CAMPBELL BIOLOGY IN FOCUS

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14

Gene Expression: From Gene to Protein

Lecture Presentations by
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Simon Fraser University

SECOND EDITION

Overview: The Flow of Genetic Information

- The information content of genes is in the form of specific sequences of nucleotides in DNA
- 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 14.1

Concept 14.1: Genes specify proteins via transcription and translation

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

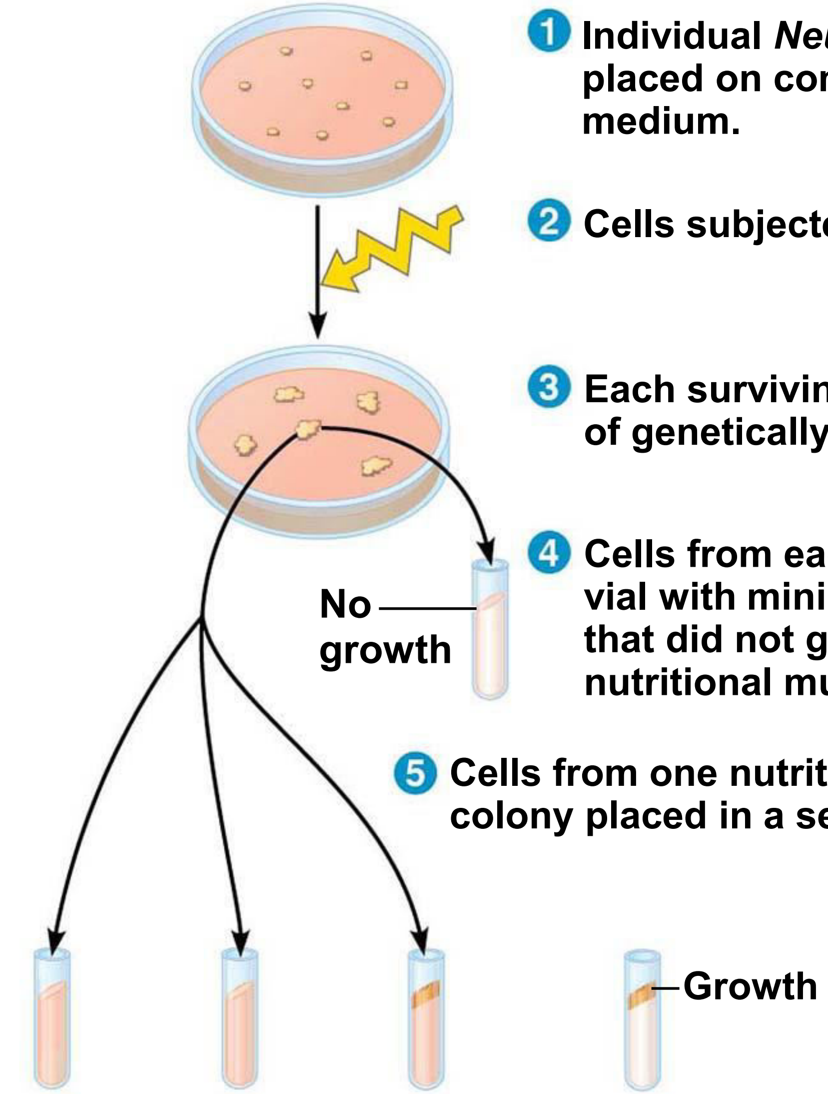
Evidence from the Study of Metabolic Defects

- 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: *Scientific Inquiry*

- Beadle and Tatum disabled genes in bread mold one by one and looked for phenotypic changes
- They studied the haploid bread mold because it would be easier to detect recessive mutations
- They studied mutations that altered the ability of the fungus to grow on minimal medium

Figure 14.2



1. Individual *Neurospora* cells placed on complete medium.
2. Cells subjected to X-rays.
3. Each surviving cell formed a colony of genetically identical cells.
4. Cells from each colony placed in a vial with minimal medium. Cells that did not grow identified as nutritional mutants.
5. Cells from one nutritional mutant colony placed in a series of vials.
6. Vials observed for growth.

No growth

Growth

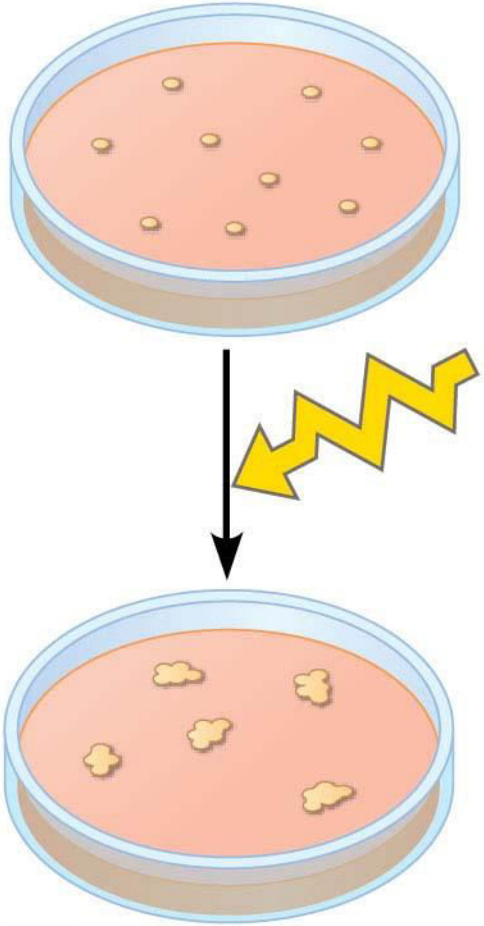
Minimal medium + valine

Minimal medium + lysine

Minimal medium + arginine

Control: Wild-type cells growing on minimal medium

Figure 14.2-1

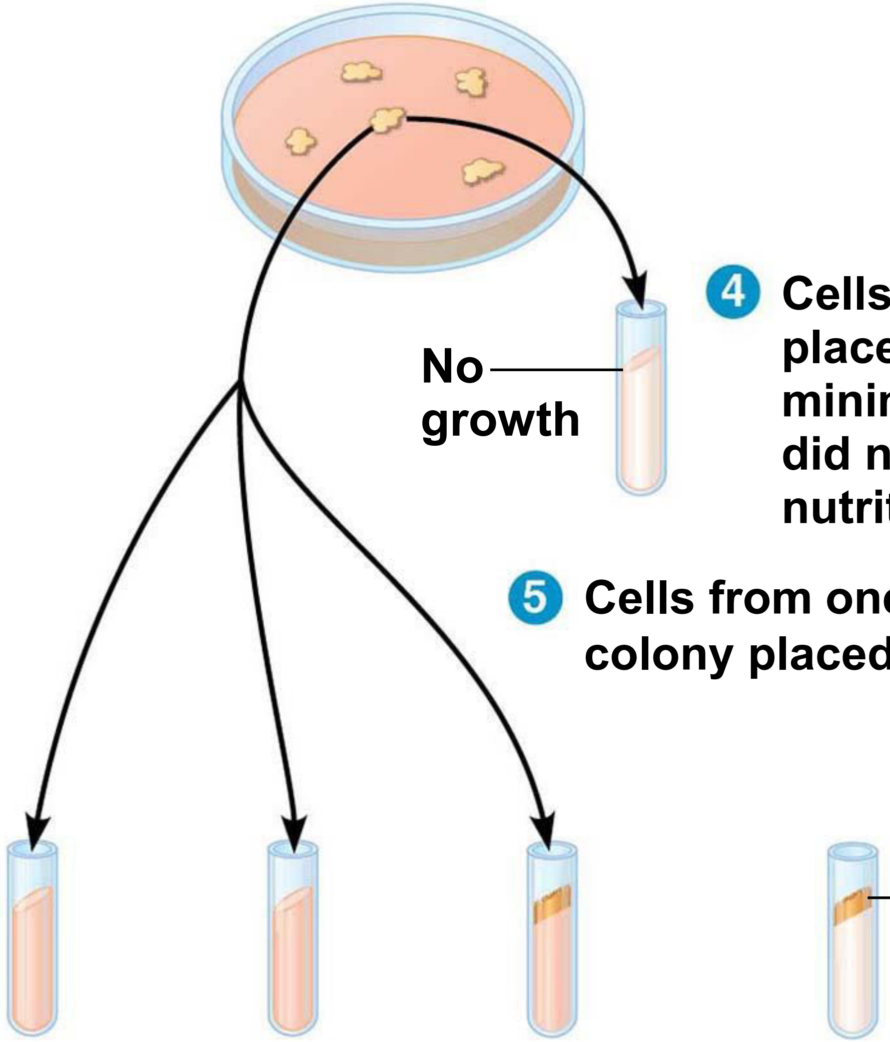


① **Individual *Neurospora* cells placed on complete medium.**

② **Cells subjected to X-rays.**

③ **Each surviving cell formed a colony of genetically identical cells.**

Figure 14.2-2



4 Cells from each colony placed in a vial with minimal medium. Cells that did not grow identified as nutritional mutants.

5 Cells from one nutritional mutant colony placed in a series of vials.

Minimal medium + valine

Minimal medium + lysine

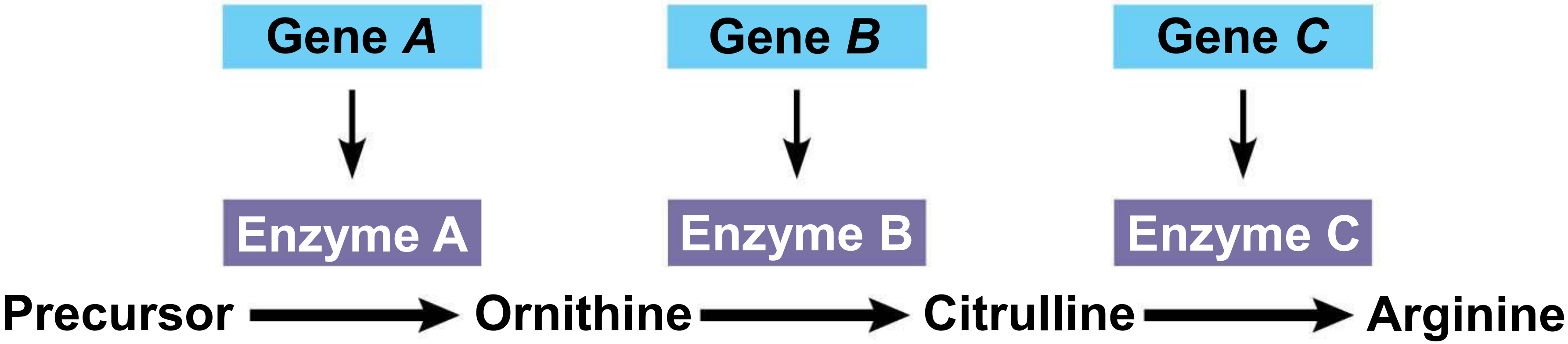
Minimal medium + arginine

Control: Wild-type cells growing on minimal medium

6 Vials observed for growth.

- The researchers amassed a valuable collection of *Neurospora* mutant strains, catalogued by their defects
- For example, one set of mutants all required arginine for growth
- It was determined that different classes of these mutants were blocked at a different step in the biochemical pathway for arginine biosynthesis

Figure 14.3



Gene *A*

Gene *B*

Gene *C*

Enzyme A

Enzyme B

Enzyme C

Precursor → Ornithine → Citrulline → Arginine

The Products of Gene Expression: A Developing Story

- Some proteins are not enzymes, so researchers later revised the one gene–one enzyme hypothesis to 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

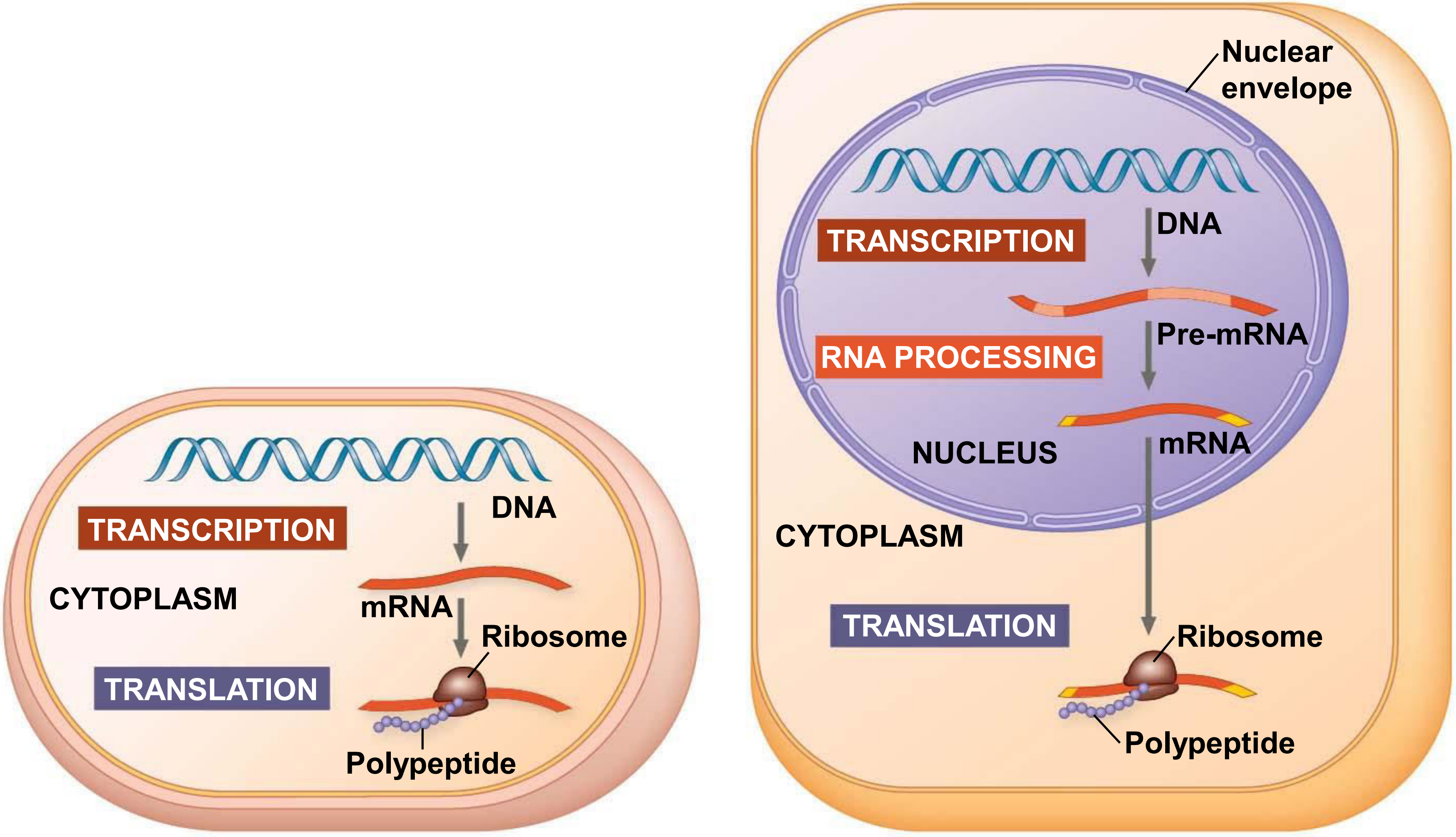
Basic Principles of Transcription and Translation

- RNA is the bridge between DNA and protein synthesis
- RNA is chemically similar to DNA, but RNA has a ribose sugar instead of deoxyribose and the base uracil (U) rather than thymine (T)
- RNA is usually single-stranded
- Getting from DNA to protein requires two stages: transcription and translation

- **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

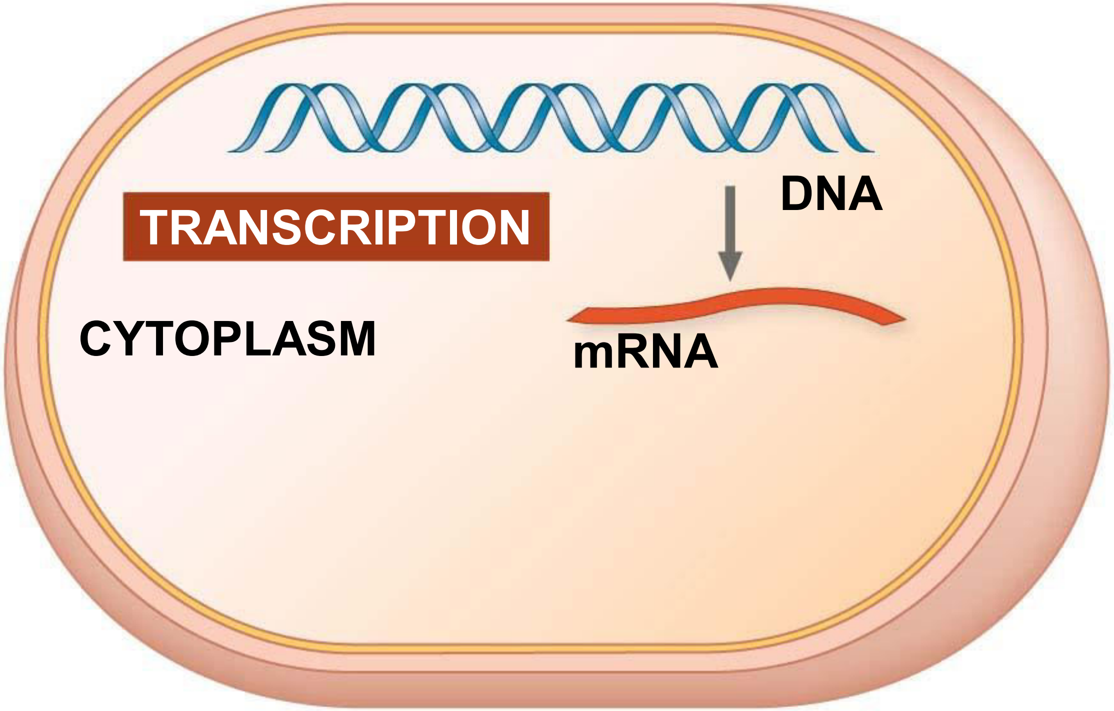
- In bacteria, translation of mRNA can begin before transcription has finished
- In eukaryotes, the nuclear envelope separates transcription from translation
- Eukaryotic RNA transcripts are modified through RNA processing to yield the finished mRNA
- Eukaryotic mRNA must be transported out of the nucleus to be translated

Figure 14.4



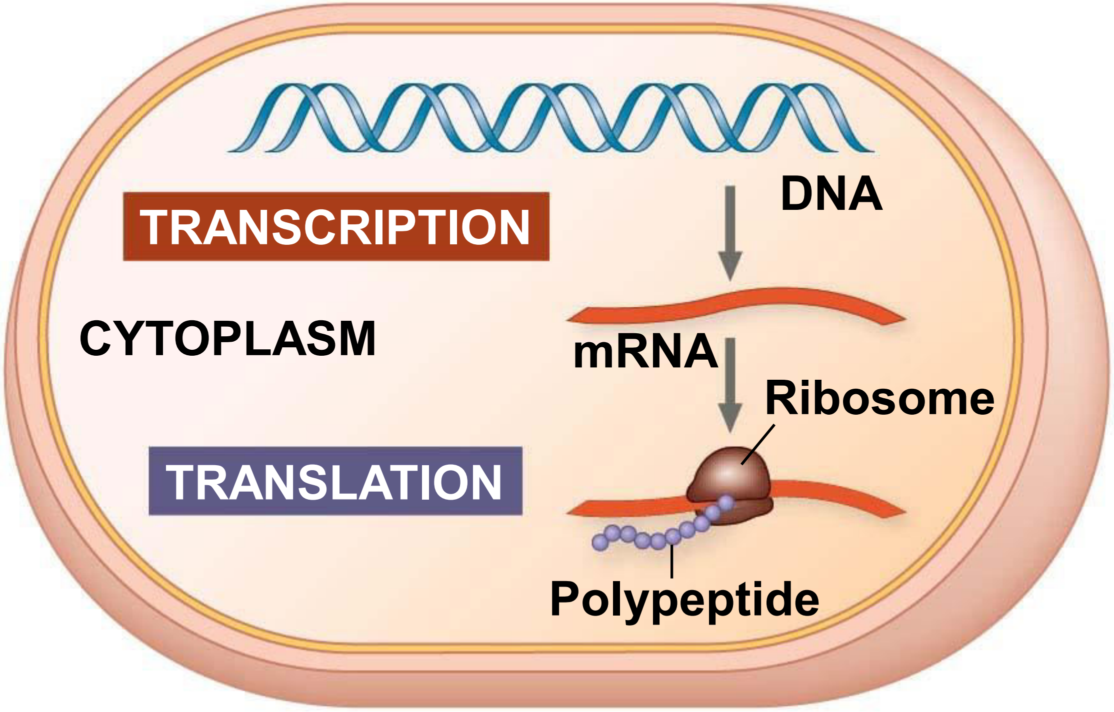
(a) Bacterial cell

(b) Eukaryotic cell

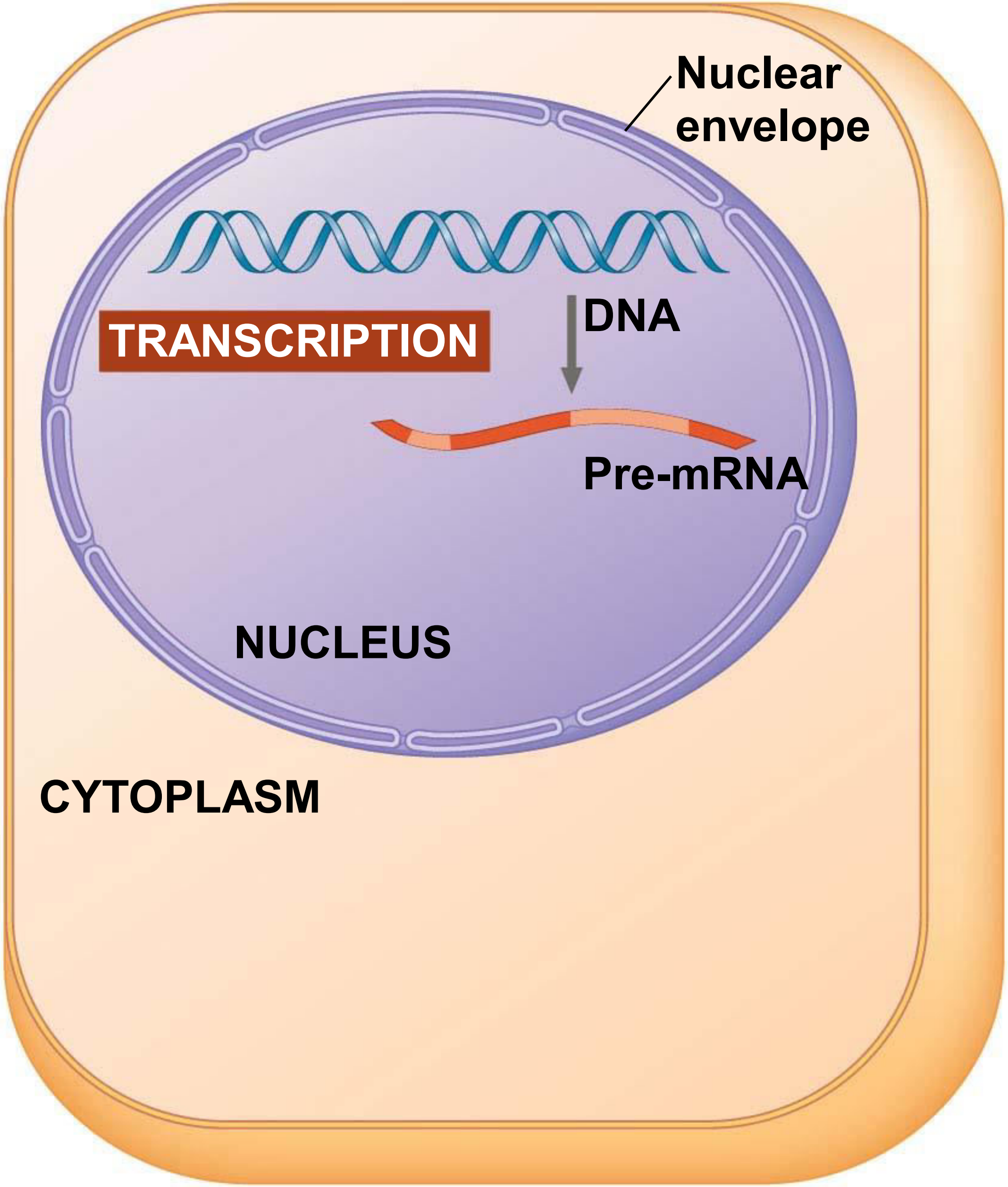


(a) Bacterial cell

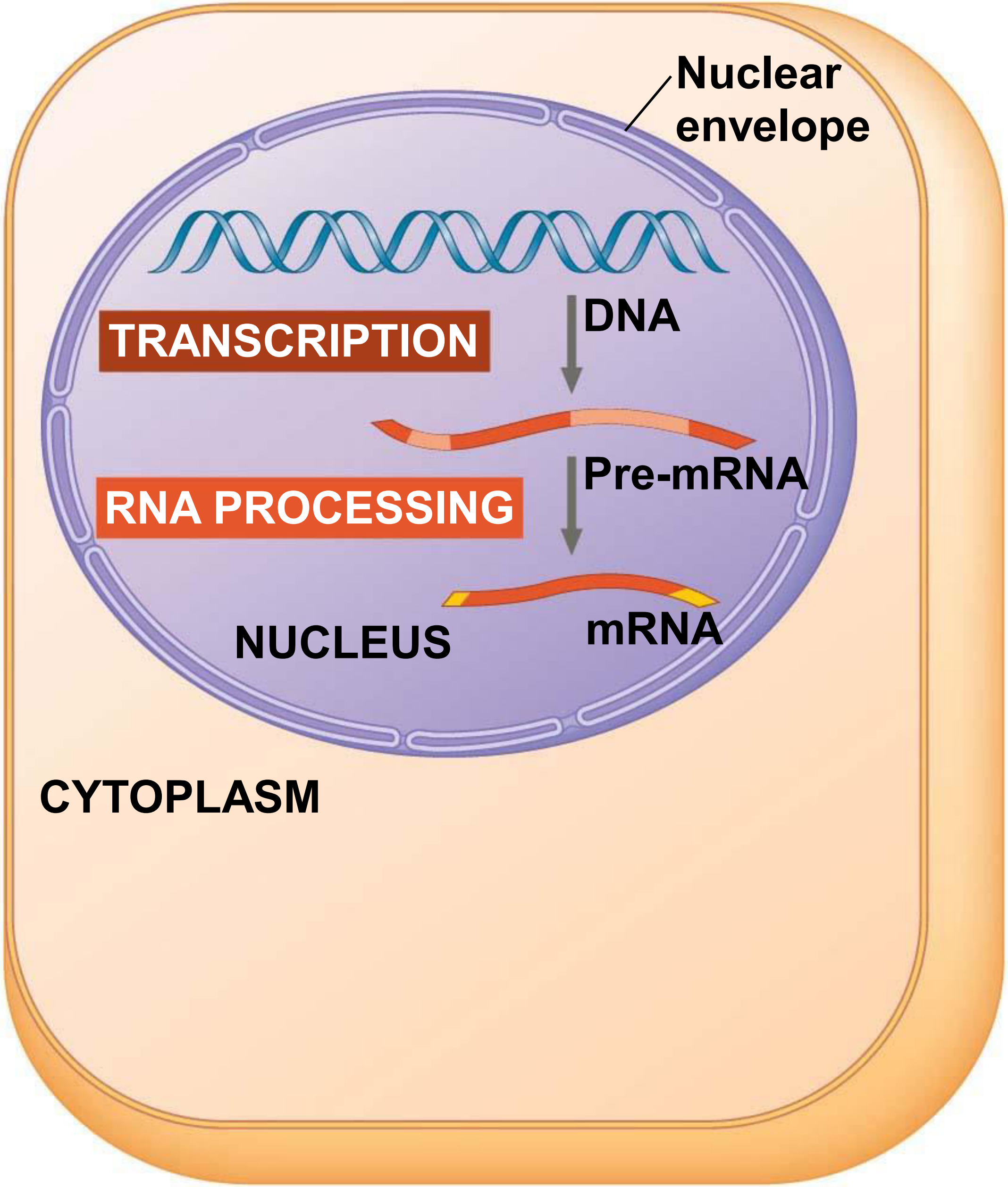
Figure 14.4-1-s2



(a) Bacterial cell

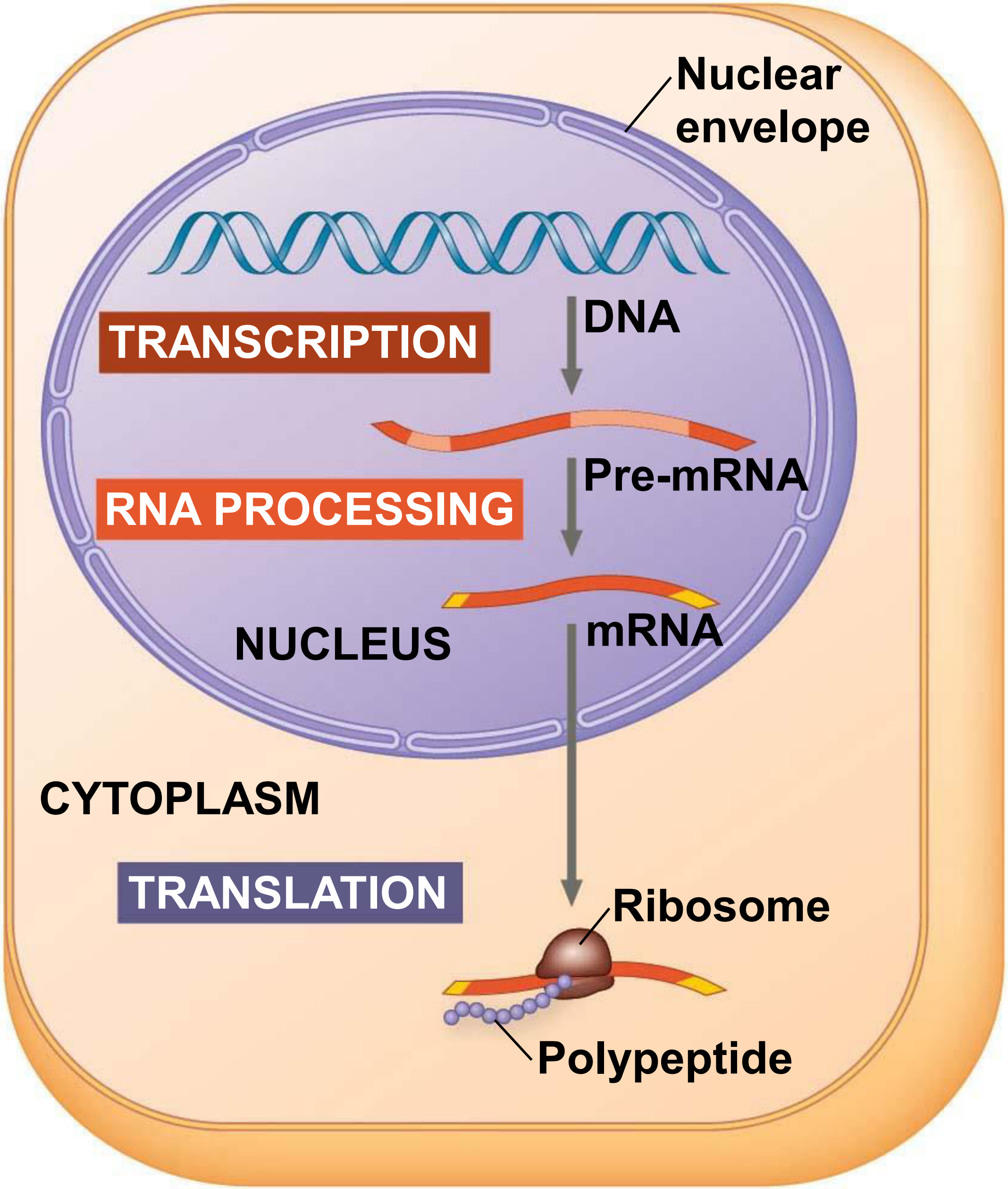


(b) Eukaryotic cell



(b) Eukaryotic cell

Figure 14.4-2-s3



(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

Figure 14.UN01

DNA → RNA → Protein

The Genetic Code

- 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 14.5

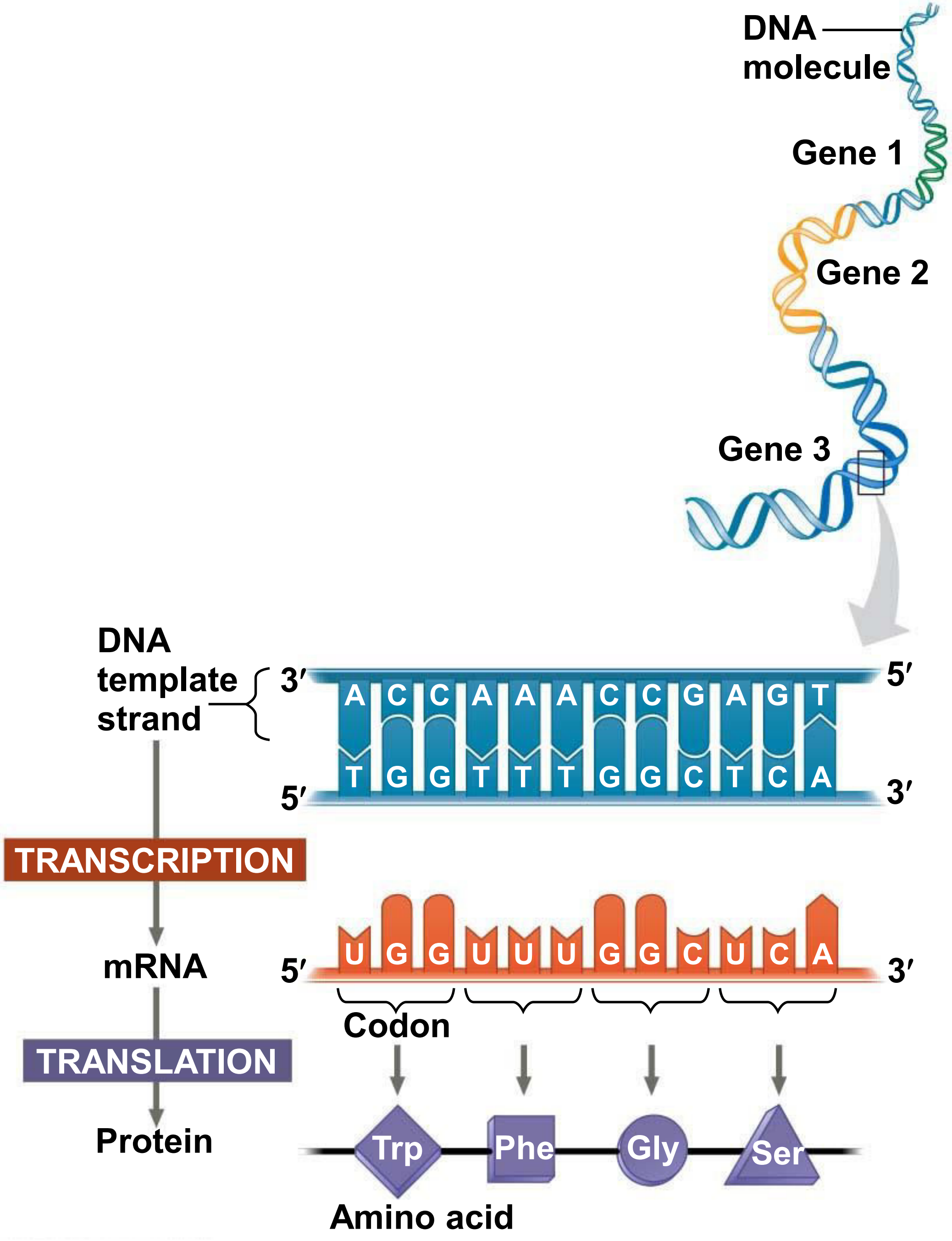
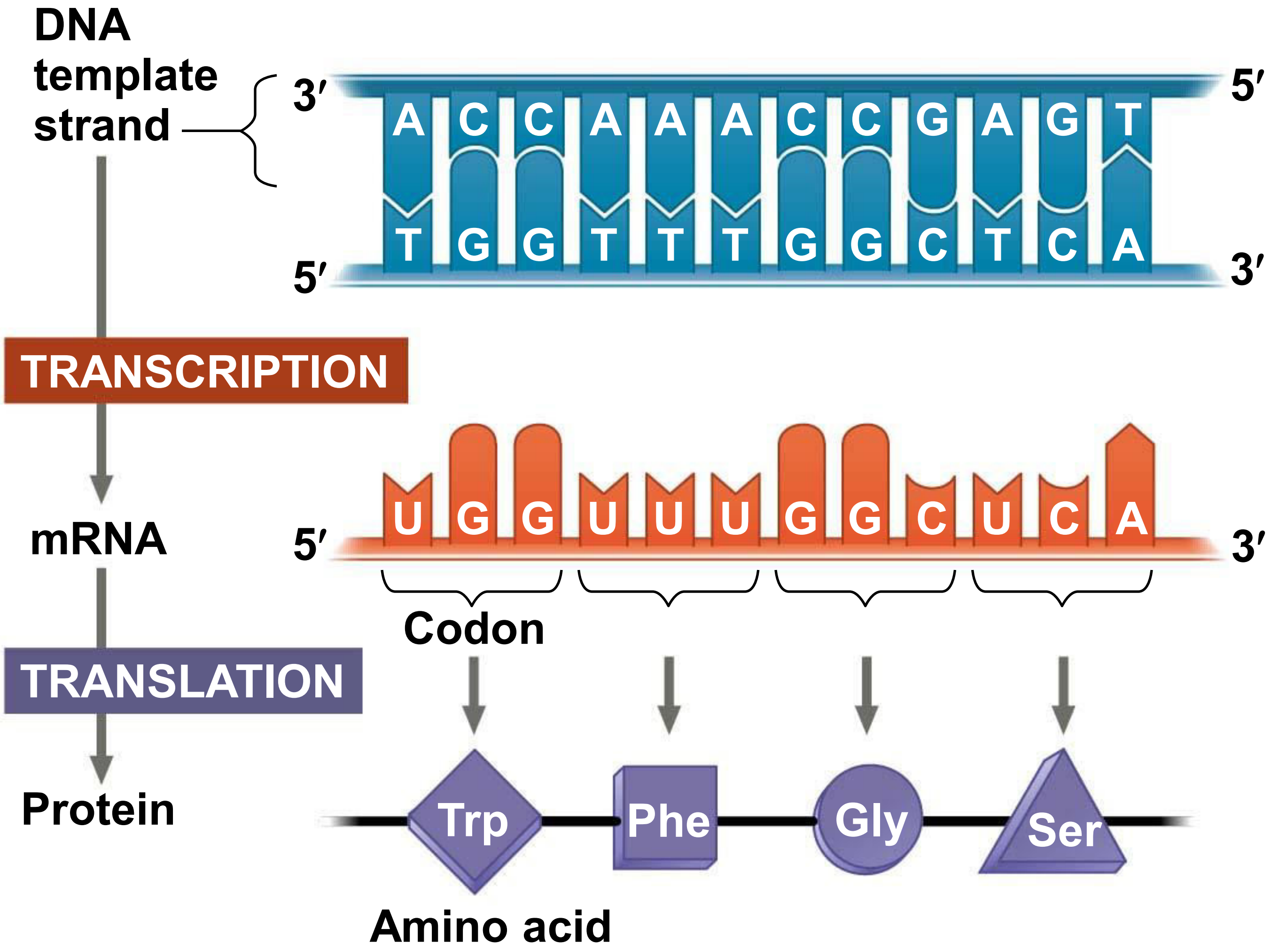

DNA molecule
Gene 1
Gene 2
Gene 3
DNA template strand
3′ A C C A A A C C G A G T 5′
5′ T G G T T T G G C T C A 3′
TRANSCRIPTION
mRNA
5′ U G G U U U G G C U C A 3′
Codon
TRANSLATION
Protein
Trp
Phe
Gly
Ser
Amino acid

Figure 14.5-1


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

- During transcription, one of the two DNA strands, called 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 any given gene

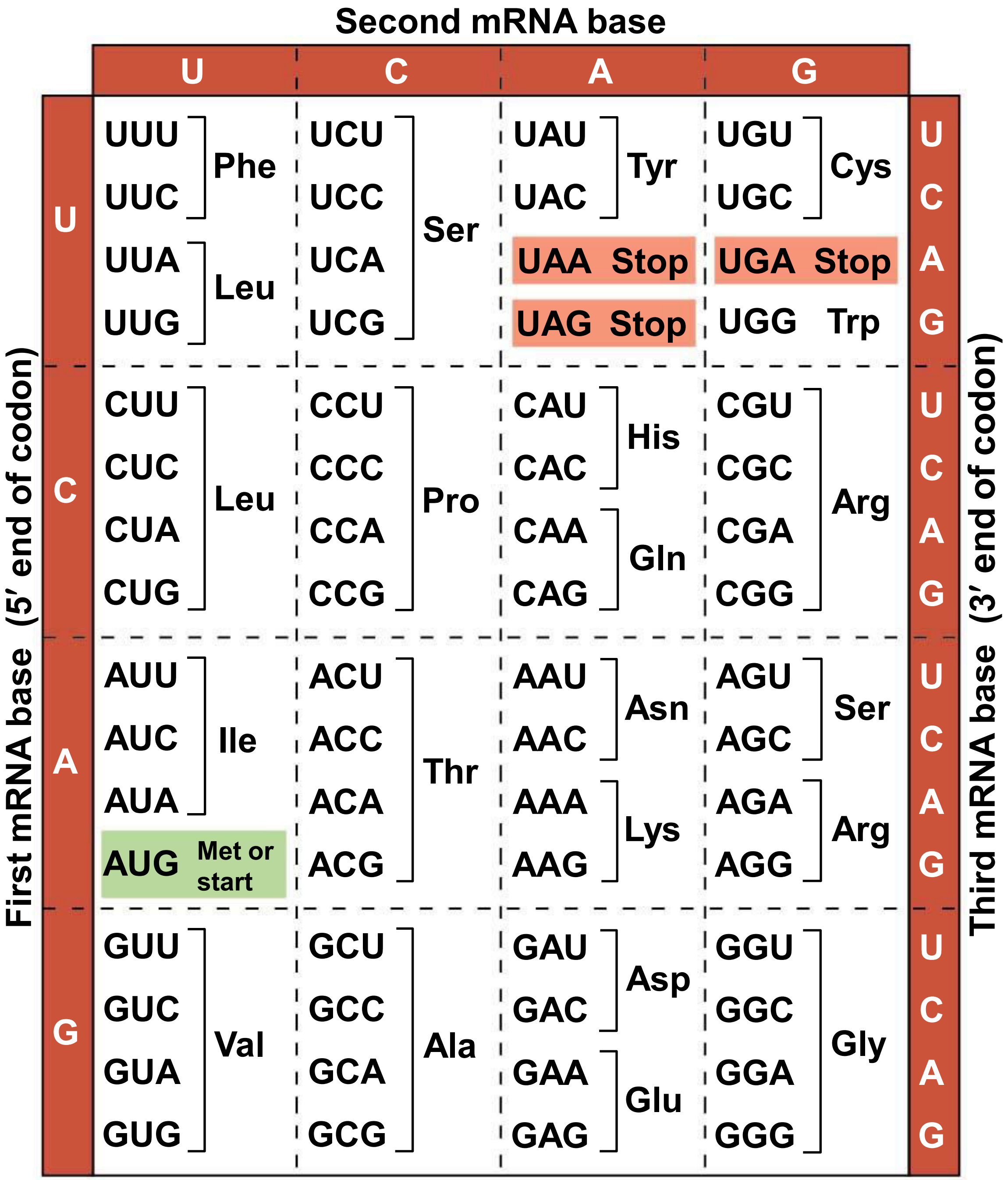
- During translation, the mRNA base triplets, called **codons**, are read in the 5′ to 3′ direction
- Each codon specifies the amino acid (one of 20) to be placed at the corresponding position along a polypeptide

Cracking the Code

- All 64 codons were deciphered by the mid-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 it is 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
- Codons are read one at a time in a nonoverlapping fashion

Figure 14.6

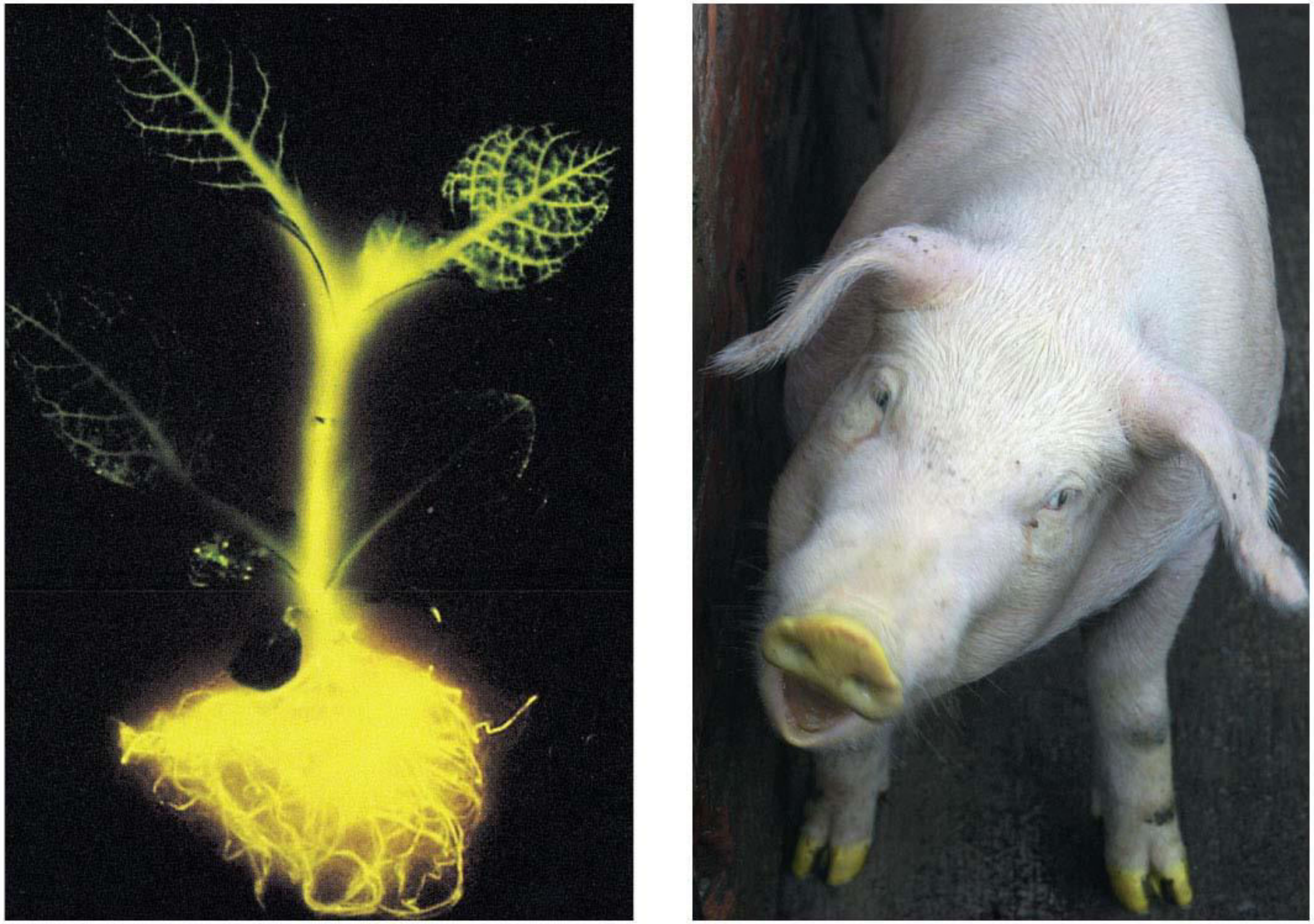


	Second mRNA base				
First mRNA base (5′ end of codon)	U	C	A	G	Third mRNA base (3′ end of codon)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC	UCC	UAC	UGC	C
	UUA Leu	UCA	UAA Stop	UGA Stop	A
	UUG	UCG	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC	CCC	CAC	CGC	C
	CUA	CCA	CAA Gln	CGA	A
	CUG	CCG	CAG	CGG	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC	ACC	AAC	AGC	C
	AUA	ACA	AAA Lys	AGA Arg	A
	AUG Met or start	ACG	AAG	AGG	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC	GCC	GAC	GGC	C
	GUA	GCA	GAA Glu	GGA	A
	GUG	GCG	GAG	GGG	G

Evolution of the Genetic Code

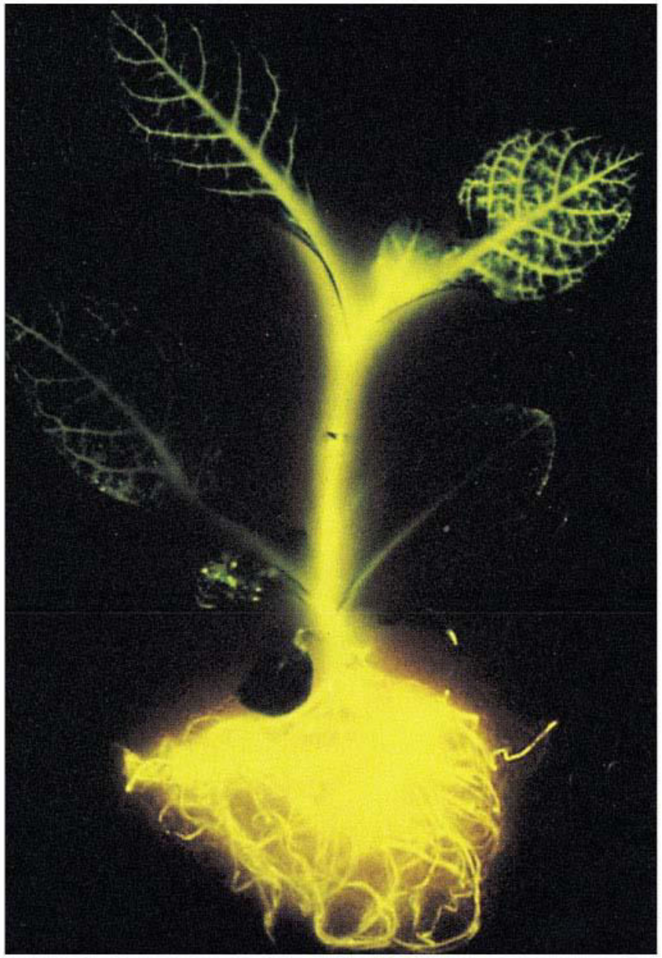
- The genetic code is nearly universal, shared by the simplest bacteria and the most complex animals
- Genes can be transcribed and translated after being transplanted from one species to another

Figure 14.7



(a) Tobacco plant expressing a firefly gene

(b) Pig expressing a jellyfish gene



(a) Tobacco plant expressing a firefly gene

Figure 14.7-2

(b) Pig expressing a jellyfish gene

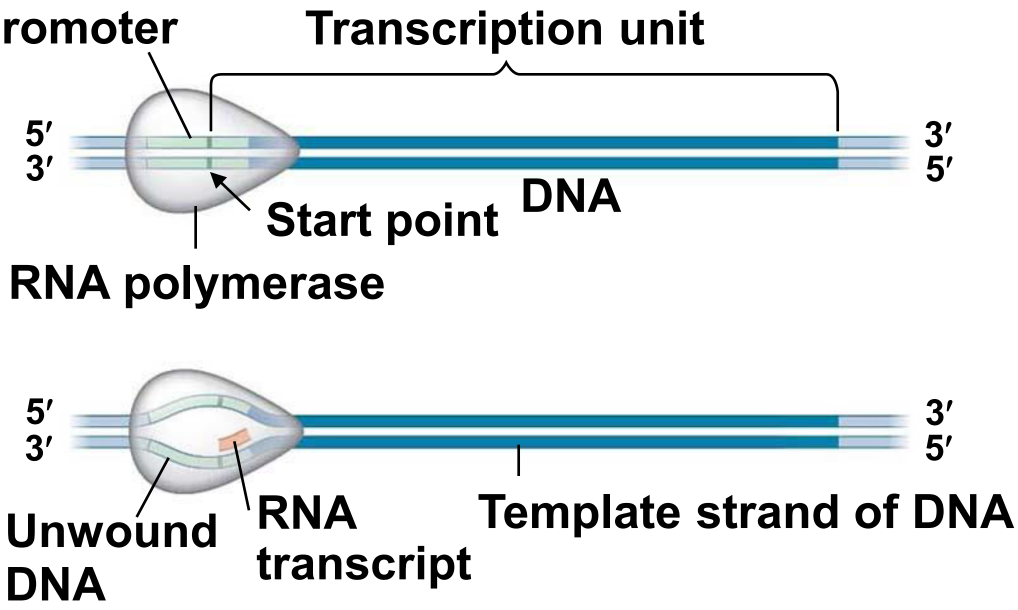
Concept 14.2: Transcription is the DNA-directed Synthesis of RNA: *A Closer Look*

- 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
- RNA polymerases assemble polynucleotides in the 5′ to 3′ direction
- Unlike DNA polymerases, RNA polymerases can start a chain without a primer

Figure 14.8-s1



① Initiation

Figure 14.8-s2

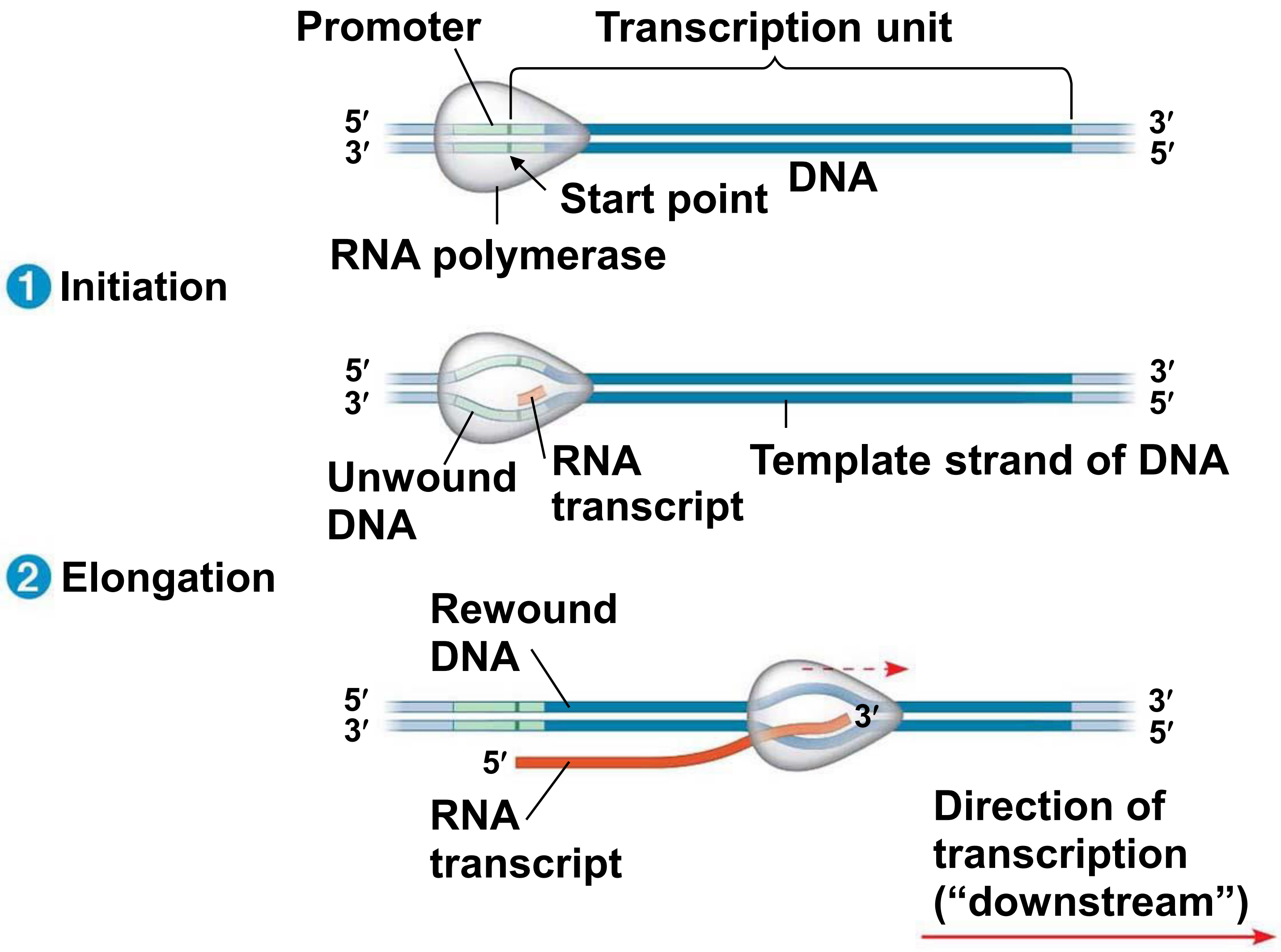
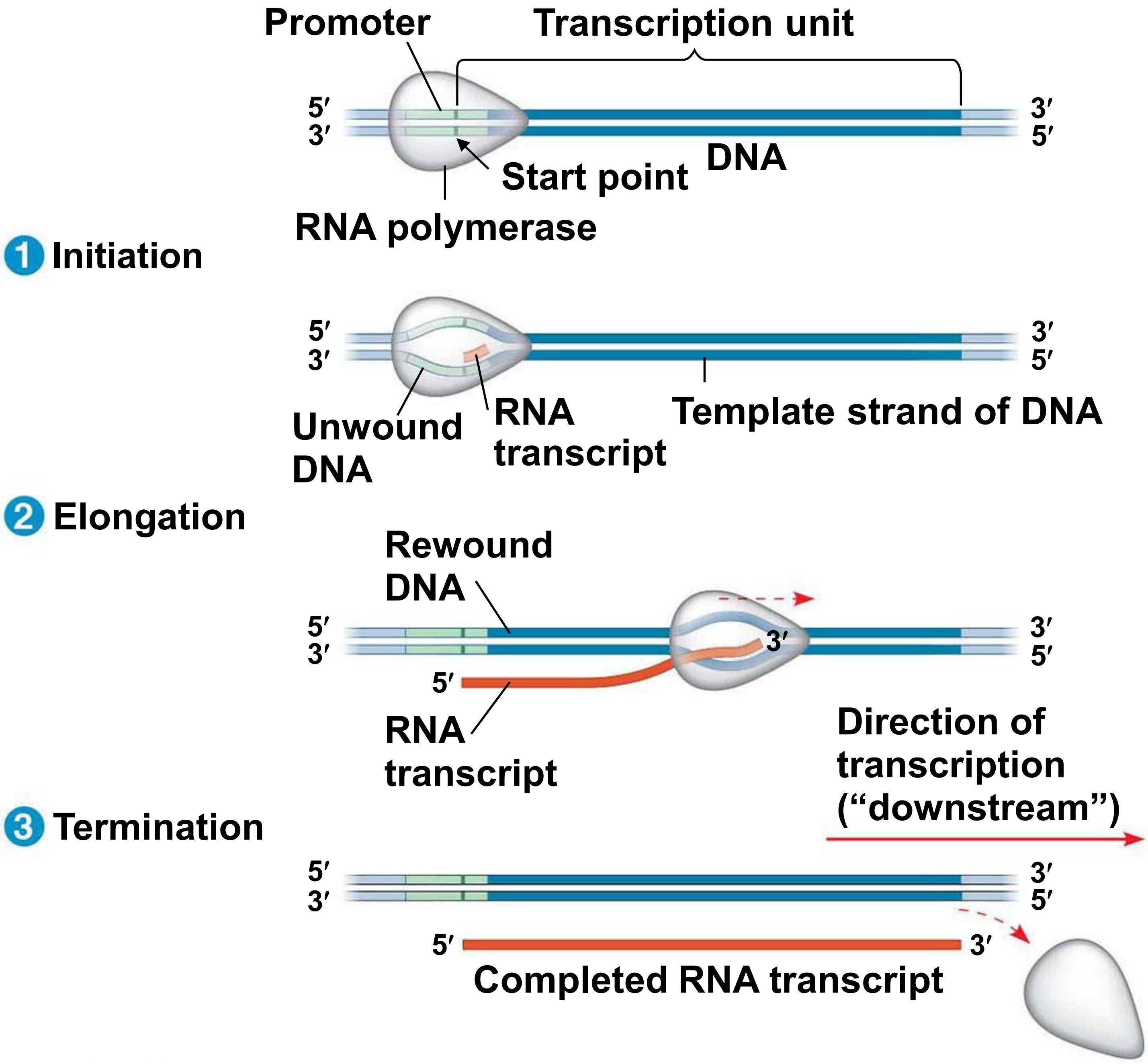


Figure 14.8-s3



- 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

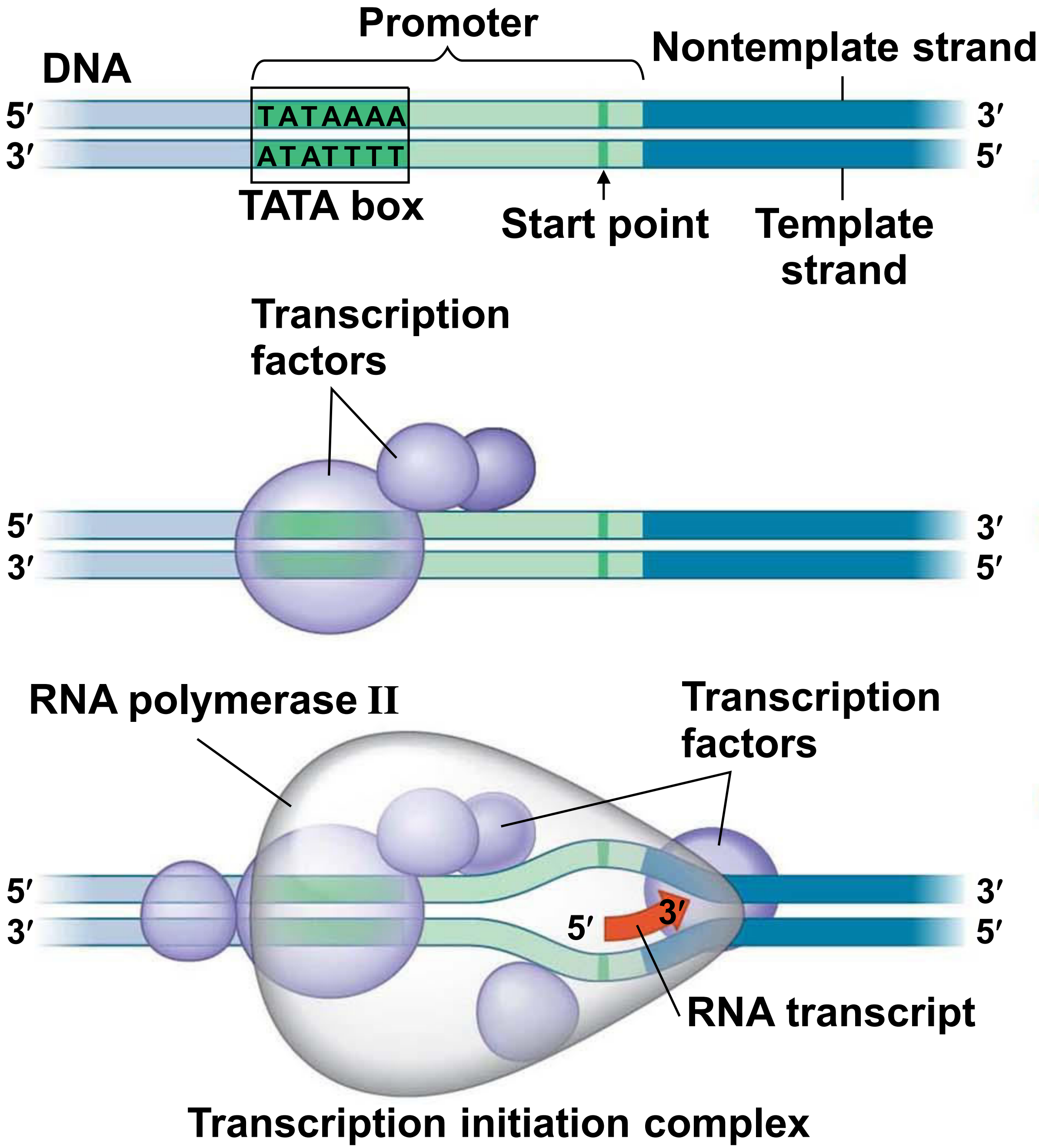
- The three stages of transcription
  - Initiation
  - Elongation
  - Termination

RNA Polymerase Binding and Initiation of Transcription

- Promoters signal the transcriptional **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 DNA sequence called a **TATA box** is crucial in forming the initiation complex in eukaryotes

Figure 14.9



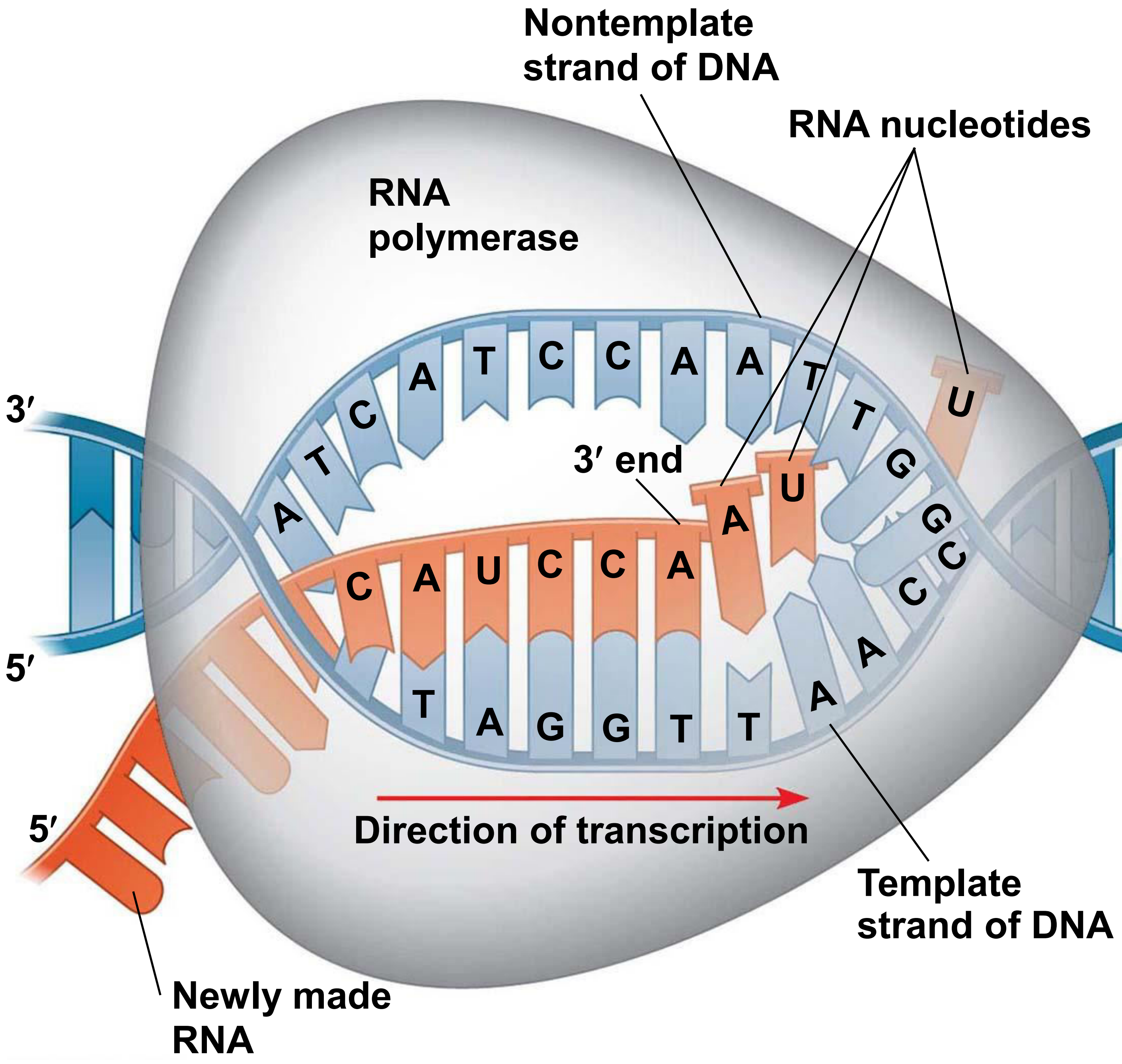
① A eukaryotic promoter

② Several transcription factors bind to DNA.

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


Nontemplate strand of DNA
RNA nucleotides
RNA polymerase
3′
5′
A T C A T C C A A T T G G
U
U
A
3′ end
C A U C C A
C C A A
T A G G T T A
5′
3′
5′
Direction of transcription
Template strand of DNA
Newly made RNA

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

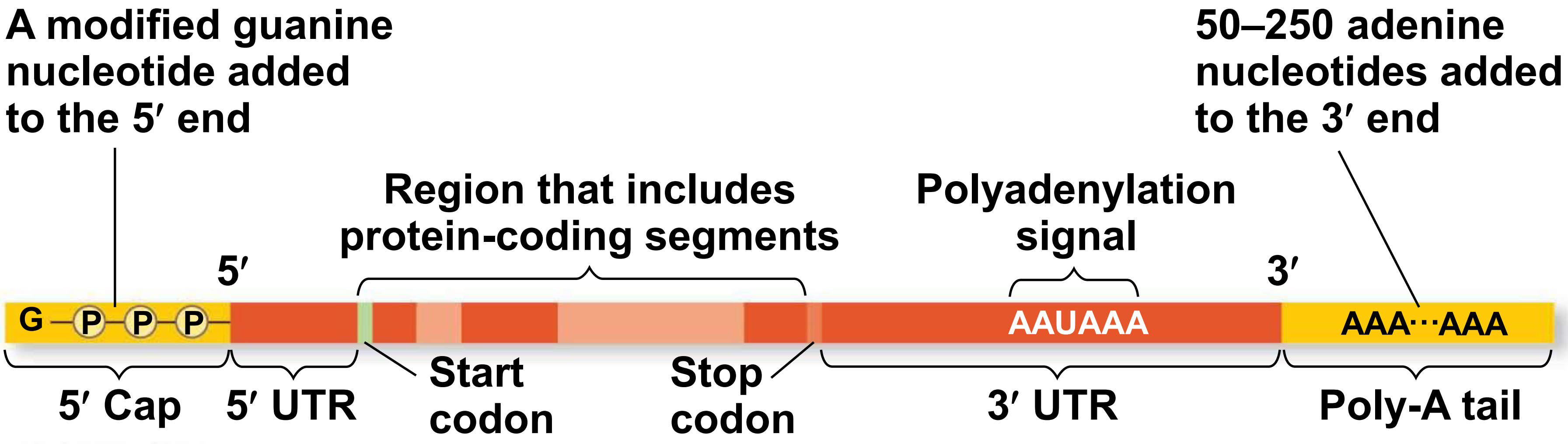
Concept 14.3: Eukaryotic cells modify RNA after transcription

- 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, usually some interior parts of the molecule are cut out and the other 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 G nucleotide **5′ cap**
  - The 3′ end gets a **poly-A tail**
- These modifications share several functions
  - Facilitating the export of mRNA to the cytoplasm
  - Protecting mRNA from hydrolytic enzymes
  - Helping ribosomes attach to the 5′ end

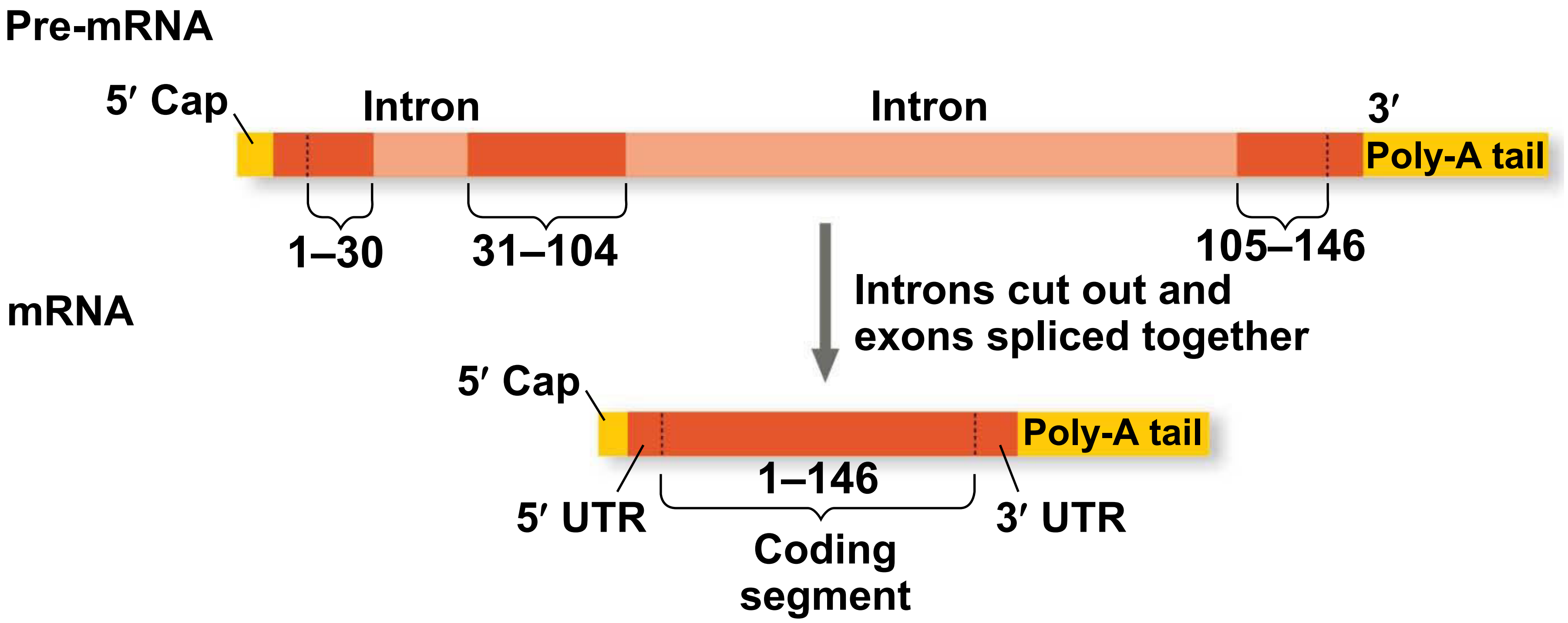
Figure 14.11


A modified guanine nucleotide added to the 5′ end
50–250 adenine nucleotides added to the 3′ end
Region that includes protein-coding segments
Polyadenylation signal
5′
3′
G–P–P–P
AAUAAA
AAA···AAA
5′ Cap
5′ UTR
Start codon
Stop codon
3′ UTR
Poly-A tail

Split Genes and RNA Splicing

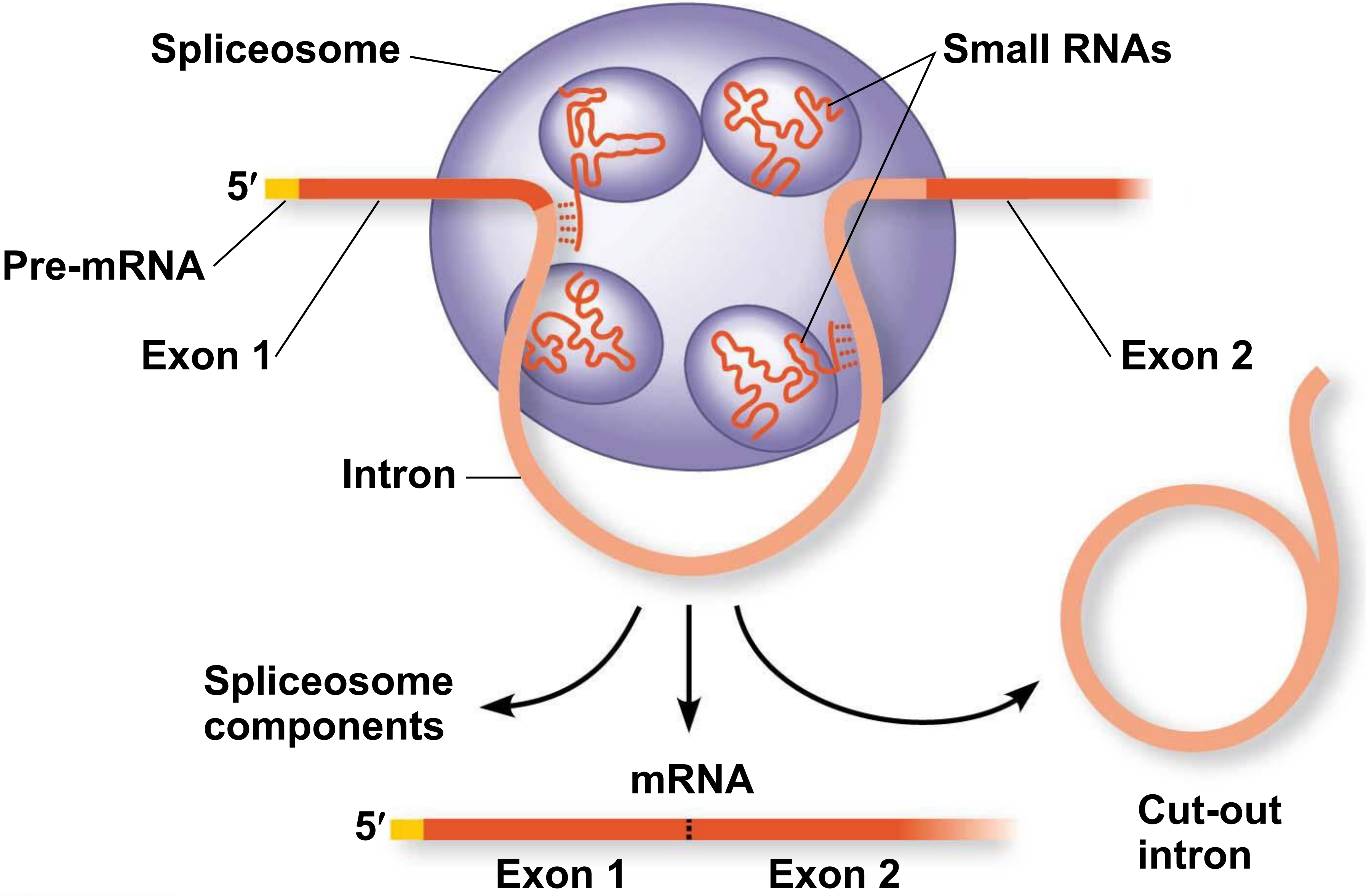
- Most eukaryotic mRNAs have long noncoding stretches of nucleotides that lie between coding regions
- The noncoding regions are called intervening sequences, or **introns**
- The other regions are called **exons** and are usually translated into amino acid sequences
- **RNA splicing** removes introns and joins exons, creating an mRNA molecule with a continuous coding sequence

Figure 14.12


Pre-mRNA
5′ Cap
Intron
Intron
3′
Poly-A tail
1–30
31–104
105–146
Introns cut out and exons spliced together
mRNA
5′ Cap
Poly-A tail
1–146
5′ UTR
3′ UTR
Coding segment

- Many genes can give rise to two or more different polypeptides, depending on which segments are used as exons
- This process is called **alternative RNA splicing**
- RNA splicing is carried out by spliceosomes
- **Spliceosomes** consist of proteins and small RNAs

Figure 14.13


Spliceosome
Small RNAs
5′
Pre-mRNA
Exon 1
Exon 2
Intron
Spliceosome components
mRNA
5′
Exon 1
Exon 2
Cut-out intron

Ribozymes

- **Ribozymes** are RNA molecules that function as enzymes
- In some organisms, RNA splicing can occur without proteins, or even additional RNA molecules
- The introns can catalyze their own splicing

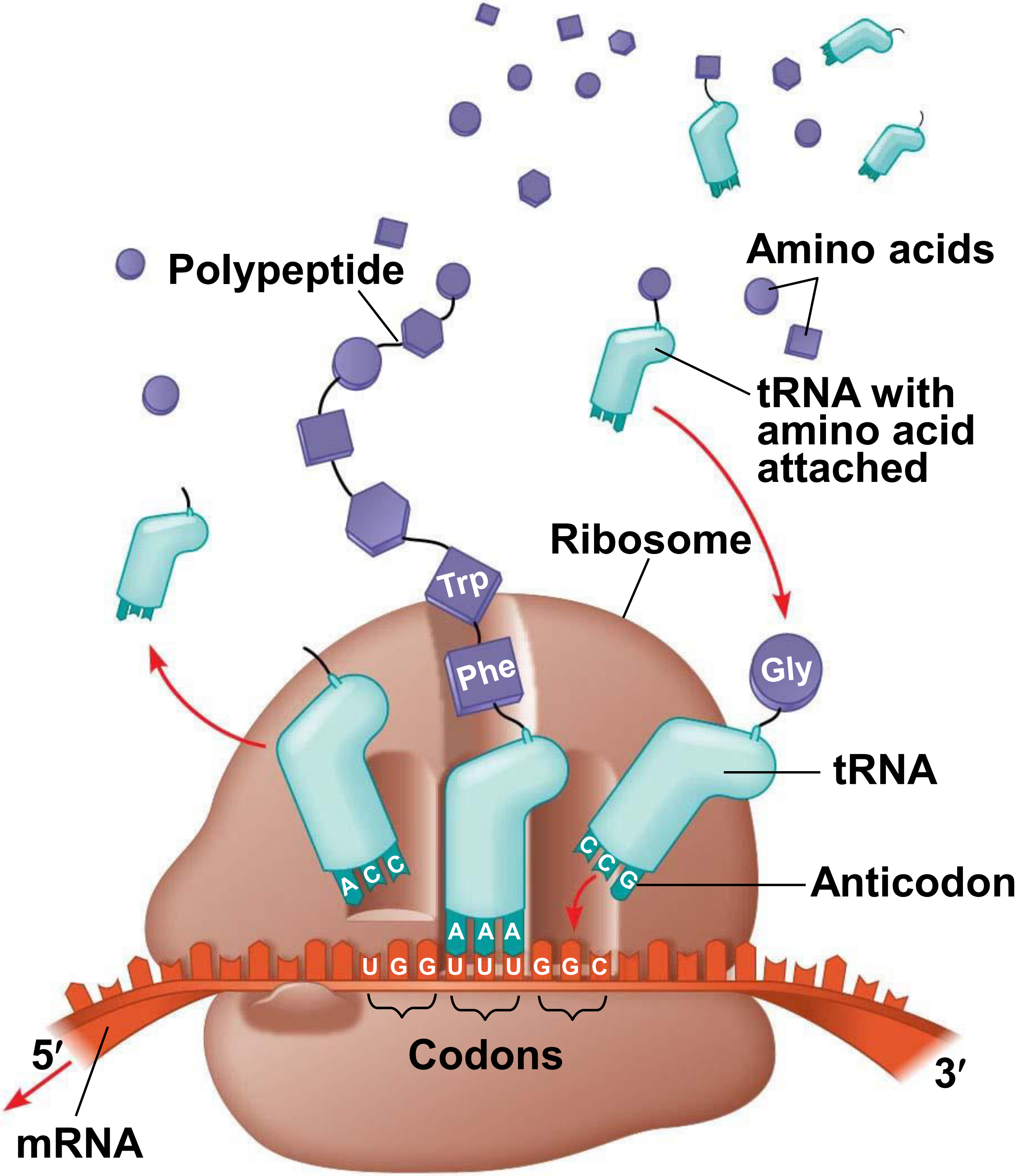
Concept 14.4: Translation is the RNA-directed Synthesis of a Polypeptide: *A Closer Look*

- 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 14.14



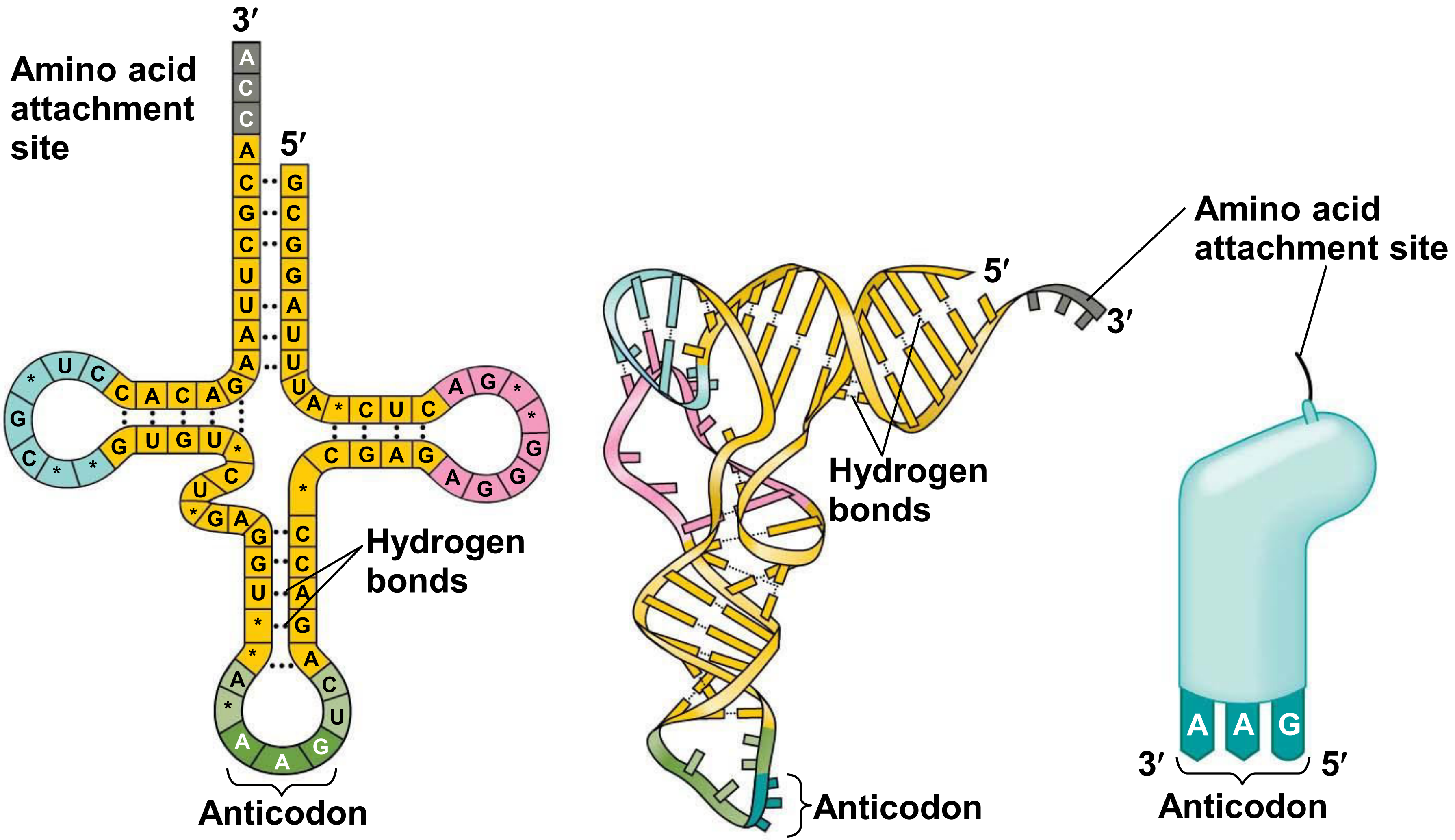
Polypeptide
Amino acids
tRNA with amino acid attached
Ribosome
Trp
Phe
Gly
tRNA
A C C
A A A
C C G
Anticodon
U G G U U U G G C
Codons
5′
3′
mRNA

The Structure and Function of Transfer RNA

- Each tRNA can translate a particular mRNA codon into a given amino acid
- The tRNA contains an amino acid at one end and at the other end has a nucleotide triplet that can base-pair with the complementary codon on mRNA

- A tRNA molecule consists of a single RNA strand that is about 80 nucleotides long
- tRNA molecules can base-pair with themselves
- Flattened into one plane, a tRNA molecule looks like a cloverleaf
- In three dimensions, tRNA is roughly L-shaped, where one end of the L contains the **anticodon** that base-pairs with an mRNA codon

Figure 14.15

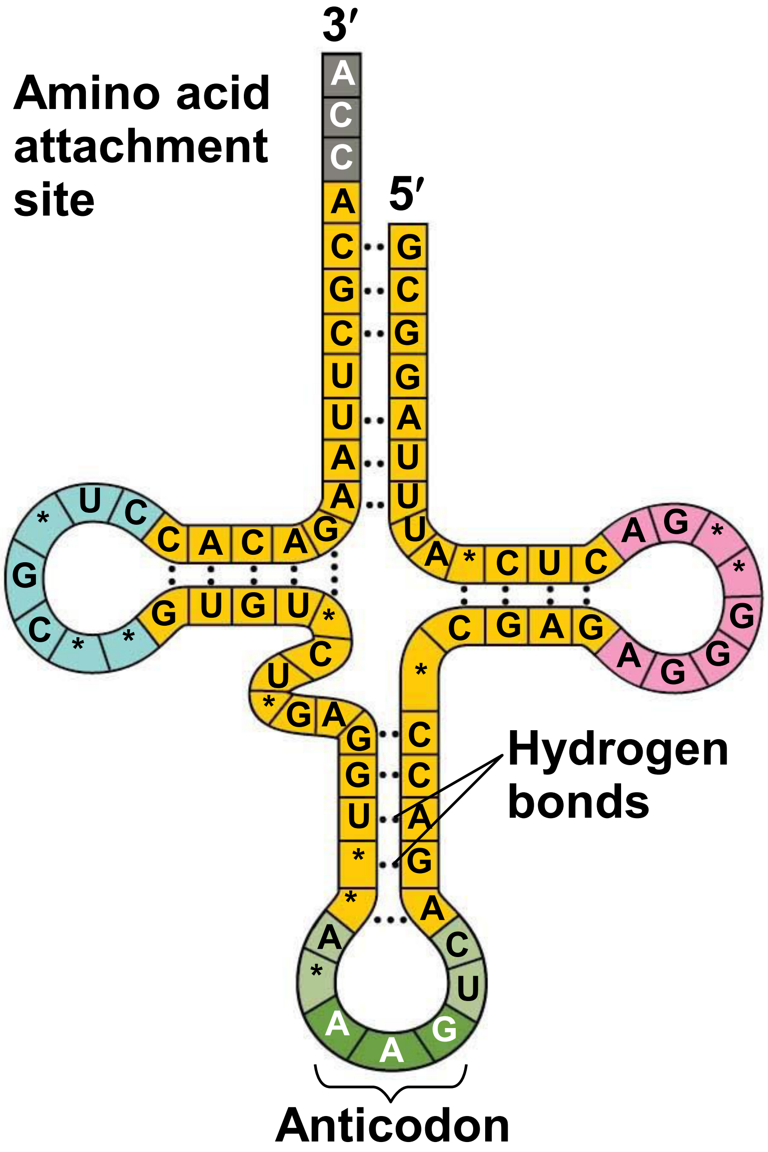


(a) Two-dimensional structure

(b) Three-dimensional structure

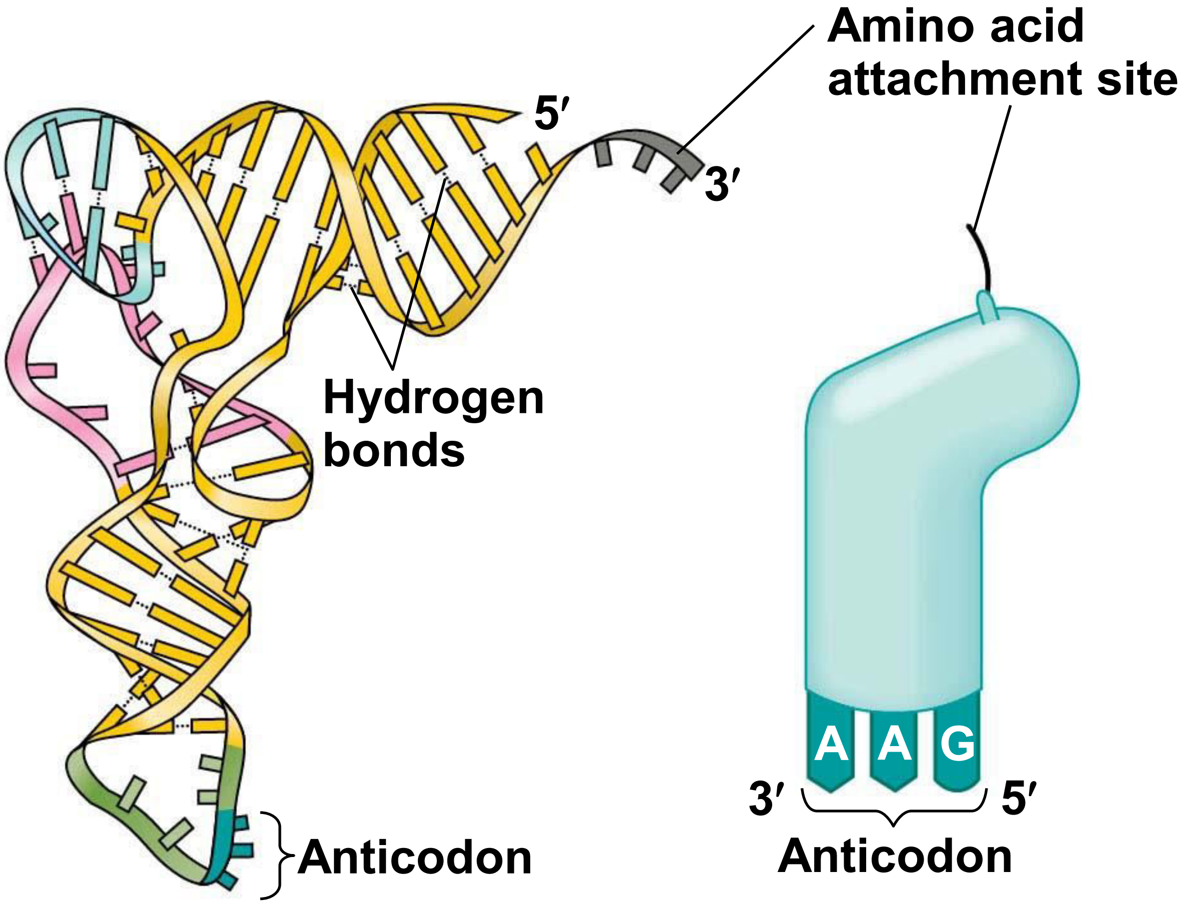
(c) Symbol used in this book

Figure 14.15-1



(a) Two-dimensional structure

Figure 14.15-2

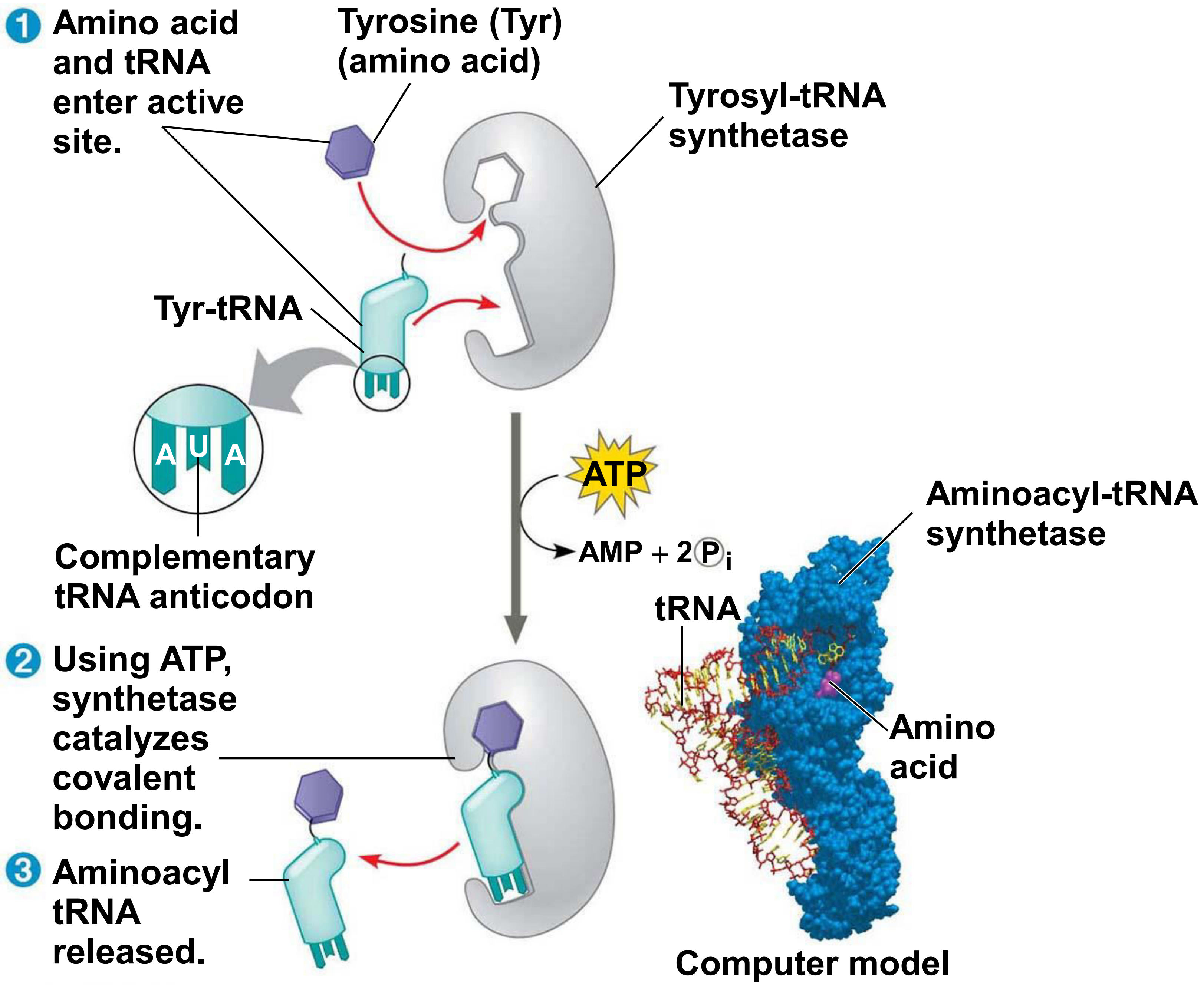


(b) Three-dimensional structure

(c) Symbol used in this book

- 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 14.16



① Amino acid and tRNA enter active site.

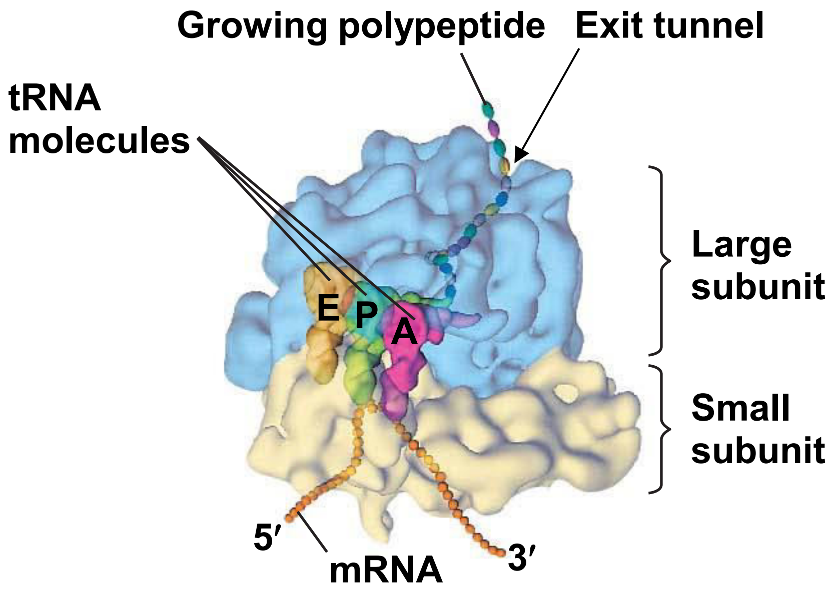
② Using ATP, synthetase catalyzes covalent bonding.

③ Aminoacyl tRNA released.

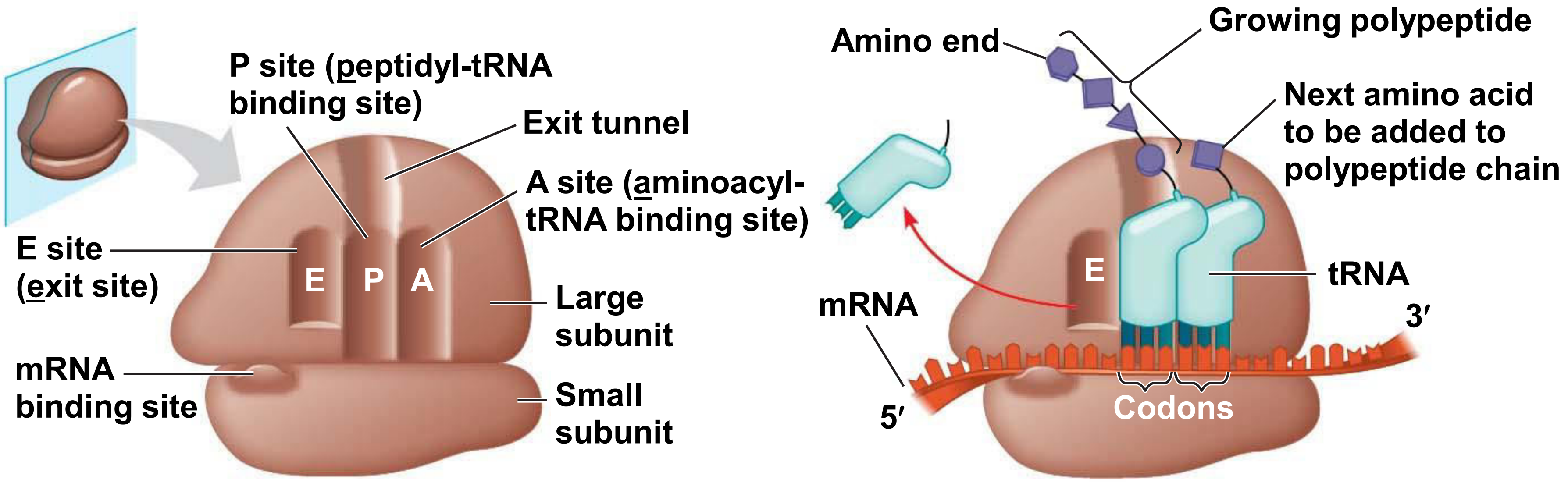
Ribosomes

- Ribosomes facilitate specific coupling of tRNA anticodons with mRNA codons during protein synthesis
- The large and small ribosomal are made of proteins and **ribosomal RNAs** (**rRNAs**)
- In bacterial and eukaryotic ribosomes the large and small subunits join to form a ribosome only when attached to an mRNA molecule

Figure 14.17



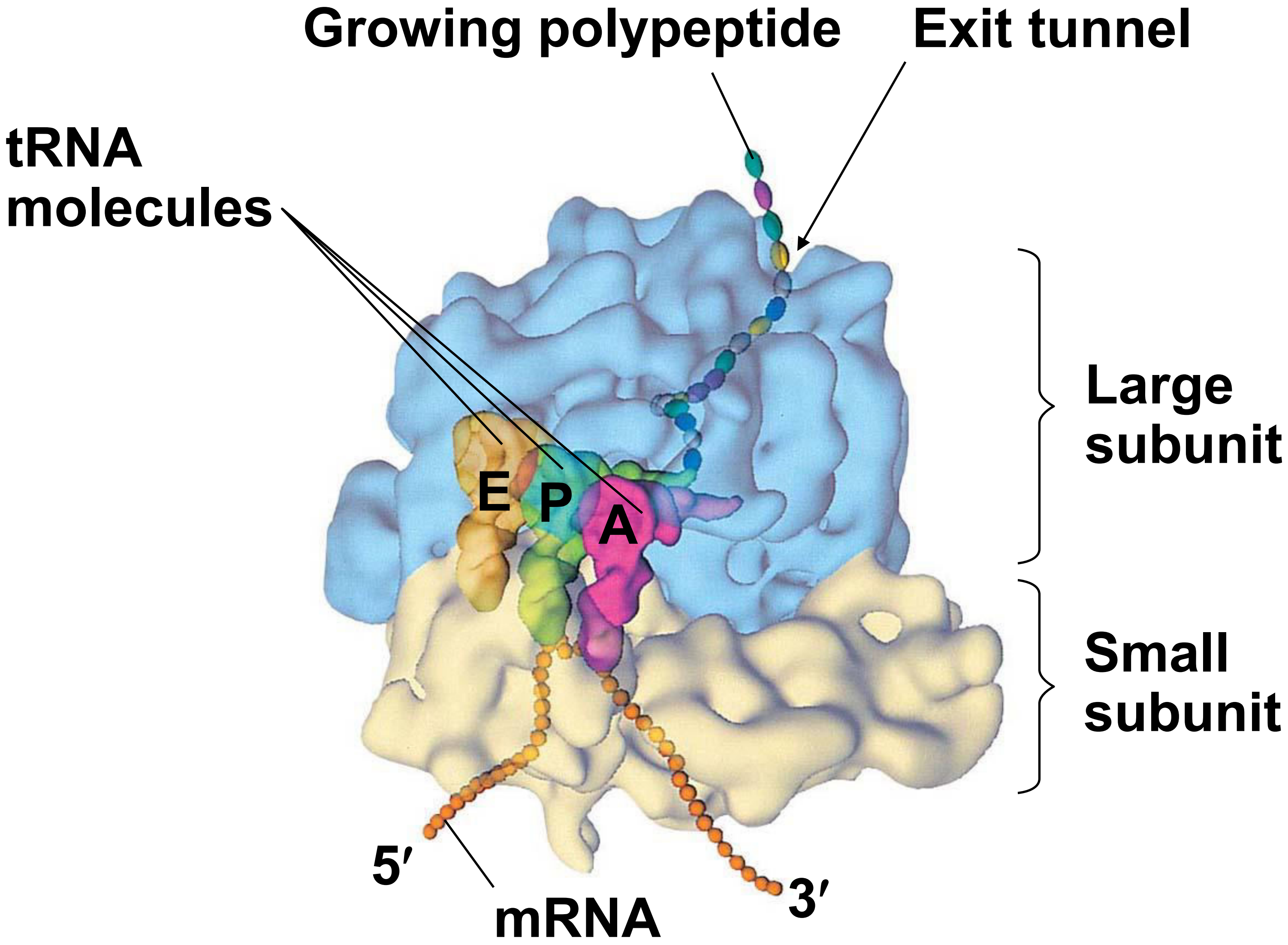
(a) Computer model of functioning ribosome



(b) Schematic model showing binding sites

(c) Schematic model with mRNA and tRNA

Figure 14.17-1



(a) Computer model of functioning ribosome

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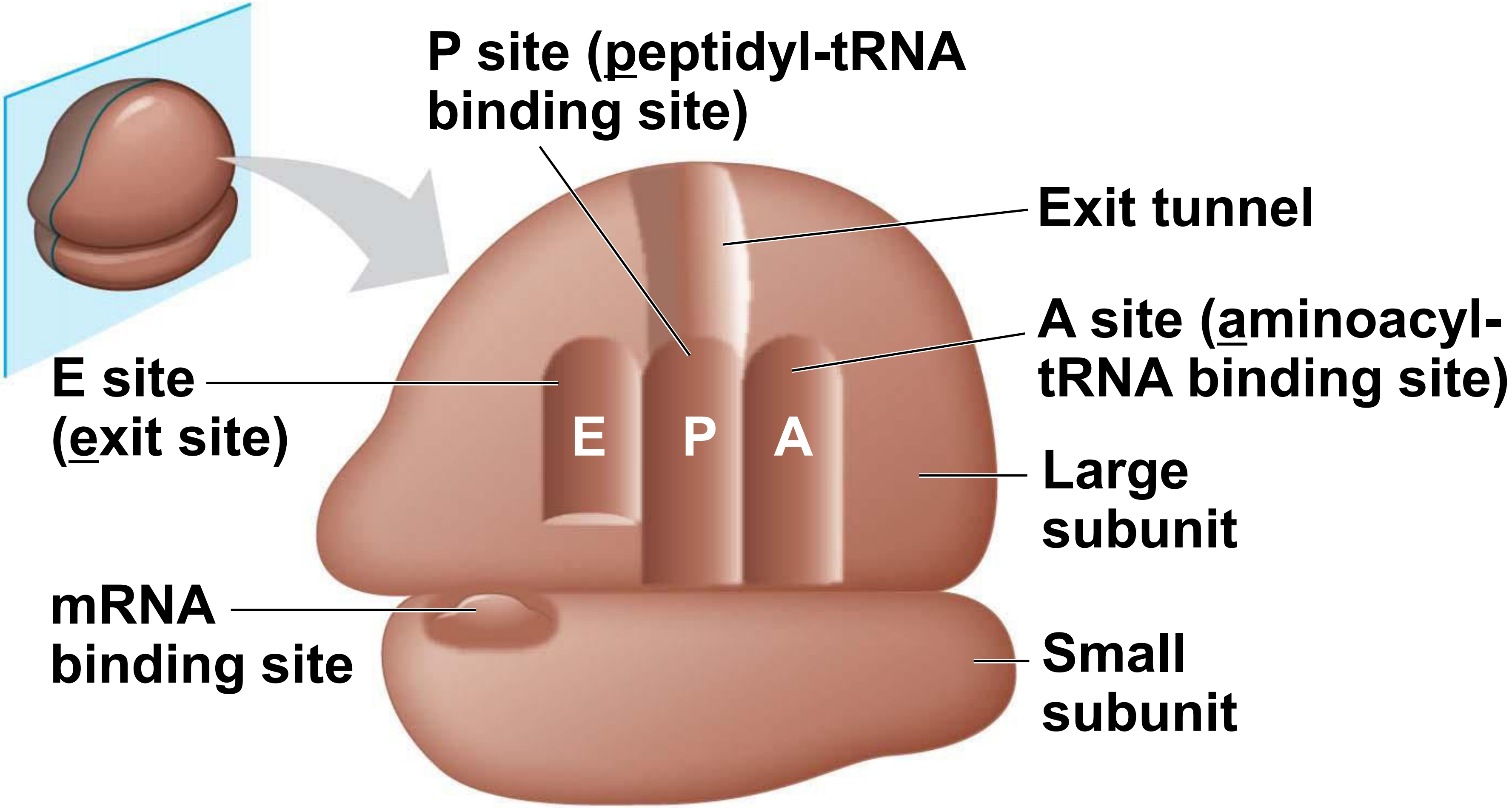
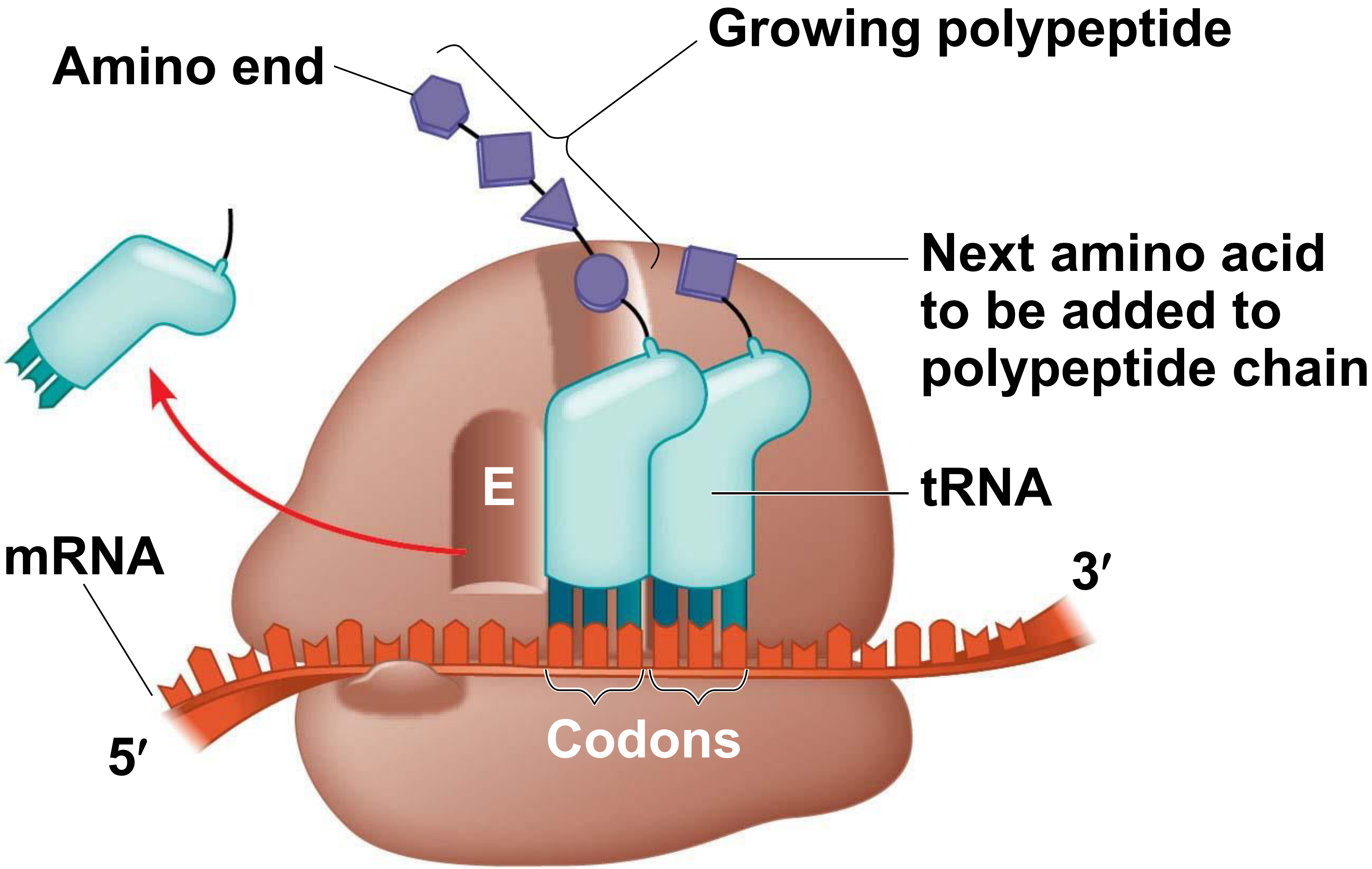


(b) Schematic model showing binding sites



(c) Schematic model with mRNA and tRNA

- 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

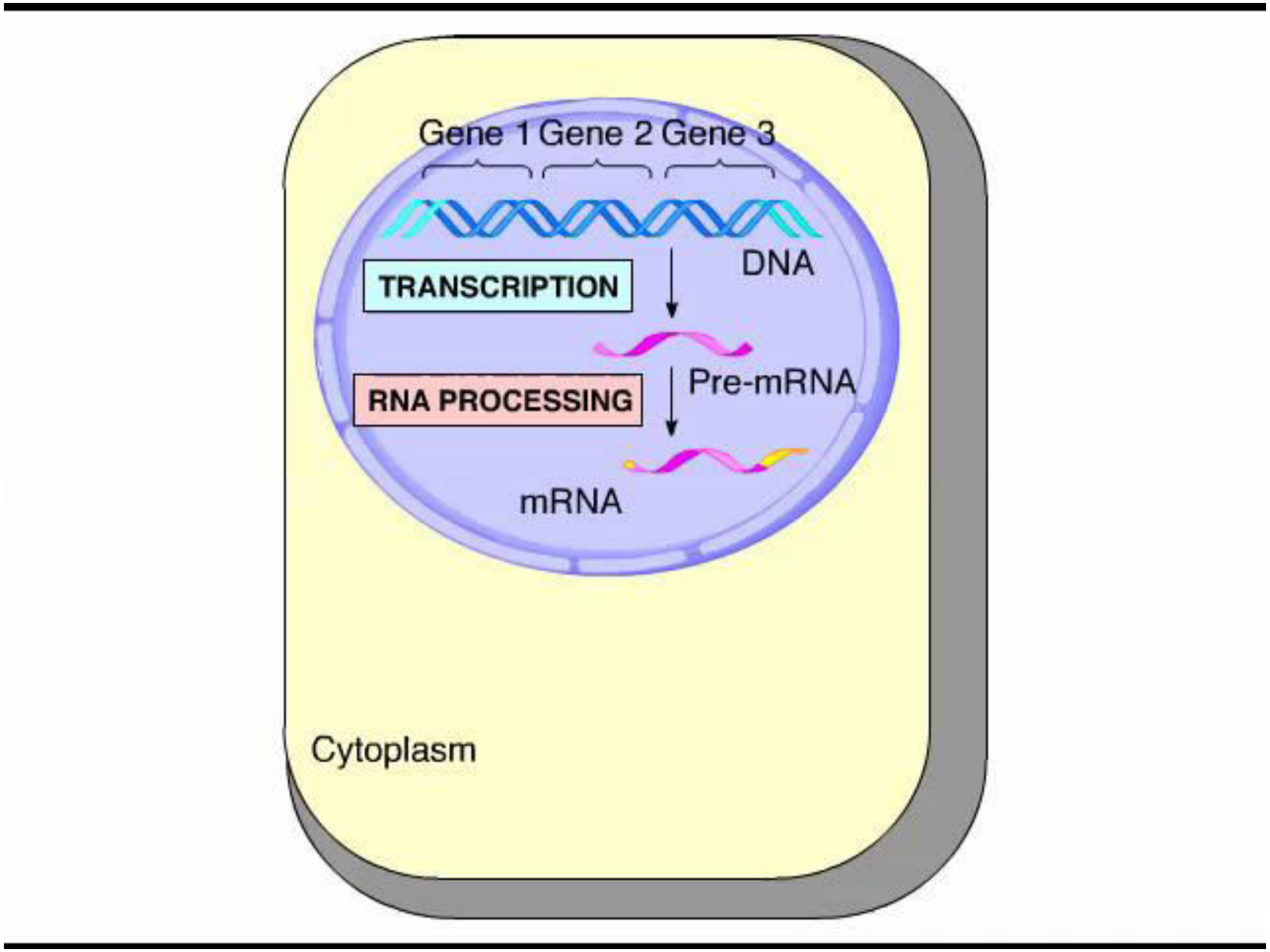
Building a Polypeptide

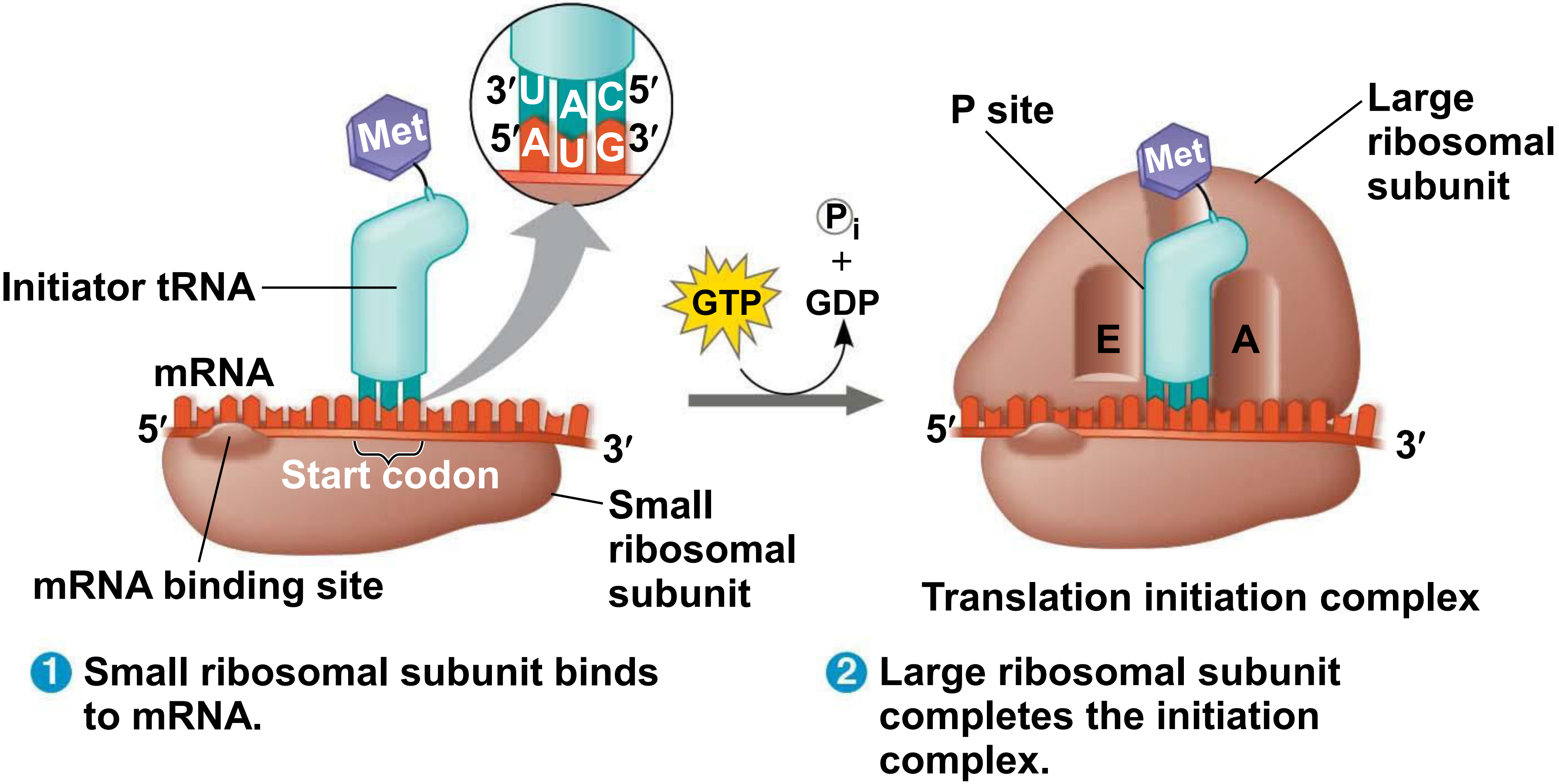
- The three stages of translation
  - Initiation
  - Elongation
  - Termination
- All three stages require protein “factors” that aid in the translation process
- Energy is provided by hydrolysis of GTP

Ribosome Association and Initiation of Translation

- The initiation stage of translation brings together mRNA, a tRNA with the first amino acid, and the two ribosomal subunits
- 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 (AUG)

Animation: Translation Introduction




3′ U A C 5′
5′ A U G 3′
Met
Initiator tRNA
mRNA
5′
3′
Start codon
Small ribosomal subunit
mRNA binding site
GTP
P_i
+
GDP
P site
Large ribosomal subunit
Met
E
A
5′
3′
Translation initiation complex
① Small ribosomal subunit binds to mRNA.
② Large ribosomal subunit completes the initiation complex.

- The start codon is important because it establishes the reading frame for the mRNA
- The addition of the large ribosomal subunit is last and completes the formation of the translation initiation complex
- Proteins called initiation factors bring all these components together

Elongation of the Polypeptide Chain

- During elongation, amino acids are added one by one to the previous amino acid at the C-terminus of the growing chain
- Each addition involves proteins called elongation factors and occurs in three steps: codon recognition, peptide bond formation, and translocation
- Translation proceeds along the mRNA in a 5′ to 3′ direction

Figure 14.19-s1

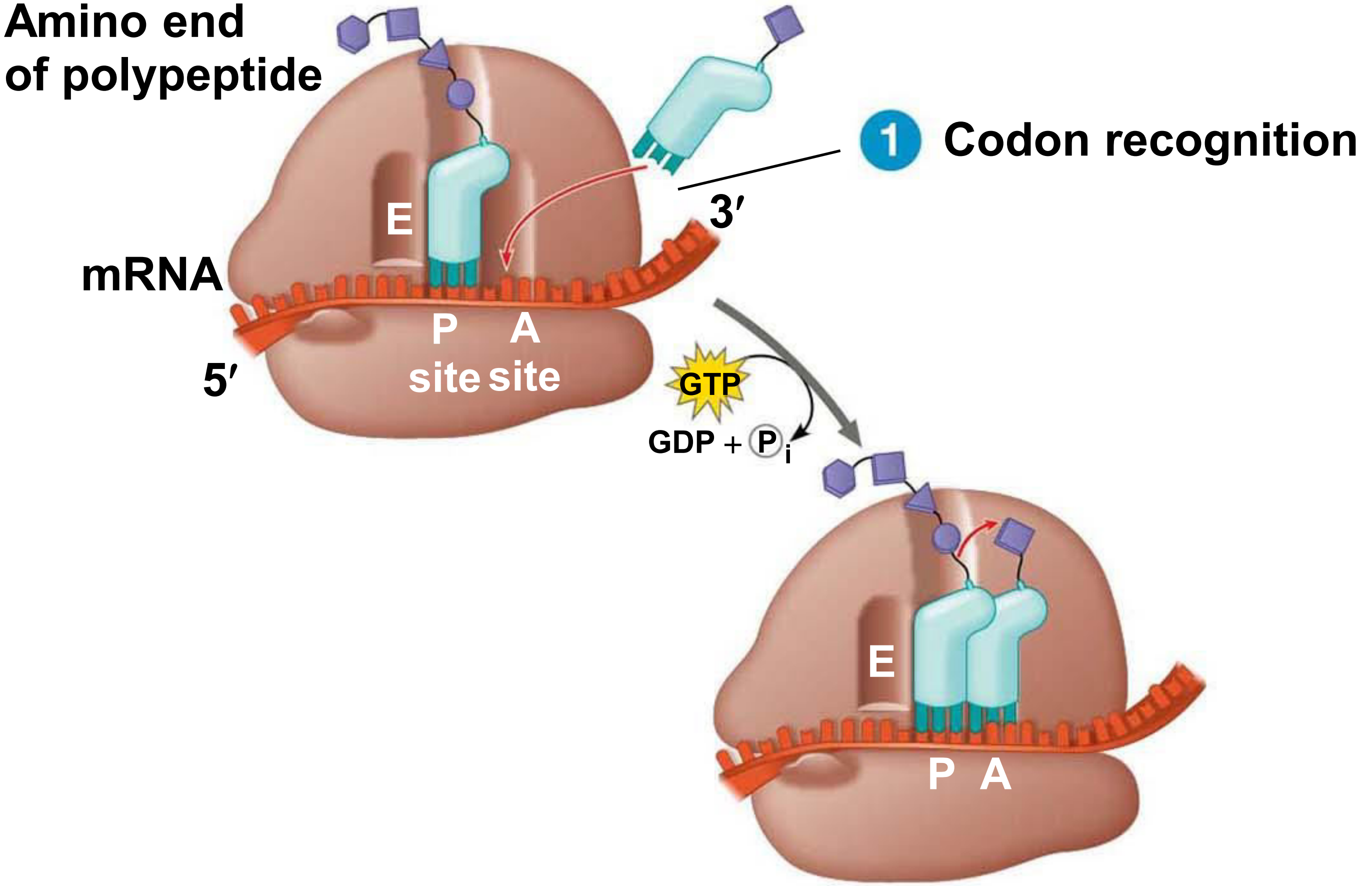
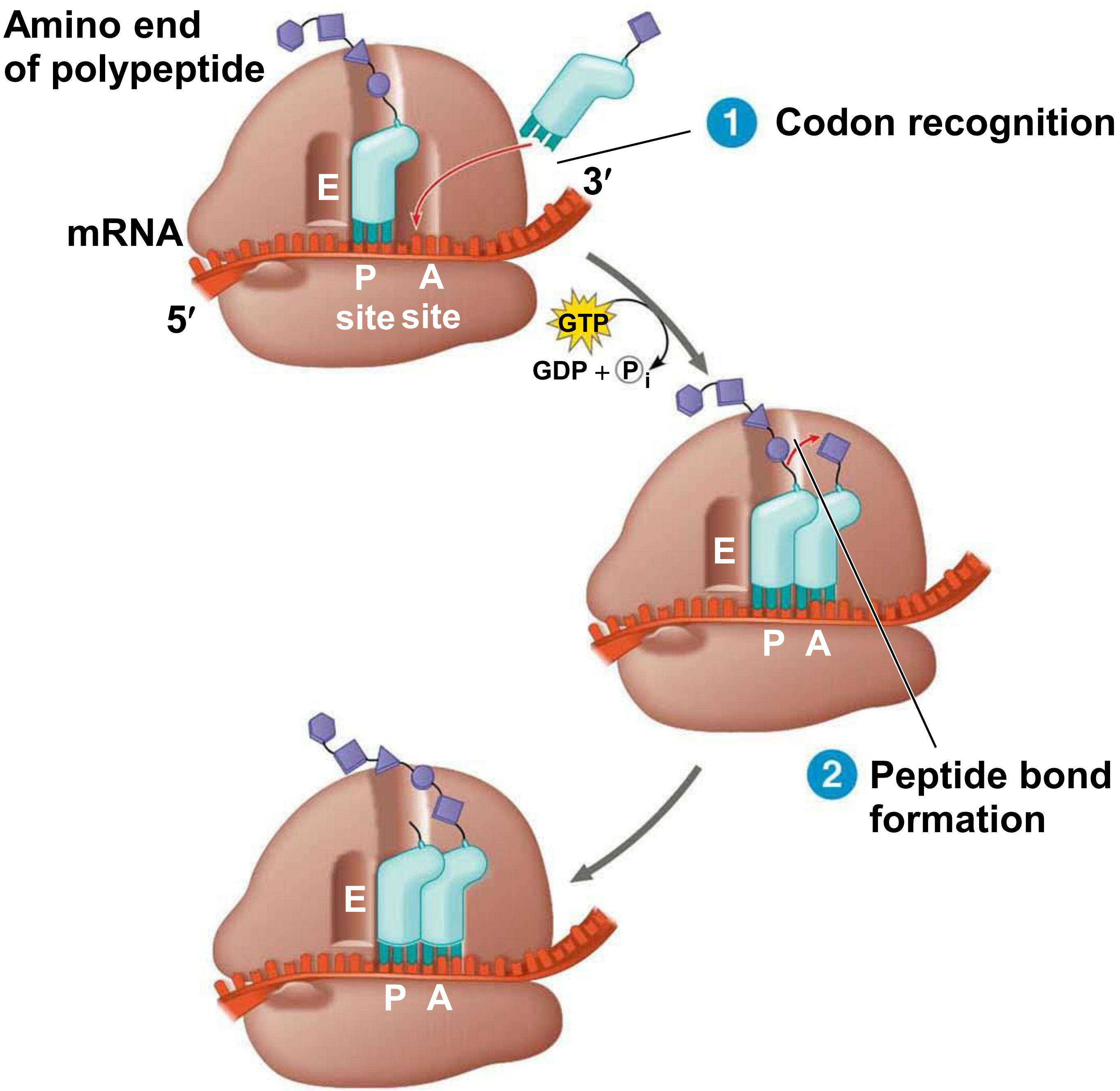
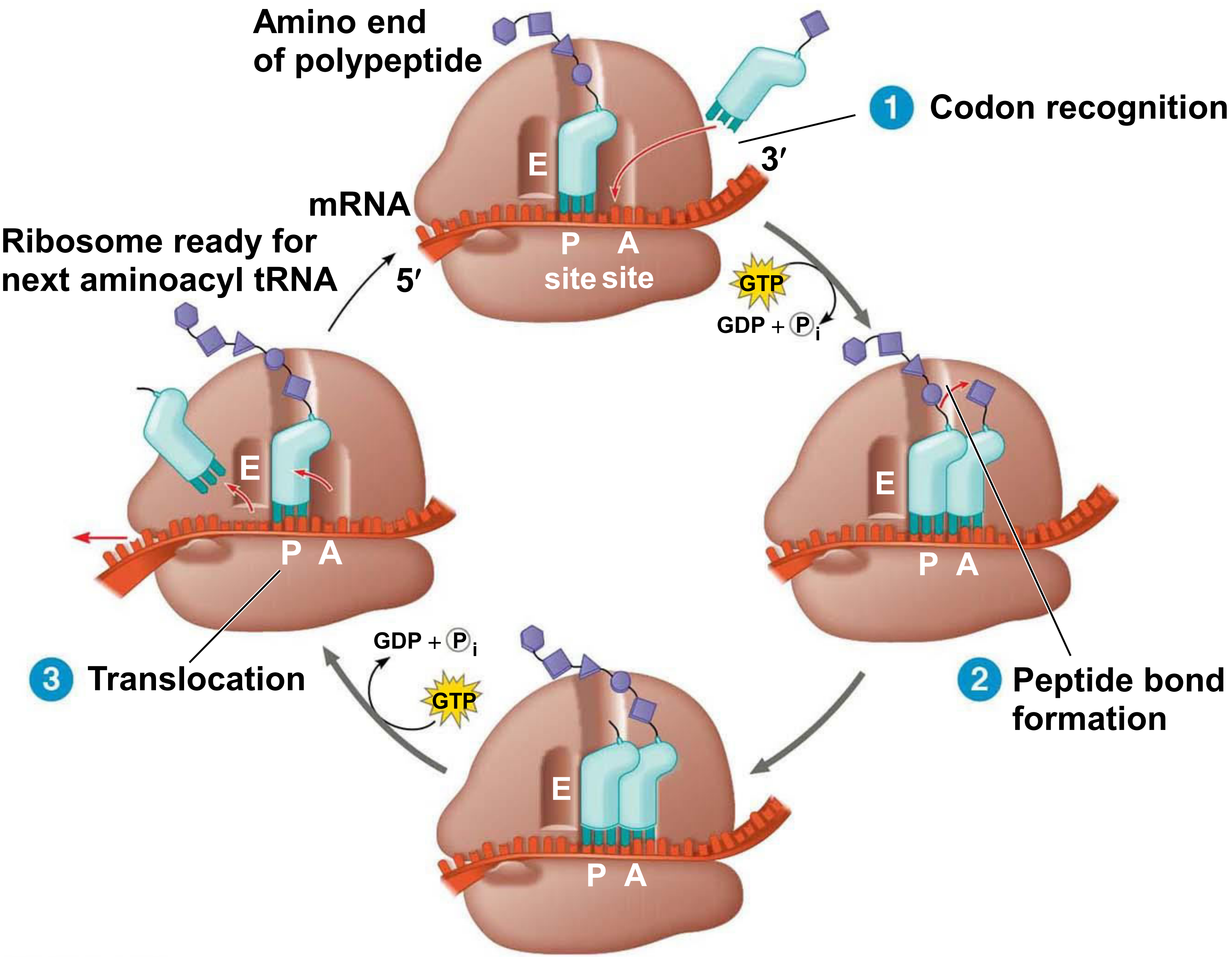


Figure 14.19-s2

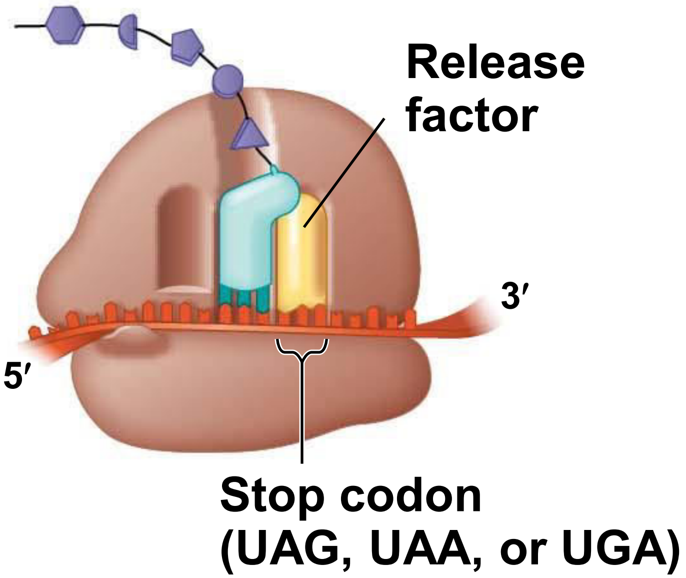



Amino end of polypeptide
E
mRNA
3′
5′
P site
A site
① Codon recognition
GTP
GDP + Ⓟi
E
P
A
② Peptide bond formation
E
P
A
GDP + Ⓟi
GTP
E
P
A
③ Translocation
Ribosome ready for next aminoacyl tRNA

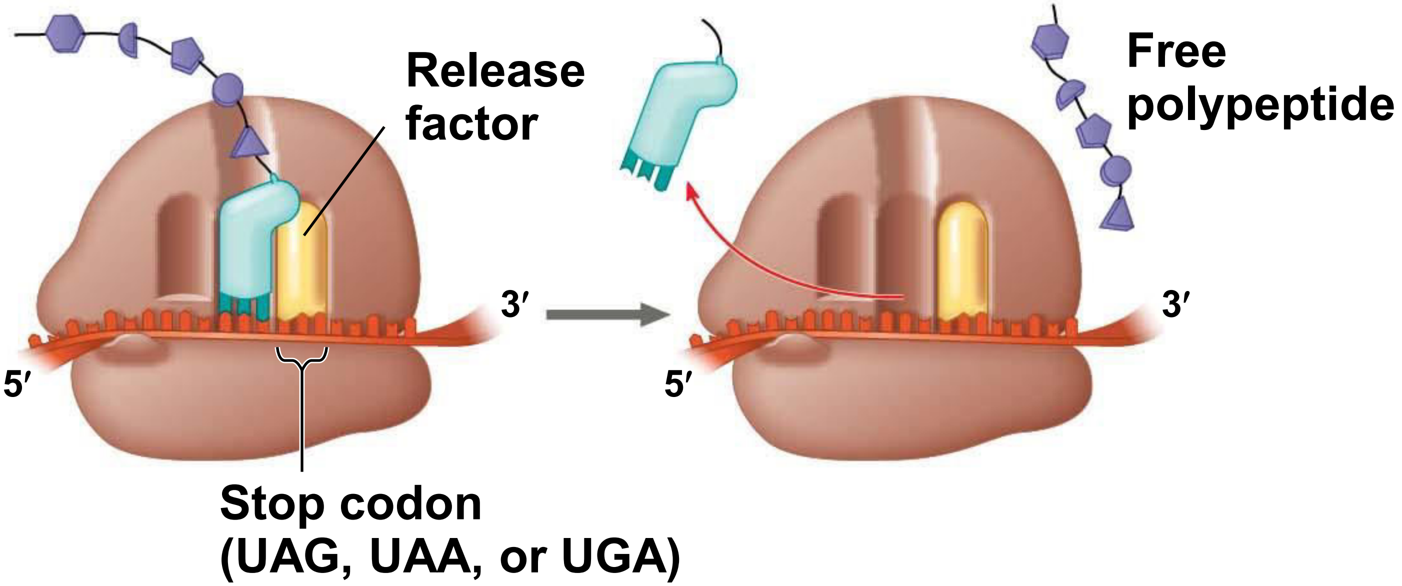
Termination of Translation

- Termination occurs when 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 then comes apart

Figure 14.20-s1

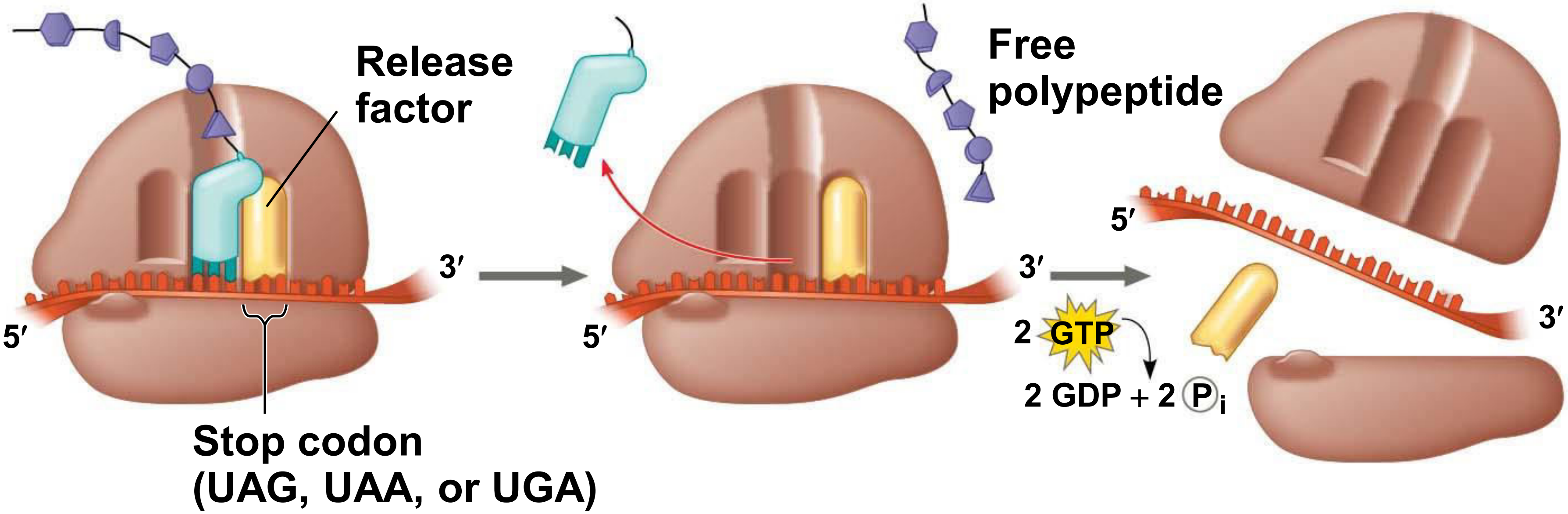


① Ribosome reaches a stop codon on mRNA.



① **Ribosome reaches a stop codon on mRNA.**

② **Release factor promotes hydrolysis.**



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 synthesis, a polypeptide chain spontaneously coils and folds into its three-dimensional shape
- Proteins may also require post-translational modifications before doing their jobs

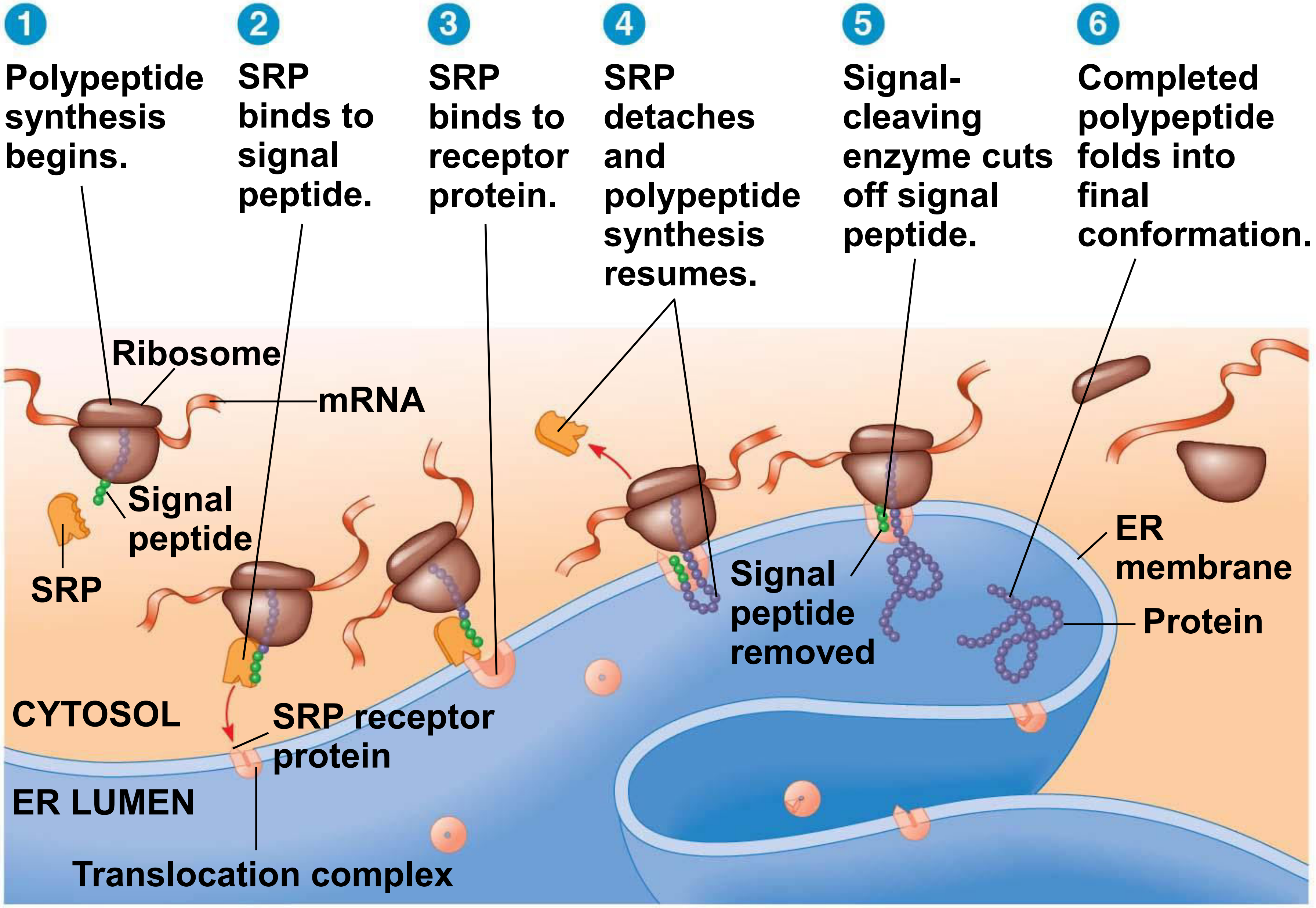
Targeting Polypeptides to Specific Locations

- 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

- 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 brings the signal peptide and its ribosome to the ER

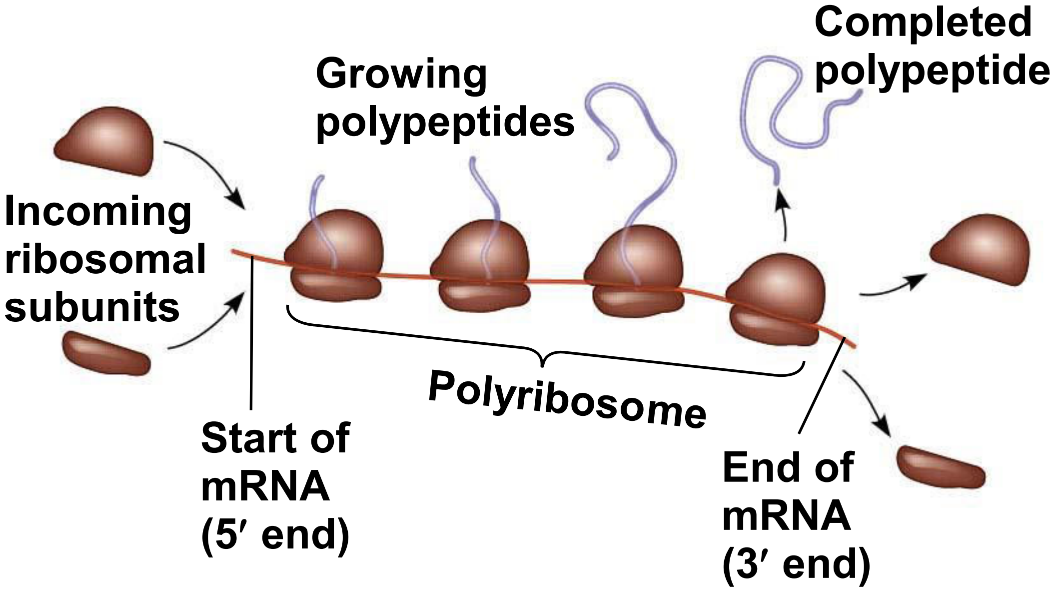
Figure 14.21


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
CYTOSOL
SRP receptor protein
ER LUMEN
Translocation complex
Signal peptide removed
ER membrane
Protein

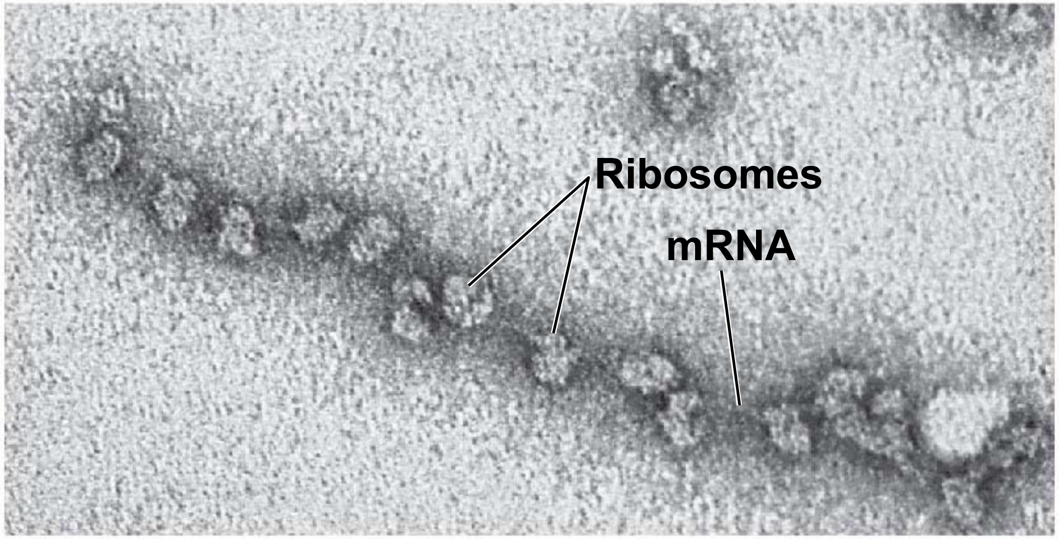
Making Multiple Polypeptides in Bacteria and Eukaryotes

- In bacteria and eukaryotes, multiple ribosomes translate an mRNA at the same time
- Once a ribosome is far enough past the start codon, another ribosome can attach to the mRNA
- Strings of ribosomes called polyribosomes (or polysomes) can be seen with an electron microscope

Figure 14.22

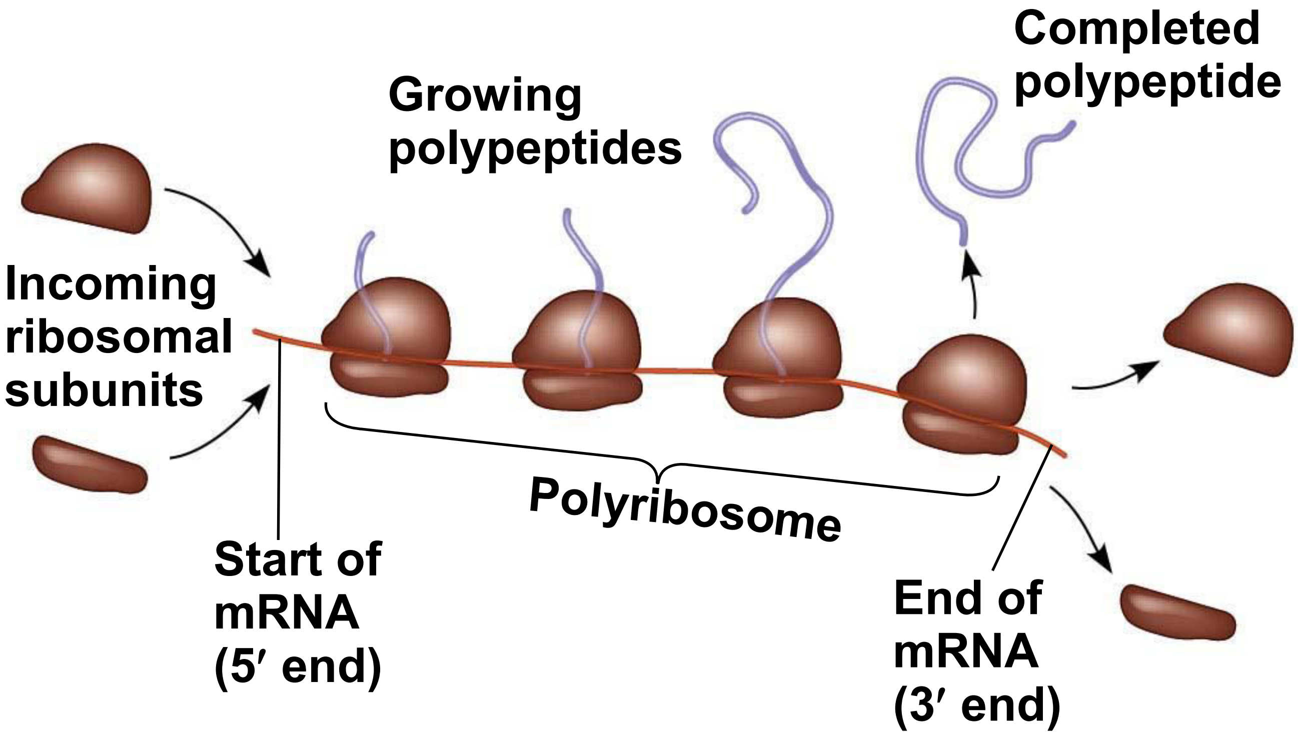


(a) An mRNA molecule translated simultaneously by several ribosomes

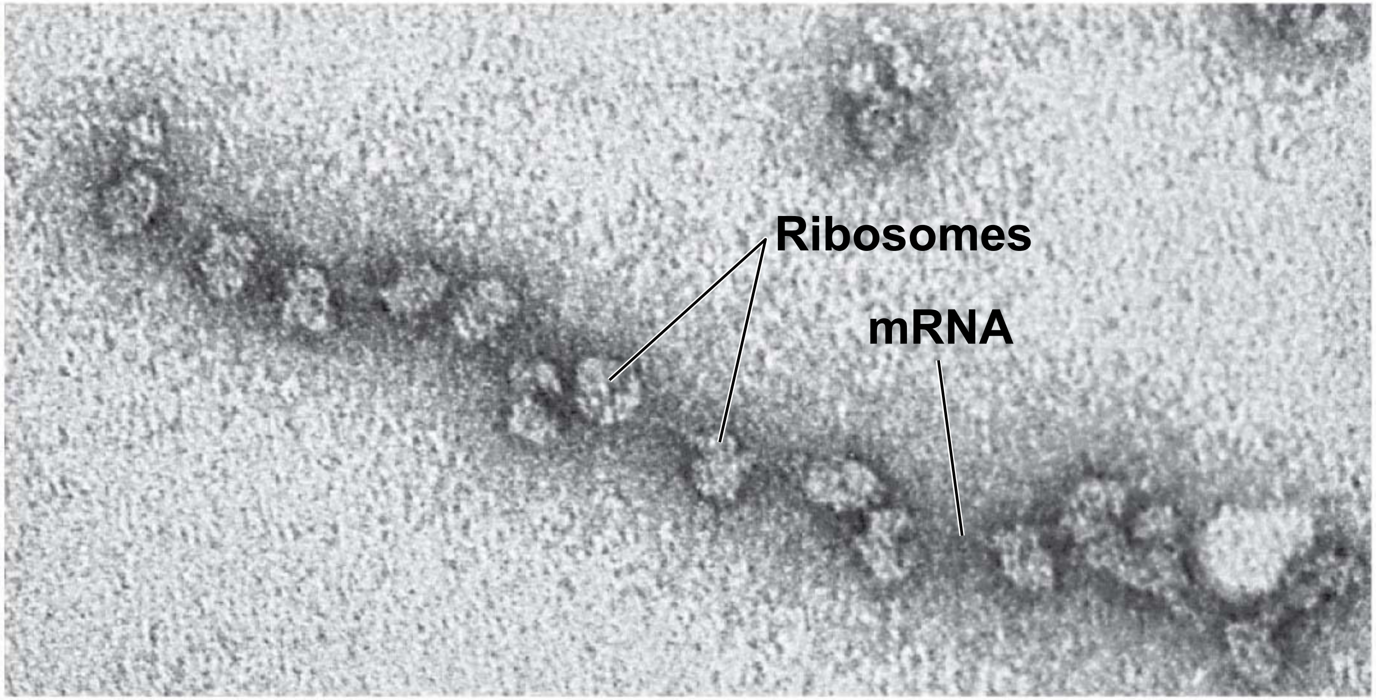


(b) A large polyribosome in a bacterial cell (TEM)

Figure 14.22-1



(a) An mRNA molecule translated simultaneously by several ribosomes



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

- Bacteria and eukaryotes can also transcribe multiple mRNAs from the same gene
- In bacteria, the transcription and translation can take place simultaneously
- In eukaryotes, the nuclear envelope separates transcription and translation

Figure 14.23

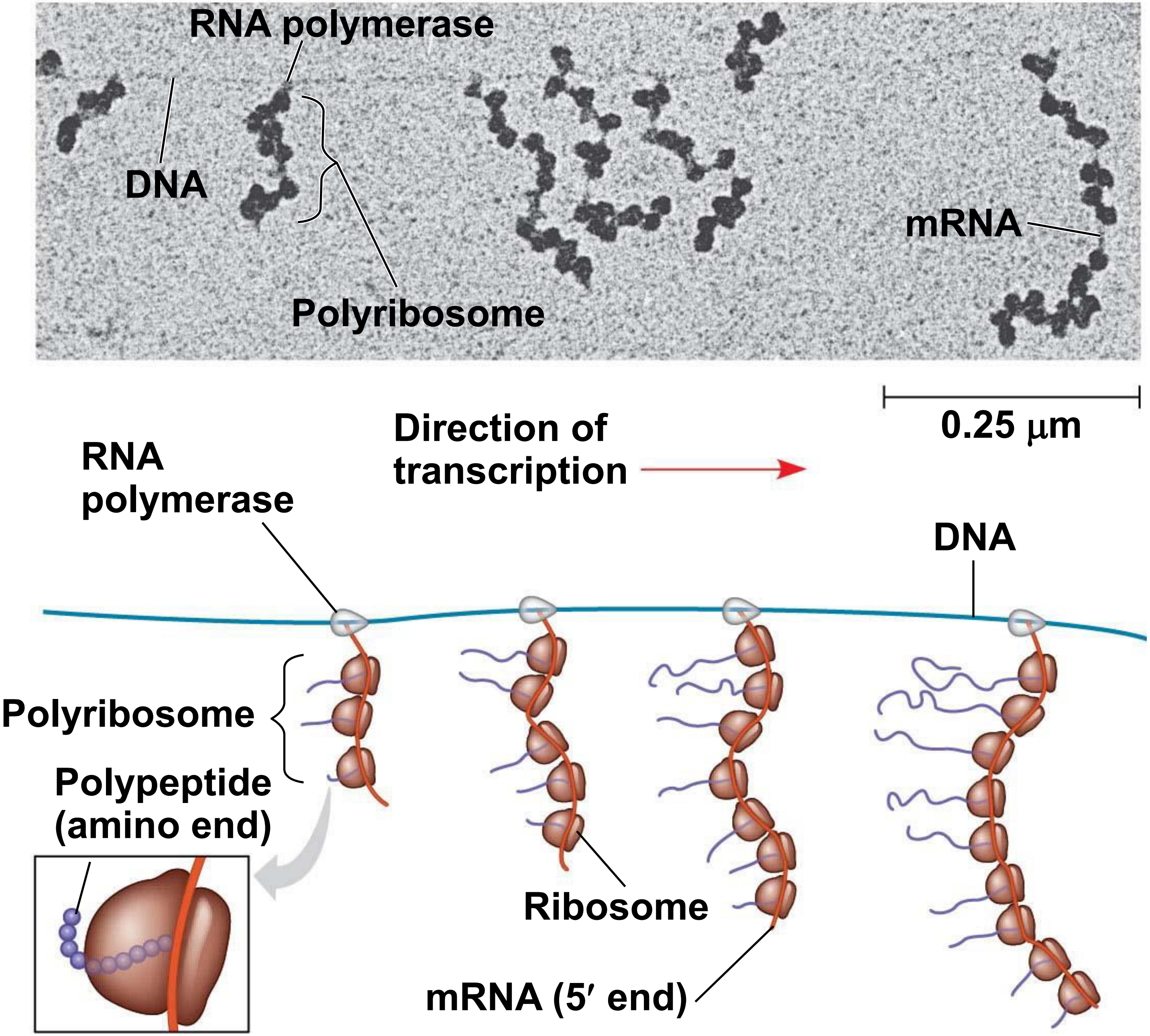

RNA polymerase
DNA
Polyribosome
mRNA
0.25 μm
Direction of transcription
RNA polymerase
DNA
Polyribosome
Polypeptide (amino end)
Ribosome
mRNA (5′ end)

Figure 14.23-1

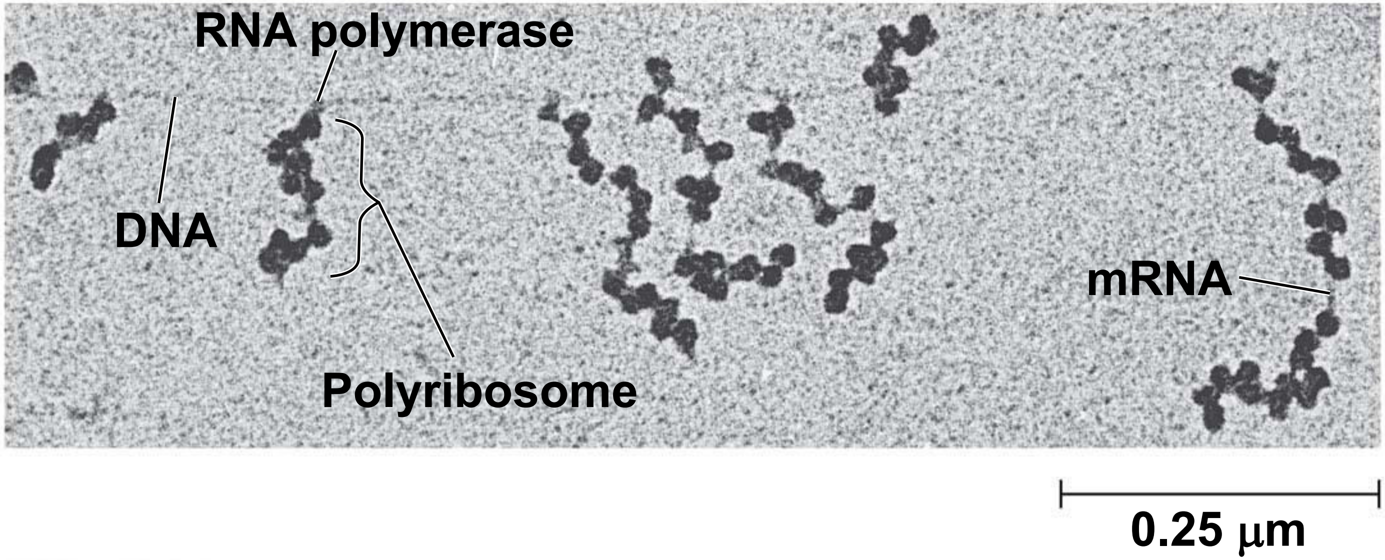


Figure 14.24

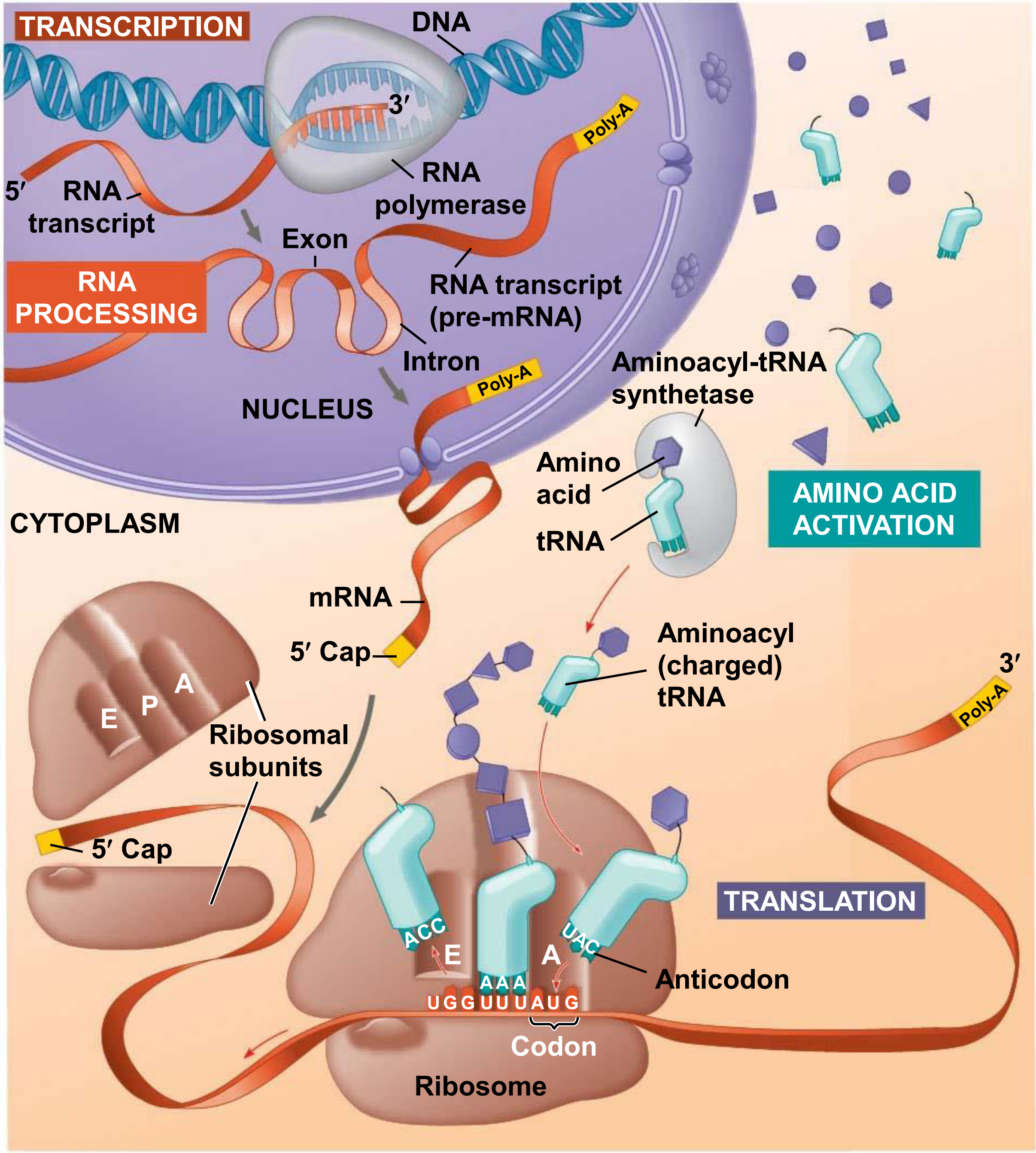

TRANSCRIPTION
DNA
3′
RNA polymerase
5′
RNA transcript
Poly-A
Exon
RNA PROCESSING
RNA transcript (pre-mRNA)
Intron
NUCLEUS
Poly-A
Aminoacyl-tRNA synthetase
Amino acid
tRNA
AMINO ACID ACTIVATION
CYTOPLASM
mRNA
5′ Cap
E
P
A
Ribosomal subunits
Aminoacyl (charged) tRNA
3′
Poly-A
5′ Cap
TRANSLATION
ACC
E
A
UAC
AAA
UGGUUUAUG
Anticodon
Codon
Ribosome

Figure 14.24-1

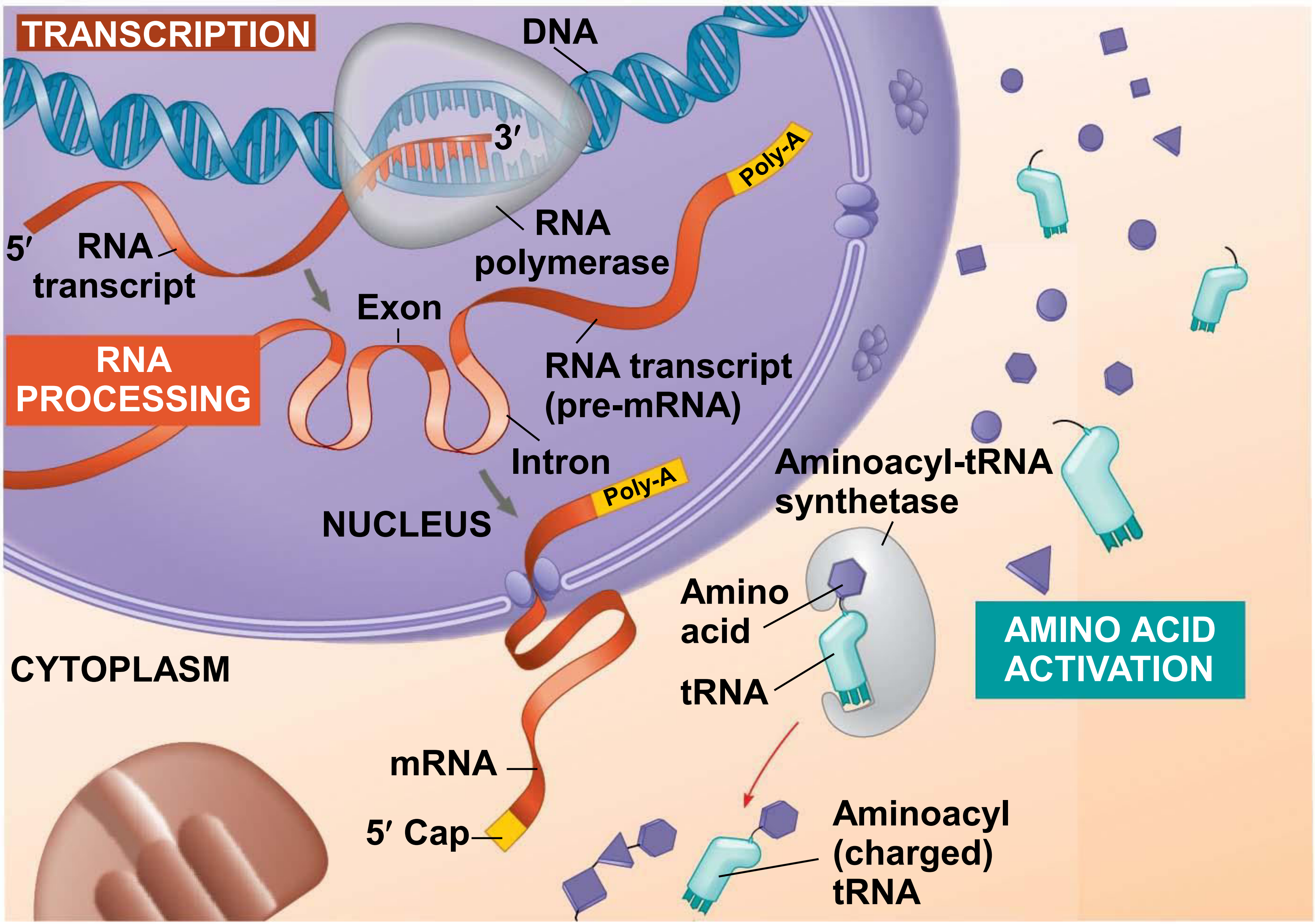
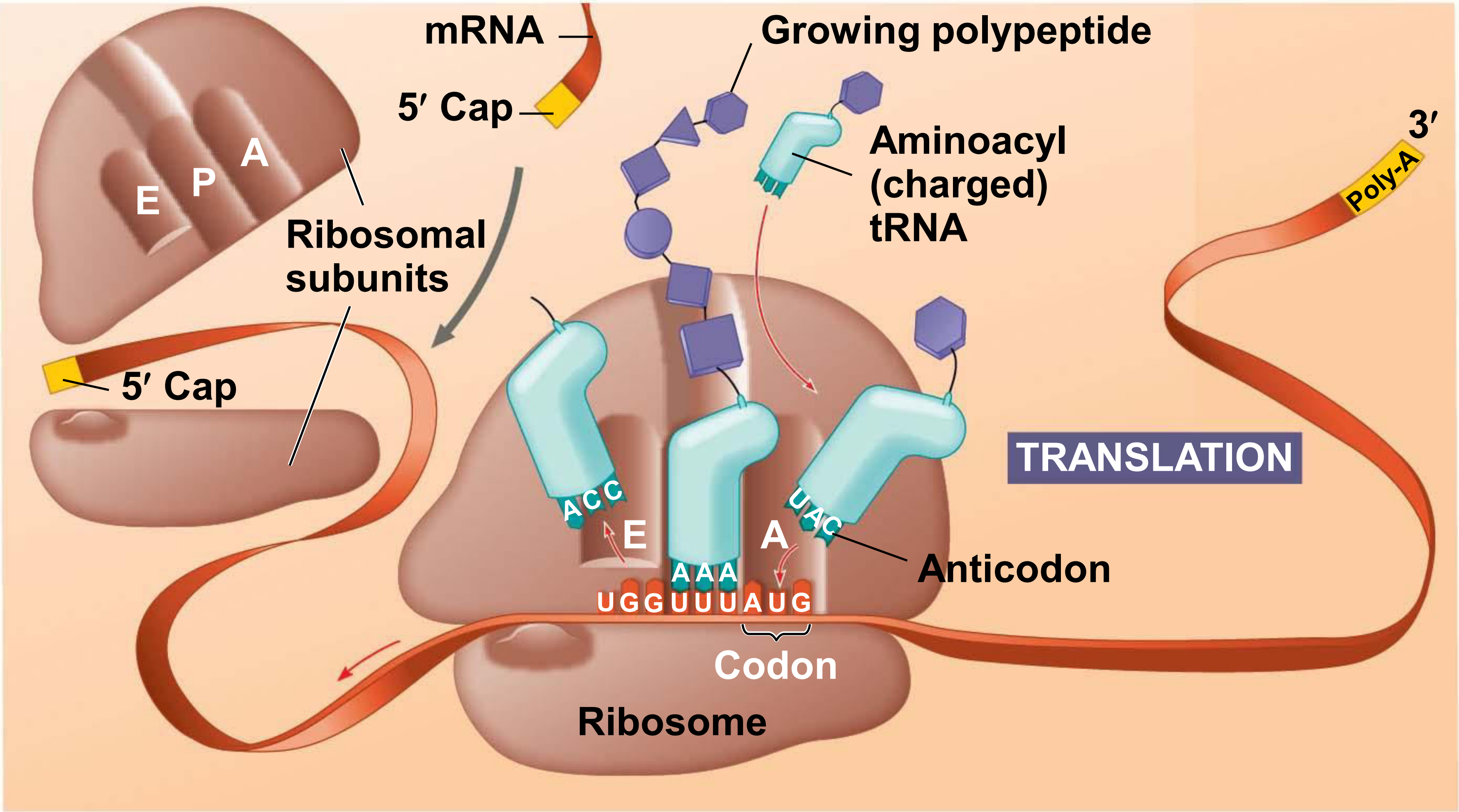


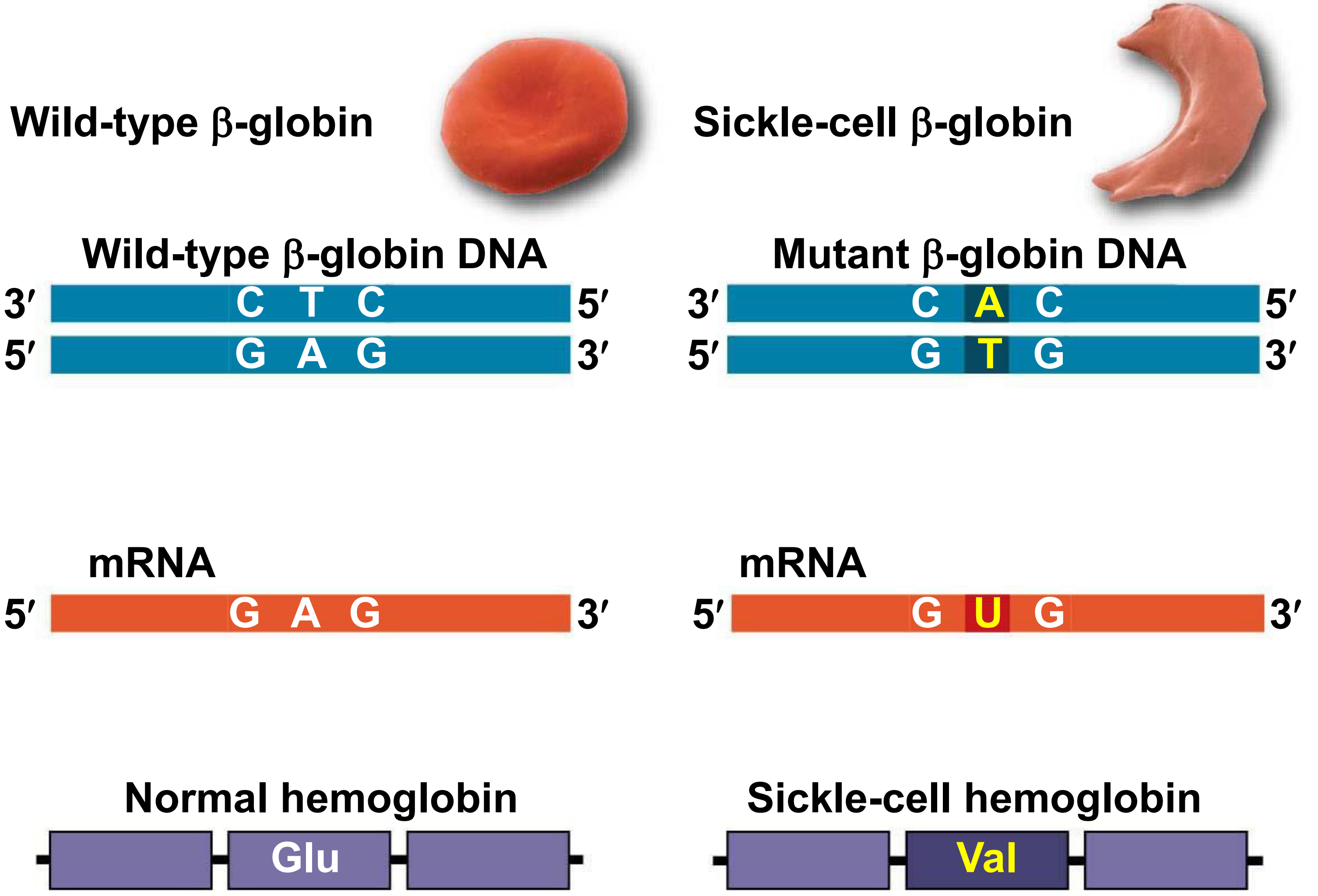
Figure 14.24-2



Concept 14.5: Mutations of one or a few nucleotides can affect protein structure and function

- **Mutations** are changes in the genetic material of a cell or virus
- **Point mutations** are chemical 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 point mutation occurs in a gamete, it may be transmitted to offspring

Figure 14.25



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

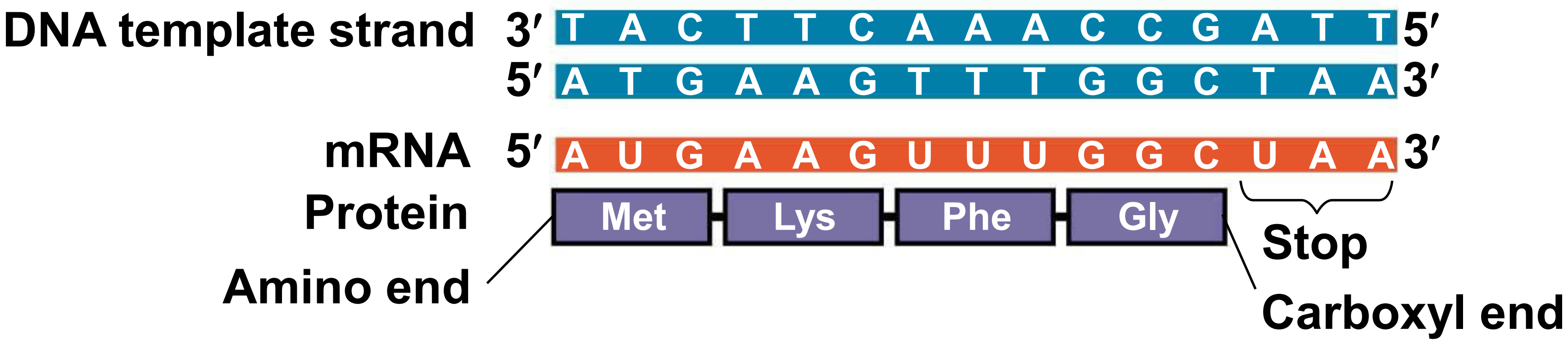
- Point mutations within a gene can be divided into two general categories
  - Single nucleotide-pair substitutions
  - Nucleotide-pair insertions or deletions

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

Figure 14.26-1

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′

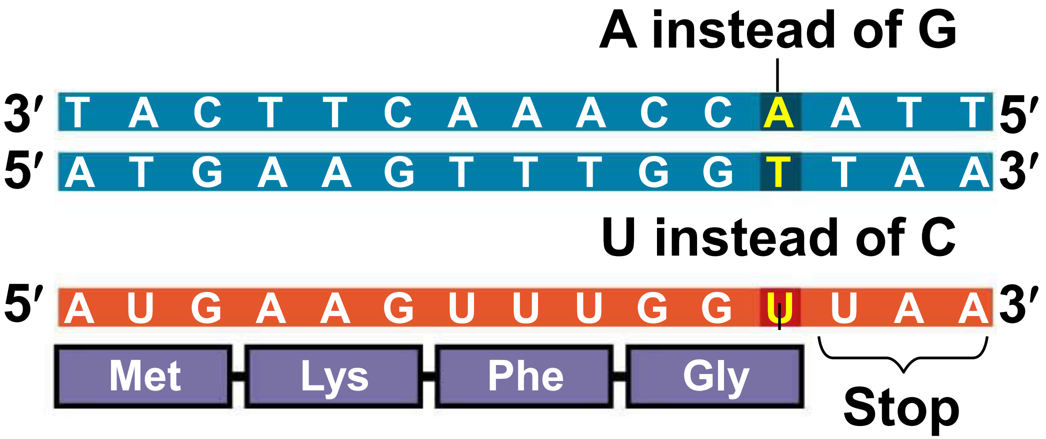
mRNA 5′ A U G A A G U U U G G C U A A 3′

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′

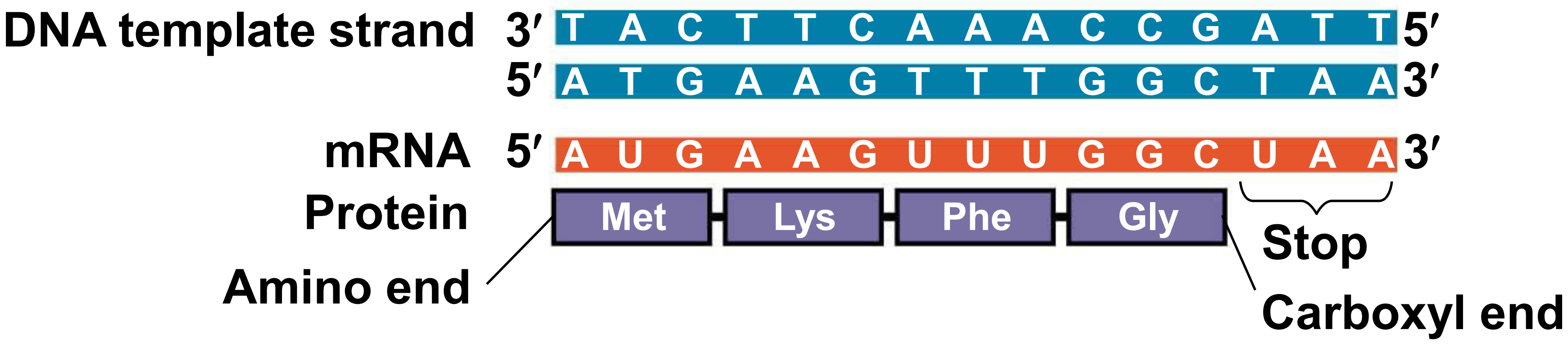
U instead of C

5′ A U G A A G U U U G G U U A A 3′

Met Lys Phe Gly Stop

Figure 14.26-2

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′

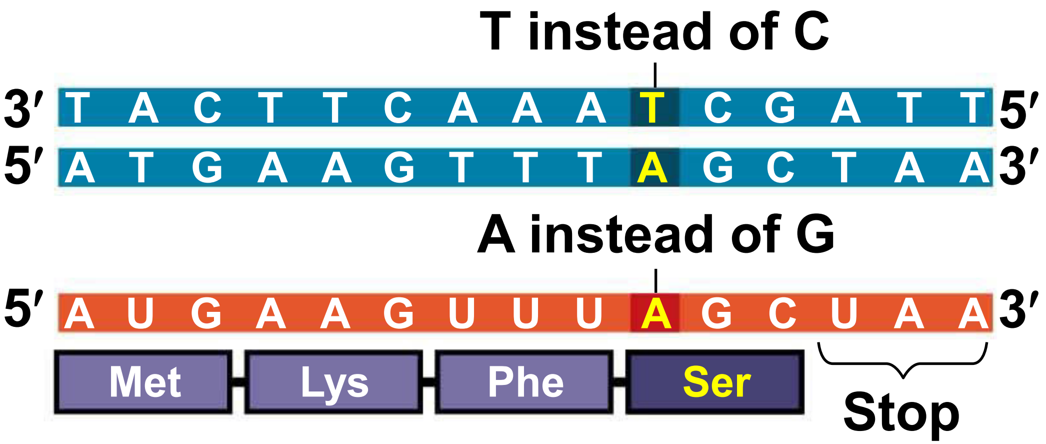
Protein Met Lys Phe Gly

Stop

Amino end

Carboxyl end

Nucleotide-pair substitution: 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

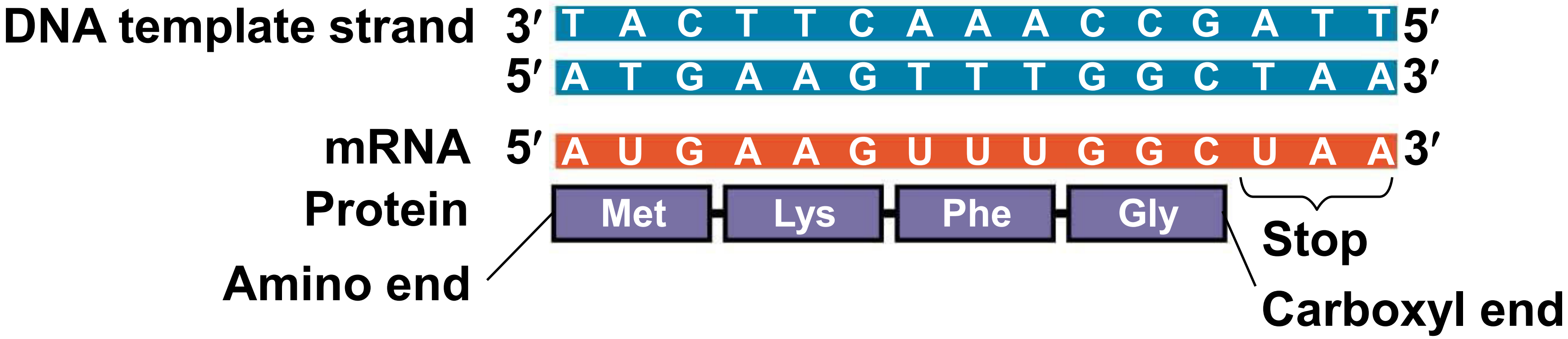
5′ A U G A A G U U U A G C U A A 3′

Met Lys Phe Ser

Stop

Figure 14.26-3

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′

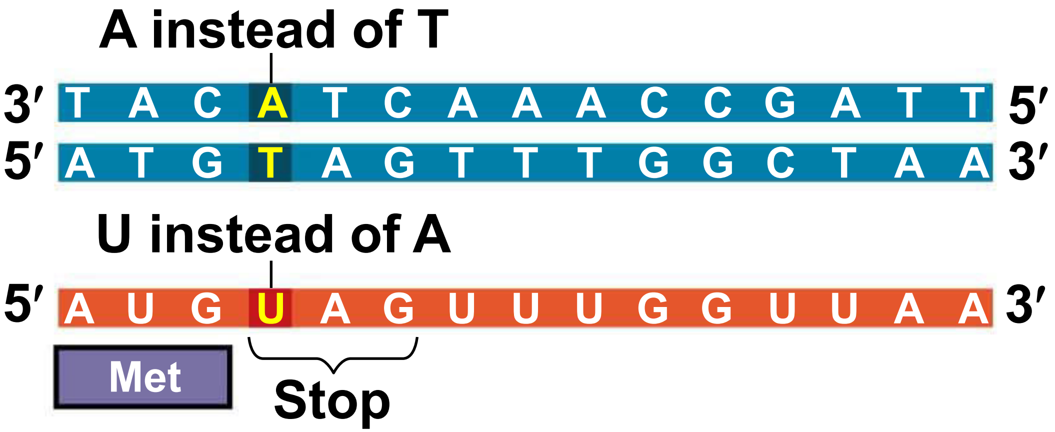
mRNA 5′ A U G A A G U U U G G C U A A 3′

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′

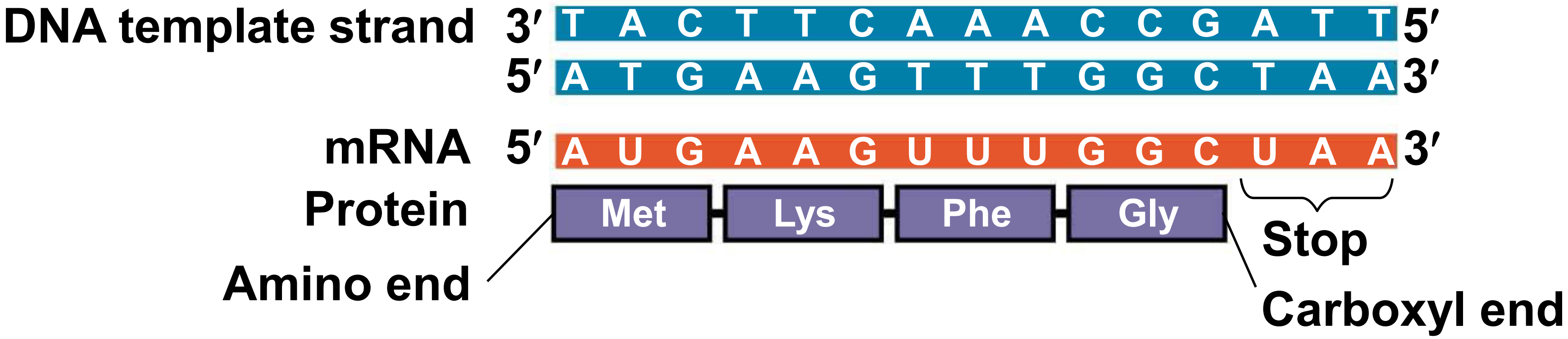
U instead of A

5′ A U G U A G U U U G G U U A A 3′

Met Stop

Figure 14.26-4

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′

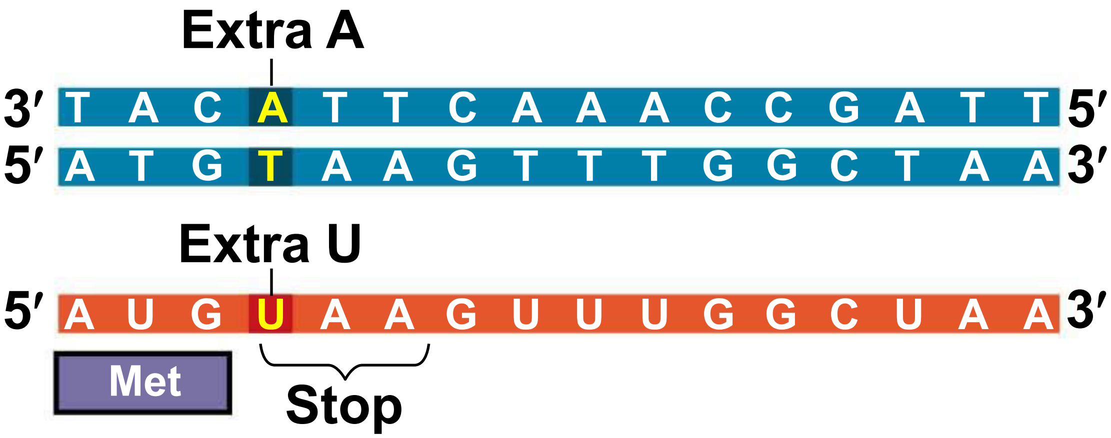
Protein: Met – Lys – Phe – Gly

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

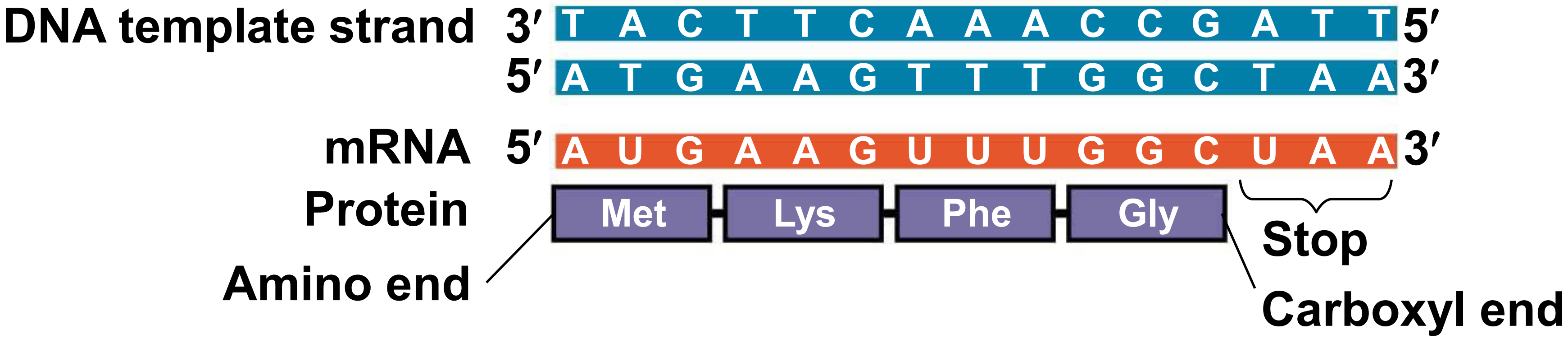
5′ A U G U A A G U U U G G C U A A 3′

Met

Stop

Figure 14.26-5

Wild type



Nucleotide-pair deletion: frameshift causing extensive missense

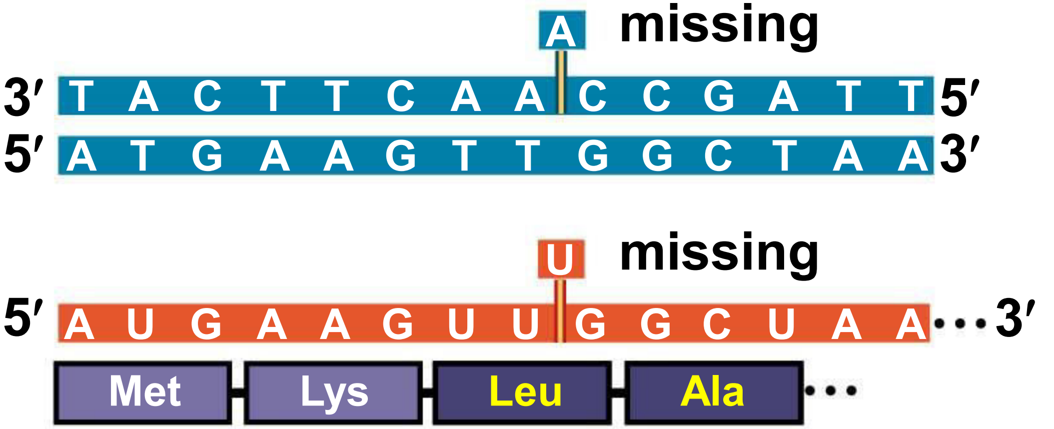
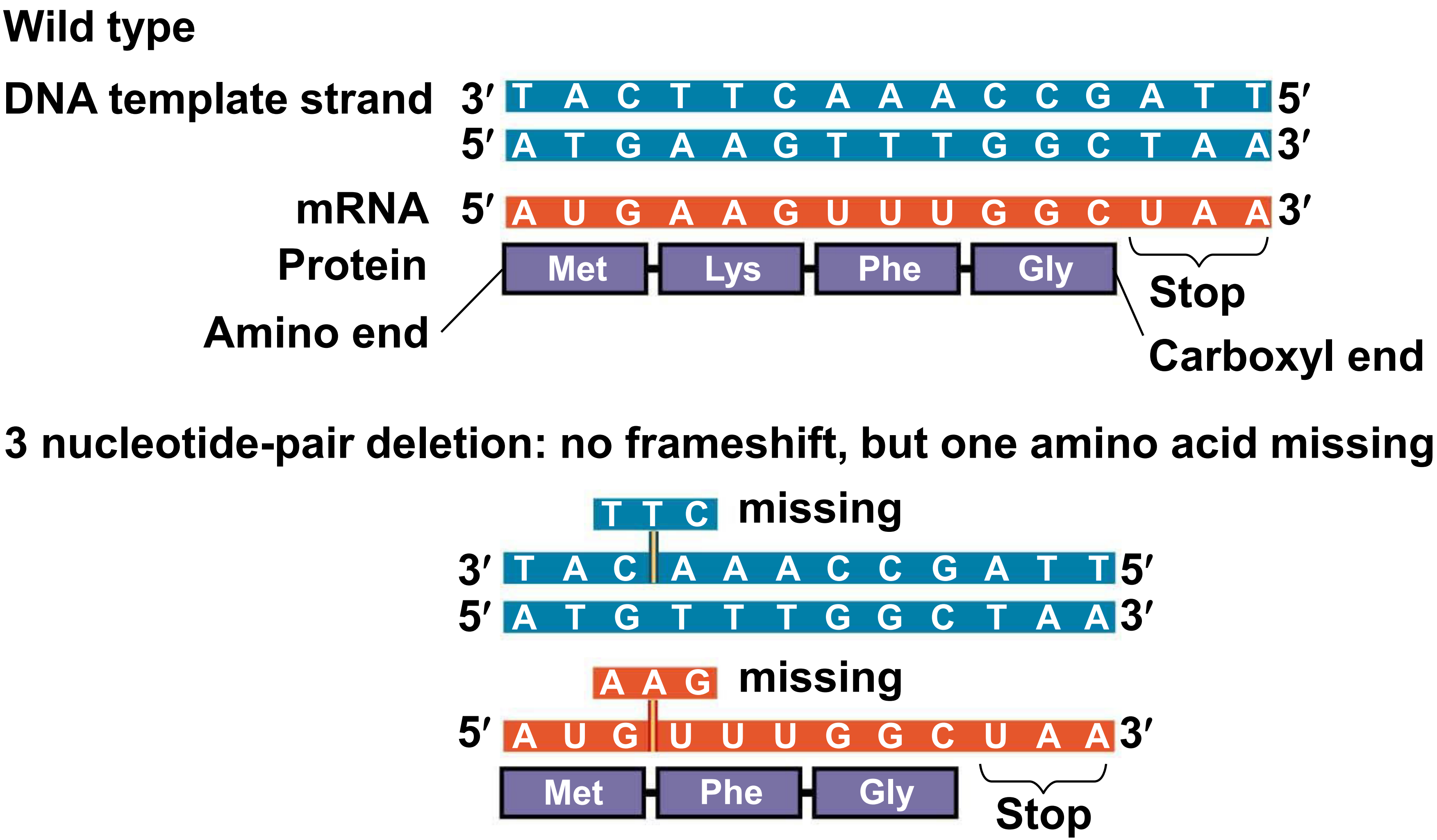


Figure 14.26-6



- **Missense mutations** still code for an amino acid, but not the correct amino acid
- Substitution mutations are usually missense mutations
- **Nonsense mutations** change an amino acid codon into a stop codon, nearly always leading to a nonfunctional protein

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 of the genetic message, producing a **frameshift mutation**

New Mutations and Mutagens

- Spontaneous mutations can occur during DNA replication, recombination, or repair
- **Mutagens** are physical or chemical agents that can cause mutations
- Researchers have developed methods to test the mutagenic activity of chemicals
- Most cancer-causing chemicals (carcinogens) are mutagenic, and the converse is also true

What Is a Gene? *Revisiting the Question*

- The definition of a 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, either a polypeptide or an RNA molecule

Figure 14.UN02

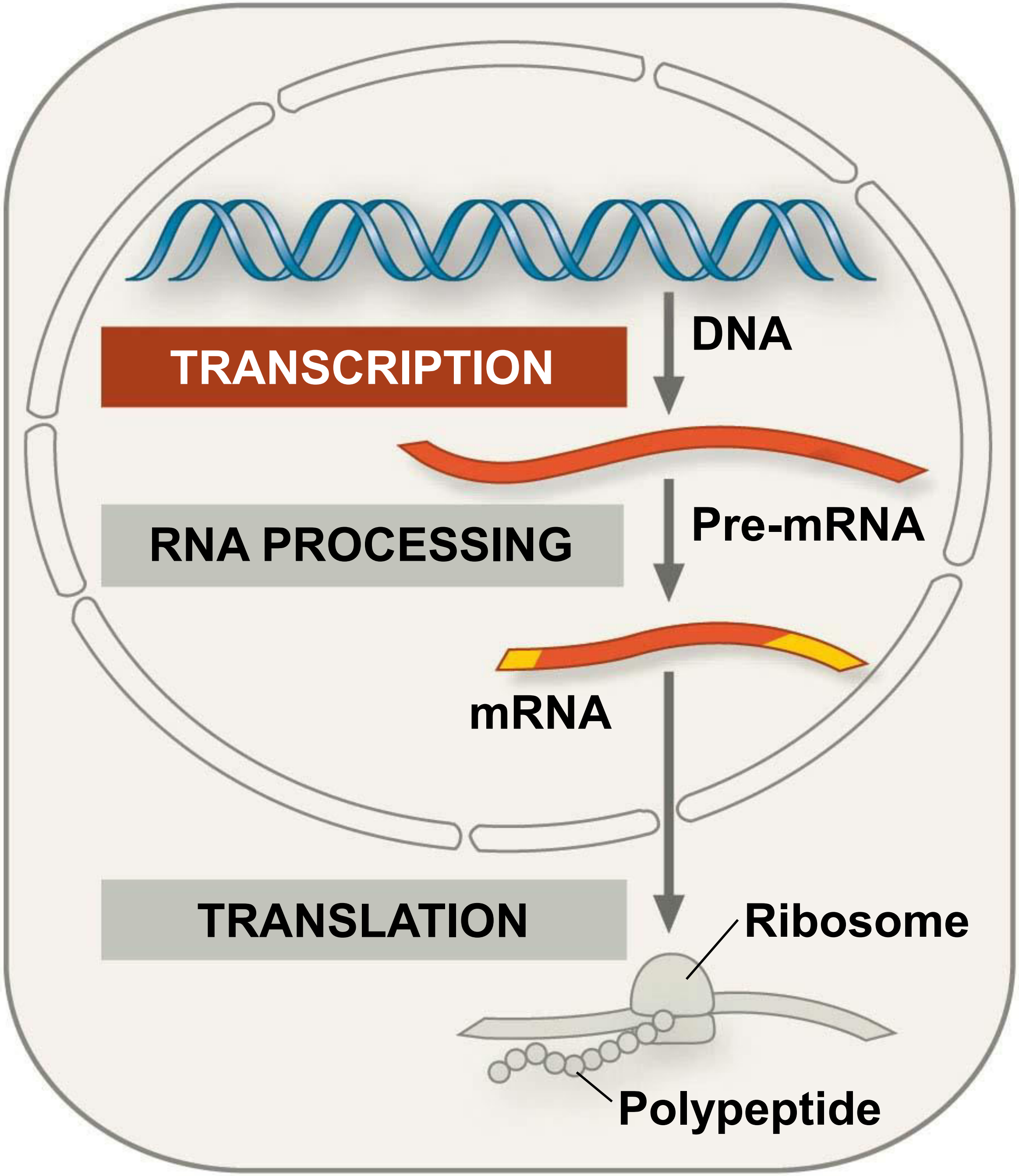


Figure 14.UN03

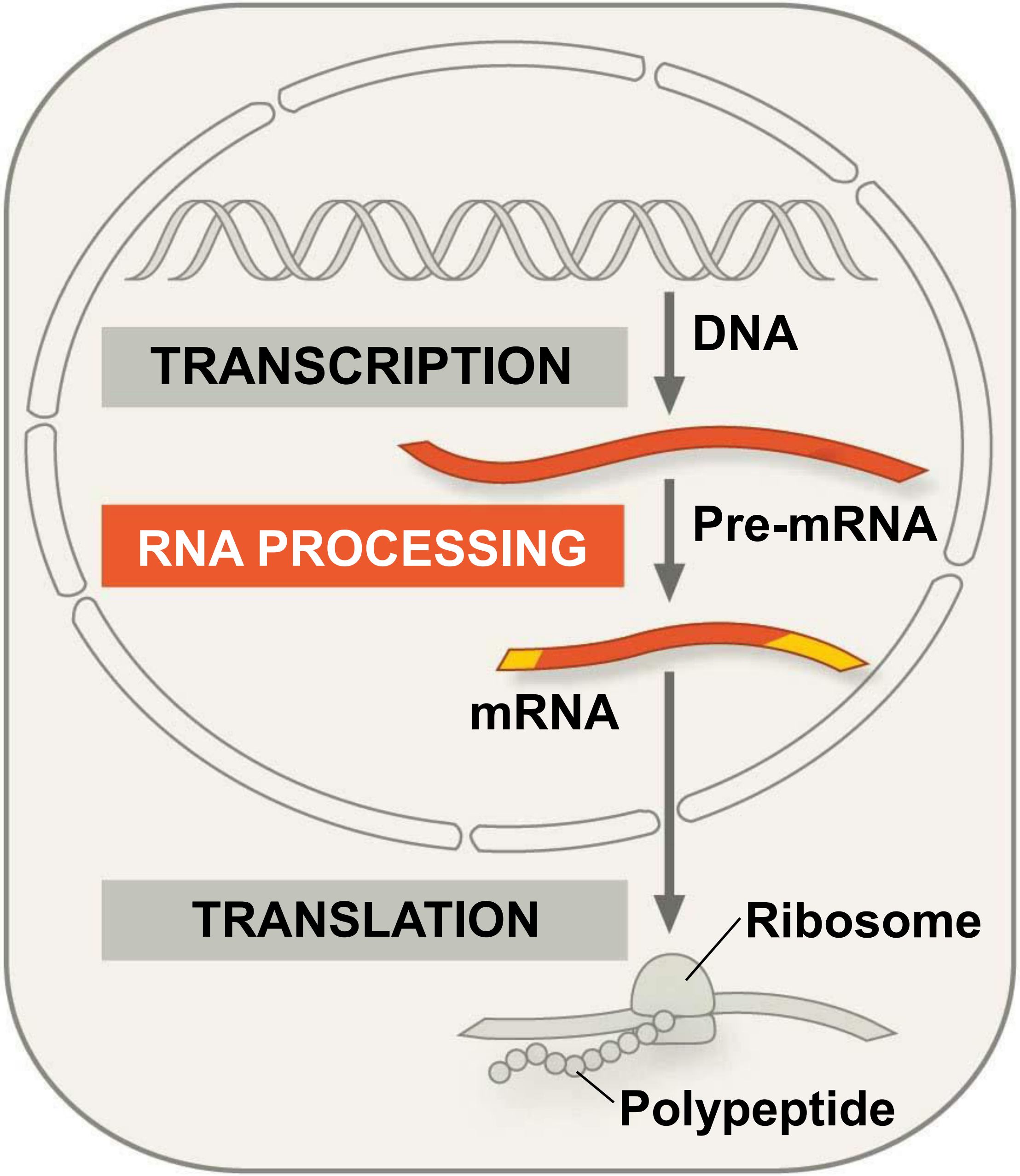


Figure 14.UN04

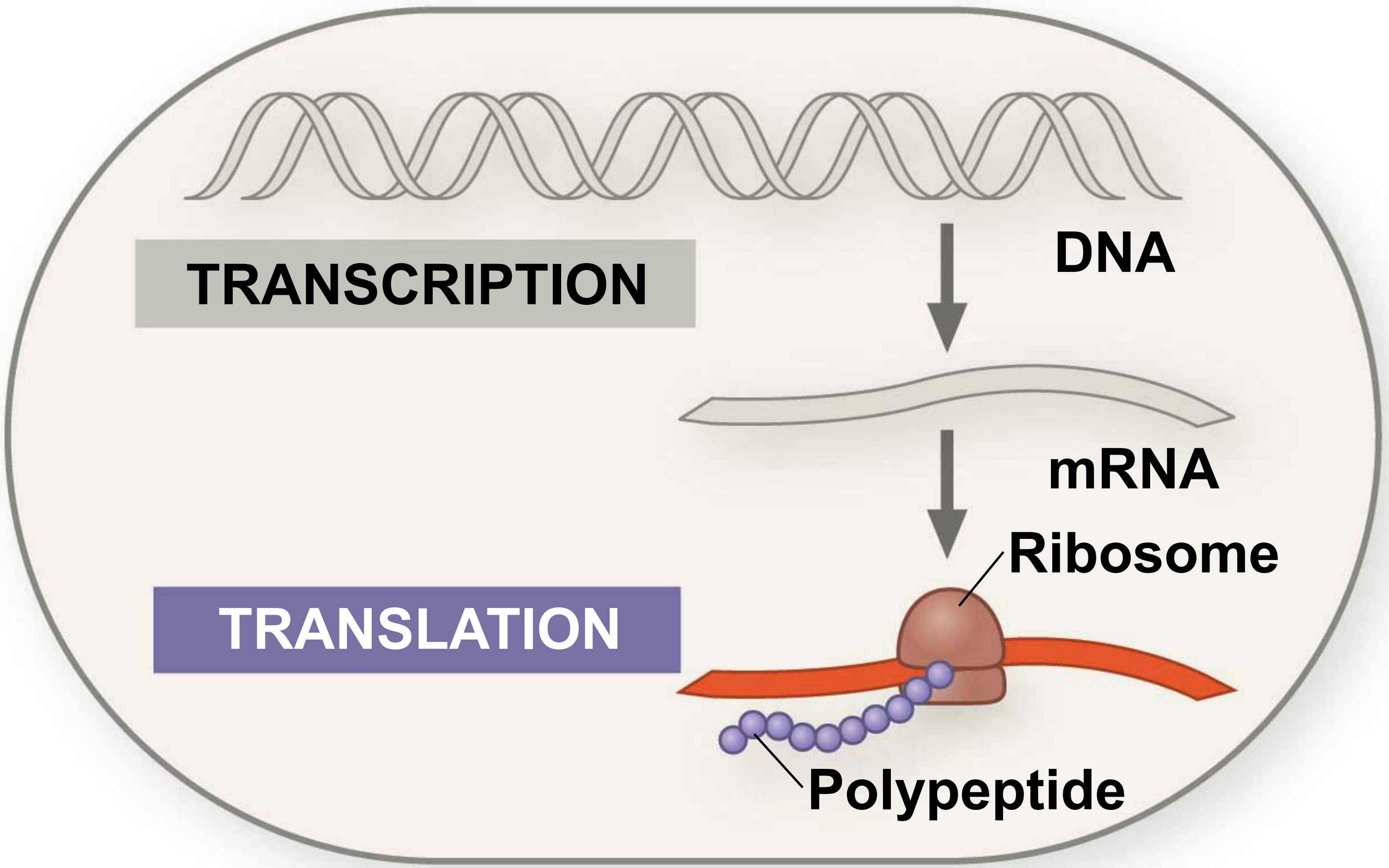
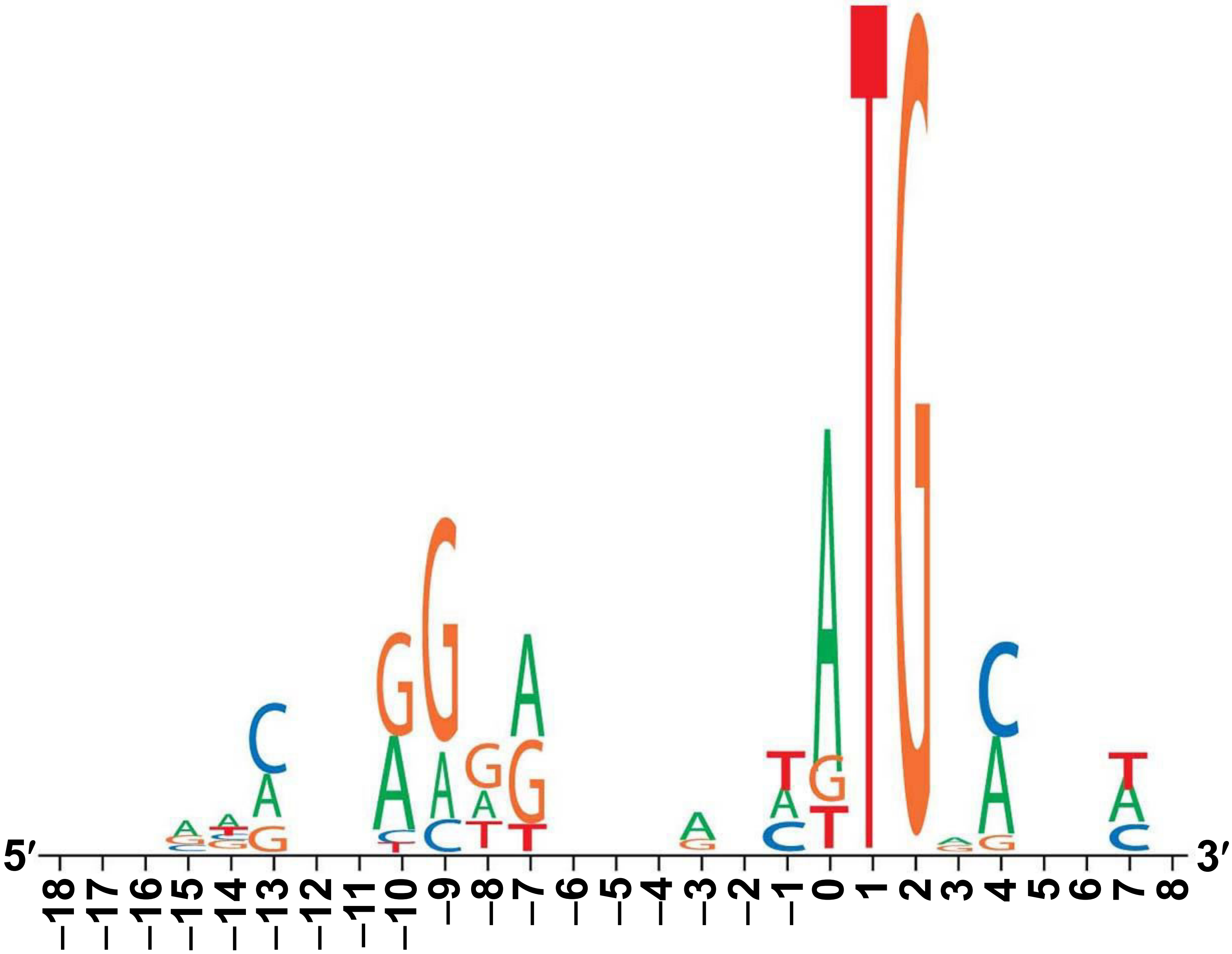


Figure 14.UN05-1

	−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	C	A	A

Sequence alignment

Figure 14.UN05-2



Sequence logo

Figure 14.UN05-3

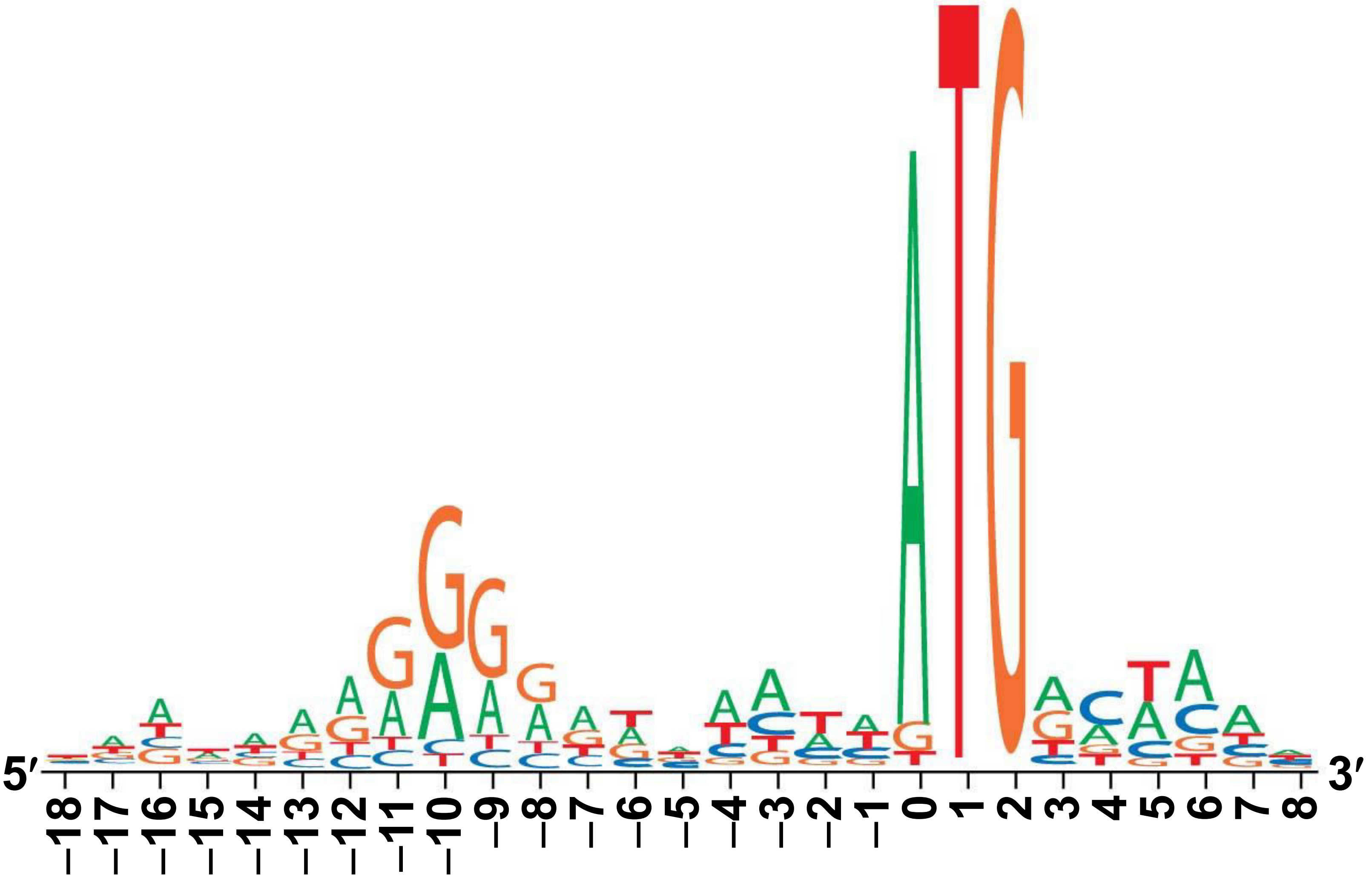


Figure 14.UN05-4

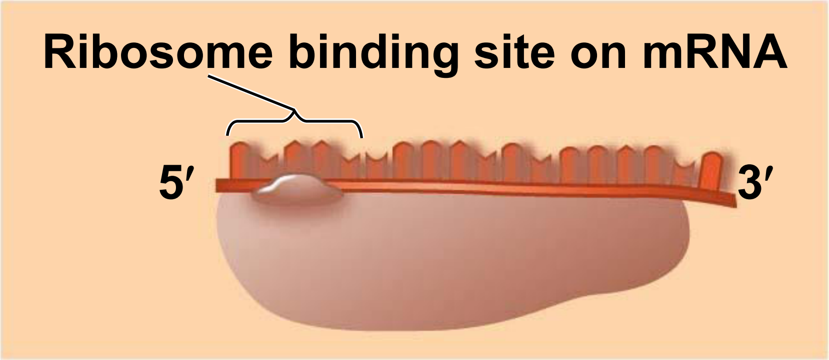


Figure 14.UN06

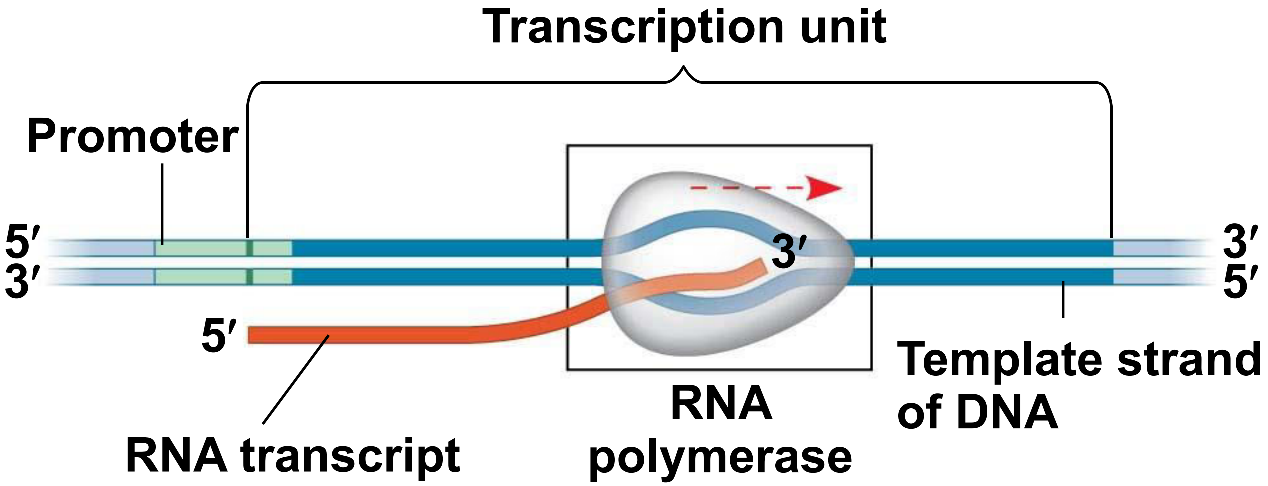


Figure 14.UN07

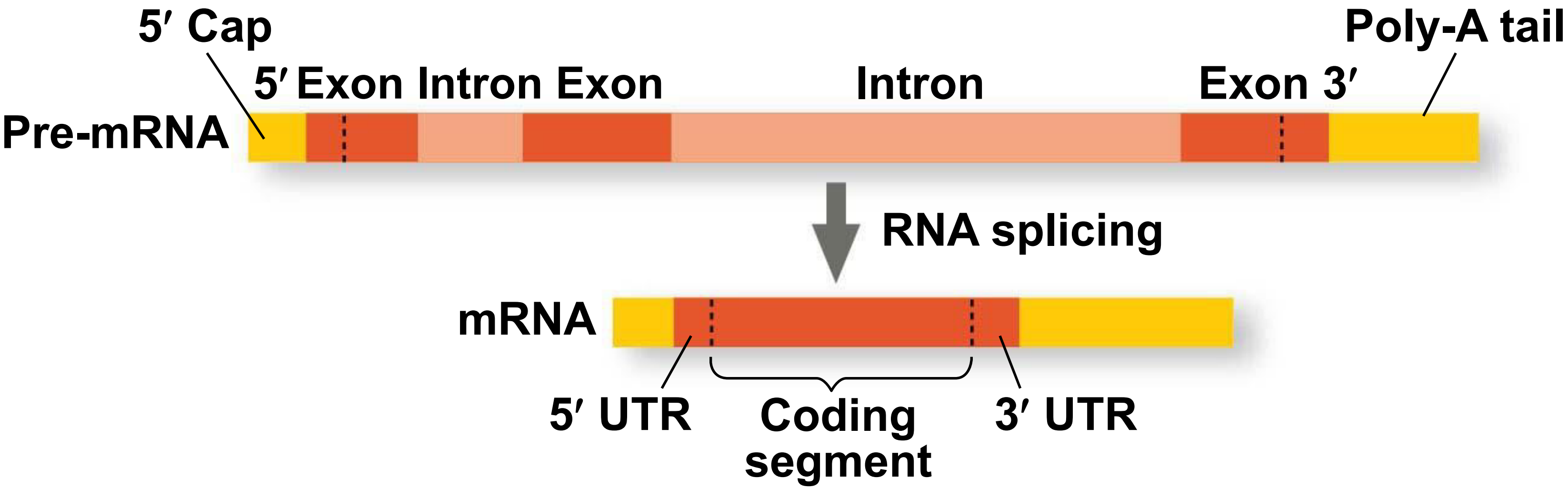


Figure 14.UN08

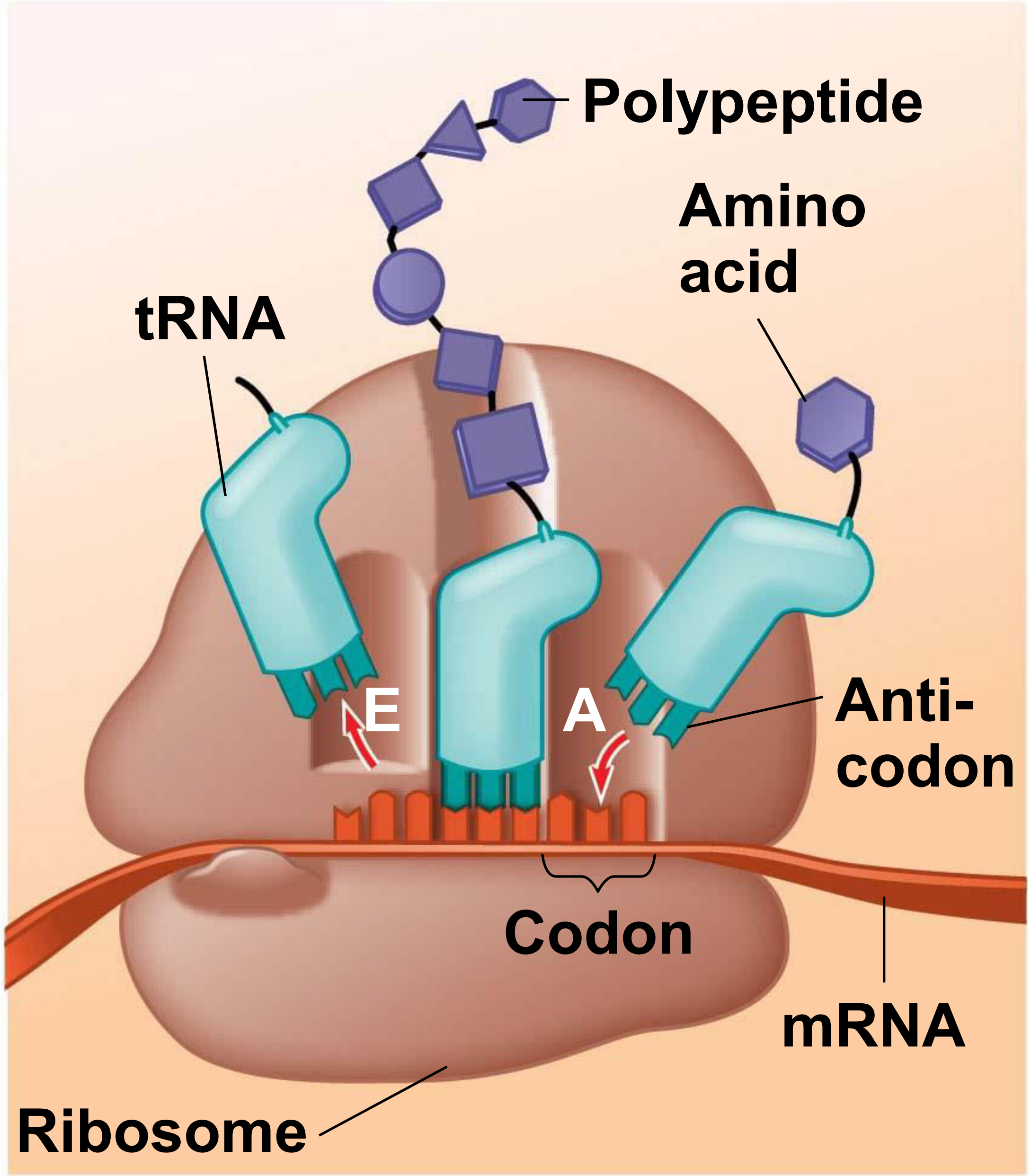


Figure 14.UN09

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 14.UN10