**Chapter 26 RNA Metabolism**

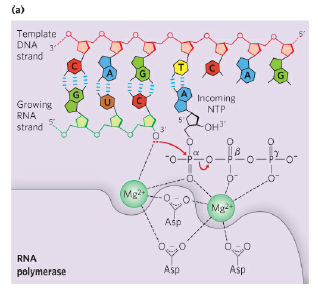
* All RNA molecules except the RNA genomes of certain viruses are derived from information permanently stored in DNA.
* During **transcription**, an enzyme system converts the genetic information in a segment of double-stranded DNA into an RNA strand with a base sequence complementary to one of the DNA strands.
* Three major kinds of RNA are produced.
* **Messenger RNAs (mRNAs)** encode the amino acid sequence of one or more polypeptides speciﬁed by a gene or set of genes.
* **Transfer RNAs (tRNAs)** read the information encoded in the mRNA and transfer the appropriate amino acid to a growing polypeptide chain during protein synthesis.
* **Ribosomal RNAs (rRNAs)** are constituents of ribosomes that synthesize proteins.
* During replication the entire chromosome is usually copied, but transcription is more selective.
* Only particular genes or groups of genes are transcribed at any one time, and some portions of the DNA genome are never transcribed.
* Speciﬁc regulatory sequences mark the beginning and end of the DNA segments to be transcribed and designate which strand in duplex DNA is to be used as the template.

**26.1 DNA-Dependent Synthesis of RNA**

* Transcription has initiation, elongation, and termination phases.

**RNA Is Synthesized by RNA Polymerases**

* *E. coli* RNA polymerase helped to define the fundamental properties of transcription.
* **DNA-dependent RNA polymerase** requires, in addition to a DNA template, all four ribonucleoside 5’-triphosphates (ATP, GTP, UTP, and CTP) as precursors of the nucleotide units of RNA **(Fig. 26–1a)**.

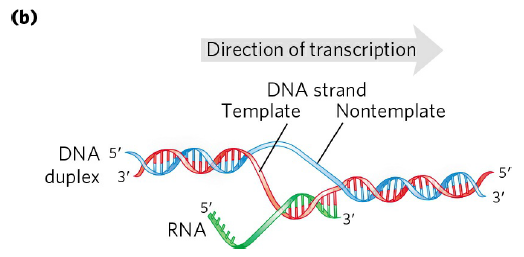


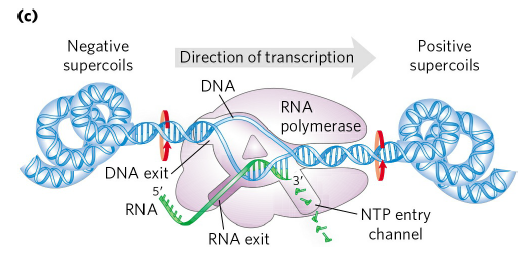
* RNA polymerase elongates an RNA strand by adding ribonucleotide units to the 3’- hydroxyl end, building RNA in the 5’  3’ direction.
* The overall reaction is

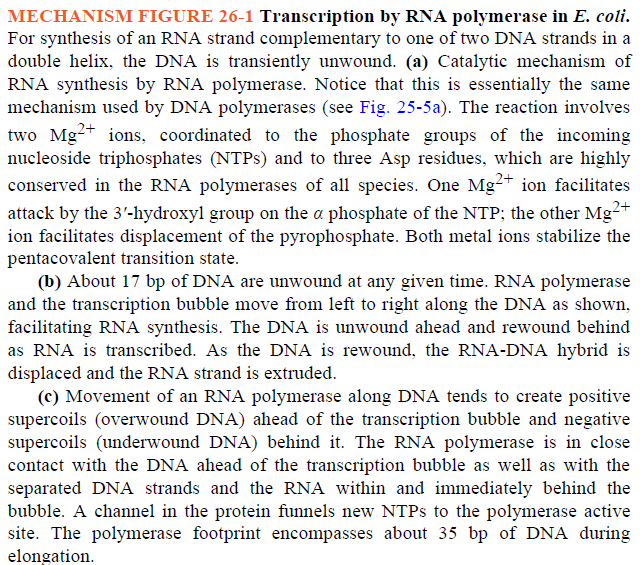
(NMP)*n +* NTP  (NMP)*n*+1 + PPi

RNA Lengthened RNA

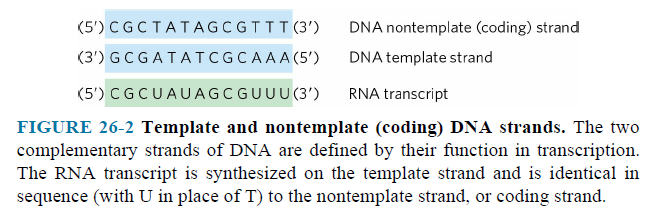
* The two complementary DNA strands have different roles in transcription **(Fig. 26–1b, c)**.



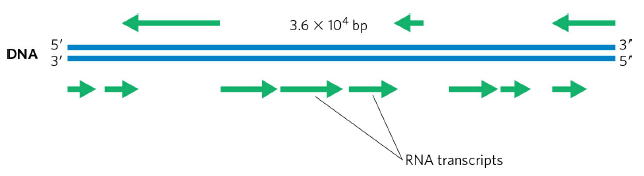


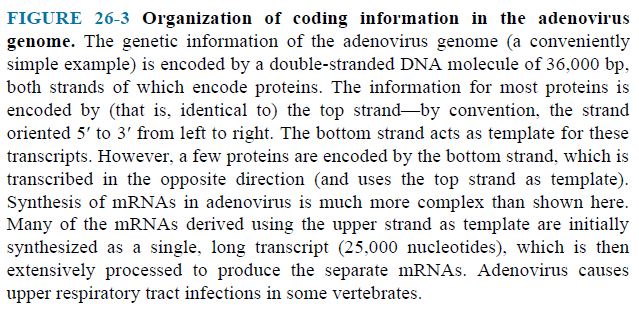


* The strand that serves as template for RNA synthesis is called the **template strand**.
* The DNA strand complementary to the template, the **nontemplate strand**, or **coding strand**,
  + is identical in base sequence to the RNA transcribed from the gene, with U in the RNA in place of T in the DNA **(Fig. 26–2)**.

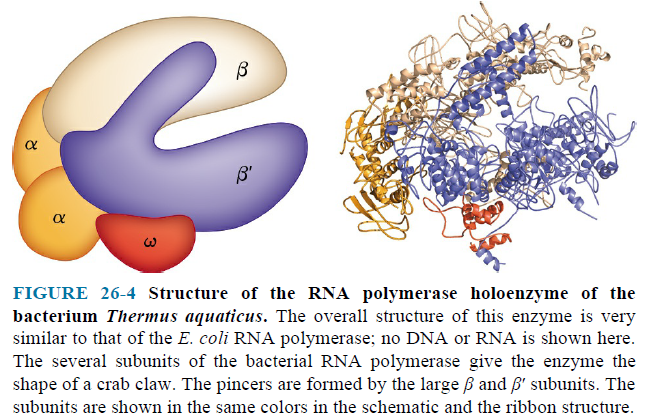


* The coding strand for a particular gene may be located in either strand of a given chromosome **(Fig. 26–3)**.





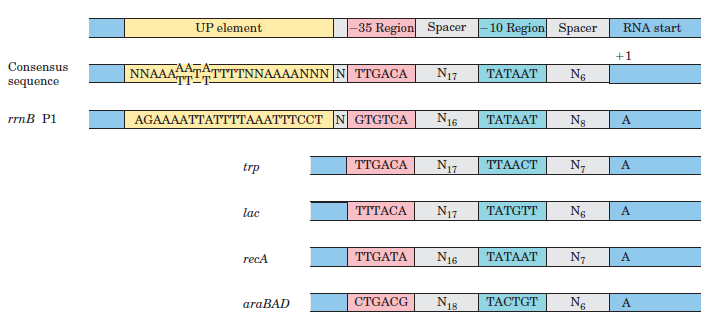
* The template DNA strand is copied in the 3’  5’ direction (antiparallel to the new RNA strand).
* Each nucleotide in the newly formed RNA is selected by base-pairing interactions; U residues are inserted in the RNA to pair with A residues in the DNA template, G residues are inserted to pair with C residues, and so on.
* Unlike DNA polymerase, RNA polymerase does not require a primer to initiate synthesis.
* Initiation occurs when RNA polymerase binds at specific DNA sequences called **promoters**.
* During the elongation phase of transcription, the growing end of the new RNA strand base-pairs temporarily with the DNA template to form a short hybrid RNA-DNA double helix, estimated to be 8 bp long **(Fig. 26–1b, c)**.
* Elongation of a transcript by *E. coli* RNA polymerase proceeds at a rate of 50 to 90 nucleotides/s.
* The DNA-dependent RNA polymerase of *E. coli* is a large, complex enzyme with ﬁve core subunits (') and a sixth subunit, one of a group designated  **(Fig. 26–4)**

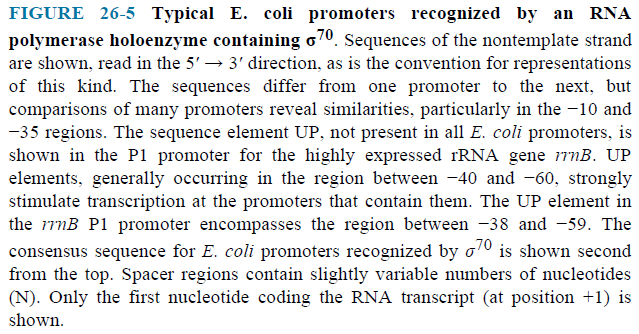


* The subunit binds transiently to the core and directs the enzyme to speciﬁc binding sites on the DNA.
* These six subunits constitute the RNA polymerase holoenzyme.

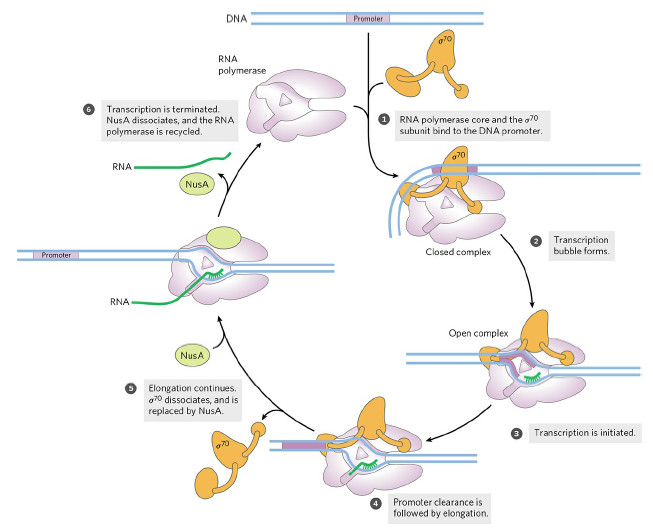
**RNA Synthesis Begins at Promoters**

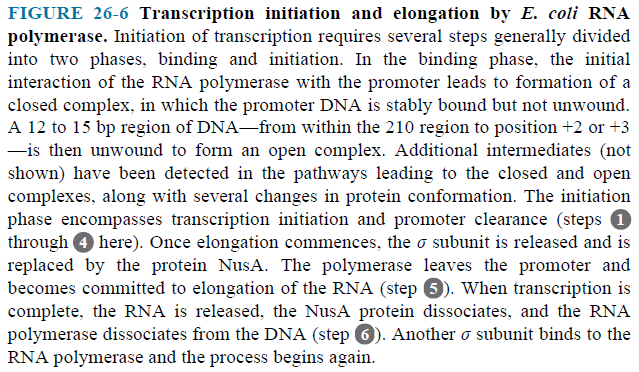
* RNA polymerase binds to speciﬁc sequences in the DNA called **promoters**.
* The promoter region extends between positions -70 and +30.
* Bacterial promoters have similarities in two short sequences centered about positions -10 and -35.
* These sequences of the nontemplate strand, read in the 5’  3’ direction, are important interaction sites for the subunit **(Fig. 26–5)**.





* The consensus sequence at the -10 region is (5’)TATAAT(3’); the consensus sequence at the -35 region is (5’)TTGACA(3’).
* RNA polymerase core binds to the DNA promoter **(Fig. 26–6)**.
* Transcription bubble forms.
* Transcription is initiated.
* Promoter clearance is followed by elongation.
* Elongation continues.  dissociates, and is replaced by protein NusA.
* Transcription is terminated. NusA dissociates, and the RNA polymerase is recycled.
* factor can again bind to the enzyme to initiate transcription.



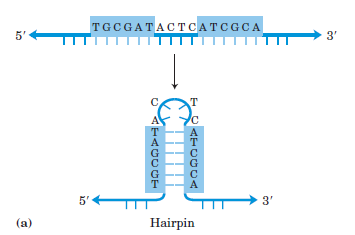


**Transcription Is Regulated at Several Levels**

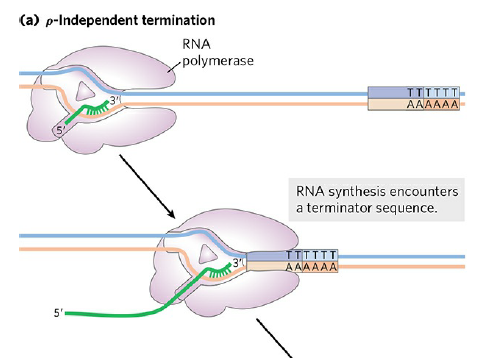
* Regulation can occur at any step in transcription, including elongation and termination.
* The binding of proteins to sequences both near to and distant from the promoter can also affect levels of gene expression.
* Protein binding can *activate* transcription by facilitating either RNA polymerase binding or steps further along in the initiation process, or it can *repress* transcription by blocking the activity of the polymerase.
* In *E. coli*, one protein that activates transcription is the **cAMP receptor protein (CRP)**, which increases the transcription of genes coding for enzymes.
* **Repressors** are proteins that block the synthesis of RNA at specific genes.

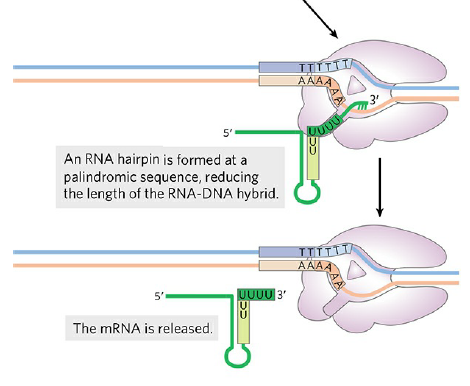
**Specific Sequences Signal Termination of RNA Synthesis**

* *E. coli* has at least two classes of termination signals: one class relies on a protein factor called  (rho) and the other is -independent.
* Most  -independent terminators have two distinguishing features.
* The first is a region that produces an RNA transcript with self-complementary sequences, permitting the formation of a hairpin structure centered 15 to 20 nucleotides before the projected end of the RNA strand **(Fig. 8–19a)**.

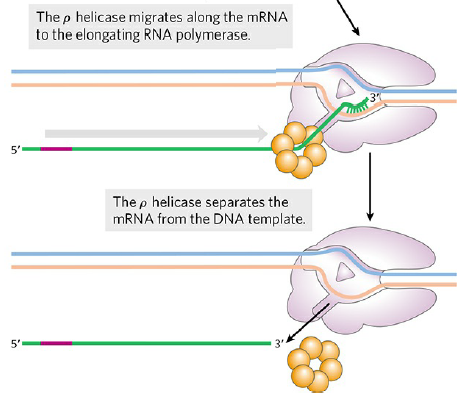
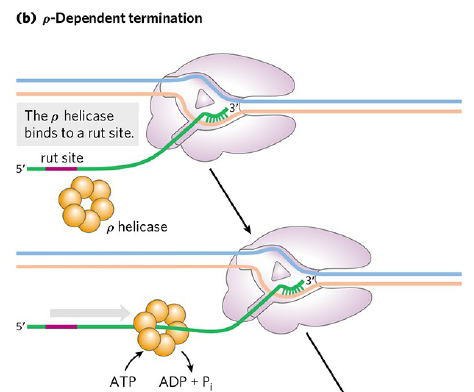


* The second feature is a highly conserved string of three A residues in the template strand that are transcribed into U residues near the 3’ end of the hairpin **(Fig. 26–7a)**.
* When a polymerase arrives at a termination site with this structure, it pauses.
* Formation of the hairpin structure in the RNA disrupts several A=U base pairs in the RNA-DNA hybrid segment and may disrupt important interactions between RNA and the RNA polymerase, facilitating dissociation of the transcript.





* The -dependent terminators lack the sequence of repeated A residues in the template strand but usually include a CA-rich sequence called a *rut* (rho utilization) element **(Fig. 26–7b)**.



* The protein associates with the RNA at specific binding sites and migrates in the 5’  3’ direction until it reaches the transcription complex that is paused at a termination site.
* Here it contributes to release of the RNA transcript.

**Eukaryotic Cells Have Three Kinds of Nuclear RNA Polymerases**

* RNA polymerases are designated RNA Pol I, RNA Pol II and RNA Pol III.
* RNA Pol I is responsible for the synthesis of rRNAs (5.8S, 18S and 28S rRNAs).
* RNA Pol II is responsible for the synthesis of mRNAs.
* RNA Pol III is responsible for the synthesis of tRNAs and 5S rRNA.

**RNA Polymerases Require Many Other Protein Factors for Its Activity**

* The other proteins are called **general** **transcription factors**.
* Transcription factors are required for initiation of transcription at the RNA polymerase promoters.