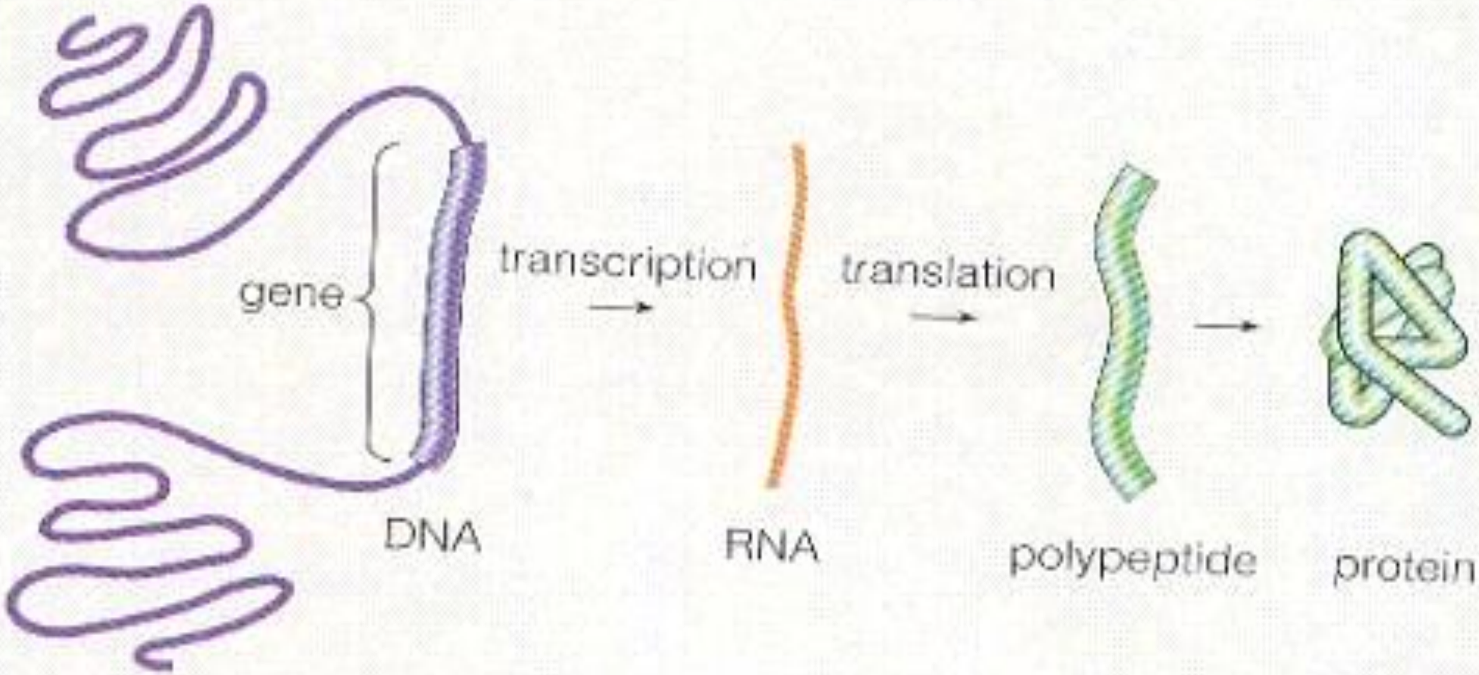
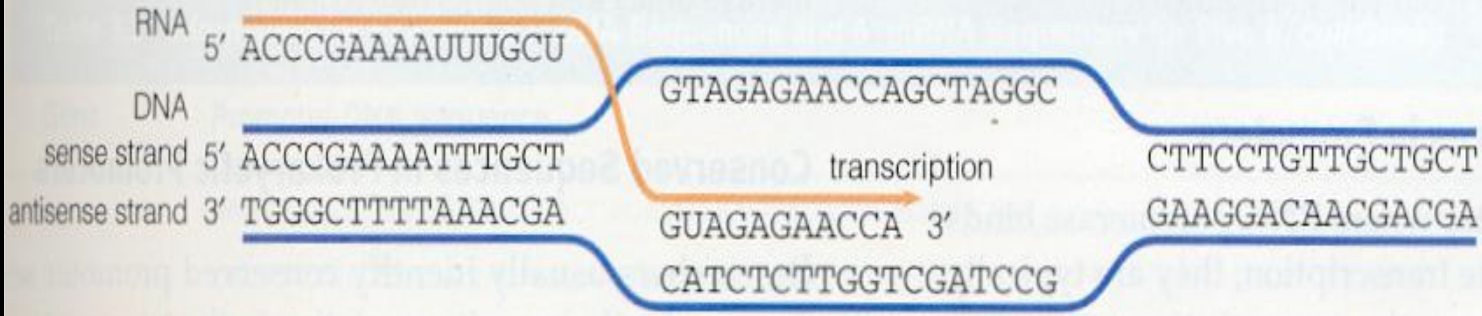


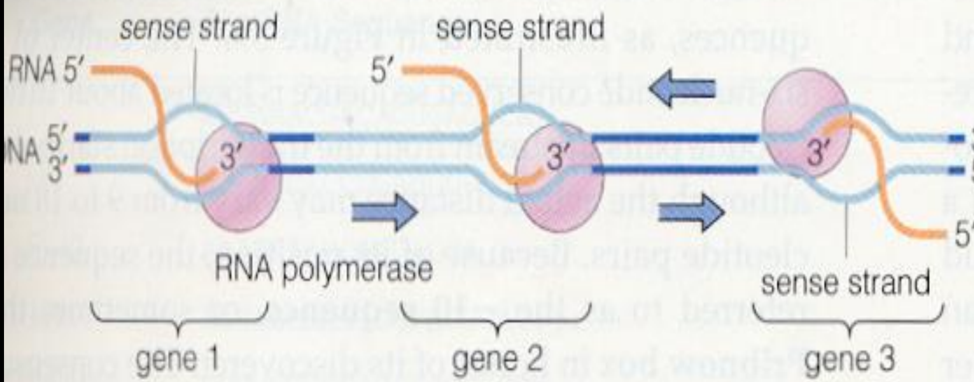
Figure 3.1 The central dogma of molecular genetics.

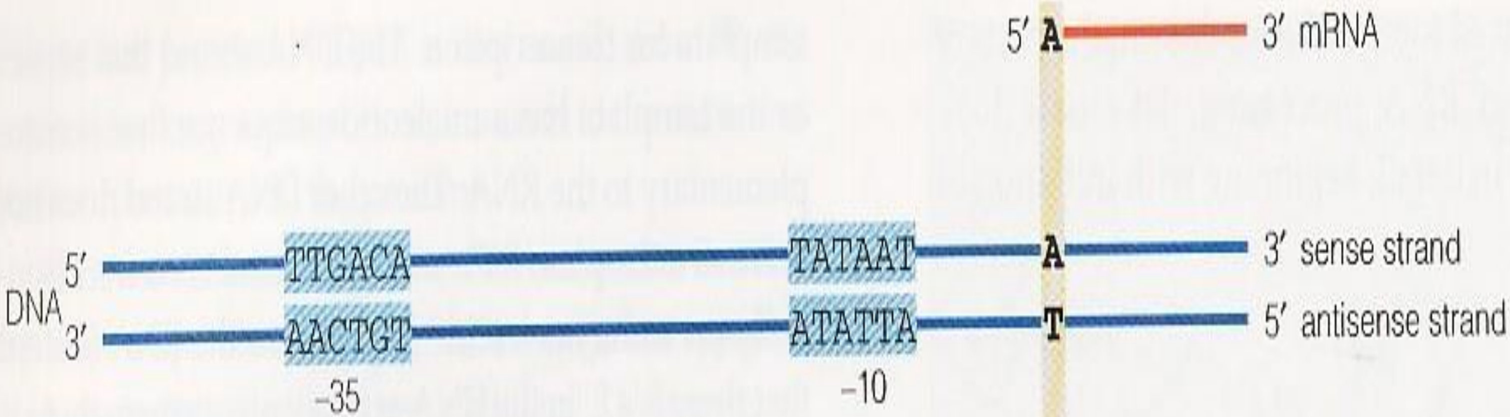
The RNA and the sense strand in the DNA have the same nucleotide sequence in the 5′ → 3′ direction (substituting U for T in the RNA).



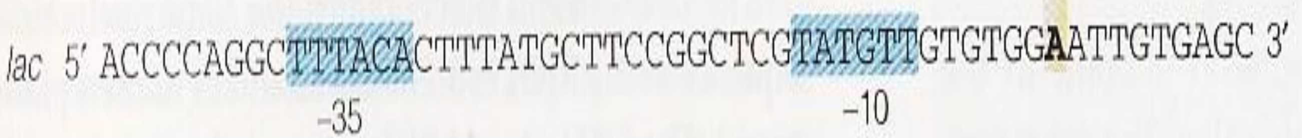
The antisense strand serves as the template for transcription.

Figure 3.4 The two strands of a gene.



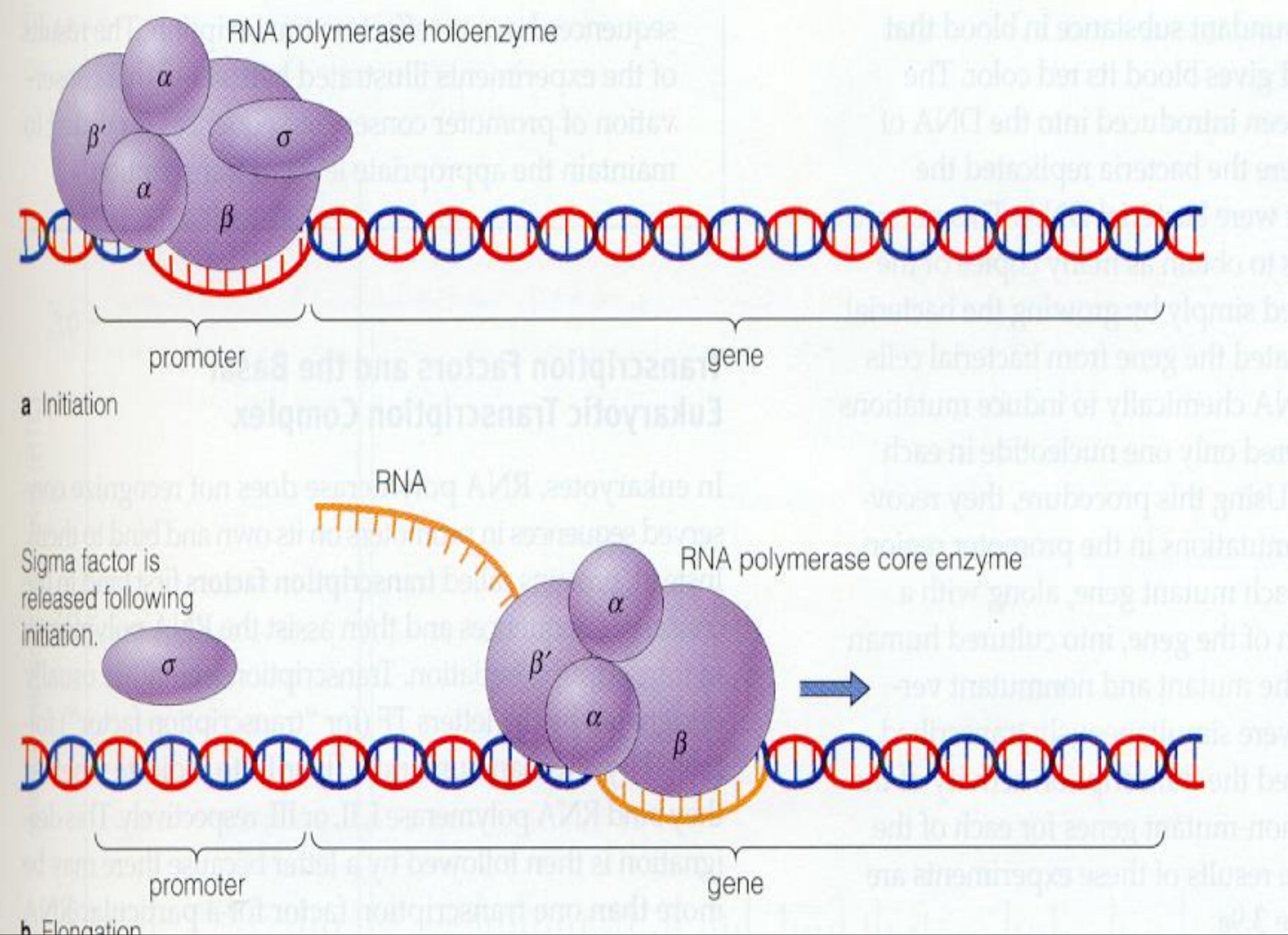


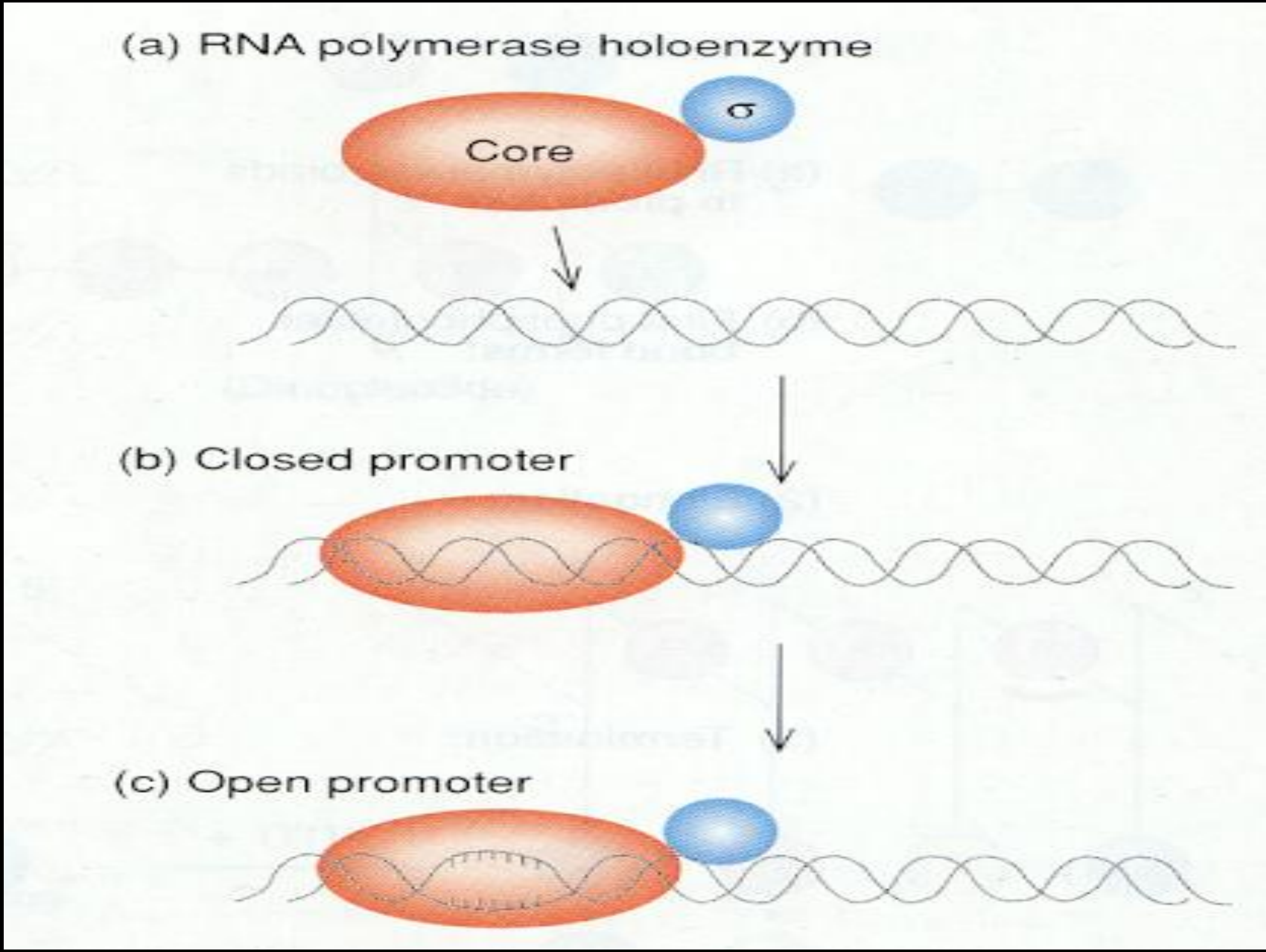
a Consensus sequences for the –35 and –10 sequences in *E. coli*.



b DNA sequence of the *lac* promoter region in *E. coli*. Conserved sequences are boxed.

Figure 3.6 Conserved sequences in prokaryotic promoters.


RNA polymerase holoenzyme
α
β′
σ
α
β
promoter
gene
a Initiation
RNA
Sigma factor is released following initiation.
σ
RNA polymerase core enzyme
α
β′
α
β
promoter
gene
b Elongation


(a) RNA polymerase holoenzyme
σ
Core
(b) Closed promoter
(c) Open promoter

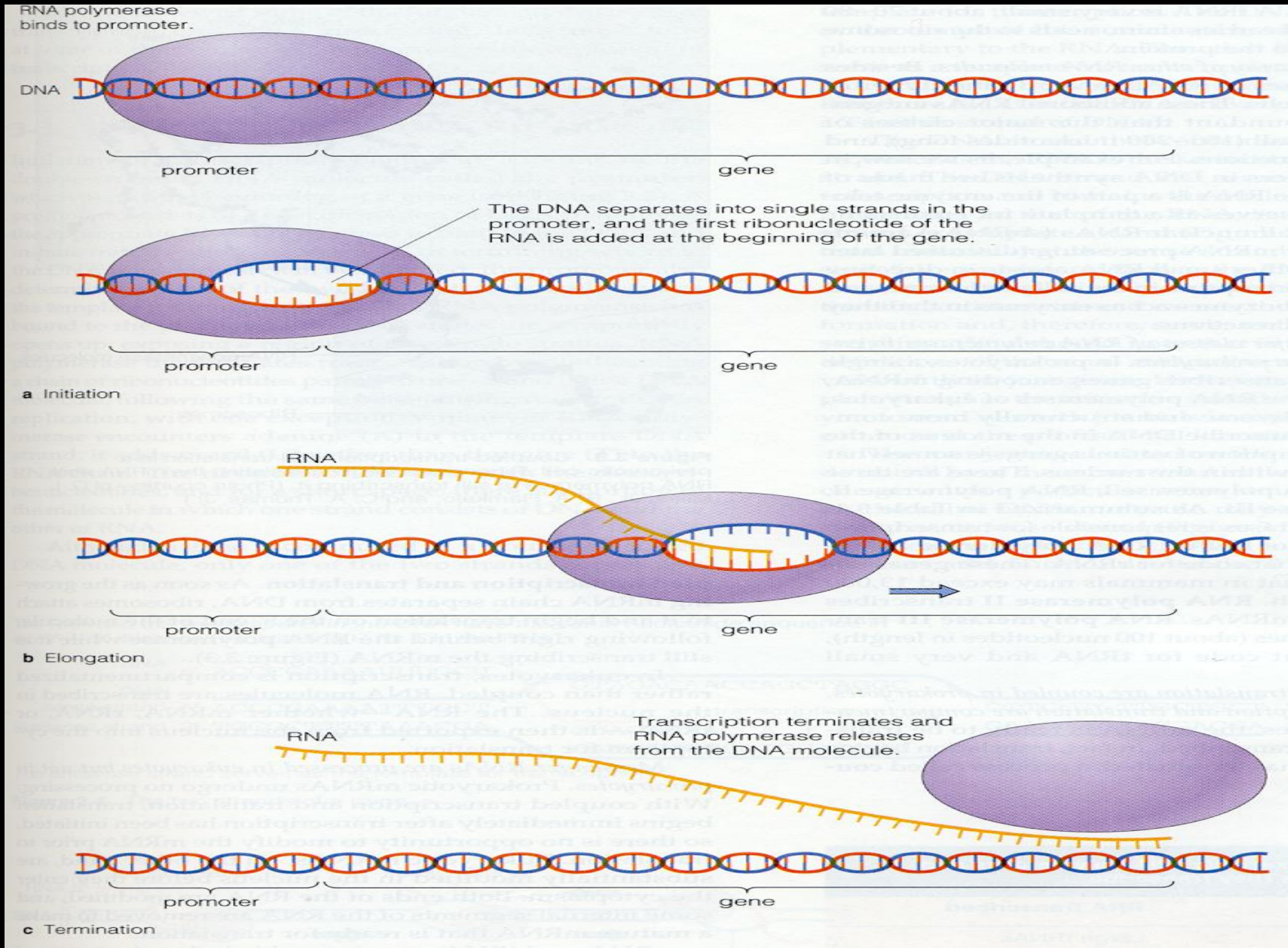
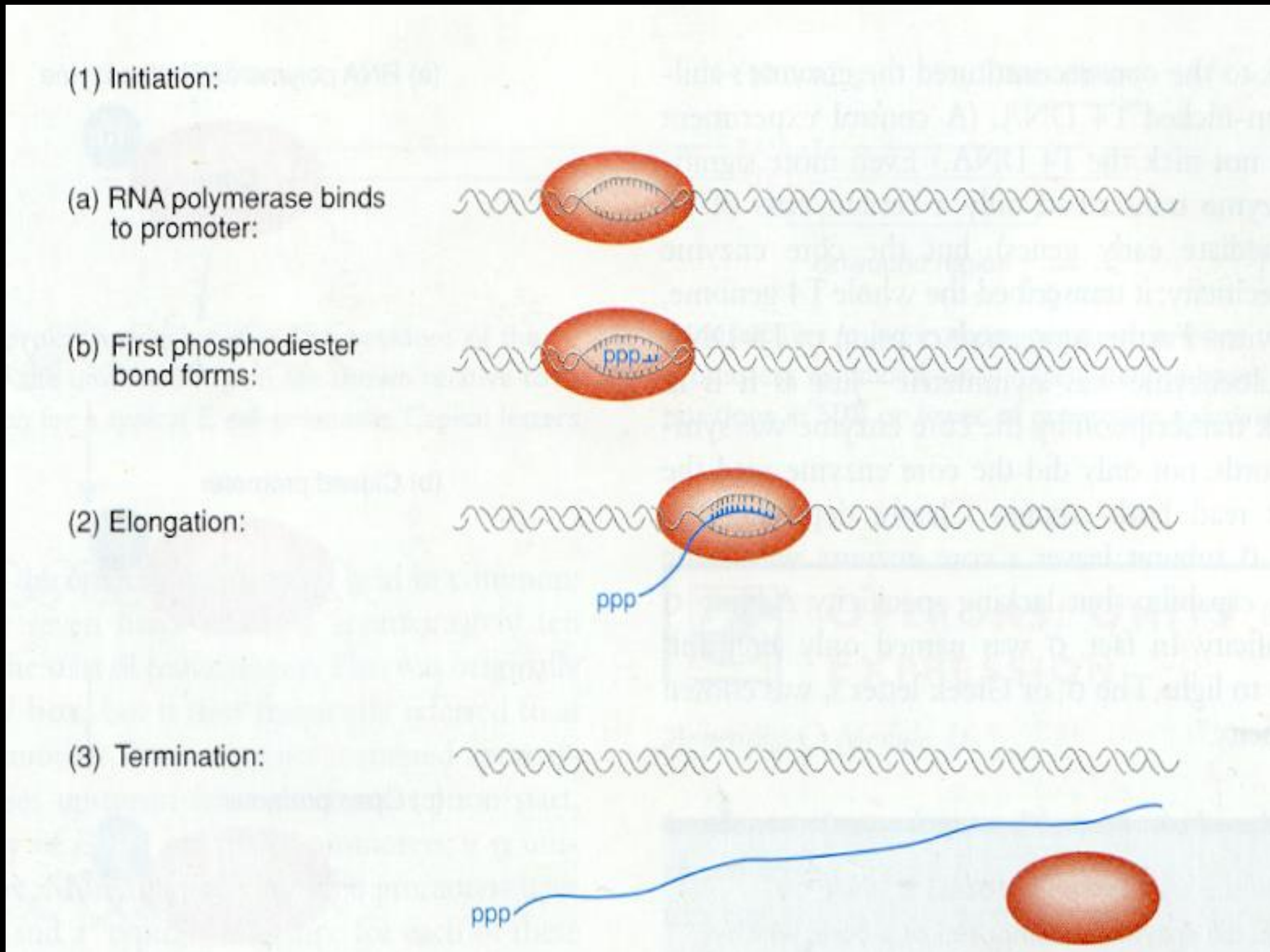
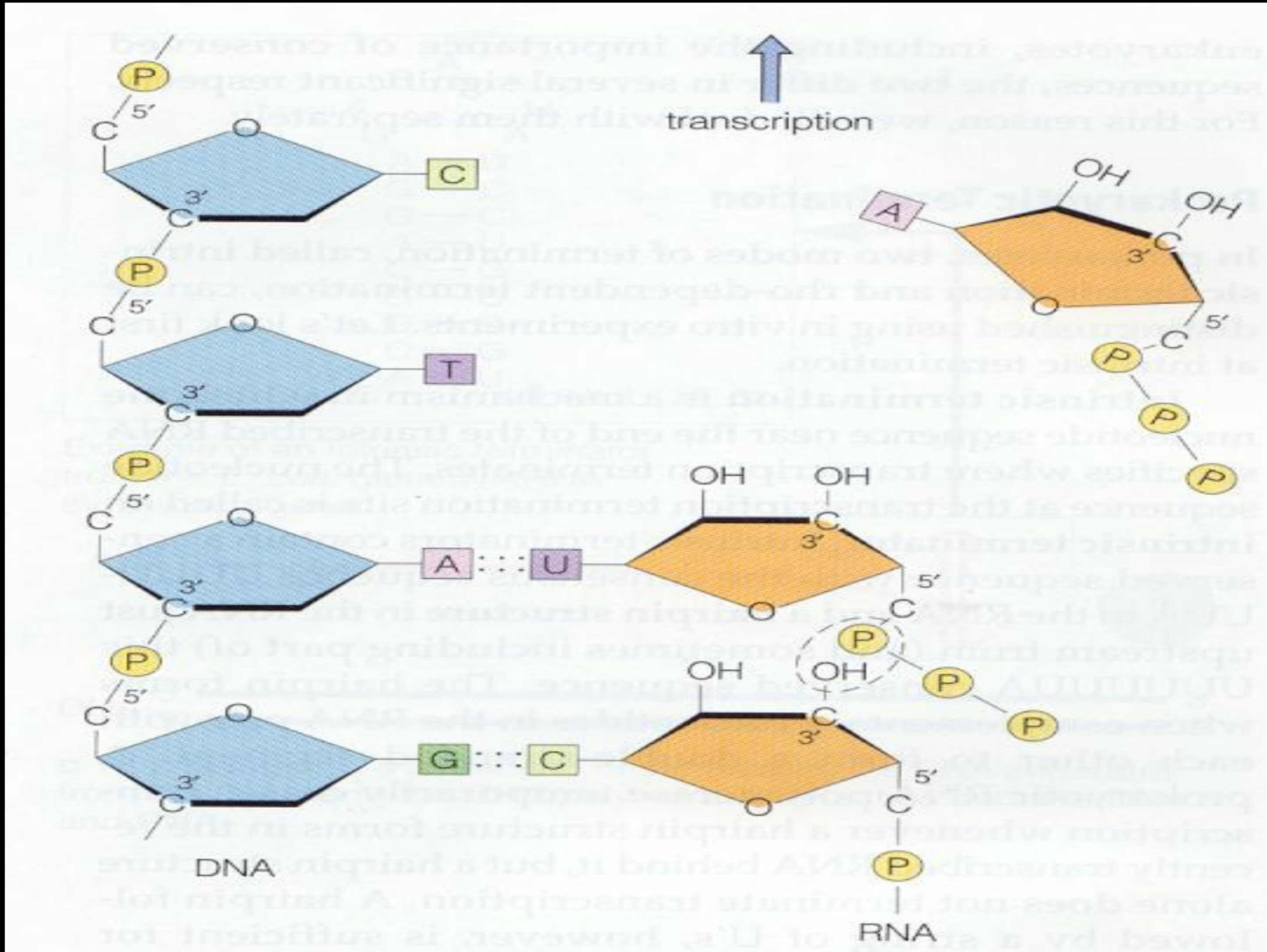


Figure 3.2 The three stages of transcription.


(1) Initiation:
(a) RNA polymerase binds to promoter:
(b) First phosphodiester bond forms:
ppp
(2) Elongation:
ppp
(3) Termination:
ppp


transcription
P
5′
C
O
3′
C
T
A
U
G
OH
DNA
RNA

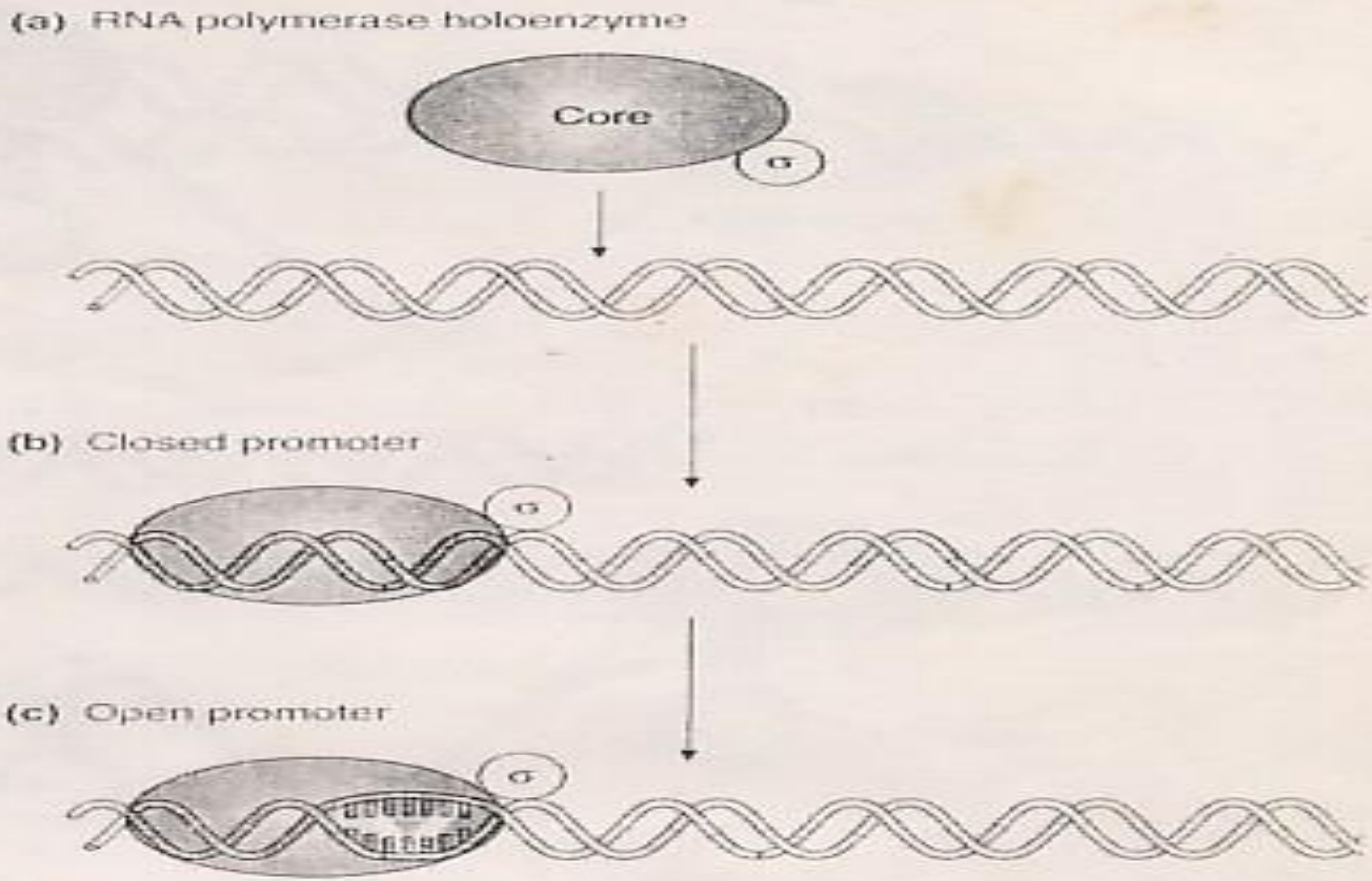


FIGURE 8.10
The binding of DNA-directed RNA polymerase plus sigma to DNA. The hydrogen bonds across the double-stranded DNA are broken and an open promoter complex is formed in preparation for mRNA synthesis (transcription).

Termination

The last stage in mRNA synthesis is chain-growth termination. Synthesis of mRNA is ended when one of two DNA sequences is reached.

The DNA sequences, often referred to as transcription terminators, are either rho-dependent or rho-independent. In either case, a so-called **stem-loop**, or hairpin structure, is formed (recall attenuation; Chapter 7). RNA synthesis terminates shortly after this structure is formed (Figure 8.11).

The stem-loop forms at the 3′ end of the mRNA, because at the 5′ end of the template DNA an unusual sequence of nucleotides occurs. This sequence is known as an inverted repeat. That is, read in a 5′ to 3′ direction, the DNA nucleotide sequences of the two strands are identical. For example:

5′ TACGAAGTTCGTA 3′
*
3′ ATGCTTCAAGCAT 5′

At the asterisk, the G-C pairing, is the point of symmetry. When mRNA is transcribed from the template strand (3′→5′), the resulting sequence is:

*
5′ UACGAAGUUCGUA 3′

The molecule is self-complementary around the point of symmetry, $\overset{*}{G}$. So a hairpin, or stem-loop, can form:

```
5′ U–A 3′
   A–U
   C–G
   G–C
   A–U
   A U
    G
    *
```

Because of the turn at the bottom, the last A-U pairing does not form, but a loop is produced.

In rho-dependent termination, the template inverted repeat of DNA is followed by a series of adenines. This series produces a run of perhaps half a dozen uracils in the mRNA.

So we have:

```
5′ U–AUUUUUU 3′
   A–U
   C–G
   G–C
   A–U
   A U
    G
```

The molecule is self-complementary around the point of symmetry, Ġ. So a hairpin, or stem-loop, can form:

```
5′ U–A 3′
   A–U
   C–G
   G–C
   A–U
   A U
    G
    *
```

Because of the turn at the bottom, the last A-U pairing does not form, but a loop is produced.

In rho-dependent termination, the template inverted repeat of DNA is followed by a series of adenines. This series produces a run of perhaps half a dozen uracils in the mRNA.

So we have:

```
5′ U–AUUUUUU 3′
   A–U
   C–G
   G–C
   A–U
   A U
    G
```

At the point where the poly-U sequence is attached to the DNA sequence, the hybrid DNA-RNA is unusually weak (A—U bonds are weak), and it requires very little energy to break the hydrogen bonds holding the two strands together. When separation occurs, mRNA synthesis, transcription, stops. This type of termination is rho-independent; no termination factor is required.

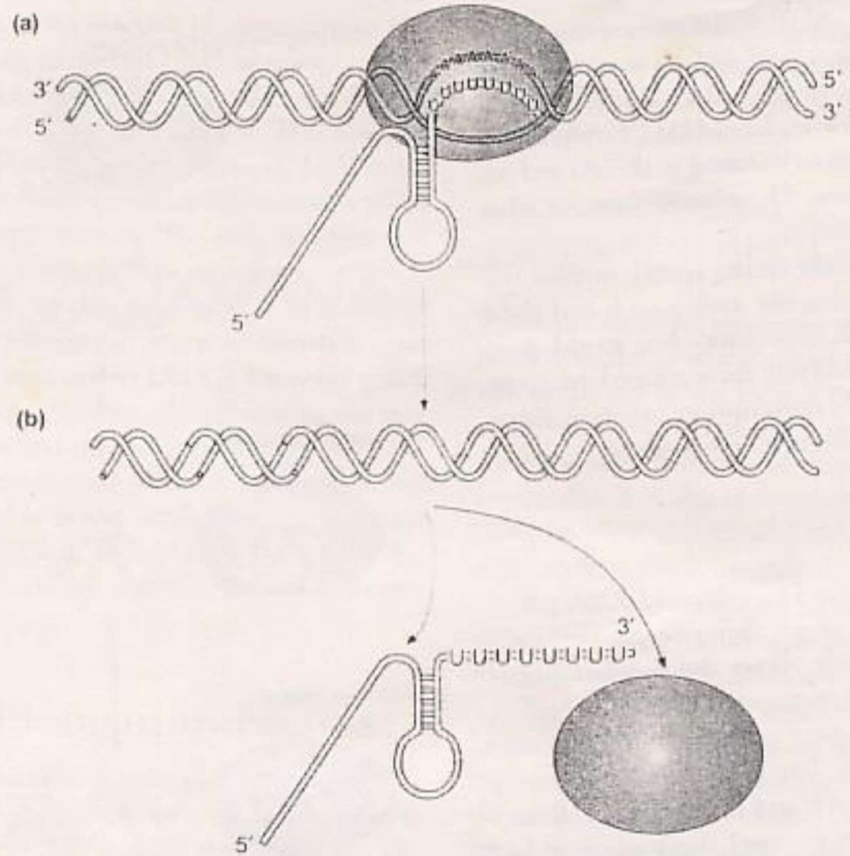


FIGURE 8.11
ρ-independent termination of mRNA synthesis/termination of transcription. (a) RNA polymerase synthesizes a poly-U 3′ end. (b) The mRNA and enzyme pull away from the DNA template.

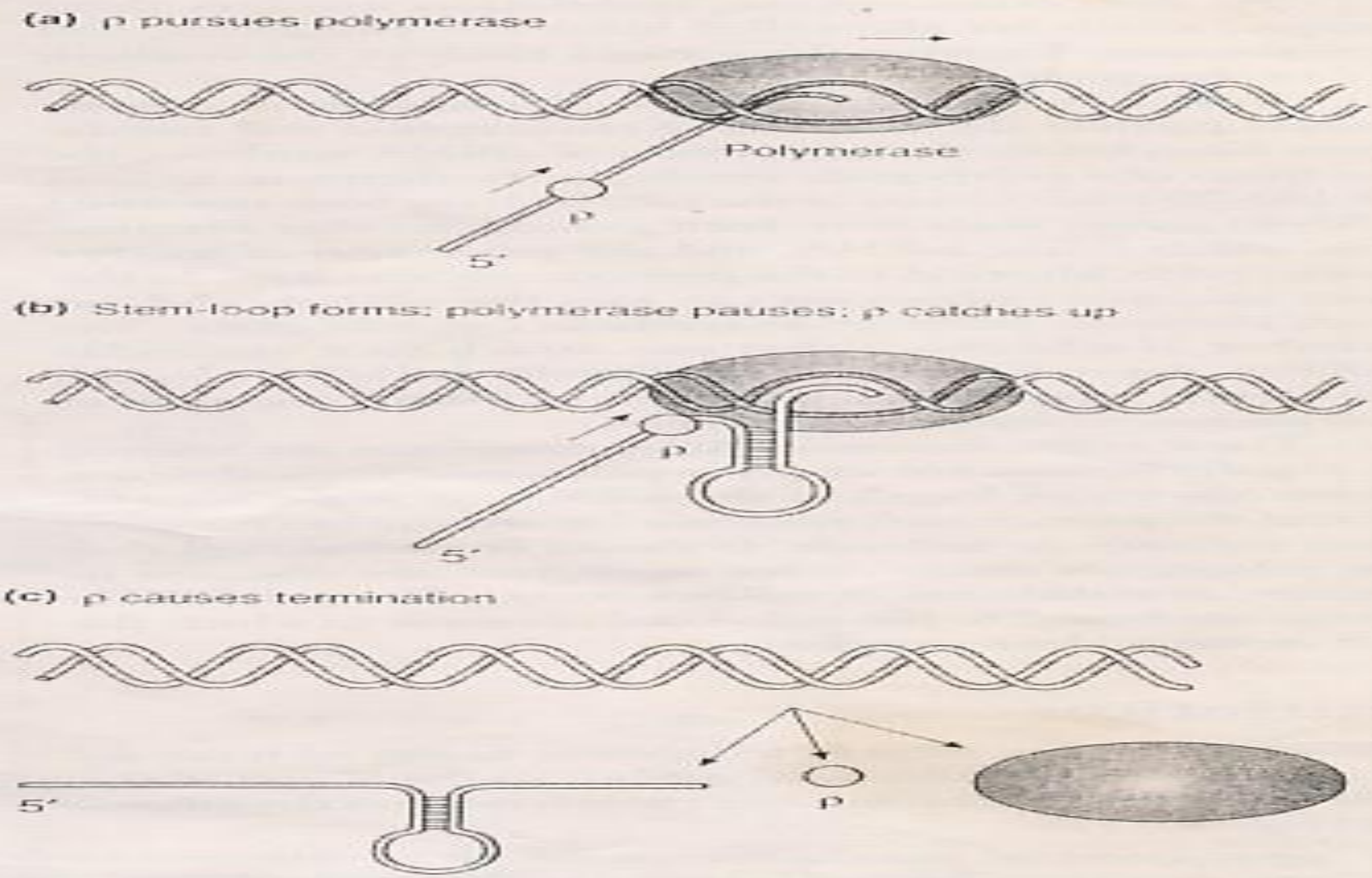


FIGURE 8.12
ρ-dependent termination of mRNA synthesis/termination of transcription. (a) Rho attaches to mRNA as it is being synthesized. (b) RNA polymerase pauses after stem-loop is synthesized, allowing ρ to catch up. (c) By some unknown mechanism, ρ causes the release of the mRNA and enzyme.

Synthesis of mRNA, then, looks like this:

Coding strand:	5′	AATGCCGTTACGCCC	3′
Template:	3′	TTACGGCAATGCGGG	5′

⟶ (reading direction)

mRNA: 5′ ppp-AAUGCCGUUACGCCC 3′

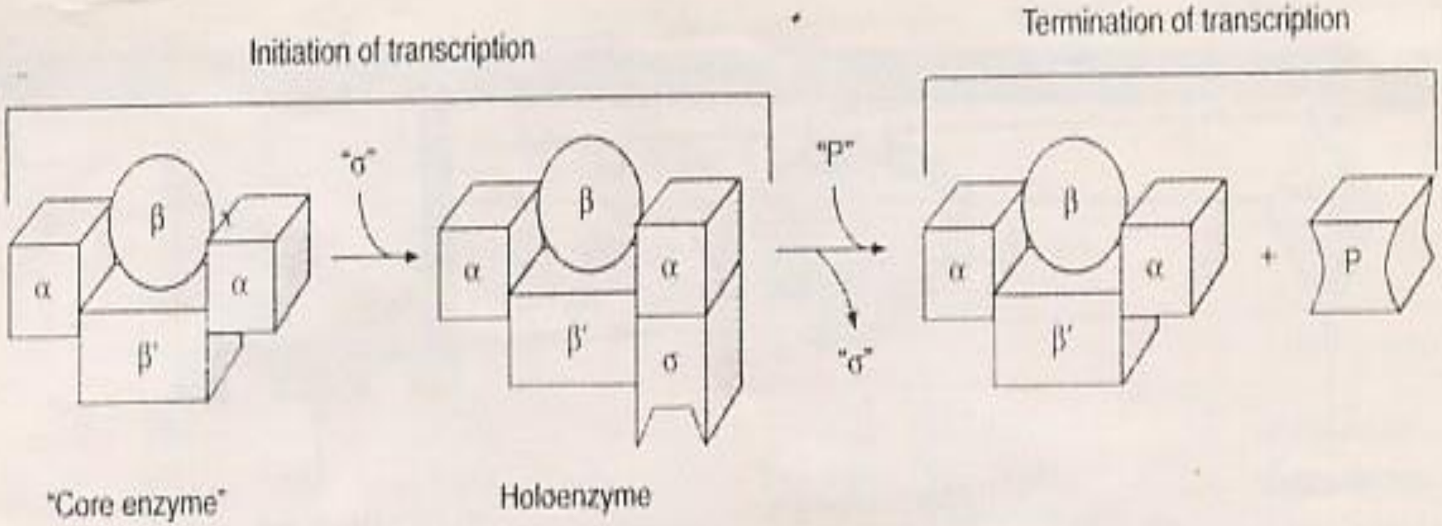
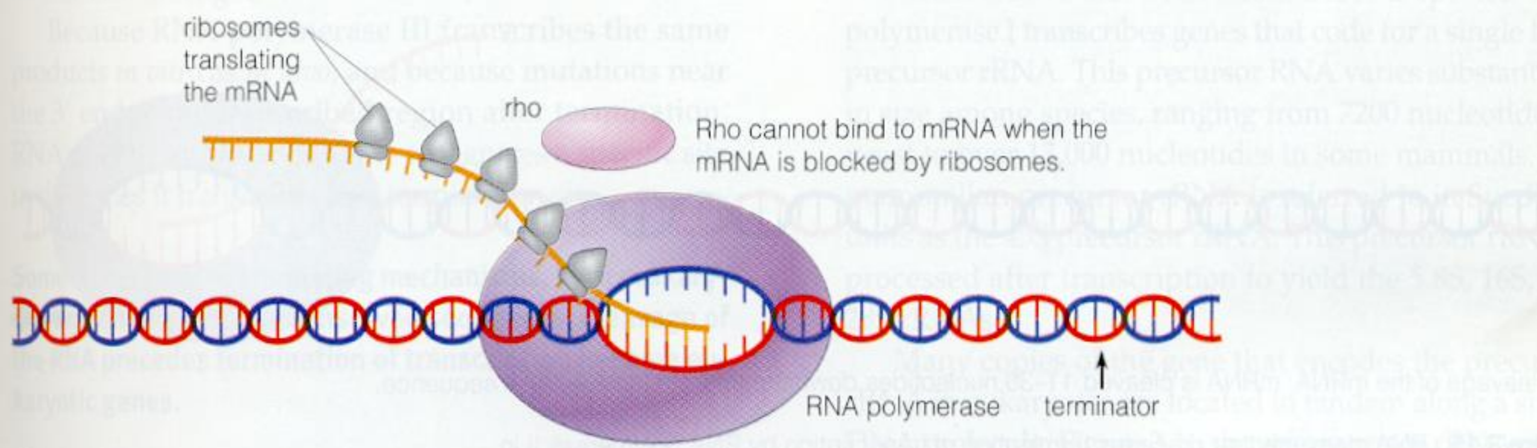
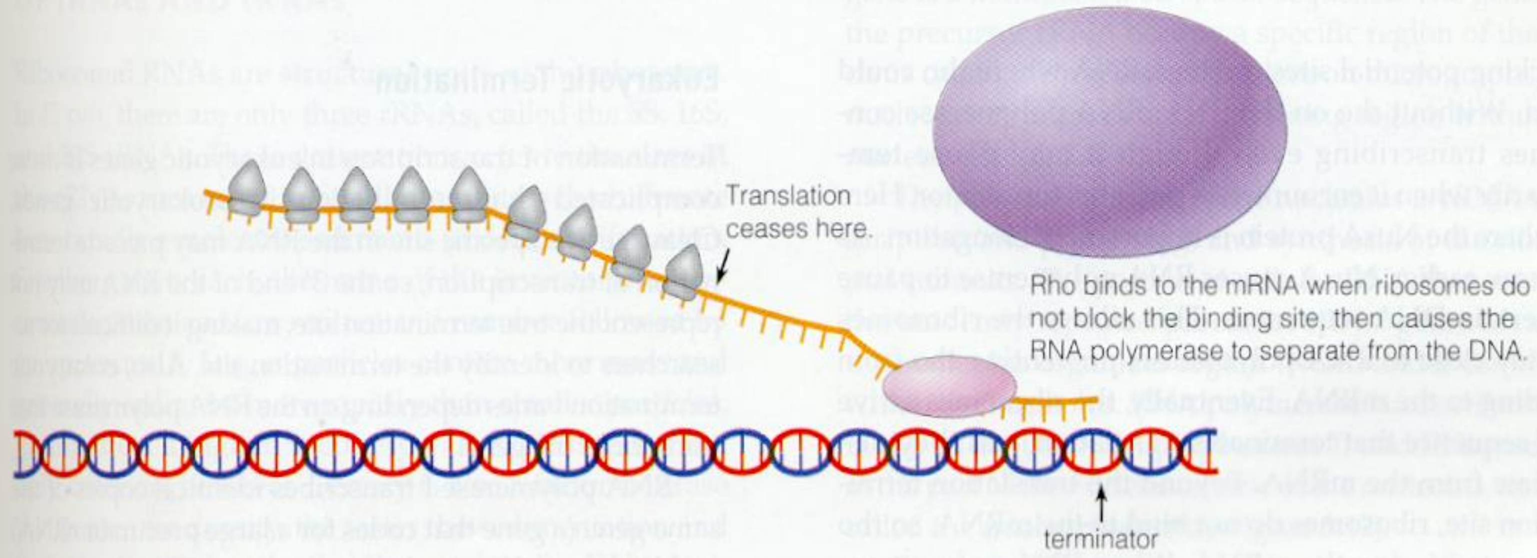
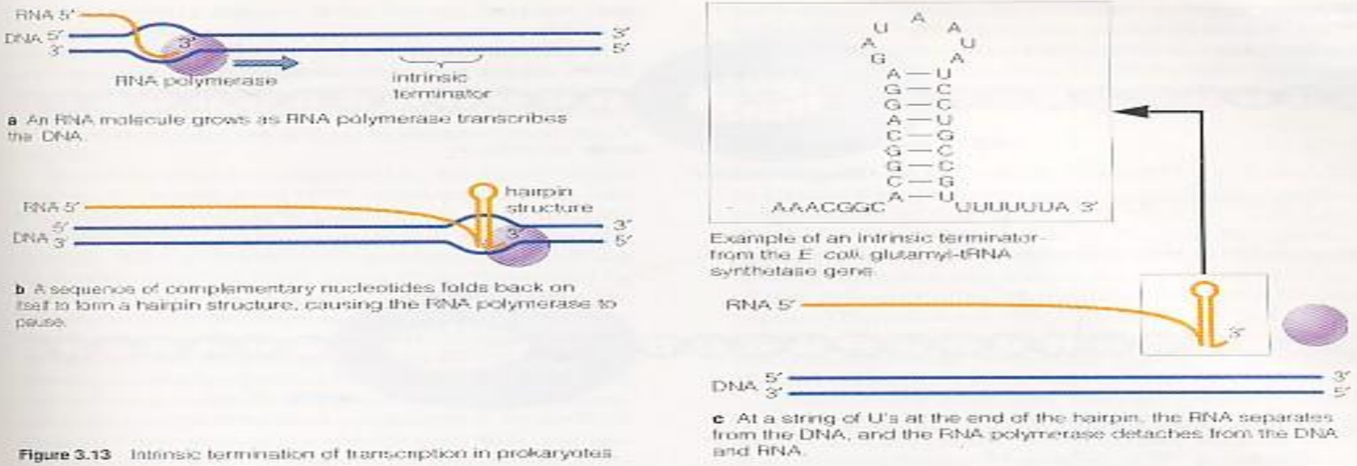


FIGURE 7.8
The core enzyme/holoenzyme (DNA-directed RNA polymerase).



a Transcription continues as long as ribosomes cover potential binding sites for rho on the mRNA.



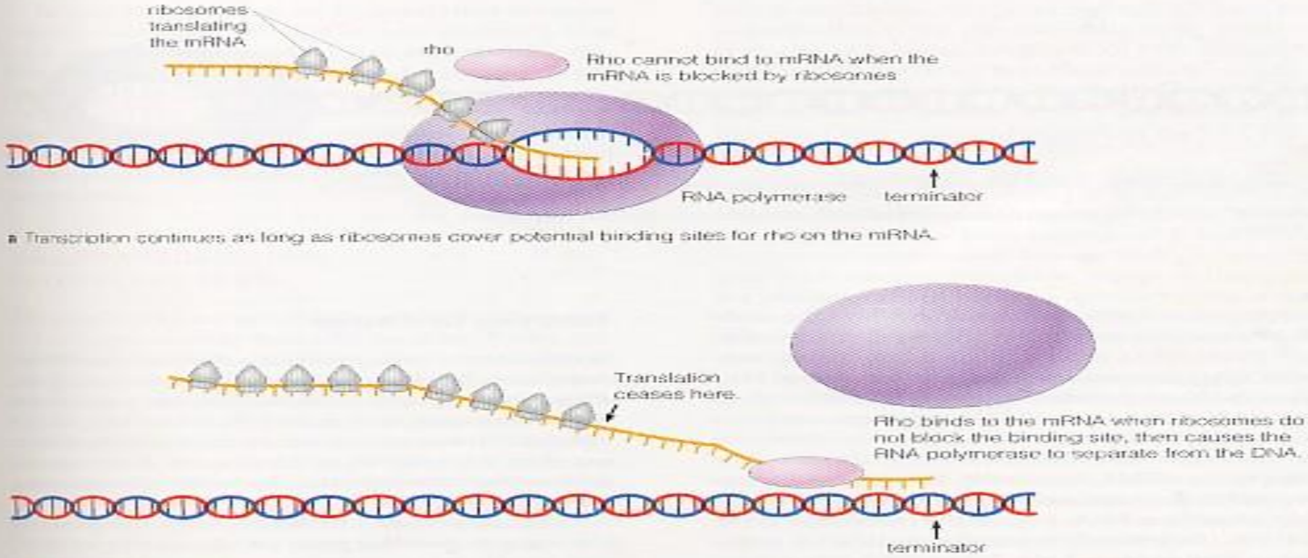


a An RNA molecule grows as RNA polymerase transcribes the DNA.

b A sequence of complementary nucleotides folds back on itself to form a hairpin structure, causing the RNA polymerase to pause.

c At a string of U's at the end of the hairpin, the RNA separates from the DNA, and the RNA polymerase detaches from the DNA and RNA.

Figure 3.13 Intrinsic termination of transcription in prokaryotes



a Transcription continues as long as ribosomes cover potential binding sites for rho on the mRNA.

b Transcription terminates beyond the termination site for translation because ribosomes do not cover a binding site for rho at the end of the mRNA.

Figure 3.14 Rho-dependent termination of transcription in prokaryotes

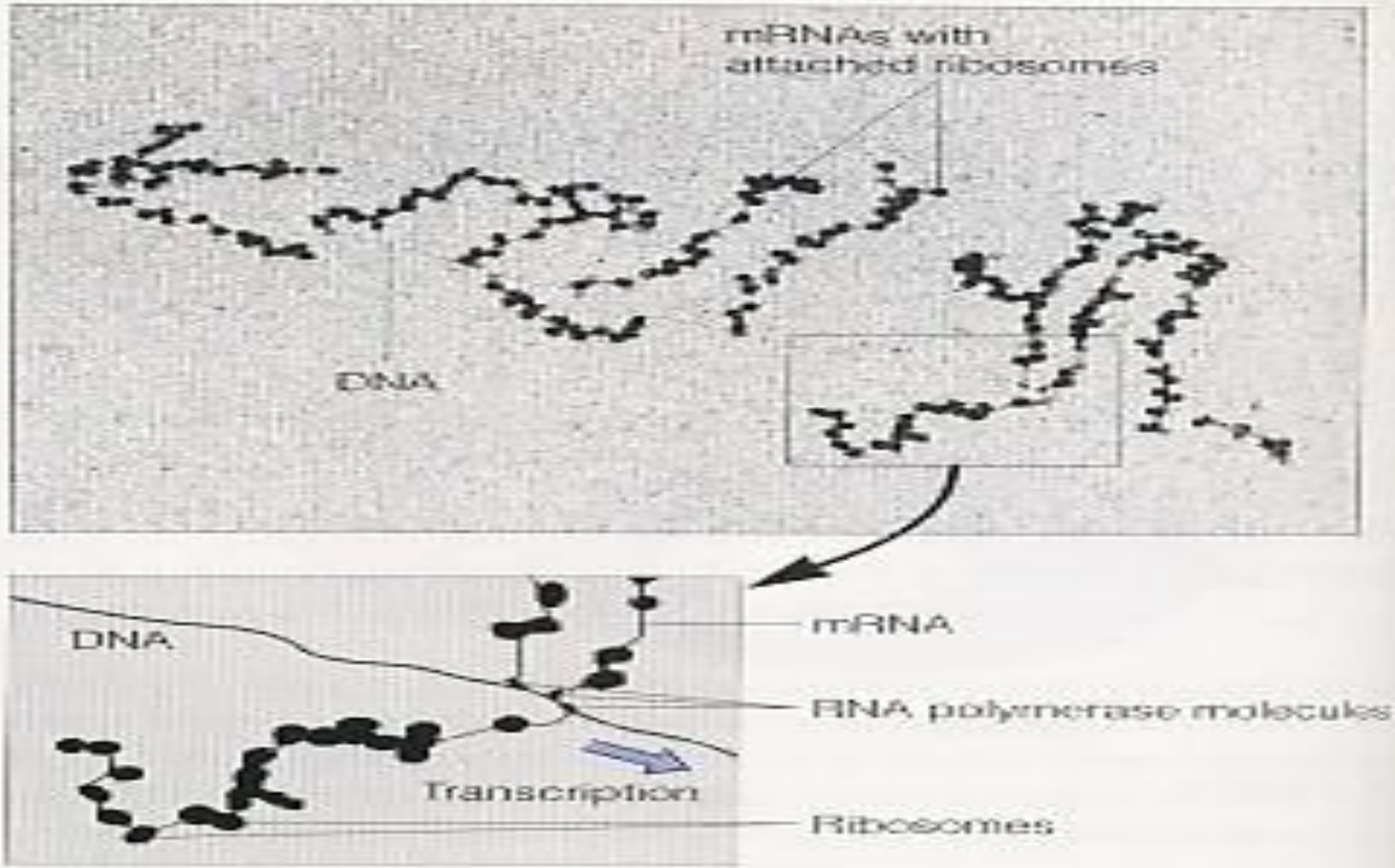


Figure 3.3 Coupled transcription and translation in a prokaryotic cell. Ribosomes begin translating the mRNA while RNA polymerase is still transcribing it. (Photo courtesy of O. L. Miller, Jr., B. A. Hamkalo, and C. A. Thomas, Jr.)

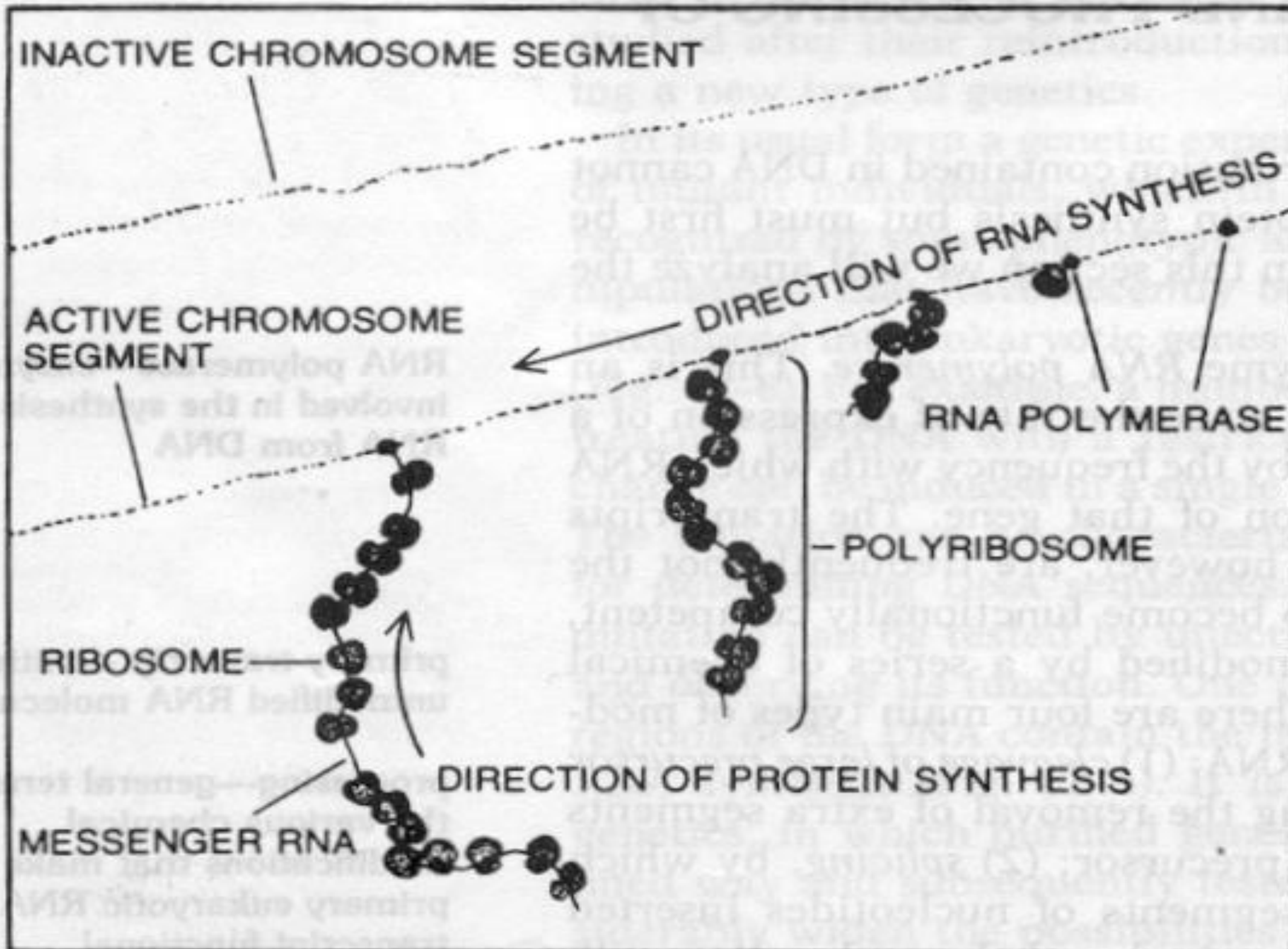
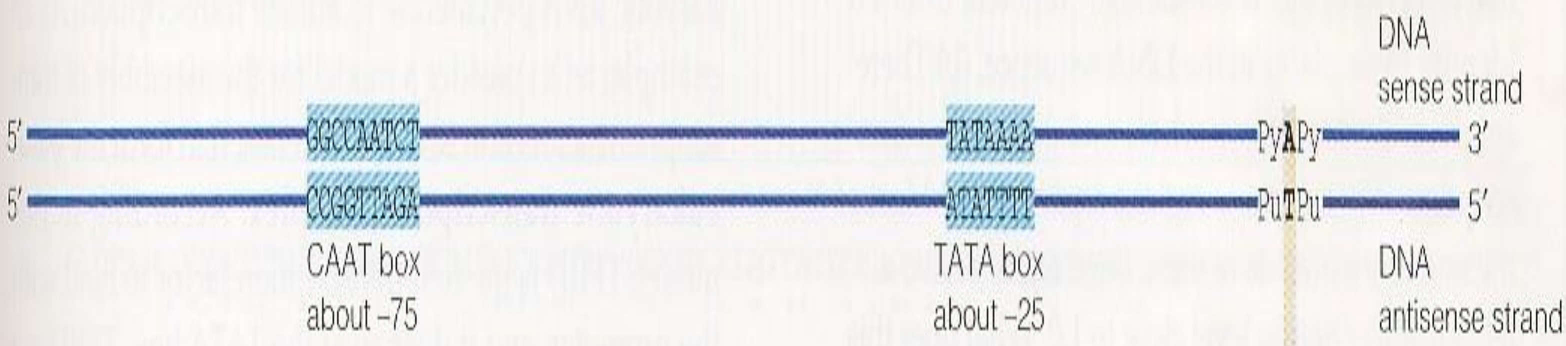
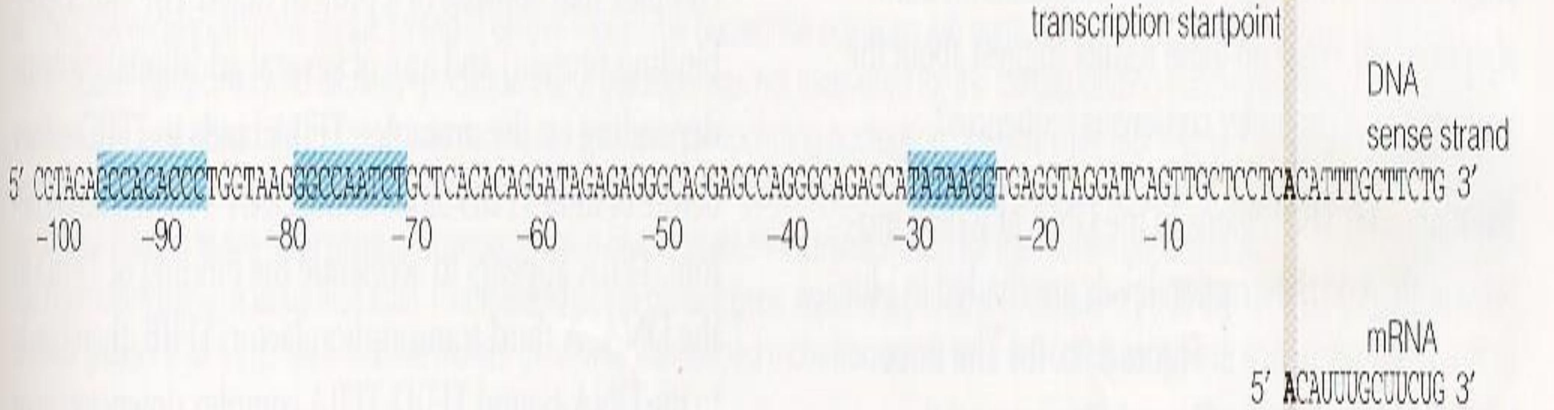

INACTIVE CHROMOSOME SEGMENT
DIRECTION OF RNA SYNTHESIS
ACTIVE CHROMOSOME SEGMENT
RNA POLYMERASE
POLYRIBOSOME
RIBOSOME
DIRECTION OF PROTEIN SYNTHESIS
MESSENGER RNA

TABLE 11-3 PROPERTIES AND FUNCTIONS OF EUKARYOTIC RNA POLYMERASES

Enzyme	Localization	Gene Transcripts	Inhibition by α-Amanitin
I	Nucleolus	18S and 28S rRNAs	Insensitive
II	Nucleoplasm	mRNA	Sensitive to low concentration
III	Nucleoplasm	tRNA, 5S RNA	Sensitive to high concentration

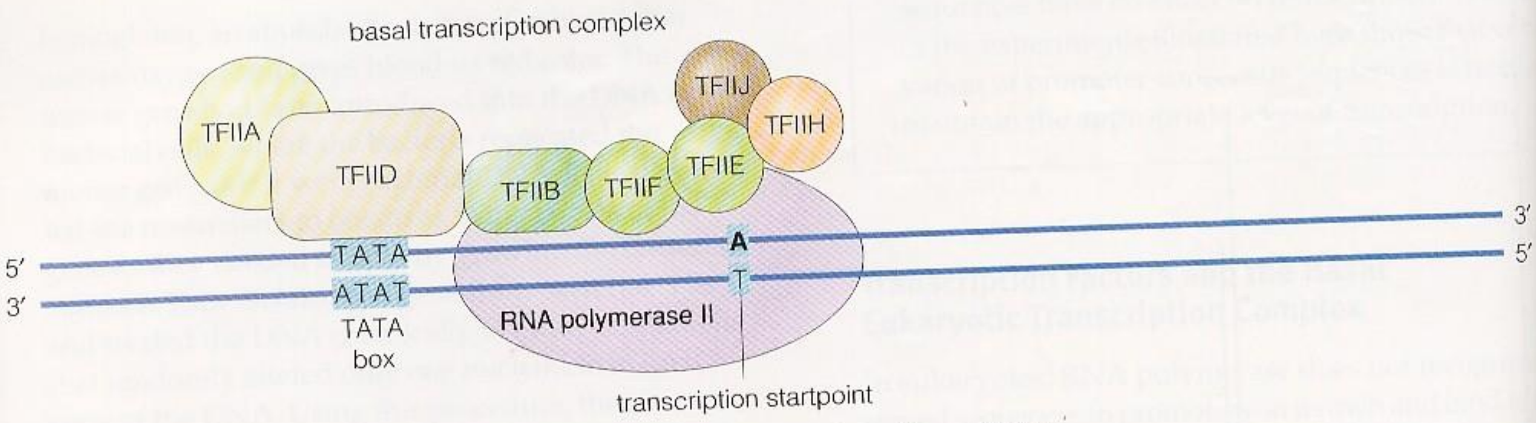


a Consensus sequences and positions of the CAAT and TATA boxes.

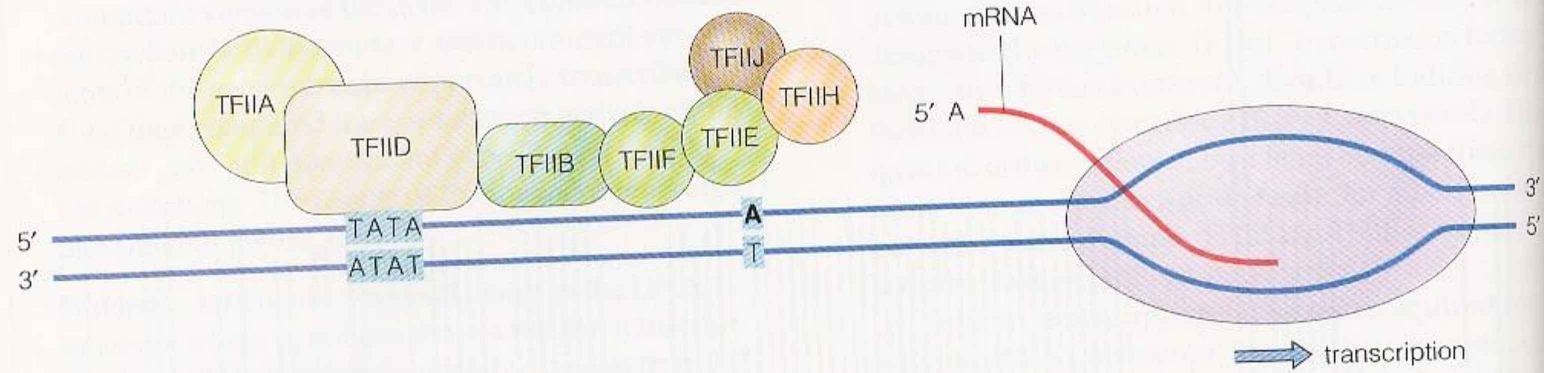


b DNA sequence of the mouse β-major globin gene promoter region. Conserved sequences are shaded in blue.

Figure 3.8 Conserved sequences in eukaryotic promoters.

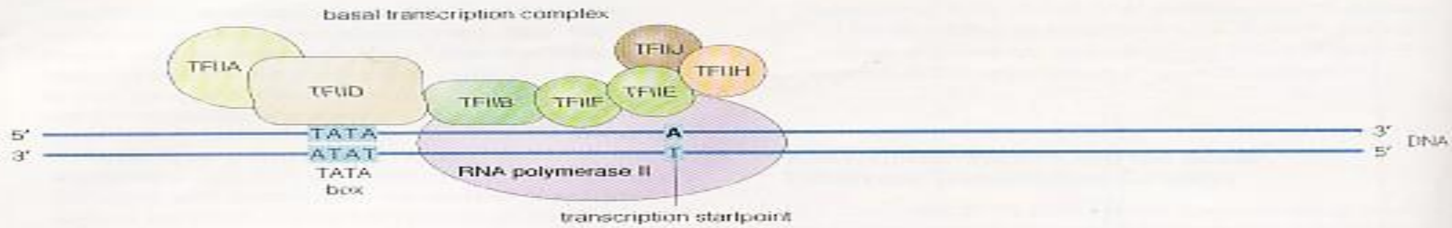


a The basal transcription complex positions RNA polymerase II for initiation of transcription.

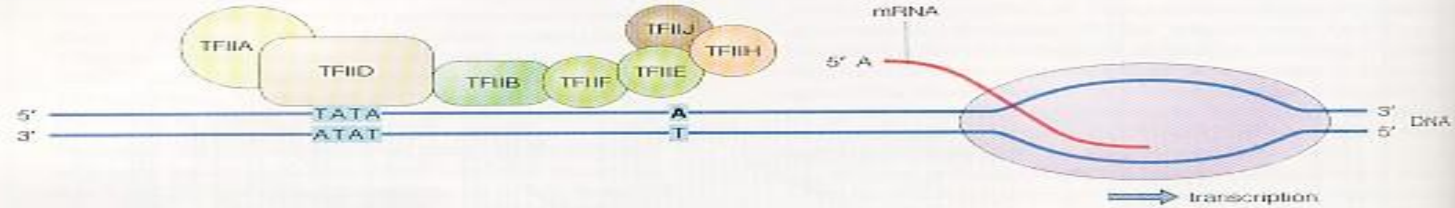


b Once transcription is initiated, RNA polymerase II separates from the basal transcription complex and proceeds to transcribe the ge

Figure 3.10 The basal eukaryotic transcription complex and initiation of transcription in eukaryotes.



a The basal transcription complex positions RNA polymerase II for initiation of transcription.



b Once transcription is initiated, RNA polymerase II separates from the basal transcription complex and proceeds to transcribe the gene.

Figure 3.10 The basal eukaryotic transcription complex and initiation of transcription in eukaryotes.

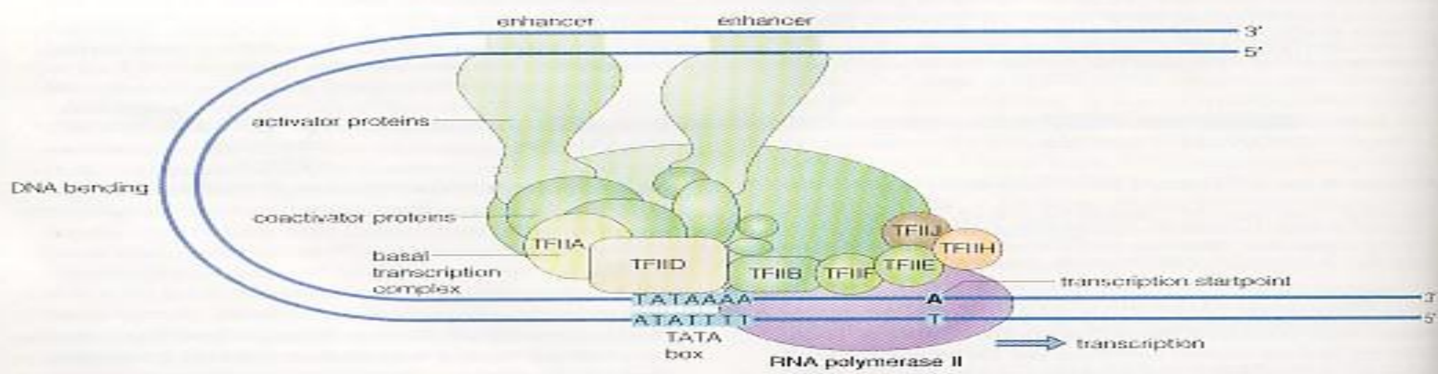
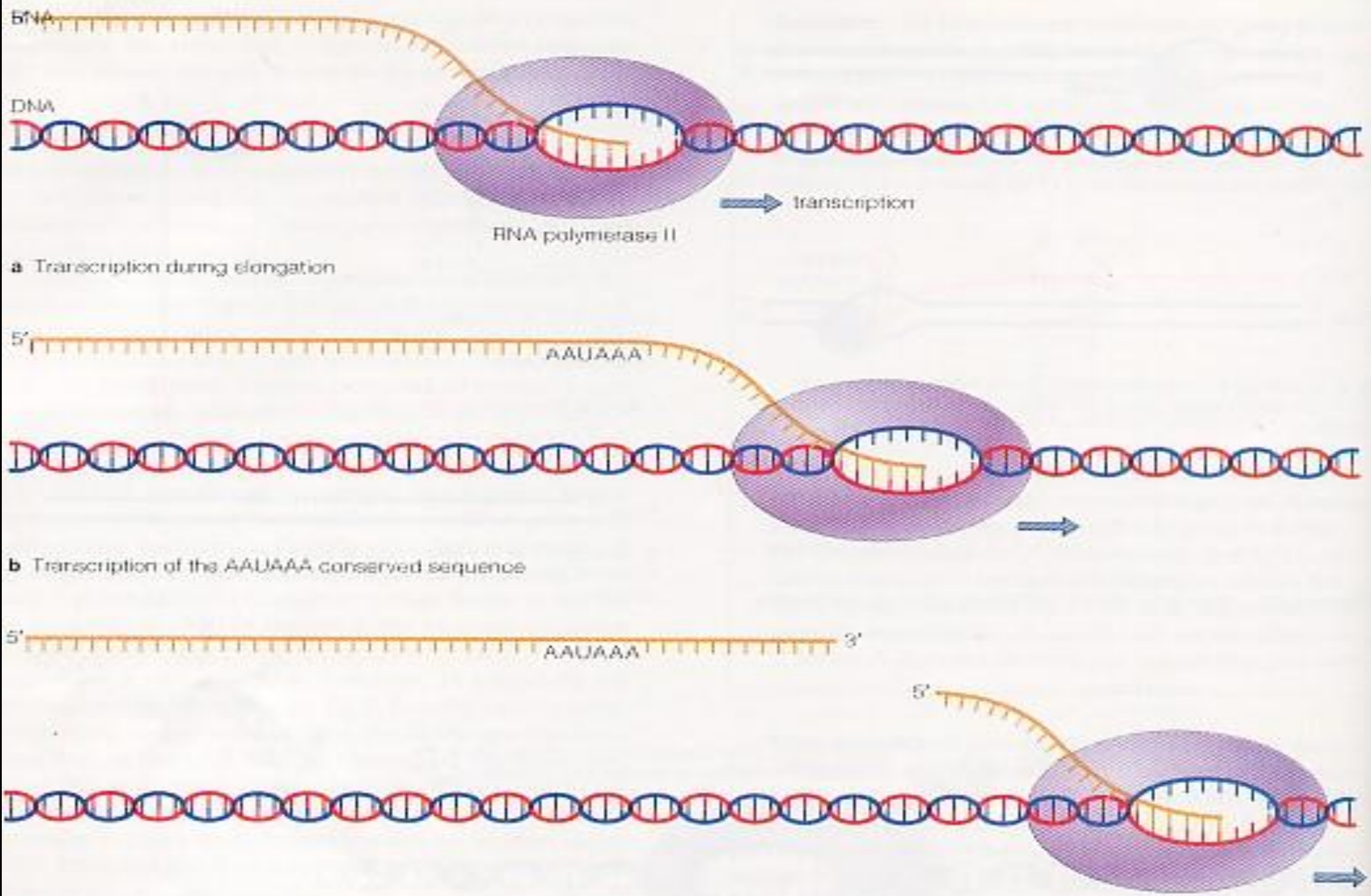


Figure 3.11 Interaction of enhancers, activators, and coactivators with the basal transcription complex for initiation of transcription in eukaryotes. The DNA bends, bringing the activator proteins into contact with coactivator proteins bound to the basal transcription complex. (Adapted from an original drawing by Jared Schneidman Design in Tjian, R. 1995. Molecular machines that control genes. *Scientific American* 272 (Feb 95):54–61. Reprinted by permission.)

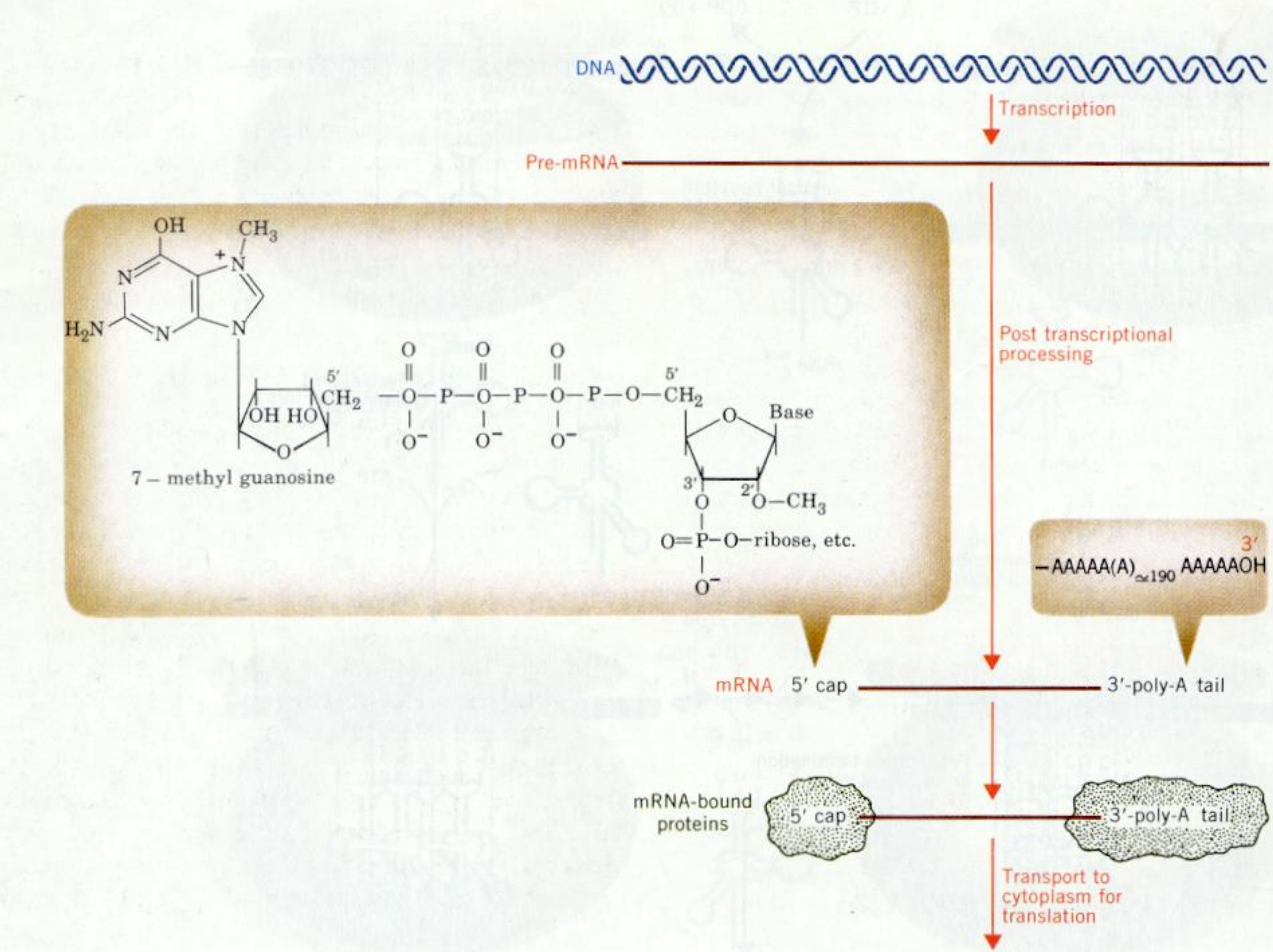


a Transcription during elongation

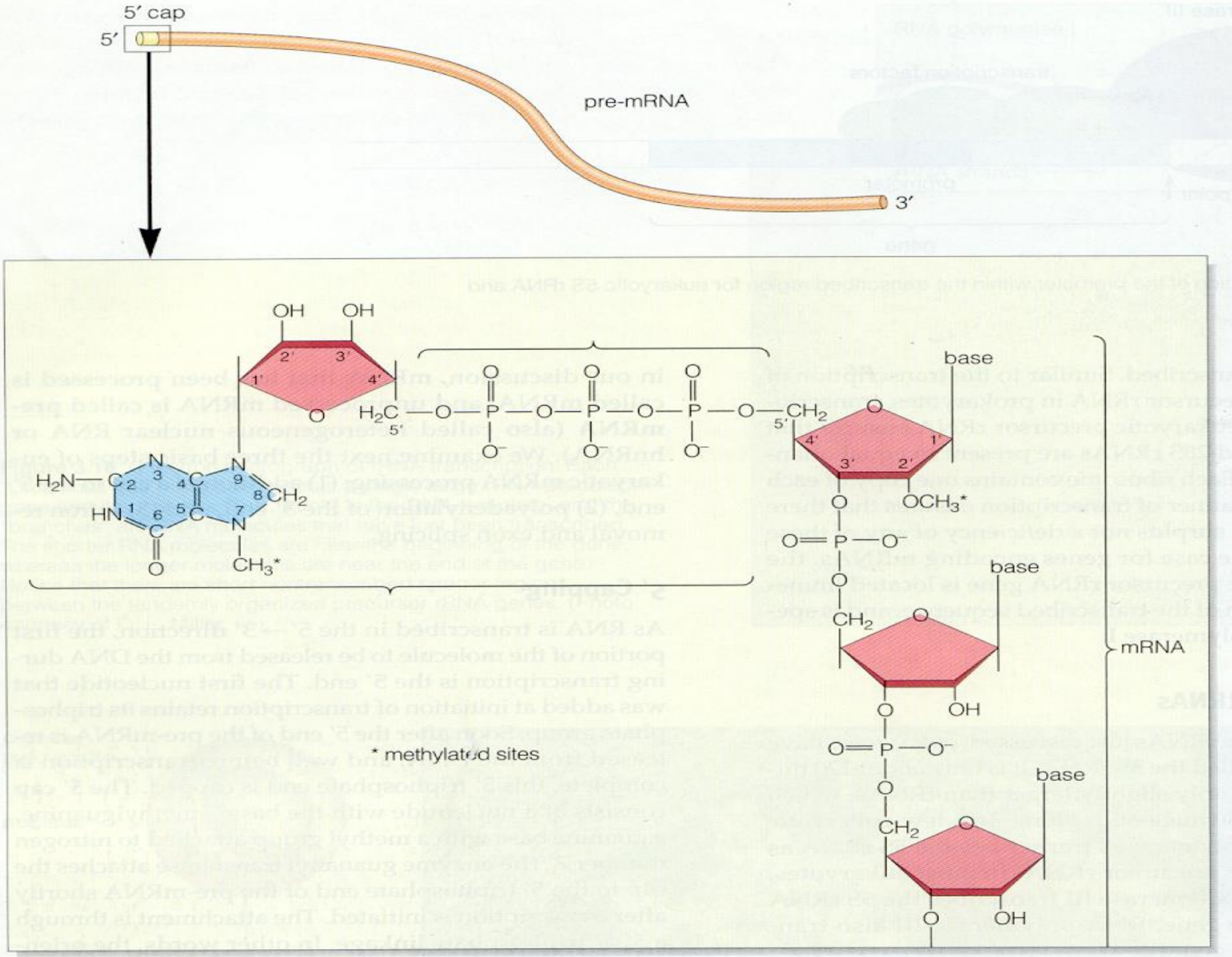
b Transcription of the AAUAAA conserved sequence

c Cleavage of the mRNA. mRNA is cleaved 11–30 nucleotides downstream from the AAUAAA sequence

Figure 3.15 RNA cleavage that precedes termination of transcription by RNA polymerase II in eukaryotes.



DNA
Transcription
Pre-mRNA
OH
CH_3
H_2N
7 – methyl guanosine
Base
O=P–O–ribose, etc.
Post transcriptional processing
3′
$-AAAAA(A)_{\approx 190}$ AAAAAOH
mRNA 5′ cap
3′-poly-A tail
mRNA-bound proteins
5′ cap
3′-poly-A tail
Transport to cytoplasm for translation



5′ cap
5′
pre-mRNA
3′
OH
OH
2′
3′
1′
4′
H_2C
5′
O
O
O
O
P
P
P
O^-
O^-
O^-
CH_2
5′
4′
1′
3′
2′
OCH_3*
base
N
3
H_2N
C
2
4
C
9
N
8
CH_2
HN
1
6
5
C
7
N
C
O
CH_3*
O=P—O^-
base
CH_2
O
OH
O=P—O^-
base
CH_2
O
OH
mRNA
* methylated sites

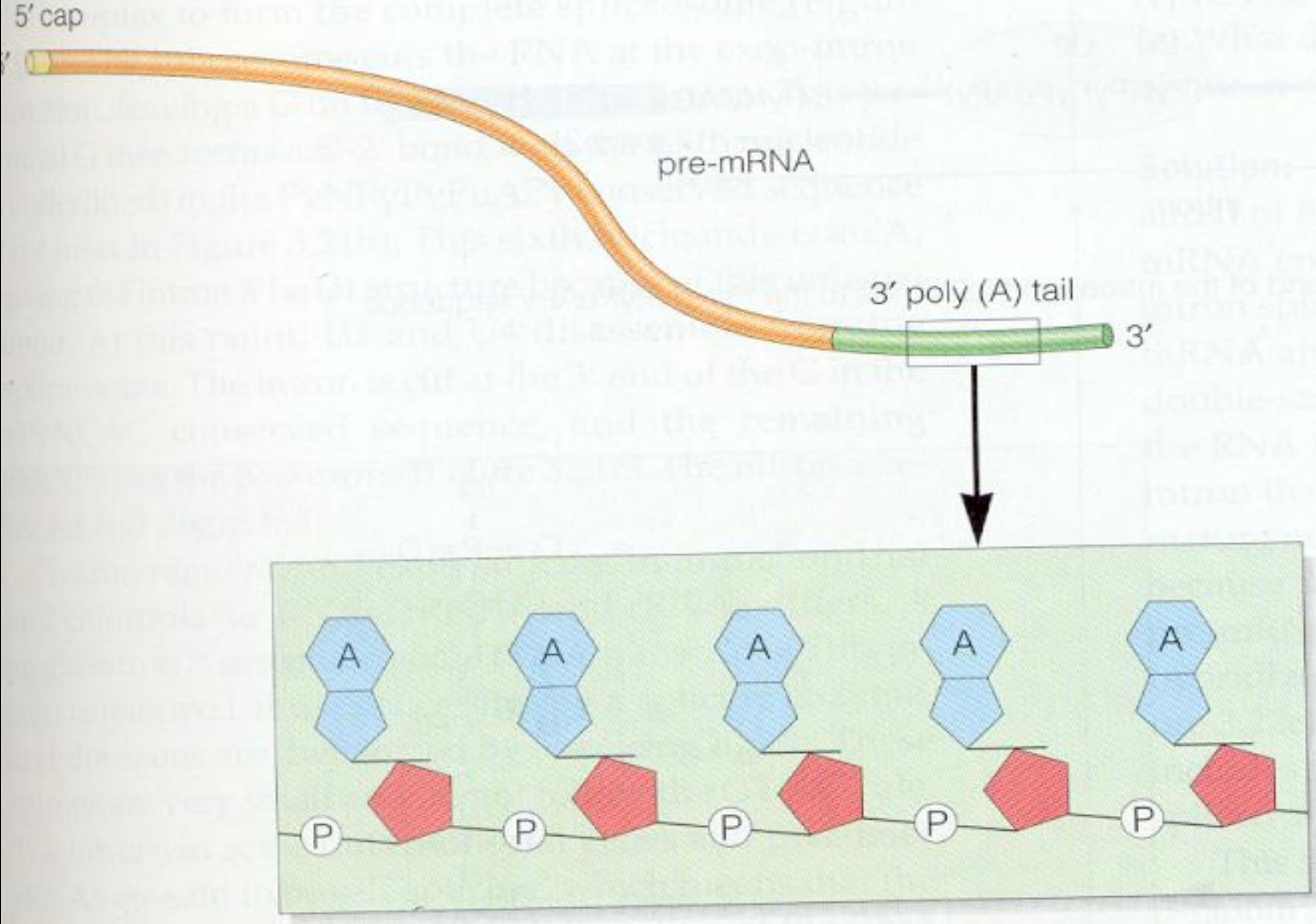


Figure 3.20 The 3′ poly (A) tail of eukaryotic mRNAs.

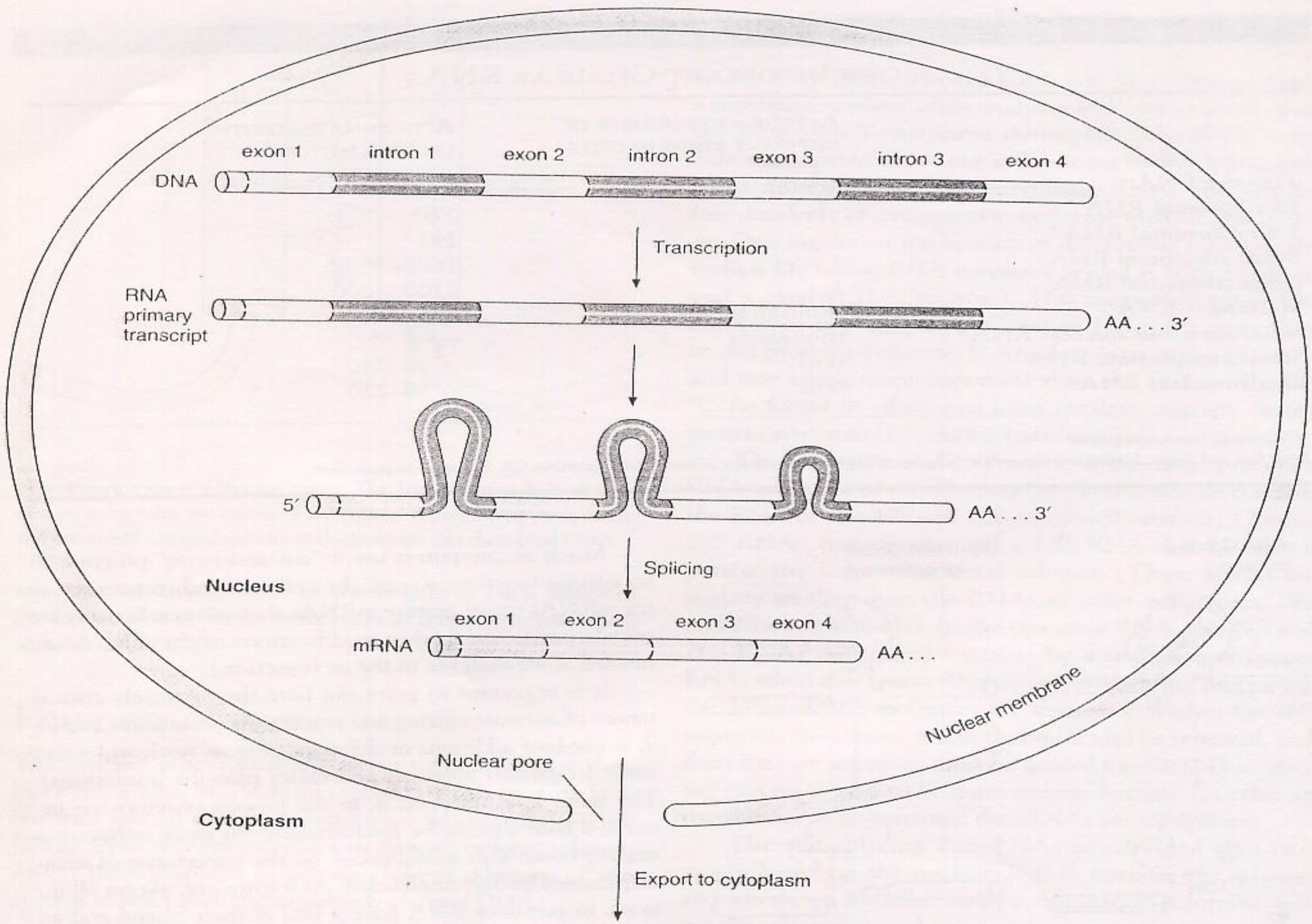


FIGURE 10.15
Splicing of hnRNA to produce mRNA by removal of introns. Capping the 5′ end and polyadenylation of the 3′ tail are also shown.

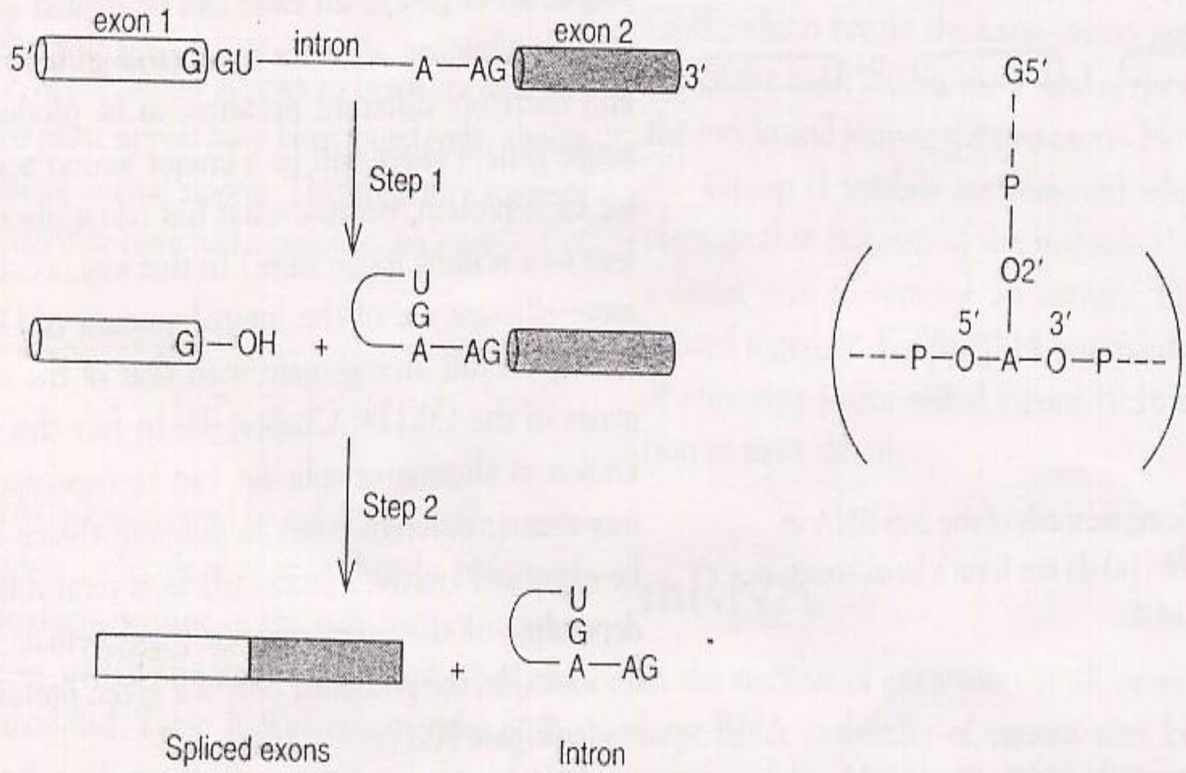


FIGURE 10.16

Lariat formation in the splicing of mRNA. The G at the 5´ end of the intron attaches an A within the intron to form the lariat at the intron's 3´ end. G attaches to the A at its 2´ OH position.

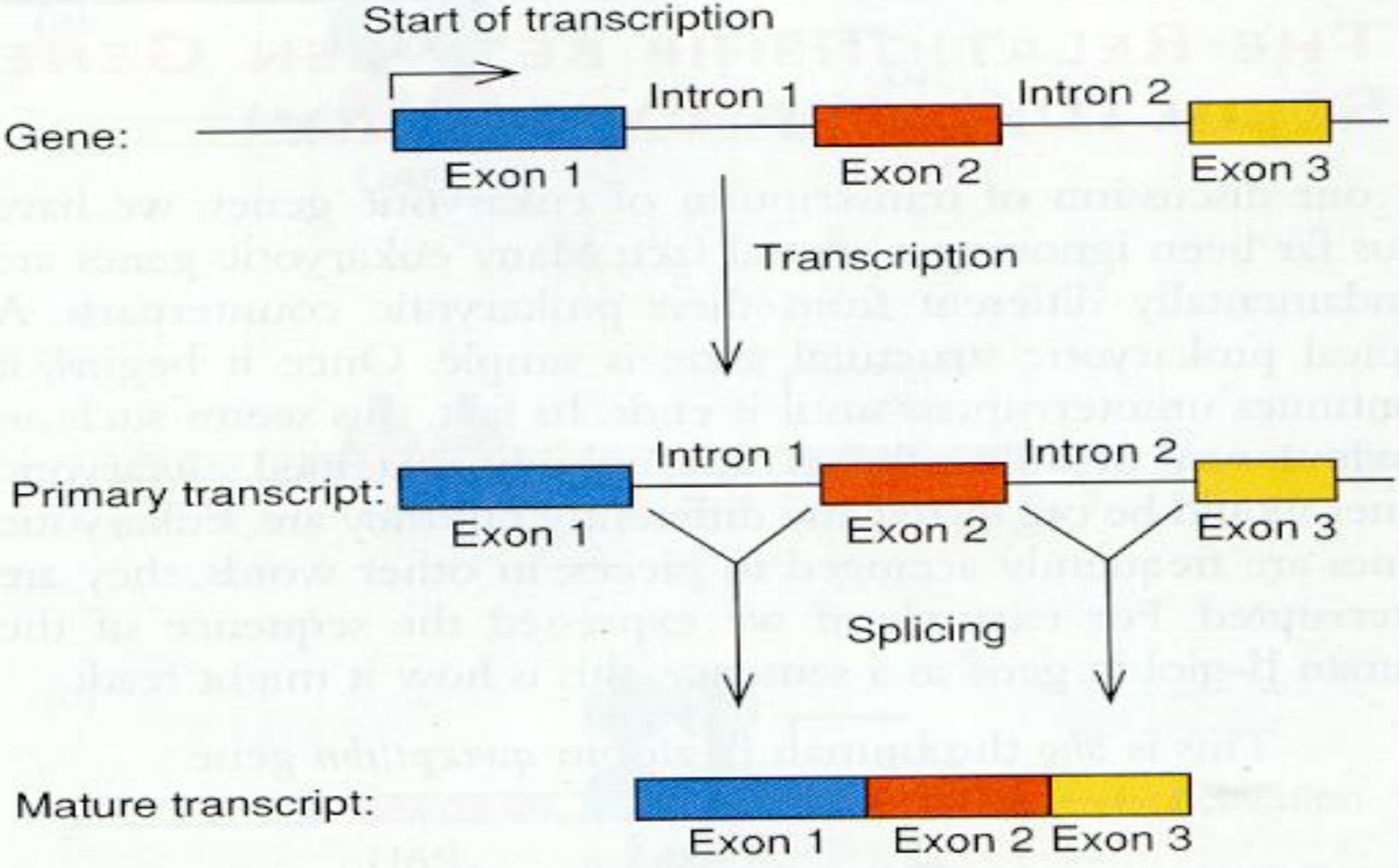


FIGURE 9.33 Outline of splicing. The introns in a gene are transcribed along with the exons (colored boxes) in the primary transcript. Then they are removed as the exons are spliced together.