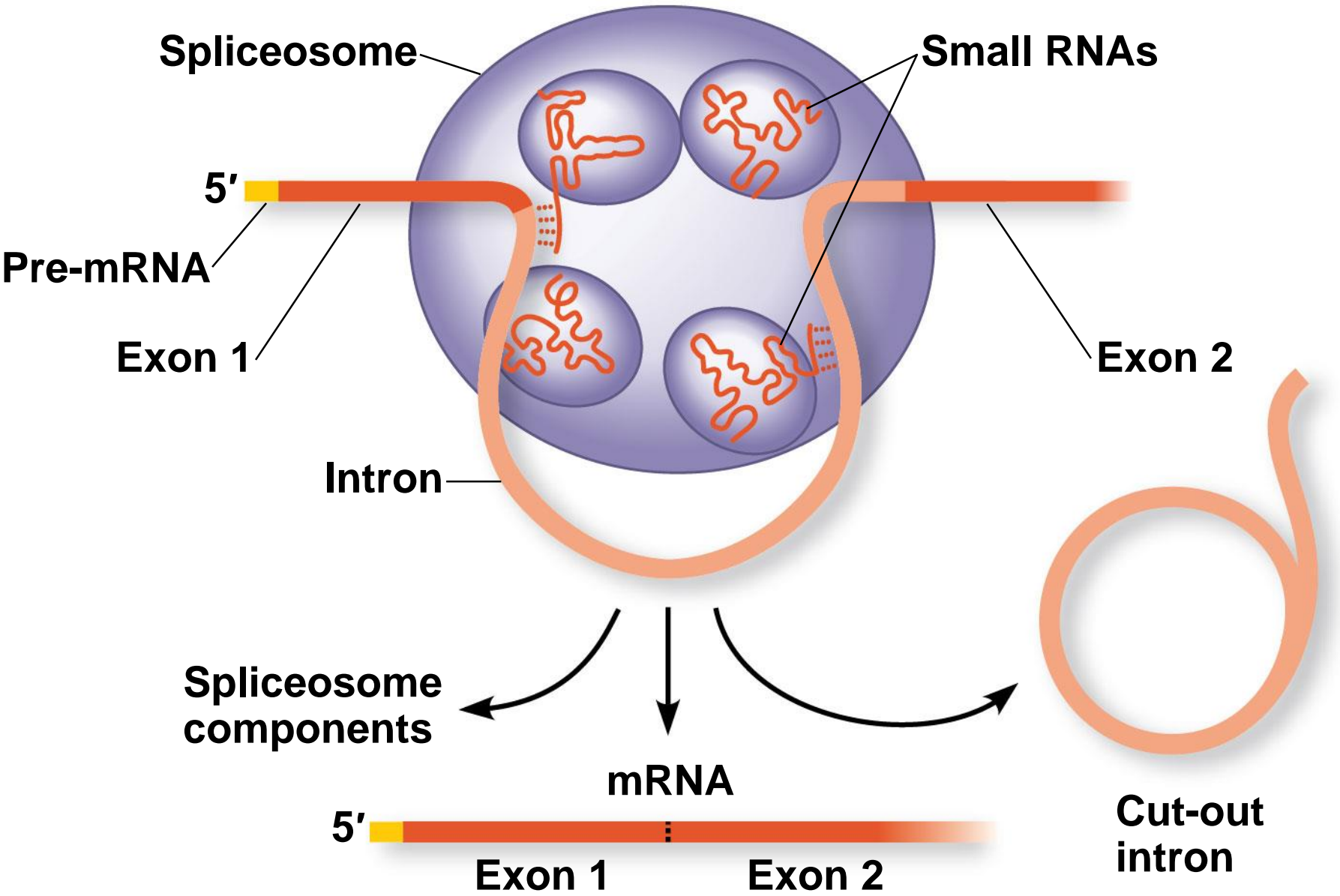
Ribozymes

- **Ribozymes** are catalytic RNA molecules that function as enzymes and can splice RNA

- The discovery of ribozymes rendered obsolete the belief that all biological catalysts were proteins

- Three properties of RNA enable it to function as an enzyme
  - It can form a three-dimensional structure because of its ability to base-pair with itself
  - Some bases in RNA contain functional groups that may participate in catalysis
  - RNA may hydrogen-bond with other nucleic acid molecules

The Functional and Evolutionary Importance of Introns

- Some introns contain sequences that may regulate gene expression

- Some genes can encode more than one kind of polypeptide, depending on which segments are treated as exons during splicing

- This is called **alternative RNA splicing**

- Consequently, the number of different proteins an organism can produce is much greater than its number of genes

- Proteins often have a modular architecture consisting of discrete regions called **domains**

- In many cases, different exons code for the different domains in a protein

- Exon shuffling may result in the evolution of new proteins

Figure 17.14

Gene

DNA

| Exon 1 | Intron | Exon 2 | Intron | Exon 3 |

Transcription

RNA processing

Translation

Domain 3

Domain 2

Domain 1
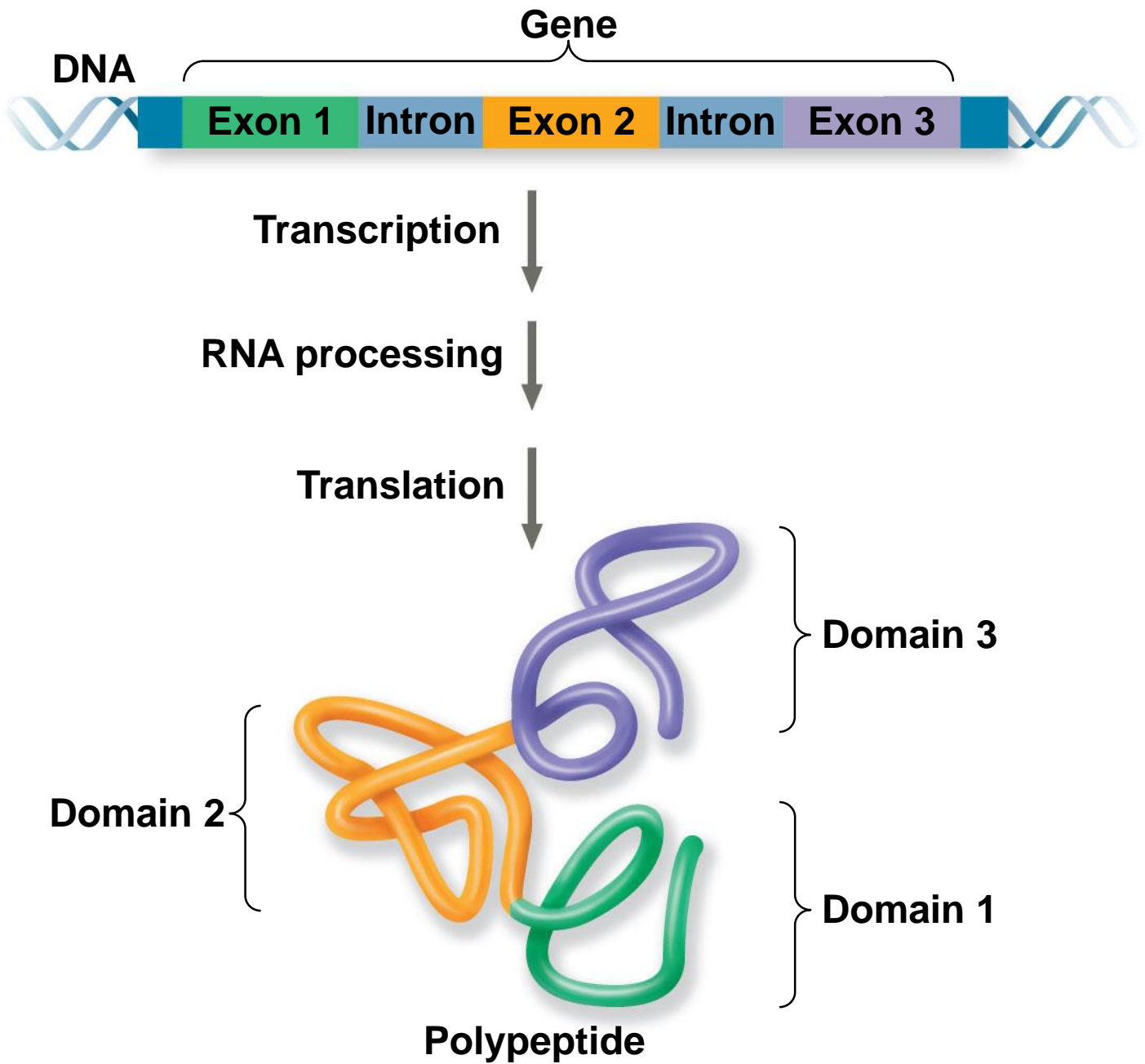
Polypeptide

Concept 17.4: Translation is the RNA-directed synthesis of a polypeptide: *a closer look*

- Genetic information flows from mRNA to protein through the process of translation

Molecular Components of Translation

- A cell translates an mRNA message into protein with the help of **transfer RNA (tRNA)**

- tRNAs transfer amino acids to the growing polypeptide in a ribosome

- Translation is a complex process in terms of its biochemistry and mechanics

Figure 17.15

Polypeptide

Amino acids

tRNA with amino acid attached

Ribosome

Trp

Phe

Gly

tRNA

Anticodon

A C C

A A A

C C G

U G G U U U G G C

Codons

5′

mRNA

3′
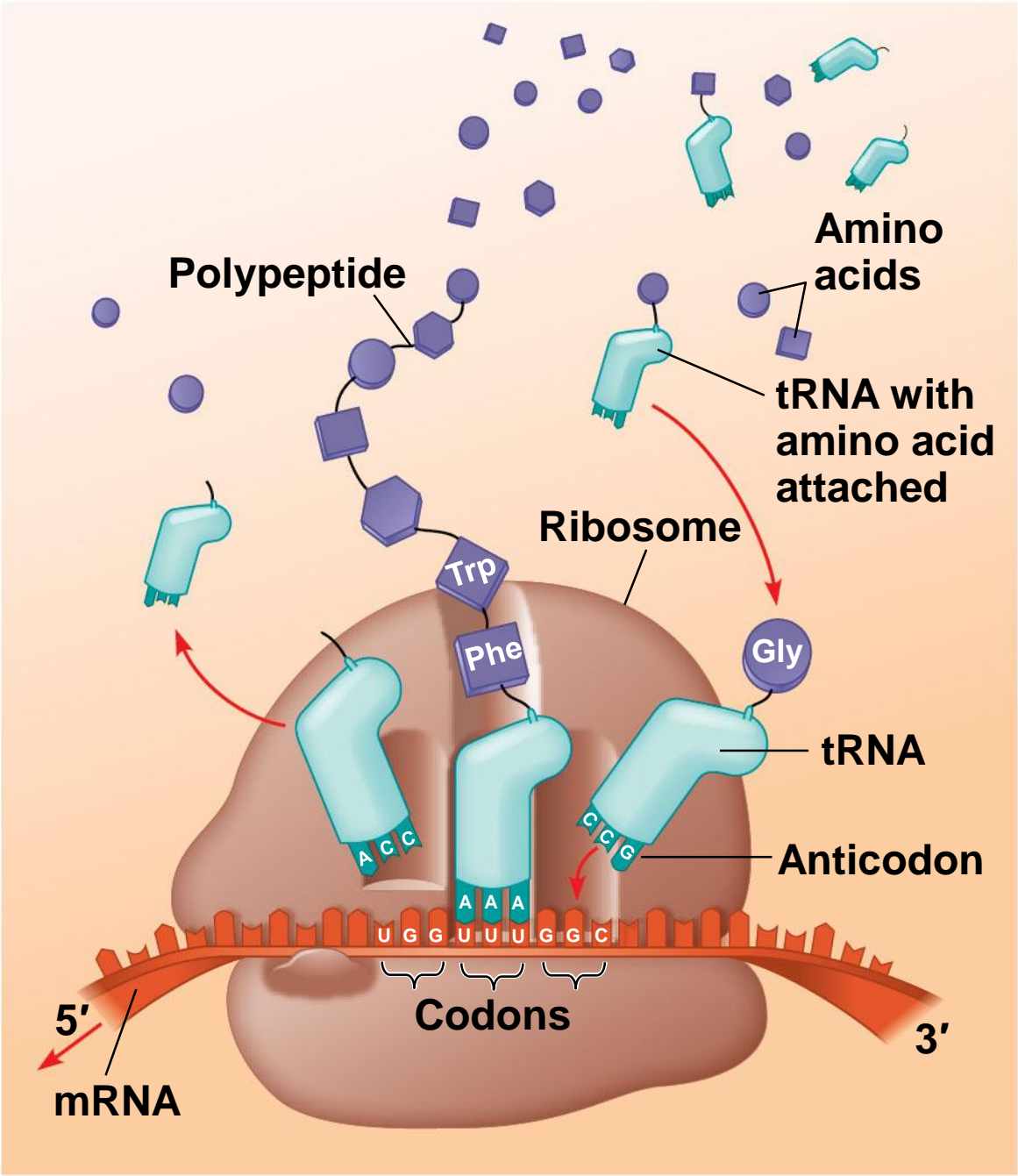
The Structure and Function of Transfer RNA

- Each tRNA molecule enables translation of a given mRNA codon into a certain amino acid
  - Each carries a specific amino acid on one end
  - Each has an **anticodon** on the other end; the anticodon base-pairs with a complementary codon on mRNA

- A tRNA molecule consists of a single RNA strand that is only about 80 nucleotides long

- Flattened into one plane to reveal its base pairing, a tRNA molecule looks like a cloverleaf

- Because of hydrogen bonds, tRNA actually twists and folds into a three-dimensional molecule

- tRNA is roughly L-shaped with the 5' and 3' ends both located near one end of the structure

- The protruding 3' end acts as an attachment site for an amino acid

Figure 17.16
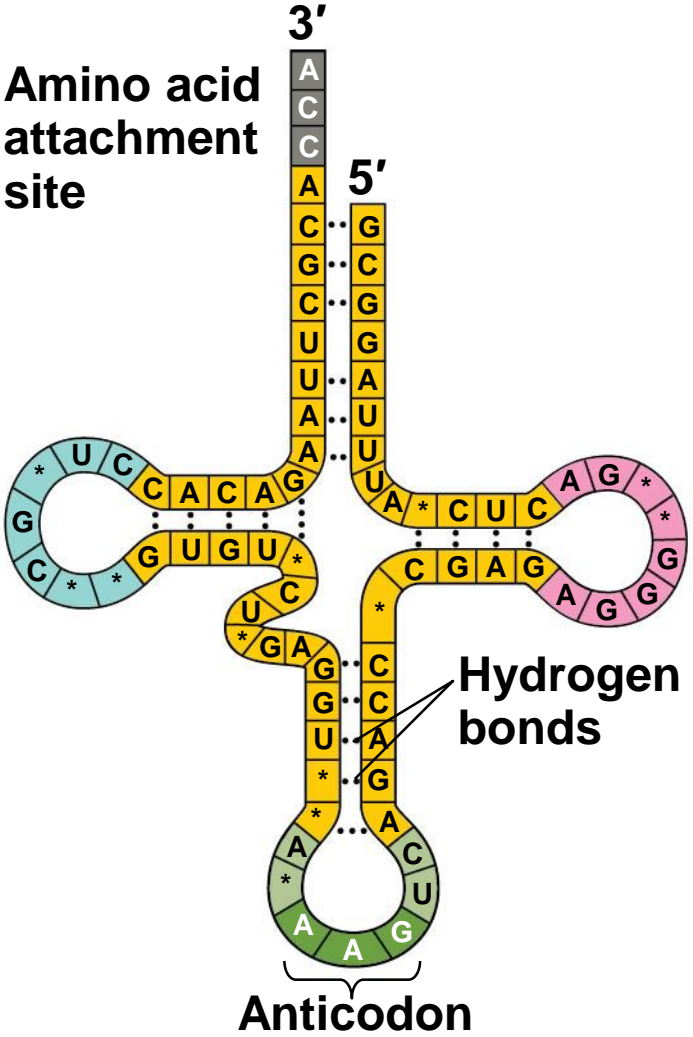
Amino acid attachment site
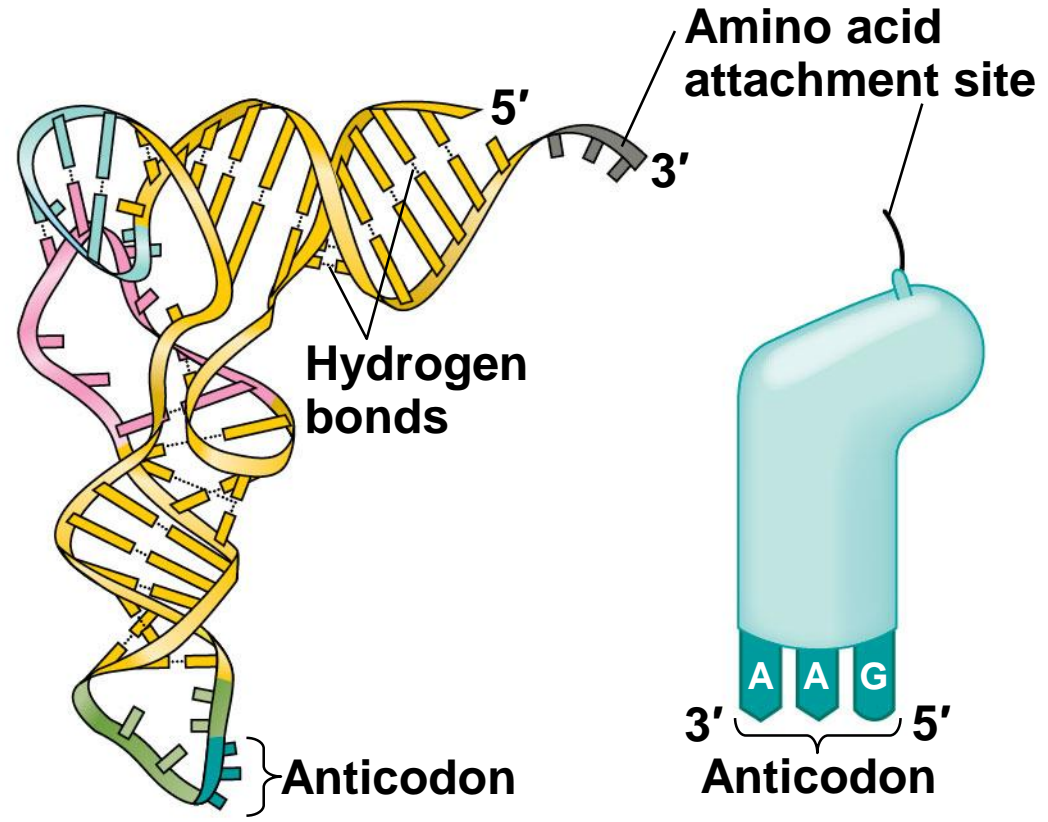
3′

5′

Hydrogen bonds

Anticodon

(a) Two-dimensional structure

Amino acid attachment site

5′

3′

Hydrogen bonds

Anticodon

(b) Three-dimensional structure

Amino acid attachment site

A A G

3′   5′

Anticodon

(c) Symbol used in this book

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Figure 17.16a

Amino acid attachment site

3′

5′

Hydrogen bonds

Anticodon

(a) Two-dimensional structure

Figure 17.16b

Amino acid
attachment site

5′

3′

Hydrogen
bonds

Anticodon

**(b) Three-dimensional
structure**

A A G

3′   5′
Anticodon
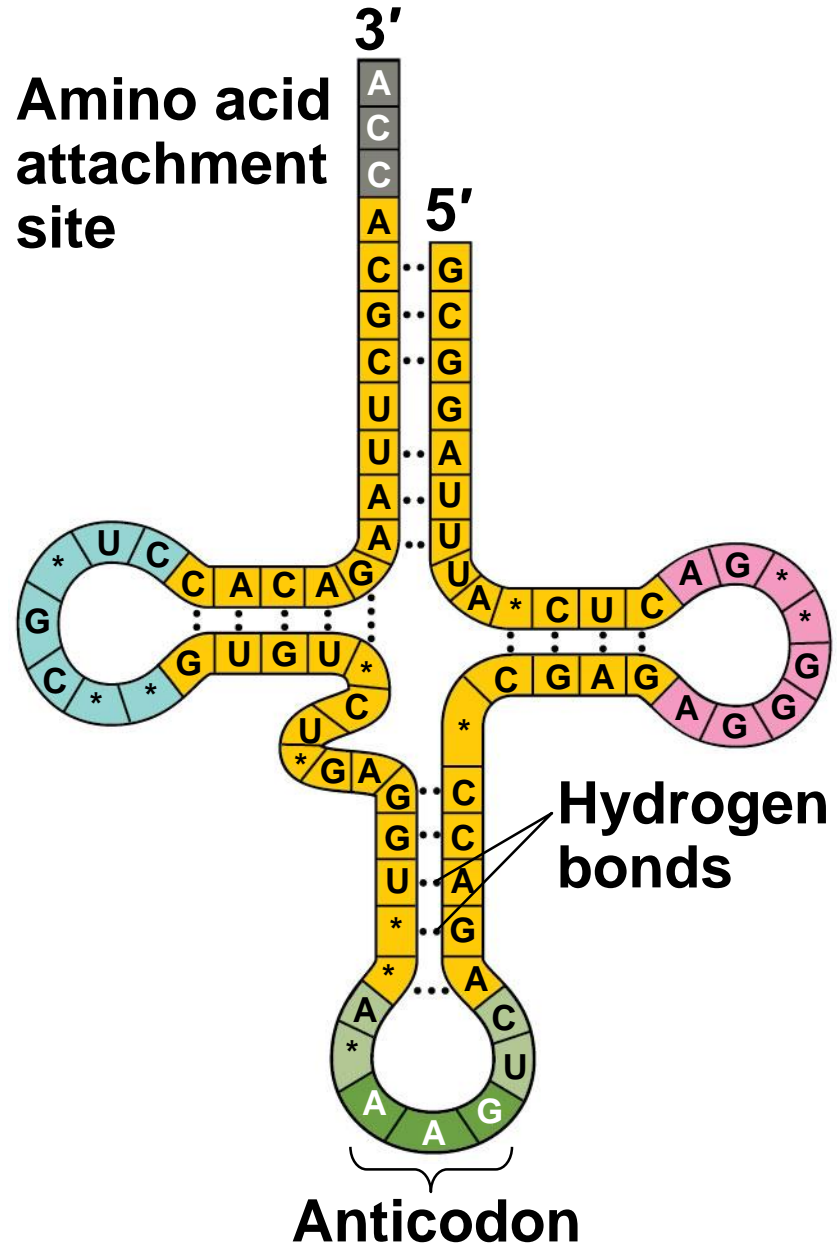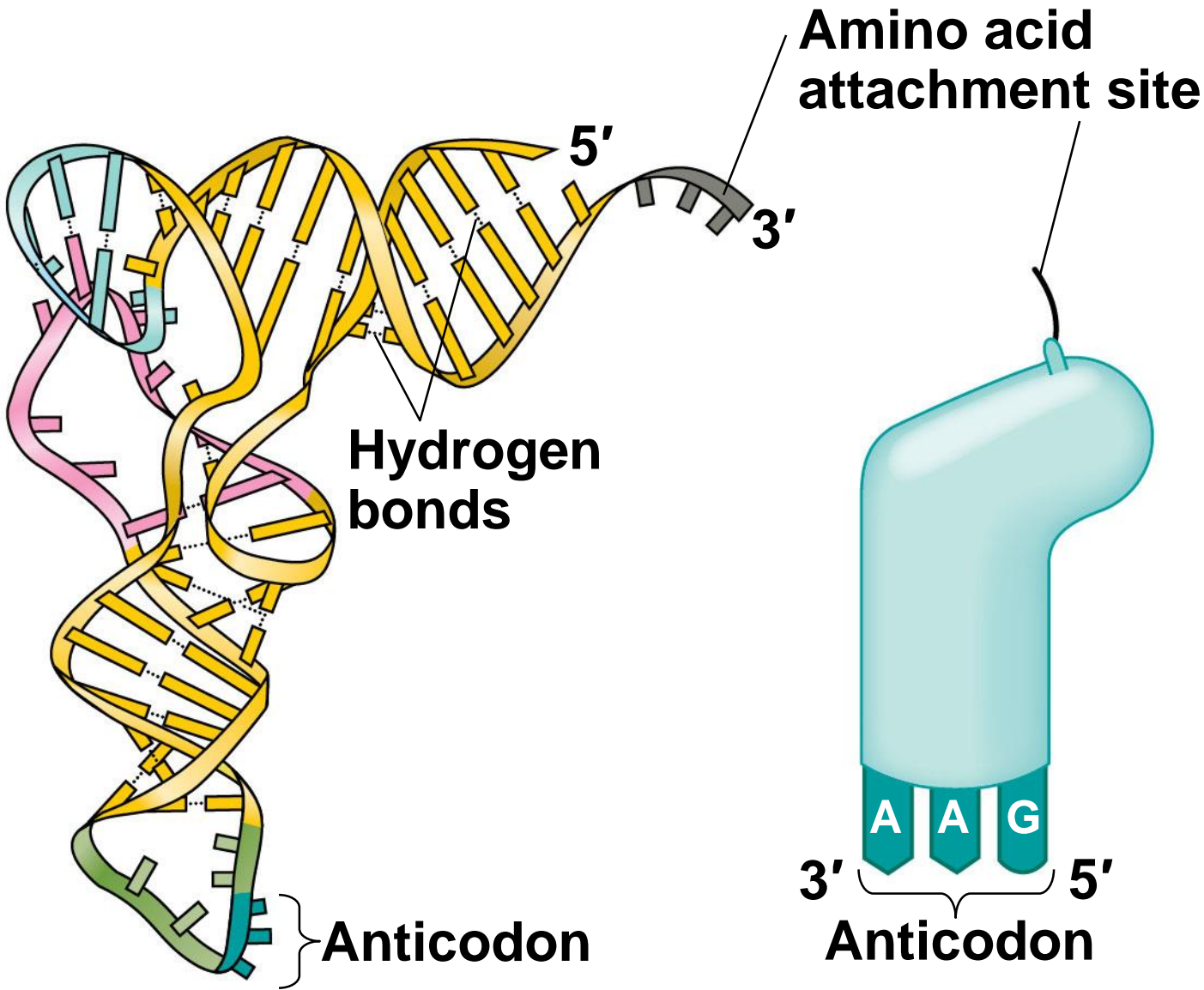
**(c) Symbol used
in this book**

Video: Stick and Ribbon Rendering of a tRNA
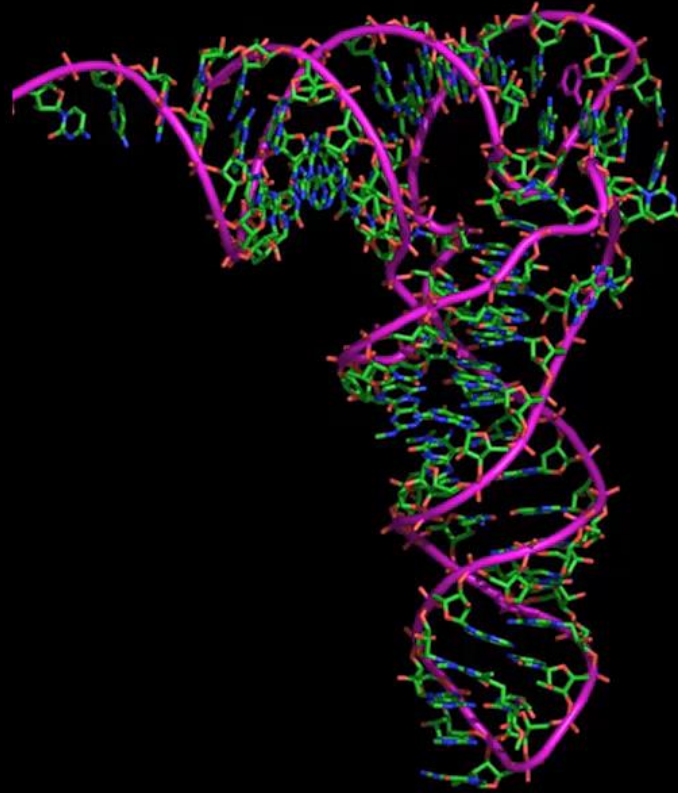
Credit: Jeff Hardin, University of Wisconsin-Madison.

- Accurate translation requires two steps
  - First: a correct match between a tRNA and an amino acid, done by the enzyme **aminoacyl-tRNA synthetase**
  - Second: a correct match between the tRNA anticodon and an mRNA codon
- Flexible pairing at the third base of a codon is called **wobble** and allows some tRNAs to bind to more than one codon

Figure 17.17_1

Tyrosine (Tyr)
(amino acid)

1 **Amino acid and tRNA enter active site.**

Tyrosyl-tRNA synthetase

Tyr-tRNA

A U A

Complementary tRNA anticodon

Figure 17.17_2

1 **Amino acid and tRNA enter active site.**

Tyrosine (Tyr) (amino acid)

Tyrosyl-tRNA synthetase

Tyr-tRNA

Aminoacyl-tRNA synthetase

A U A

Complementary tRNA anticodon

ATP

AMP + 2 P_i

tRNA

Amino acid

2 **Using ATP, synthetase catalyzes covalent bonding.**

Computer model

Figure 17.17_3

Tyrosine (Tyr) (amino acid)

Tyrosyl-tRNA synthetase

1 **Amino acid and tRNA enter active site.**

Tyr-tRNA

A U A

Complementary tRNA anticodon

ATP

AMP + **2 P**$_i$

Aminoacyl-tRNA synthetase

tRNA

Amino acid

3 **Aminoacyl tRNA released.**

2 **Using ATP, synthetase catalyzes covalent bonding.**

Computer model

Figure 17.17a

Aminoacyl-tRNA synthetase

tRNA

Amino acid

Computer model

The Structure and Function of Ribosomes

- Ribosomes facilitate specific coupling of tRNA anticodons with mRNA codons in protein synthesis

- The two ribosomal subunits (large and small) are made of proteins and **ribosomal RNA (rRNA)**

- Bacterial and eukaryotic ribosomes are somewhat similar but have significant differences

- Some antibiotic drugs specifically target bacterial ribosomes without harming eukaryotic ribosomes

- A ribosome has three binding sites for tRNA
  - The **P site** holds the tRNA that carries the growing polypeptide chain
  - The **A site** holds the tRNA that carries the next amino acid to be added to the chain
  - The **E site** is the exit site, where discharged tRNAs leave the ribosome

Figure 17.18
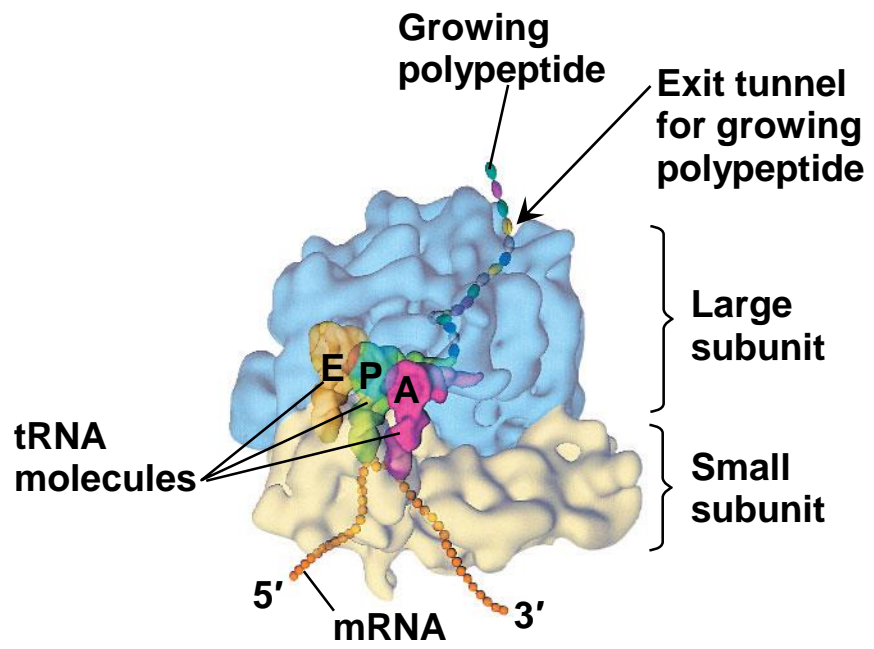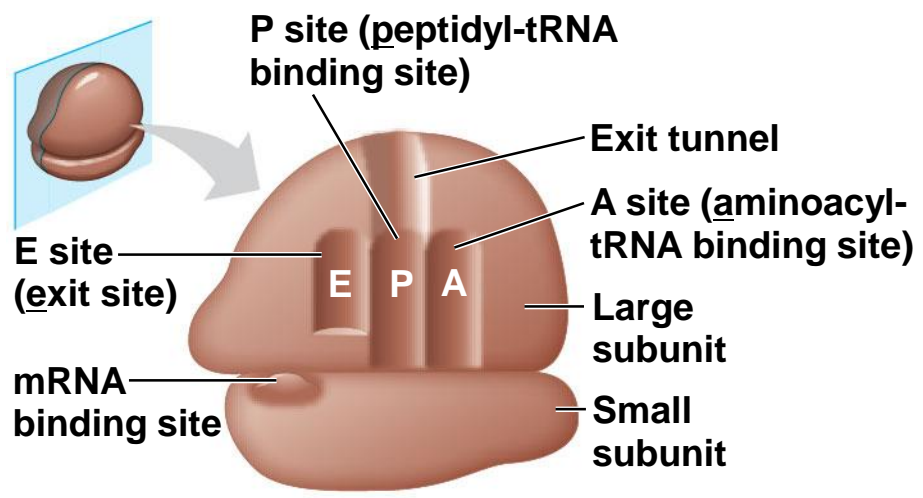
Growing polypeptide

Exit tunnel for growing polypeptide

Large subunit

E P A

tRNA molecules

Small subunit

5′

mRNA

3′

(a) Computer model of functioning ribosome

P site (peptidyl-tRNA binding site)

Exit tunnel

A site (aminoacyl-tRNA binding site)

E site (exit site)

E P A

Large subunit

mRNA binding site

Small subunit

(b) Schematic model showing binding sites

Amino end

Growing polypeptide

Carboxyl end

Next amino acid to be added to polypeptide chain

E

mRNA

tRNA

3′

5′

Codons

(c) Schematic model with mRNA and tRNA

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Figure 17.18a

Growing polypeptide

Exit tunnel for growing polypeptide

Large subunit

E P A

tRNA molecules

Small subunit

5′

mRNA

3′
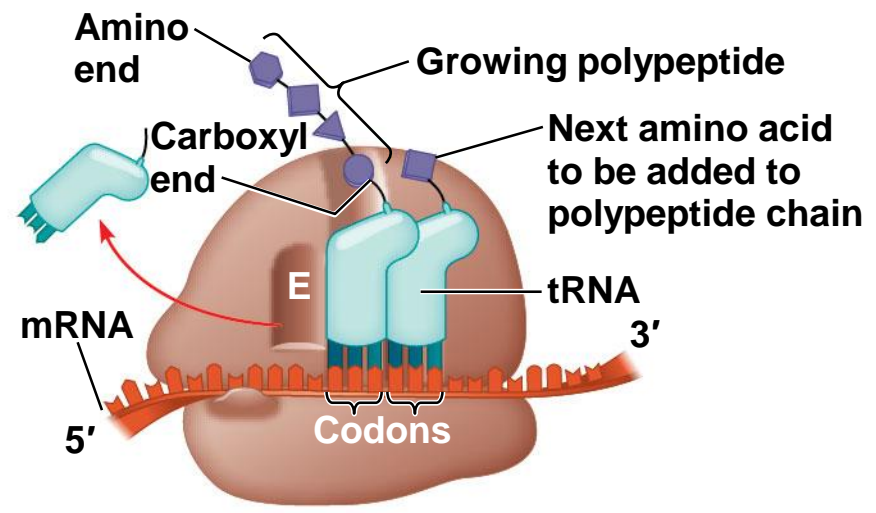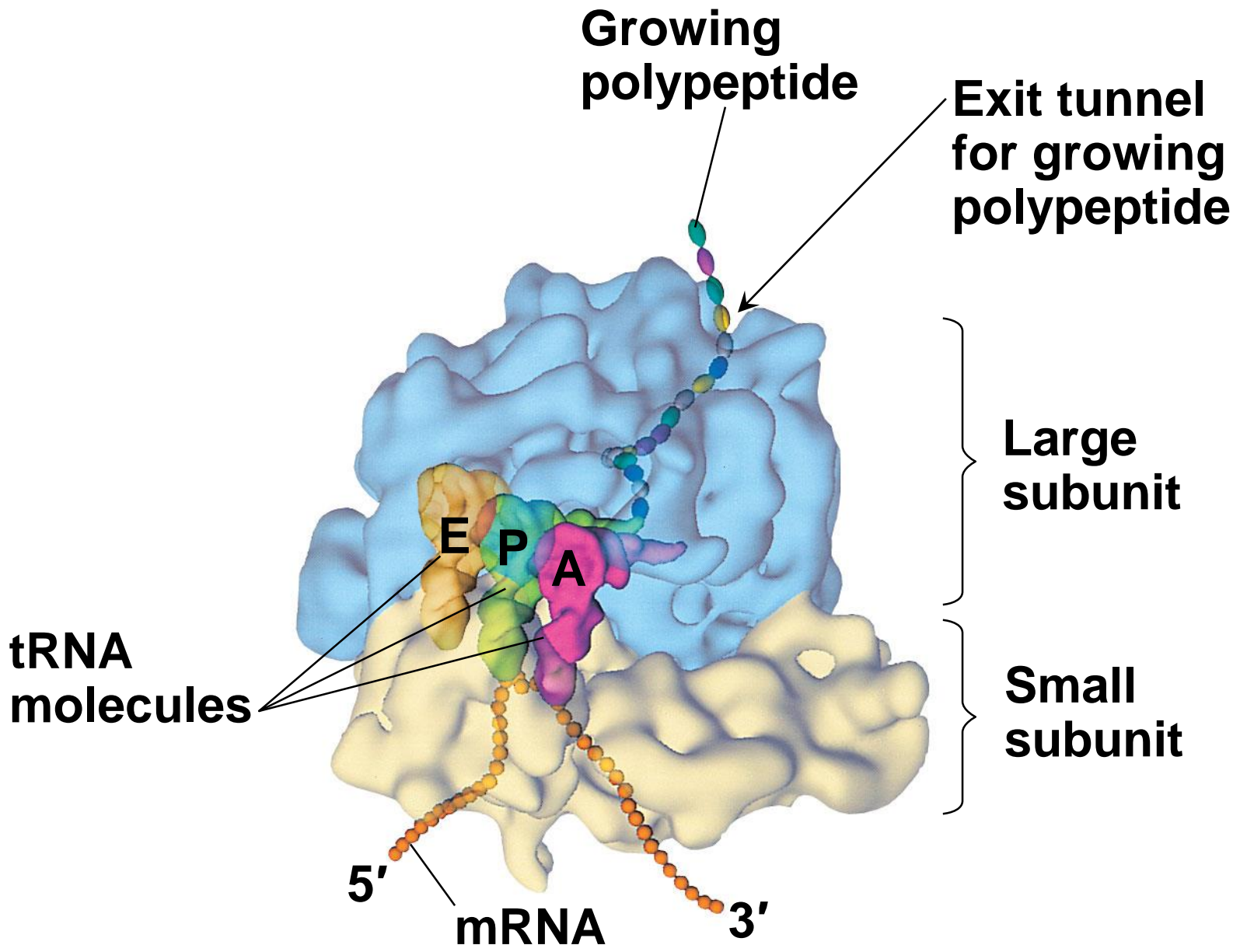
(a) Computer model of functioning ribosome

Figure 17.18b

P site (peptidyl-tRNA binding site)

Exit tunnel

E site (exit site)

A site (aminoacyl-tRNA binding site)

E   P   A

Large subunit

mRNA binding site

Small subunit
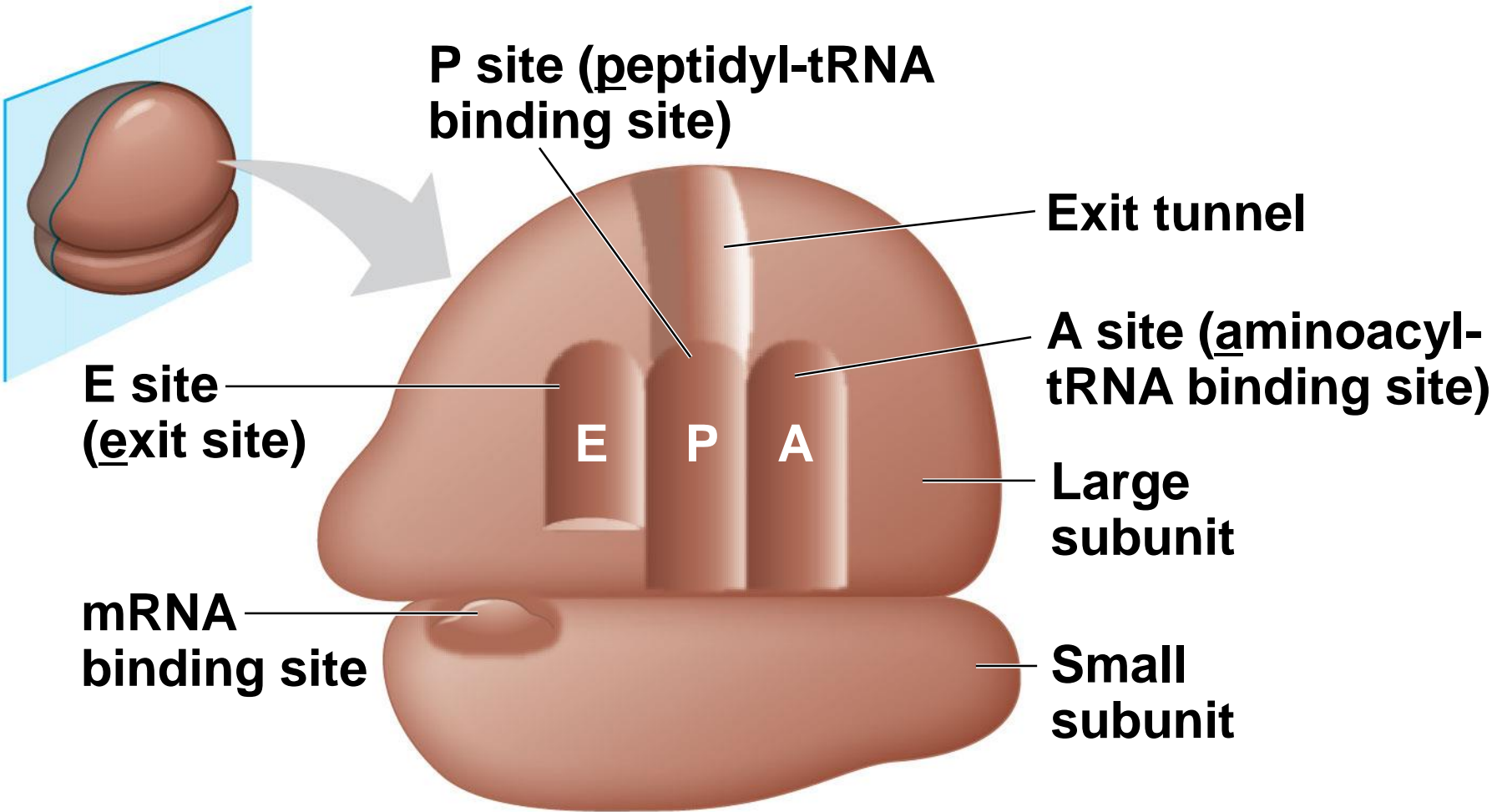
(b) Schematic model showing binding sites

Figure 17.18c

Amino end

Growing polypeptide

Carboxyl end

Next amino acid to be added to polypeptide chain

E

tRNA

mRNA

3′

5′

Codons
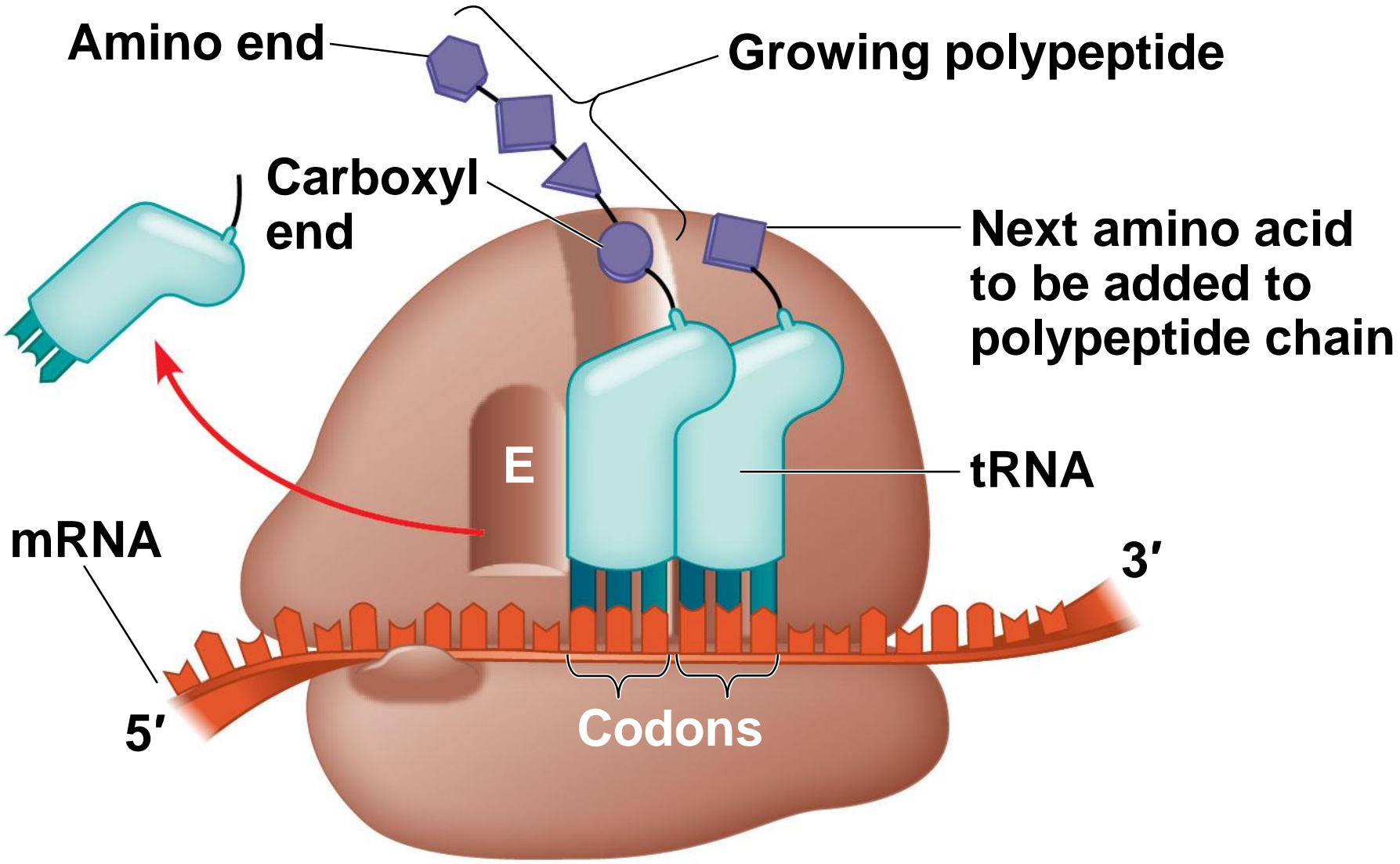
(c) Schematic model with mRNA and tRNA

Building a Polypeptide

- The three stages of translation:
  - Initiation
  - Elongation
  - Termination
- All three stages require protein "factors" that aid in the translation process
- Energy is required for some steps, too

Ribosome Association and Initiation of Translation

- The start codon (AUG) signals the start of translation

- First, a small ribosomal subunit binds with mRNA and a special initiator tRNA

- Then the small subunit moves along the mRNA until it reaches the start codon

- Proteins called initiation factors bring in the large subunit that completes the translation initiation complex

Figure 17.19

Initiator tRNA

mRNA

5′

Met

3′U A C 5′
5′A U G 3′

Start codon

mRNA binding site

Small ribosomal subunit
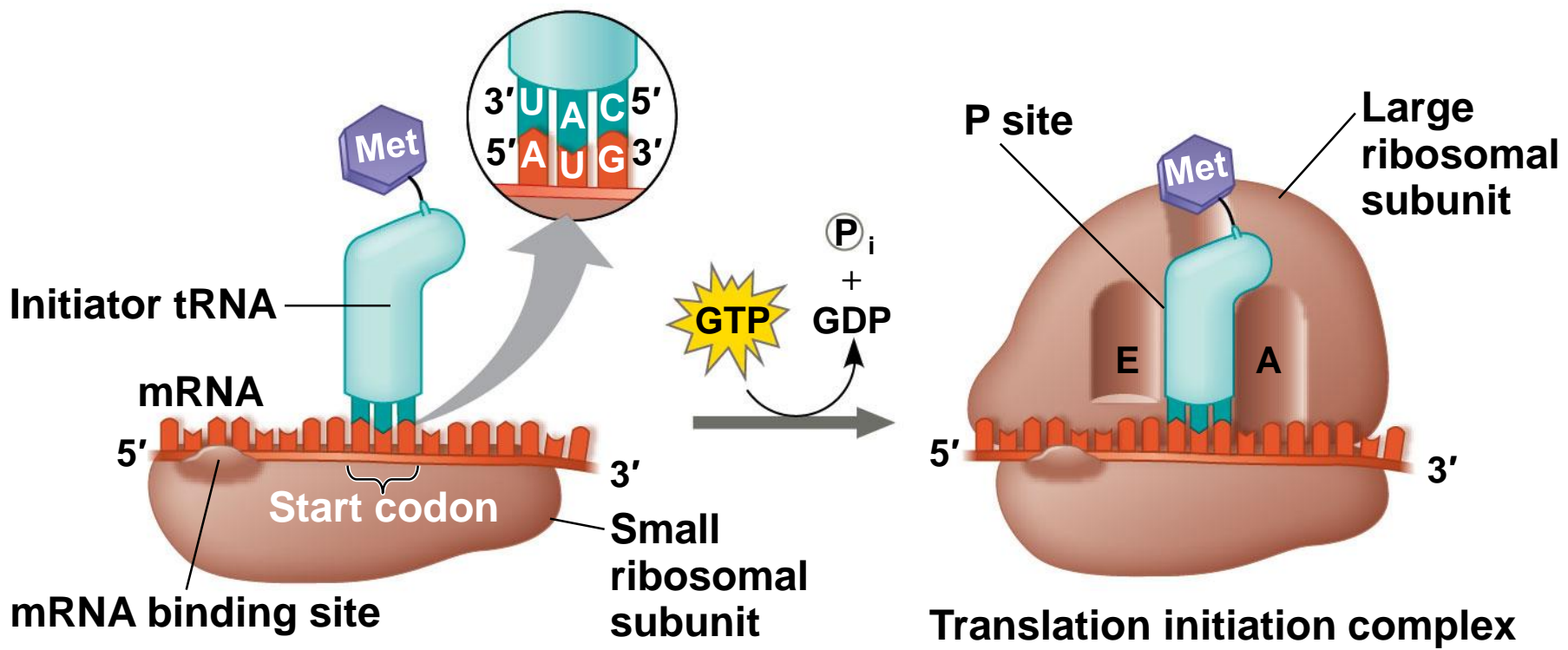
1 Small ribosomal subunit binds to mRNA.

GTP + GDP

P_i +

P site

Met

Large ribosomal subunit

5′   3′

E   A

Translation initiation complex

2 Large ribosomal subunit completes the initiation complex.

Elongation of the Polypeptide Chain

- During elongation, amino acids are added one by one to the C-terminus of the growing chain

- Each addition involves proteins called elongation factors

- Elongation occurs in three steps: codon recognition, peptide bond formation, and translocation

- Energy expenditure occurs in the first and third steps

- Translation proceeds along the mRNA in a $5' \rightarrow 3'$ direction

- The ribosome and mRNA move relative to each other, codon by codon

- The elongation cycles takes less than a tenth of a second in bacteria

Figure 17.20_1

Amino end
of polypeptide

Carboxyl end of
polypeptide

1 Codon recognition

E

mRNA

5′

3′

P   A
site site

GTP

GDP + P$_i$

E

P A

Figure 17.20_2

Amino end of polypeptide

Carboxyl end of polypeptide

1 Codon recognition

mRNA

3′

5′

E

P site A site

GTP

GDP + P_i

E

P A

2 Peptide bond formation

E

P A

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Figure 17.20_3

Amino end of polypeptide

Carboxyl end of polypeptide

1 Codon recognition

3′

E

P site A site

mRNA

Ribosome ready for next aminoacyl tRNA

5′

GTP

GDP + Pi

E

P A

2 Peptide bond formation

E

P A

3 Translocation

GDP + Pi

GTP

E

P A

Termination of Translation

- Elongation continues until a stop codon in the mRNA reaches the A site of the ribosome

- The A site accepts a protein called a release factor

- The release factor causes the addition of a water molecule instead of an amino acid

- This reaction releases the polypeptide, and the translation assembly comes apart

Figure 17.21_1

Release factor

3′

5′

Stop codon (UAG, UAA, or UGA)
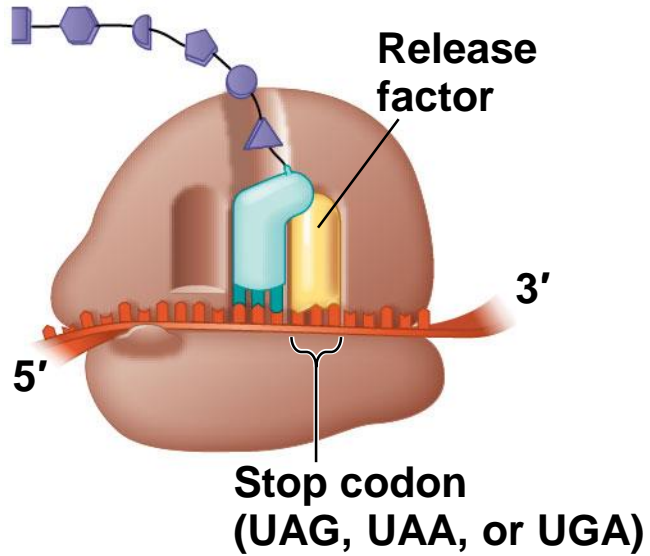
1 **Ribosome reaches a stop codon on mRNA.**

Figure 17.21_2

Release factor

Free polypeptide

3′

3′

5′

5′

Stop codon (UAG, UAA, or UGA)
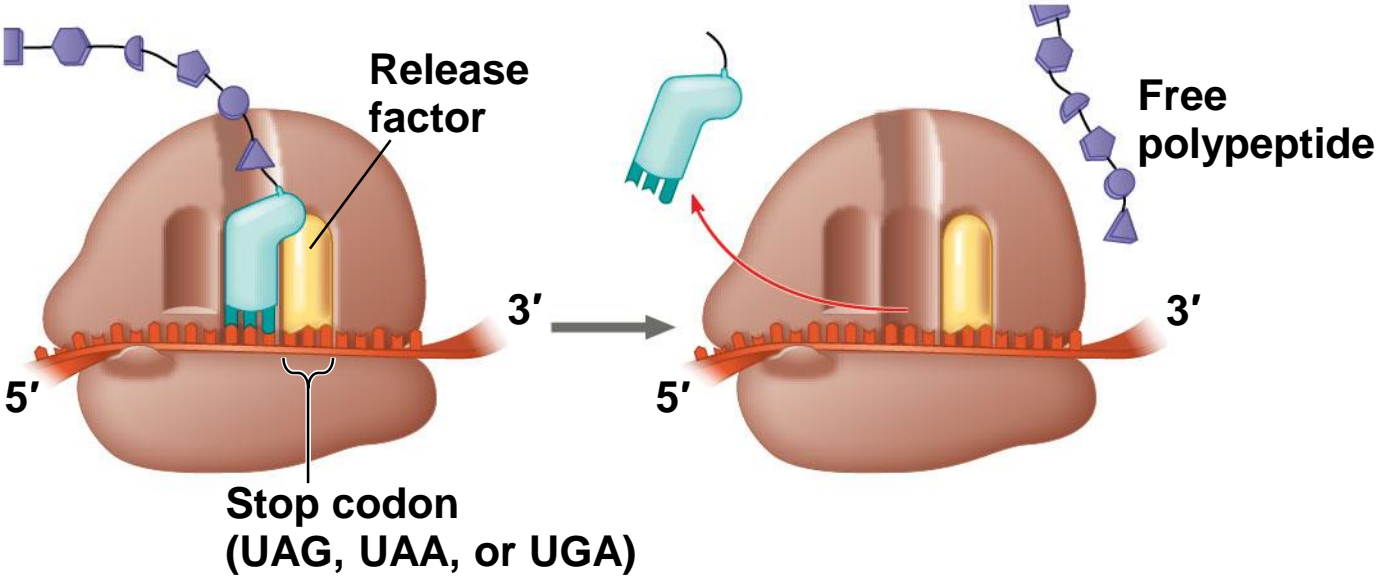
1 Ribosome reaches a stop codon on mRNA.

2 Release factor promotes hydrolysis.

Figure 17.21_3

Release factor

Free polypeptide

3′

3′

5′

5′

5′

3′

2 **GTP**

2 GDP + 2 P_i

Stop codon (UAG, UAA, or UGA)
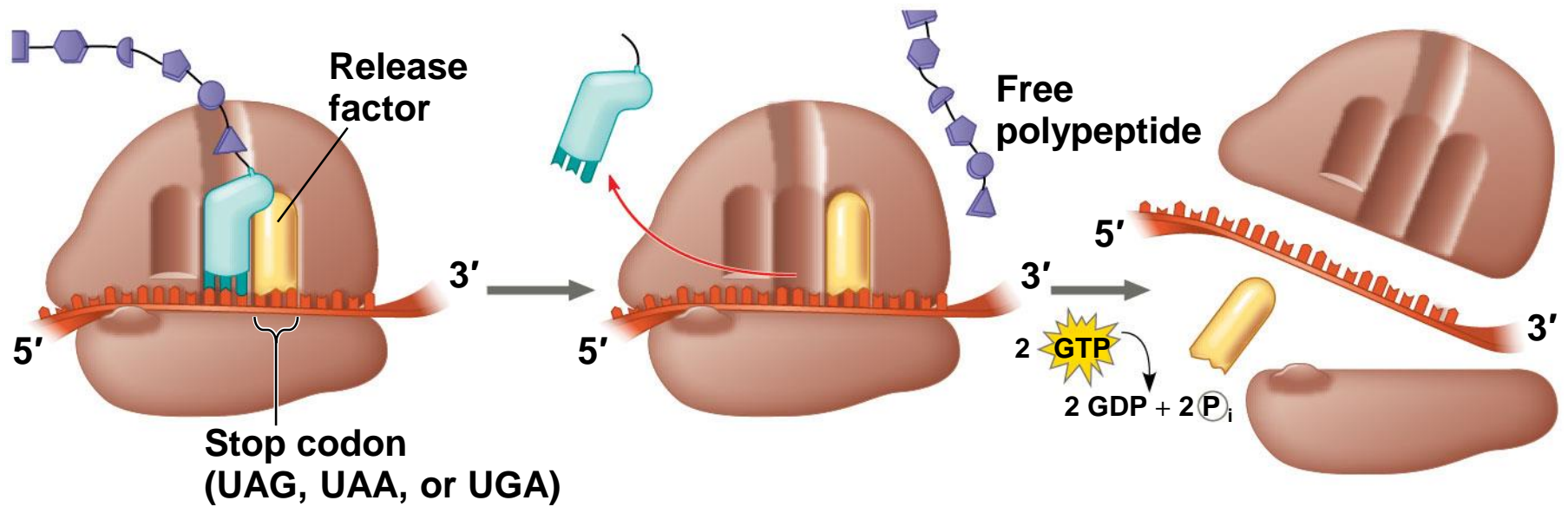
1 **Ribosome reaches a stop codon on mRNA.**

2 **Release factor promotes hydrolysis.**

3 **Ribosomal subunits and other components dissociate.**

Completing and Targeting the Functional Protein

- Often translation is not sufficient to make a functional protein

- Polypeptide chains are modified after translation or targeted to specific sites in the cell

Protein Folding and Post-Translational Modifications

- During its synthesis, a polypeptide chain begins to coil and fold spontaneously into a specific shape—a three-dimensional molecule with secondary and tertiary structure

- A gene determines primary structure, and primary structure in turn determines shape

- Post-translational modifications may be required before the protein can begin doing its particular job in the cell

Targeting Polypeptides to Specific Locations

- Two populations of ribosomes are evident in cells: free ribosomes (in the cytosol) and bound ribosomes (attached to the ER)

- Free ribosomes mostly synthesize proteins that function in the cytosol

- Bound ribosomes make proteins of the endomembrane system and proteins that are secreted from the cell

- Ribosomes are identical and can switch from free to bound

- Polypeptide synthesis always begins in the cytosol

- Synthesis finishes in the cytosol unless the polypeptide signals the ribosome to attach to the ER

- Polypeptides destined for the ER or for secretion are marked by a **signal peptide**

- A **signal-recognition particle (SRP)** binds to the signal peptide

- The SRP escorts the ribosome to a receptor protein built into the ER membrane

Figure 17.22

1 Polypeptide synthesis begins.

2 SRP binds to signal peptide.

3 SRP binds to receptor protein.

4 SRP detaches and polypeptide synthesis resumes.

5 Signal-cleaving enzyme cuts off signal peptide.

6 Completed polypeptide folds into final conformation.

Ribosome

mRNA

Signal peptide

SRP

Signal peptide removed

ER membrane

Protein

CYTOSOL

SRP receptor protein

ER LUMEN

Translocation complex

Making Multiple Polypeptides in Bacteria and Eukaryotes

- Multiple ribosomes can translate a single mRNA simultaneously, forming a **polyribosome** (or **polysome**)

- Polyribosomes enable a cell to make many copies of a polypeptide very quickly

Figure 17.23

Growing polypeptides

Incoming ribosomal subunits

Completed polypeptide

Polyribosome

Start of mRNA (5′ end)

End of mRNA (3′ end)
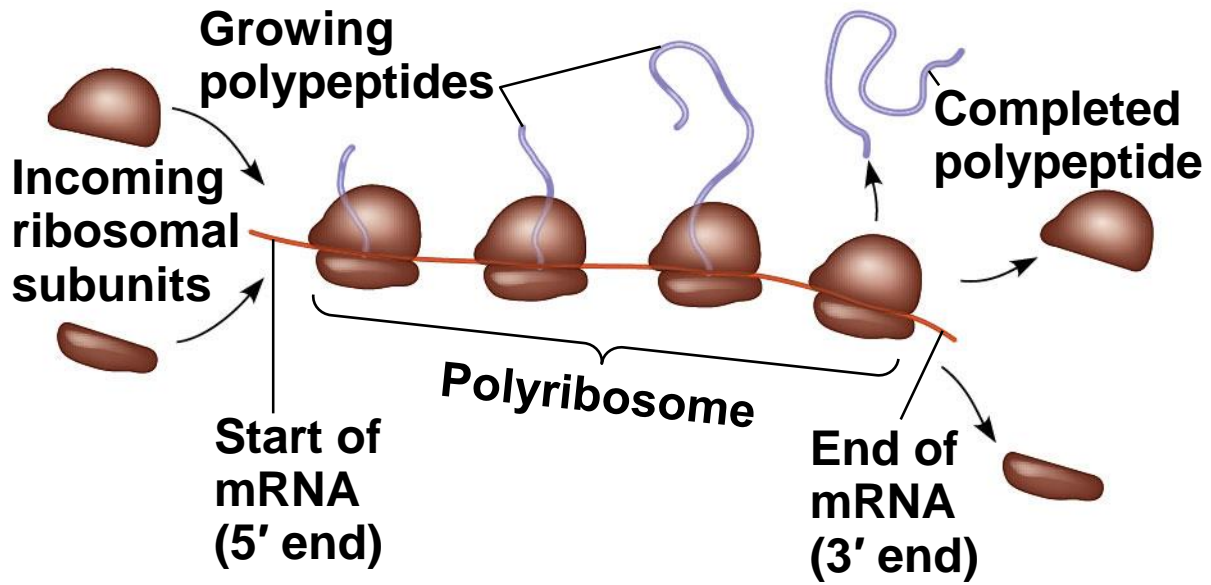
(a) Several ribosomes simultaneously translating one mRNA molecule
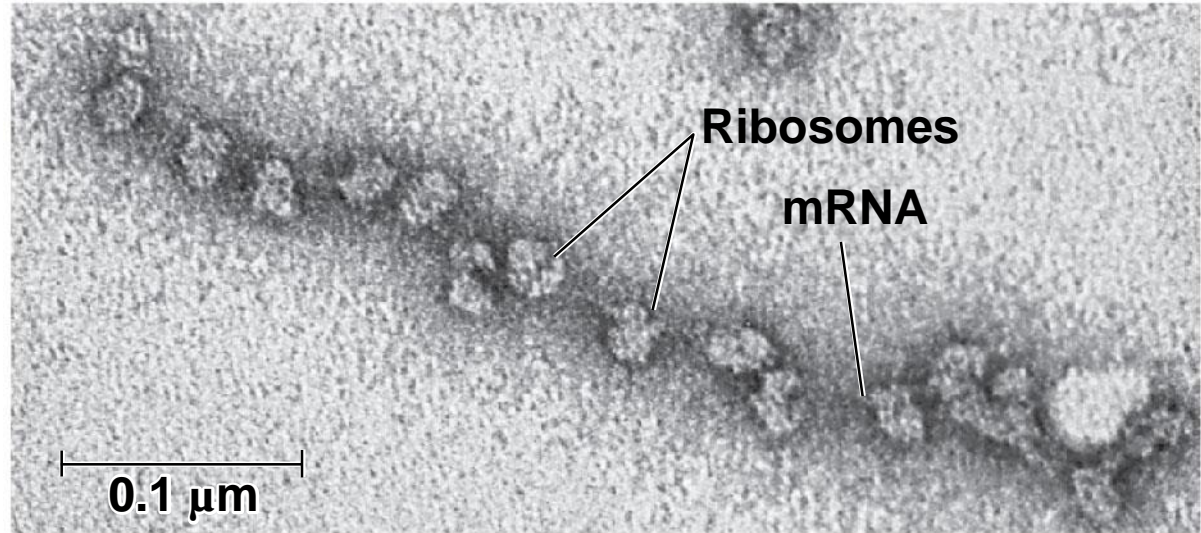
Ribosomes

mRNA

0.1 μm

(b) A large polyribosome in a bacterial cell (TEM)

Figure 17.23a

Ribosomes

mRNA

0.1 μm
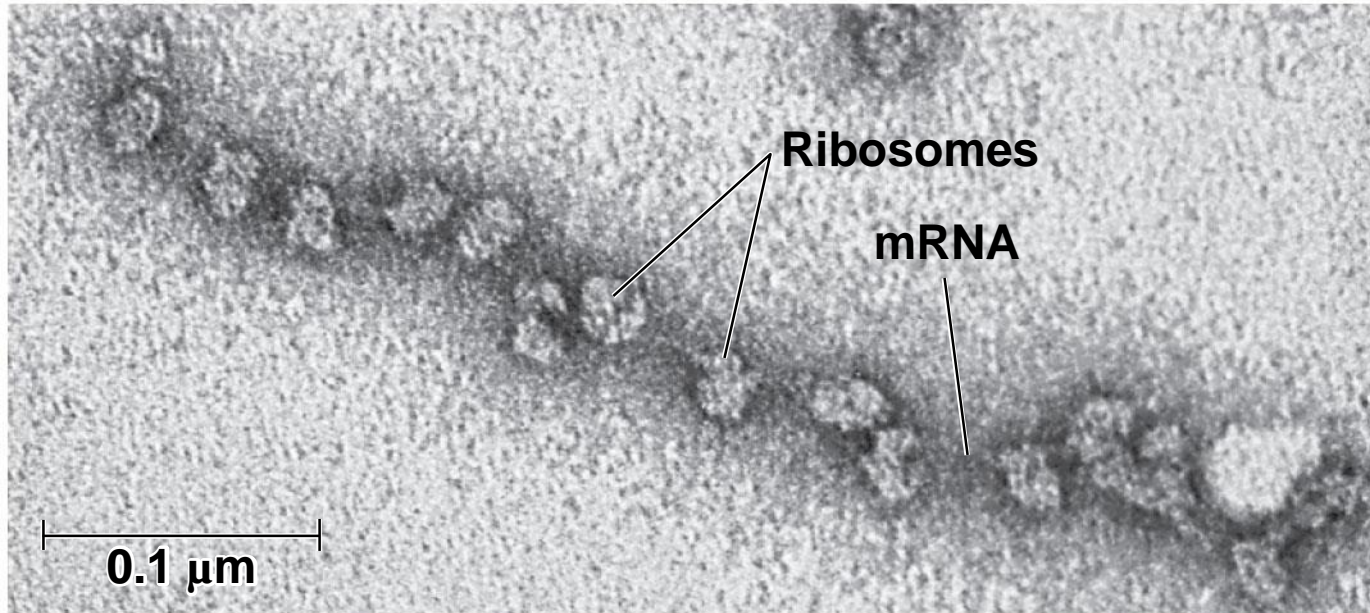
(b) A large polyribosome in a bacterial cell (TEM)

- A bacterial cell ensures a streamlined process by coupling transcription and translation

- In this case the newly made protein can quickly diffuse to its site of function

Figure 17.24

RNA polymerase

DNA

Polyribosome

0.25 μm

mRNA

RNA polymerase

Direction of transcription

DNA

Polyribosome

Polypeptide (amino end)

Ribosome

mRNA (5′ end)

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Figure 17.24a

RNA polymerase

DNA

Polyribosome

mRNA

0.25 μm
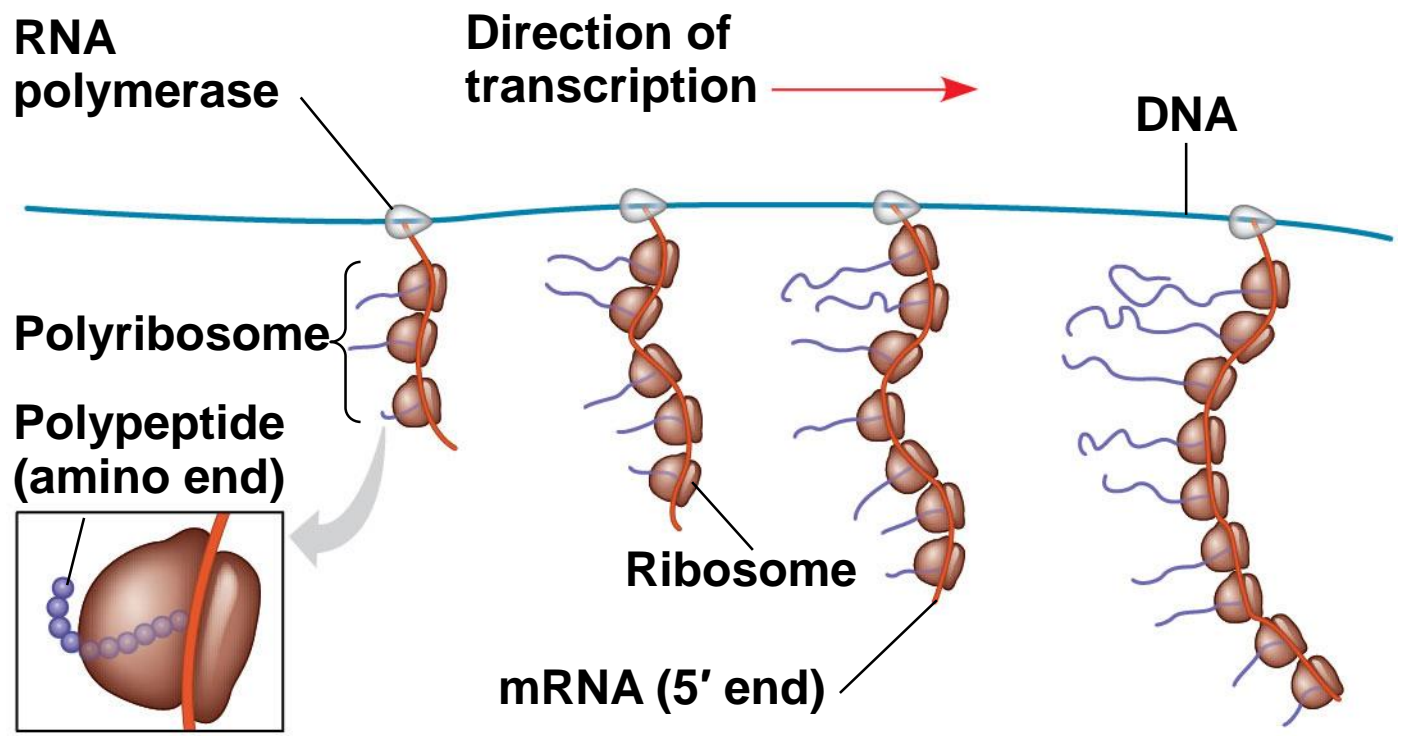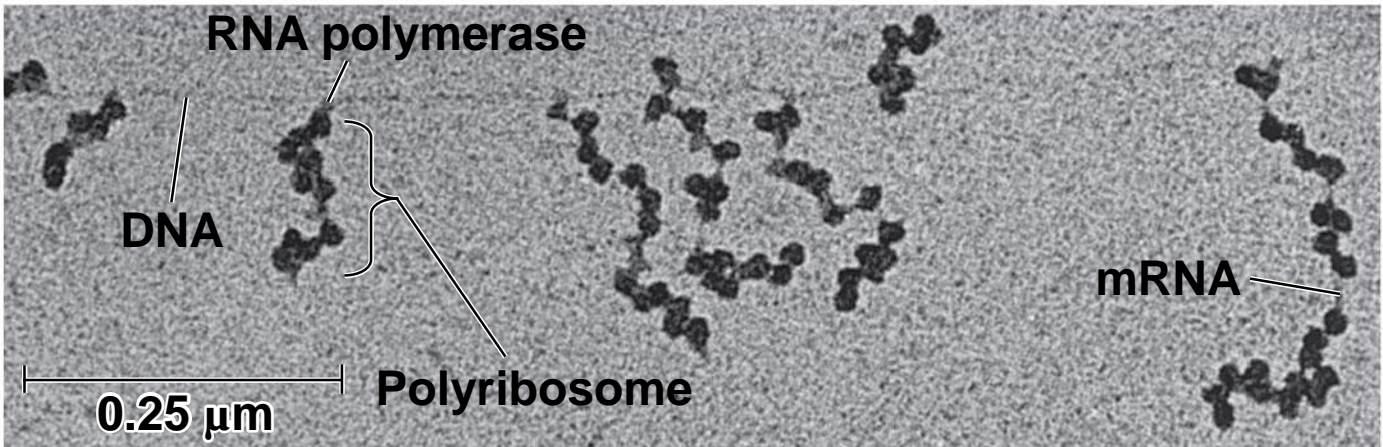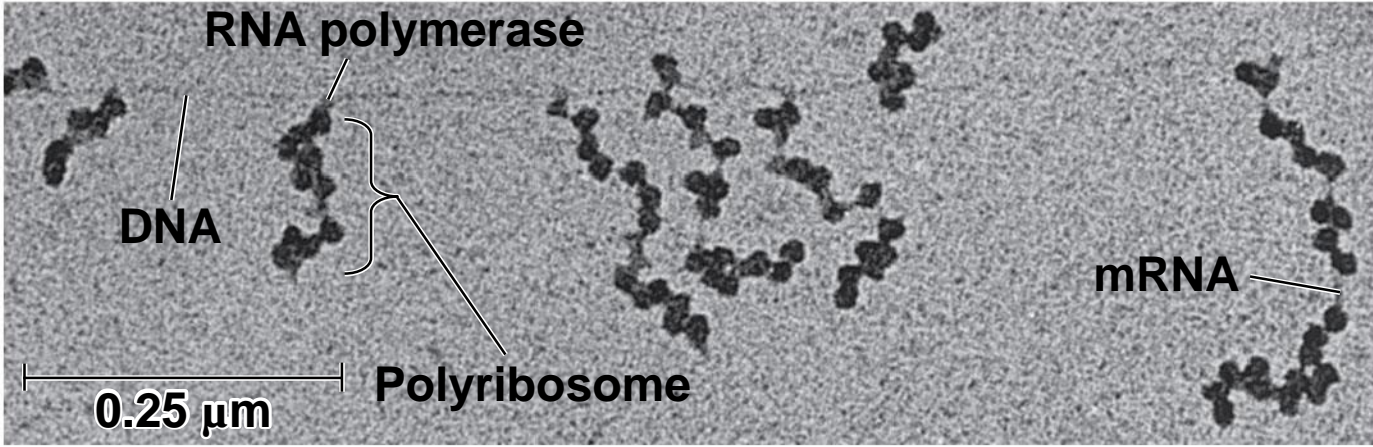
- In eukaryotes, the nuclear envelope separates the processes of transcription and translation

- RNA undergoes processing before leaving the nucleus

Figure 17.25

TRANSCRIPTION

DNA

5′ RNA transcript

RNA PROCESSING

Exon

RNA polymerase

3′

RNA transcript (pre-mRNA)

Intron

Poly-A

NUCLEUS

Poly-A

CYTOPLASM

Aminoacyl-tRNA synthetase

Amino acid

tRNA

AMINO ACID ACTIVATION

mRNA

5′ Cap

E P A

Ribosomal subunits

5′ Cap

Aminoacyl (charged) tRNA

3′

Poly-A

TRANSLATION

A C C

E

A A A

U G G U U U A U G

Codon

U A C

A

Anticodon

Ribosome

Figure 17.25a

TRANSCRIPTION

DNA

3′

5′

RNA polymerase

Poly-A

RNA transcript

RNA PROCESSING

Exon

RNA transcript (pre-mRNA)

Intron

Poly-A

NUCLEUS

Aminoacyl-tRNA synthetase

Amino acid

AMINO ACID ACTIVATION

CYTOPLASM

tRNA

mRNA

5′ Cap

Aminoacyl (charged) tRNA

Figure 17.25b

mRNA

Growing polypeptide

5′ Cap

3′

Poly-A

E P A

Ribosomal subunits

Aminoacyl (charged) tRNA

5′ Cap

TRANSLATION

A C C

E A

A A A

U G G U U U A U G

U A C

Anticodon

Codon

Ribosome

BioFlix Animation: Protein Synthesis
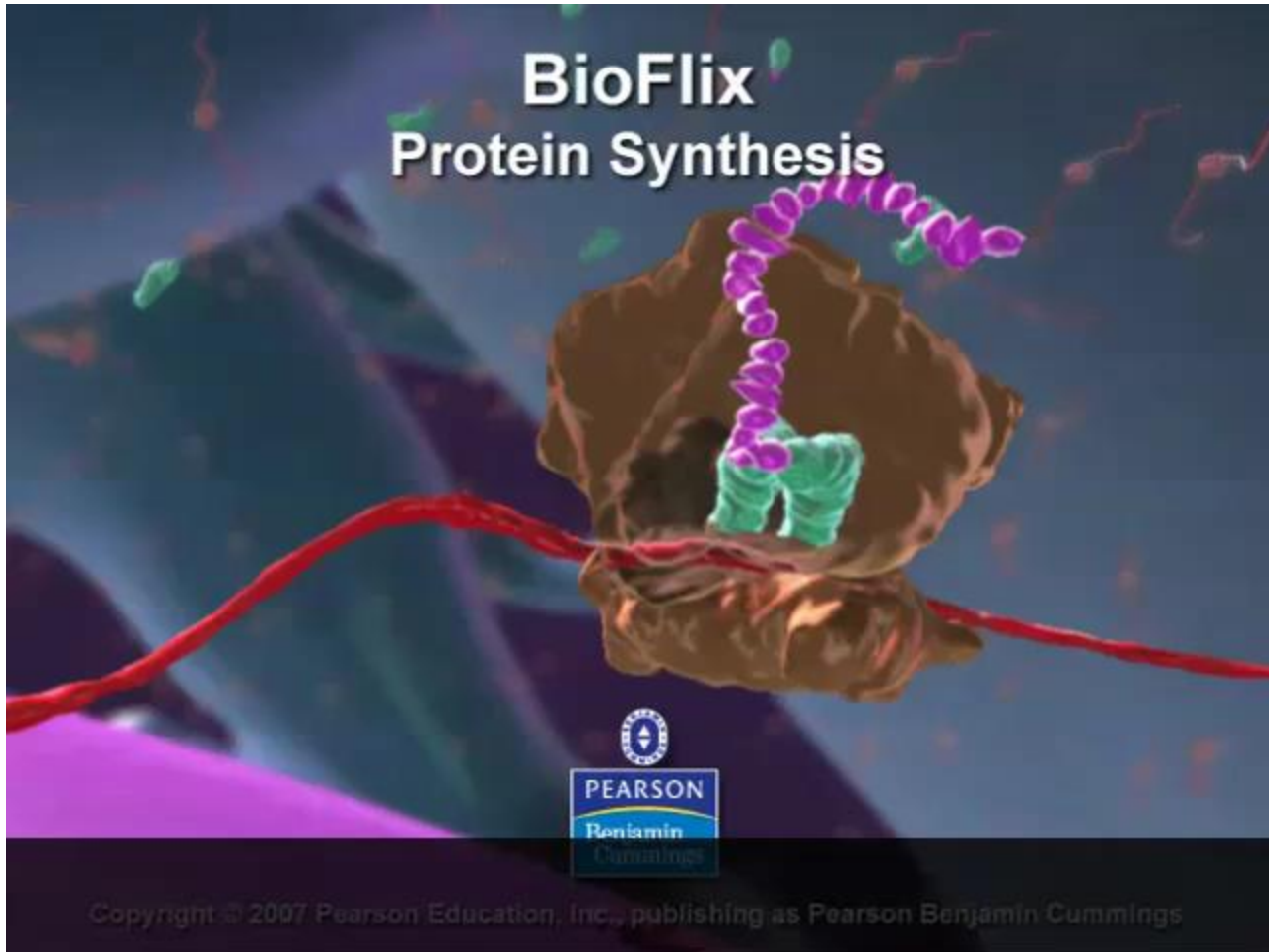
Animation: Translation
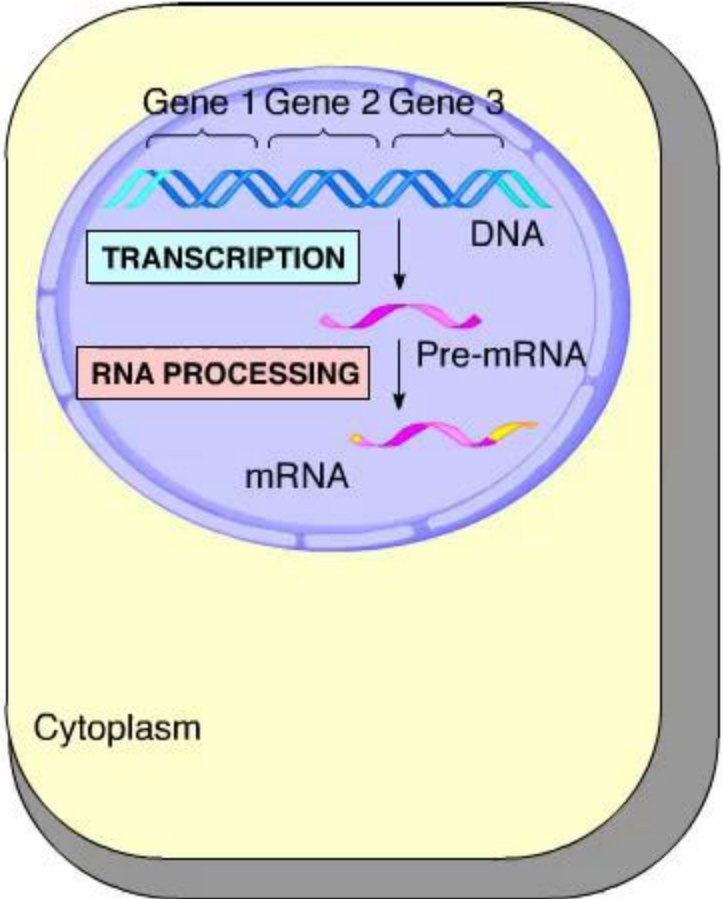
Concept 17.5: Mutations of one or a few nucleotides can affect protein structure and function

- **Mutations** are changes in the genetic information of a cell

- **Point mutations** are changes in just one nucleotide pair of a gene

- The change of a single nucleotide in a DNA template strand can lead to the production of an abnormal protein

- If a mutation has an adverse effect on the phenotype of the organism, the condition is referred to as a genetic disorder or hereditary disease

Figure 17.26

Wild-type β-globin

Sickle-cell β-globin

Wild-type β-globin DNA

3′   C   T   C   5′

5′   G   A   G   3′

Mutant β-globin DNA
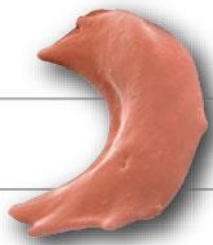
3′   C   A   C   5′

5′   G   T   G   3′

mRNA

5′   G   A   G   3′

mRNA

5′   G   U   G   3′

Normal hemoglobin

Glu

Sickle-cell hemoglobin

Val

Types of Small-Scale Mutations
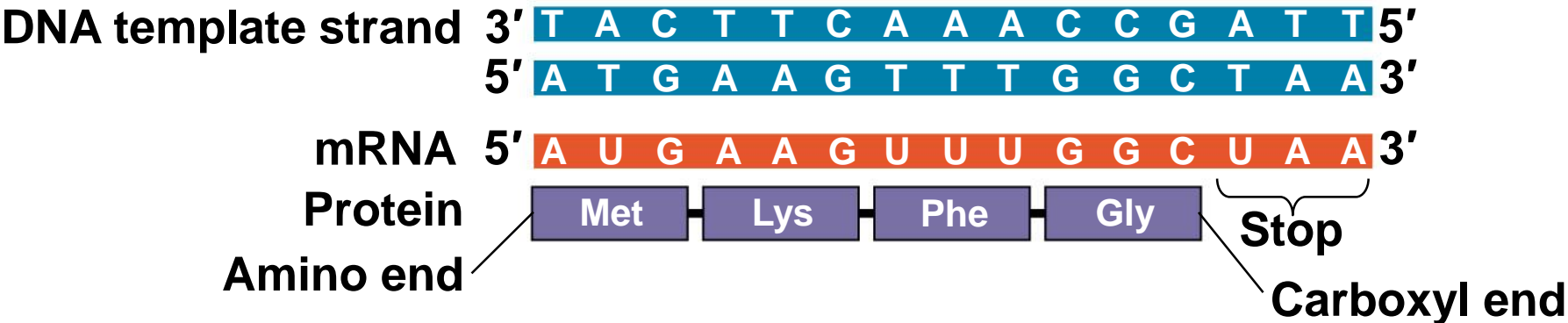
- Point mutations within a gene can be divided into two general categories:

    - Single nucleotide-pair substitutions

    - Nucleotide-pair insertions or deletions

Substitutions

- A **nucleotide-pair substitution** replaces one nucleotide and its partner with another pair of nucleotides

- **Silent mutations** have no effect on the amino acid produced by a codon because of redundancy in the genetic code

- **Missense mutations** still code for an amino acid, but not the correct amino acid

- **Nonsense mutations** change an amino acid codon into a stop codon; most lead to a nonfunctional protein

Figure 17.27a

Wild type

DNA template strand 3′ T A C T T C A A A C C G A T T 5′
5′ A T G A A G T T T G G C T A A 3′

mRNA 5′ A U G A A G U U U G G C U A A 3′
Protein Met ▪ Lys ▪ Phe ▪ Gly **Stop**
Amino end **Carboxyl end**

Nucleotide-pair substitution: silent

A instead of G

3′ T A C T T C A A A C C A A T T 5′
5′ A T G A A G T T T G G T T A A 3′

U instead of C

5′ A U G A A G U U U G G U U A A 3′
Met ▪ Lys ▪ Phe ▪ Gly **Stop**
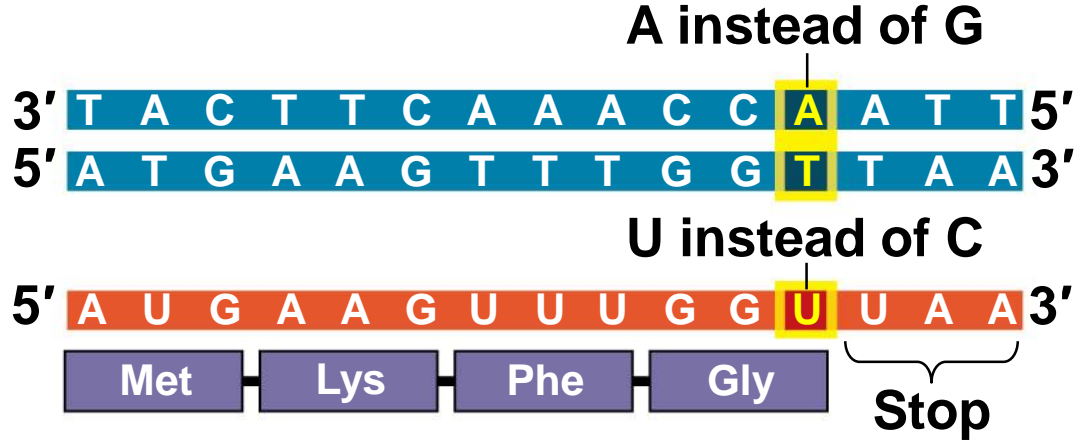
Insertions and Deletions

- **Insertions** and **deletions** are additions or losses of nucleotide pairs in a gene

- These mutations have a disastrous effect on the resulting protein more often than substitutions do

- Insertion or deletion of nucleotides may alter the reading frame, producing a **frameshift mutation**

Figure 17.27b

Wild type

DNA template strand 3′ | T A C T T C A A A C C G A T T | 5′
5′ | A T G A A G T T T G G C T A A | 3′

mRNA 5′ | A U G A A G U U U G G C U A A | 3′
Protein

| Met | Lys | Phe | Gly |

Amino end

Stop

Carboxyl end
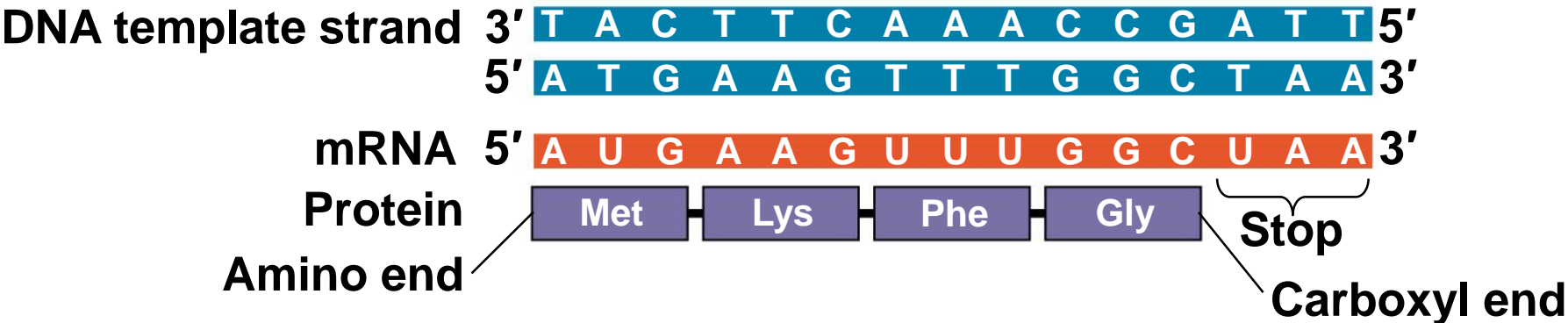
Nucleotide-pair substitution: missense

T instead of C

3′ | T A C T T C A A A **T** C G A T T | 5′
5′ | A T G A A G T T T **A** G C T A A | 3′

A instead of G

5′ | A U G A A G U U U **A** G C U A A | 3′

| Met | Lys | Phe | Ser |

Stop
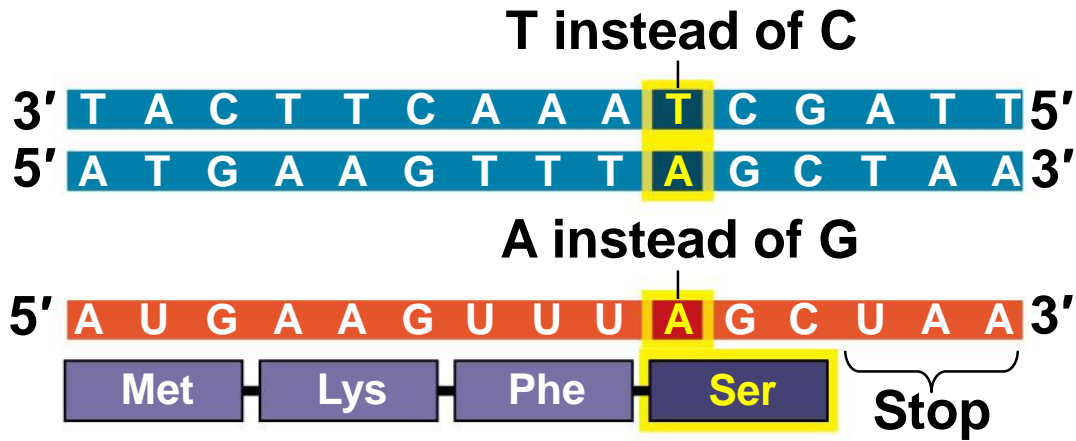
New Mutations and Mutagens

- Spontaneous mutations can occur during errors in DNA replication, recombination, or repair

- **Mutagens** are physical or chemical agents that can cause mutations

- Chemical mutagens fall into a variety of categories

- Most carcinogens (cancer-causing chemicals) are mutagens, and most mutagens are carcinogenic

What Is a Gene? *Revisiting the Question*

- The idea of the gene has evolved through the history of genetics

- We have considered a gene as

    - a discrete unit of inheritance

    - a region of specific nucleotide sequence in a chromosome

    - a DNA sequence that codes for a specific polypeptide chain

- A gene can be defined as a region of DNA that can be expressed to produce a final functional product that is either a polypeptide or an RNA molecule

Figure 17.27

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Figure 17.27c

Wild type

DNA template strand 3′ | T | A | C | T | T | C | A | A | A | C | C | G | A | T | T |5′
5′ | A | T | G | A | A | G | T | T | T | G | G | C | T | A | A |3′

mRNA 5′ | A | U | G | A | A | G | U | U | U | G | G | C | U | A | A |3′

Protein   Met – Lys – Phe – Gly   **Stop**

Amino end

Carboxyl end
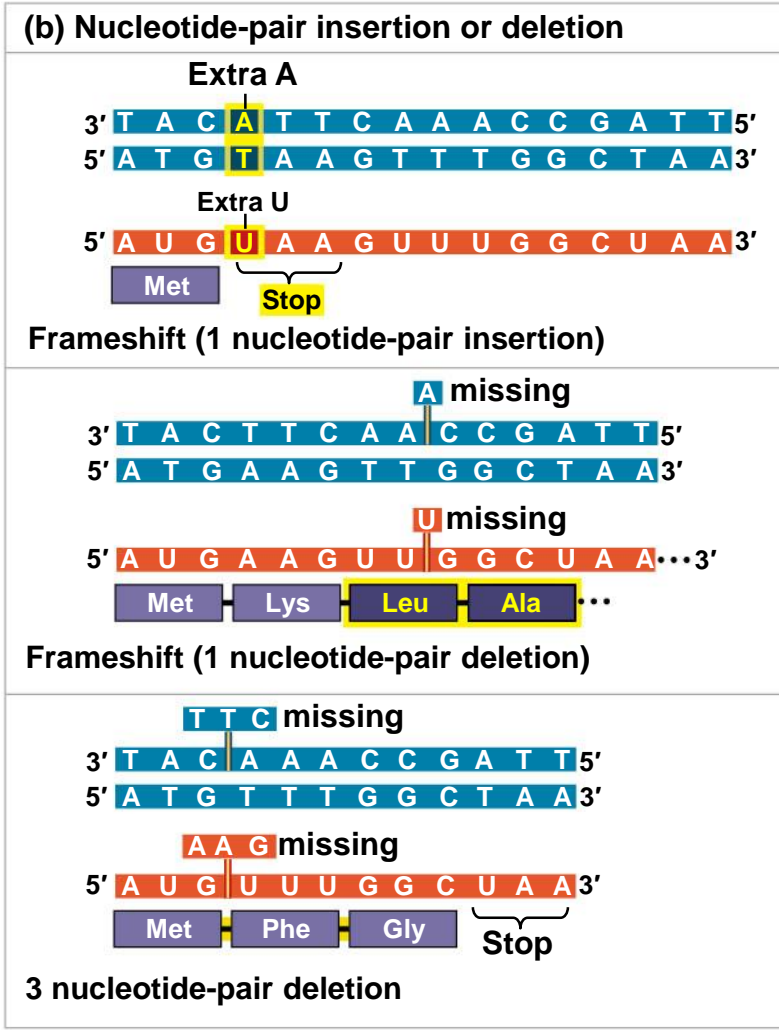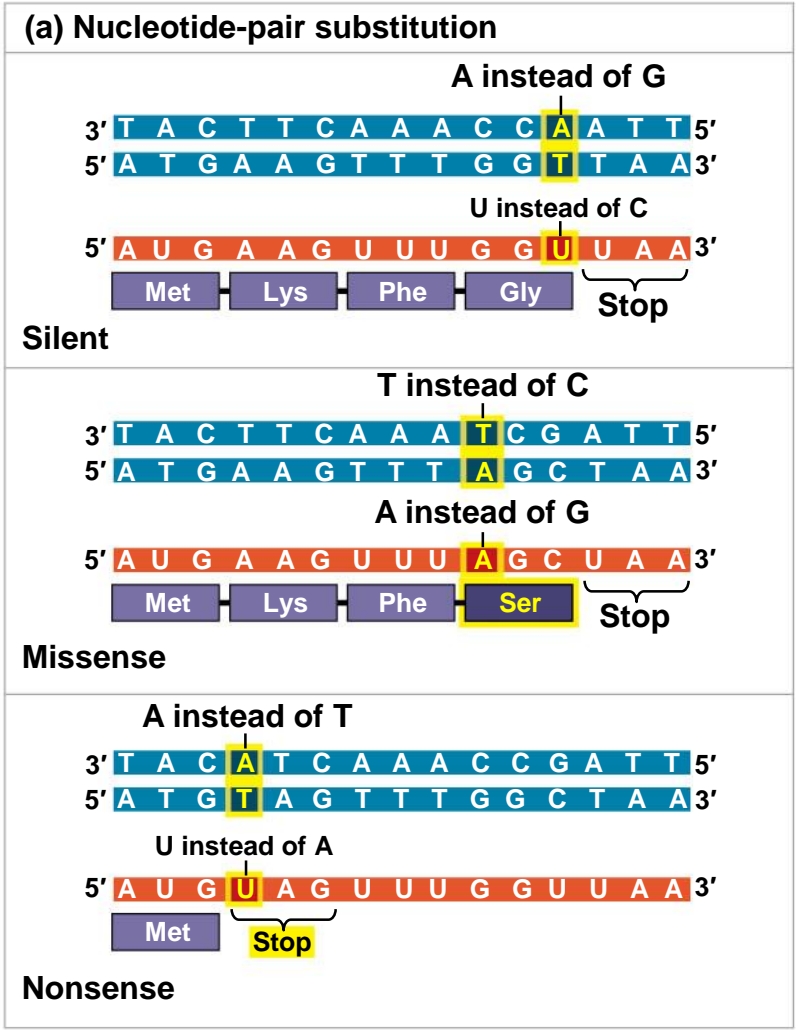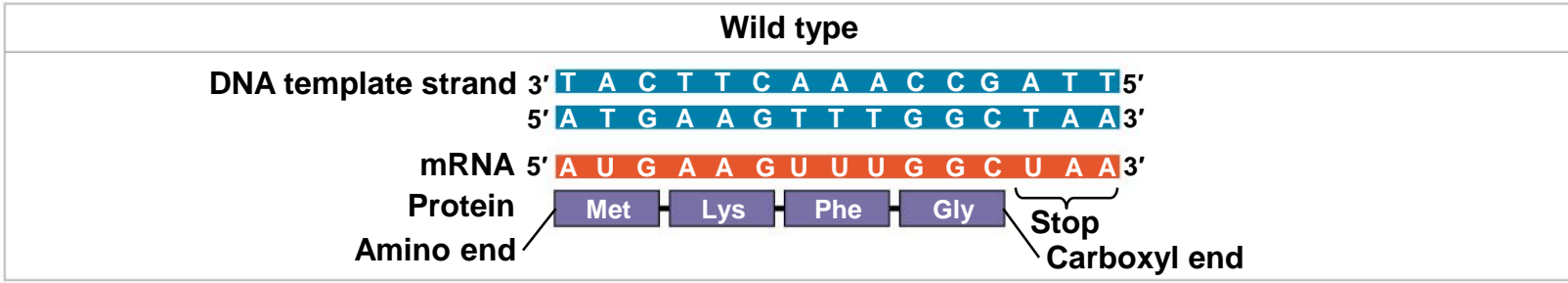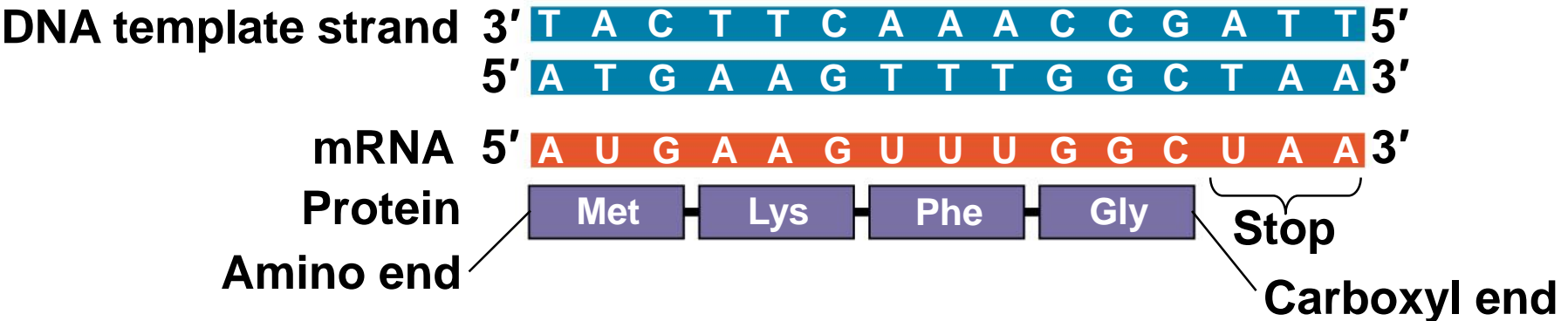
Nucleotide-pair substitution: nonsense

A instead of T

3′ | T | A | C | A | T | C | A | A | A | C | C | G | A | T | T |5′
5′ | A | T | G | T | A | G | T | T | T | G | G | C | T | A | A |3′

U instead of A

5′ | A | U | G | U | A | G | U | U | U | G | G | U | U | A | A |3′

Met   **Stop**

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Figure 17.27d

Wild type

DNA template strand 3′ | T | A | C | T | T | C | A | A | A | C | C | G | A | T | T | 5′
5′ | A | T | G | A | A | G | T | T | T | G | G | C | T | A | A | 3′

mRNA 5′ | A | U | G | A | A | G | U | U | U | G | G | C | U | A | A | 3′

Protein | Met | Lys | Phe | Gly | Stop
Amino end
Carboxyl end
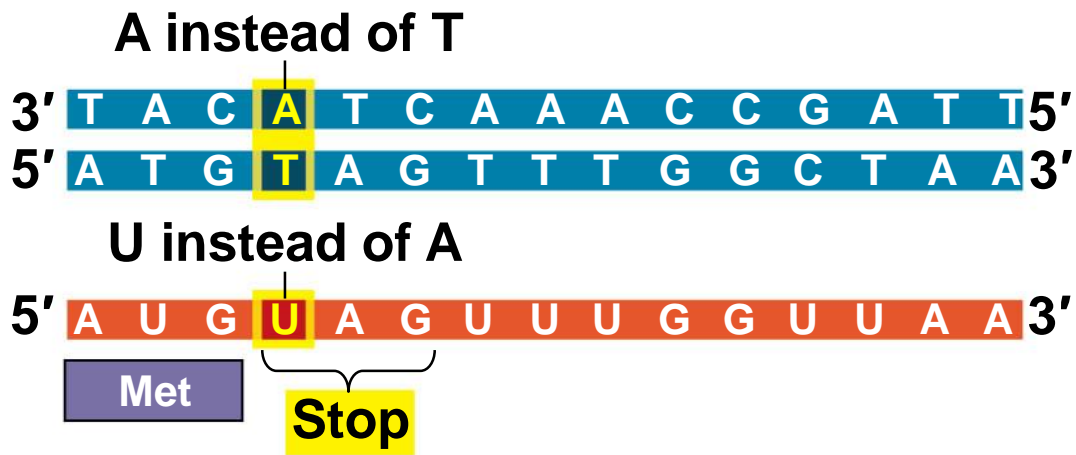
Nucleotide-pair insertion: frameshift causing immediate nonsense

Extra A

3′ | T | A | C | A | T | T | C | A | A | A | C | C | G | A | T | T | 5′
5′ | A | T | G | T | A | A | G | T | T | T | G | G | C | T | A | A | 3′

Extra U

5′ | A | U | G | U | A | A | G | U | U | U | G | G | U | U | A | A | 3′

| Met | Stop

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Figure 17.27e

Wild type

DNA template strand 3′ | T | A | C | T | T | C | A | A | A | C | C | G | A | T | T |5′

5′ | A | T | G | A | A | G | T | T | T | G | G | C | T | A | A |3′

mRNA 5′ | A | U | G | A | A | G | U | U | U | G | G | C | U | A | A |3′

Protein

| Met | Lys | Phe | Gly | Stop

Amino end

Carboxyl end
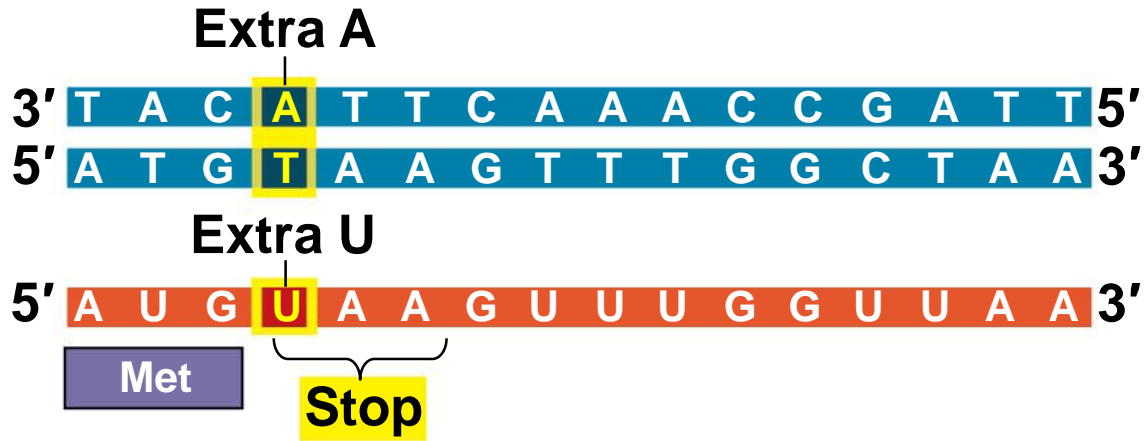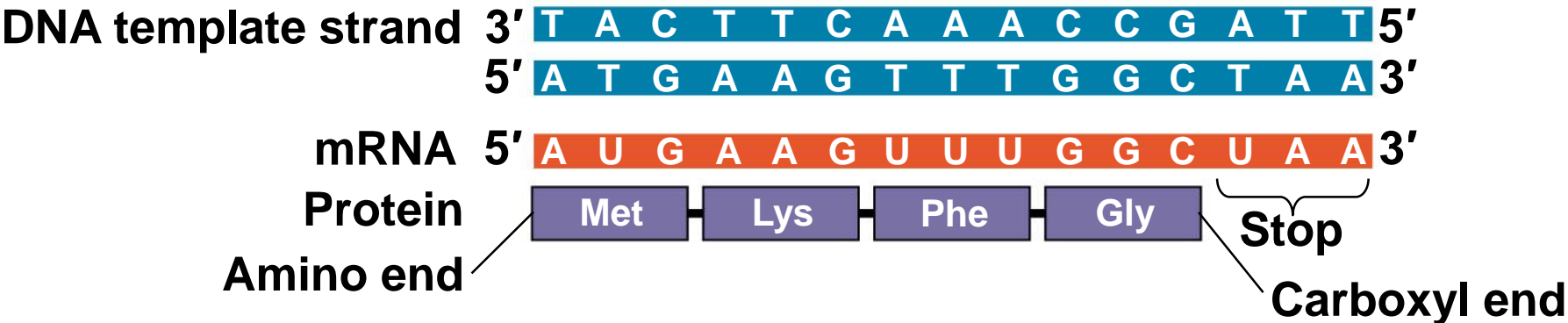
Nucleotide-pair deletion: frameshift causing extensive missense

A **missing**

3′ | T | A | C | T | T | C | A | A | C | G | A | T | T |5′

5′ | A | T | G | A | A | G | T | T | G | G | C | T | A | A |3′

U **missing**

5′ | A | U | G | A | A | G | U | U | G | G | G | U | A | A |···3′

| Met | Lys | Leu | Ala |···

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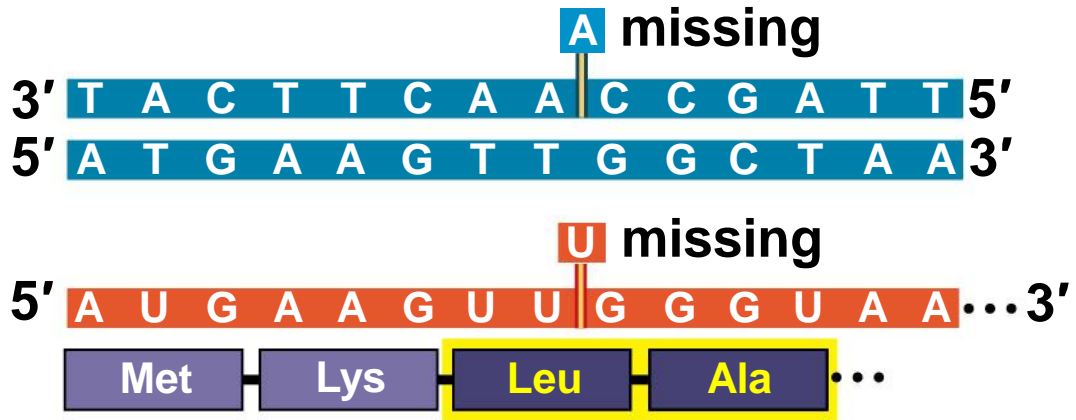
Figure 17.27f

Wild type

DNA template strand 3′ T A C T T C A A A C C G A T T 5′
5′ A T G A A G T T T G G C T A A 3′

mRNA 5′ A U G A A G U U U G G C U A A 3′

Protein

| Met | Lys | Phe | Gly | Stop |

Amino end

Carboxyl end
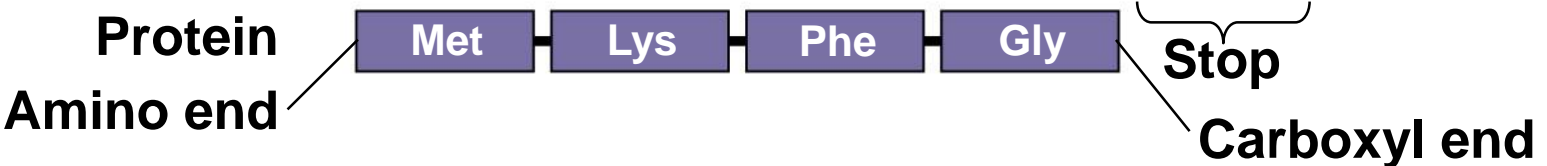
3 nucleotide-pair deletion: no frameshift, but one amino acid missing

T T C **missing**

3′ T A C A A A C C G A T T 5′
5′ A T G T T T G G C T A A 3′

A A G **missing**

5′ A U G U U U G G G U A A 3′

| Met | Phe | Gly | Stop |

Figure 17.UN02

DNA

TRANSCRIPTION

Pre-mRNA

RNA PROCESSING

mRNA

TRANSLATION

Ribosome

Polypeptide
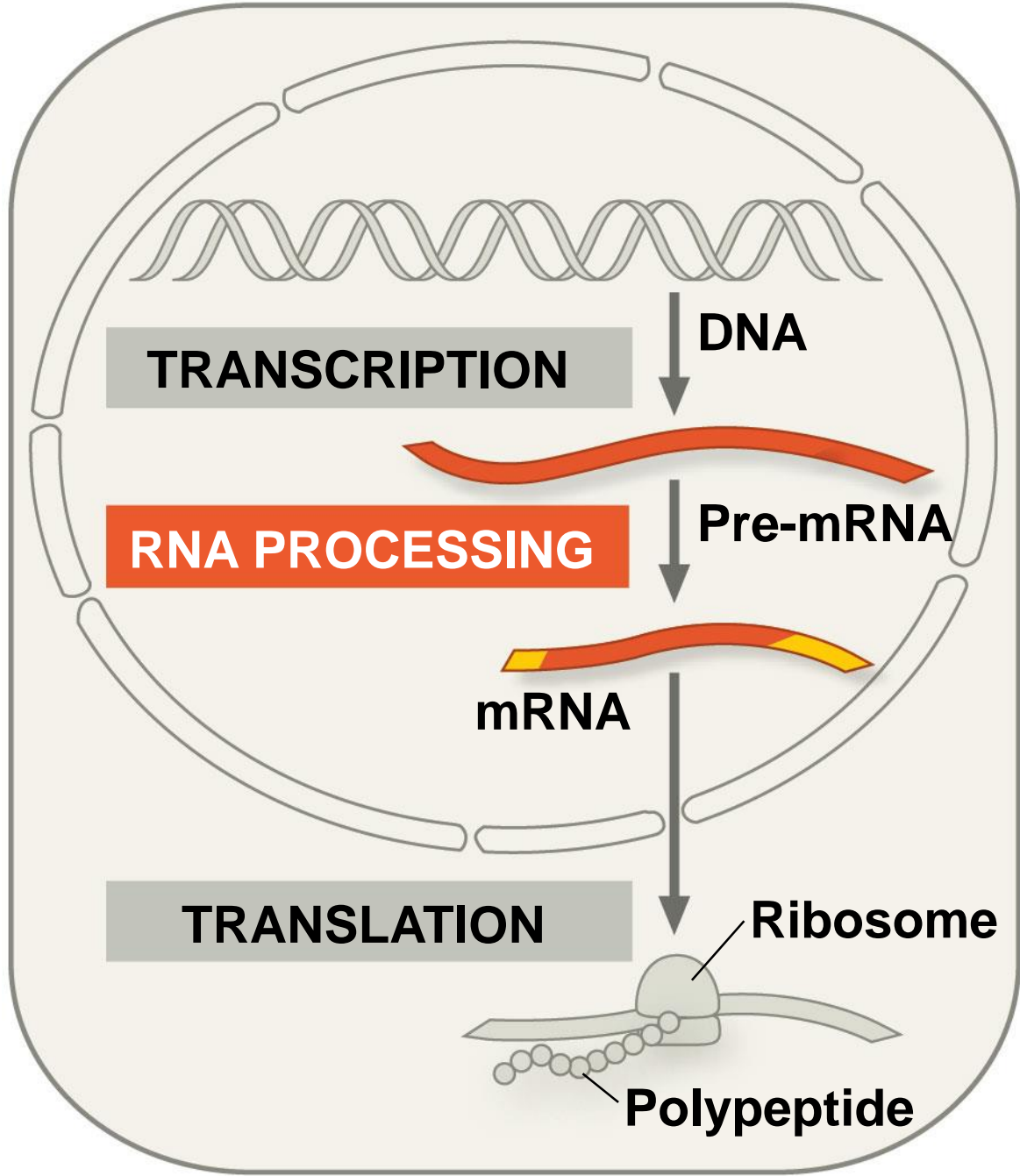
Figure 17.UN03

Figure 17.UN04

Figure 17.UN05a

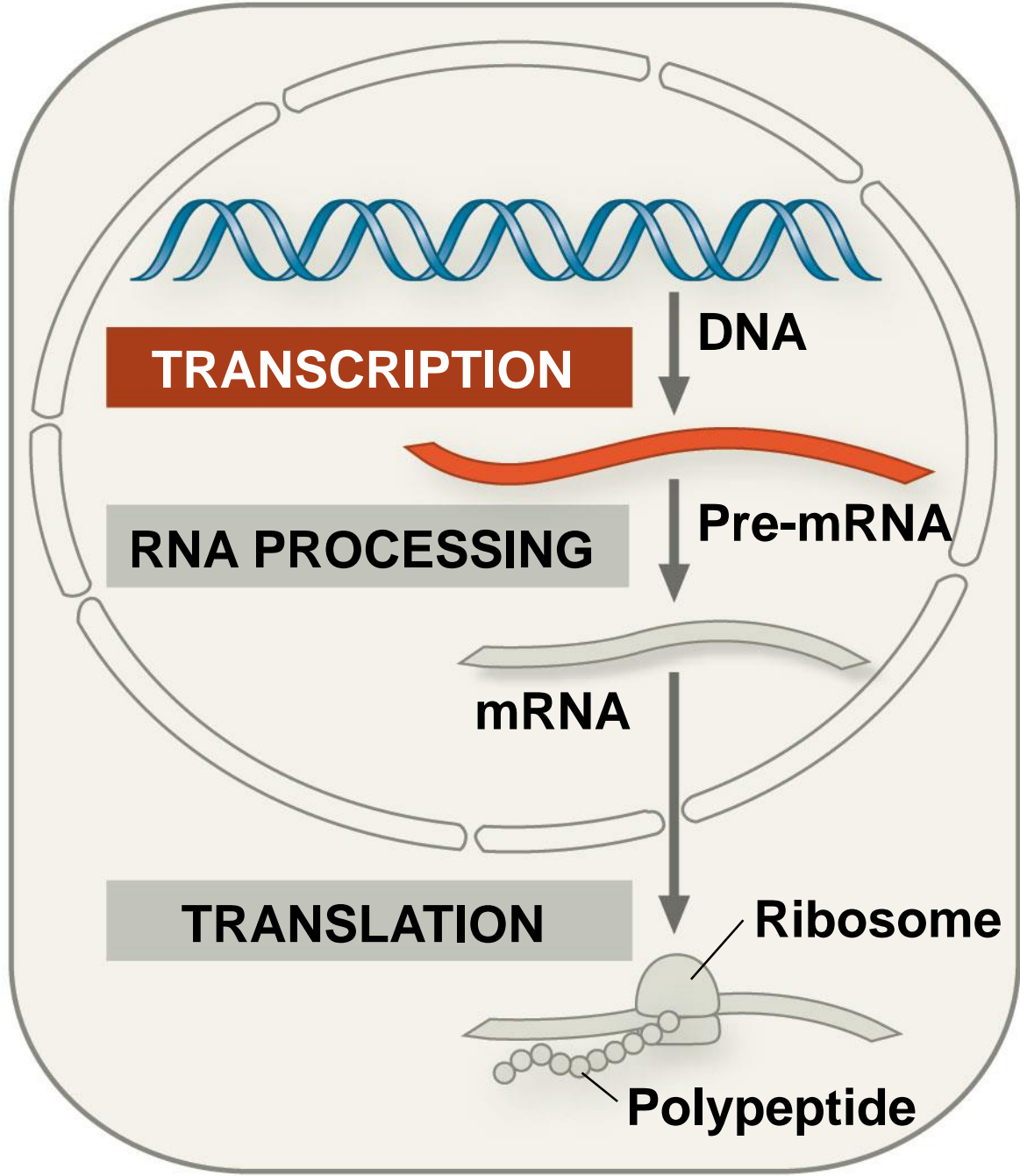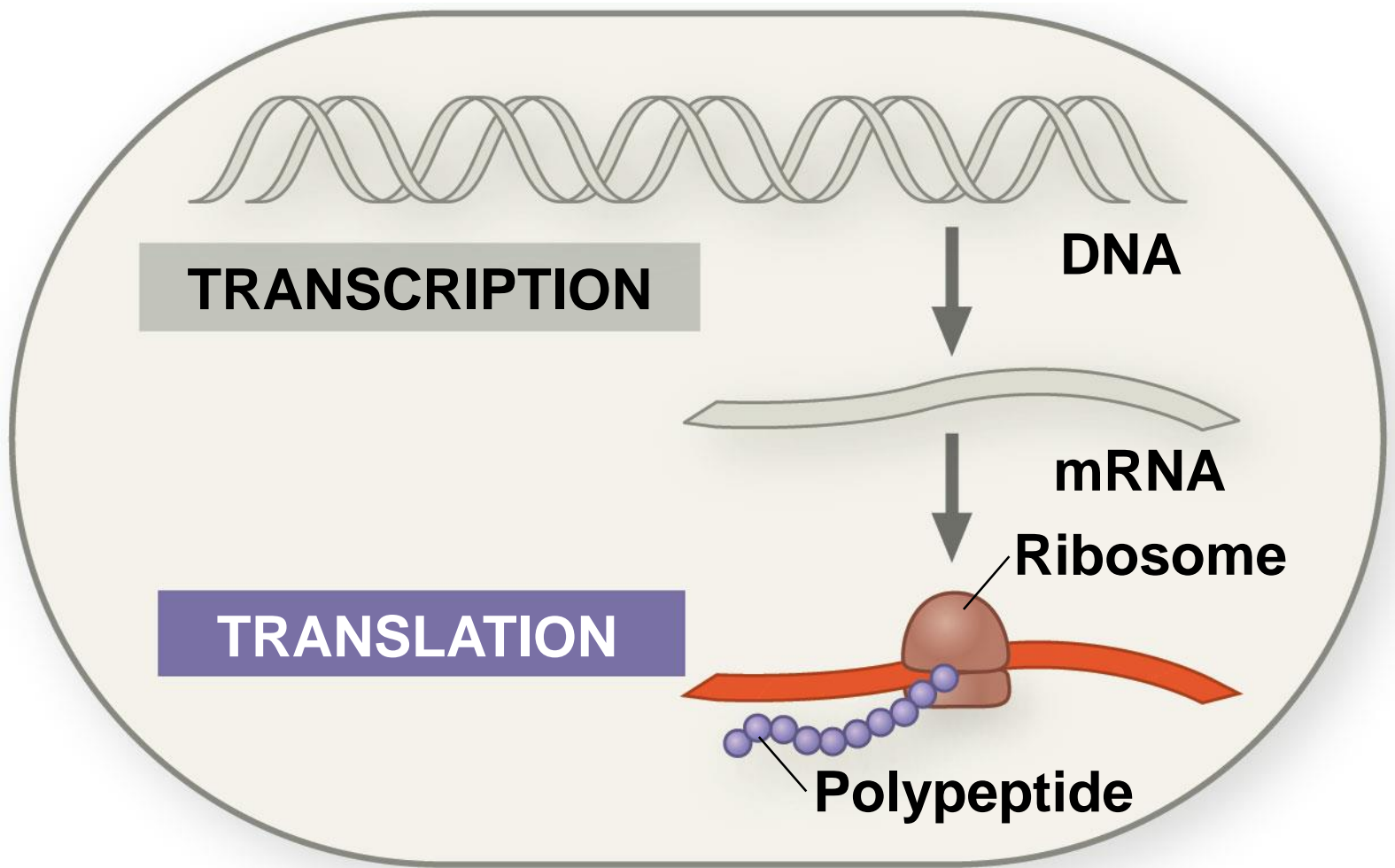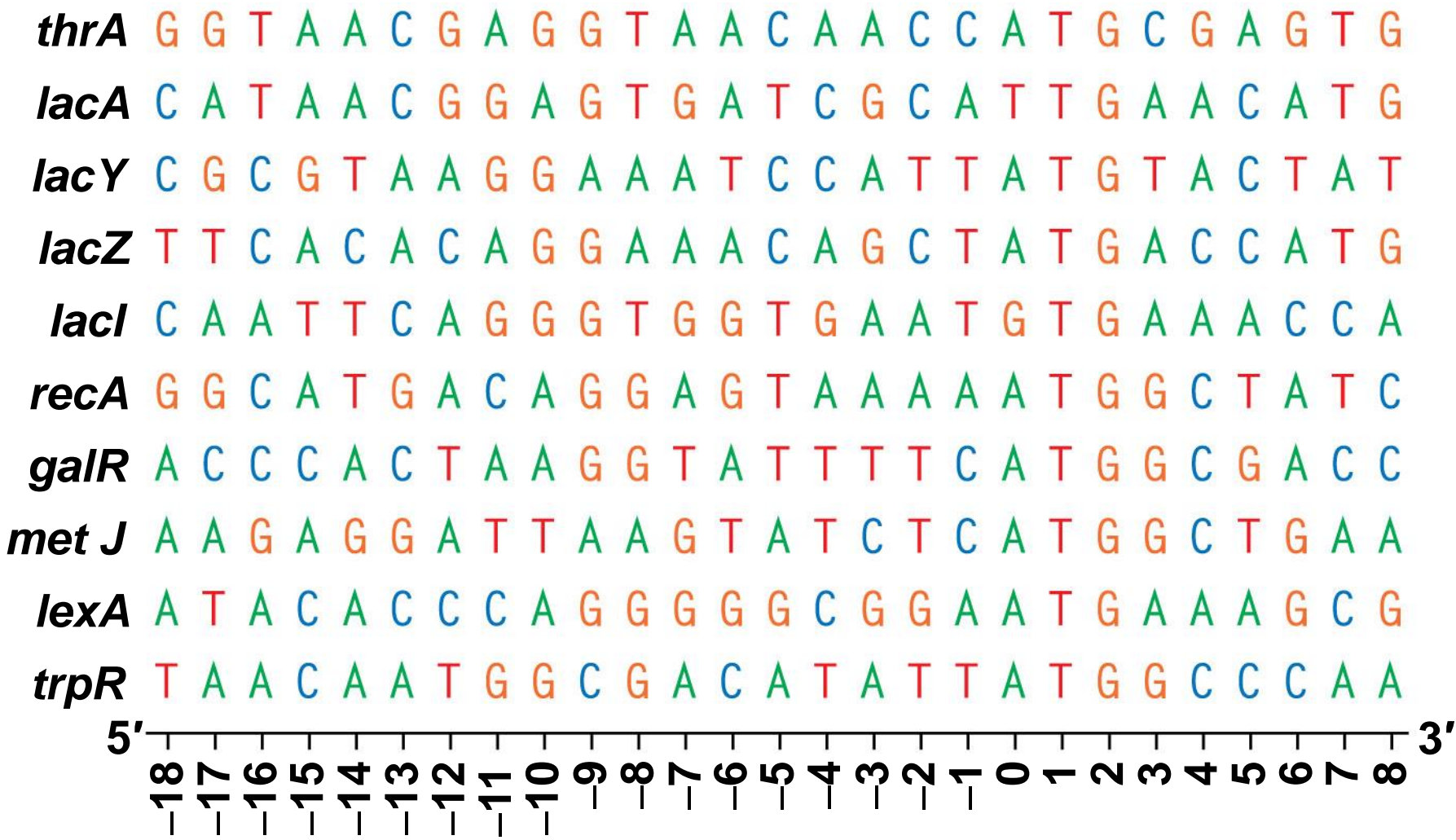|	-18	-17	-16	-15	-14	-13	-12	-11	-10	-9	-8	-7	-6	-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8
thrA	G	G	T	A	A	C	G	A	G	G	T	A	A	C	A	A	C	C	A	T	G	C	G	A	G	T	G
lacA	C	A	T	A	A	C	G	G	A	G	T	G	A	T	C	G	C	A	T	T	G	A	A	C	A	T	G
lacY	C	G	C	G	T	A	A	G	G	A	A	A	T	C	C	A	T	T	A	T	G	T	A	C	T	A	T
lacZ	T	T	C	A	C	A	C	A	G	G	A	A	A	C	A	G	C	T	A	T	G	A	C	C	A	T	G
lacI	C	A	A	T	T	C	A	G	G	G	T	G	G	T	G	A	A	T	G	T	G	A	A	A	C	C	A
recA	G	G	C	A	T	G	A	C	A	G	G	A	G	T	A	A	A	A	A	T	G	G	C	T	A	T	C
galR	A	C	C	C	A	C	T	A	A	G	G	T	A	T	T	T	T	C	A	T	G	G	C	G	A	C	C
met J	A	A	G	A	G	G	A	T	T	A	A	G	T	A	T	C	T	C	A	T	G	G	C	T	G	A	A
lexA	A	T	A	C	A	C	C	C	A	G	G	G	G	G	C	G	G	A	A	T	G	A	A	A	G	C	G
trpR	T	A	A	C	A	A	T	G	G	C	G	A	C	A	T	A	T	T	A	T	G	G	C	C	A	A	A

5′ ——————————————————————————————— 3′

Sequence alignment

Further Reading T. D. Schneider and R. M. Stephens, Sequence logos: A new way to display consensus sequences, *Nucleic Acids Research* 18:6097–6100 (1990).

Figure 17.UN05b

5′   3′
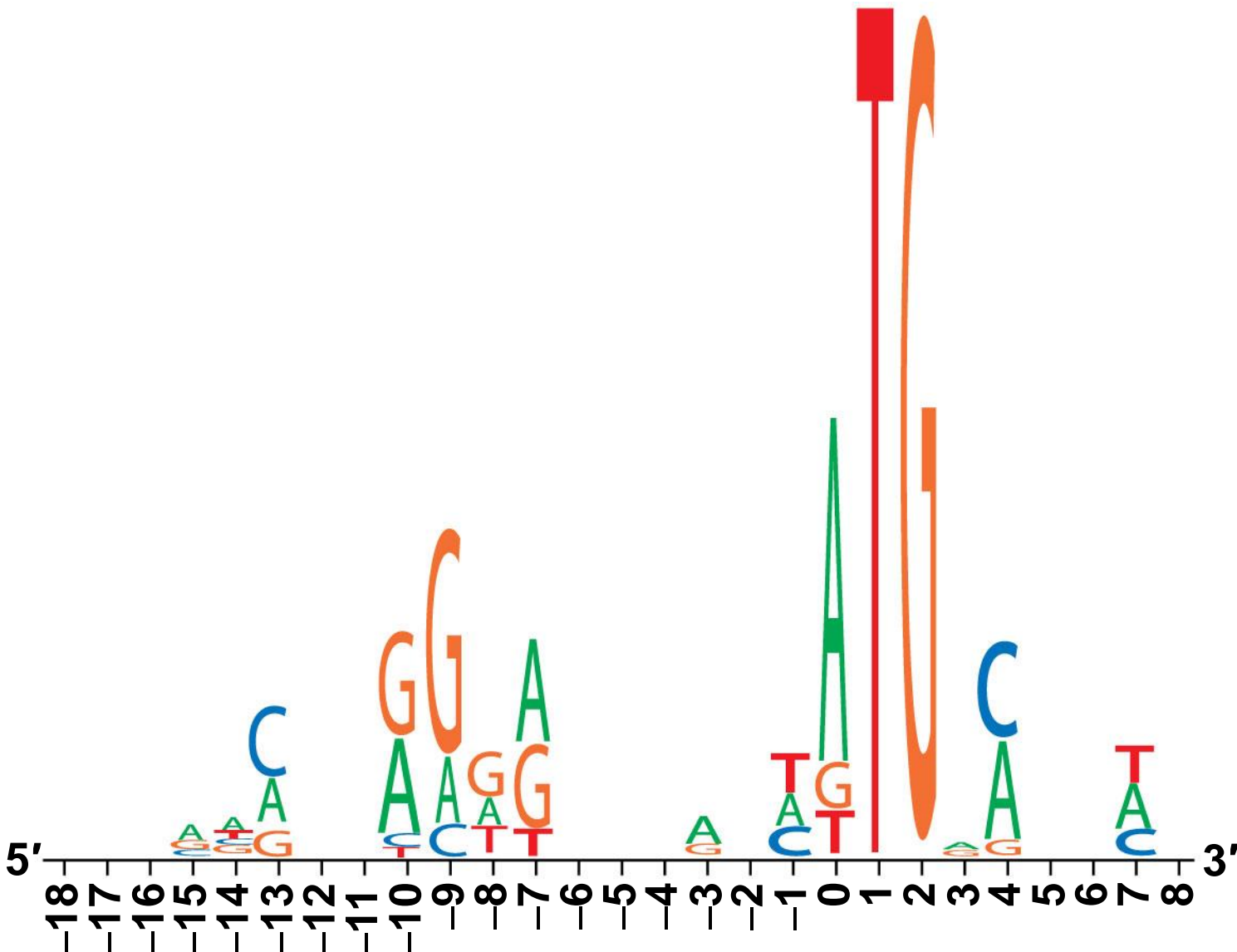
Sequence logo

Further Reading T. D. Schneider and R. M. Stephens, Sequence logos: A new way to display consensus sequences, *Nucleic Acids Research* **18:6097–6100 (1990).**

Figure 17.UN05c

Further Reading T. D. Schneider and R. M. Stephens, Sequence logos: A new way to display consensus sequences, *Nucleic Acids Research* **18:6097–6100 (1990).**

Figure 17.UN05d

Ribosome binding site on mRNA

5′   3′

Figure 17.UN06a
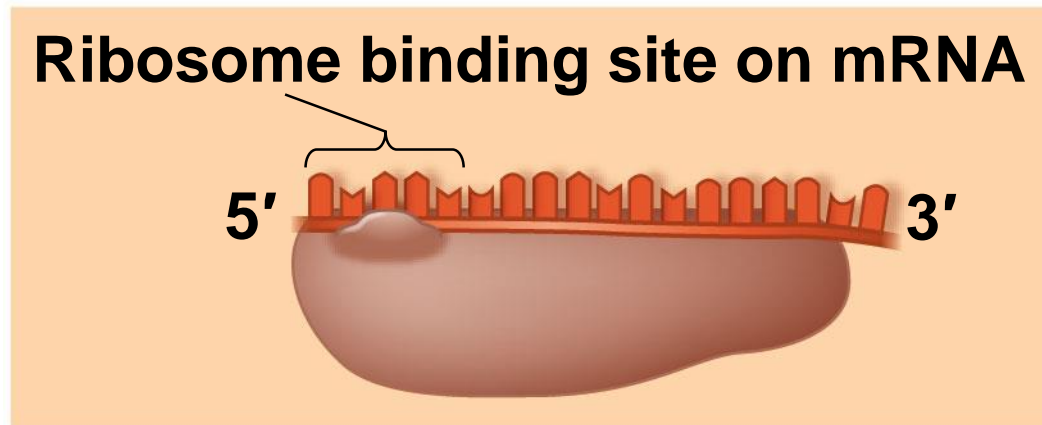
Wild-type cDNA   5′–CTG GTG GAA GCT CTC TAC CTA GTG TGC GGG GAA CGA GGC TTC TTC TAC ACA CCC AAG ACC –3′

Patient 1 cDNA   5′–CTG GTG GAA GCT CTC TAC CTA GTG TGC GGG GAA CGA GGC TGC TTC TAC ACA CCC AAG ACC –3′

Patient 2 cDNA   5′–CTG GTG GAA GCT CTC TAC CTA GTG TGC GGG GAA CGA GGC TCC TTC TAC ACA CCC AAG ACC –3′

Patient 3 cDNA   5′–CTG GTG GAA GCT CTC TAC CTA GTG TGC GGG GAA CGA GGC TTC TTG TAC ACA CCC AAG ACC –3′

Data from N. Nishi and K. Nanjo, Insulin gene mutations and diabetes, *Journal of Diabetes Investigation* 2:92–100 (2011).

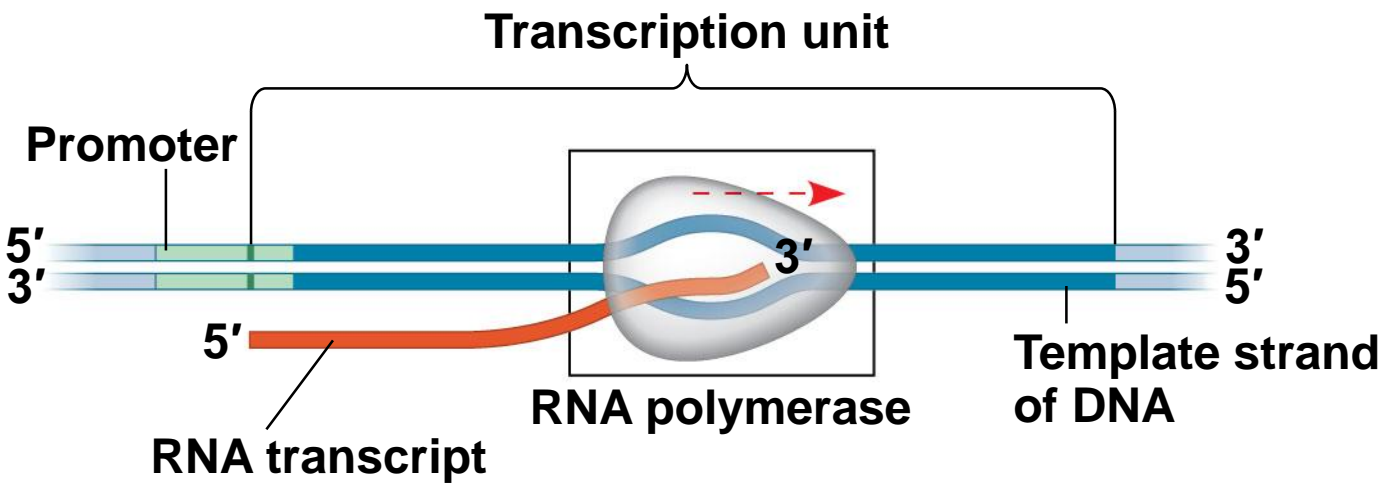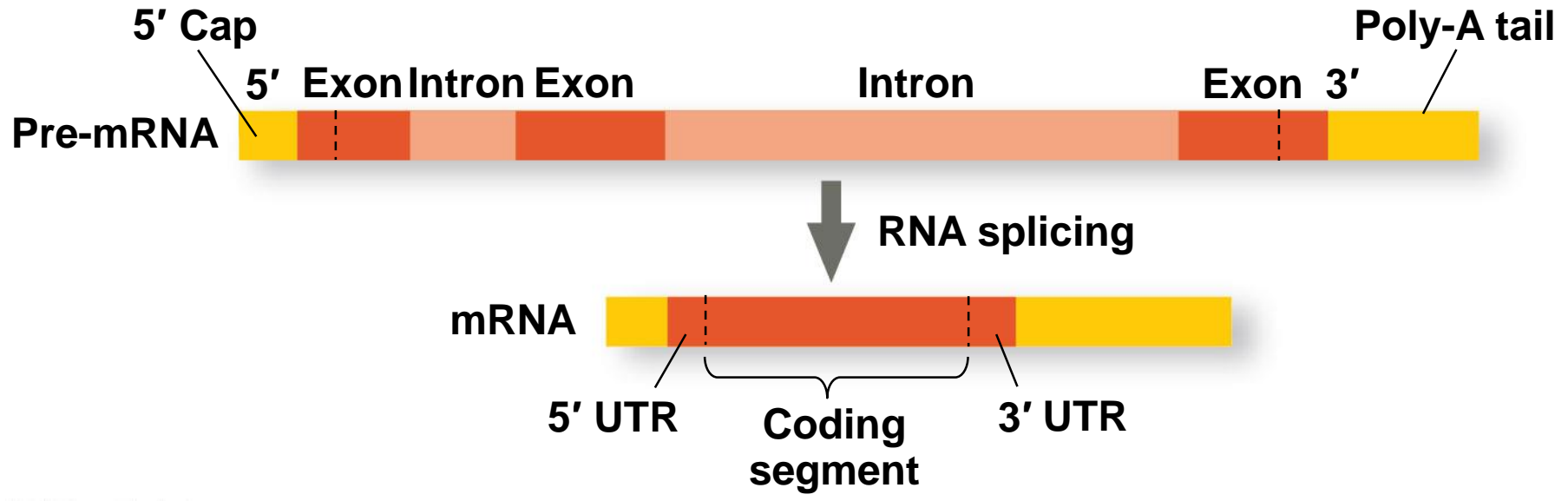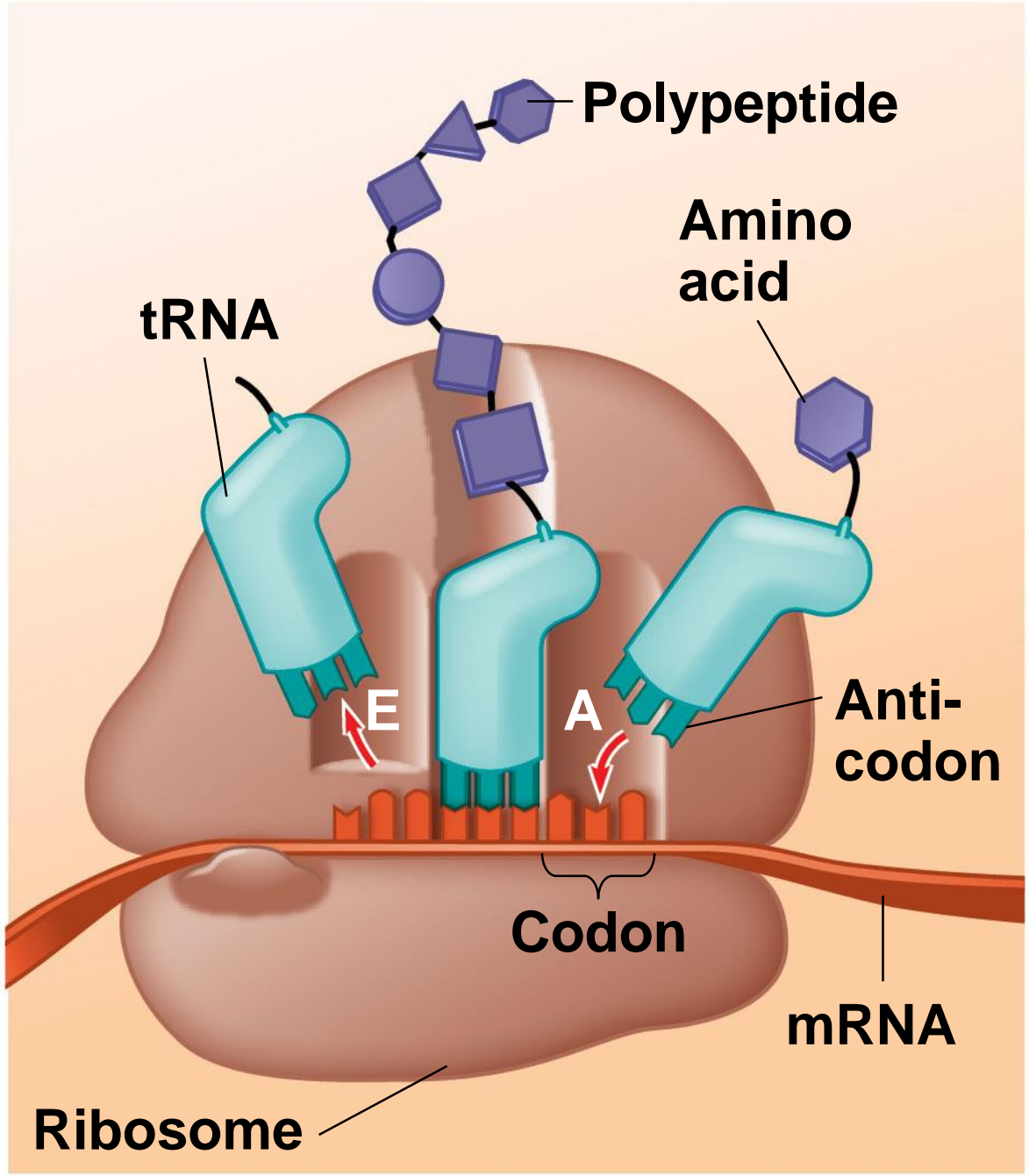Figure 17.UN06b

Figure 17.UN07

Transcription unit

Promoter

5′
3′

3′

5′

RNA polymerase

Template strand of DNA

RNA transcript

3′
5′

Figure 17.UN08

Figure 17.UN09

Figure 17.UN10

Type of RNA	Functions
Messenger RNA (mRNA)	
Transfer RNA (tRNA)	
	Plays catalytic (ribozyme) roles and structural roles in ribosomes
Primary transcript	
Small RNAs in the spliceosome	

Figure 17.UN11