Chapter 4: Transcription of Genes

Transcription

Regulation of transcription

Storage and Transmission of Information with Simple Codes

(1) how the *genetic* information of living creatures is written in an alphabet with just four letters, the four base pairs in DNA, and

(2) how this *genetic* information is expressed during the growth and development of an organism.

James Watson's idea on RNA

Of course Francis and I talked about protein synthesis and there was evidence that protein synthesis occurred in the cytoplasm of cells, not in the nucleus, so protein synthesis occurred removed from the chromosomes, or seemingly removed from the chromosomes, it occurred on particles which contained RNA. So I thought there must be some system by which the information is transferred from DNA to RNA and then RNA provides the information, is the direct template for protein synthesis. I wrote that on a little piece of paper and taped it above my desk.

Transfer of Genetic Information: The Central Dogma

(1) **transcription**, the transfer of the genetic information from DNA to RNA, and

(2) **translation**, the transfer of information from RNA to protein.

In addition, genetic information flows from RNA to DNA

The central dogma

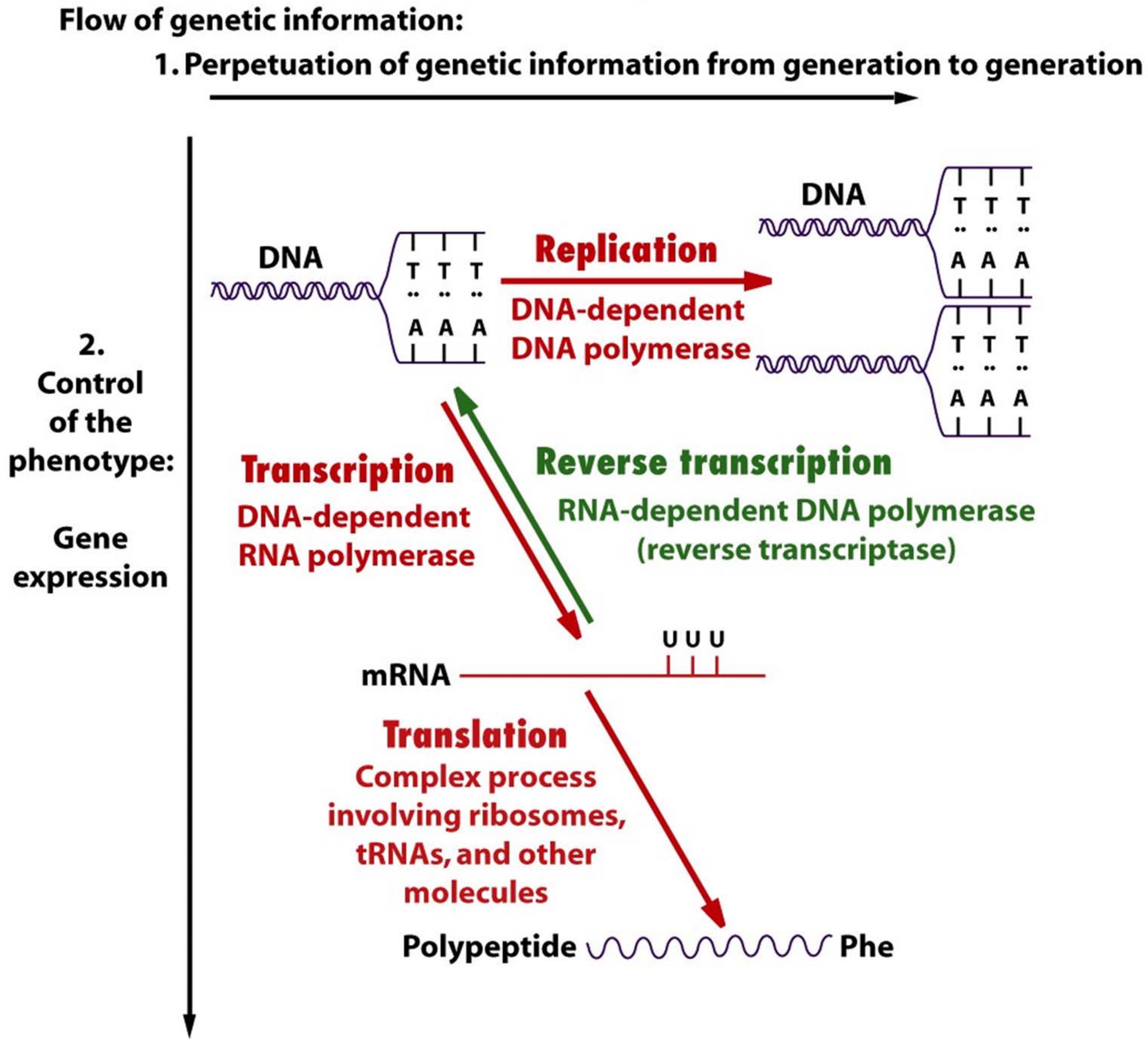
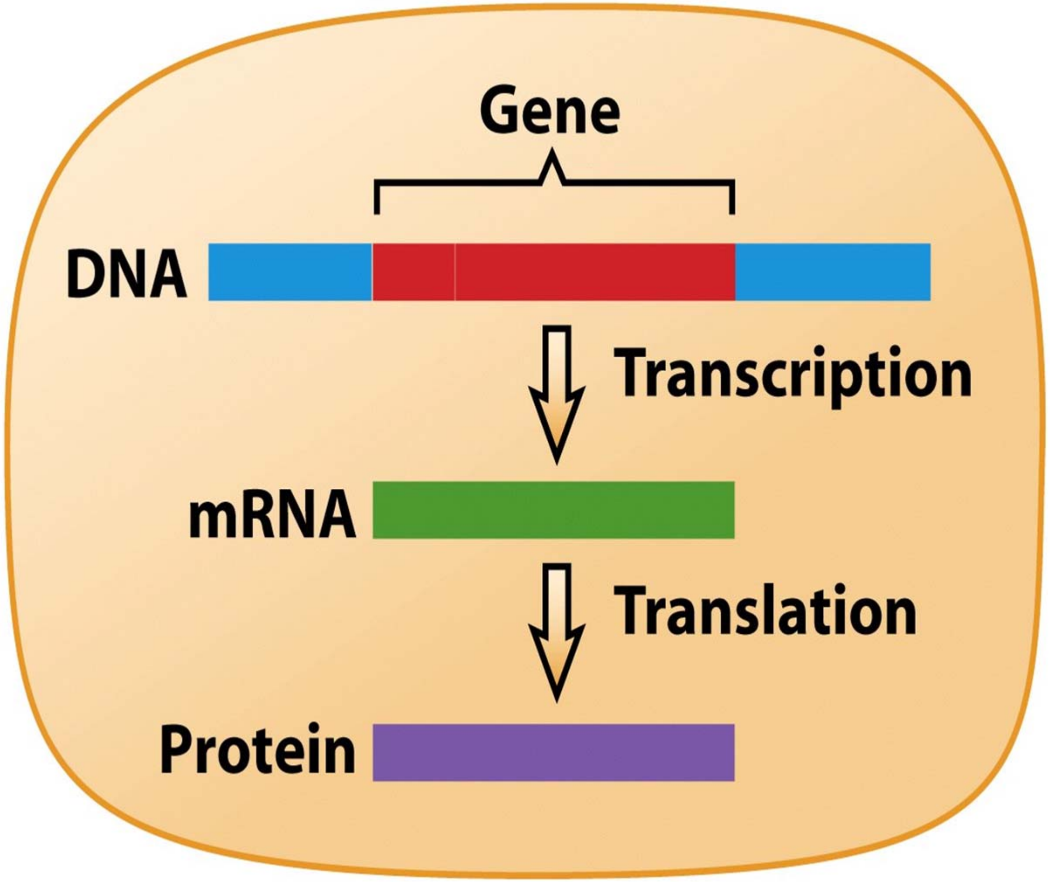


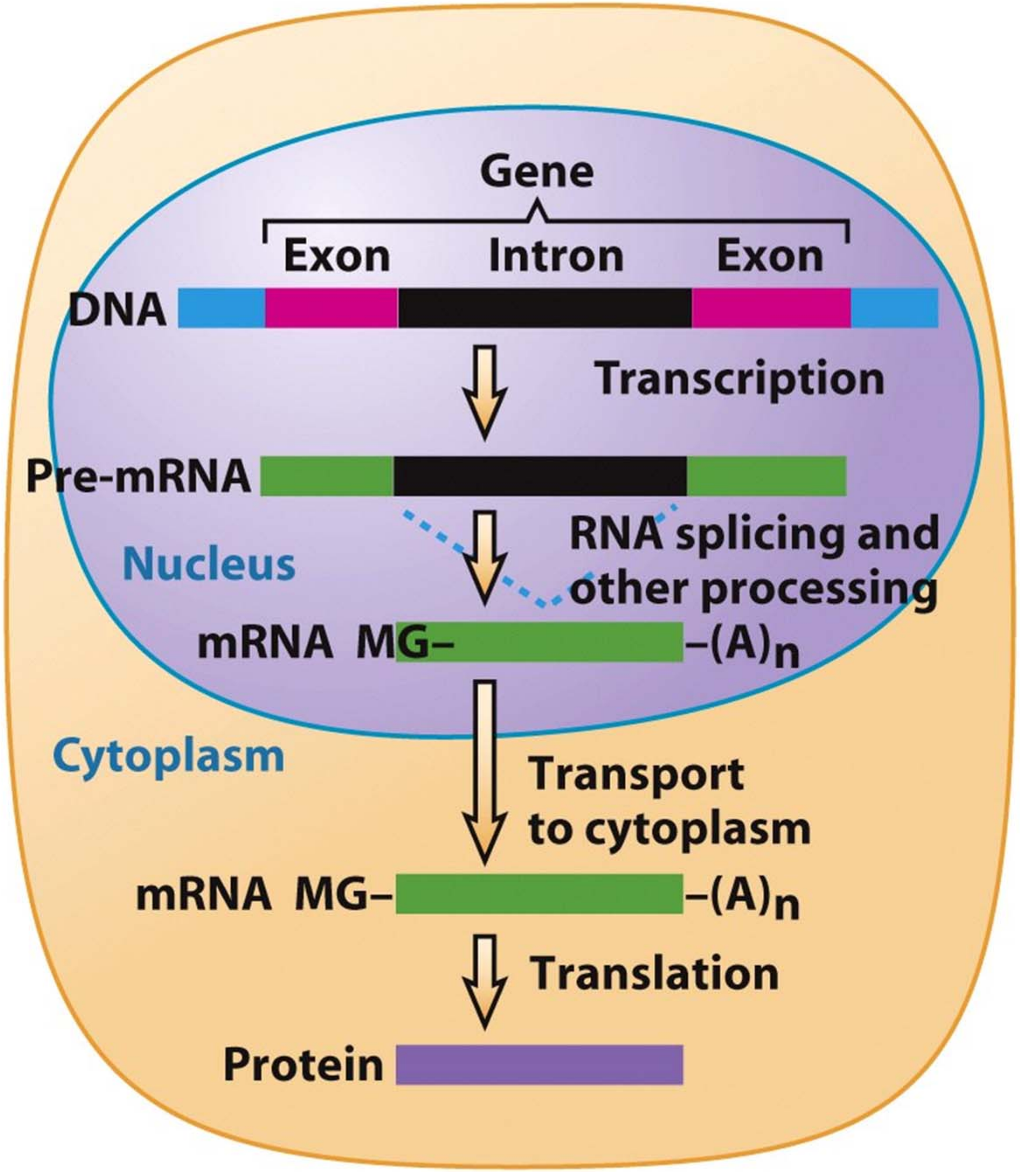
Figure 11-3 Principles of Genetics, 4/e



Prokaryotes

Figure 11-4a Principles of Genetics, 4/e

In prokaryotes, the product of transcription, the **primary transcript**, usually is equivalent to the mRNA molecule



Eukaryotes

Figure 11-4b Principles of Genetics, 4/e

In eukaryotes, the primary transcripts or pre-mRNAs often must be processed by the excision of introns and the addition of 5′ 7-methyl guanosine caps (MG) and 3′ poly(A) tails [(A)n].

Transcription

- Transcription: the transfer of information from DNA to messenger RNA

- Chemical differences between DNA and RNA

  1) In DNA the sugar is deoxyribose, whereas in RNA the sugar is ribose
  2) In RNA the base thymine (T) is replaced by uracil (U)
  3) DNA is double stranded (ds), whereas RNA is single stranded (ss)
  [At transcription, only one of the strands (=non-coding strand) of DNA is copied]

- RNA is made by an enzyme called RNA polymerase (=sigma subunit + core enzyme), which binds to the DNA at the start of a gene, opens the double helix, and then manufactures an RNA message

- Sigma subunit binds to promoter sequences at -10 (TATAAT) and -35 (TTGACA) region of the gene and then core enzyme makes the mRNA

- core enzyme stops at the terminator sequence (two inverted repeats and poly As) at the end of the gene

Five Types of RNA Molecules

mRNAs

Transfer RNAs (tRNAs) are small RNA molecules that function as adaptors between amino acids and the codons in mRNA during translation.

Ribosomal RNAs (rRNAs) are structural and catalytic components of the ribosomes, the intricate machines that translate nucleotide sequences of mRNAs into amino acid sequences of polypeptides.

Small nuclear RNAs (snRNAs) are structural components of spliceosomes, the nuclear structures that excise introns from nuclear genes.

Micro RNAs (miRNAs) are short 20 to 22-nucleotide single-stranded RNAs that are cleaved from small hairpin-shaped precursors and block the expression of complementary or partially complementary mRNAs by either causing their degradation or repressing their translation.

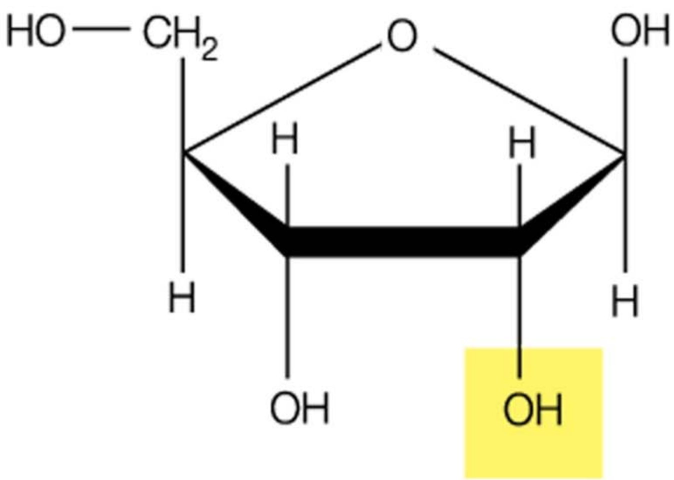
General Features of RNA Synthesis

RNA synthesis occurs by a mechanism that is similar to that of DNA synthesis except that

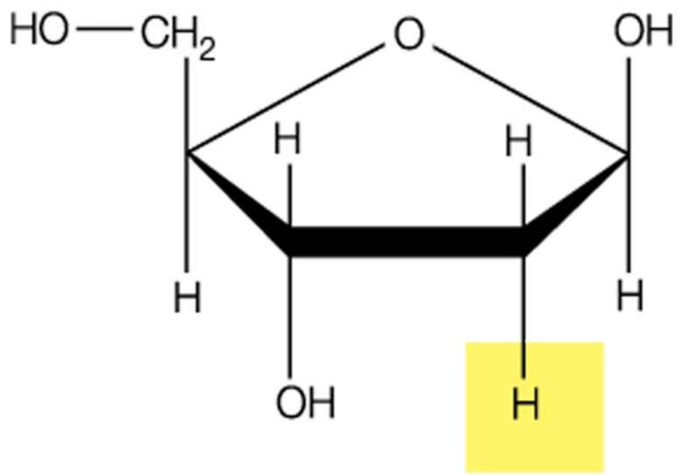
(1) the precursors are **ribonucleoside triphosphates** rather than deoxyribonucleoside triphosphates,

(2) only one strand of DNA is used as a template for the synthesis of a complementary RNA chain in any given region, and

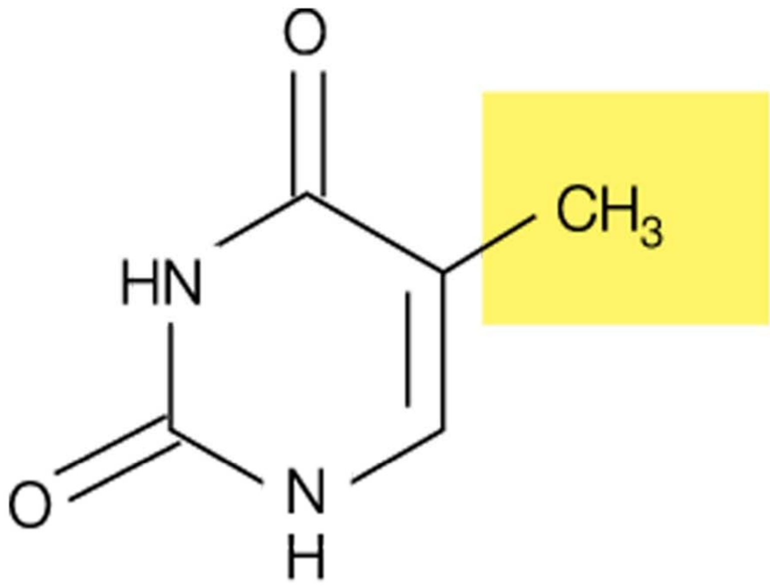
(3) RNA chains can be initiated *de novo,* without any requirement for a preexisting primer strand.



리보오스



데옥시리보오스



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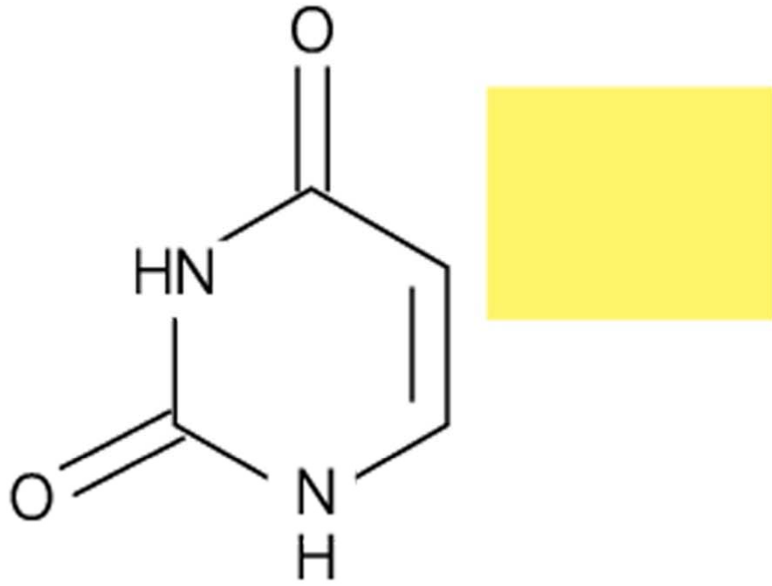


우라실

General Features of RNA Synthesis

The RNA molecule produced will be <u>complementary</u> to the DNA **template strand** and identical, except that uridine residues replace thymidines, to the DNA **nontemplate strand**

mRNA molecules are coding strands of RNA. They are also called **sense strands** of RNA because their nucleotide sequences "make sense" in that they specify sequences of amino acids in the protein gene products.

An RNA molecule that is complementary to an mRNA is referred to as **antisense RNA**.

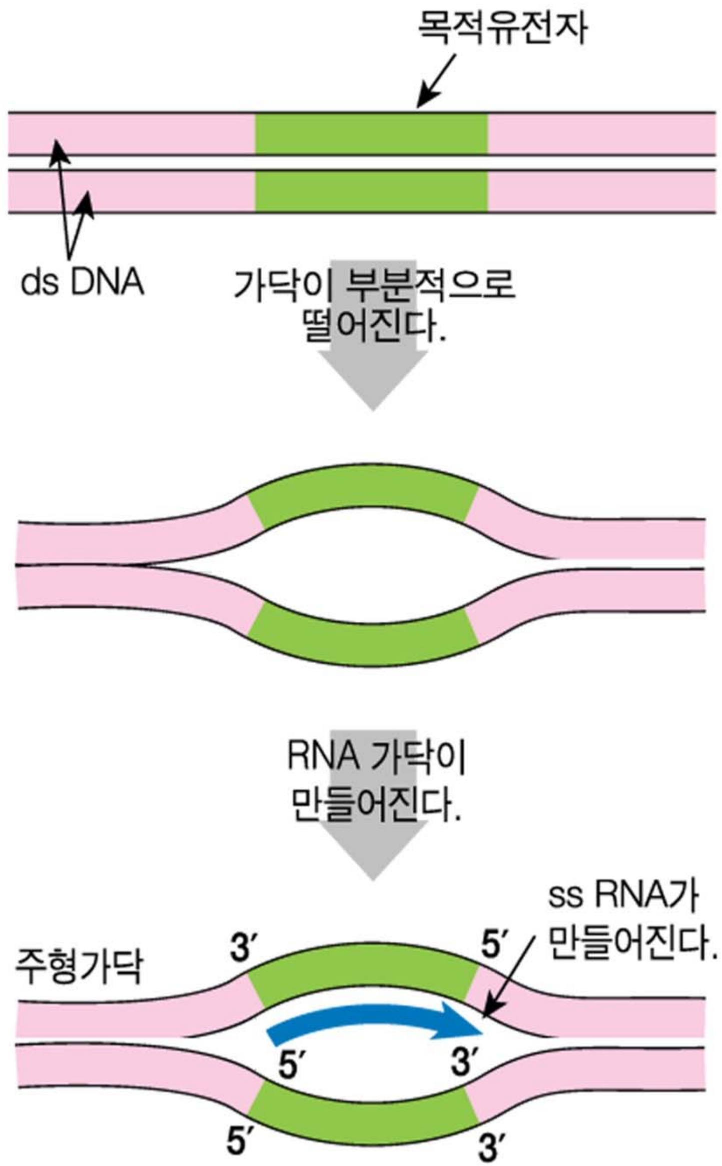

목적유전자
ds DNA
가닥이 부분적으로
떨어진다.
RNA 가닥이
만들어진다.
ss RNA가
만들어진다.
주형가닥
3′
5′
5′
3′
5′
3′

그림 6-1

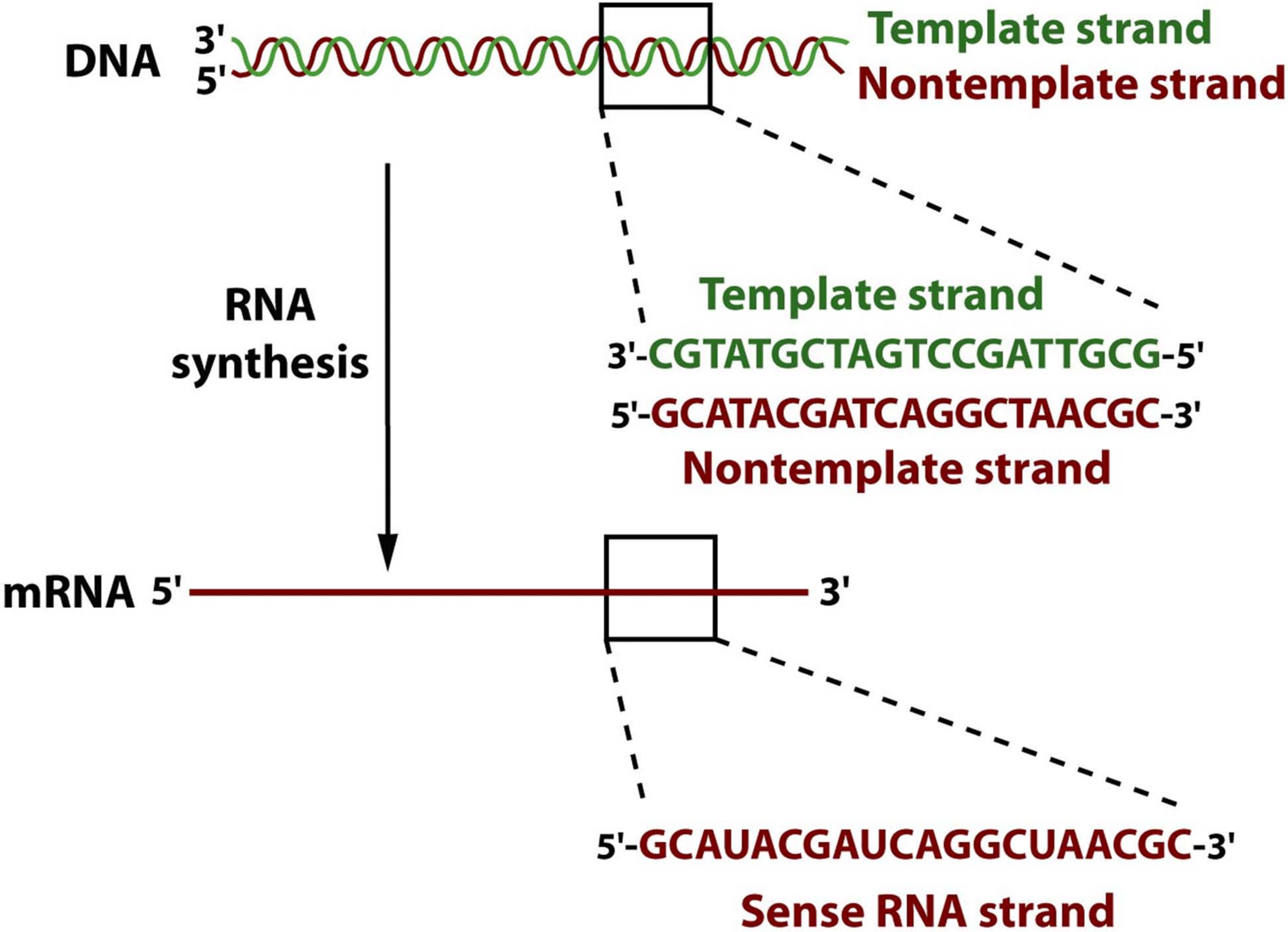


Figure 11-7 Principles of Genetics, 4/e

RNA Polymerases: Complex Enzymes

RNA polymerases initiate transcription <u>at specific nucleotide sequences</u> called **promoters**.

A single RNA polymerase carries out all transcription in most prokaryotes, whereas three different RNA polymerases are present in eukaryotes, with each polymerase responsible for the synthesis of a distinct class of RNAs.

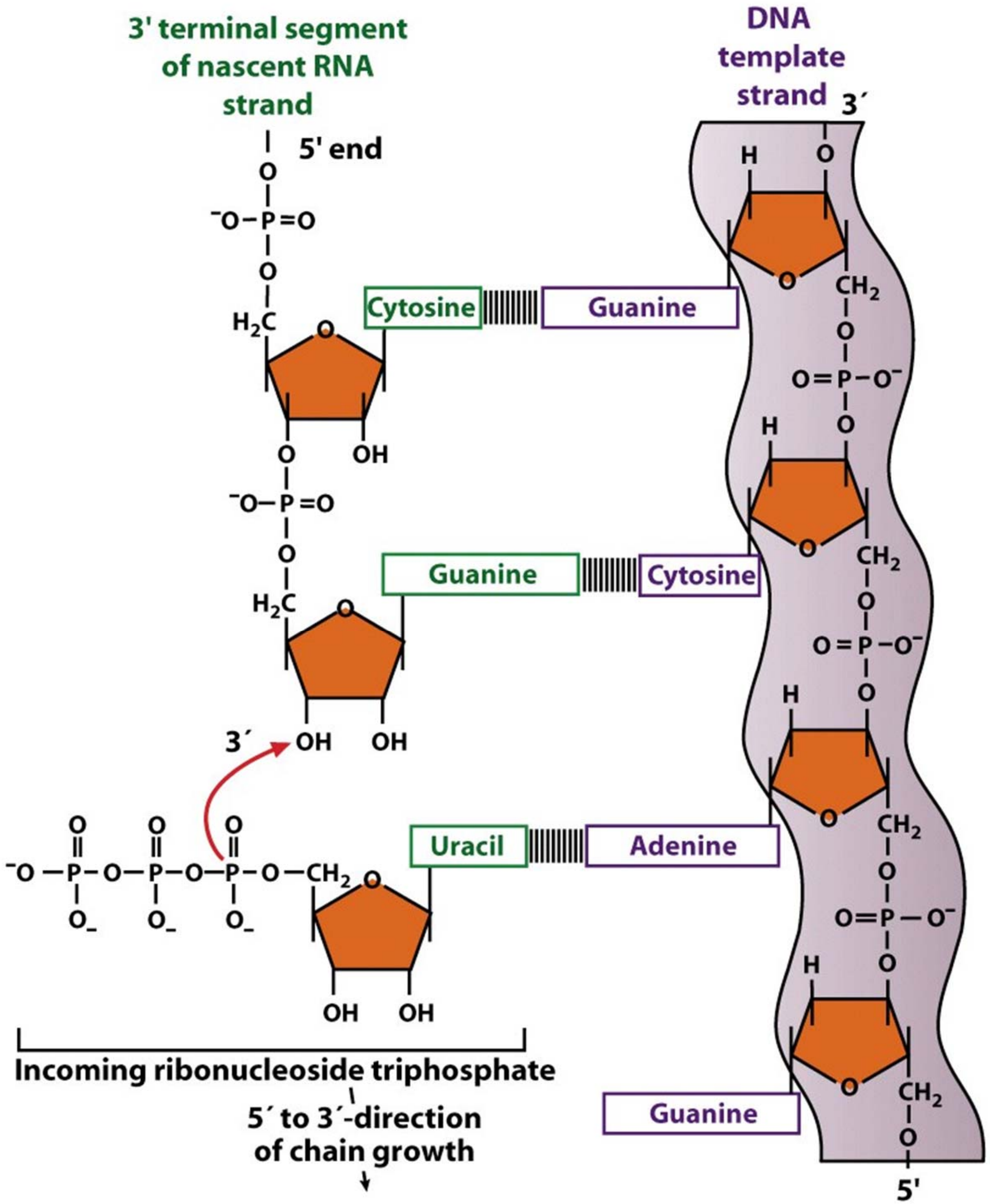
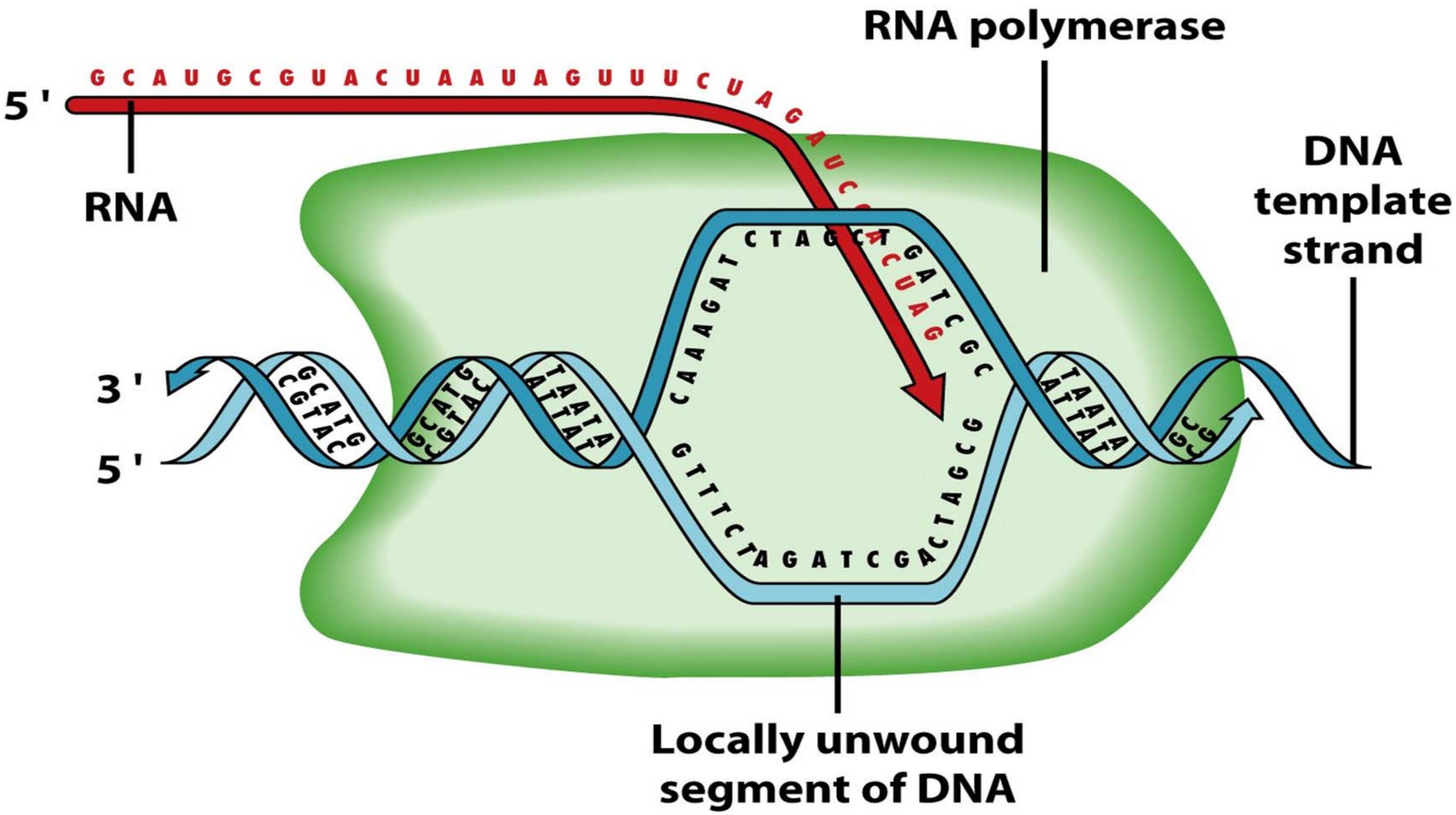


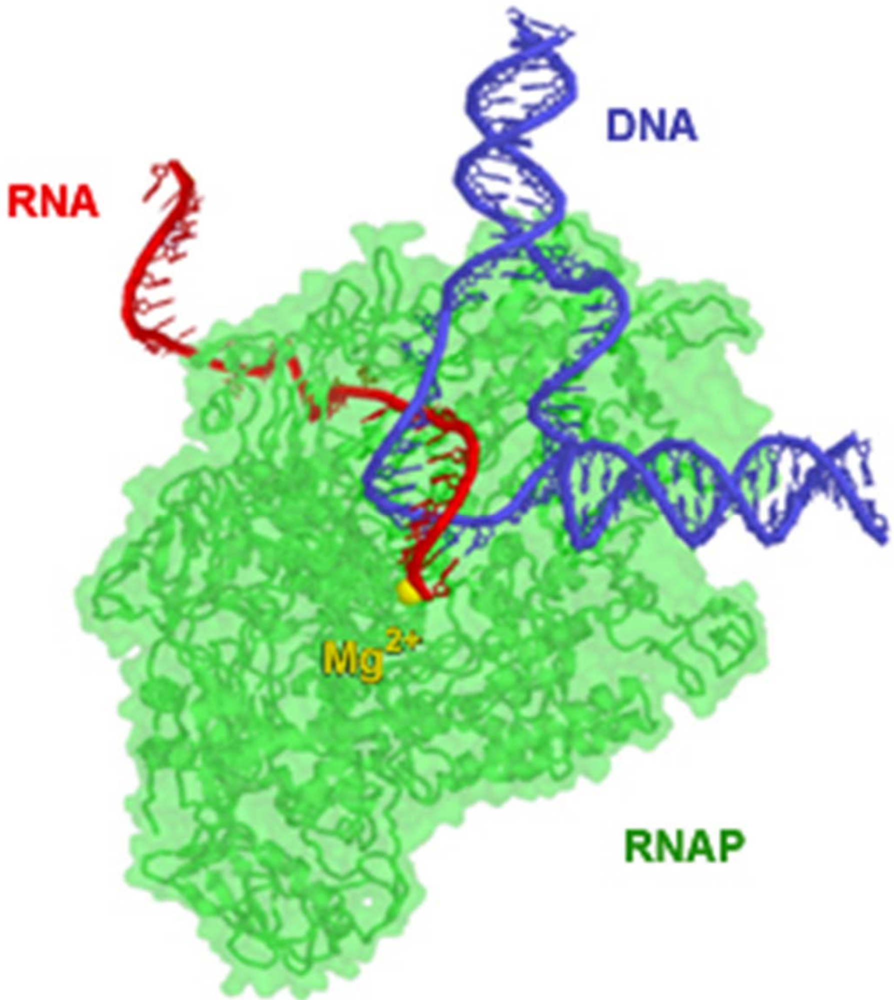
Figure 11-8 Principles of Genetics, 4/e

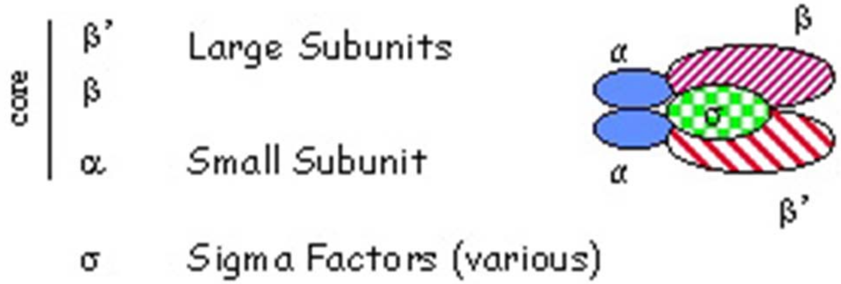
The synthesis of RNA chains, like DNA chains, occurs in the 5′ → 3′ direction, with the addition of ribonucleotides to the 3′-hydroxyl group at the end of the chain.



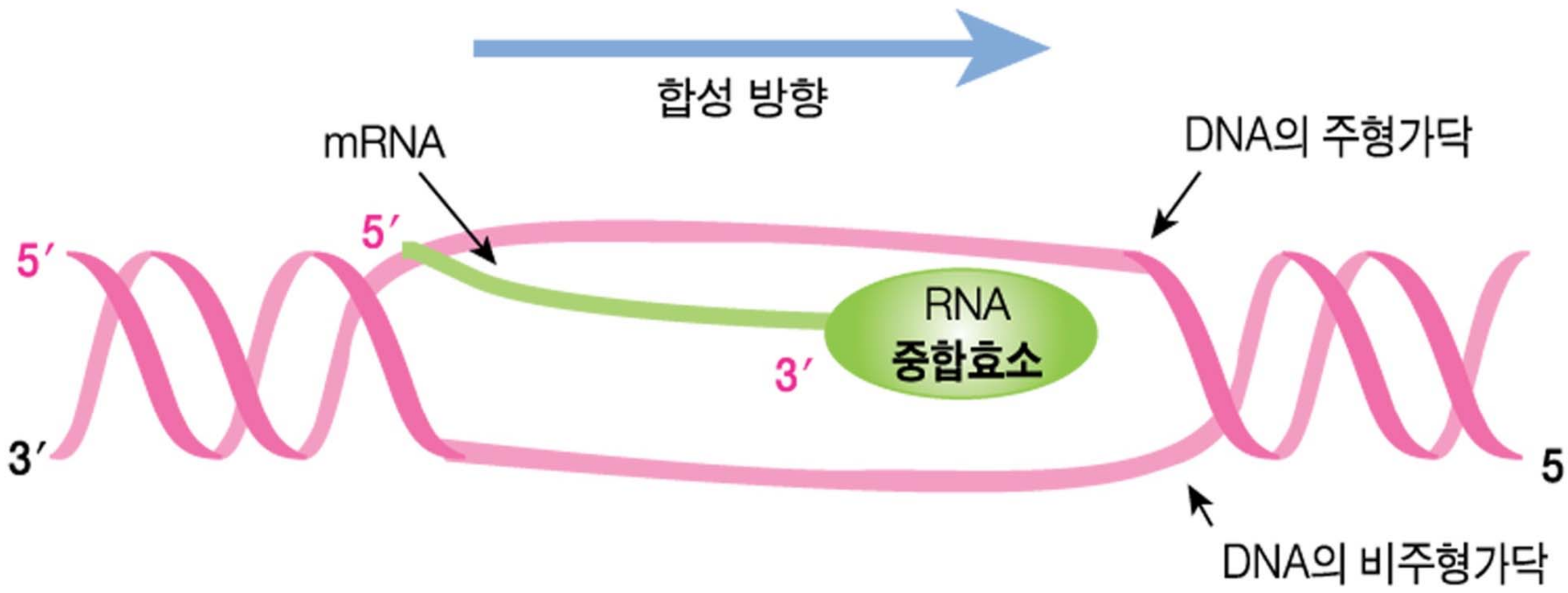
This reaction is catalyzed by enzymes called **RNA polymerases.**

RNA synthesis takes place within a locally unwound segment of DNA, sometimes called a **transcription bubble**, which is produced by RNA polymerase

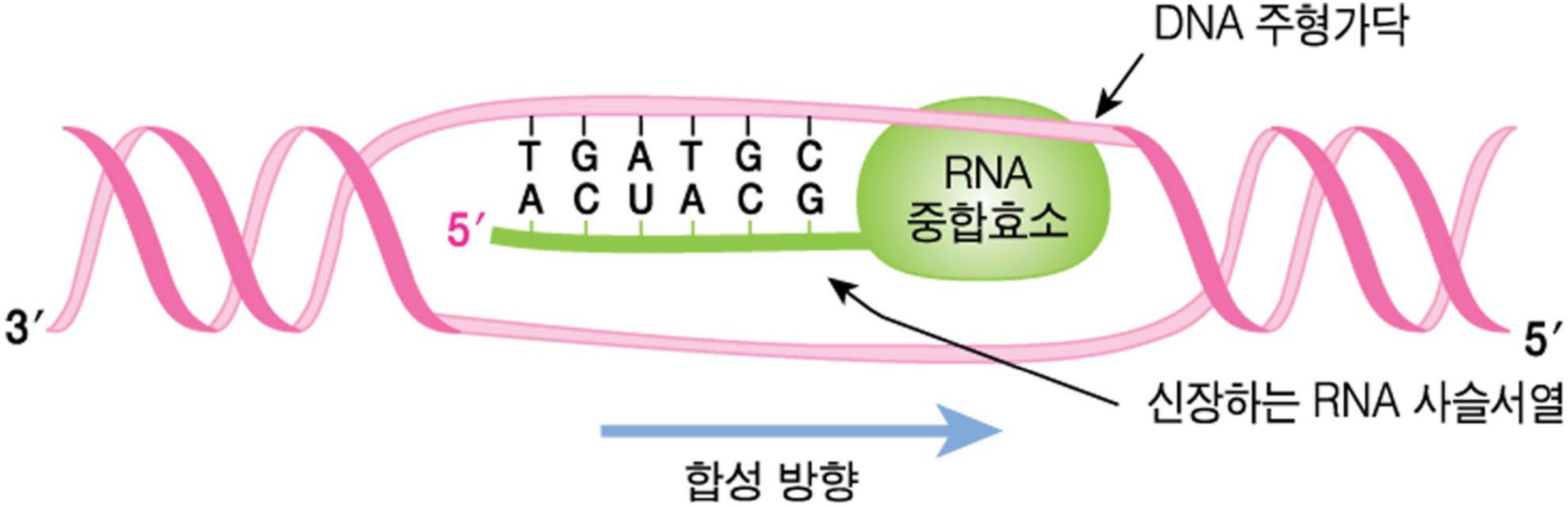




RNAP from *T. aquaticus* pictured during elongation. Prokaryotic RNAP is composed of sigma factor and core enzyme(large and small subunit)



합성 방향
mRNA
DNA의 주형가닥
5′
5′
RNA
중합효소
3′
3′
5′
DNA의 비주형가닥


DNA 주형가닥
T G A T G C
A C U A C G
5′
RNA
중합효소
3′
5′
신장하는 RNA 사슬서열
합성 방향

RNA Synthesis Procedure

1) RNA chain **initiation**

2) RNA chain **elongation**

3) RNA chain **termination**

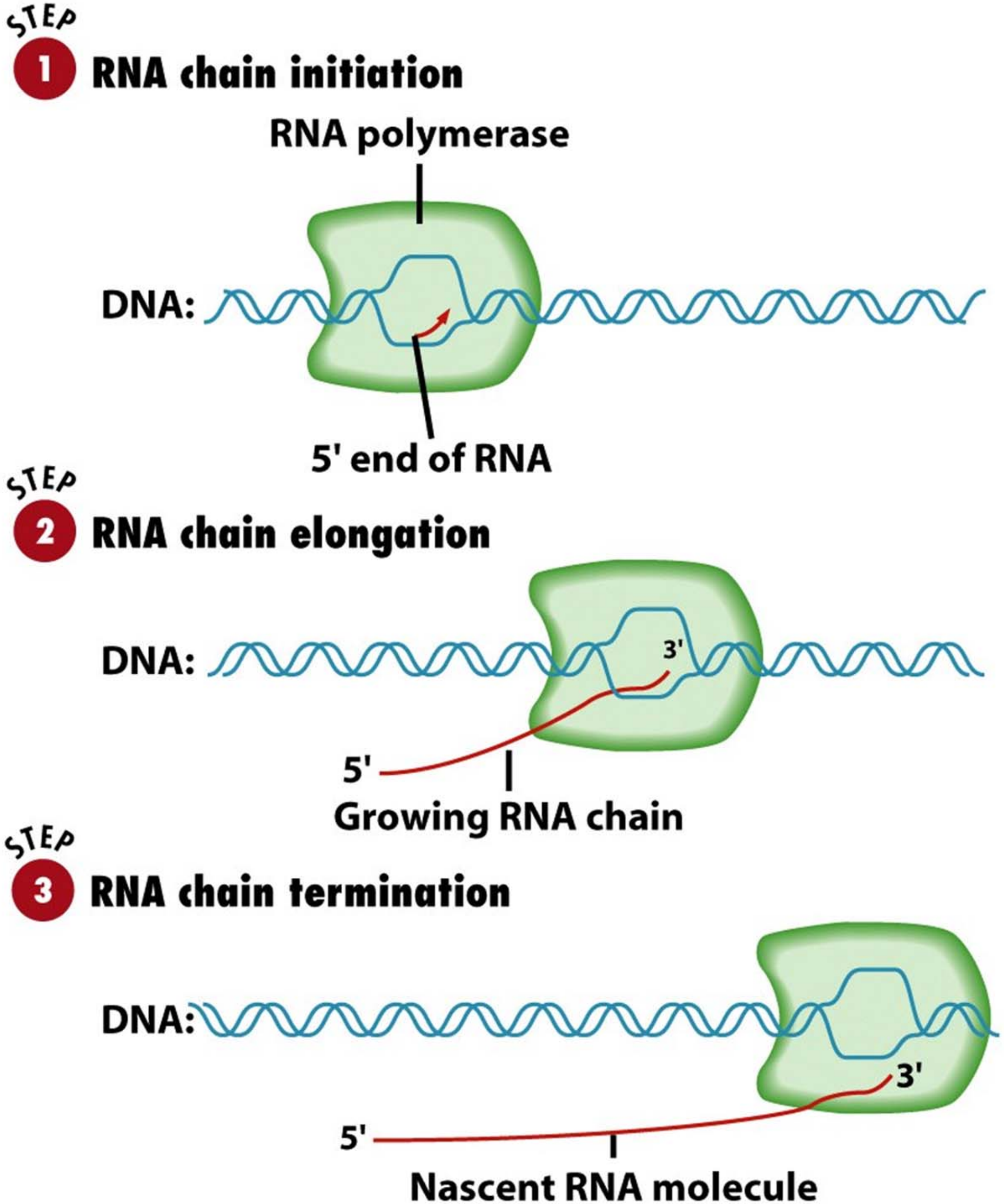


Figure 11-10 Principles of Genetics, 4/e

Initiation of RNA Chains

Initiation of RNA chains involves three steps:

(1) binding of the RNA polymerase holoenzyme to a promoter region in DNA;

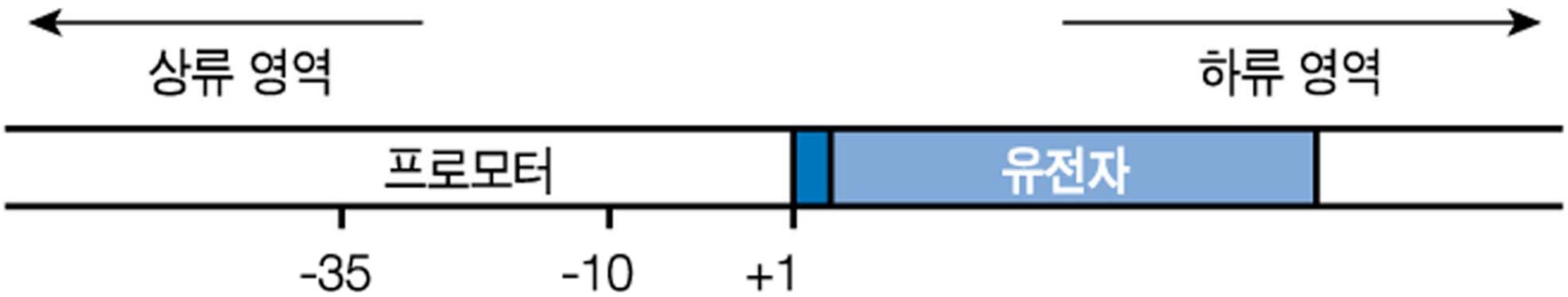
(2) the localized unwinding of the two strands of DNA by RNA polymerase, providing a template strand free to base-pair with incoming ribonucleotides; and

(3) the formation of phosphodiester bonds between the first few ribonucleotides in the nascent RNA chain.

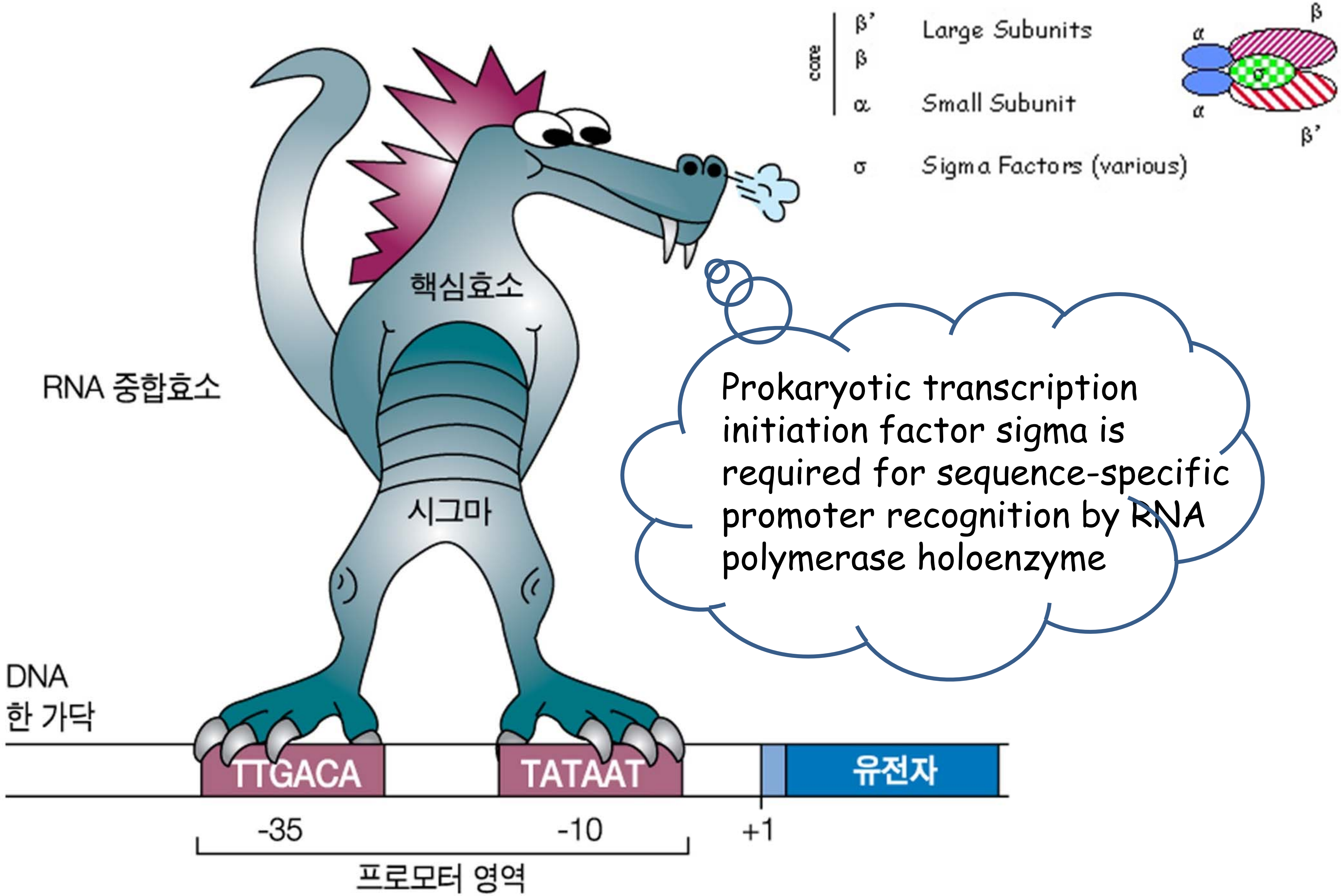
By convention, the nucleotide pairs or nucleotides within and adjacent to transcription units are numbered relative to the transcript initiation site (designated +1)—the nucleotide pair corresponding to the first (5′) nucleotide of the RNA transcript.

Base pairs preceding the initiation site are given minus (–) prefixes; those following (relative to the direction of transcription) the initiation site are given plus (+) prefixes.

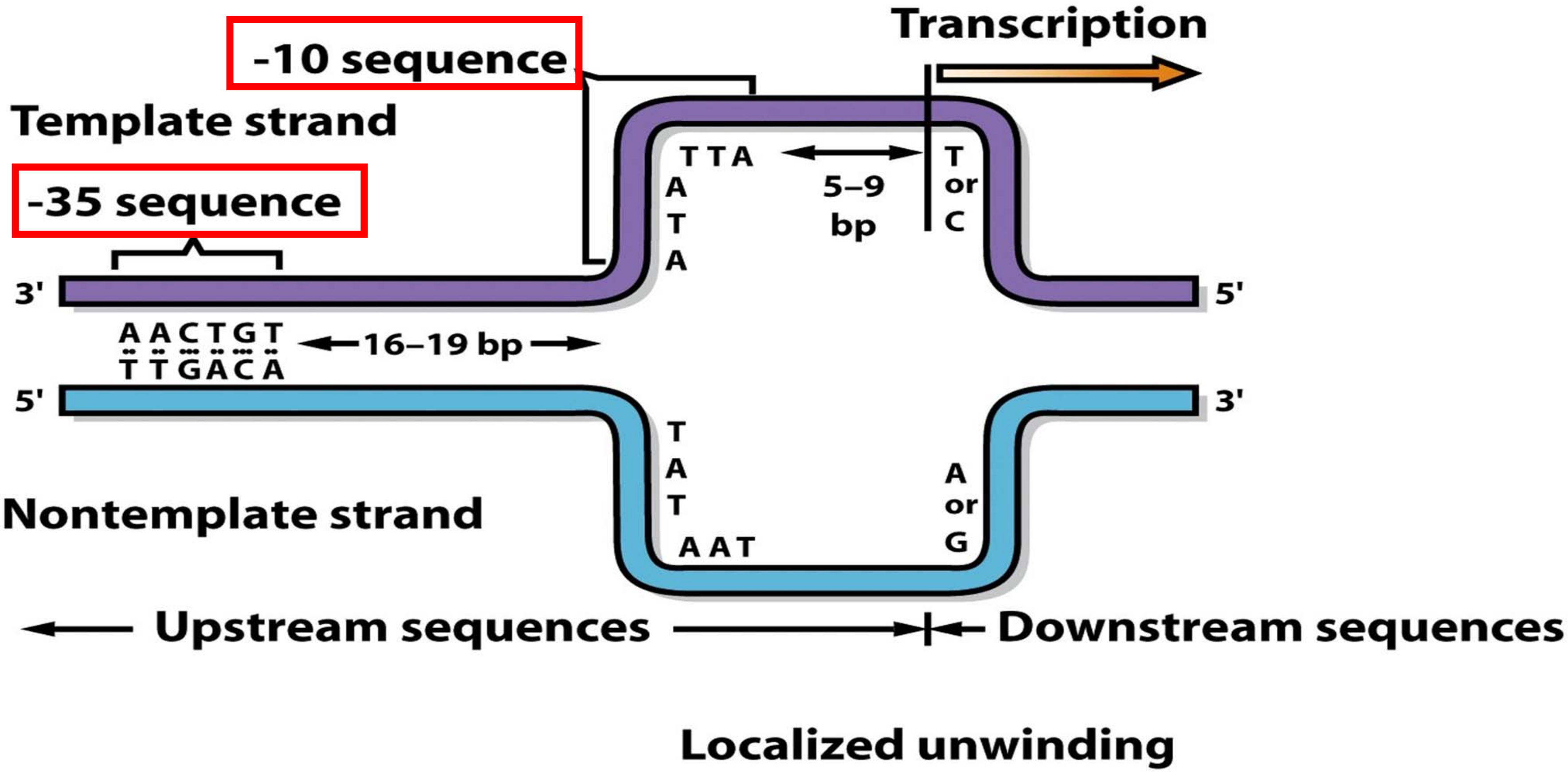
Nucleotide sequences preceding the initiation site are referred to as **upstream sequences**; those following the initiation site are called **downstream sequences.**



상류 영역
하류 영역
프로모터
유전자
-35
-10
+1



RNA 중합효소
핵심효소
시그마
DNA
한 가닥
TTGACA
TATAAT
유전자
-35
-10
+1
프로모터 영역
core
β' β Large Subunits
α Small Subunit
σ Sigma Factors (various)
Prokaryotic transcription initiation factor sigma is required for sequence-specific promoter recognition by RNA polymerase holoenzyme

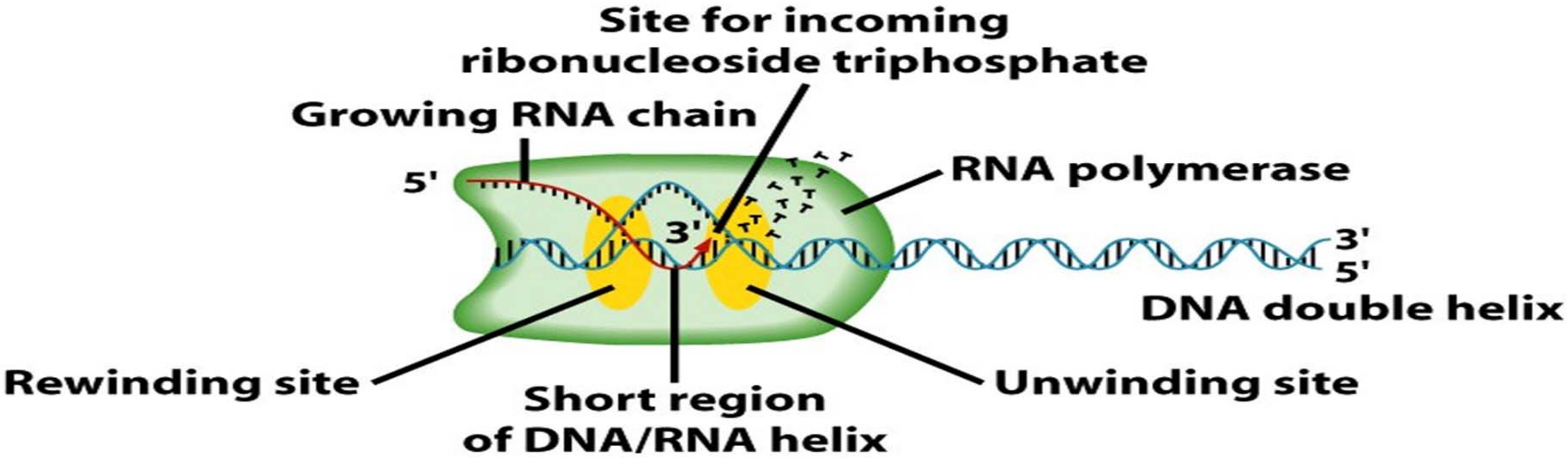


Structure of a typical promoter in *E. coli*. RNA polymerase binds to the −35 sequence of the promoter and initiates unwinding of the DNA strands at the A:T-rich −10 sequence. Transcription begins within the transcription bubble at a site five to nine base pairs beyond the −10 sequence.

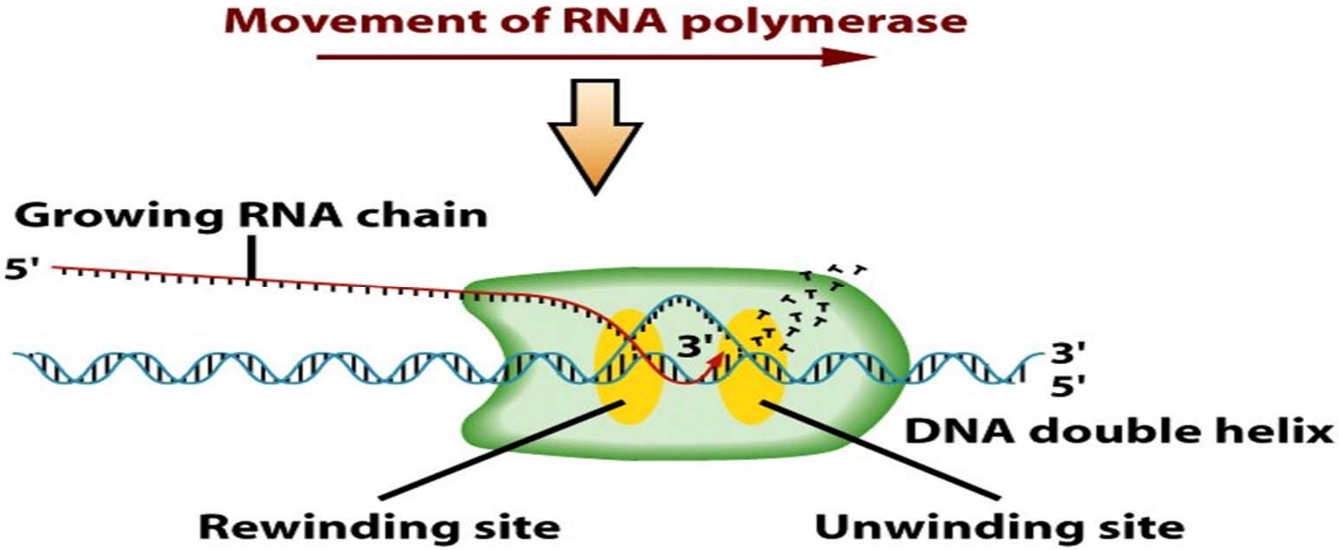
Elongation of RNA Chains

Elongation of RNA chains is catalyzed by the RNA polymerase core enzyme

RNA polymerase continuously unwinds the DNA double helix ahead of the polymerization site and rewinds the complementary DNA strands behind the polymerization site as it moves along the double helix



(a) **RNA polymerase is bound to DNA and is covalently extending the RNA chain.**



(b) **RNA polymerase has moved downstream from its position in *(a)*, processively extending the nascent RNA chain.**

Figure 11-12 Principles of Genetics, 4/e

Termination of RNA Chains

Termination of RNA chains occurs when RNA polymerase encounters a **termination signal**. When it does, the transcription complex dissociates, releasing the nascent RNA molecule.

core enzyme stops at the terminator sequence (two inverted repeats and poly As) at the end of the gene

Terminator sequences contain a G:C-rich region followed by at least six A:T base pairs with A's present.

역위 반복

DNA:

비주형가닥 ATTA - TAGCGGCCATC - ACTGTTACA - GATGGCCGCTA - TTTTTTT

주형가닥 TAAT - ATCGCCGGTAG - TGACAATGT - CTACCGGCGAT - AAAAAAA

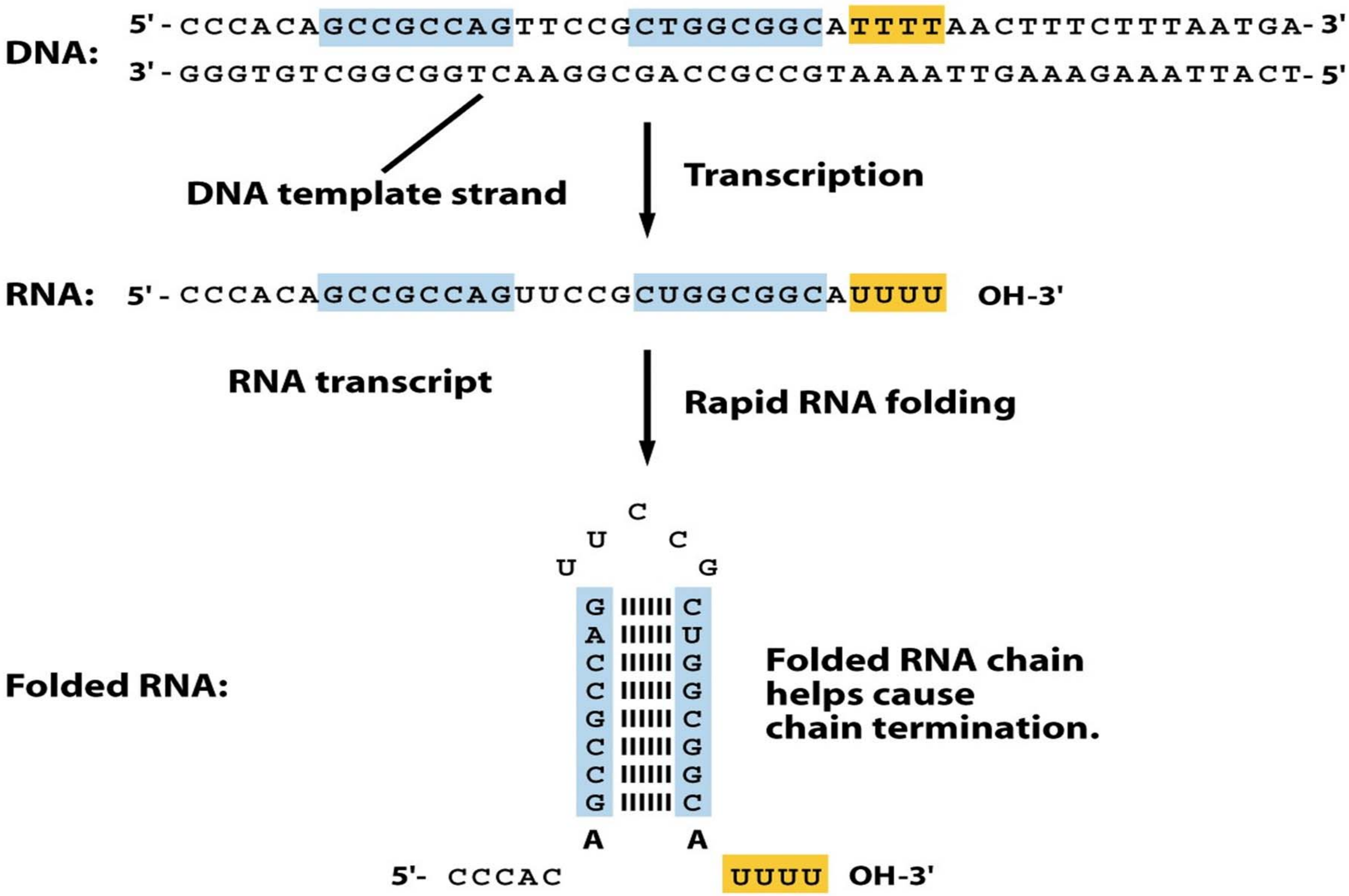
전사

전령 RNA
(T 대신 U가 삽입 됨을 기억하기)

5′ AUUA - UAGCGGCCAUC - ACUGUUACA - GAUGGCCGCUA - UUUUUUU 3′

Palindrome sequence (inverted repeat) as termination signal

Hairpin (stem and loop) structure formation by palindrome sequence



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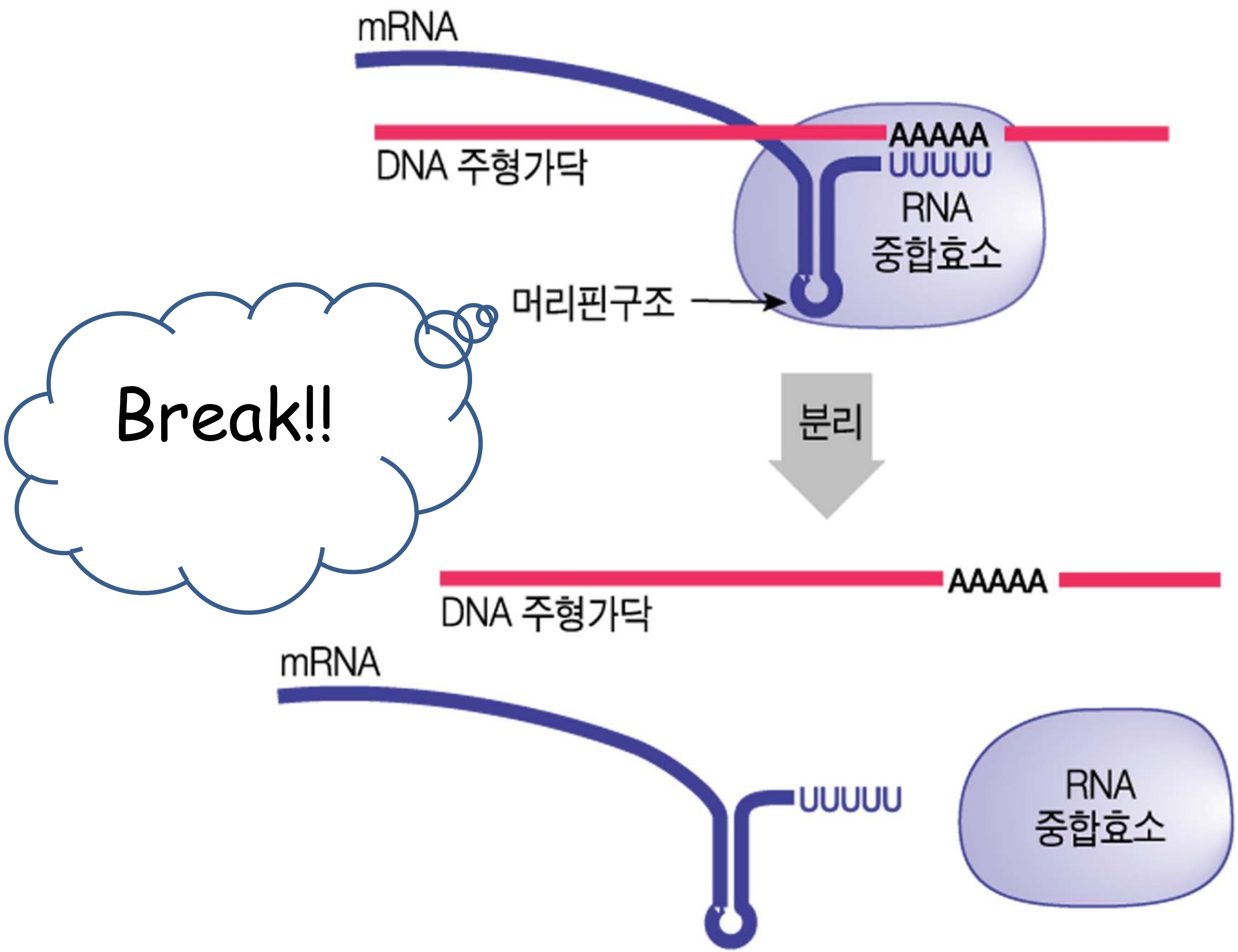

Releasing of newly synthesized nascent RNA molecular