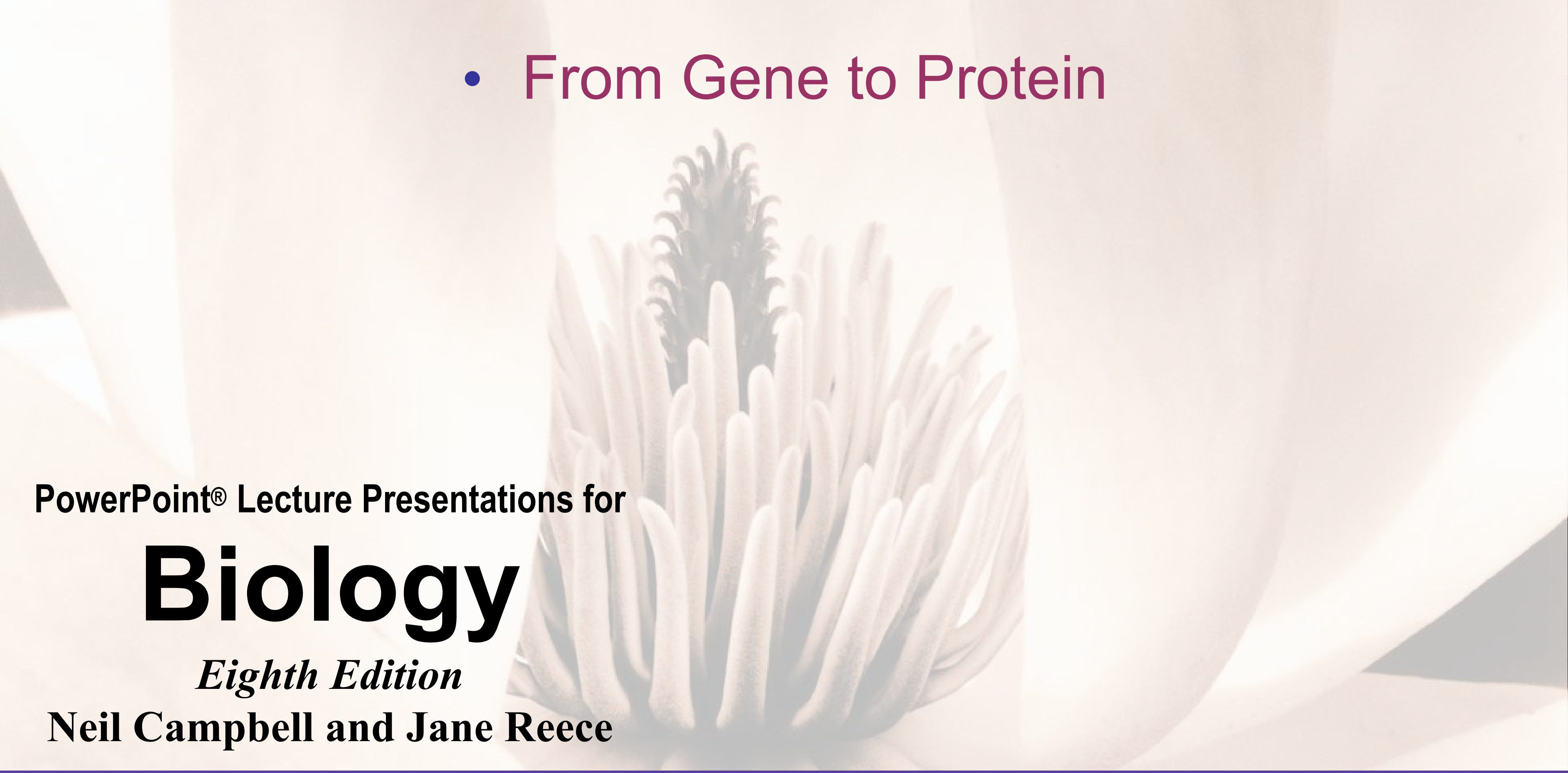
Chapter 17

- From Gene to Protein



PowerPoint® Lecture Presentations for

Biology

Eighth Edition

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Lectures by Chris Romero, updated by Erin Barley with contributions from Joan Sharp

Overview: The Flow of Genetic Information

- The information content of DNA is in the form of 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

Fig. 17-1

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

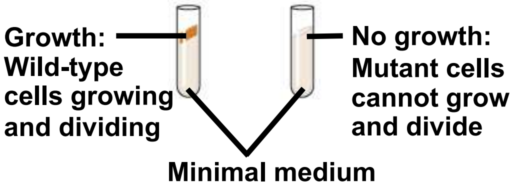
- In 1909, British physician Archibald Garrod first suggested that genes dictate phenotypes through enzymes that catalyze specific chemical reactions
- He thought symptoms of an inherited disease reflect an inability to synthesize a certain enzyme
- Linking genes to enzymes required understanding that cells synthesize and degrade molecules in a series of steps, a metabolic pathway

Nutritional Mutants in Neurospora: Scientific Inquiry

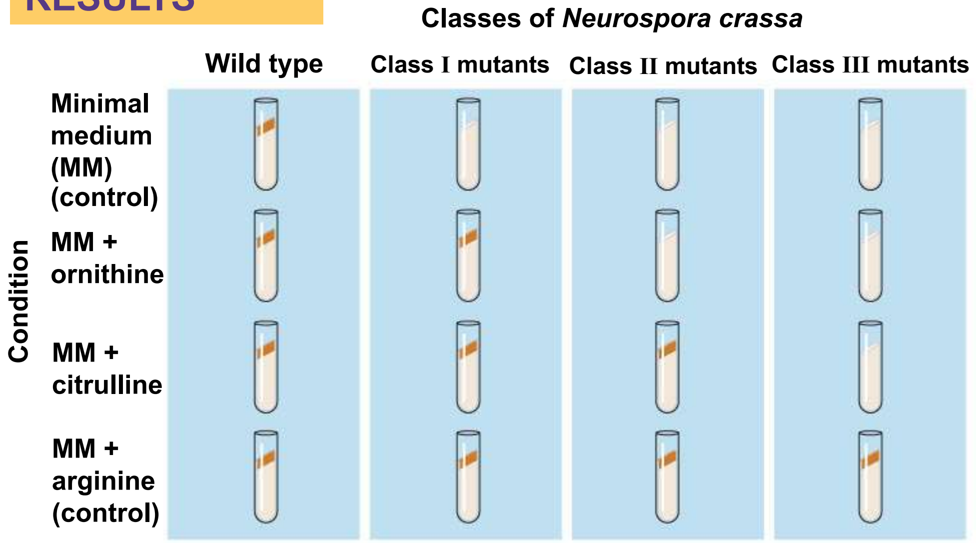
- George Beadle and Edward Tatum exposed bread mold to X-rays, creating mutants that were unable to survive on minimal medium as a result of inability to synthesize certain molecules
- Using crosses, they identified three classes of arginine-deficient mutants, each lacking a different enzyme necessary for synthesizing arginine
- They developed a *one gene–one enzyme hypothesis*, which states that each gene dictates production of a specific enzyme

Fig. 17-2

EXPERIMENT



RESULTS



CONCLUSION

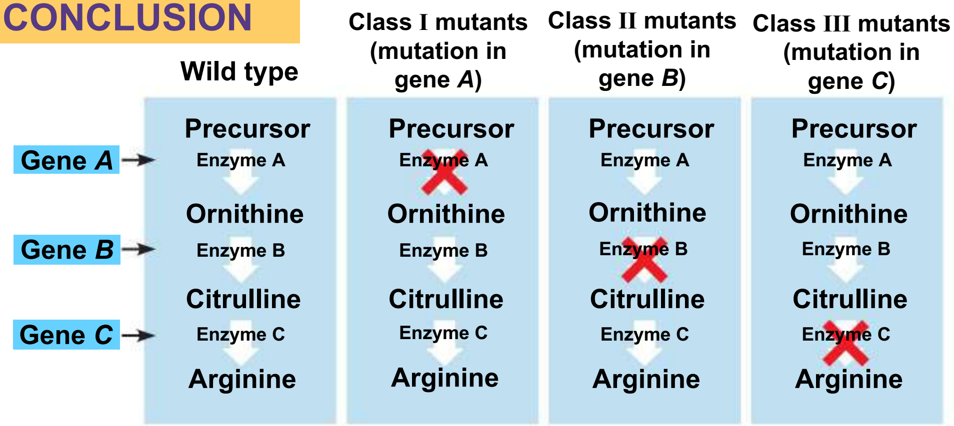
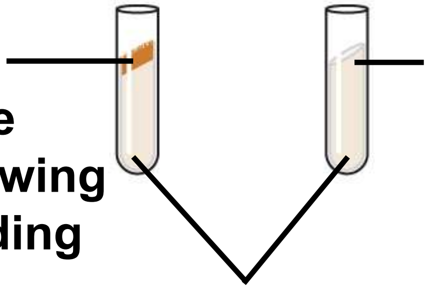


Fig. 17-2a

EXPERIMENT



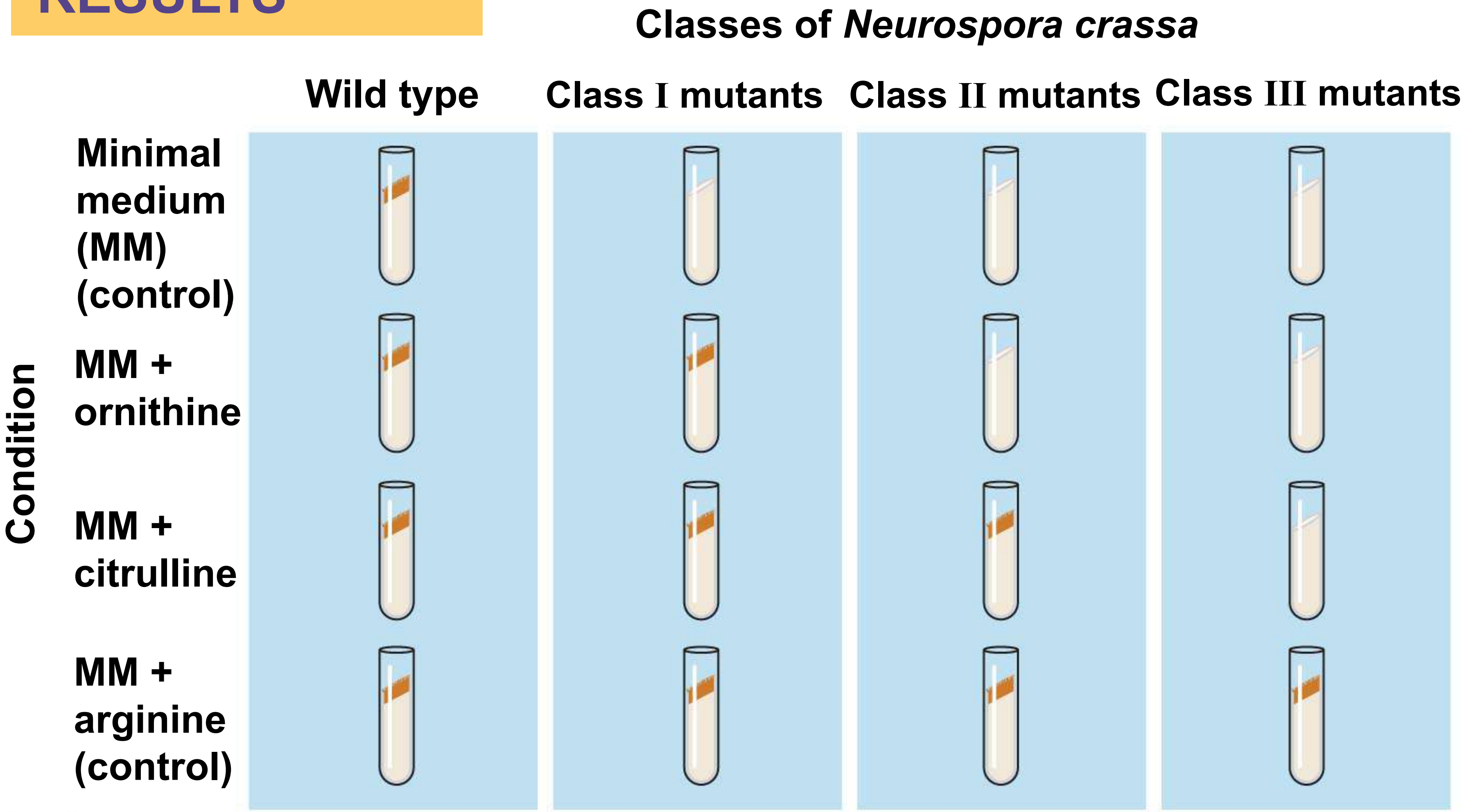
Growth: Wild-type cells growing and dividing

No growth: Mutant cells cannot grow and divide

Minimal medium

Fig. 17-2b

RESULTS



Classes of *Neurospora crassa*

Wild type

Class I mutants

Class II mutants

Class III mutants

Condition

Minimal medium (MM) (control)

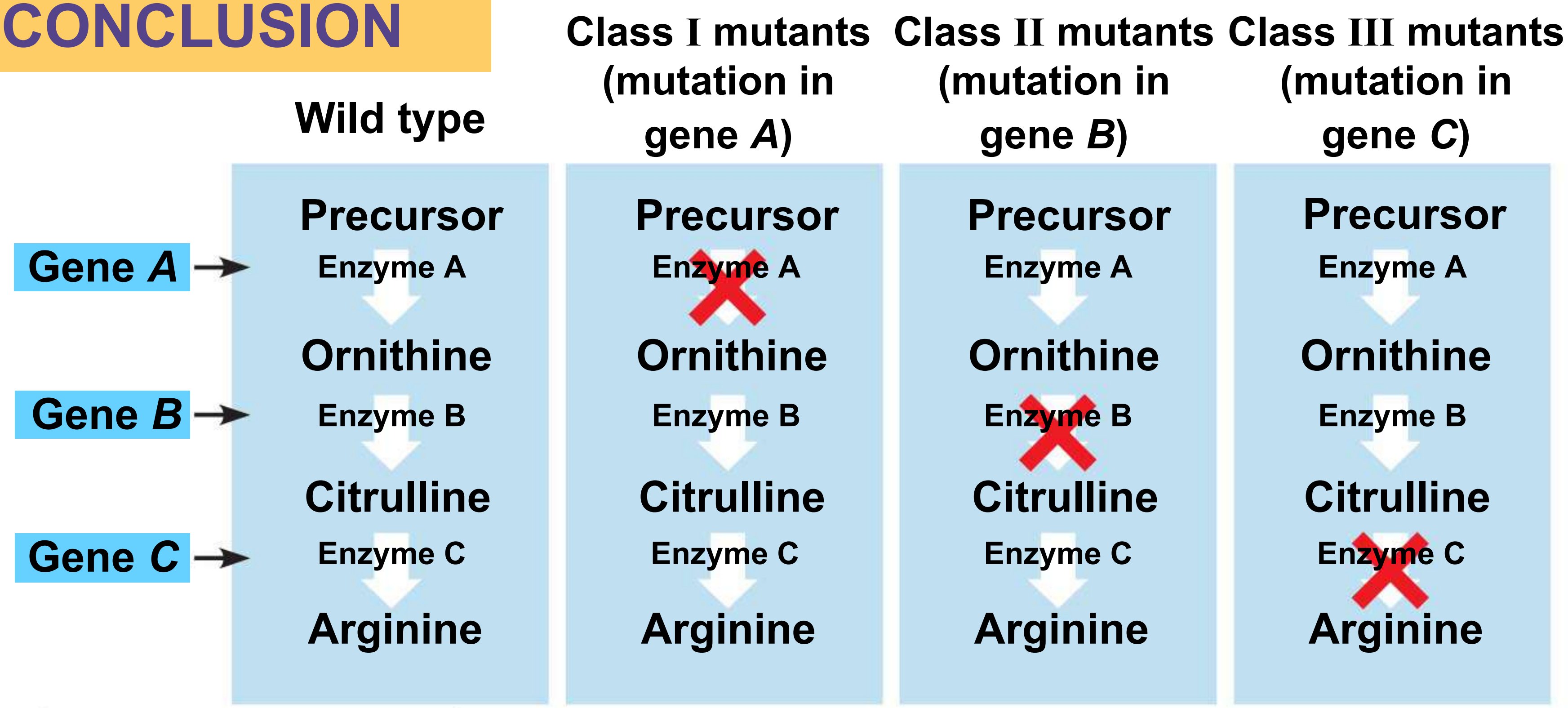
MM + ornithine

MM + citrulline

MM + arginine (control)

Fig. 17-2c

CONCLUSION



	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

The Products of Gene Expression: A Developing Story

- Some proteins aren’t 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*
- Note that it is common to refer to gene products as proteins rather than polypeptides

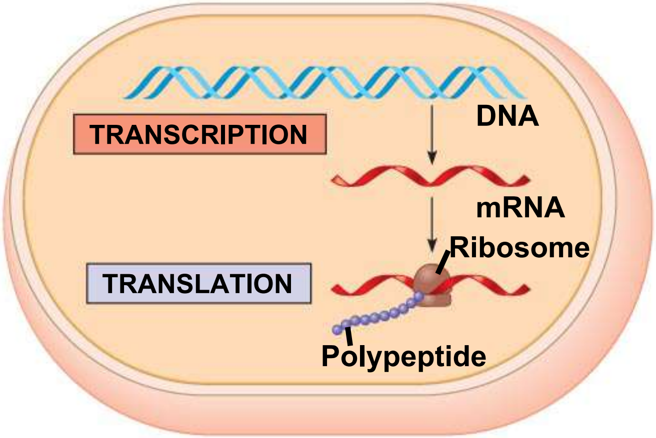
Basic Principles of Transcription and Translation

- RNA is the intermediate between genes and the proteins for which they code
- **Transcription** is the synthesis of RNA under the direction of DNA
- Transcription produces **messenger RNA (mRNA)**
- **Translation** is the synthesis of a polypeptide, which occurs under the direction of mRNA
- **Ribosomes** are the sites of translation

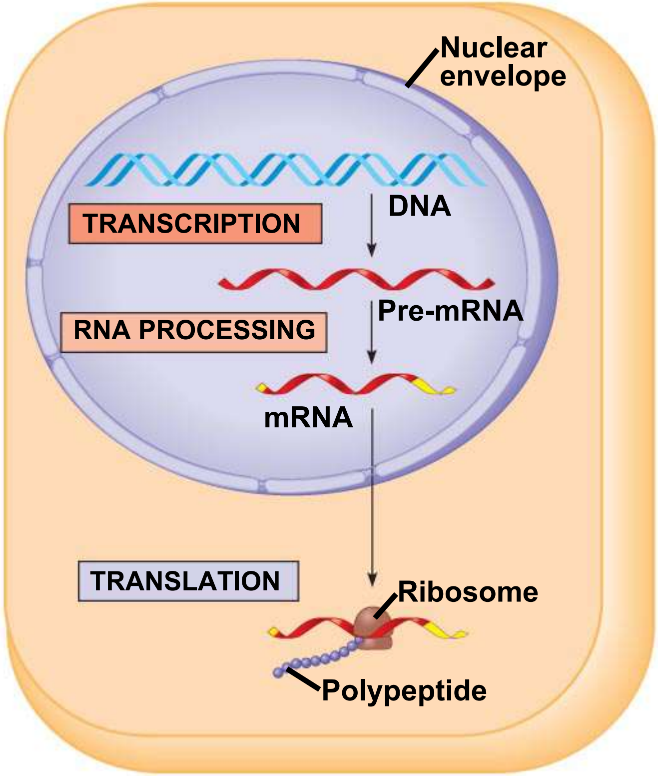
- In prokaryotes, mRNA produced by transcription is immediately translated without more processing
- In a eukaryotic cell, the nuclear envelope separates transcription from translation
- Eukaryotic RNA transcripts are modified through **RNA processing** to yield finished mRNA

- A **primary transcript** is the initial RNA transcript from any gene
- The central dogma is the concept that cells are governed by a cellular chain of command: DNA → RNA → protein

Fig. 17-3

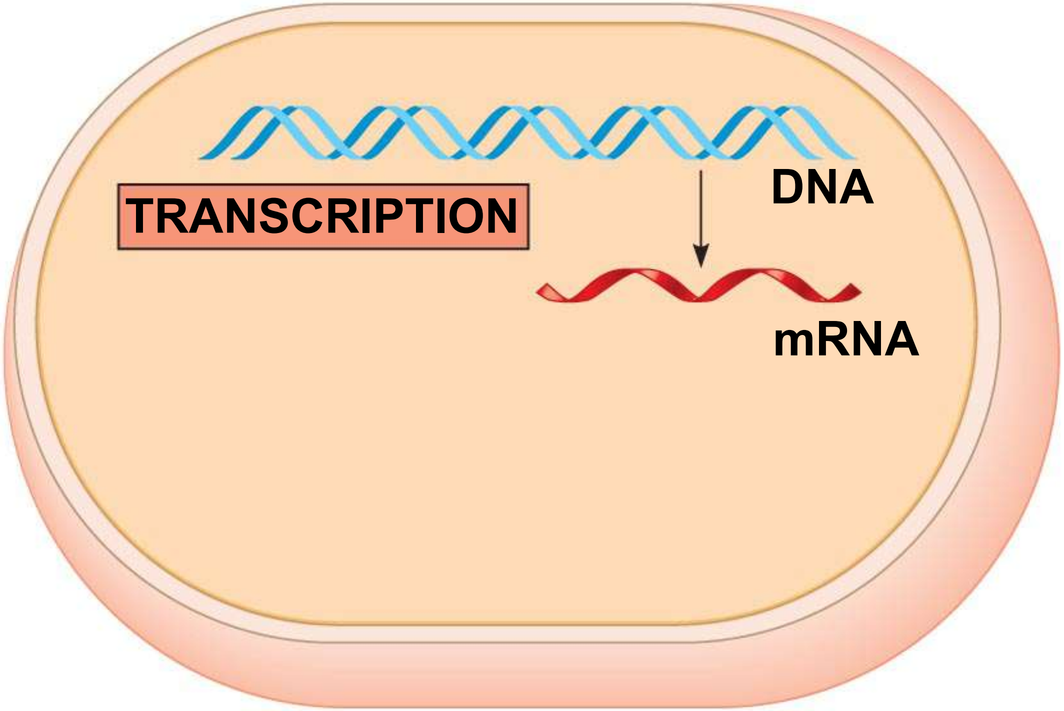


(a) Bacterial cell



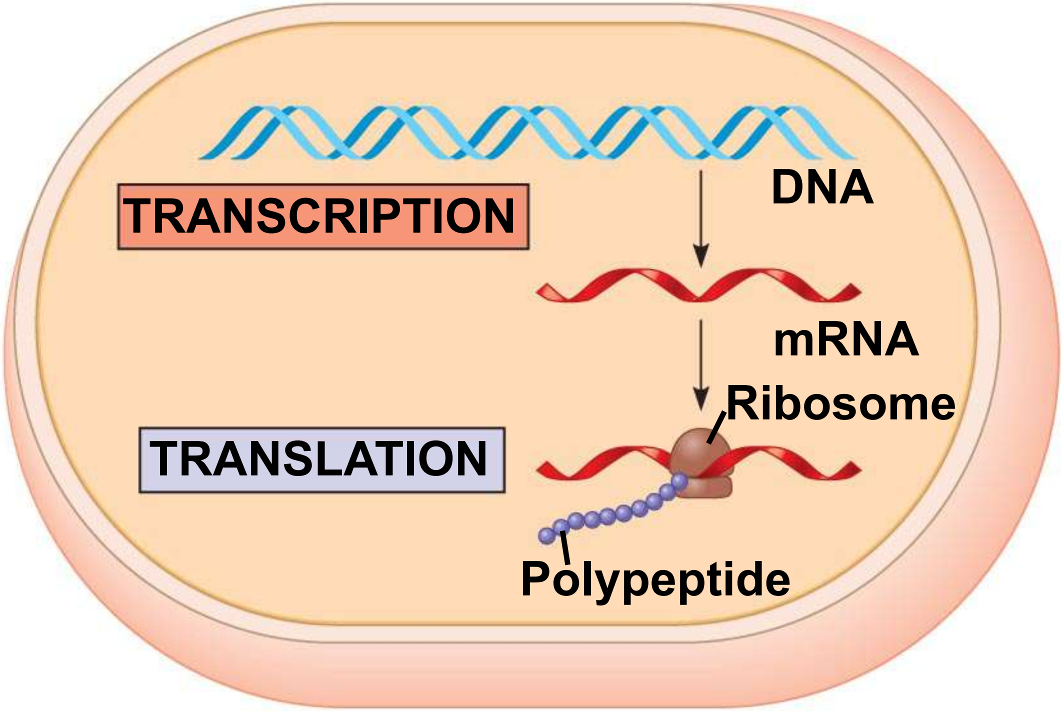
(b) Eukaryotic cell

Fig. 17-3a-1

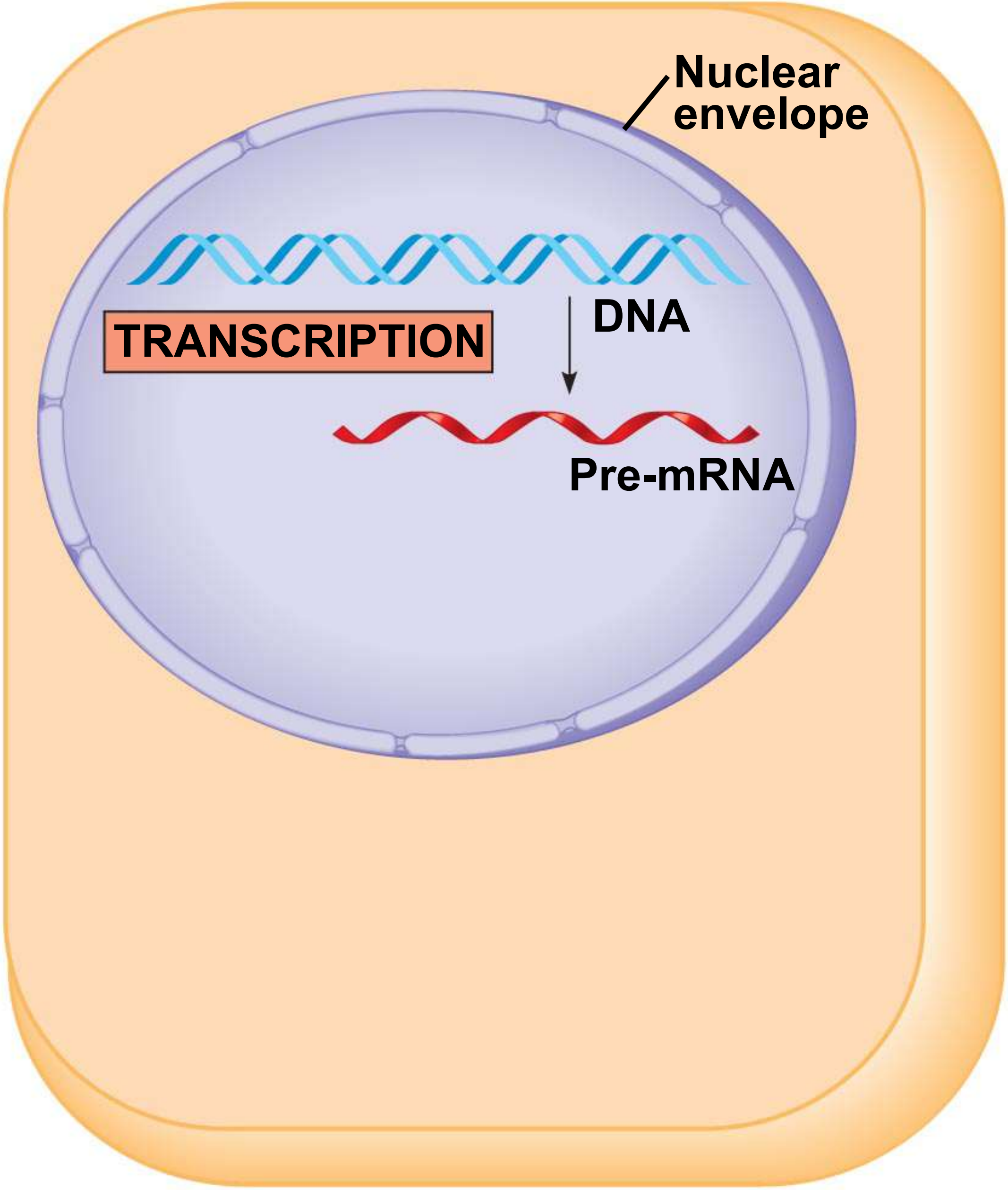


(a) Bacterial cell

Fig. 17-3a-2

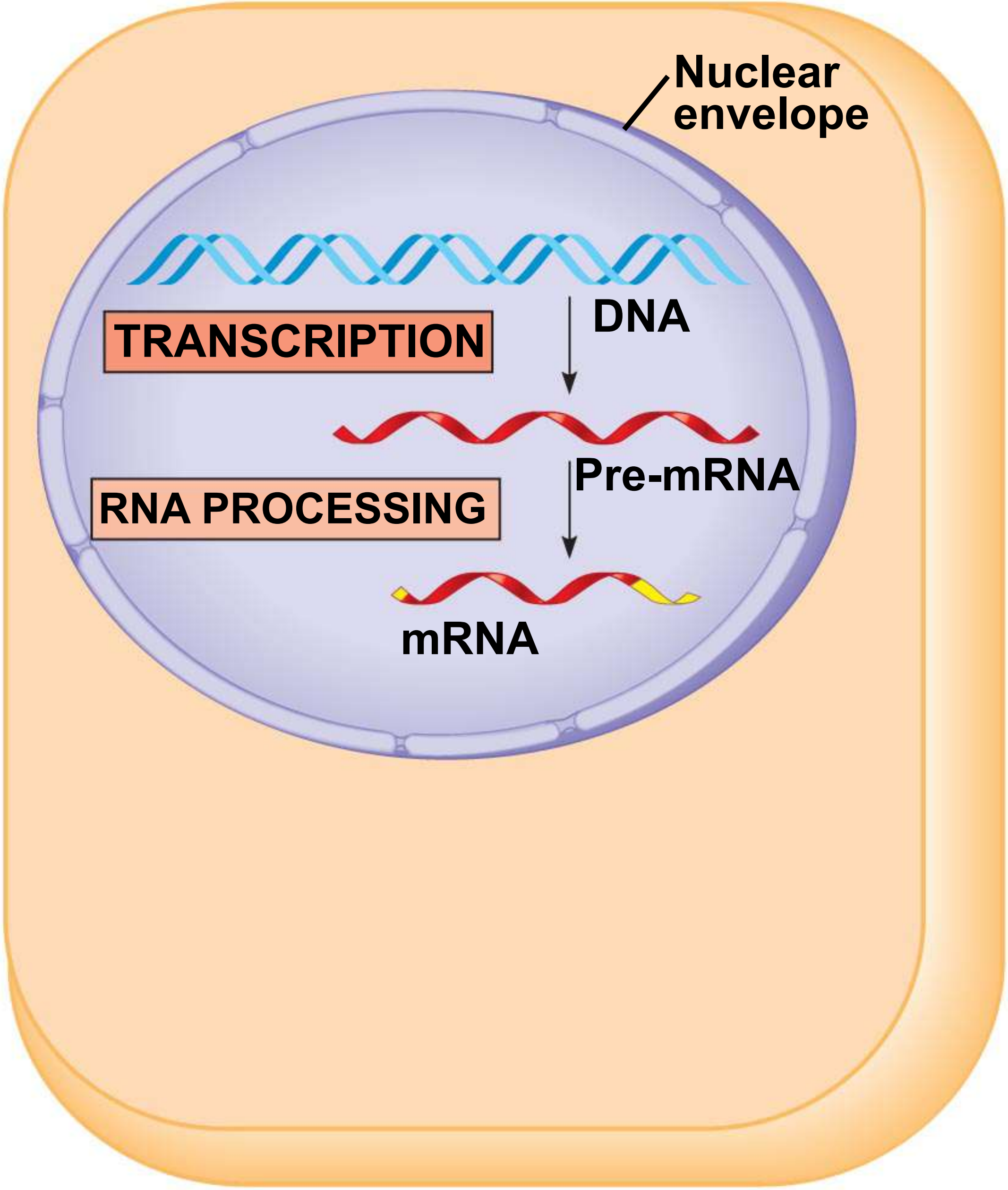


(a) Bacterial cell

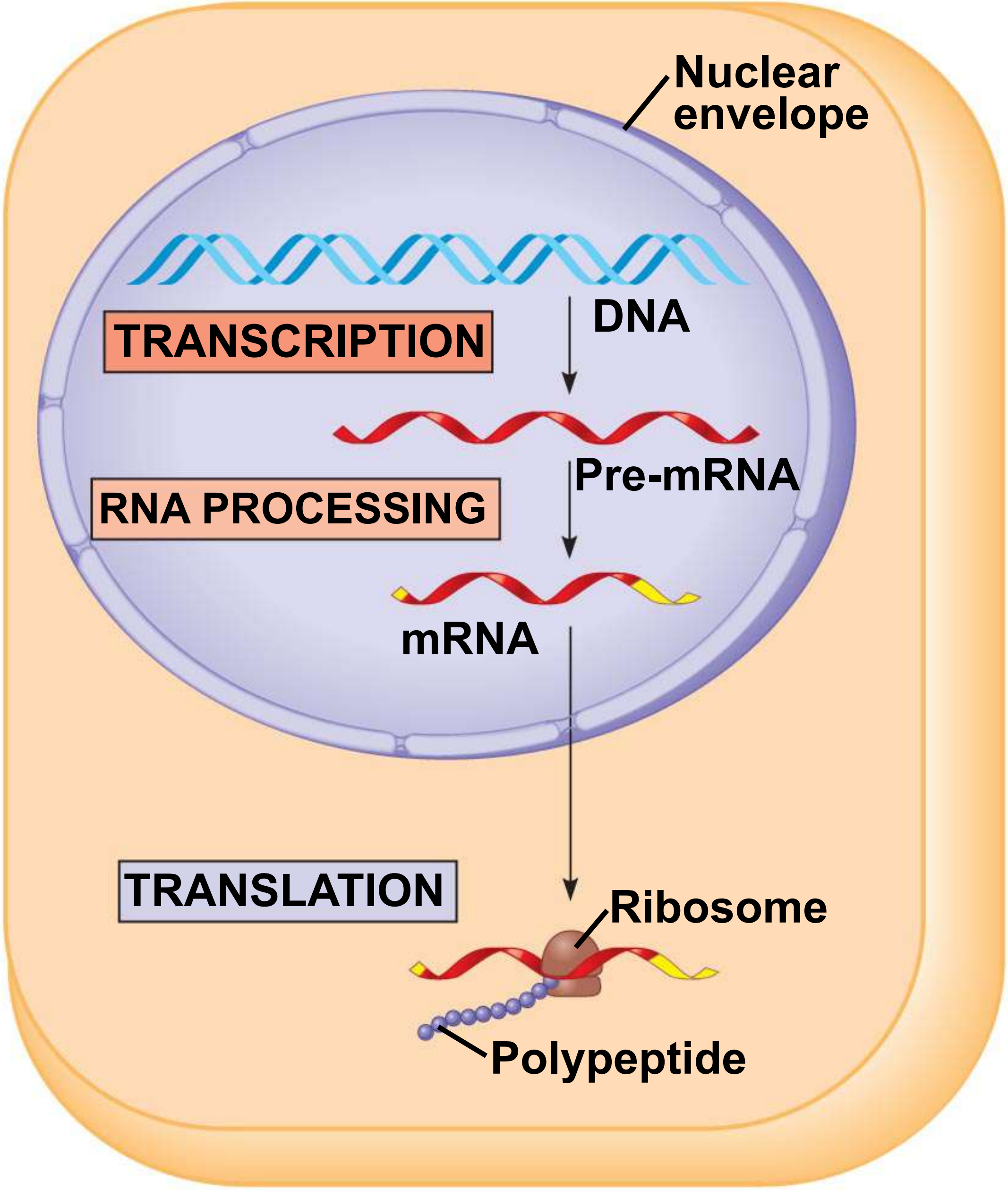


(b) Eukaryotic cell

Fig. 17-3b-2



(b) Eukaryotic cell



(b) Eukaryotic cell

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 bases correspond to an amino acid?

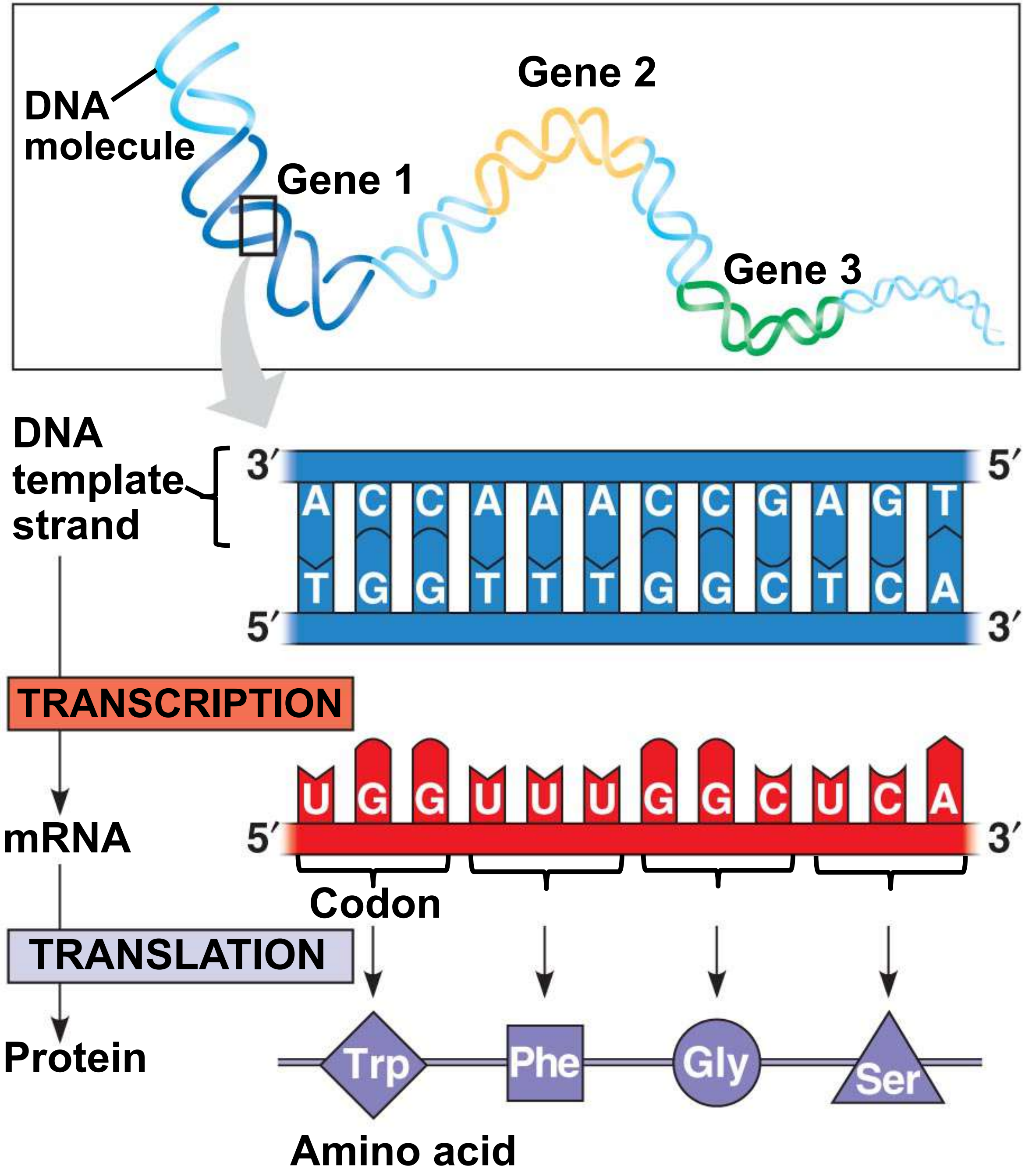
Codons: Triplets of Bases

- The flow of information from gene to protein is based on a **triplet code**: a series of nonoverlapping, three-nucleotide words
- These triplets are the smallest units of uniform length that can code for all the amino acids
- Example: AGT at a particular position on a DNA strand results in the placement of the amino acid serine at the corresponding position of the polypeptide to be produced

- During transcription, one of the two DNA strands called the **template strand** provides a template for ordering the sequence of nucleotides in an RNA transcript
- During translation, the mRNA base triplets, called **codons**, are read in the 5′ to 3′ direction
- Each codon specifies the amino acid to be placed at the corresponding position along a polypeptide

- Codons along an mRNA molecule are read by translation machinery in the 5′ to 3′ direction
- Each codon specifies the addition of one of 20 amino acids

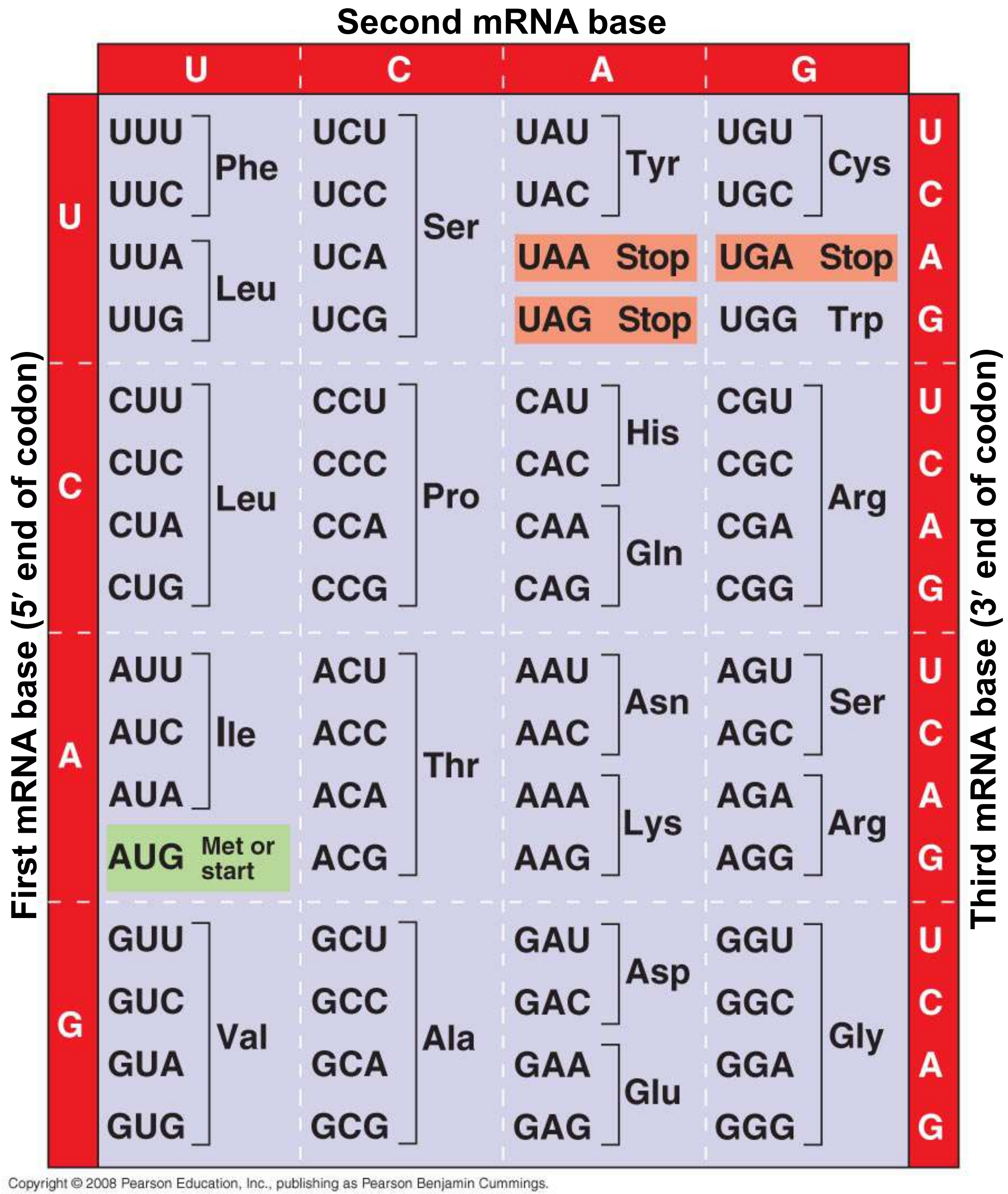
Fig. 17-4


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

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 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

Fig. 17-5



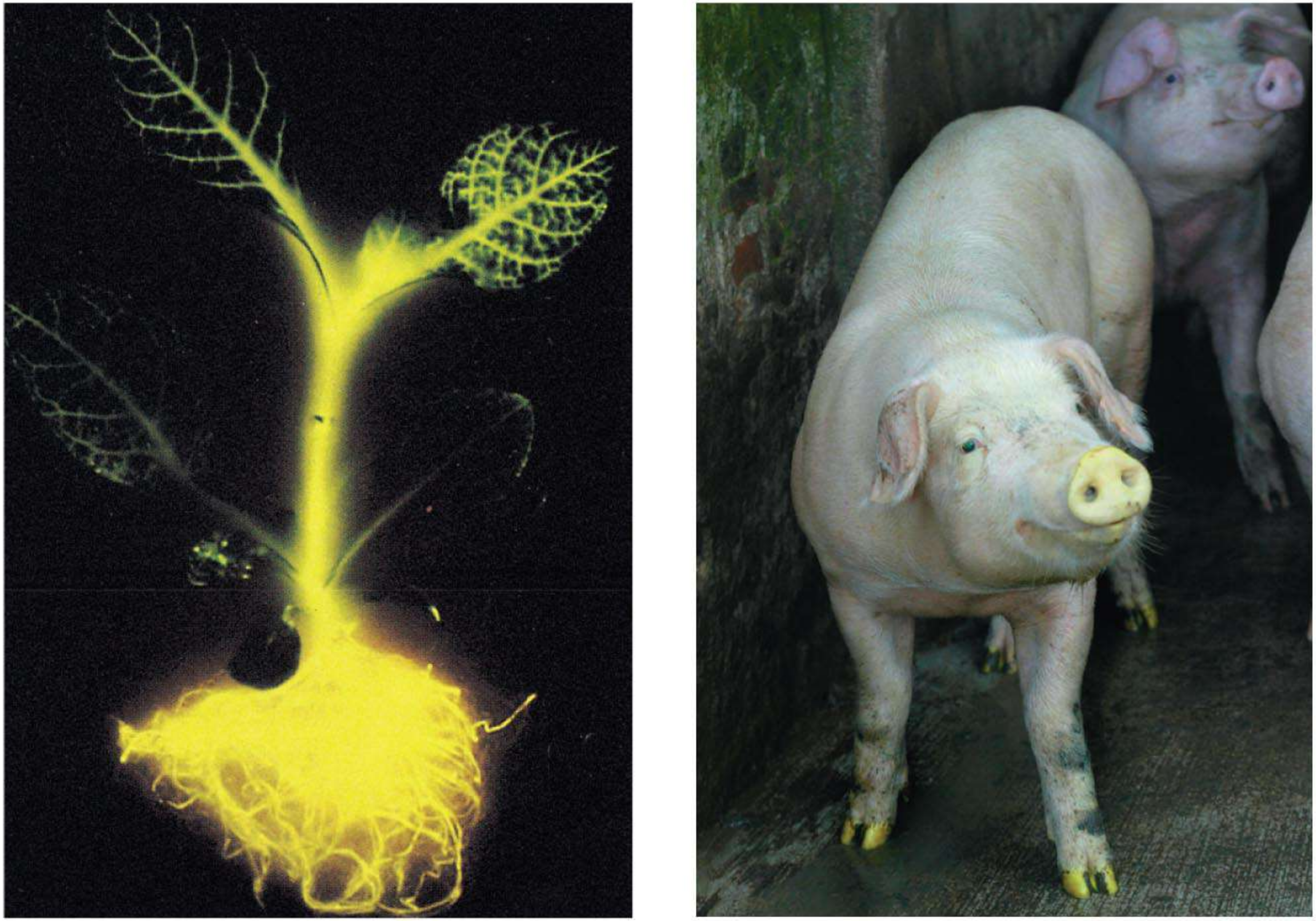
Second mRNA base

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 to the most complex animals
- Genes can be transcribed and translated after being transplanted from one species to another

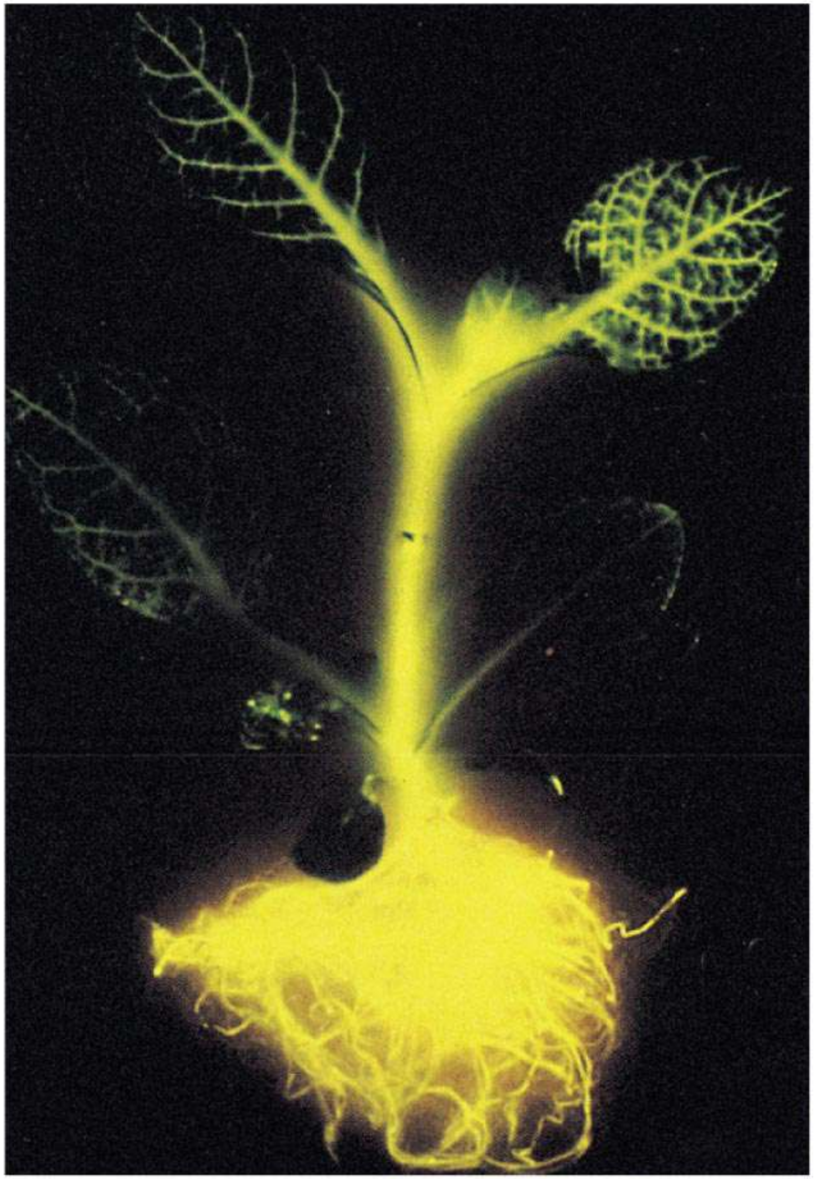
Fig. 17-6



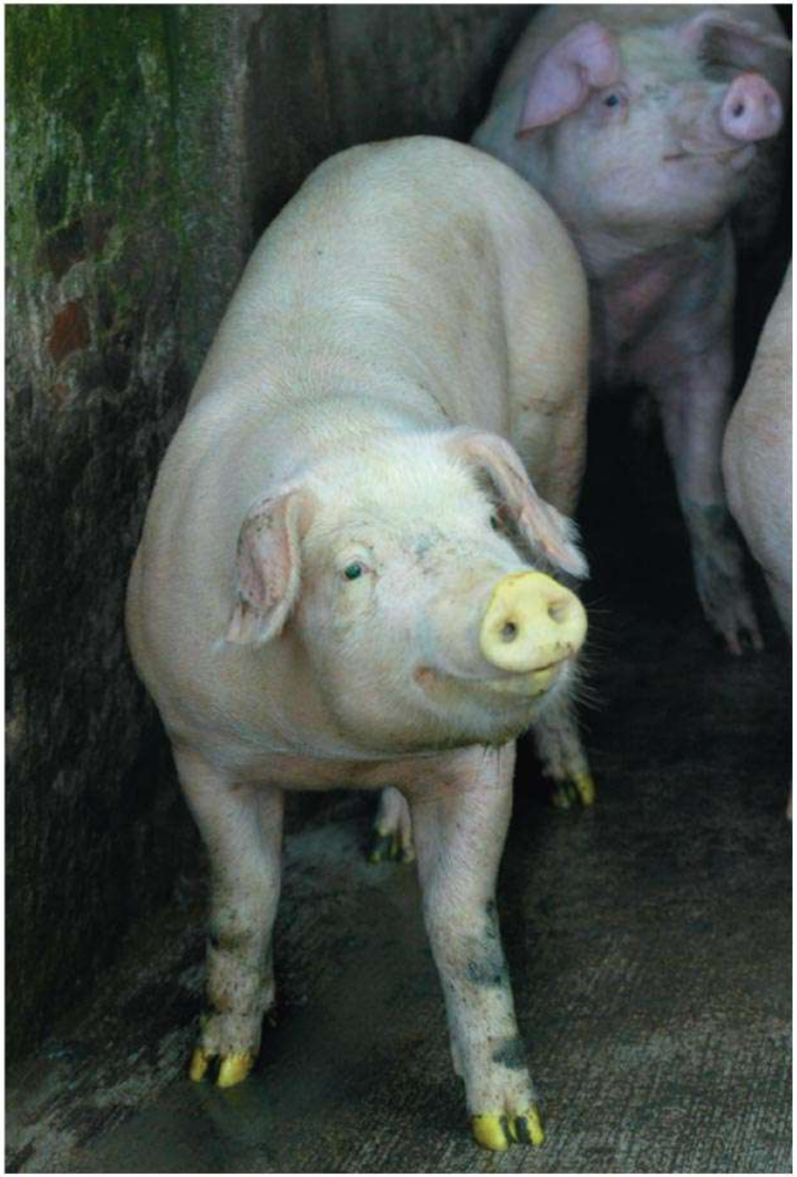
(a) Tobacco plant expressing a firefly gene

(b) Pig expressing a jellyfish gene

Fig. 17-6a



(a) Tobacco plant expressing
a firefly gene



(b) Pig expressing a jellyfish gene

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

- Transcription, the first stage of gene expression, can be examined in more detail

Molecular Components of Transcription

- RNA synthesis is catalyzed by **RNA polymerase**, which pries the DNA strands apart and hooks together the RNA nucleotides
- RNA synthesis follows the same base-pairing rules as DNA, except uracil substitutes for thymine

- 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**

PLAY **Animation: Transcription**

Fig. 17-7

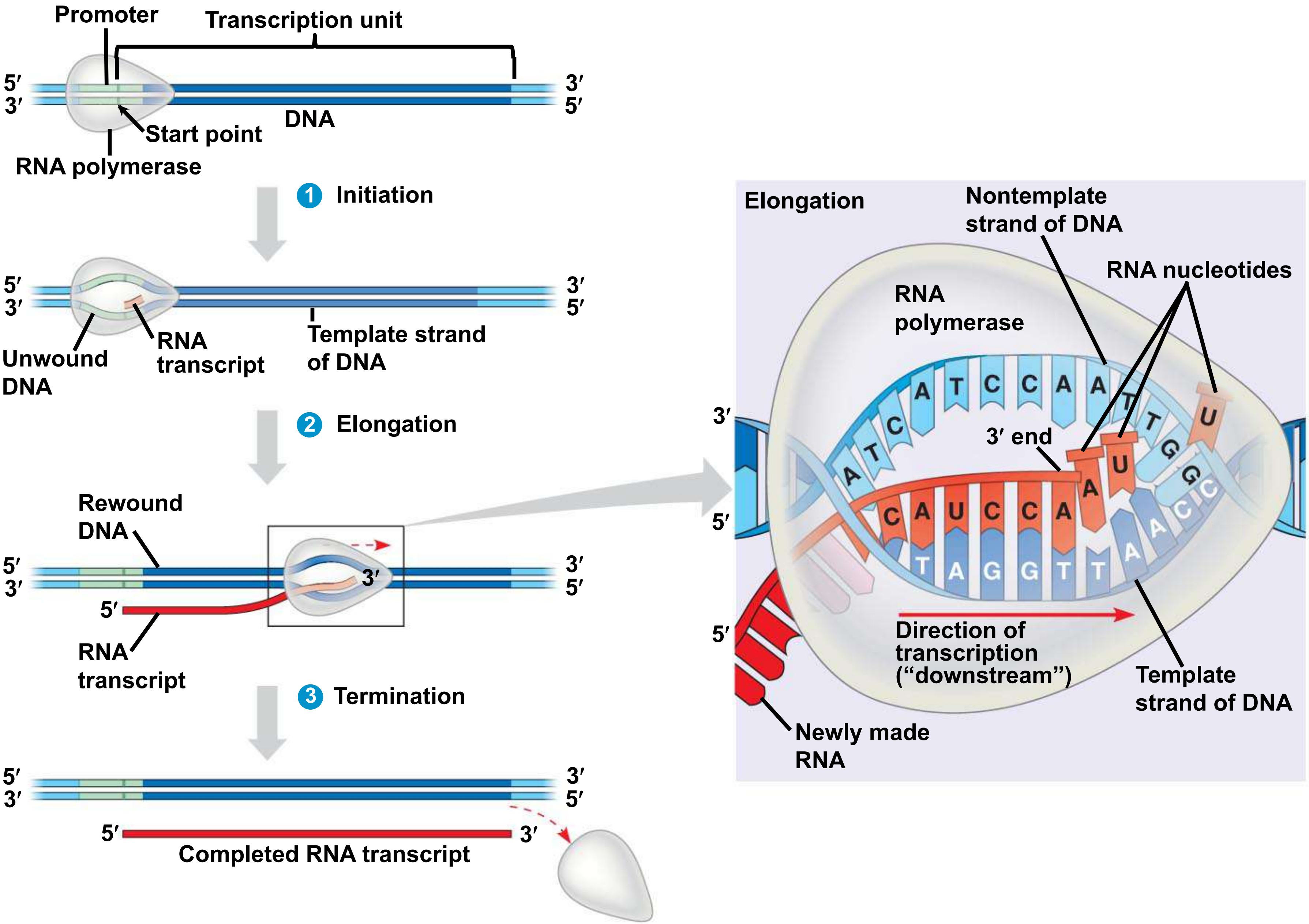

Promoter
Transcription unit
5′
3′
3′
5′
Start point
DNA
RNA polymerase
1 Initiation
5′
3′
3′
5′
Unwound DNA
RNA transcript
Template strand of DNA
2 Elongation
Rewound DNA
5′
3′
3′
3′
5′
5′
RNA transcript
3 Termination
5′
3′
3′
5′
5′
3′
Completed RNA transcript
Elongation
Nontemplate strand of DNA
RNA nucleotides
RNA polymerase
A T C A T C C A A T T G G
3′ end
U U
C A U C C A A
T A G G T T A A C C
3′
5′
5′
Direction of transcription (“downstream”)
Template strand of DNA
Newly made RNA

Fig. 17-7a-1

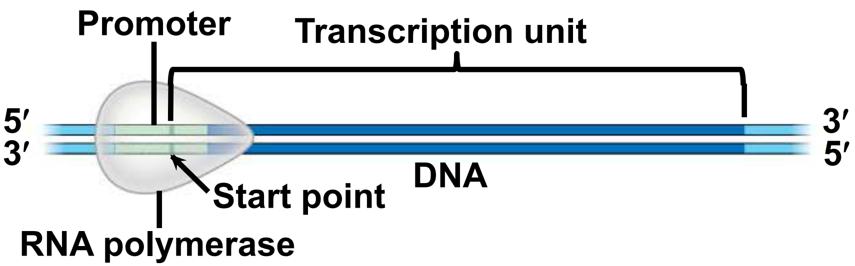

Promoter
Transcription unit
5′
3′
3′
5′
Start point
DNA
RNA polymerase

Fig. 17-7a-2

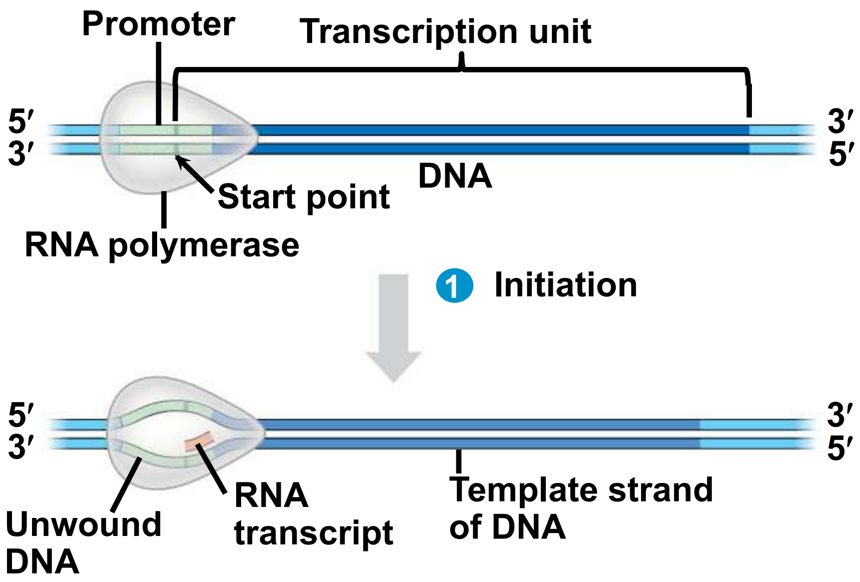

Promoter
Transcription unit
5′
3′
3′
5′
Start point
DNA
RNA polymerase
1 Initiation
5′
3′
3′
5′
Unwound DNA
RNA transcript
Template strand of DNA

Fig. 17-7a-3

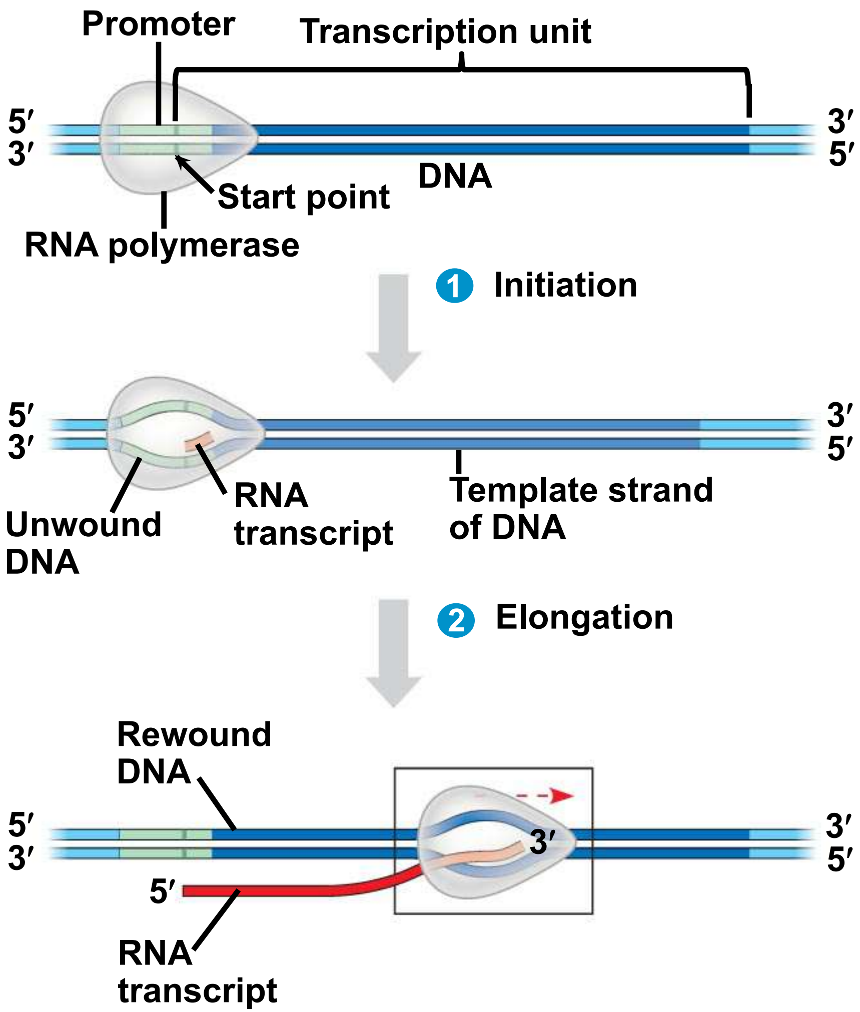

Promoter
Transcription unit
5′
3′
3′
5′
Start point
DNA
RNA polymerase
1 Initiation
5′
3′
3′
5′
Unwound DNA
RNA transcript
Template strand of DNA
2 Elongation
Rewound DNA
5′
3′
3′
3′
5′
5′
RNA transcript

Fig. 17-7a-4

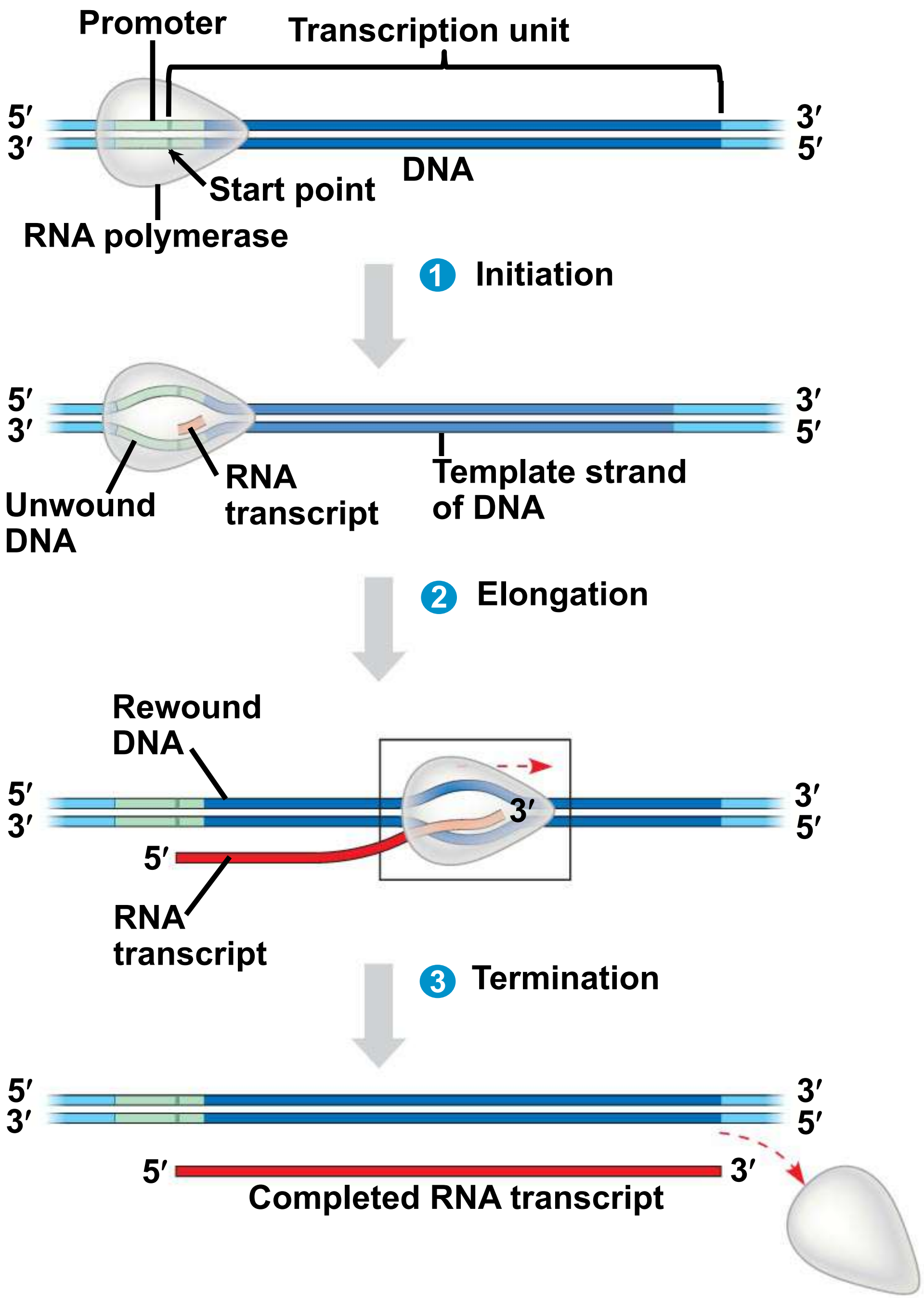
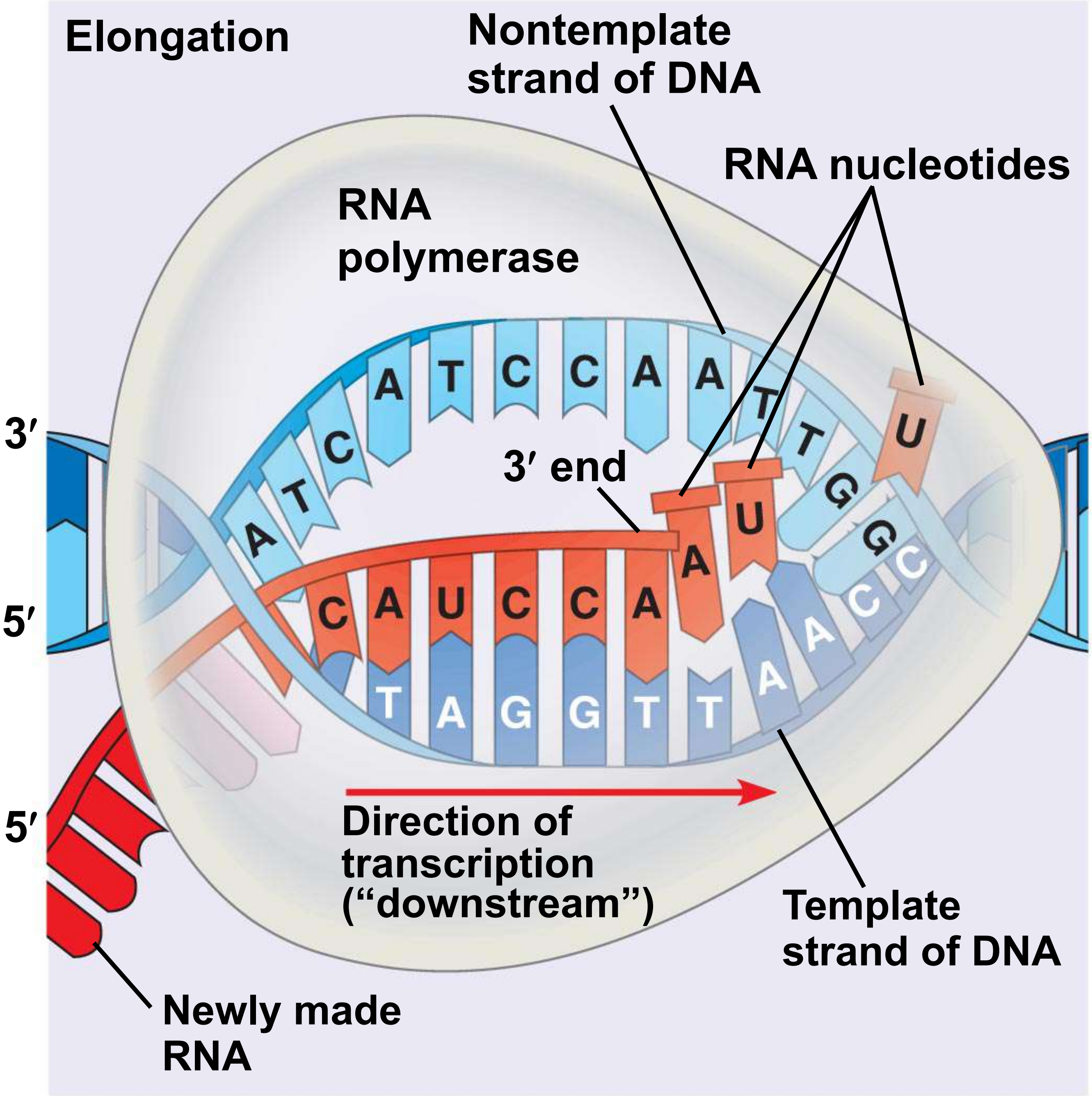

Promoter
Transcription unit
5′
3′
3′
5′
Start point
DNA
RNA polymerase
1 Initiation
5′
3′
3′
5′
Unwound DNA
RNA transcript
Template strand of DNA
2 Elongation
Rewound DNA
5′
3′
3′
3′
5′
5′
RNA transcript
3 Termination
5′
3′
3′
5′
5′
3′
Completed RNA transcript

Fig. 17-7b


Elongation
Nontemplate strand of DNA
RNA nucleotides
RNA polymerase
A T C C A A T T G G
A T C
3′
3′ end
U
U
A
C A U C C A
A
5′
T A G G T T A A C C
5′
Direction of transcription (“downstream”)
Template strand of DNA
Newly made RNA

Synthesis of an RNA Transcript

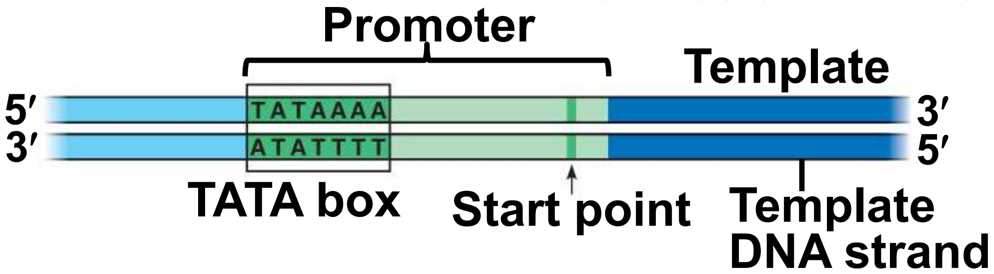
- The three stages of transcription:
  - Initiation
  - Elongation
  - Termination

RNA Polymerase Binding and Initiation of Transcription

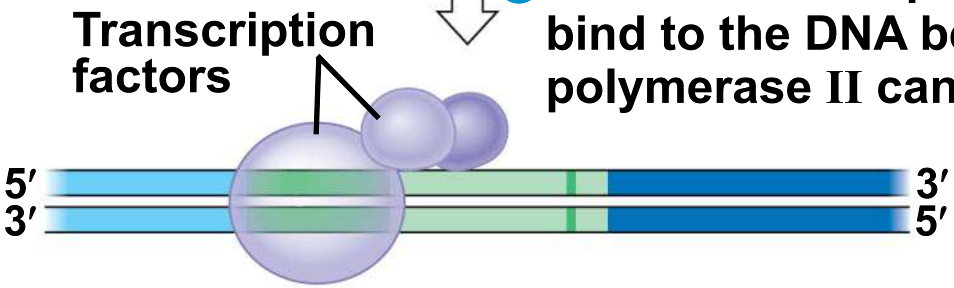
- Promoters signal the initiation of RNA synthesis
- **Transcription factors** mediate the binding of RNA polymerase and the initiation of transcription
- The completed assembly of transcription factors and RNA polymerase II bound to a promoter is called a **transcription initiation complex**
- A promoter called a **TATA box** is crucial in forming the initiation complex in eukaryotes

Fig. 17-8

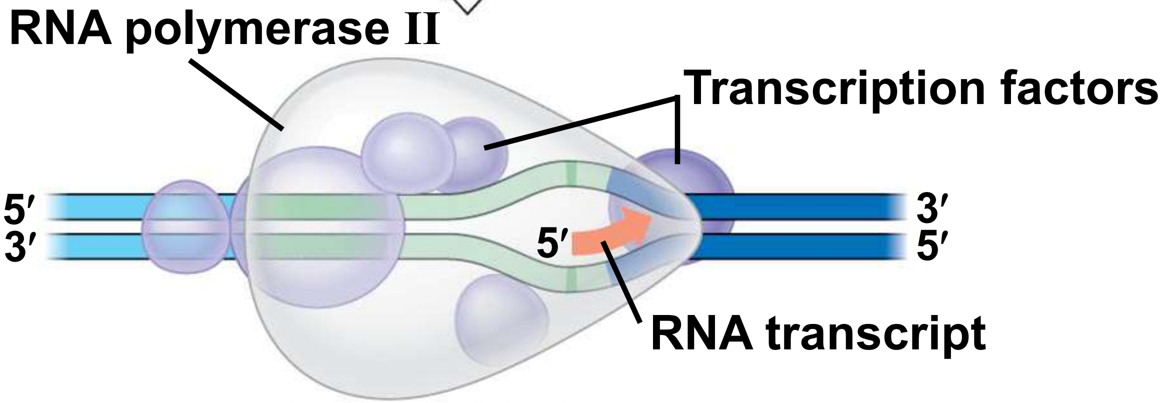
① A eukaryotic promoter includes a TATA box



② Several transcription factors must bind to the DNA before RNA polymerase II can do so.



③ Additional transcription factors bind to the DNA along with RNA polymerase II, forming the transcription initiation complex.



Transcription initiation complex

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

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
- In eukaryotes, the polymerase continues transcription after the pre-mRNA is cleaved from the growing RNA chain; the polymerase eventually falls off the DNA

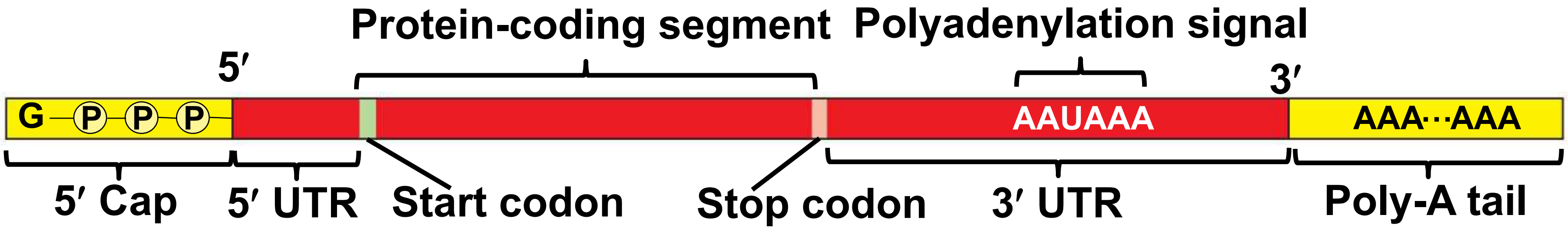
Concept 17.3: Eukaryotic cells modify RNA after transcription

- Enzymes in the eukaryotic nucleus modify pre-mRNA before the genetic messages are dispatched to the cytoplasm
- During RNA processing, both ends of the primary transcript are usually 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 nucleotide **5′ cap**
  - The 3′ end gets a **poly-A tail**
- These modifications share several functions:
  - They seem to facilitate the export of mRNA
  - They protect mRNA from hydrolytic enzymes
  - They help ribosomes attach to the 5′ end

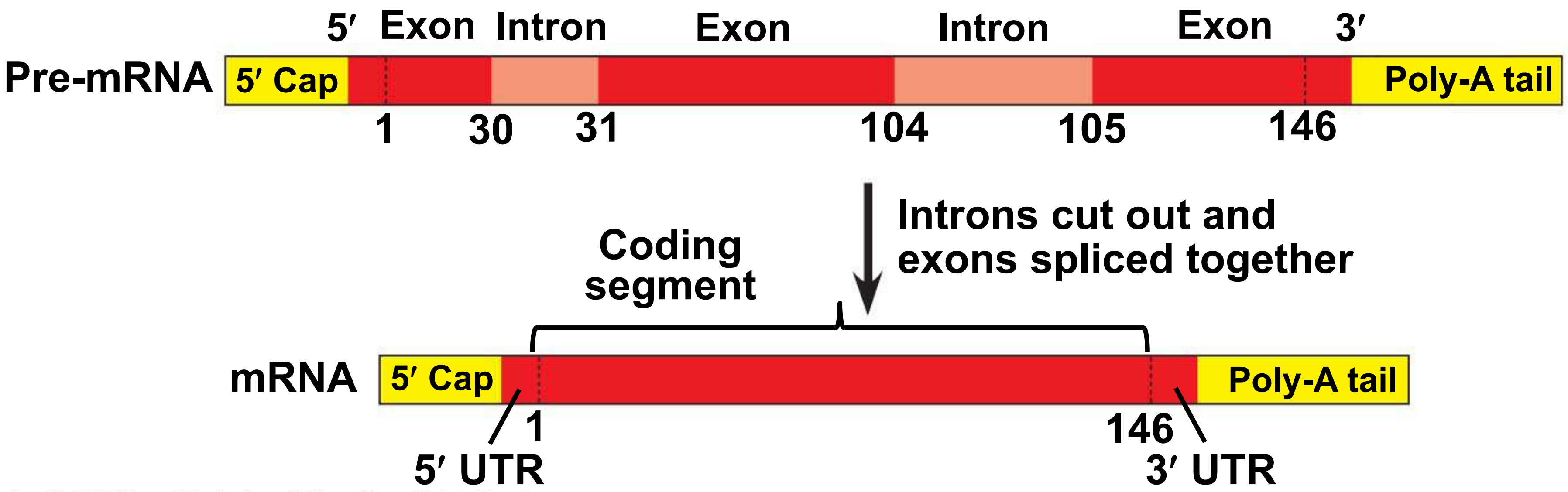
Fig. 17-9


Protein-coding segment
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 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

Fig. 17-10


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

- In some cases, RNA splicing is carried out by spliceosomes
- **Spliceosomes** consist of a variety of proteins and several small nuclear ribonucleoproteins (snRNPs) that recognize the splice sites

Fig. 17-11-1

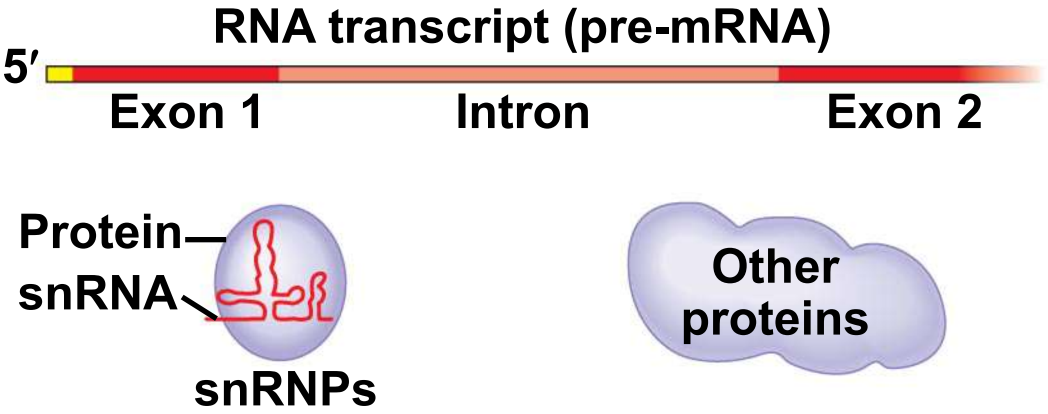

RNA transcript (pre-mRNA)
5′
Exon 1
Intron
Exon 2
Protein
snRNA
snRNPs
Other proteins

Fig. 17-11-2

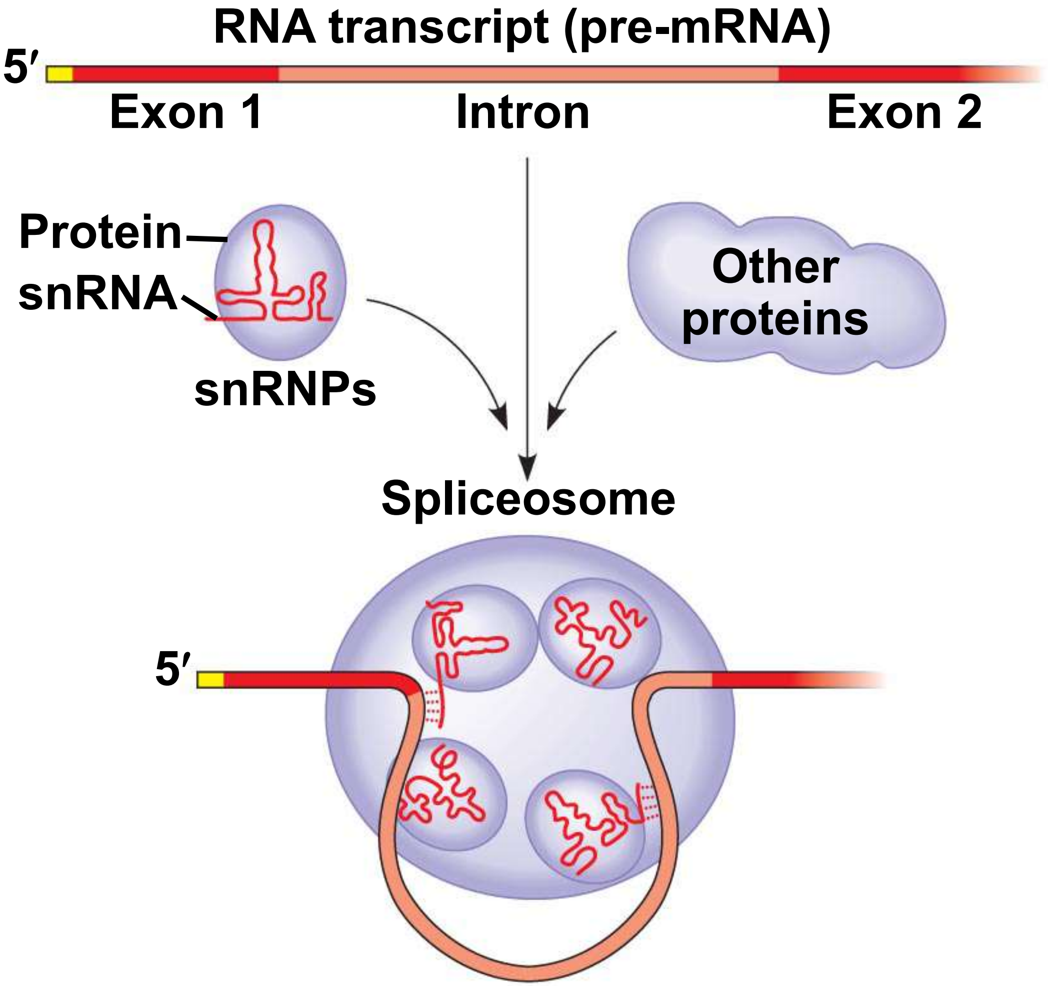
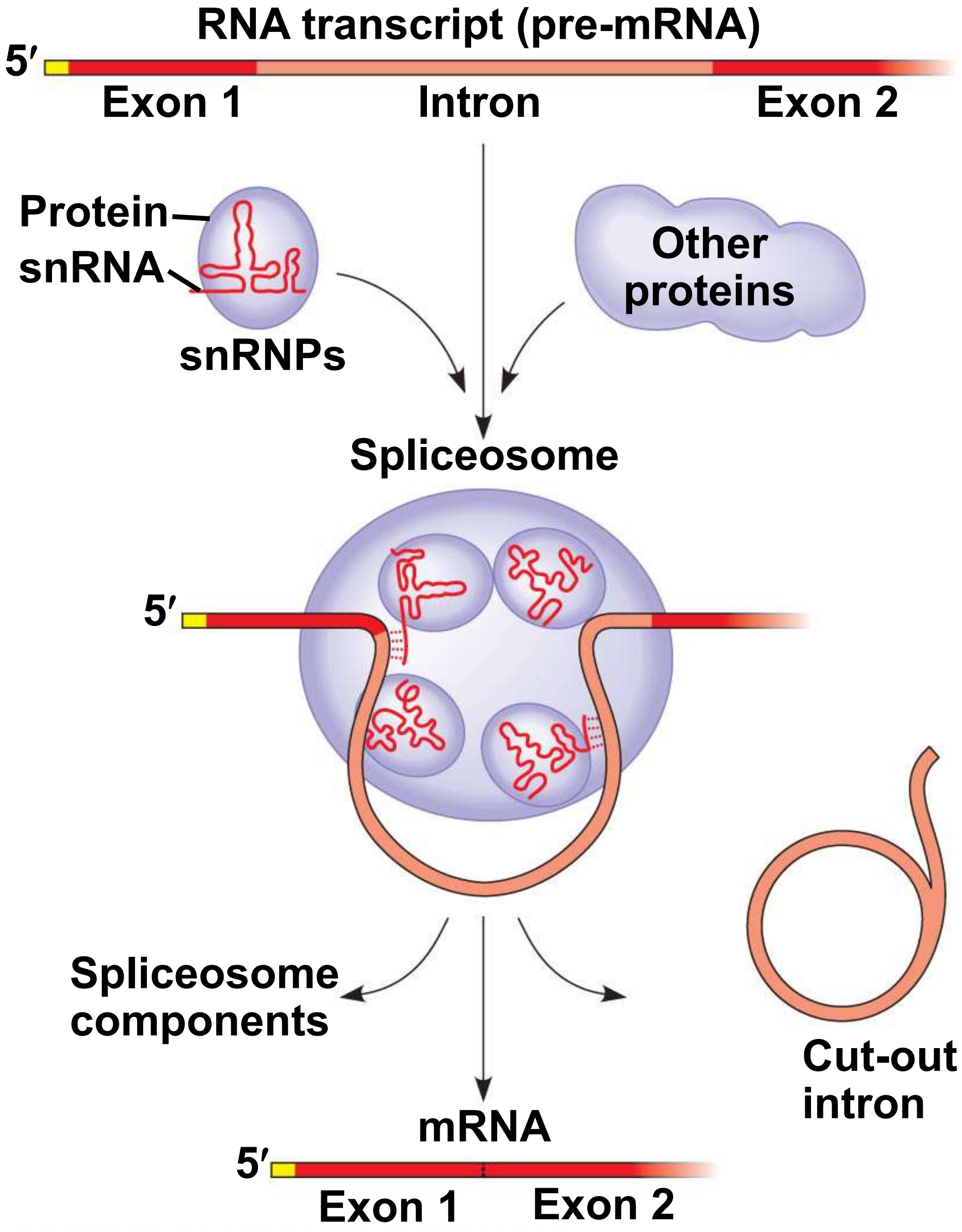

RNA transcript (pre-mRNA)
5′
Exon 1
Intron
Exon 2
Protein
snRNA
snRNPs
Other proteins
Spliceosome
5′

Fig. 17-11-3


RNA transcript (pre-mRNA)
5′
Exon 1
Intron
Exon 2
Protein
snRNA
snRNPs
Other proteins
Spliceosome
5′
Spliceosome components
Cut-out intron
mRNA
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

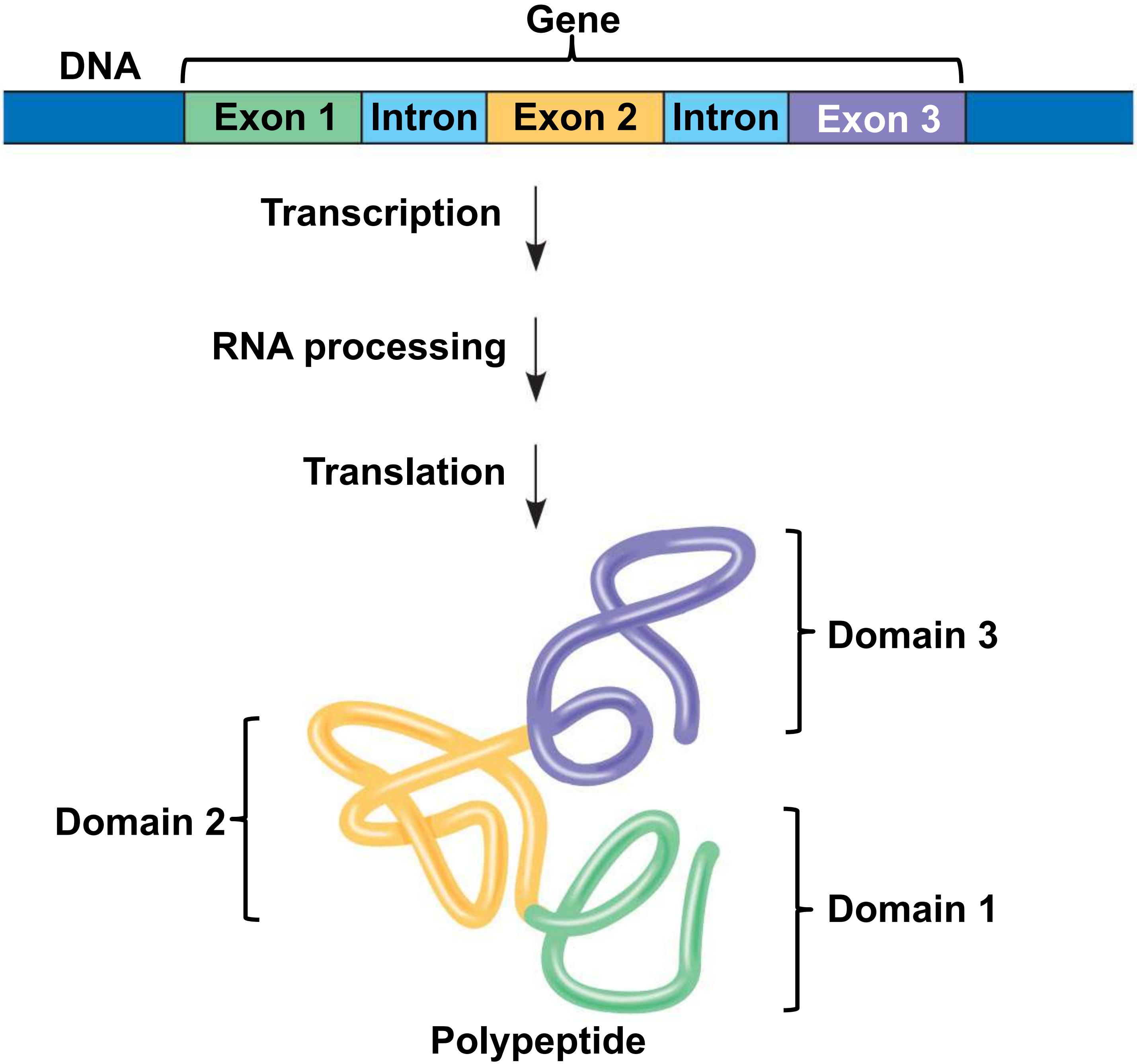
- Three properties of RNA enable it to function as an enzyme
  - It can form a three-dimensional structure because of its ability to base pair with itself
  - Some bases in RNA contain functional groups
  - RNA may hydrogen-bond with other nucleic acid molecules

The Functional and Evolutionary Importance of Introns

- Some genes can encode more than one kind of polypeptide, depending on which segments are treated as exons during RNA splicing
- Such variations are called **alternative RNA splicing**
- Because of alternative splicing, 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

Fig. 17-12



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*

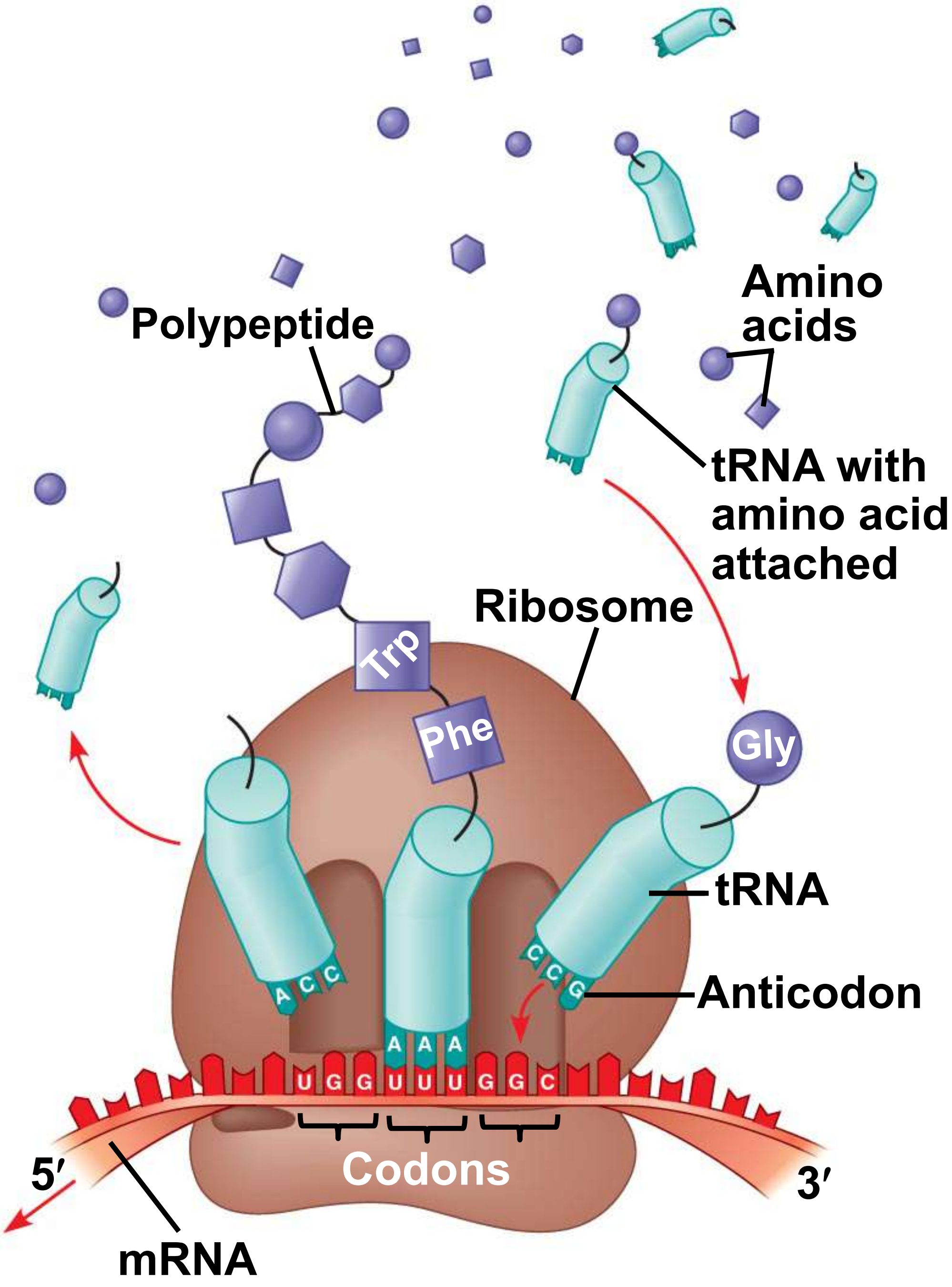
- The translation of mRNA to protein can be examined in more detail

Molecular Components of Translation

- A cell translates an mRNA message into protein with the help of **transfer RNA (tRNA)**
- Molecules of tRNA are not identical:
  - 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

PLAY **BioFlix: Protein Synthesis**

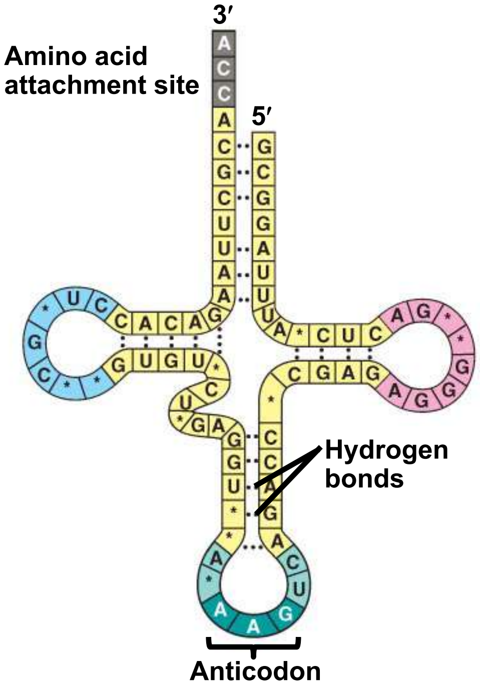
Fig. 17-13


Amino acids
Polypeptide
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′
3′
mRNA

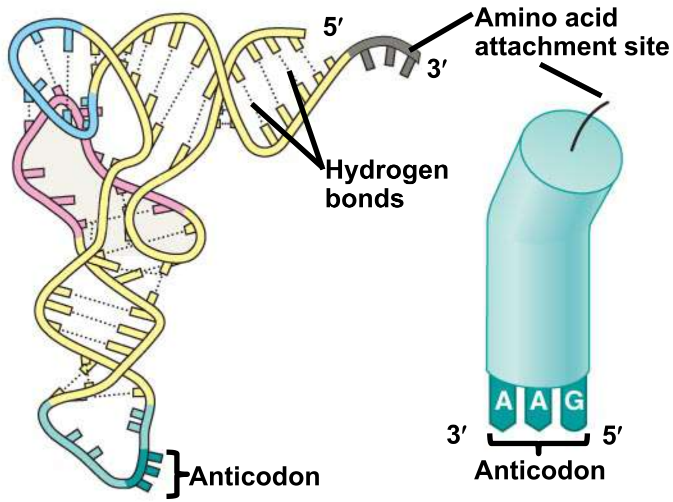
The Structure and Function of Transfer RNA

- 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

Fig. 17-14



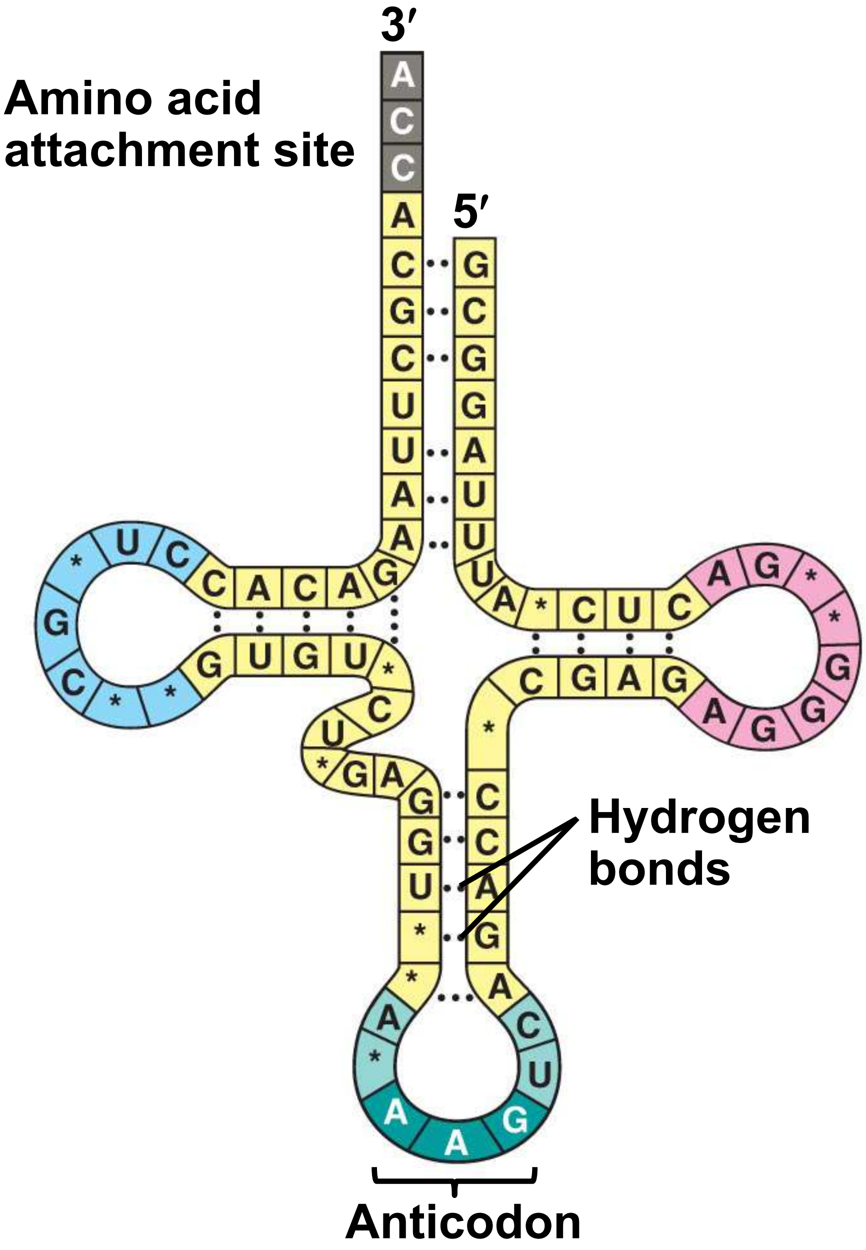
(a) Two-dimensional structure



(b) Three-dimensional structure

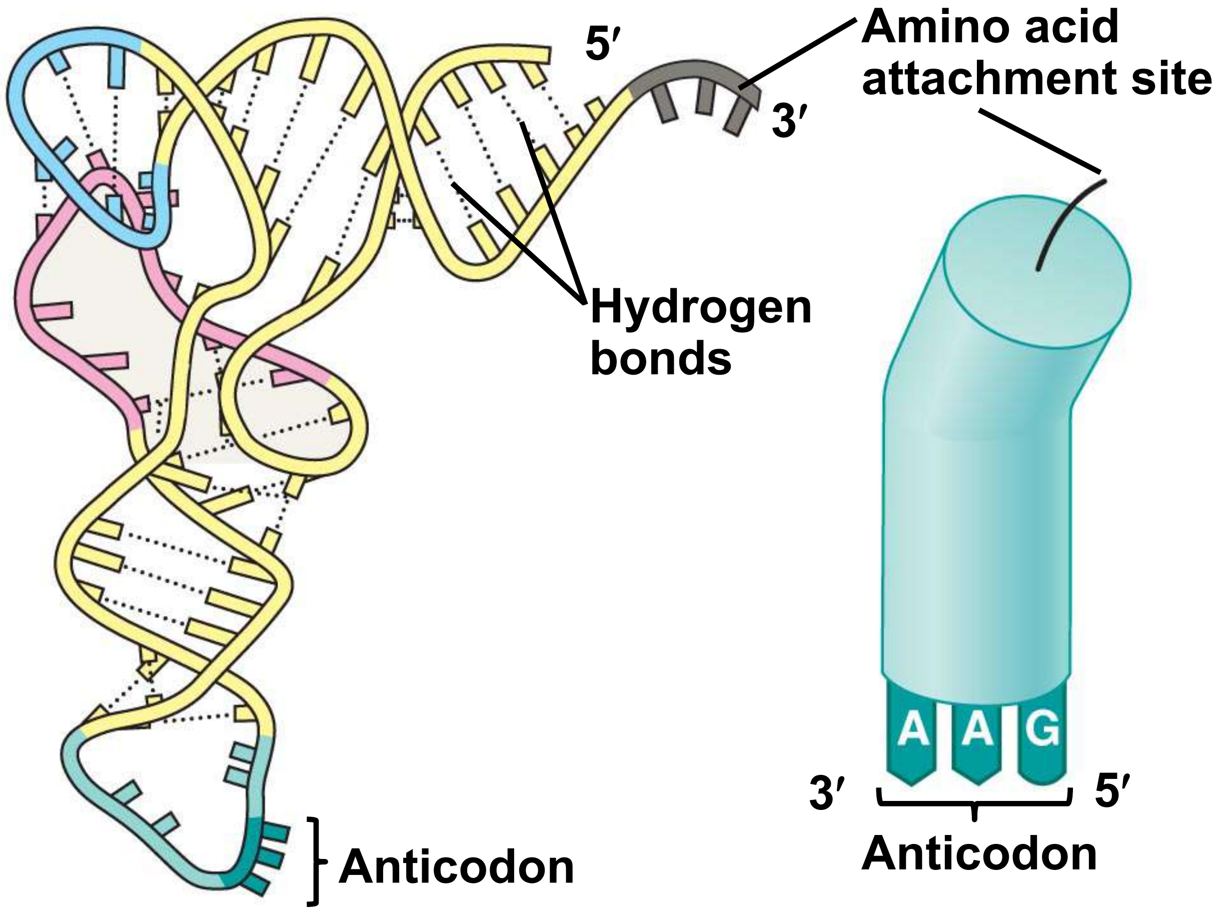
(c) Symbol used in this book

Fig. 17-14a



(a) Two-dimensional structure

Fig. 17-14b



(b) Three-dimensional structure

(c) Symbol used in this book

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

- 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

Fig. 17-15-1

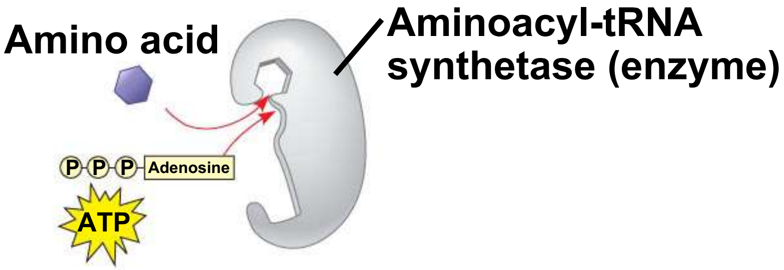

Amino acid
Aminoacyl-tRNA synthetase (enzyme)
P
P
P
Adenosine
ATP

Fig. 17-15-2

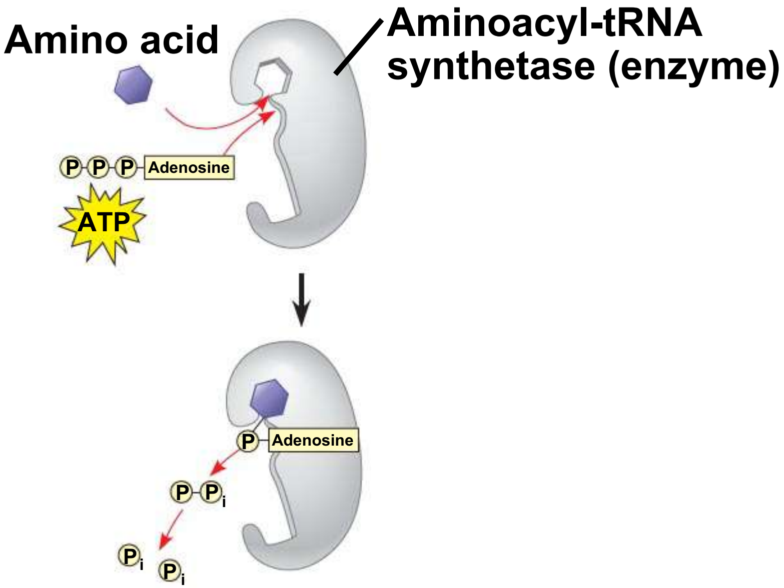
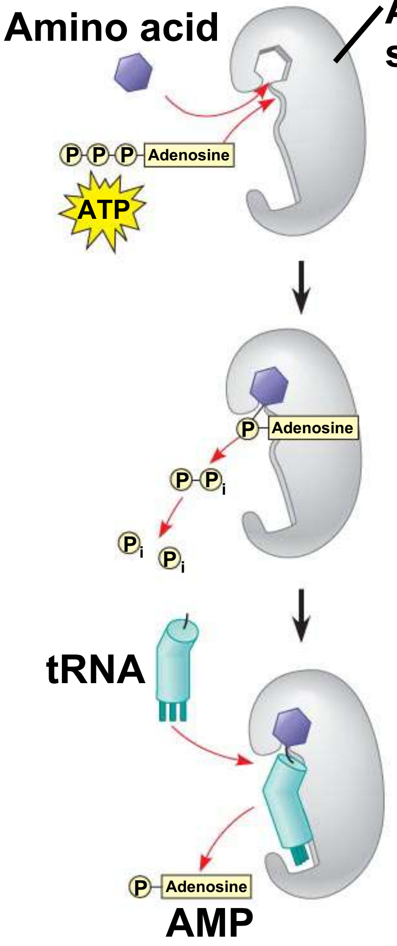
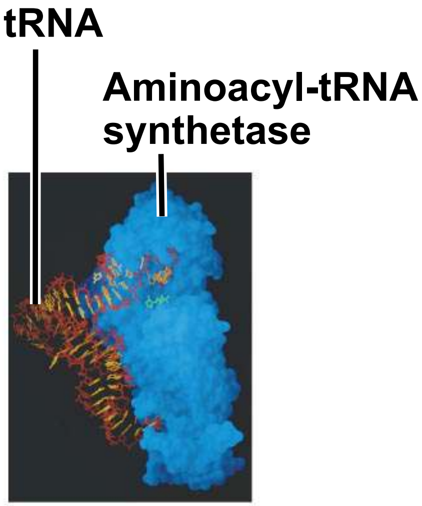

Amino acid
Aminoacyl-tRNA synthetase (enzyme)
P P P Adenosine
ATP
P Adenosine
P P$_i$
P$_i$
P$_i$

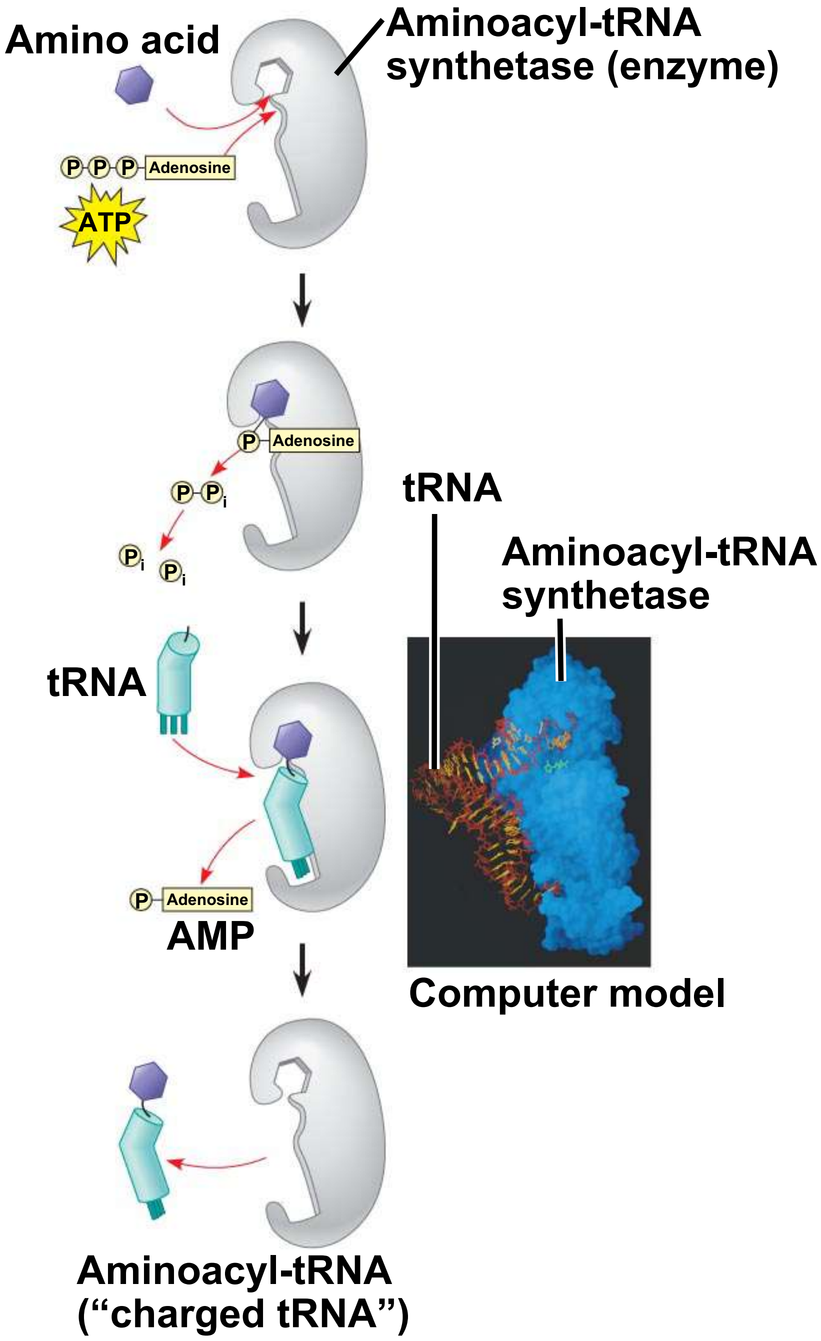
Fig. 17-15-3





Computer model

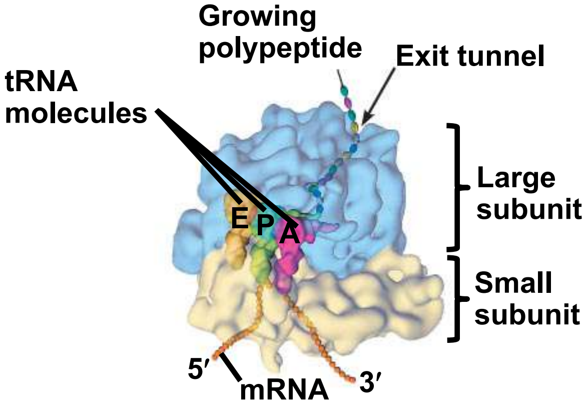
Fig. 17-15-4


Amino acid
Aminoacyl-tRNA synthetase (enzyme)
P P P Adenosine
ATP
P Adenosine
P P$_i$
P$_i$ P$_i$
tRNA
P Adenosine
AMP
Aminoacyl-tRNA ("charged tRNA")
tRNA
Aminoacyl-tRNA synthetase
Computer model

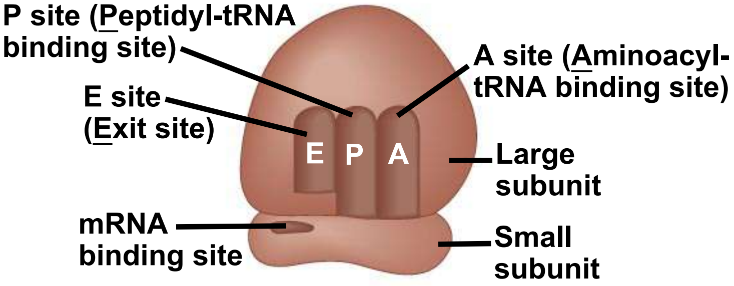
Ribosomes

- 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)**

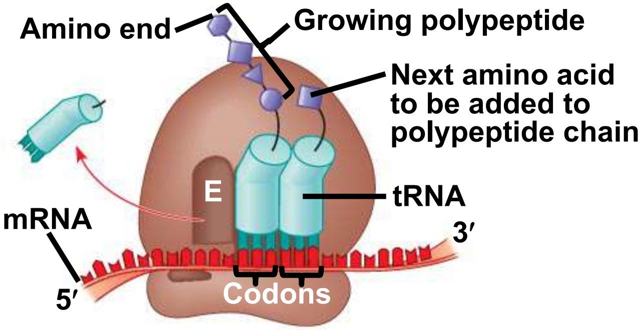
Fig. 17-16



(a) Computer model of functioning ribosome

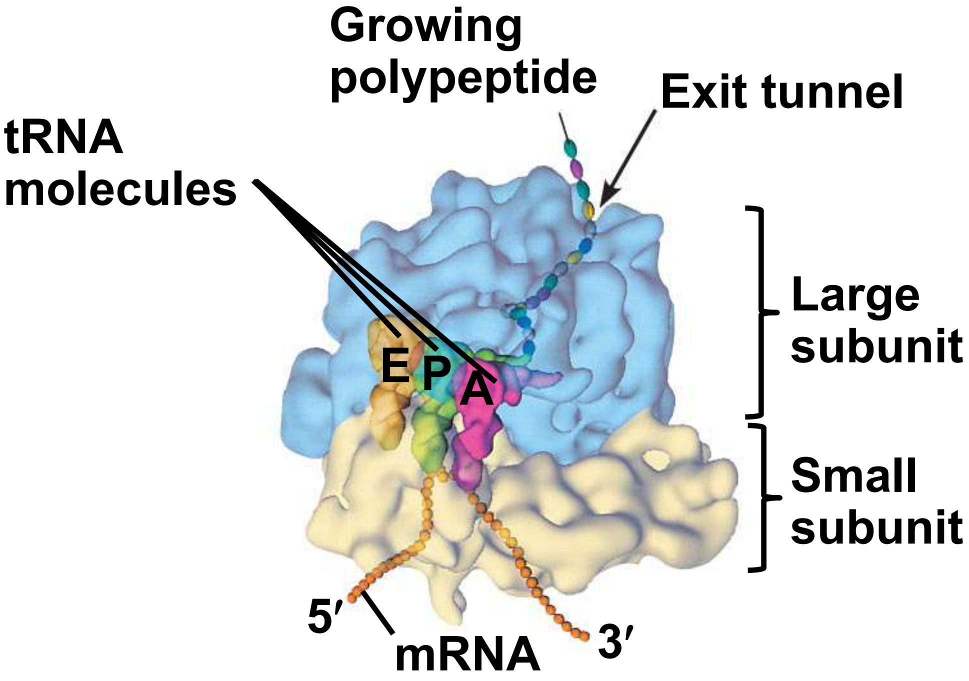


(b) Schematic model showing binding sites



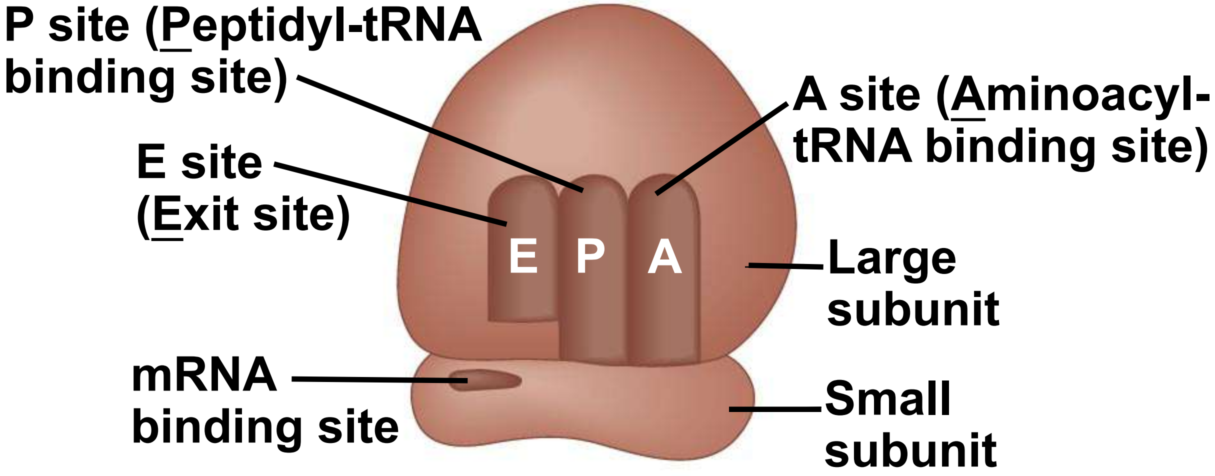
(c) Schematic model with mRNA and tRNA

Fig. 17-16a

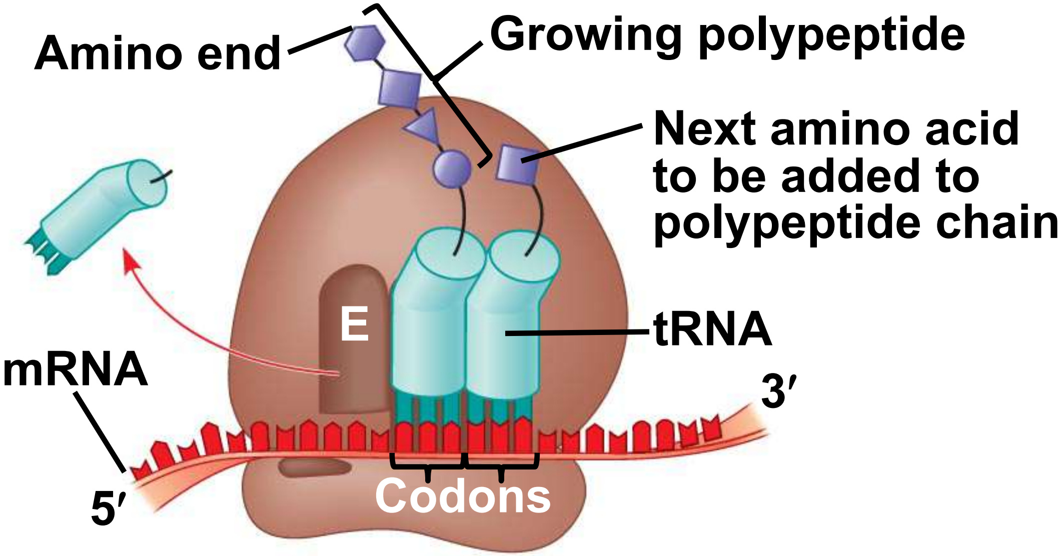


(a) Computer model of functioning ribosome

Fig. 17-16b



(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

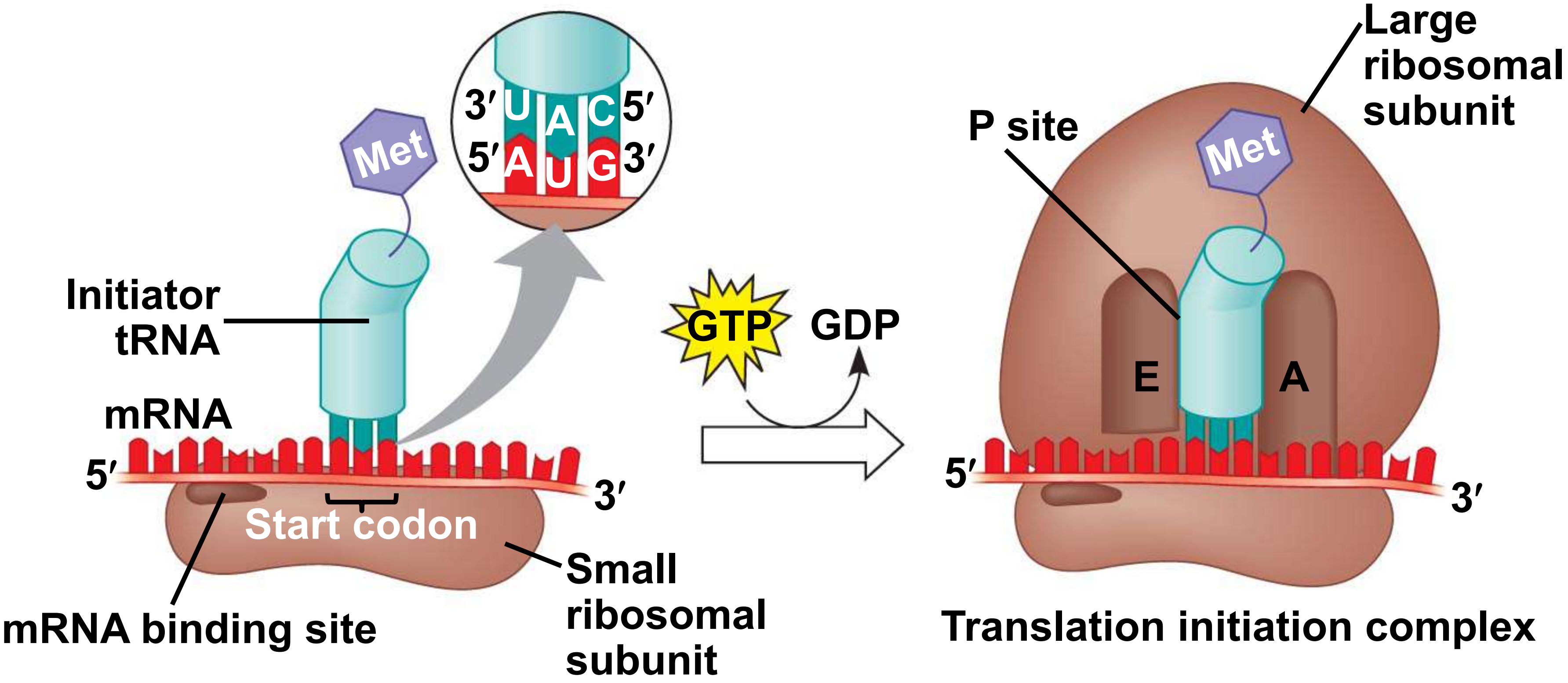
Building a Polypeptide

- The three stages of translation:
  - Initiation
  - Elongation
  - Termination
- All three stages require protein “factors” that aid in the translation process

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

Fig. 17-17


Met
3′ U A C 5′
5′ A U G 3′
Initiator tRNA
mRNA
5′
3′
Start codon
mRNA binding site
Small ribosomal subunit
GTP
GDP
Large ribosomal subunit
P site
Met
E
A
5′
3′
Translation initiation complex

Elongation of the Polypeptide Chain

- During the elongation stage, amino acids are added one by one to the preceding amino acid
- Each addition involves proteins called elongation factors and occurs in three steps: codon recognition, peptide bond formation, and translocation

Fig. 17-18-1

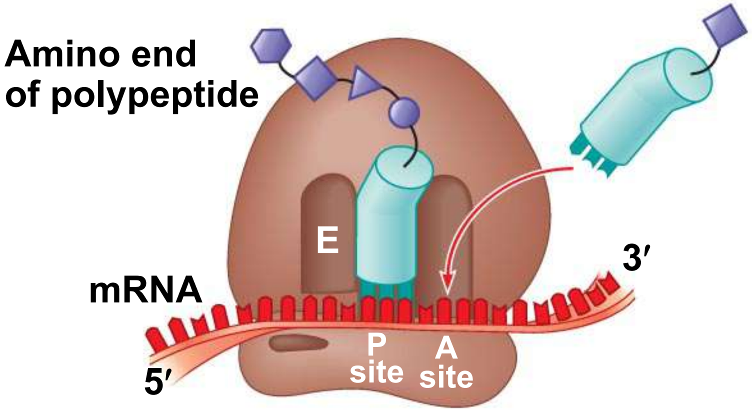


Fig. 17-18-2

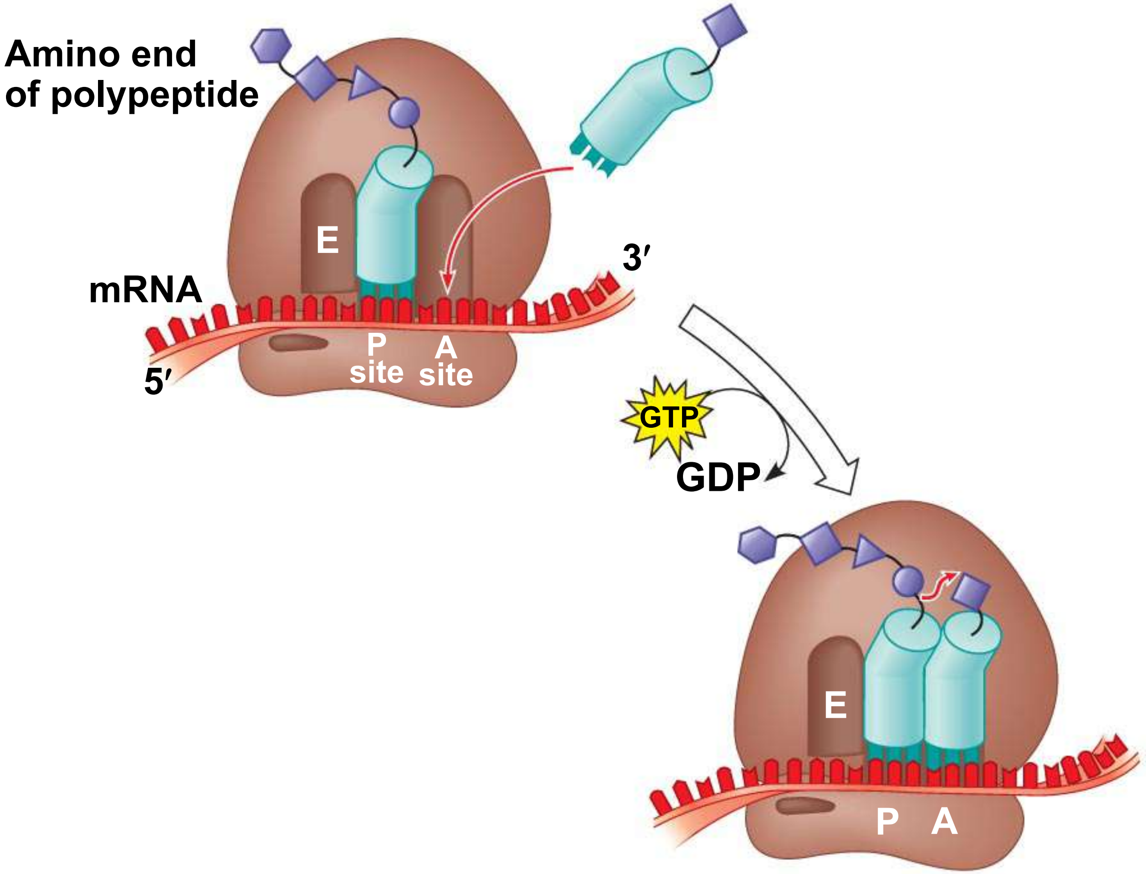


Fig. 17-18-3

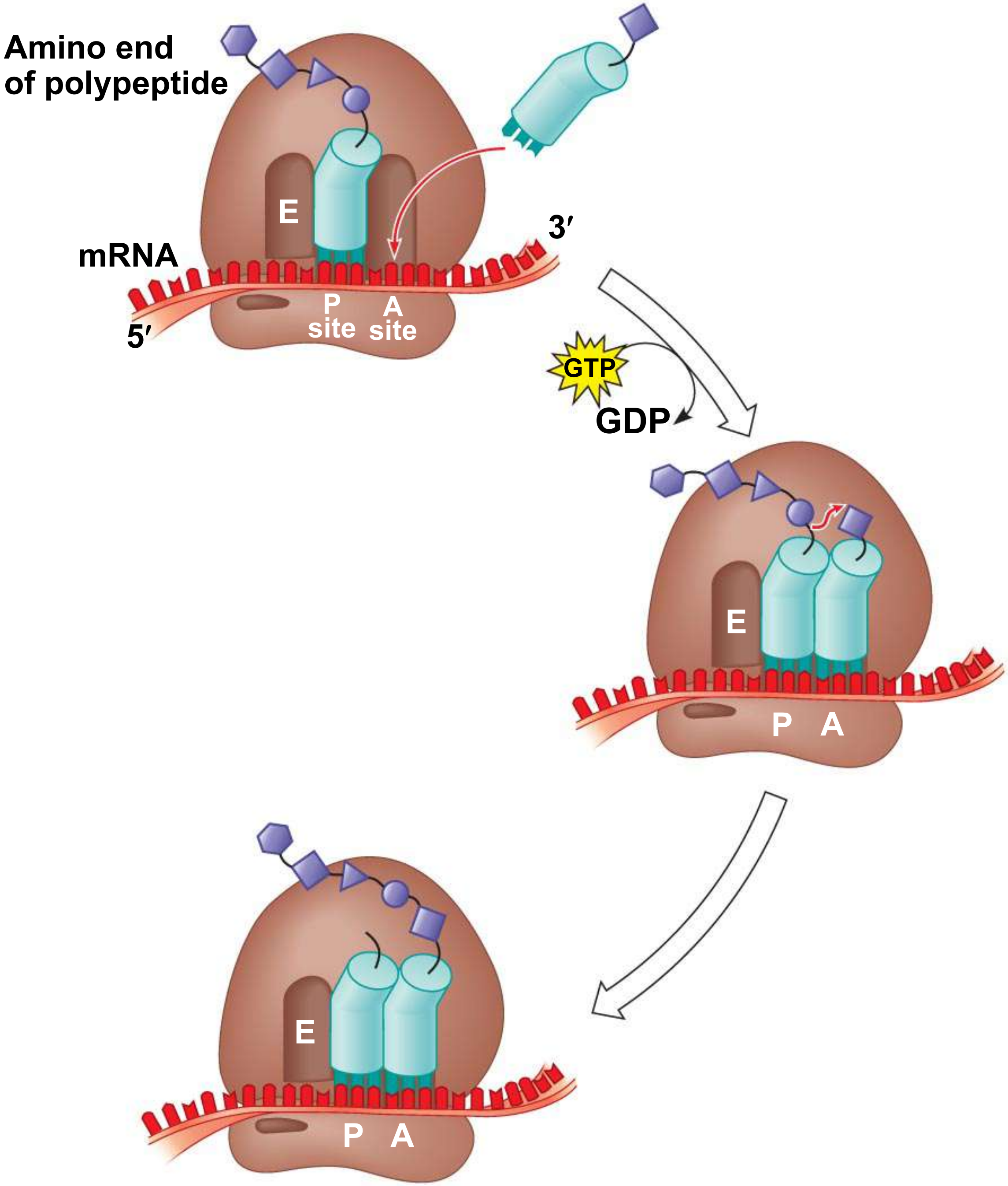
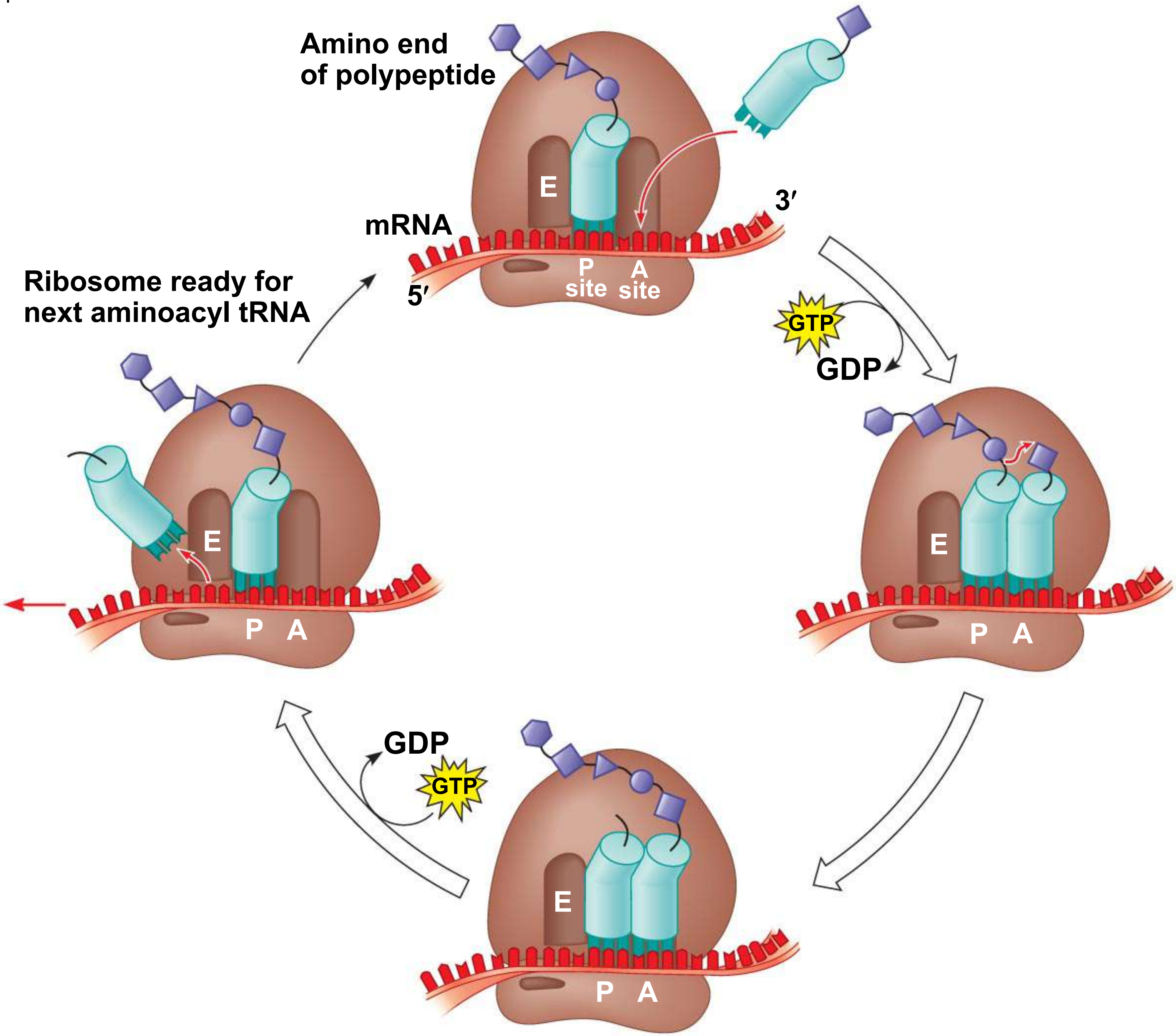

Amino end of polypeptide
E
mRNA
3′
5′
P site
A site
GTP
GDP
E
P
A
E
P
A

Fig. 17-18-4


Amino end
of polypeptide
E
mRNA
3′
5′
P
site
A
site
Ribosome ready for
next aminoacyl tRNA
GTP
GDP
E
P
A
E
P
A
GDP
GTP
E
P
A

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

PLAY **Animation: Translation**

Fig. 17-19-1

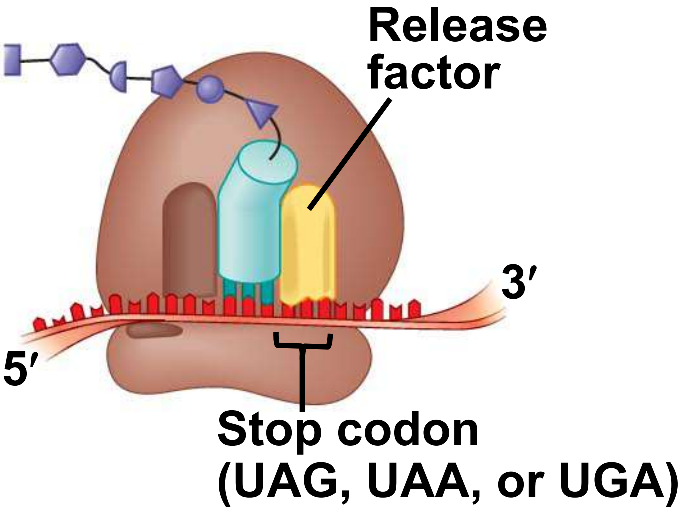


Fig. 17-19-2

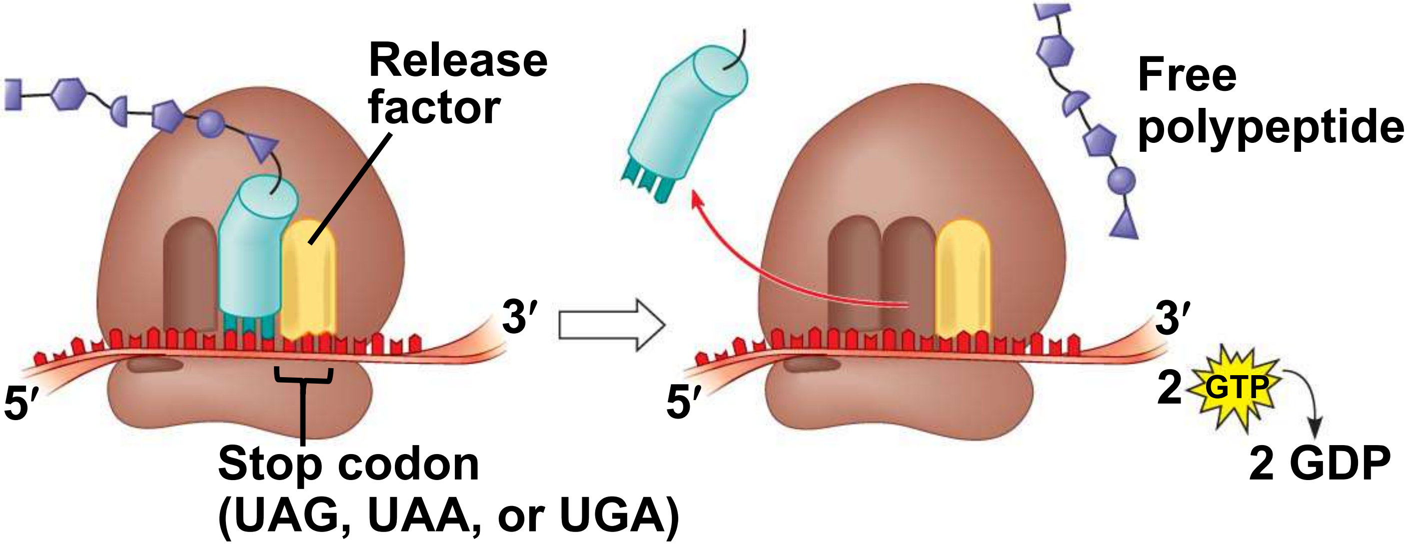
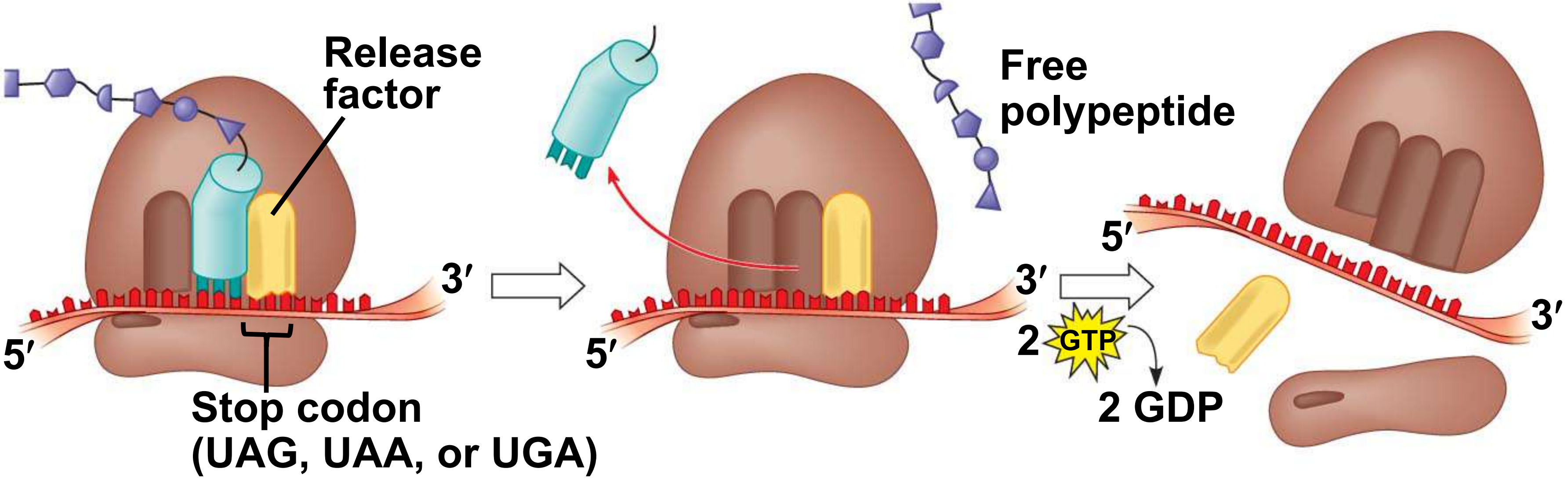

Release factor
Stop codon (UAG, UAA, or UGA)
3′
5′
Free polypeptide
3′
5′
2 GTP
2 GDP

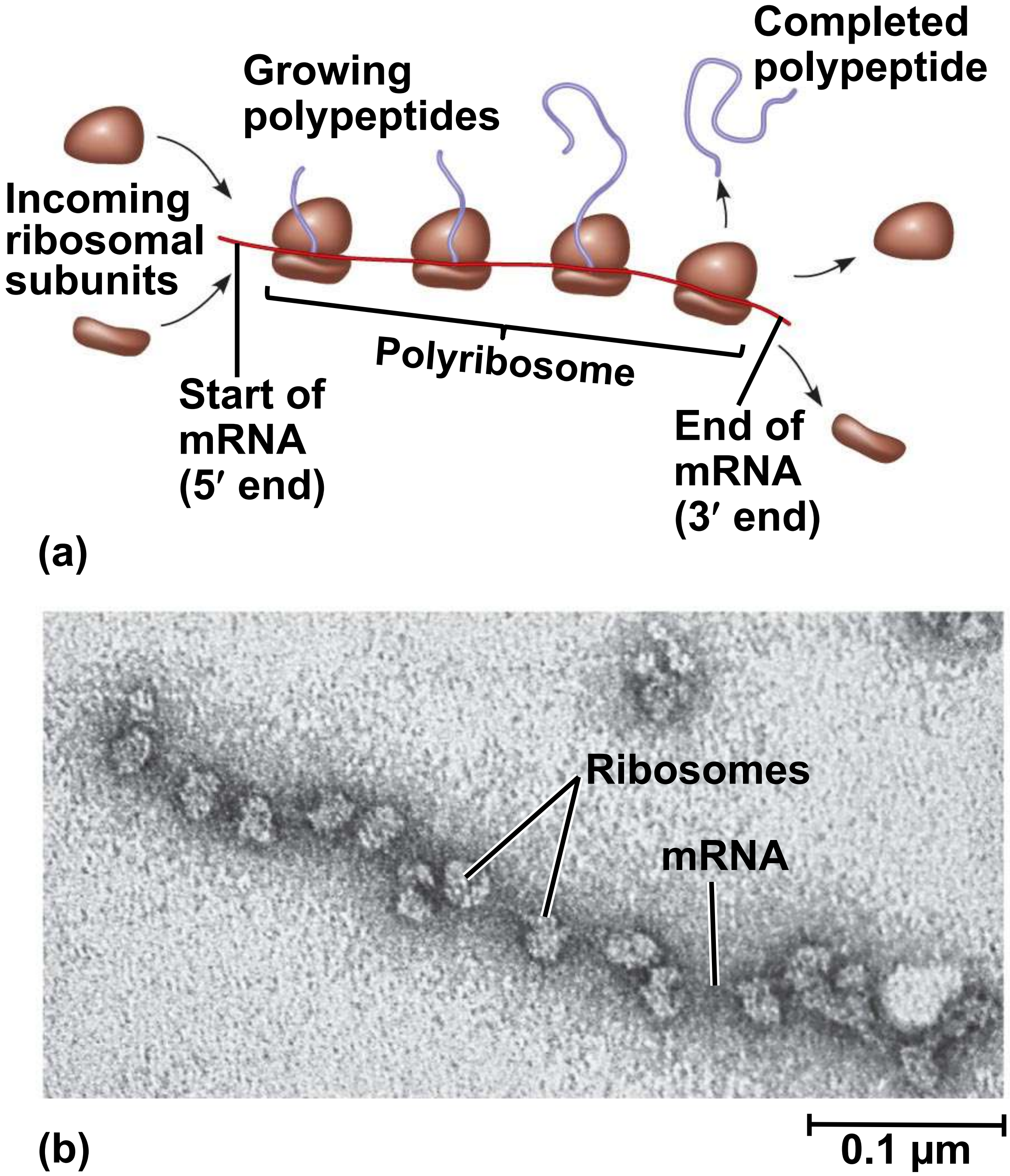
Fig. 17-19-3


Release factor
3′
5′
Stop codon (UAG, UAA, or UGA)
5′
Free polypeptide
3′
2 GTP
2 GDP
5′
3′

Polyribosomes

- A number of 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

Fig. 17-20


Completed polypeptide
Growing polypeptides
Incoming ribosomal subunits
Polyribosome
Start of mRNA (5′ end)
End of mRNA (3′ end)
(a)
Ribosomes
mRNA
(b)
0.1 µm

Completing and Targeting the Functional Protein

- Often translation is not sufficient to make a functional protein
- Polypeptide chains are modified after translation
- Completed proteins are targeted to specific sites in the cell

Protein Folding and Post-Translational Modifications

- During and after synthesis, a polypeptide chain spontaneously coils and folds into its three-dimensional shape
- Proteins may also require post-translational modifications before doing their job
- Some polypeptides are activated by enzymes that cleave them
- Other polypeptides come together to form the subunits of a protein

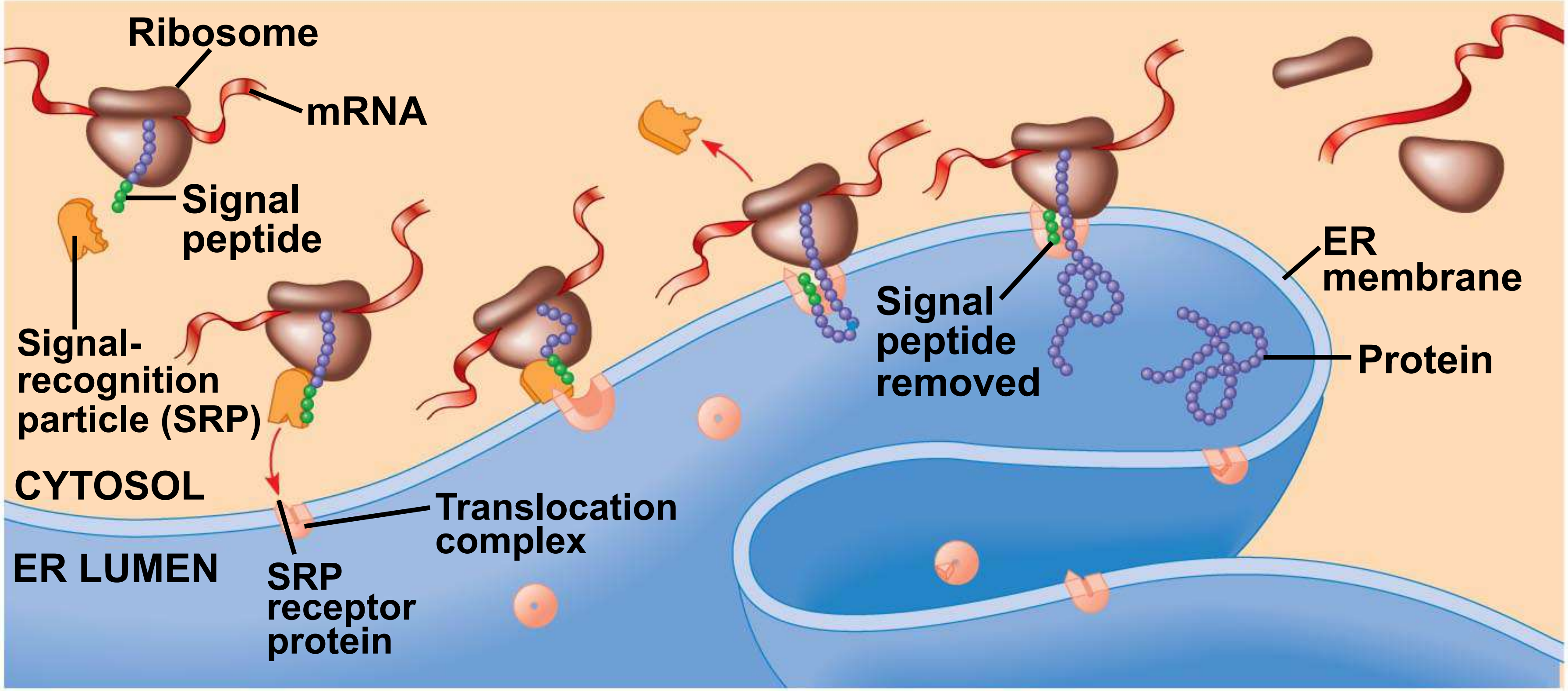
Targeting Polypeptides to Specific Locations

- Two populations of ribosomes are evident in cells: free ribsomes (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 brings the signal peptide and its ribosome to the ER

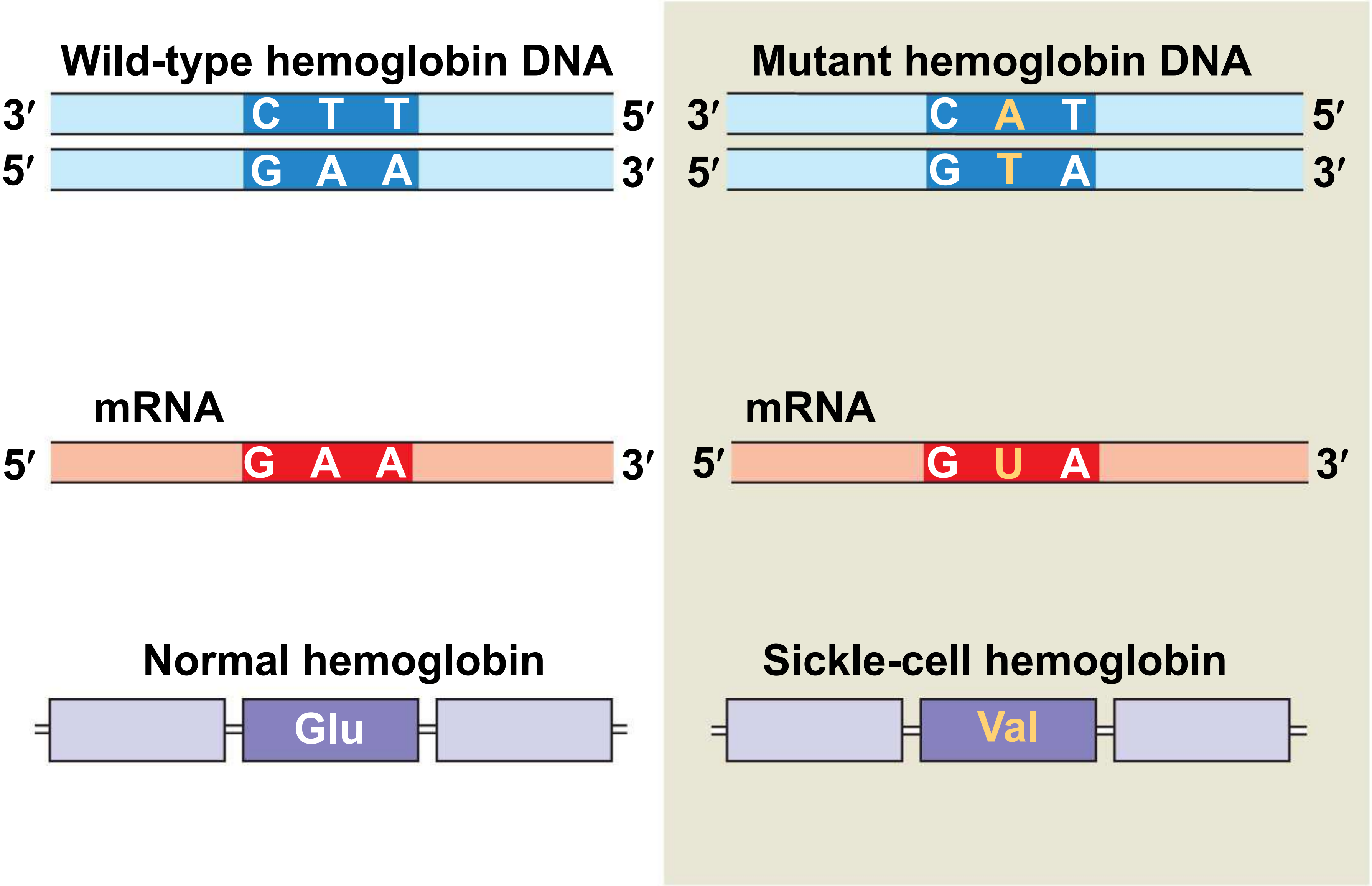
Fig. 17-21


Ribosome
mRNA
Signal peptide
Signal-recognition particle (SRP)
CYTOSOL
ER LUMEN
SRP receptor protein
Translocation complex
Signal peptide removed
ER membrane
Protein

Concept 17.5: Point mutations 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 base pair of a gene
- The change of a single nucleotide in a DNA template strand can lead to the production of an abnormal protein

Fig. 17-22


Wild-type hemoglobin DNA
3′ C T T 5′
5′ G A A 3′
mRNA
5′ G A A 3′
Normal hemoglobin
Glu
Mutant hemoglobin DNA
3′ C A T 5′
5′ G T A 3′
mRNA
5′ G U A 3′
Sickle-cell hemoglobin
Val

Types of Point Mutations

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

Fig. 17-23

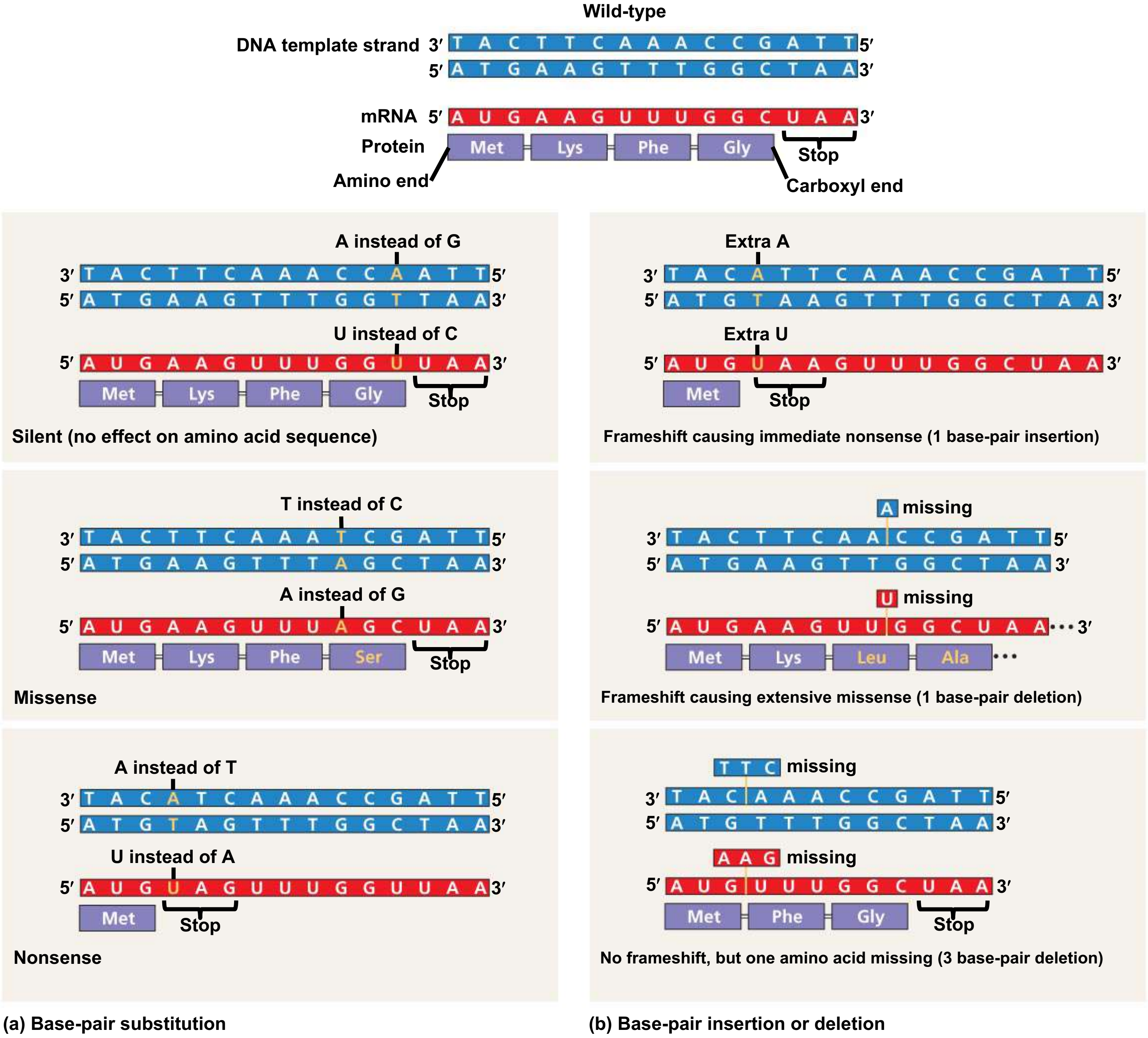

Wild-type
DNA template strand 3′ T A C T T C A A A C C G A T T 5′
5′ A T G A A G T T T G G C T A A 3′
mRNA 5′ A U G A A G U U U G G C U A A 3′
Protein
Met
Lys
Phe
Gly
Stop
Amino end
Carboxyl end
A instead of G
3′ T A C T T C A A A C C A A T T 5′
5′ A T G A A G T T T G G T T A A 3′
U instead of C
5′ A U G A A G U U U G G U U A A 3′
Met
Lys
Phe
Gly
Stop
Silent (no effect on amino acid sequence)
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
Missense
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
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
Frameshift causing immediate nonsense (1 base-pair insertion)
A missing
3′ T A C T T C A A C 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 C U A A • • • 3′
Met
Lys
Leu
Ala
• • •
Frameshift causing extensive missense (1 base-pair deletion)
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 C U A A 3′
Met
Phe
Gly
Stop
No frameshift, but one amino acid missing (3 base-pair deletion)
(a) Base-pair substitution
(b) Base-pair insertion or deletion

Fig. 17-23a

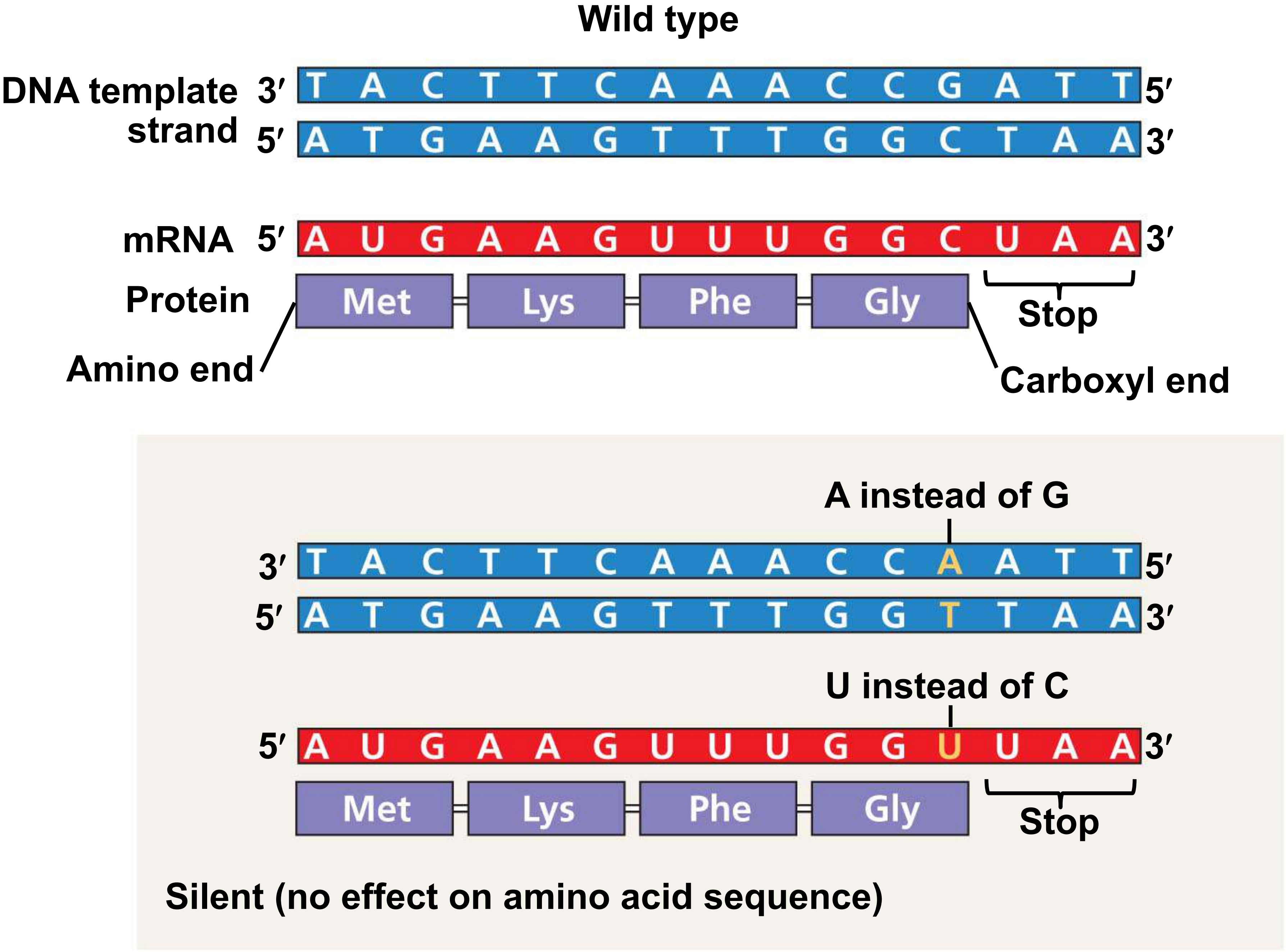
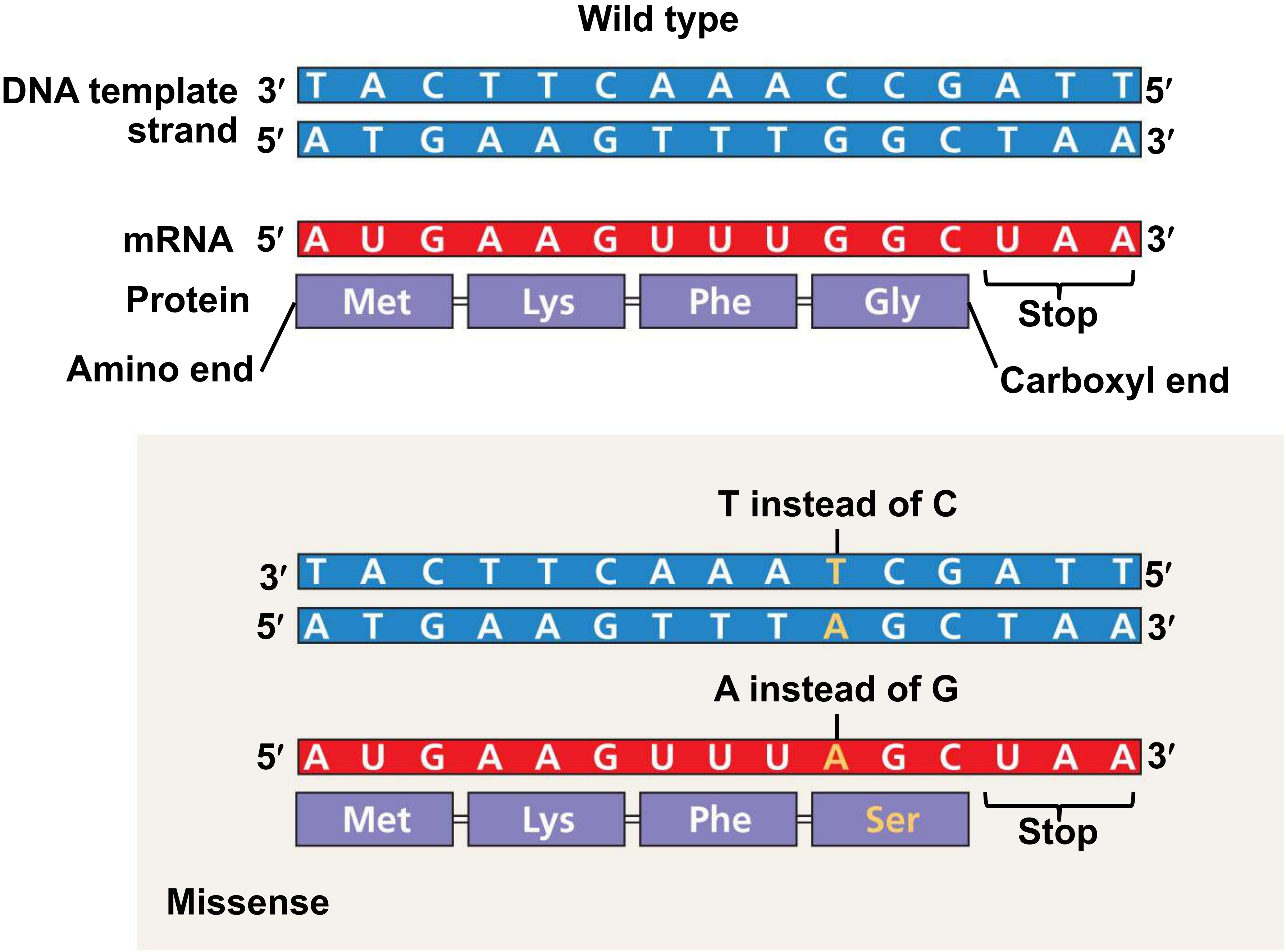

Wild type
DNA template strand
3′ T A C T T C A A A C C G A T T 5′
5′ A T G A A G T T T G G C T A A 3′
mRNA 5′ A U G A A G U U U G G C U A A 3′
Protein
Met Lys Phe Gly
Stop
Amino end
Carboxyl end
A instead of G
3′ T A C T T C A A A C C A A T T 5′
5′ A T G A A G T T T G G T T A A 3′
U instead of C
5′ A U G A A G U U U G G U U A A 3′
Met Lys Phe Gly
Stop
Silent (no effect on amino acid sequence)

Fig. 17-23b



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

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

Missense

Fig. 17-23c

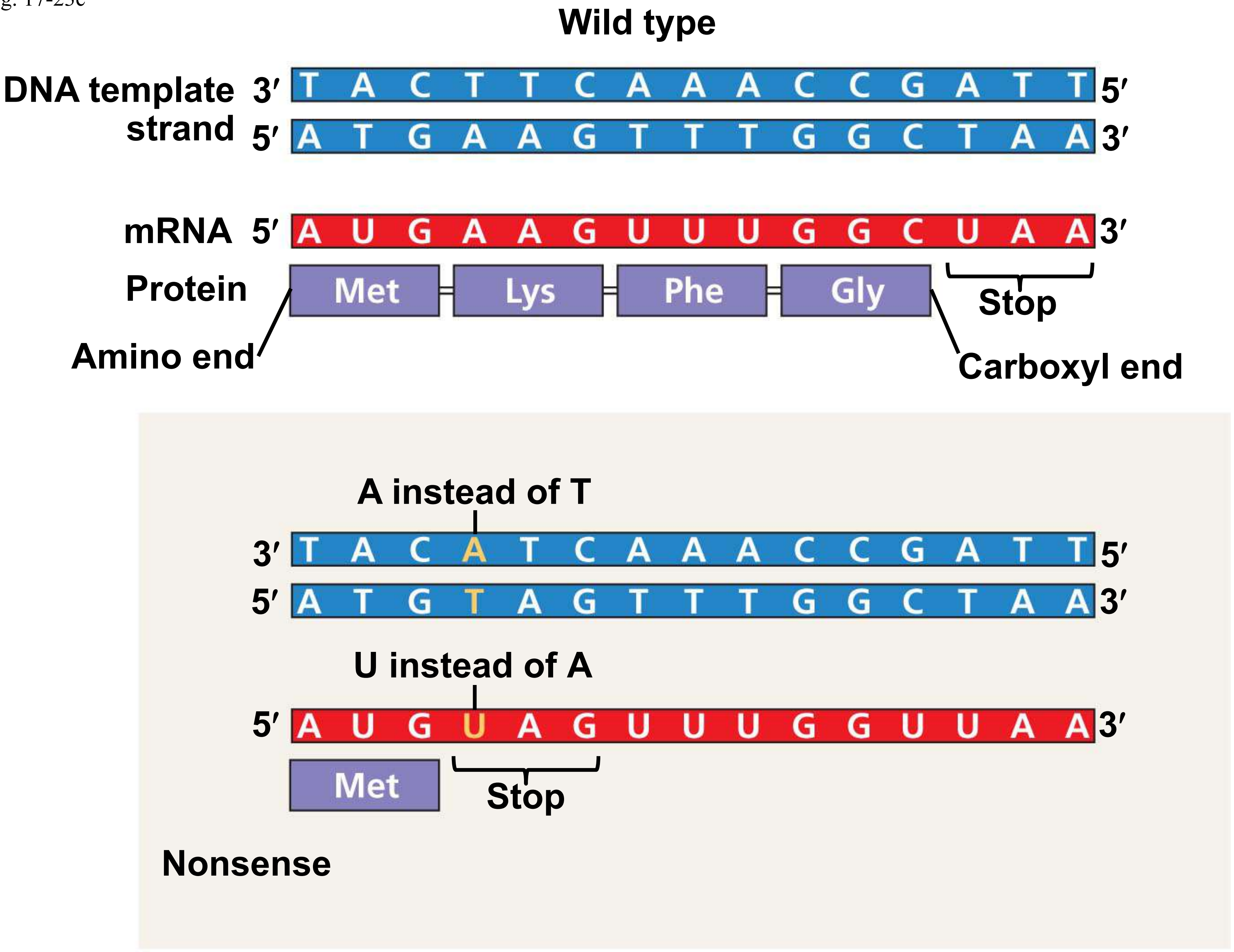
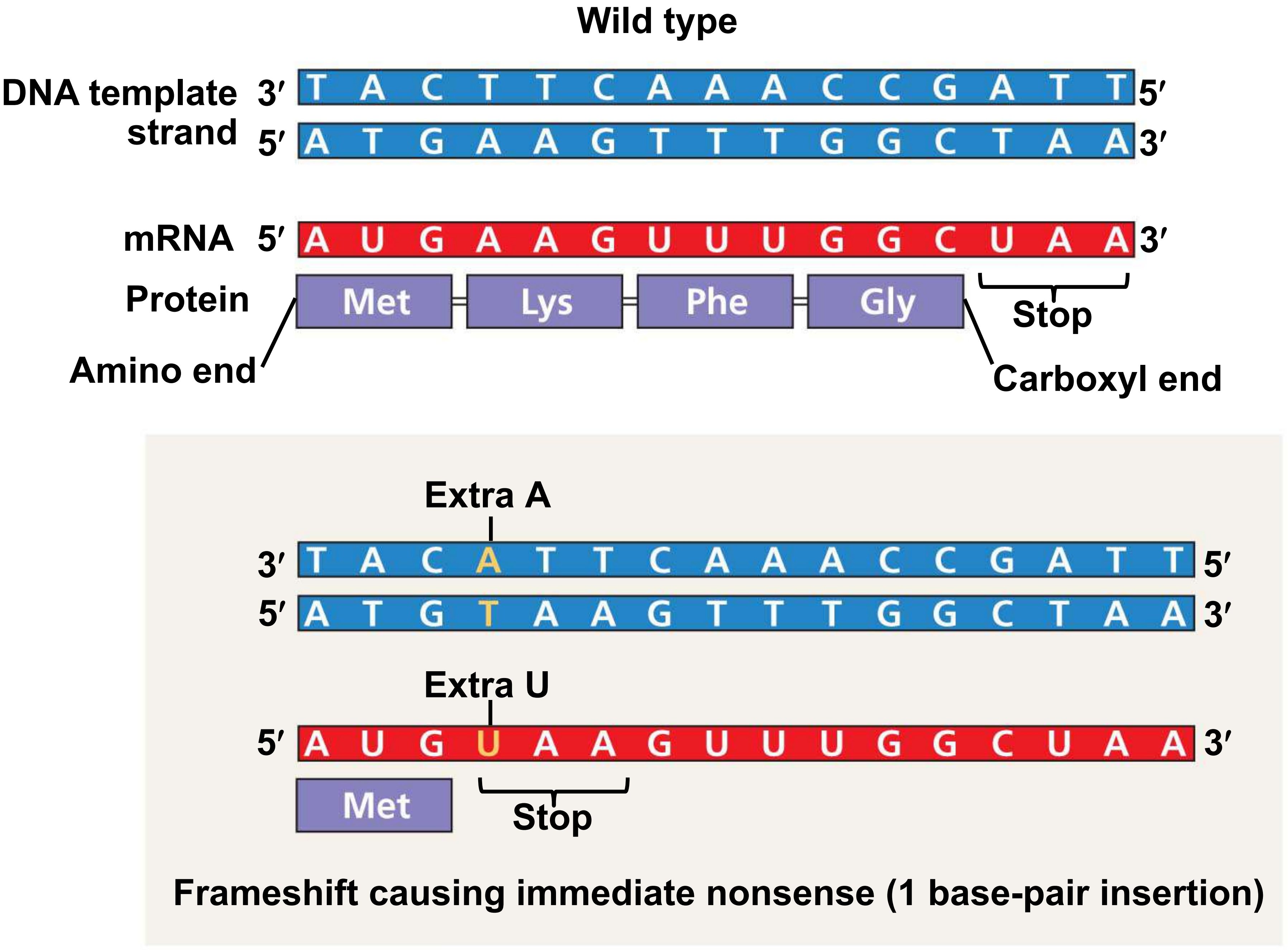

Wild type
DNA template strand
3′ T A C T T C A A A C C G A T T 5′
5′ A T G A A G T T T G G C T A A 3′
mRNA 5′ A U G A A G U U U G G C U A A 3′
Protein
Met
Lys
Phe
Gly
Stop
Amino end
Carboxyl end
A instead of T
3′ T A C A T C A A A C C G A T T 5′
5′ A T G T A G T T T G G C T A A 3′
U instead of A
5′ A U G U A G U U U G G U U A A 3′
Met
Stop
Nonsense

Fig. 17-23d



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

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

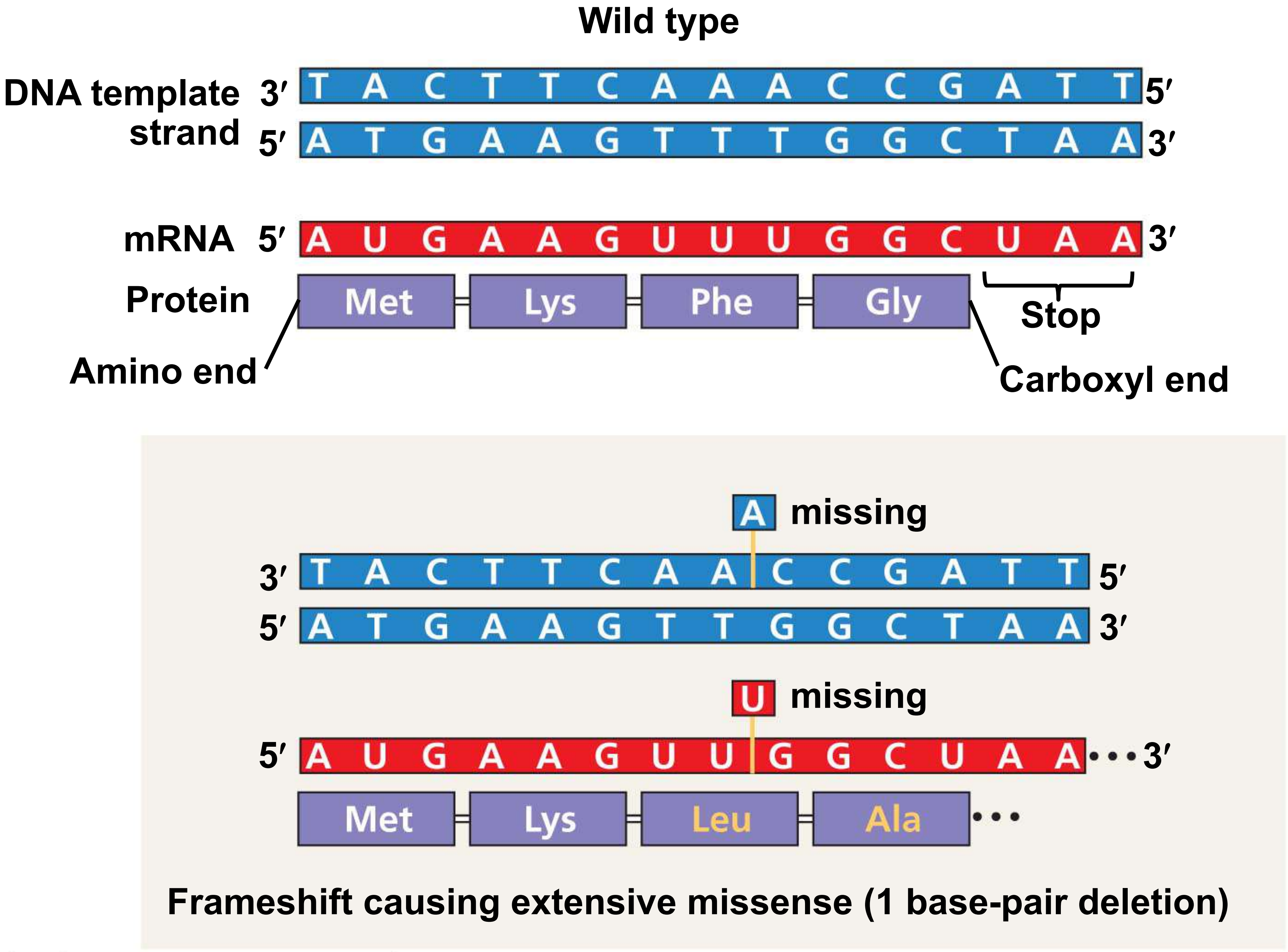
5′ A U G U A A G U U U G G C U A A 3′

Met

Stop

Frameshift causing immediate nonsense (1 base-pair insertion)

Fig. 17-23e



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

A missing

3′ T A C T T C A A C C G A T T 5′

5′ A T G A A G T T G G C T A A 3′

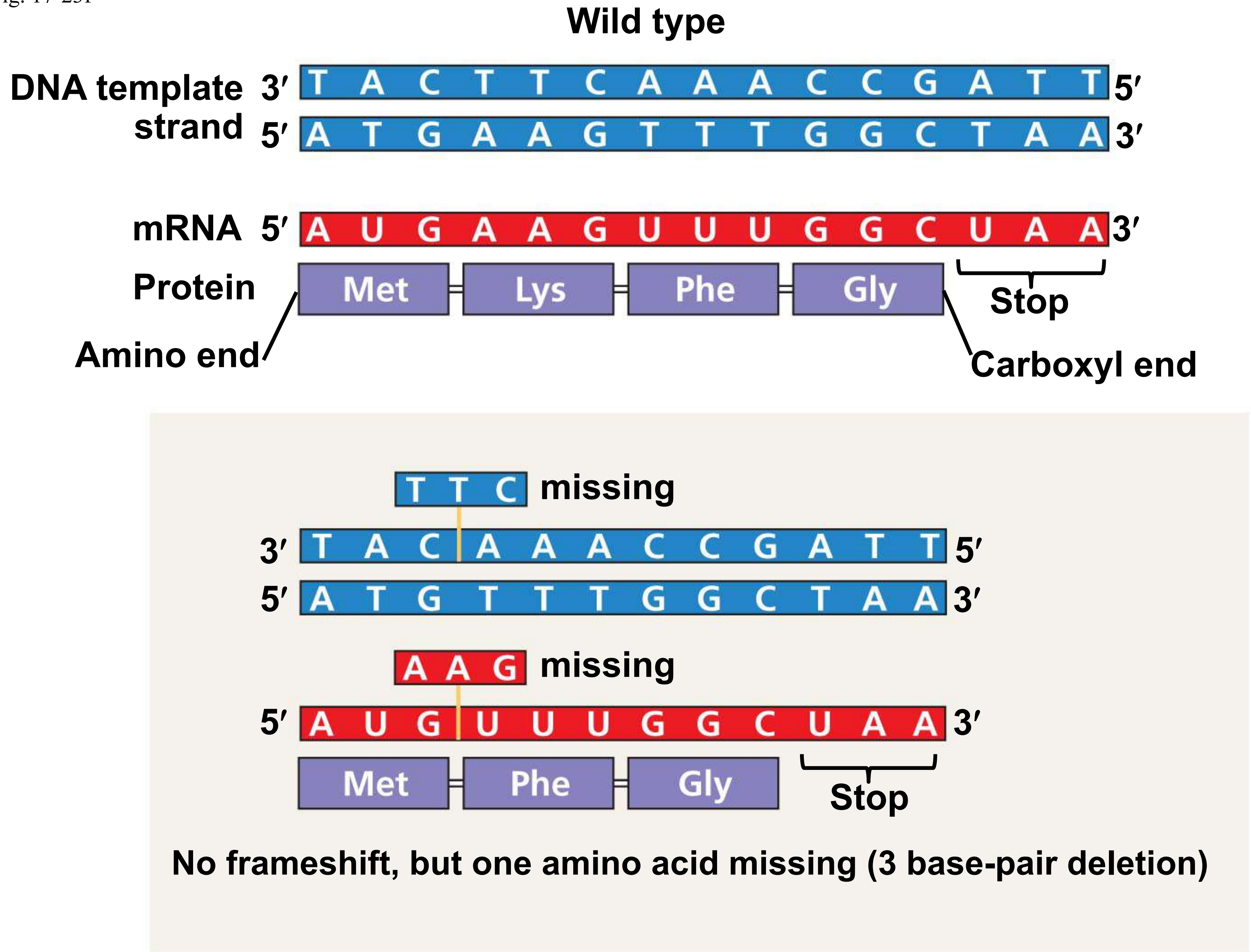
U missing

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

Met – Lys – Leu – Ala • • •

Frameshift causing extensive missense (1 base-pair deletion)

Fig. 17-23f



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

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 C U A A 3′

Met Phe Gly Stop

No frameshift, but one amino acid missing (3 base-pair deletion)

Substitutions

- A **base-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 necessarily the right amino acid
- **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, producing a **frameshift mutation**

Mutagens

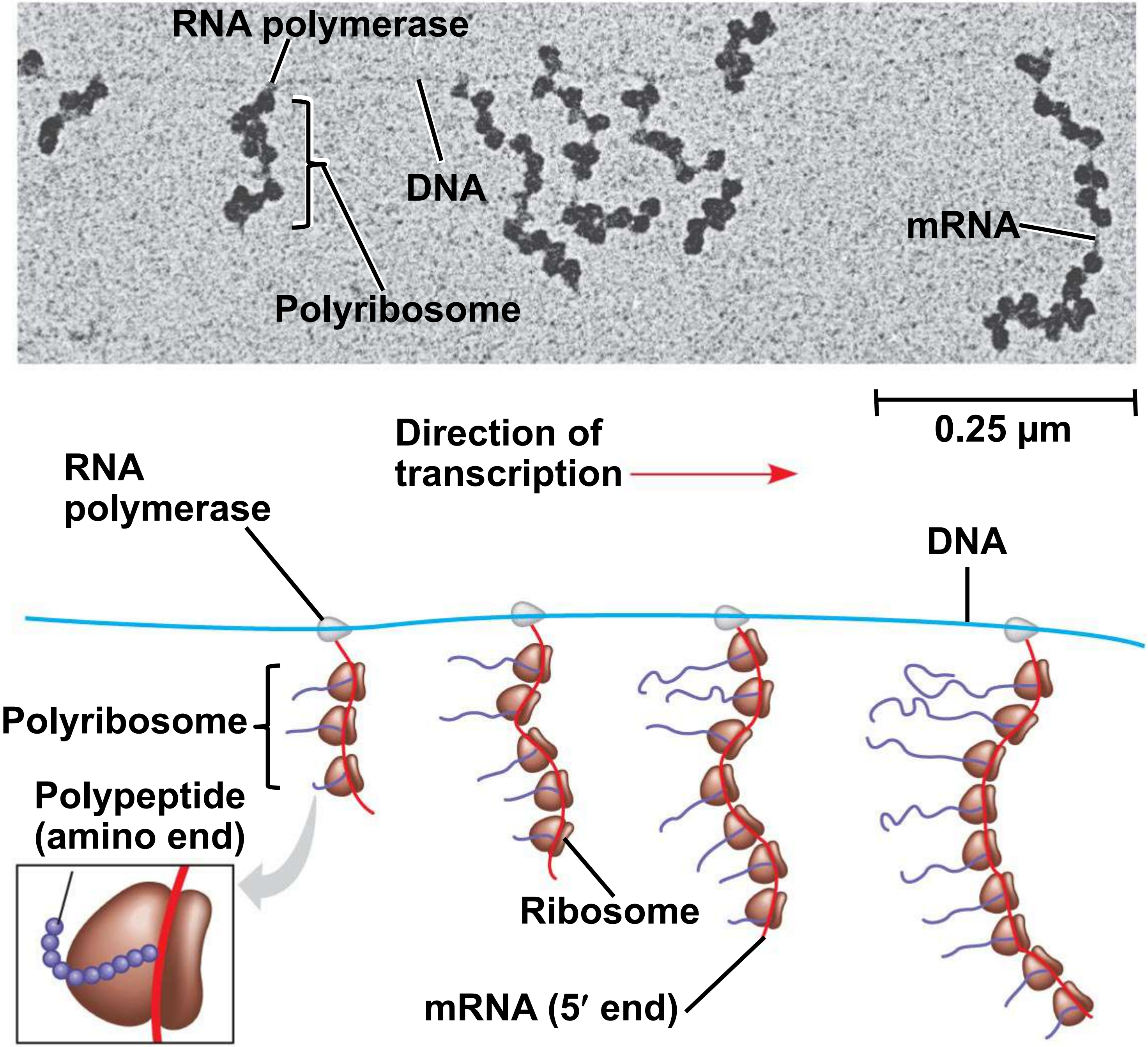
- Spontaneous mutations can occur during DNA replication, recombination, or repair
- **Mutagens** are physical or chemical agents that can cause mutations

Concept 17.6: While gene expression differs among the domains of life, the concept of a gene is universal

- Archaea are prokaryotes, but share many features of gene expression with eukaryotes

Comparing Gene Expression in Bacteria, Archaea, and Eukarya

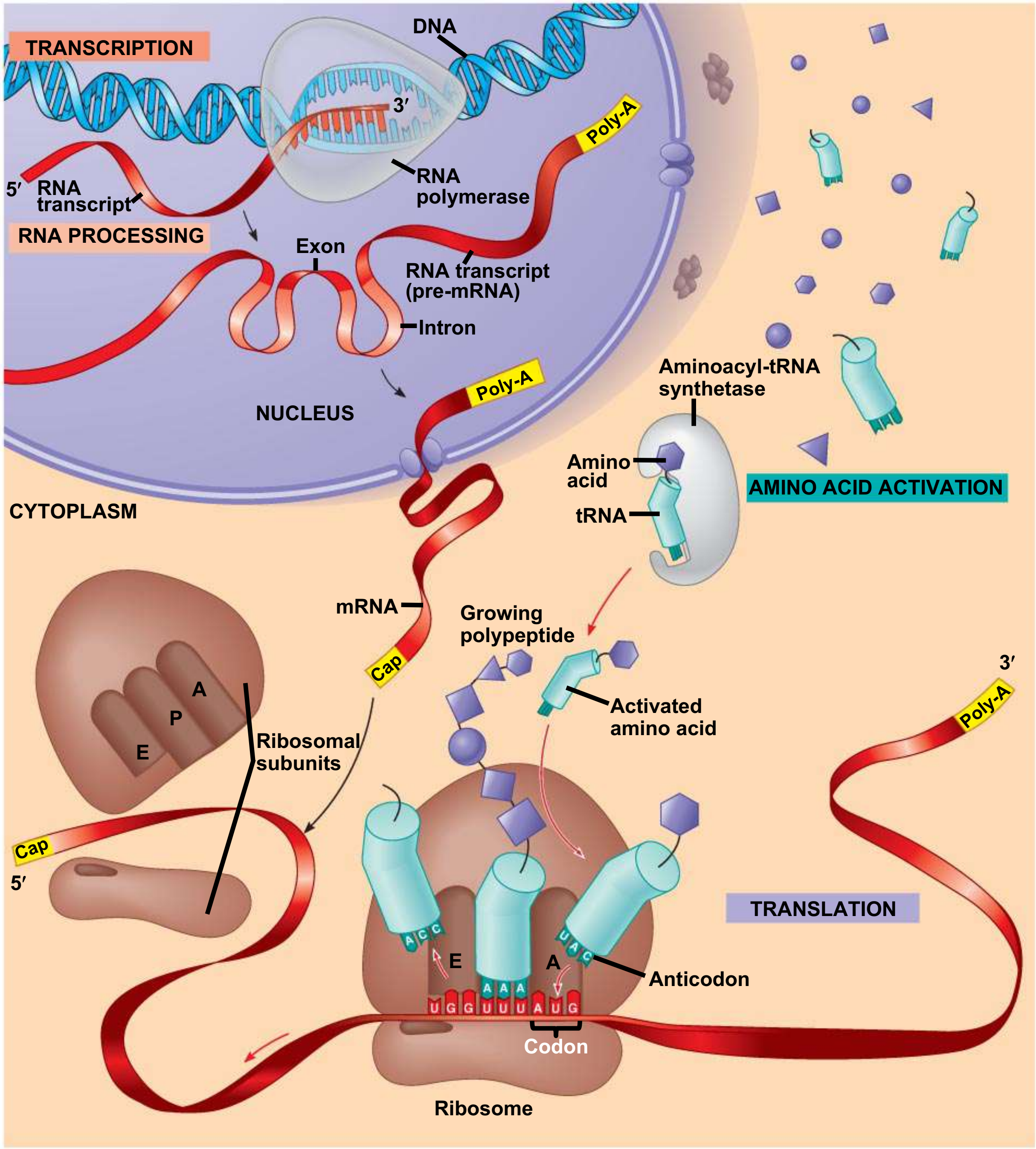
- Bacteria and eukarya differ in their RNA polymerases, termination of transcription and ribosomes; archaea tend to resemble eukarya in these respects
- Bacteria can simultaneously transcribe and translate the same gene
- In eukarya, transcription and translation are separated by the nuclear envelope
- In archaea, transcription and translation are likely coupled


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

What Is a Gene? *Revisiting the Question*

- The idea of the gene itself is a unifying concept of life
- 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

Fig. 17-25


TRANSCRIPTION
DNA
3′
5′
RNA transcript
RNA polymerase
RNA PROCESSING
Exon
RNA transcript (pre-mRNA)
Intron
Poly-A
Poly-A
NUCLEUS
CYTOPLASM
Aminoacyl-tRNA synthetase
Amino acid
tRNA
AMINO ACID ACTIVATION
mRNA
Cap
Growing polypeptide
Activated amino acid
A
P
E
Ribosomal subunits
3′
Poly-A
Cap
5′
TRANSLATION
A C C
A A A
U A C
E
A
Anticodon
U G G U U U A U G
Codon
Ribosome

- In summary, 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

Fig. 17-UN1

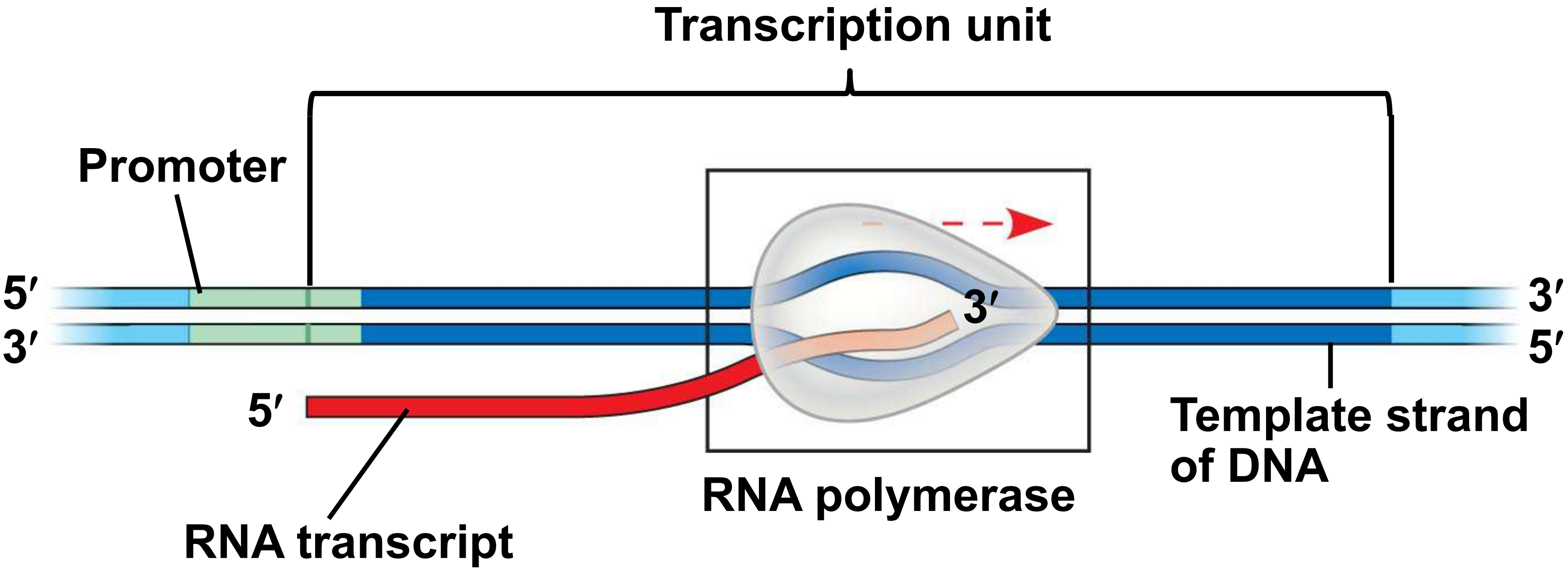

Transcription unit
Promoter
5′
3′
3′
5′
3′
5′
RNA transcript
RNA polymerase
Template strand of DNA

Fig. 17-UN2

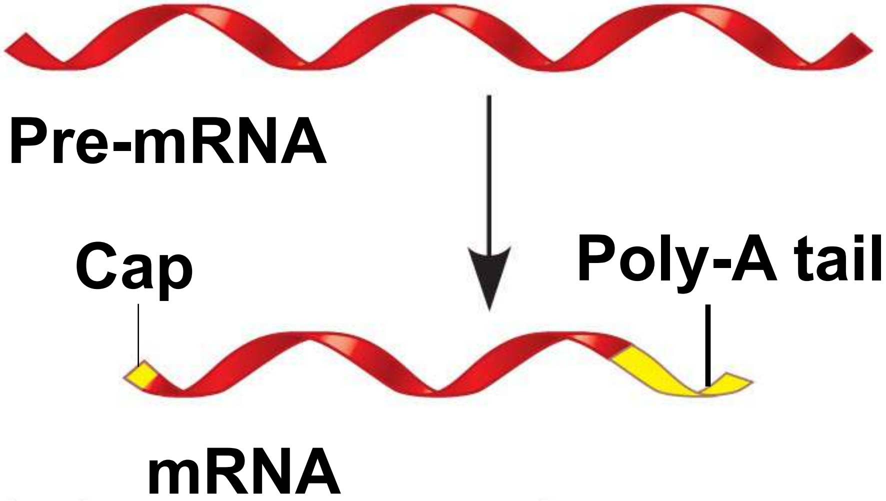


Fig. 17-UN3

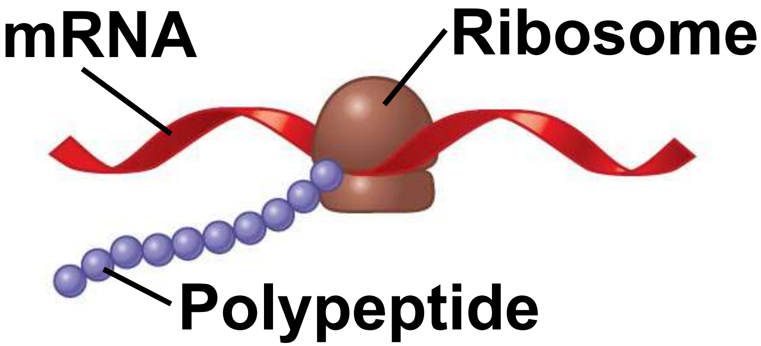


Fig. 17-UN4

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

Fig. 17-UN5

Template sequence (from problem): 3′-TTCAGTCGT-5′

Nontemplate sequence: 5′-AAGTCAGCA-3′

mRNA sequence: 5′-AAGUCAGCA-3′

Fig. 17-UN6

Template sequence (from "nontemplate" sequence in problem, written 3′ → 5′):	3′–ACGACTGAA–5′
mRNA sequence:	5′–UGCUGACAA–3′
Translated:	Cys–STOP–Gln

Fig. 17-UN7

Normal DNA sequence
(template strand is on top): 3′-TACTTGTCCGATATC-5′
5′-ATGAACAGGCTATAG-3′

mRNA sequence: 5′-AUGAACAGGCUAUAG-3′

Amino acid sequence: Met-Asn-Arg-Leu-STOP

Mutated DNA sequence
(template strand is on top): 3′-TACTTGTCCAATATC-5′
5′-ATGAACAGGTTATAG-3′

mRNA sequence: 5′-AUGAACAGGUUAUAG-3′

Amino acid sequence: Met-Asn-Arg-Leu-STOP

Fig. 17-UN8

Type of RNA	Functions
Messenger RNA (mRNA)	Carries information specifying amino acid sequences of proteins from DNA to ribosomes.
Transfer RNA (tRNA)	Serves as adapter molecule in protein synthesis; translates mRNA codons into amino acids.
Ribosomal RNA (rRNA)	Plays catalytic (ribozyme) roles and structural roles in ribosomes.
Primary transcript	Is a precursor to mRNA, rRNA, or tRNA, before being processed. Some intron RNA acts as a ribozyme, catalyzing its own splicing.
Small nuclear RNA (snRNA)	Plays structural and catalytic roles in spliceosomes, the complexes of protein and RNA that splice pre-mRNA.

You should now be able to:

- Describe the contributions made by Garrod, Beadle, and Tatum to our understanding of the relationship between genes and enzymes
- Briefly explain how information flows from gene to protein
- Compare transcription and translation in bacteria and eukaryotes
- Explain what it means to say that the genetic code is redundant and unambiguous

- Include the following terms in a description of transcription: mRNA, RNA polymerase, the promoter, the terminator, the transcription unit, initiation, elongation, termination, and introns
- Include the following terms in a description of translation: tRNA, wobble, ribosomes, initiation, elongation, and termination