تنظیم بیان ژن

زیست شناسی مولکولی

منابع:

بیوشیمی لنینجر، ژنوم ۳

Molecular biology, Weaver

Genetics, Brooker

فرآیند های تاثیر گذار بر غلظت پروتئین

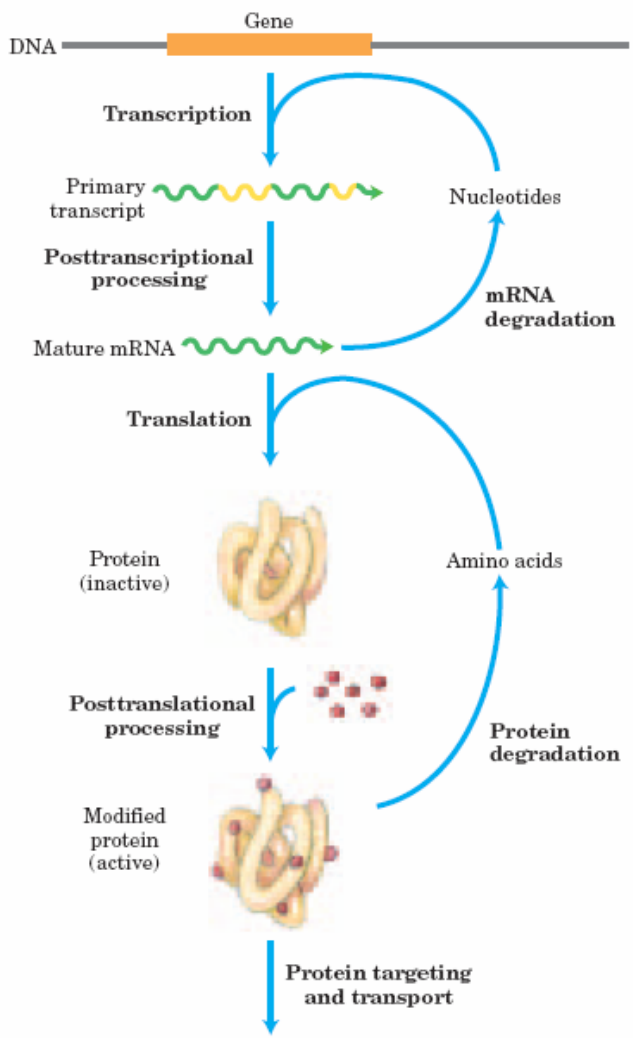


FIGURE 28–1 **Seven processes that affect the steady-state concentration of a protein.** Each process has several potential points of regulation.

انواع بیان ژن

- بیان دائمی ژن (constitutive gene expression)
  - Housekeeping genes –
- بیان تنظیم شده ژن (regulated gene expression)
  - Inducible – (آنزیم های متابولیسم لاکتوز، ترمیم DNA)
  - Repressible – (اپران تریپتوفان)

تنظیم شروع رونویسی

- تفاوت در توالی پروموتر ژنها
- تفاوت در توالی پروموتر ژنها = تنظیم میزان مناسب محصول ژن

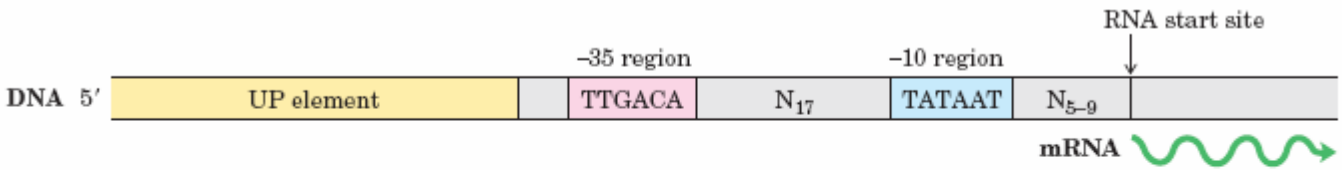


FIGURE 28–2 Consensus sequence for many *E. coli* promoters. Most base substitutions in the −10 and −35 regions have a negative effect on promoter function. Some promoters also include the UP (*u*pstream *p*romoter) element (see Fig. 26–5). By convention, DNA sequences are shown as they exist in the nontemplate strand, with the 5′ terminus on the left. Nucleotides are numbered from the transcription start site, with positive numbers to the right (in the direction of transcription) and negative numbers to the left. N indicates any nucleotide.

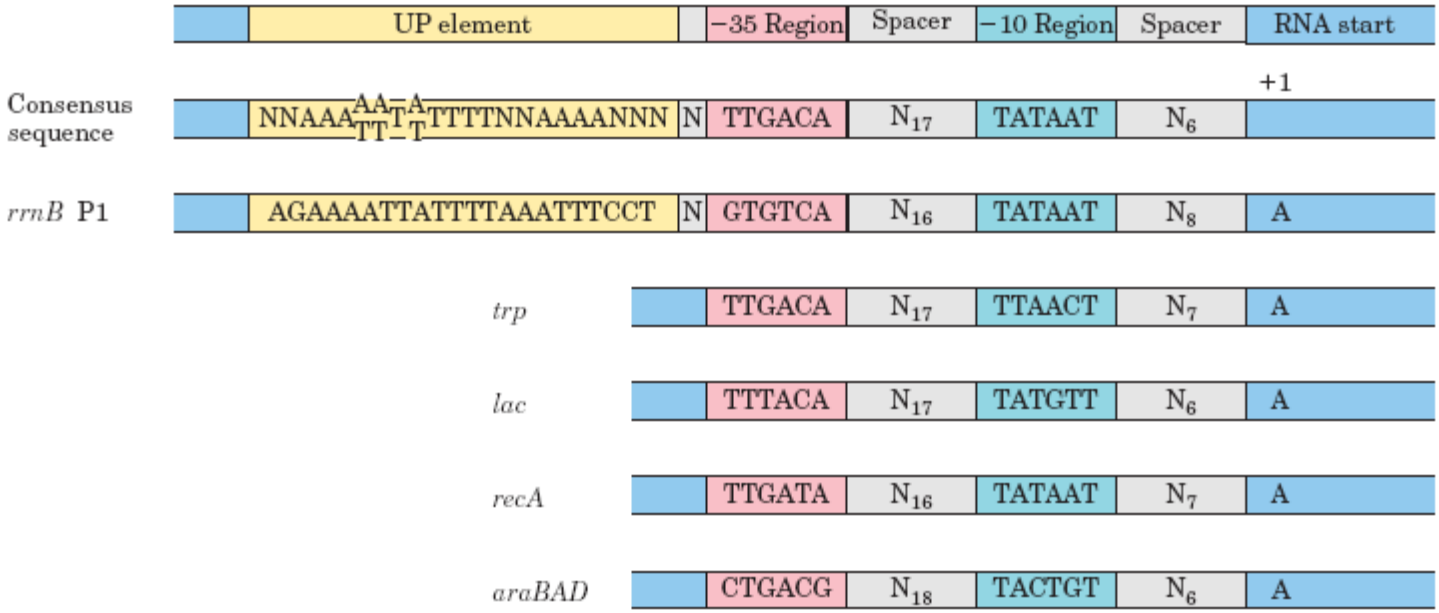


FIGURE 26–5 Typical *E. coli* promoters recognized by an RNA polymerase holoenzyme containing σ^{70}. Sequences of the nontemplate strand are shown, read in the 5′⟶3′ direction, as is the convention for representations of this kind. The sequences vary from one promoter to the next, but comparisons of many promoters reveal similarities, particularly in the −10 and −35 regions. The sequence element UP, not present in all *E. coli* promoters, is shown in the P1 promoter for the highly expressed rRNA gene *rrnB*. UP elements, generally occurring in the region between −40 and −60, strongly stimulate transcription at the promoters that contain them. The UP element in the *rrnB* P1 promoter encompasses the region between −38 and −59. The consensus sequence for *E. coli* promoters recognized by σ^{70} is shown second from the top. Spacer regions contain slightly variable numbers of nucleotides (N). Only the first nucleotide coding the RNA transcript (at position +1) is shown.

تنظیم شروع رونویسی

- پروتئین های درگیر:
  - فاکتور های رونویسی خاص (specifity factors)
  - رپرسور ها (repressors)
    - تنظیم منفی
  - فعال کننده ها (activators)
    - تنظیم مثبت

توالی پروموتر ژنهای شوک حرارتی

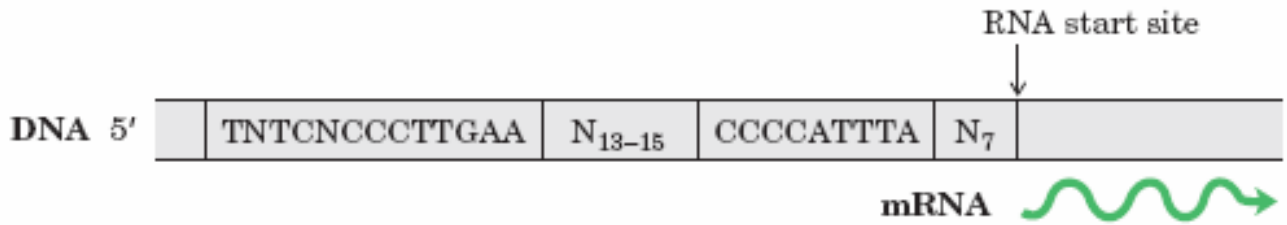
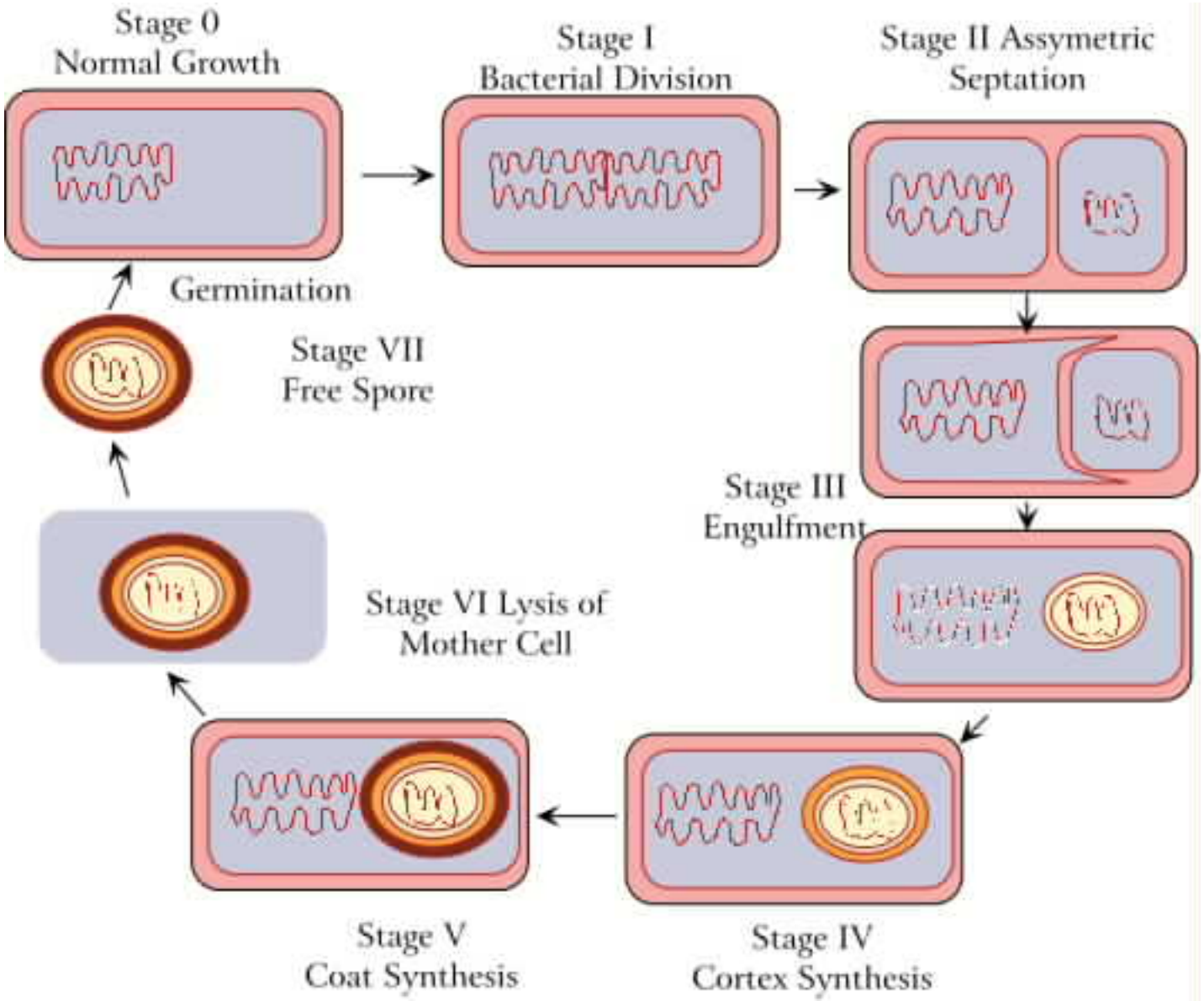


FIGURE 28–3 **Consensus sequence for promoters that regulate expression of the *E. coli* heat-shock genes.** This system responds to temperature increases as well as some other environmental stresses, resulting in the induction of a set of proteins. Binding of RNA polymerase to heat-shock promoters is mediated by a specialized σ subunit of the polymerase, σ^{32}, which replaces σ^{70} in the RNA polymerase initiation complex.


Stage 0
Normal Growth
Stage I
Bacterial Division
Stage II Assymetric
Septation
Germination
Stage VII
Free Spore
Stage III
Engulfment
Stage VI Lysis of
Mother Cell
Stage V
Coat Synthesis
Stage IV
Cortex Synthesis

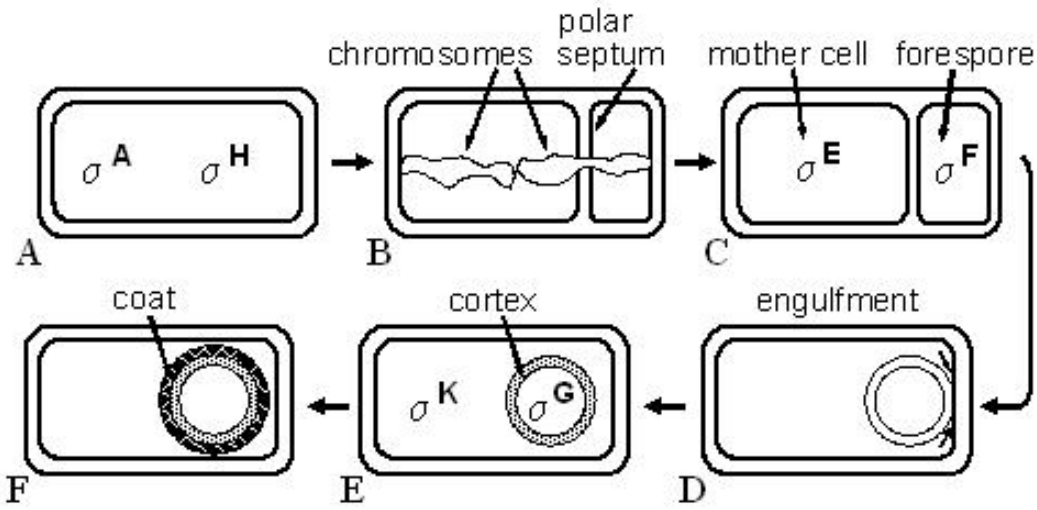


Fig. 1. Morphological changes during B. subtilis sporulation, and the approximate time and location at which different σ factors become active. (A) σ^A and σ^H RNA polymerase transcribe genes whose products cause polar septation and axial filament formation. (B) The axial filament consists of two chromosomes extending the length of the cell with their replication origin proximal regions attached at opposite ends of the cell. The polar septum forms around the axial filament, capturing one-third of one chromosome in the forespore. The remaining two-thirds of that chromosome is translocated into the forespore. (C) Upon completion of polar septation, σ^F becomes active in the forespore, and this leads to activation of σ^E in the mother cell. (D) Products of genes under σ^F and σ^E control drive migration of the septal membranes around the forespore in the phagocytic-like process of engulfment. (E) Completion of engulfment pinches off the forespore as a free protoplast within the mother cell. Two membranes surround the forespore and separate its contents from the mother cell cytoplasm. σ^G becomes active in the forespore, leading to activation of σ^K in the mother cell. Primarily, genes under σ^E and σ^K control cause synthesis of a loosely crosslinked peptidoglycan termed cortex, between the two membranes surrounding the forespore, and (F) synthesis of proteins that assemble on the surface of the forespore to produce the spore coat. Not shown are subsequent steps which include spore maturation and release of the spore via lysis of the mother cell. From Kroos and Maddock (2003) J. Bacteriol. 185:1128-1146.

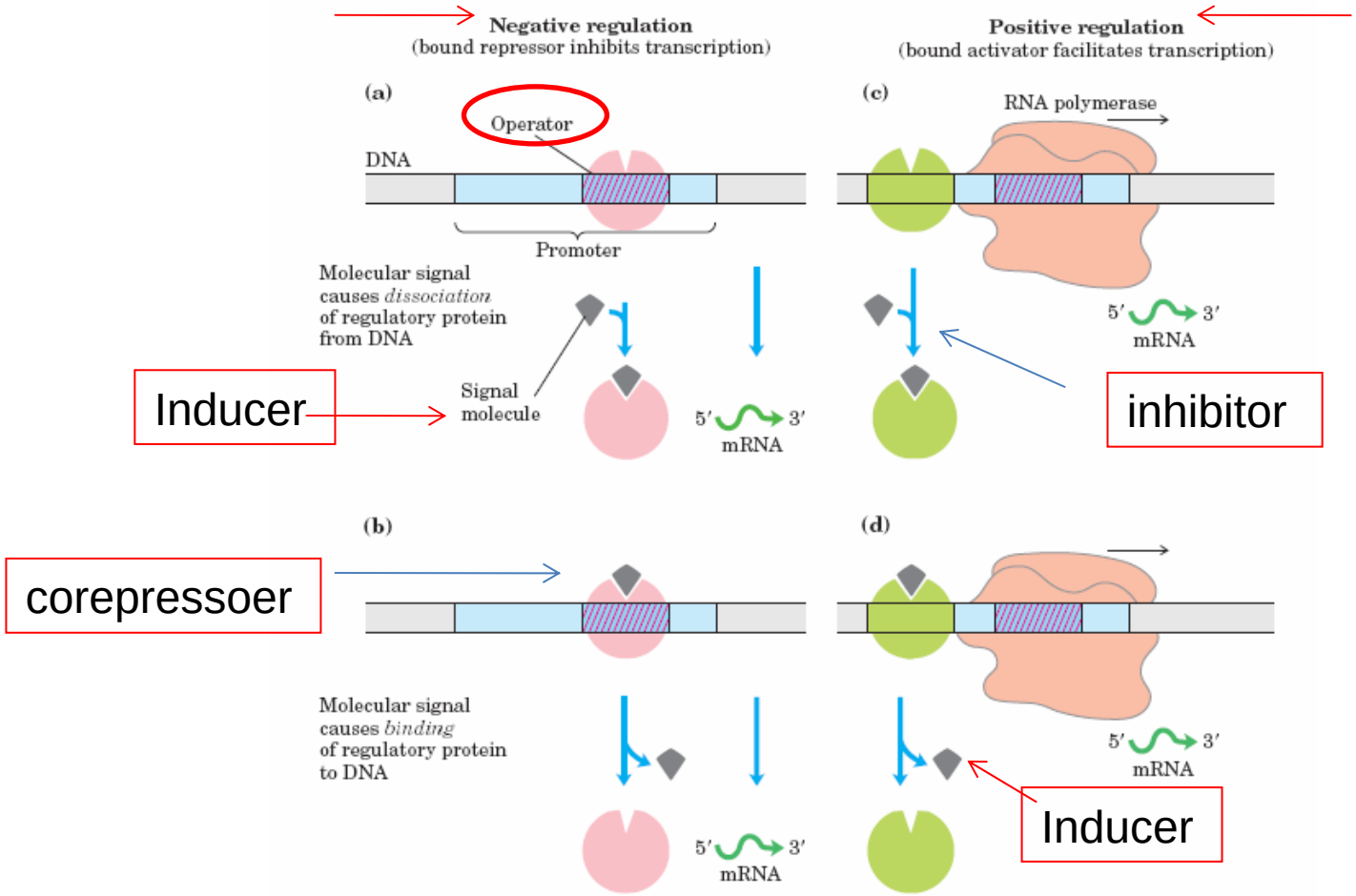


FIGURE 28–4 Common patterns of regulation of transcription initiation. Two types of negative regulation are illustrated. **(a)** Repressor

lecular signal and transcription proceeds; when the signal is added, the activator dissociates and transcription is inhibited. **(d)** Activator

اپرون پروکاریوتی

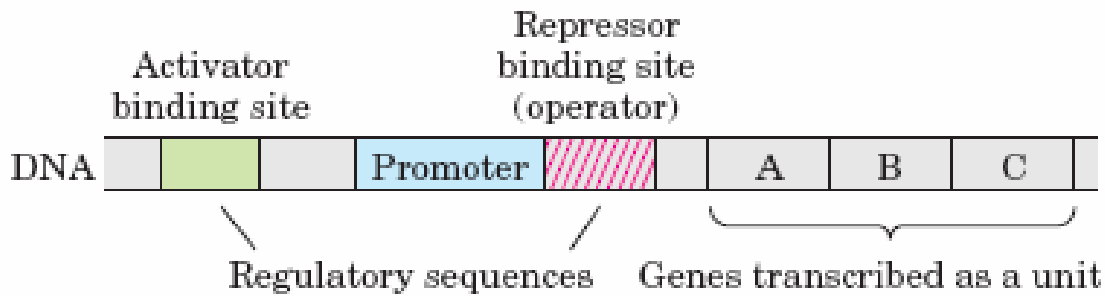
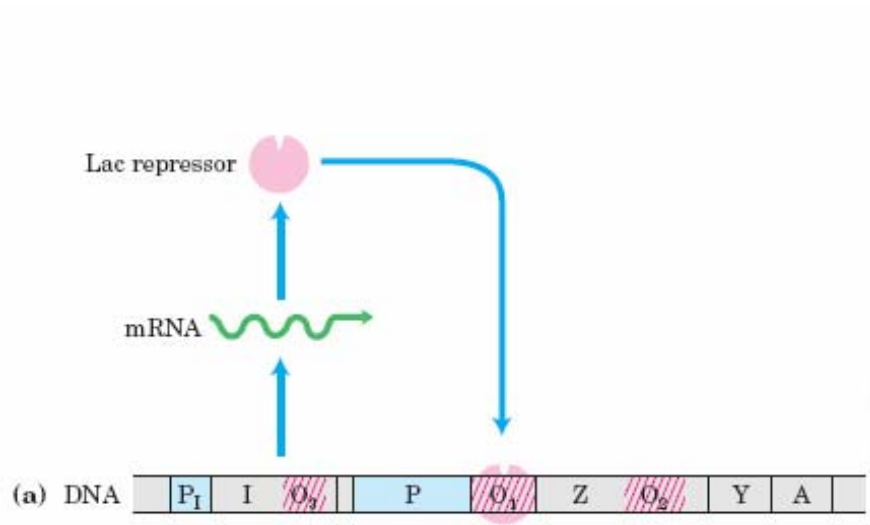


FIGURE 28–5 **Representative prokaryotic operon.** Genes A, B, and C are transcribed on one polycistronic mRNA. Typical regulatory sequences include binding sites for proteins that either activate or repress transcription from the promoter.

تنظیم منفی اپرون *lac*



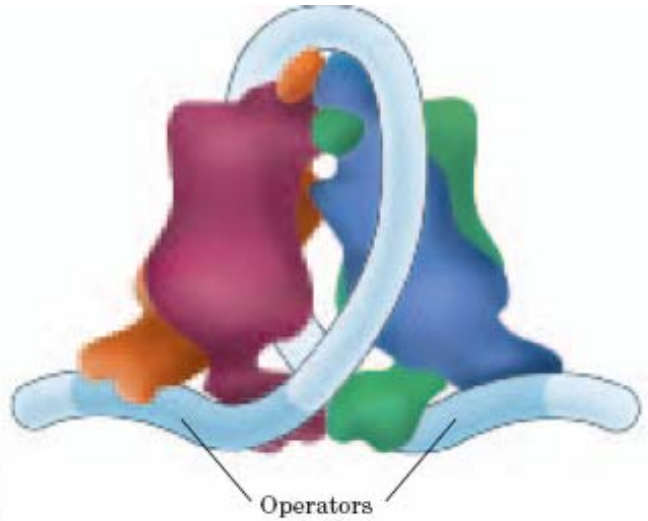


FIGURE 28–7 The *lac* operon. **(a)** The *lac* operon in the repressed state. The *I* gene encodes the Lac repressor. The *lac Z, Y,* and *A* genes encode β-galactosidase, galactoside permease, and thiogalactoside transacetylase, respectively. P is the promoter for the *lac* genes, and P_I is the promoter for the *I* gene. O_1 is the main operator for the *lac* operon; O_2 and O_3 are secondary operator sites of lesser affinity for the Lac repressor. **(b)** The Lac repressor binds to the main operator and O_2 or O_3, apparently forming a loop in the DNA that might wrap around the repressor as shown. **(c)** Lac repressor bound to DNA (de-

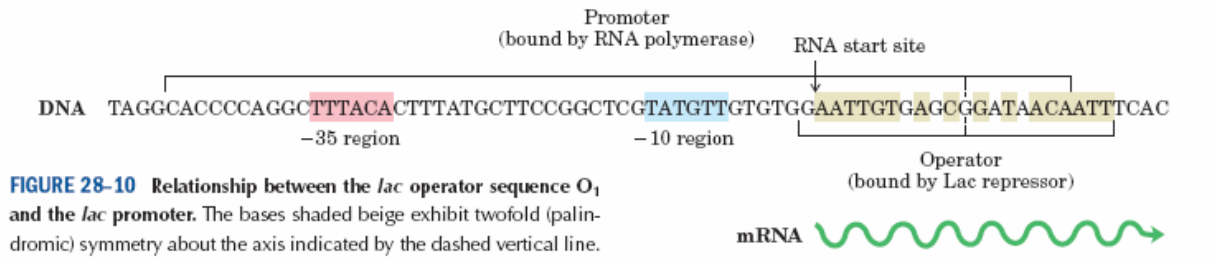


FIGURE 28–10 Relationship between the *lac* operator sequence O_1 and the *lac* promoter. The bases shaded beige exhibit twofold (palindromic) symmetry about the axis indicated by the dashed vertical line.

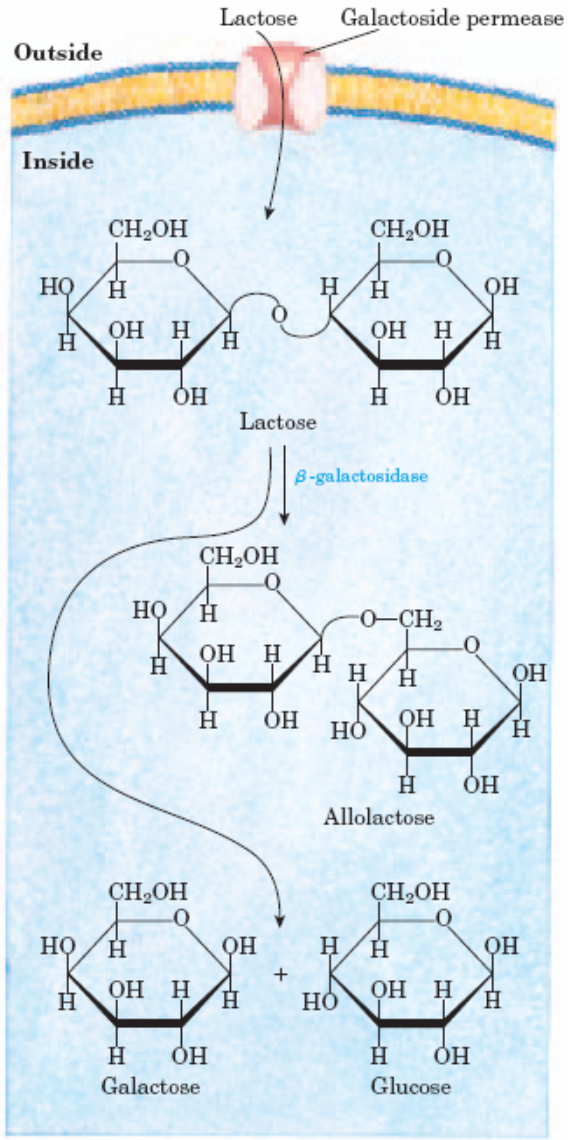


FIGURE 28–6 **Lactose metabolism in *E. coli*.** Uptake and metabolism of lactose require the activities of galactoside permease and β-galactosidase. Conversion of lactose to allolactose by transglycosylation is a minor reaction also catalyzed by β-galactosidase.

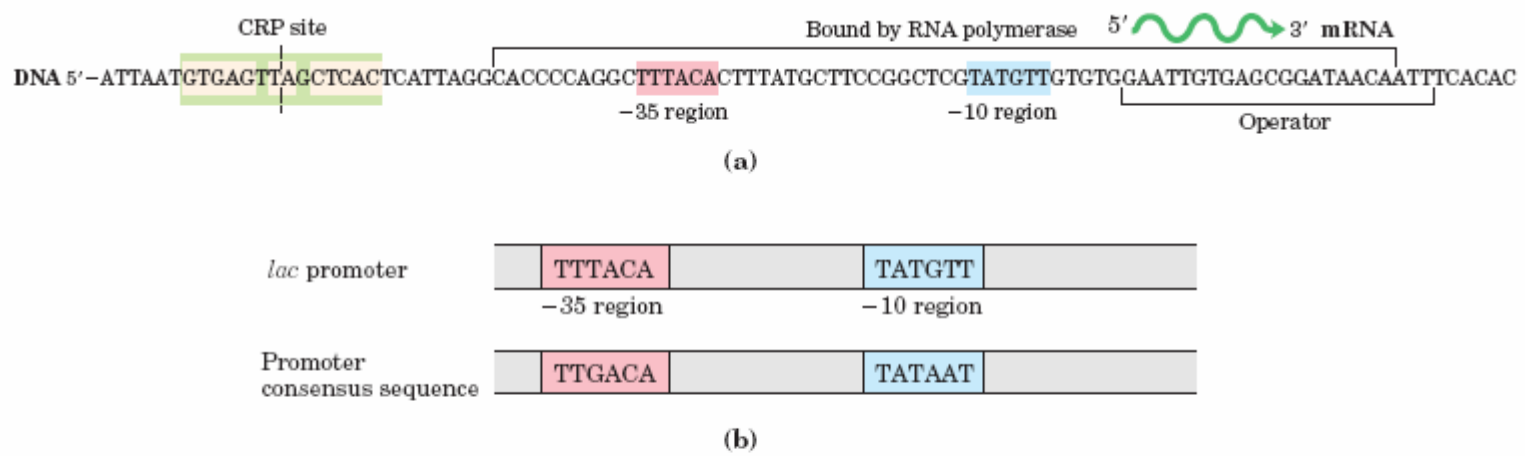


FIGURE 28–17 **Activation of transcription of the *lac* operon by CRP.** **(a)** The binding site for CRP-cAMP is near the promoter. As in the case of the *lac* operator, the CRP site has twofold symmetry (bases shaded beige) about the axis indicated by the dashed line. **(b)** Sequence of the *lac* promoter compared with the promoter consensus sequence. The differences mean that RNA polymerase binds relatively weakly to the *lac* promoter until the polymerase is activated by CRP-cAMP.

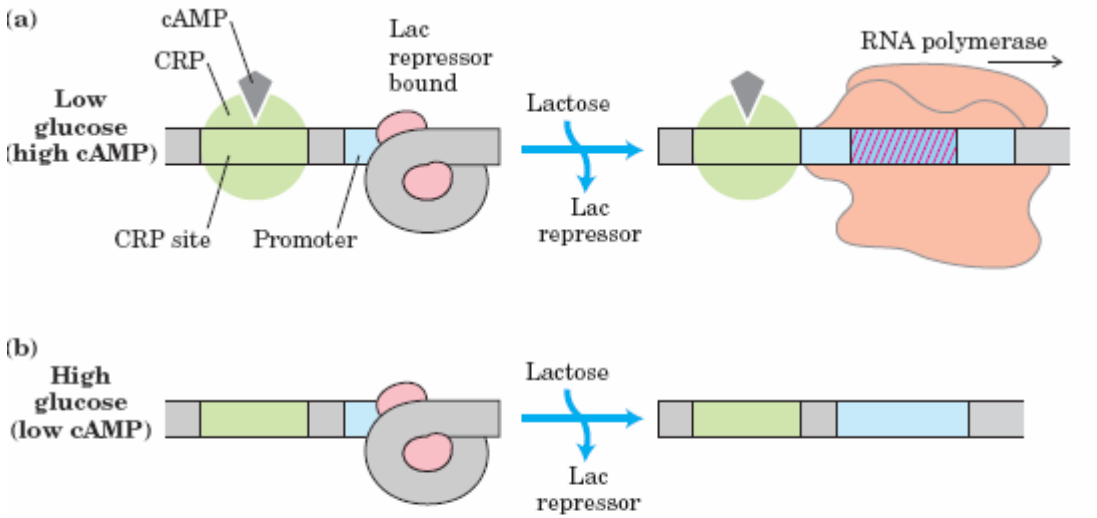
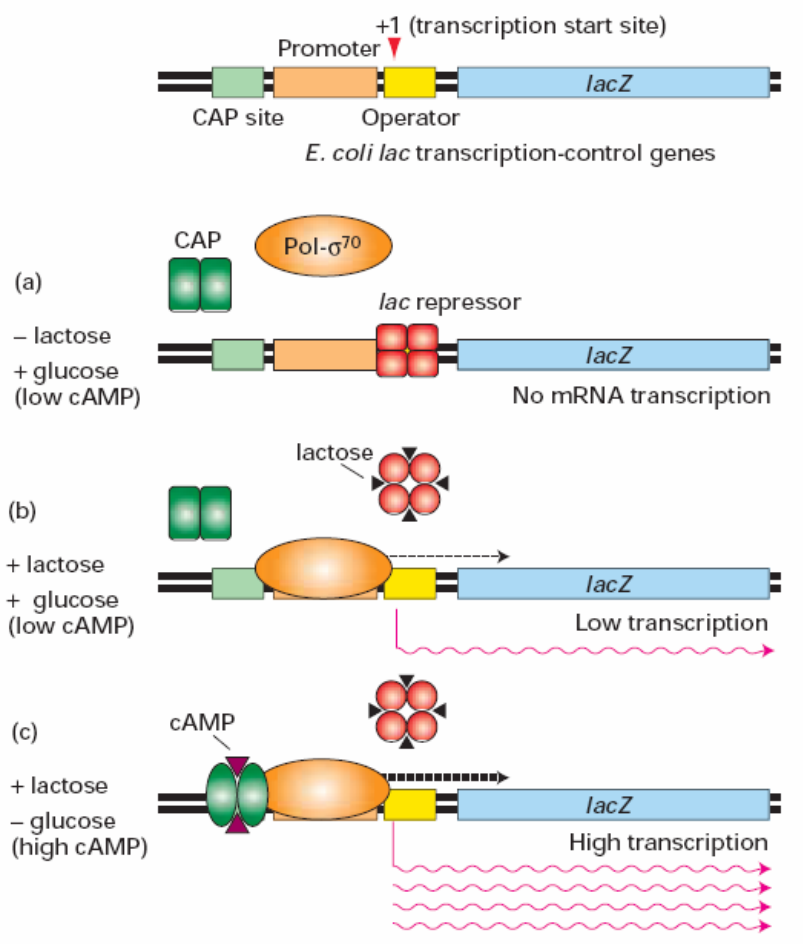


FIGURE 28–18 Combined effects of glucose and lactose on expression of the *lac* operon. **(a)** High levels of transcription take place only when glucose concentrations are low (so cAMP levels are high and CRP-cAMP is bound) and lactose concentrations are high (so the Lac repressor is not bound). **(b)** Without bound activator (CRP-cAMP), the *lac* promoter is poorly transcribed even when lactose concentrations are high and the Lac repressor is not bound.



▲ FIGURE 4-16 Regulation of transcription from the *lac* operon of *E. coli*. (*Top*) The transcription-control region, composed of ≈100 base pairs, includes three protein-binding regions: the CAP site, which binds catabolite activator protein; the *lac* promoter, which binds the RNA polymerase–σ^{70} complex; and the *lac* operator, which binds *lac* repressor. The *lacZ* gene, the first of three genes in the operon, is shown to the right. (a) In the absence of lactose, very little *lac* mRNA is produced because the *lac* repressor binds to the operator, inhibiting transcription initiation by RNA polymerase–σ^{70}. (b) In the presence of glucose and lactose, *lac* repressor binds lactose and dissociates from the operator, allowing RNA polymerase–σ^{70} to initiate transcription at a low rate. (c) Maximal transcription of the *lac* operon occurs in the presence of lactose and absence of glucose. In this situation, cAMP increases in response to the low glucose concentration and forms the CAP-cAMP complex, which binds to the CAP site, where it interacts with RNA polymerase to stimulate the rate of transcription initiation.

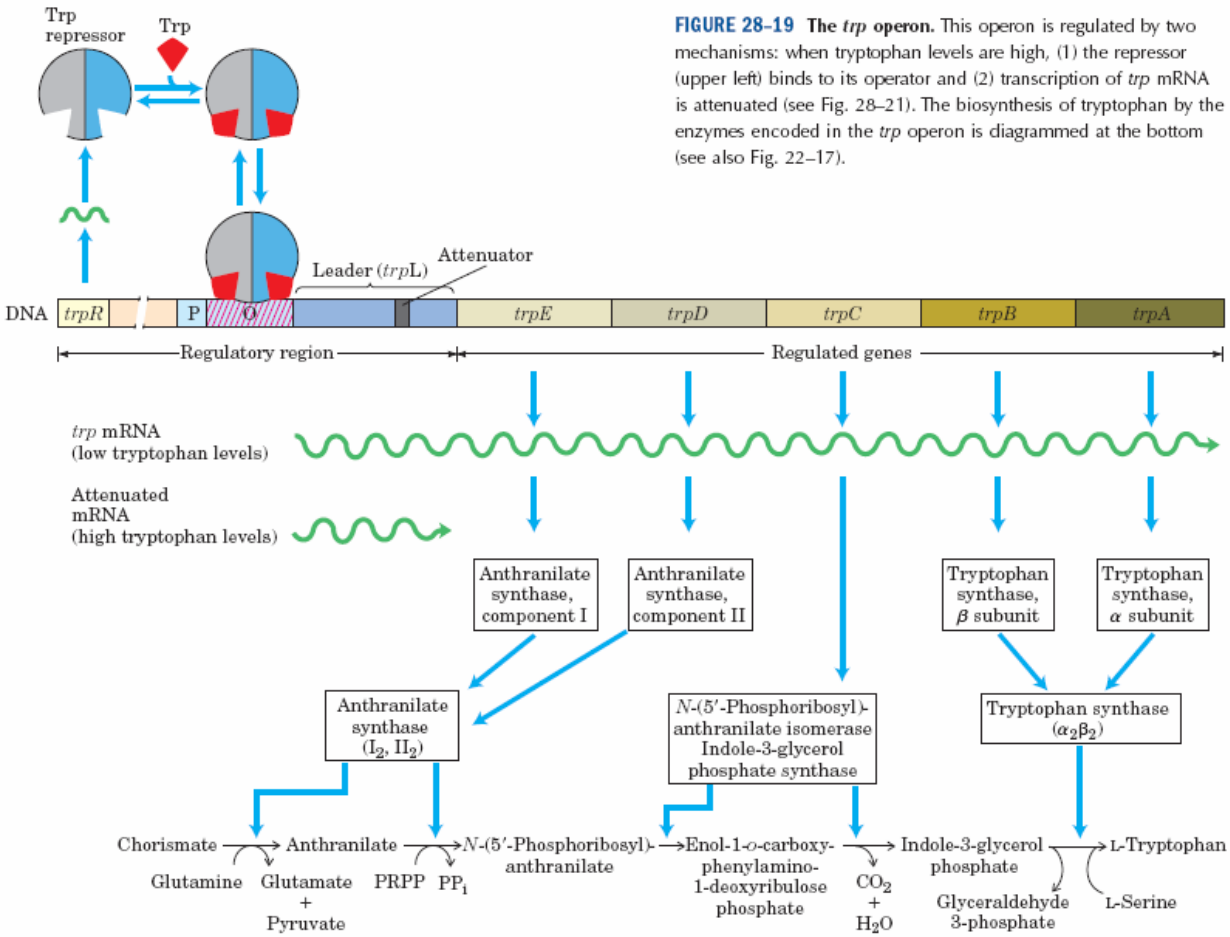


FIGURE 28–19 The *trp* operon. This operon is regulated by two mechanisms: when tryptophan levels are high, (1) the repressor (upper left) binds to its operator and (2) transcription of *trp* mRNA is attenuated (see Fig. 28–21). The biosynthesis of tryptophan by the enzymes encoded in the *trp* operon is diagrammed at the bottom (see also Fig. 22–17).

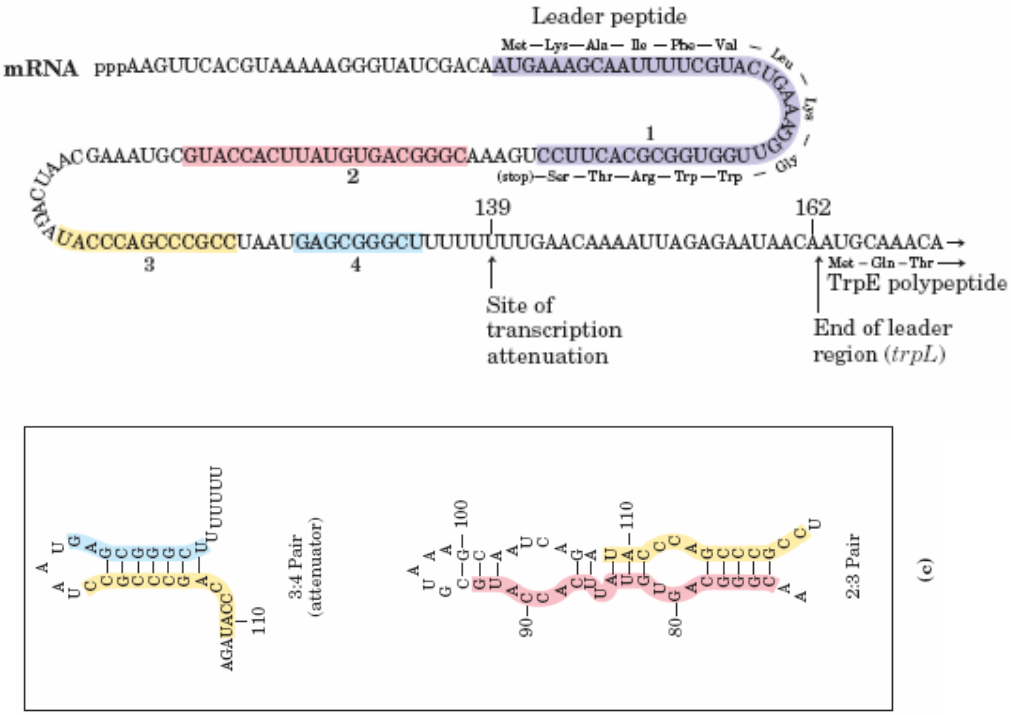
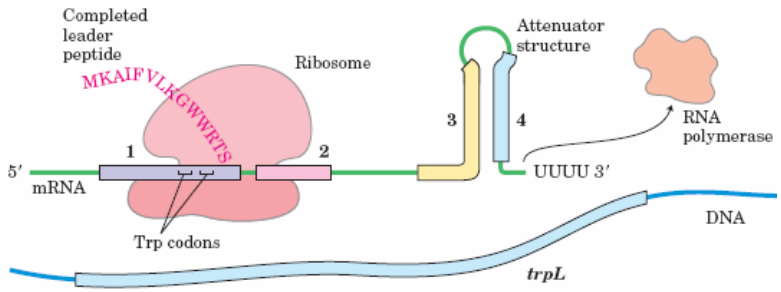
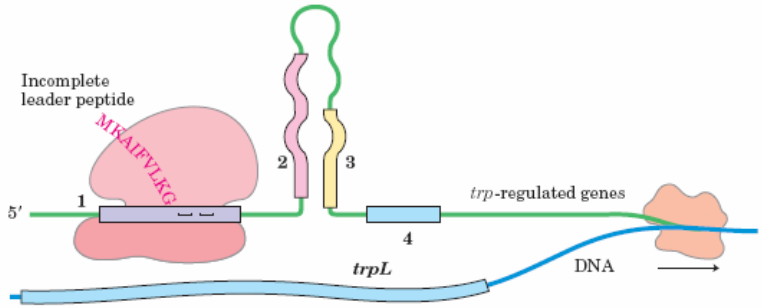


FIGURE 28–21 **Transcriptional attenuation in the *trp* operon.** Transcription is initiated at the beginning of the 162 nucleotide mRNA leader encoded by a DNA region called *trpL* (see Fig. 28-19). A regulatory mechanism determines whether transcription is attenuated at the end of the leader or continues into the structural genes. **(a)** The *trp* mRNA leader (*trpL*). The attenuation mechanism in the *trp* operon involves sequences 1 to 4 (highlighted). **(b)** Sequence 1 encodes a small peptide, the leader peptide, containing two Trp residues (W); it is translated immediately after transcription begins. Sequences 2 and 3 are complementary, as are sequences 3 and 4. The attenuator structure forms by the pairing of sequences 3 and 4 (top). Its structure and function are similar to those of a transcription terminator (see Fig. 26–7). Pairing of sequences 2 and 3 (bottom) prevents the attenuator structure from forming. Note that the leader peptide has no other cellular function. Translation of its open reading frame has a purely regulatory role that determines which complementary sequences (2 and 3 or 3 and 4) are paired. **(c)** Base-pairing schemes for the complementary regions of the *trp* mRNA leader.

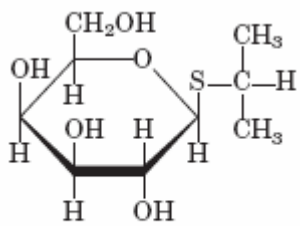


When tryptophan levels are high, the ribosome quickly translates sequence 1 (open reading frame encoding leader peptide) and blocks sequence 2 before sequence 3 is transcribed. Continued transcription leads to attenuation at the terminator-like attenuator structure formed by sequences 3 and 4.



When tryptophan levels are low, the ribosome pauses at the Trp codons in sequence 1. Formation of the paired structure between sequences 2 and 3 prevents attenuation, because sequence 3 is no longer available to form the attenuator structure with sequence 4. The 2:3 structure, unlike the 3:4 attenuator, does not prevent transcription.

(b)



Isopropylthiogalactoside
(IPTG)