Die Zellfabrik - Genexpression und Regulation

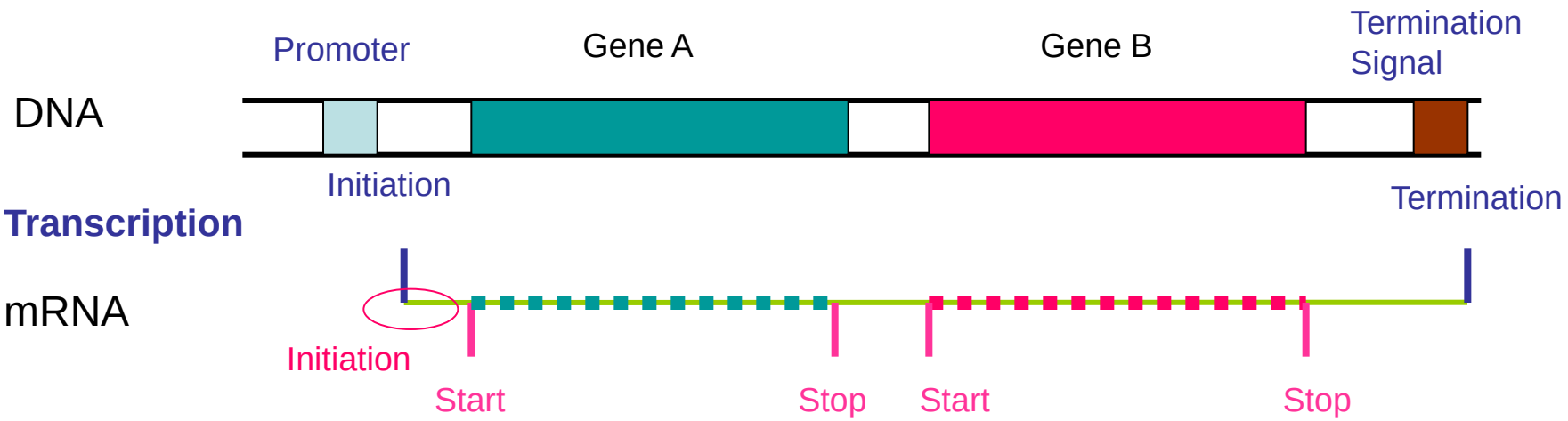
Transkription

Regulation der Transkription
- negative Kontrolle
- positive Kontrolle
- Induktion
- Repression

Translation

Postranslationale Modifikationen

Genexpression bei Prokaryoten



Codon Structure is important for gene function

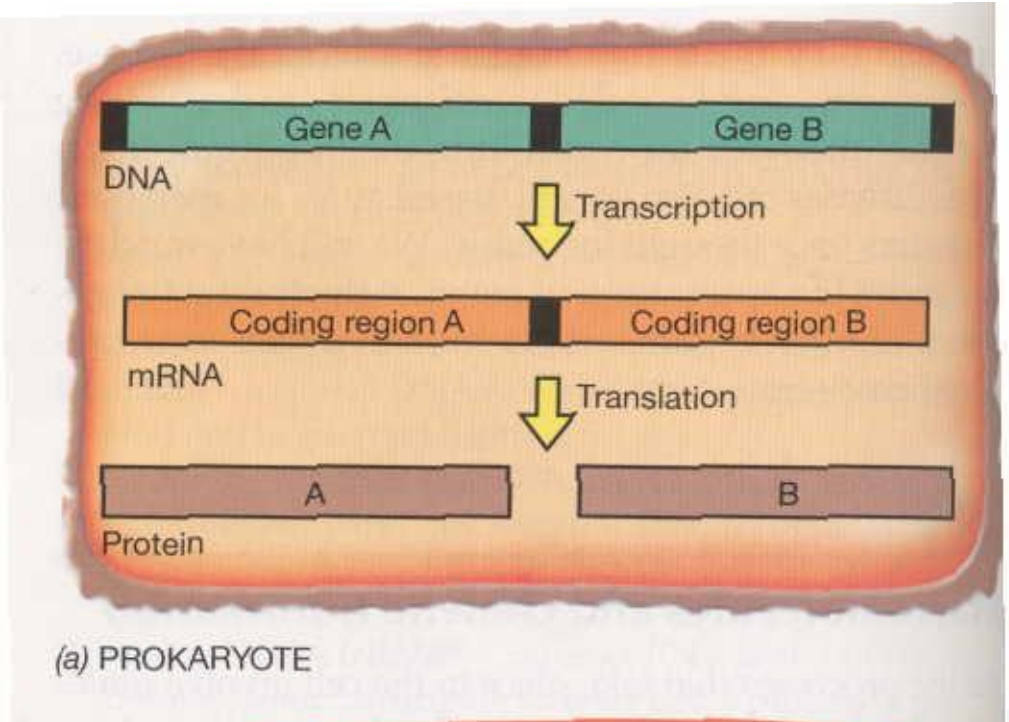
TABLE 6.5 The genetic code as expressed by triplet base sequences of mRNA[a]

Codon	Amino acid	Codon	Amino acid	Codon	Amino acid	Codon	Amino acid
UUU	Phenylalanine	UCU	Serine	UAU	Tyrosine	UGU	Cysteine
UUC	Phenylalanine	UCC	Serine	UAC	Tyrosine	UGC	Cysteine
UUA	Leucine	UCA	Serine	UAA	None (stop signal)	UGA	None (stop signal)
UUG	Leucine	UCG	Serine	UAG	None (stop signal)	UGG	Tryptophan
CUU	Leucine	CCU	Proline	CAU	Histidine	CGU	Arginine
CUC	Leucine	CCC	Proline	CAC	Histidine	CGC	Arginine
CUA	Leucine	CCA	Proline	CAA	Glutamine	CGA	Arginine
CUG	Leucine	CCG	Proline	CAG	Glutamine	CGG	Arginine
AUU	Isoleucine	ACU	Threonine	AAU	Asparagine	AGU	Serine
AUC	Isoleucine	ACC	Threonine	AAC	Asparagine	AGC	Serine
AUA	Isoleucine	ACA	Threonine	AAA	Lysine	AGA	Arginine
AUG (start)[b]	Methionine	ACG	Threonine	AAG	Lysine	AGG	Arginine
GUU	Valine	GCU	Alanine	GAU	Aspartic acid	GGU	Glycine
GUC	Valine	GCC	Alanine	GAC	Aspartic acid	GGC	Glycine
GUA	Valine	GCA	Alanine	GAA	Glutamic acid	GGA	Glycine
GUG	Valine	GCG	Alanine	GAG	Glutamic acid	GGG	Glycine

a The boxes of codons are colored according to the scheme: ionizable: acidic, ionizable: basic, nonionizable polar, and nonpolar (Figure 2.12). The nucleotide on the left is at the 5′-end of the triplet.

b AUG encodes *N*-formylmethionine at the beginning of mRNAs of Bacteria.

Eukaryotes have a complex expression machinery



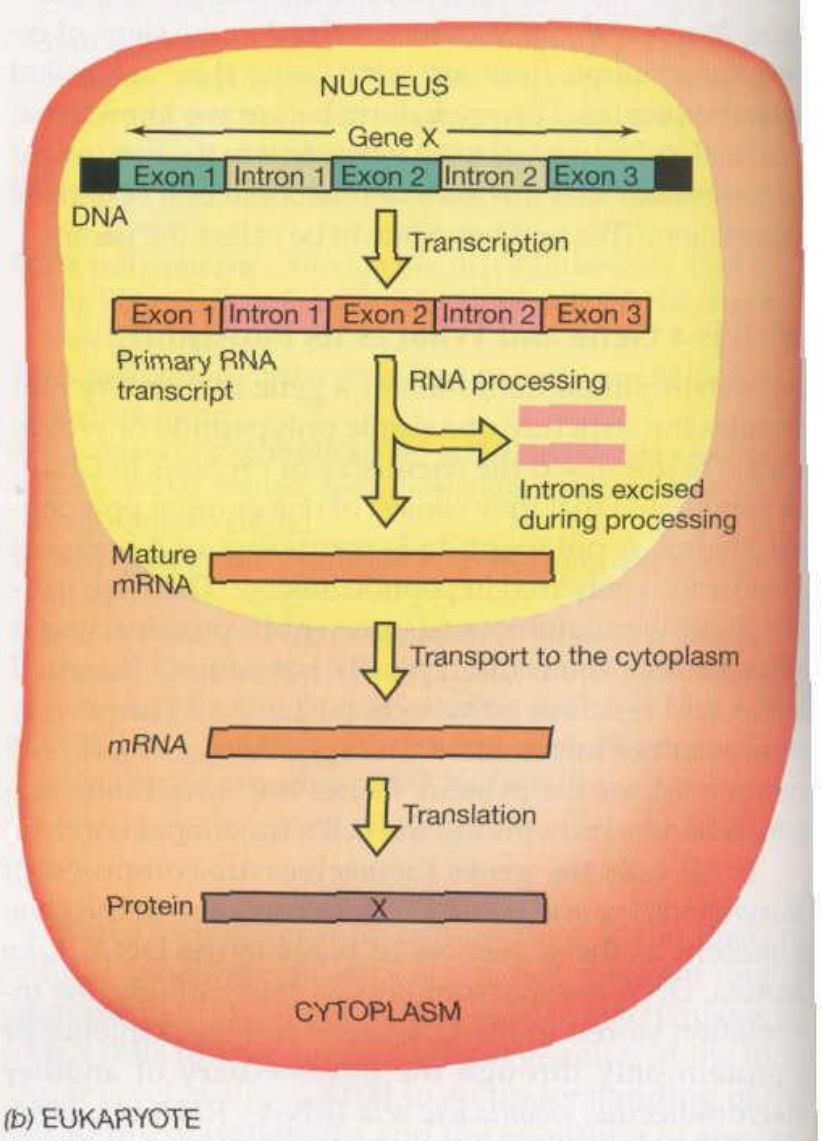


FIGURE 6.2 Contrast of information transfer in prokaryotes and eukaryotes. (a) Prokaryote. A single mRNA often contains more than one coding region (such mRNAs are called *polycistronic*). (b) Eukaryote. Noncoding regions (*introns*) are removed from the primary RNA transcript before translation. The mRNAs of eukaryotes are almost always *monocistronic*.

Processing of eukaryotic mRNA

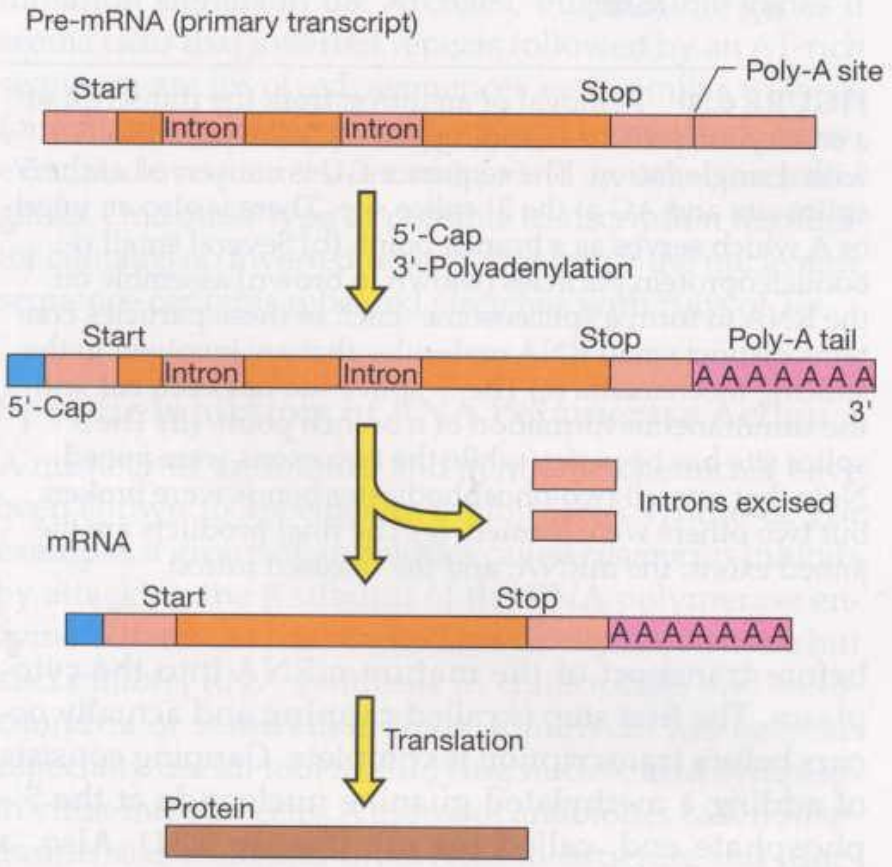


FIGURE 6.32 An overview of the processing of the pre-mRNA into mature mRNA in eukaryotes. The processing steps including adding a cap at the 5′-end, removing the introns, and clipping of the 3′-end of the transcript while adding a poly-A tail. All these steps are carried out in the nucleus. The location of the start and stop codons to be used during translation are also indicated.

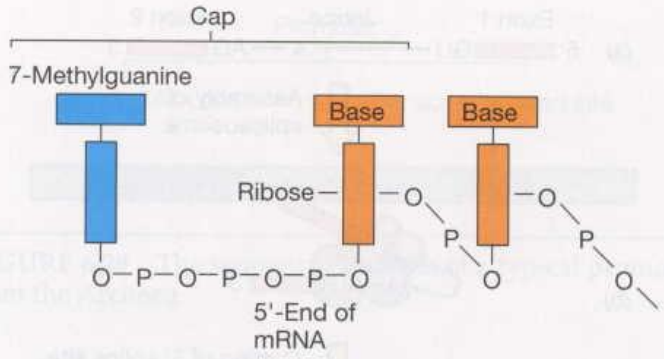
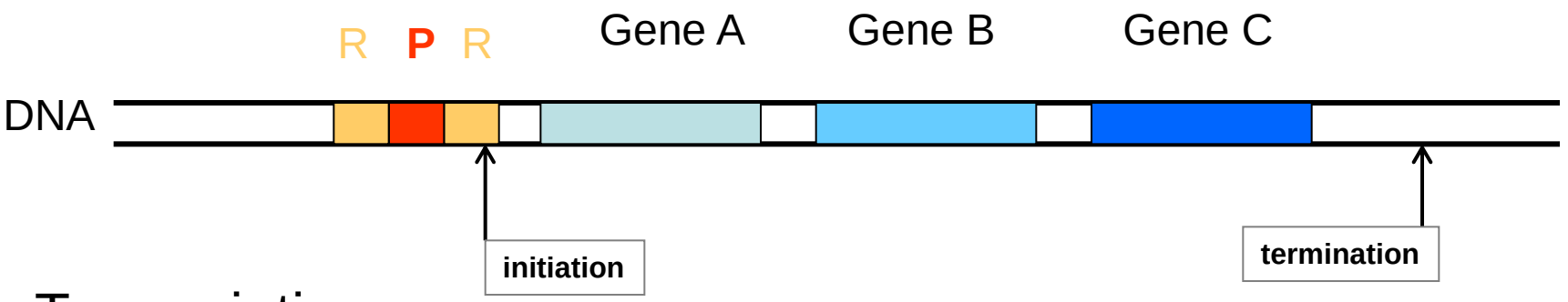
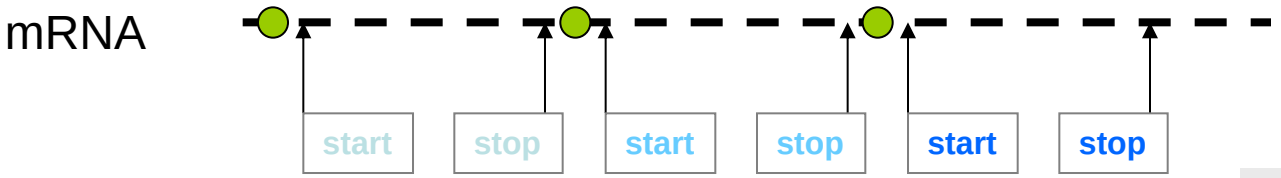


FIGURE 6.31 Structure of the cap added to the 5′-end of eukaryotic mRNA.

Gene Expression in Prokaryotes
Multicistronic mRNAs



Transcription



Translation

Ribosome Binding Site (Shine Dalgarno)

P **Promoter**

R **Regulatory Region (e.g. Operator)**

Transkription Initiation

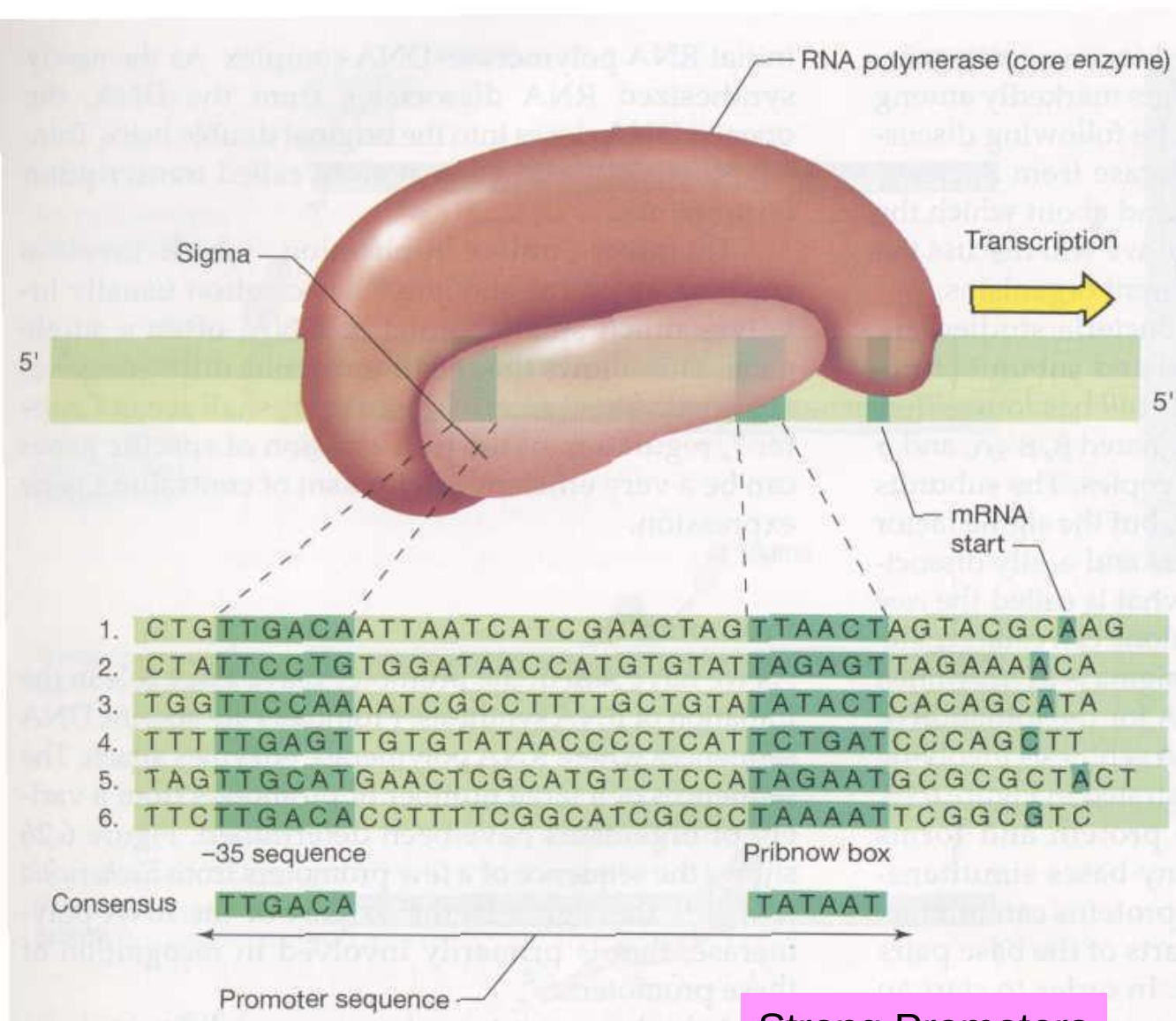
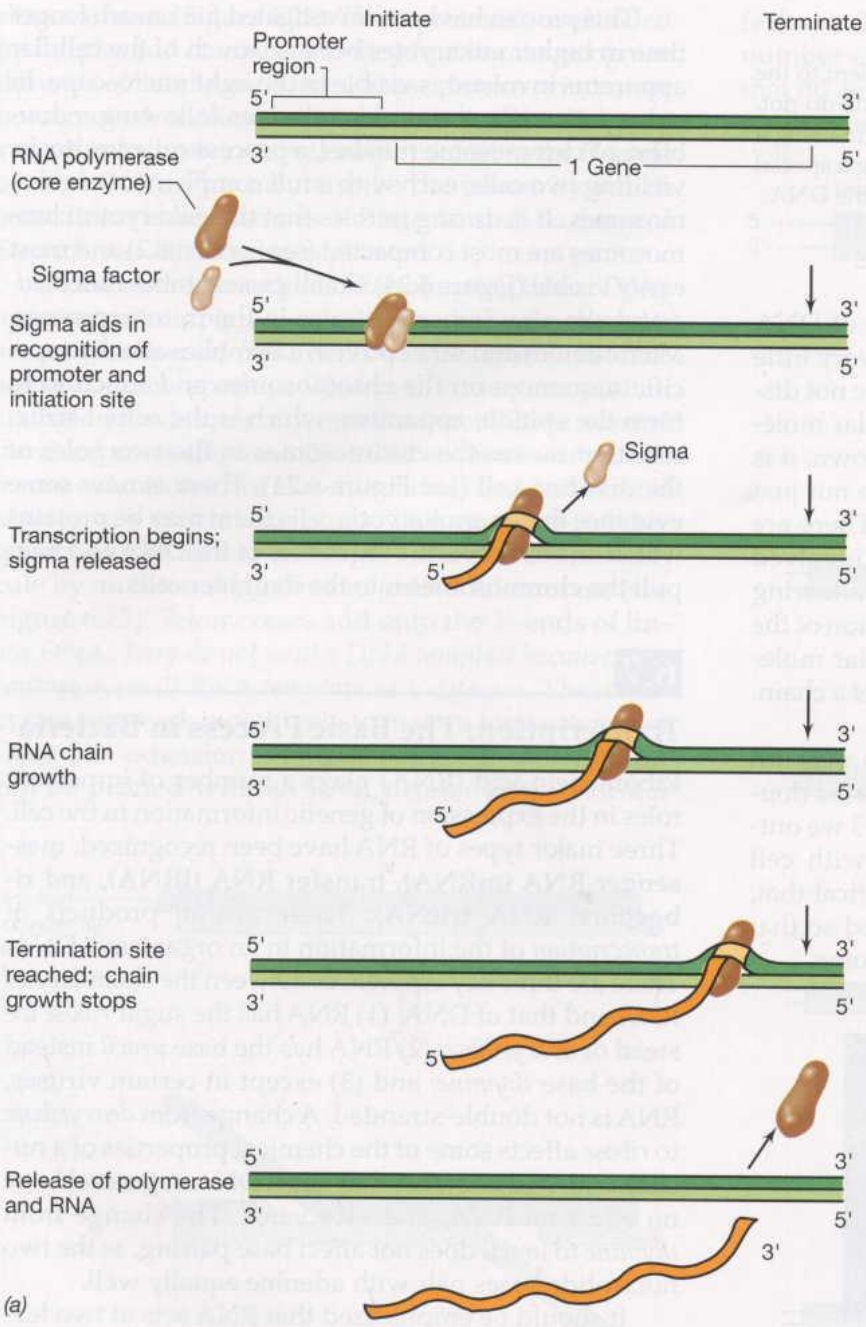
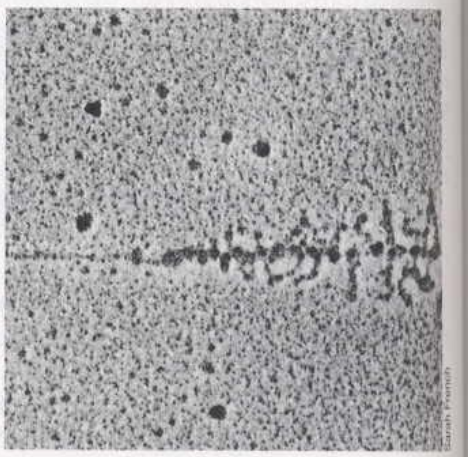


FIGURE 6.26 The interaction of RNA polymerase with the promoter. Shown below the diagram are six different promoter sequences identified in *Escherichia coli*. The contacts of the RNA polymerase with the −35 sequence and the Pribnow box are shown. Transcription begins at a unique base just downstream from the Pribnow box. Below the actual sequences at the −35 and Pribnow box regions are consensus sequences derived from comparing many promoters.

Strong Promoters
Weak Promoters





Transkription

FIGURE 6.25 Transcription. (a) Steps in messenger RNA synthesis. The initiation and termination sites are specific nucleotide sequences on the DNA. RNA polymerase moves down the DNA chain, causing temporary opening of the double helix and transcription of one of the DNA strands. When a termination site is reached, chain growth stops, and the mRNA and polymerase are released. (b) Electron micrograph of transcription occurring along a gene on the *Escherichia coli* chromosome. The region of active transcription represents about two kilobase pairs of DNA. Transcription proceeds from left to right.

Transcription Termination

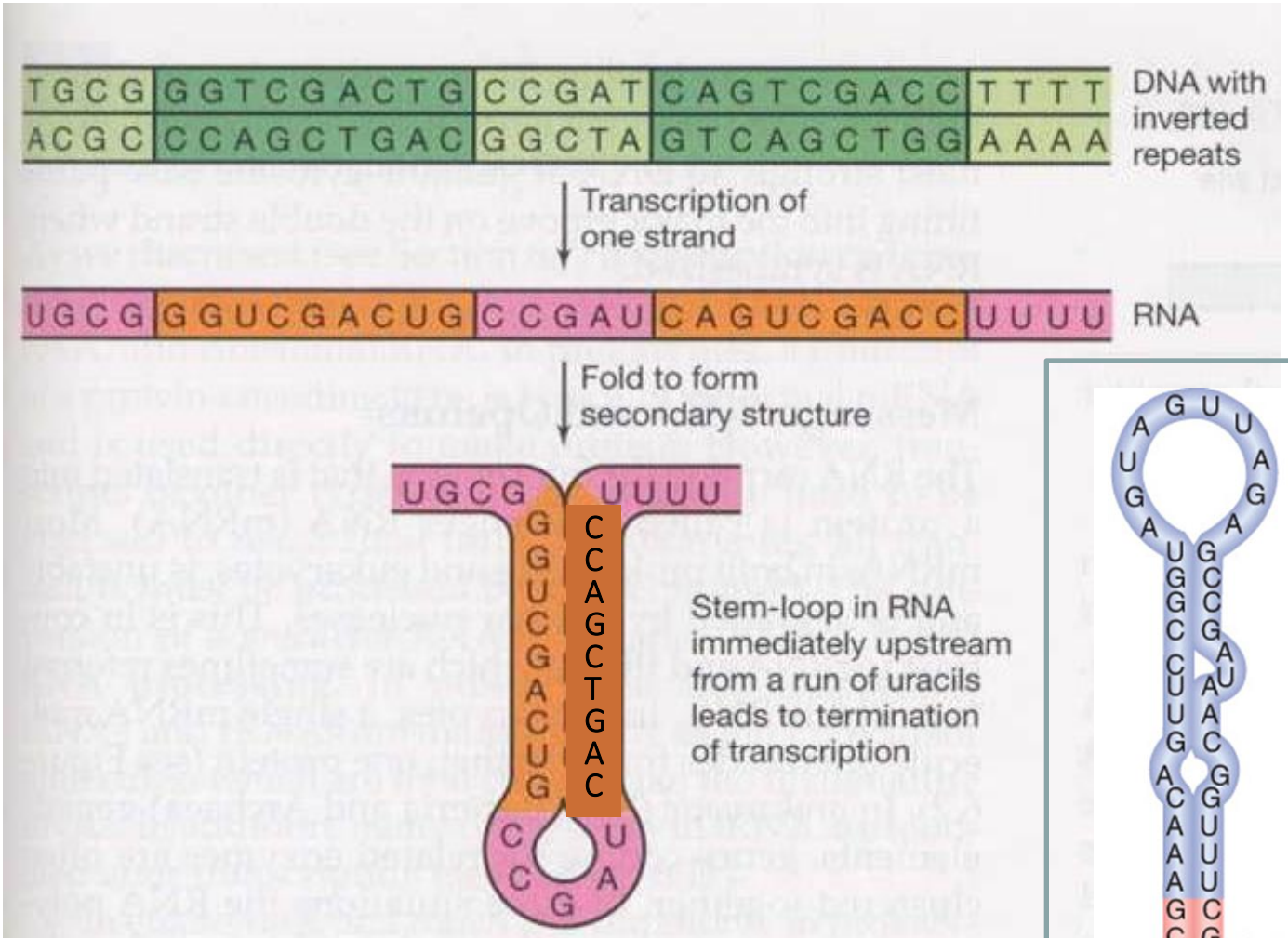
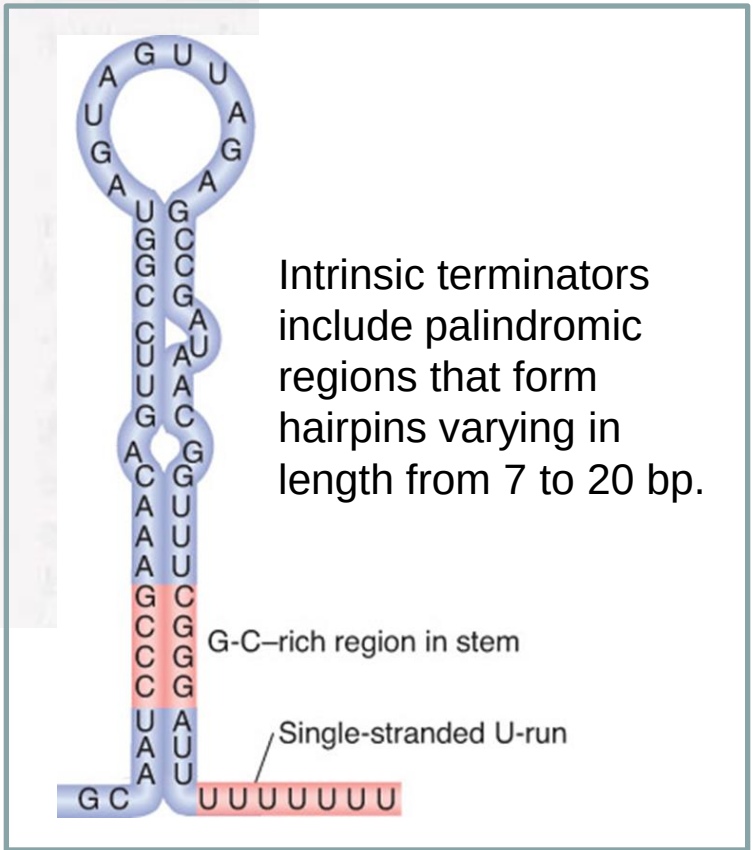


FIGURE 6.27 Inverted repeats in transcribed DNA lead to formation of a stem-loop structure in the RNA, which can result in termination of transcription.



Intrinsic terminators include palindromic regions that form hairpins varying in length from 7 to 20 bp.

Transcription Initiation in Eukayotes

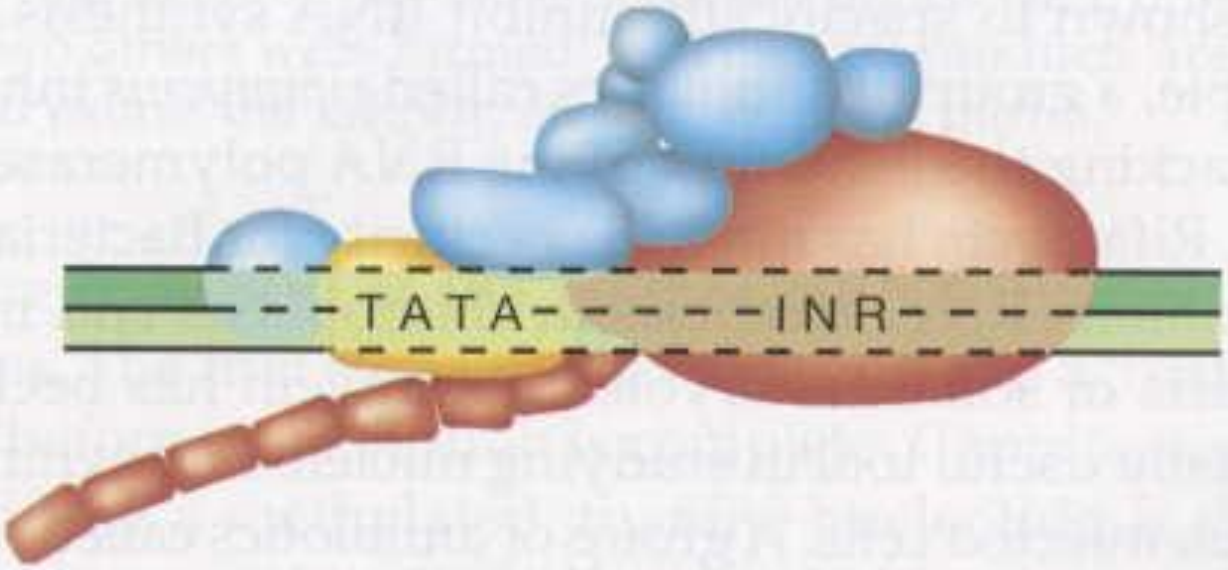


FIGURE 6.28 The interaction of eukaryotic RNA polymerase II with a promoter. The polymerase itself (shown in brown) is positioned at the initiator element (INR) of the promoter. A TATA box binding protein (shown in yellow) is shown bound at the TATA box. The polymerase has a repetitive sequence at one end (shown as a tail-like structure) that can be phosphorylated. The other proteins shown in blue are a few of the very large number of accessory factors required for initiation.

Regulation Processes

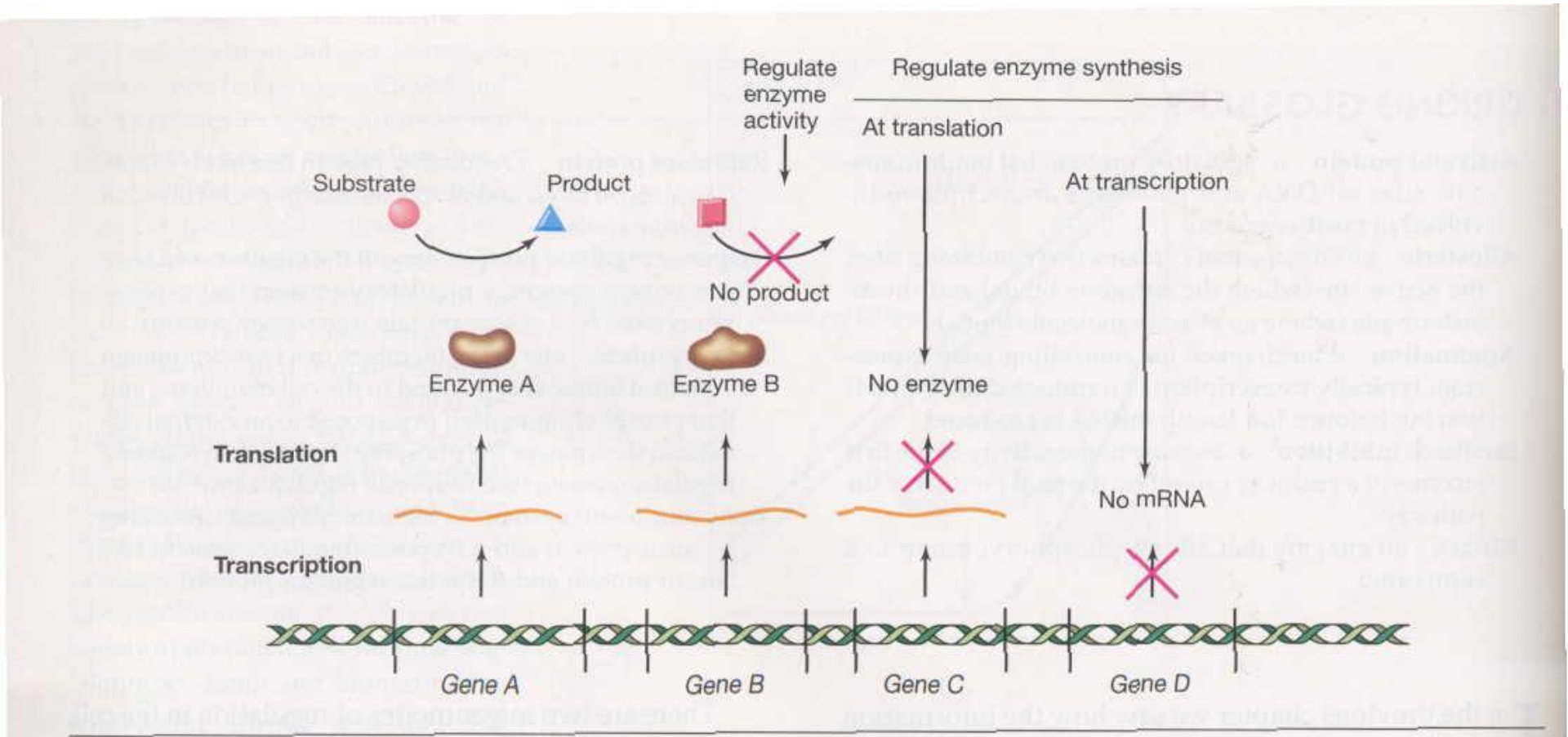


FIGURE 7.1 An overview of the mechanisms that can be used in regulation. The product of gene A is enzyme A, which is synthesized constitutively and carries out its reaction. Enzyme B is also synthesized constitutively but its activity can be inhibited. The synthesis of the product of gene C can be prevented by control at the level of translation. The synthesis of the product of gene D can be prevented by control at the level of transcription.

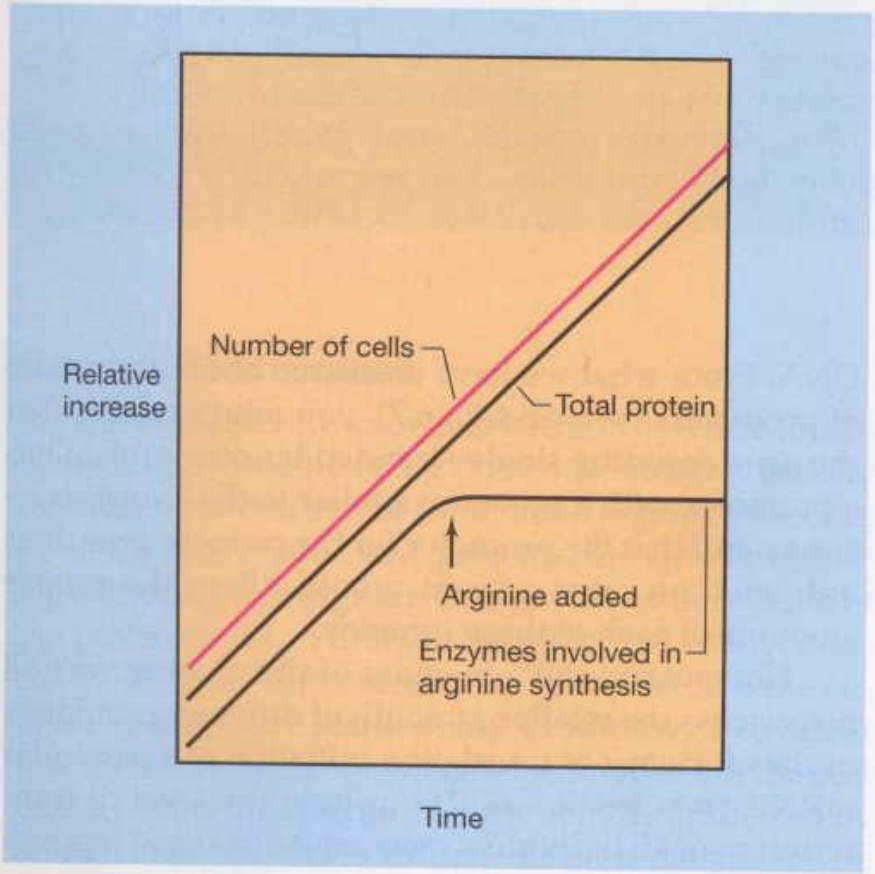


FIGURE 7.6 Repression of enzymes involved in arginine synthesis by addition of arginine to the medium. Note that the rate of total protein synthesis remains unchanged.

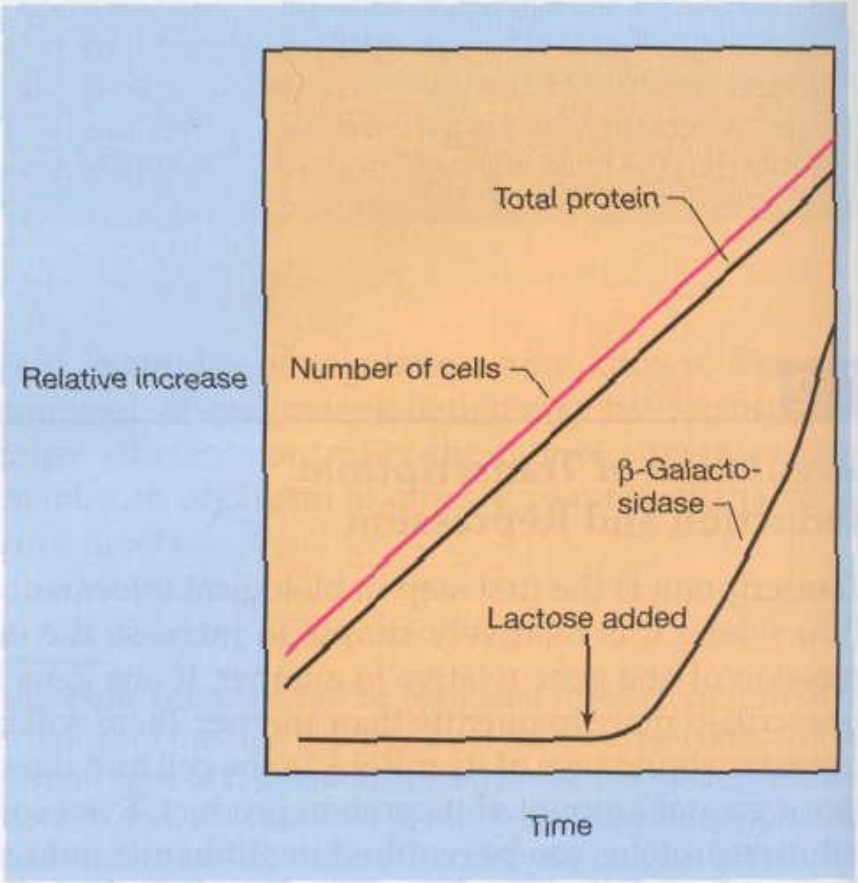


FIGURE 7.7 Induction of the enzyme β-galactosidase on the addition of lactose to the medium. Note that the rate of total protein synthesis remains unchanged.

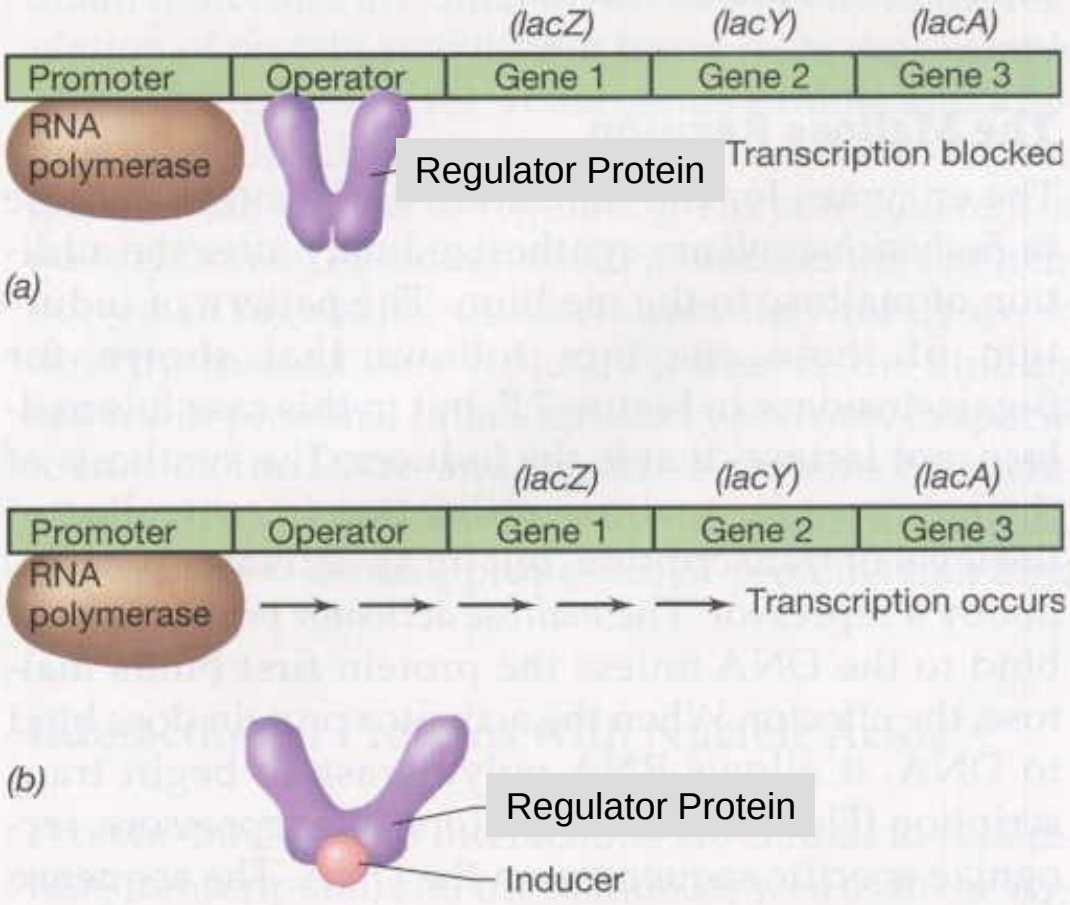
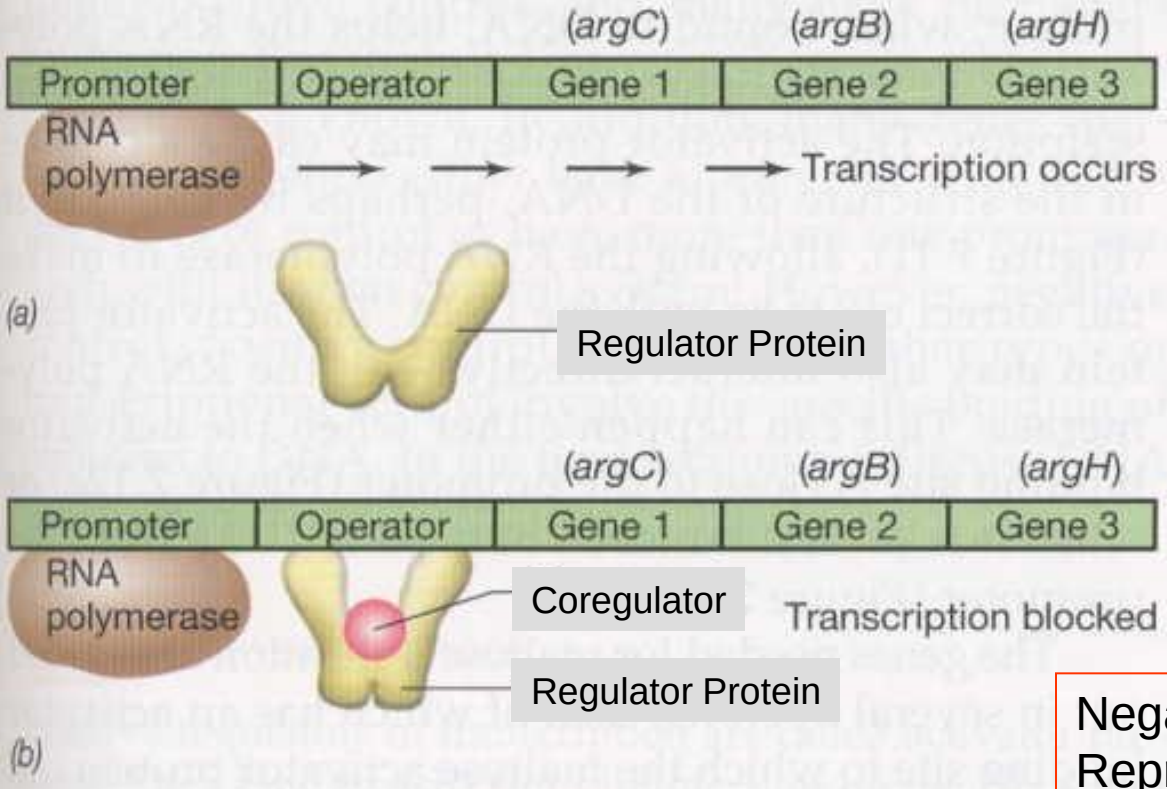


FIGURE 7.9 The process of enzyme induction using a repressor. (a) A repressor protein binds to the operator region and blocks the action of RNA polymerase. (b) An inducer molecule binds to the repressor and inactivates it. Transcription by RNA polymerase occurs and an mRNA for that operon is formed. In the case of the *lac* operon the repressor would be the *lac* repressor, and the inducer would be allolactose.

Negative Kontrolle
Induktion



Negative Kontrolle
Repression

FIGURE 7.8 The process of enzyme repression. (a) Transcription of the operon occurs because the repressor is unable to bind to the operator. (b) After a corepressor (small molecule) binds to the repressor, the repressor binds to the operator and blocks transcription; mRNA and the proteins it encodes are not made. In the case of the *argCBH* operon the repressor would be the arginine repressor and the corepressor would be the amino acid arginine.

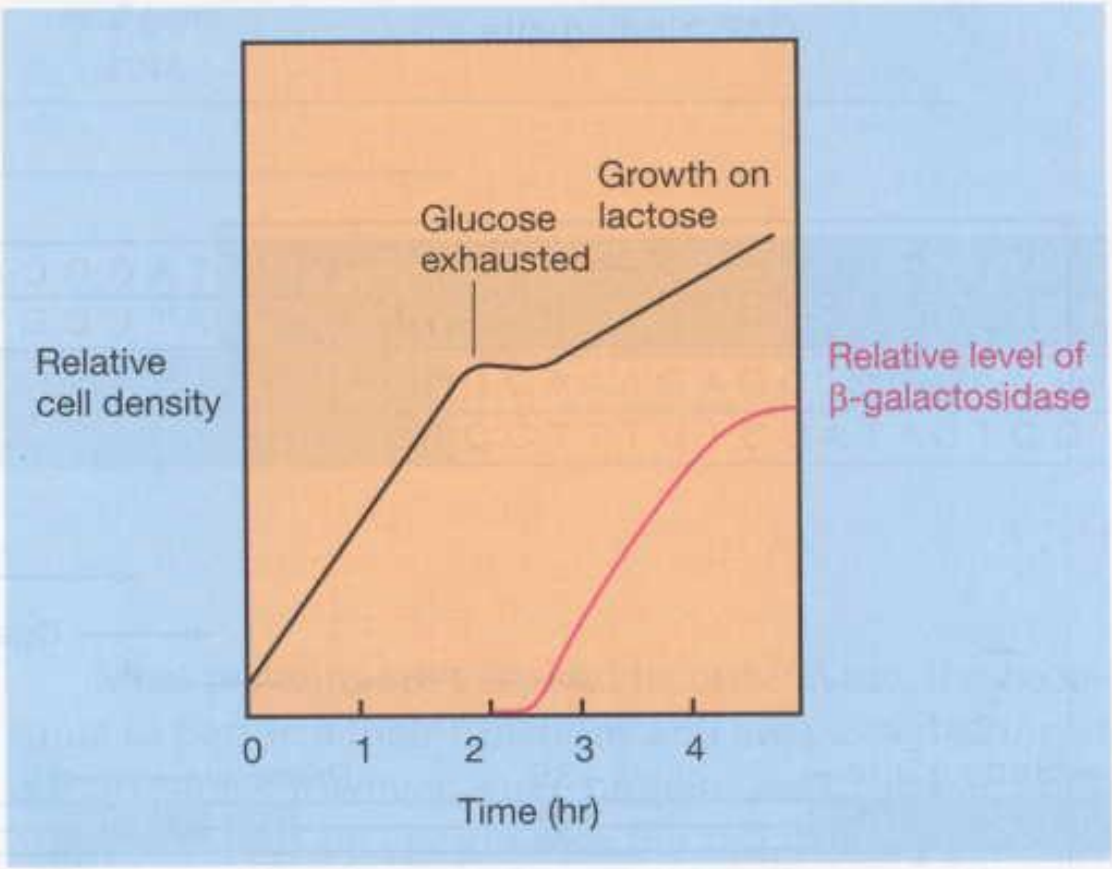


FIGURE 7.18 Diauxic growth on a mixture of glucose and lactose. Glucose represses the synthesis of β-galactosidase. After glucose is exhausted, a lag occurs until β-galactosidase is synthesized, and then growth can resume on lactose.

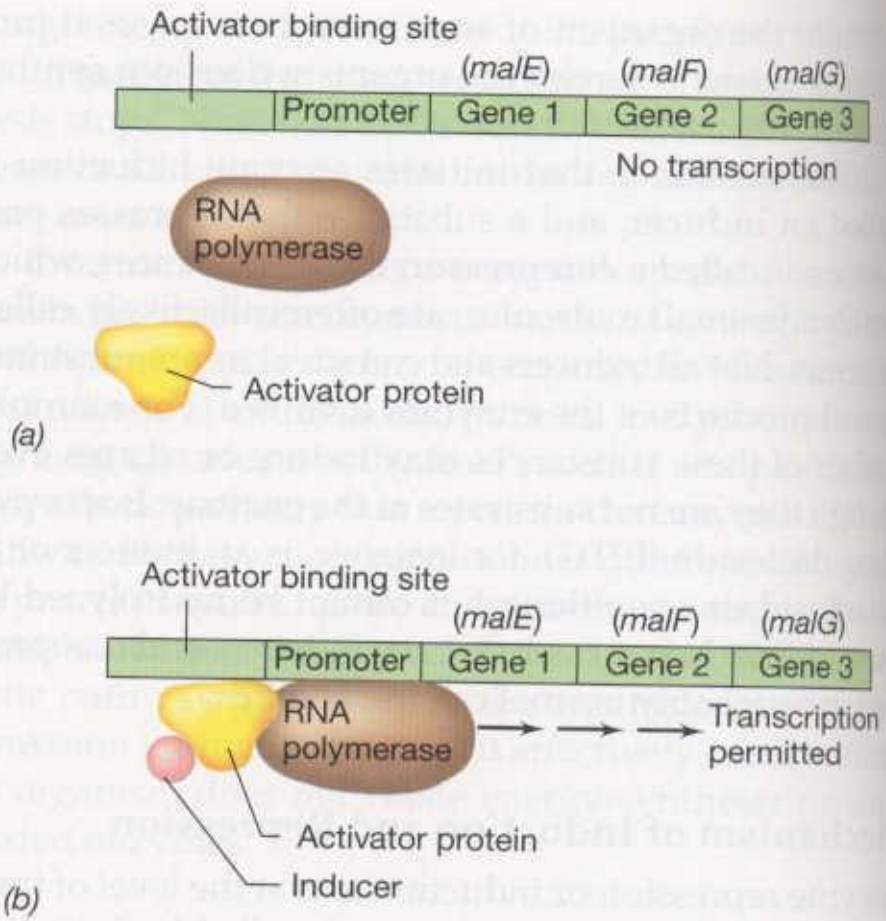


FIGURE 7.10 Positive control of enzyme induction. (a) In the absence of an inducer, neither the activator protein nor the RNA polymerase can bind to the DNA. (b) An inducer molecule binds to the activator protein, which in turn binds to the activator binding site. This allows RNA polymerase to bind to the promoter and begin transcription. In the case of the *malEFG* operon, the activator protein would be the maltose activator protein and the inducer would be the sugar maltose.

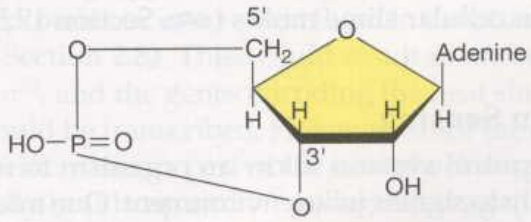


FIGURE 7.19 Cyclic adenosine monophosphate (cyclic AMP, cAMP) is produced from ATP by the enzyme adenylate cyclase.

Positive Kontrolle

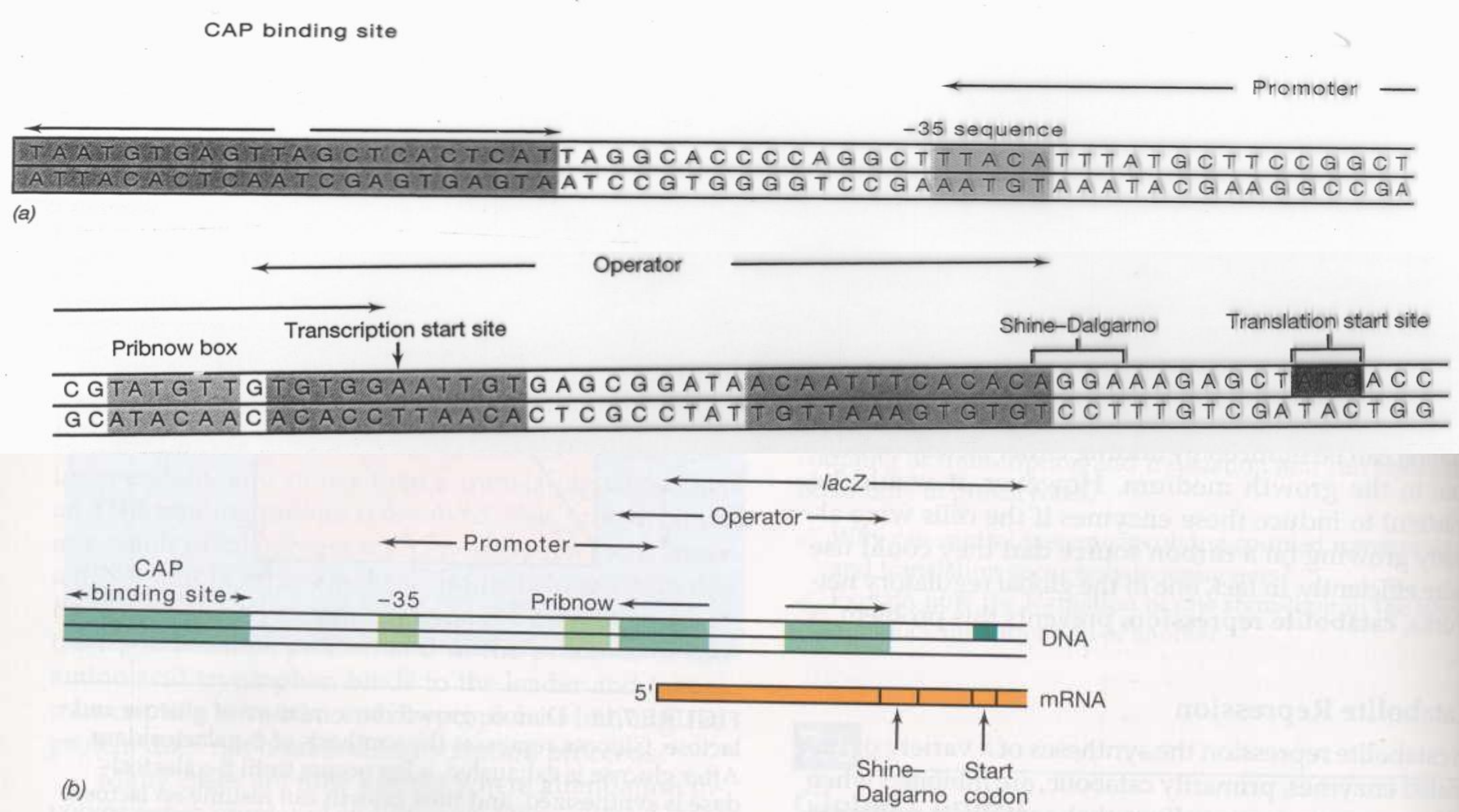


FIGURE 7.20 The genetic elements involved in regulation of the lactose operon. The first gene in this operon, *lacZ*, encodes the enzyme β-galactosidase, which breaks down lactose (see Figure 7.9). The operon contains two other genes that are also involved in lactose metabolism. (a) Part a shows the nucleotide sequence of the control region of this operon. Notice that the two halves of the operator (where the repressor would bind) are almost perfect inverted repeats. There are also inverted repeats in the CAP binding site although these are less perfect. Also shown are the transcriptional start site and the −35 sequence and the Pribnow box, which are part of the promoter (Figure 6.26). In addition, the location of the base pairs encoding the Shine–Dalgarno sequence and the start codon are also given. These two sequences would function on the mRNA (Section 6.10). (b) Part b shows a diagram of this region that also includes the beginning (5′ end) of the mRNA that would be formed.

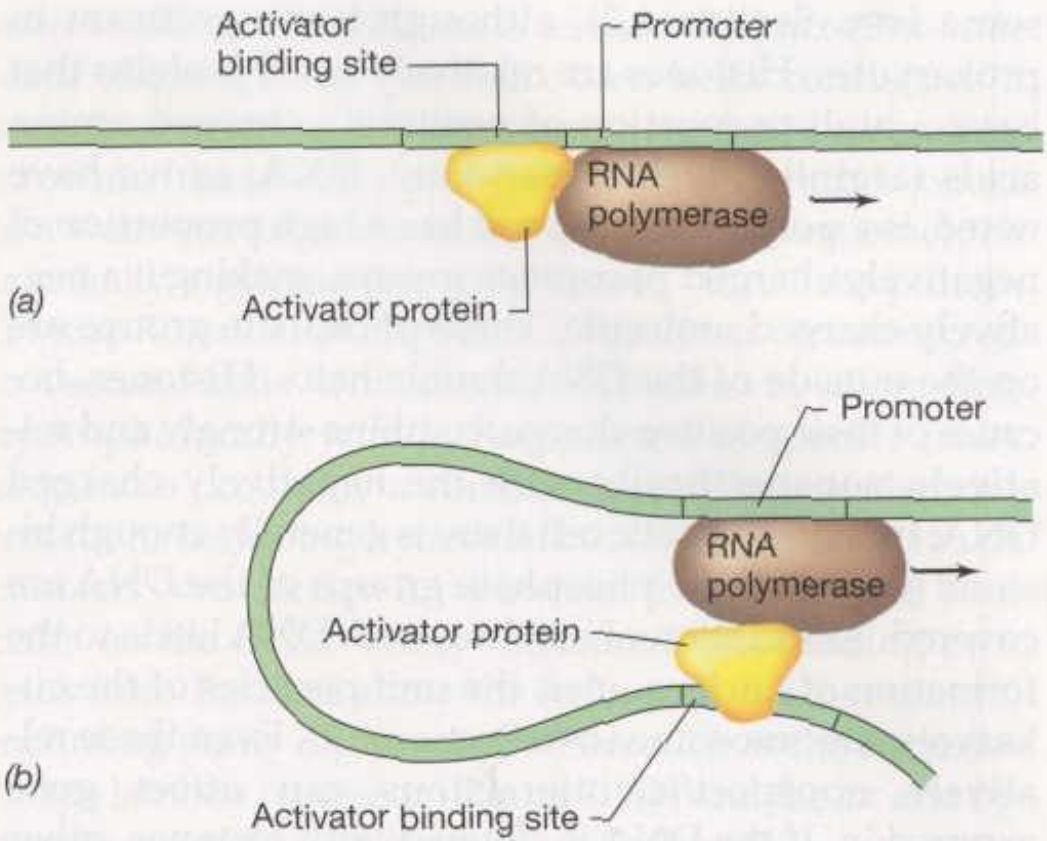


FIGURE 7.12 Some activator proteins interact with RNA polymerase. (a) The activator binding site is near the promoter. (b) The activator binding site is several hundred base pairs from the promoter. In this case, the DNA must be looped to allow the activator and the RNA polymerase to contact.

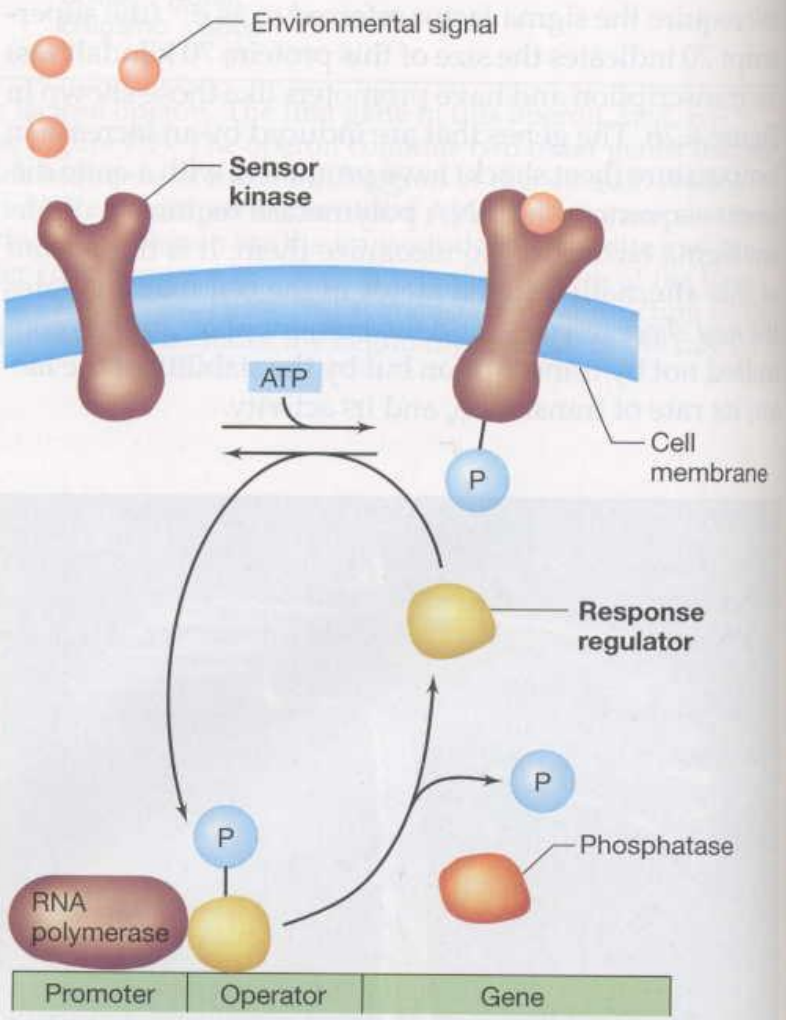


FIGURE 7.22 The control of gene expression by a two-component system. The main components of the system include a *sensor kinase* in the cell membrane that phosphorylates itself in response to an environmental signal. The phosphoryl group is then transferred to the other main component, a *response regulator*. In the system diagrammed in this figure the phosphorylated response regulator serves as a repressor. There must also be a phosphatase in the system to cycle the response regulator.

Signaltransduktion

TABLE 7.1 A few of the global control systems known in *Escherichia coli*[a]

System	Signal	Primary activity of regulatory protein	Number of genes regulated
Aerobic respiration	Presence of O_2	Repressor (ArcA)	50+
Anaerobic respiration	Lack of O_2	Activator (FNR)	70
Catabolite repression	Cyclic AMP concentration	Activator (CAP)	300+
Heat shock	Temperature	Alternative sigma (σ^{32})	36
Nitrogen utilization	NH_3 limitation	Activator (NR_I)/alternative sigma (σ^{54})	12+
Oxidative stress	Oxidizing agent	Activator (OxyR)	30+
SOS response	Damaged DNA	Repressor (LexA)	20+

a For many of the global control systems, regulation is complex. A single regulatory protein can play more than one role. For instance, the regulatory protein for aerobic respiration is a repressor for many promoters but an activator for others, whereas the regulatory protein for anaerobic respiration is an activator protein for many promoters but a repressor for others. Regulation can also be indirect or require more than one regulatory protein. Some of the regulatory proteins involved are members of two-component systems (see Section 7.7). Many genes are regulated by more than one global system. (For a discussion of the SOS response, see Section 9.3.)

TABLE 7.2 Some two-component regulatory systems from *Escherichia coli* that regulate transcription

System	Environmental signal	Sensor kinase	Response regulator	Activity of response regulator[a]
Arc system	O_2	ArcB	ArcA	Repressor/Activator
Nitrate and nitrite anaerobic regulation (Nar)	Nitrate and nitrite	NarX and NarQ	NarL	Activator/Repressor
			NarP	Activator/Repressor
Nitrogen utilization (Ntr)	NH_4^+	NR_{II}, the product of *glnL*	NR_I, the product of *glnG*	Activates RNA polymerase at promoters requiring σ^{54}.
Pho regulon	Inorganic phosphate	PhoR	PhoB	Activator
Porin regulation	Osmotic pressure	EnvZ	OmpR	Activator/Repressor

a Note that several of the response regulator proteins act as both activators and repressors depending on the genes being regulated. Although ArcA can function as either an activator or a repressor, it functions as a repressor on most operons that it regulates.

13.11.15