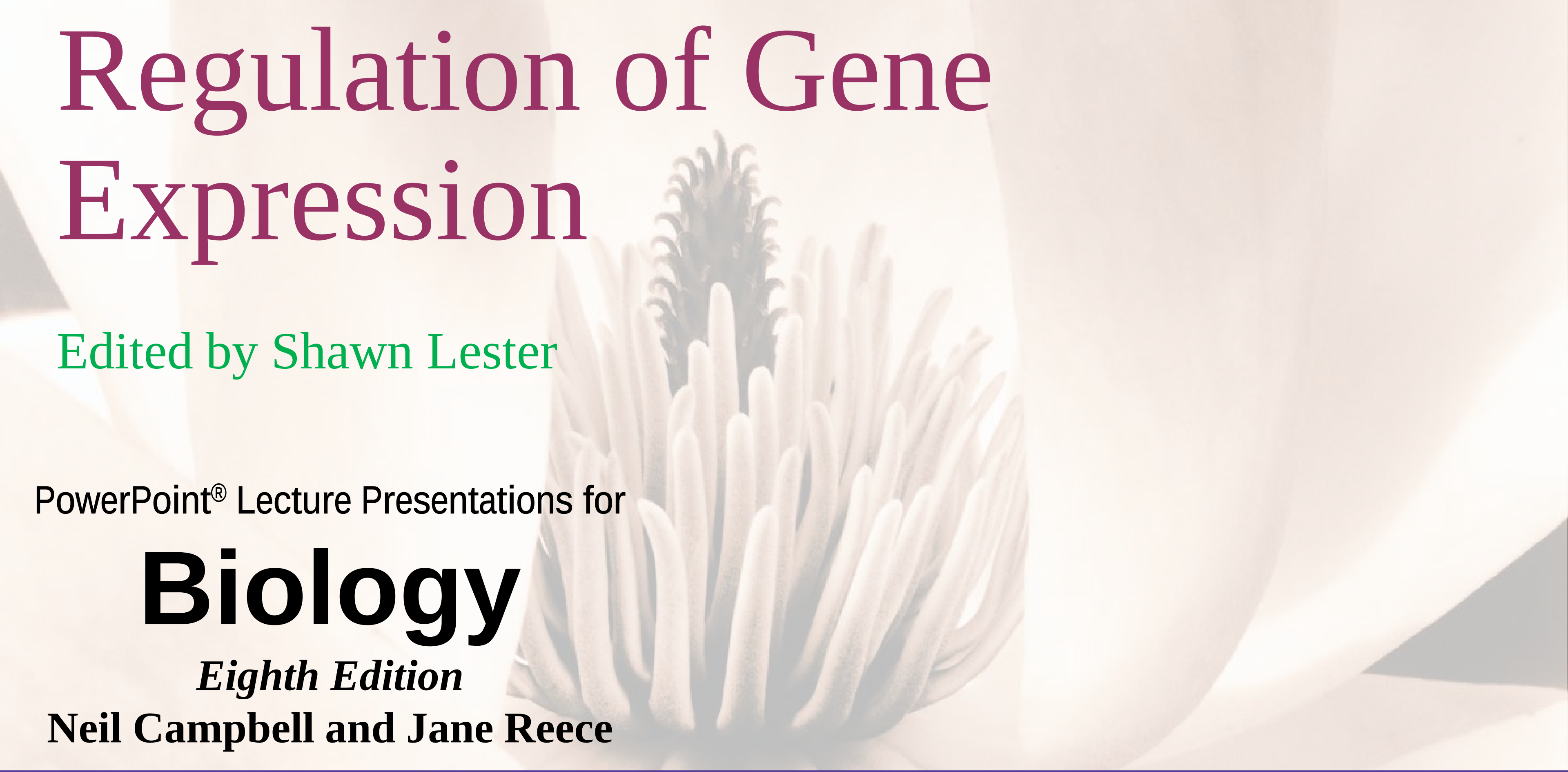
Chapter 18

Regulation of Gene Expression

Edited by Shawn Lester



PowerPoint® Lecture Presentations for

Biology

Eighth Edition

Neil Campbell and Jane Reece

Lectures by Chris Romero, updated by Erin Barley with contributions from Joan Sharp

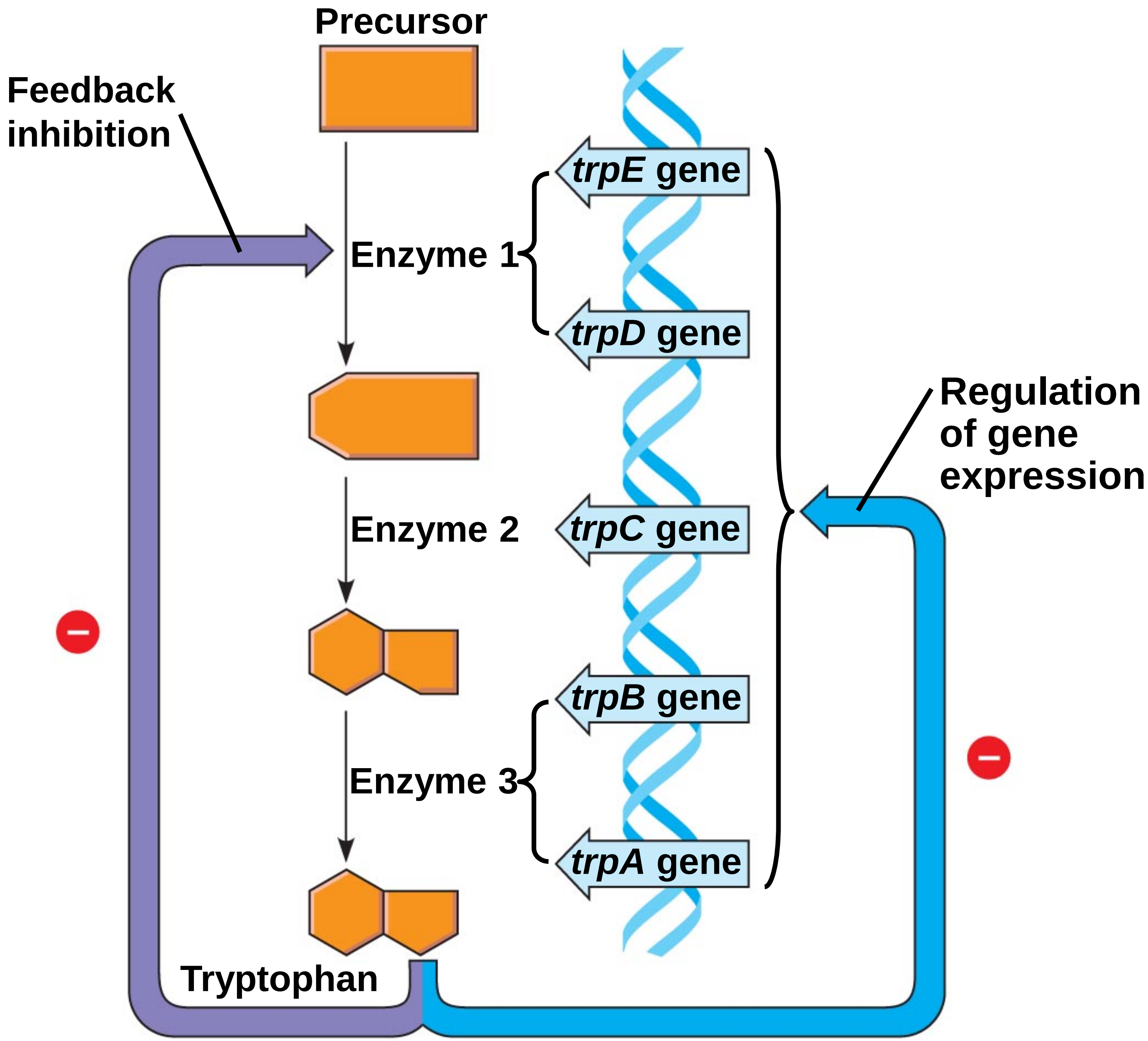
Overview: Conducting the Genetic Orchestra

- Prokaryotes and eukaryotes alter gene expression in response to their changing environment
- In multicellular eukaryotes, gene expression regulates development and is responsible for differences in cell types
- RNA molecules play many roles in regulating gene expression in eukaryotes

Concept 18.1: Bacteria often respond to environmental change by regulating transcription

- Natural selection has favored bacteria that produce only the products needed by that cell
- A cell can regulate the production of enzymes by feedback inhibition or by gene regulation
- Gene expression in bacteria is controlled by the operon model

Fig. 18-2



(a) Regulation of enzyme activity

(b) Regulation of enzyme production

Operons: The Basic Concept

- A cluster of functionally related genes can be under coordinated control by a single on-off “switch”
- The regulatory “switch” is a segment of DNA called an **operator** usually positioned within the promoter
- An **operon** is the entire stretch of DNA that includes the operator, the promoter, and the genes that they control

- The operon can be switched off by a protein **repressor**

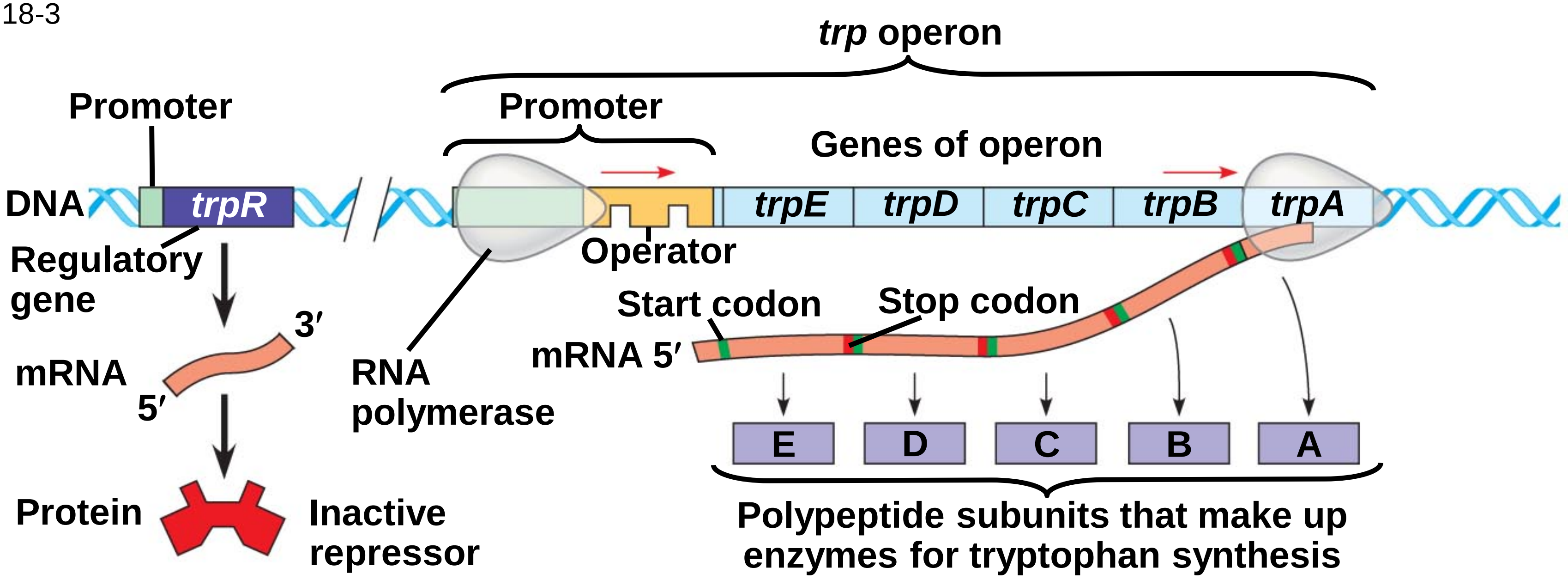
- The repressor prevents gene transcription by binding to the operator and blocking RNA polymerase

- The repressor is the product of a separate **regulatory gene**

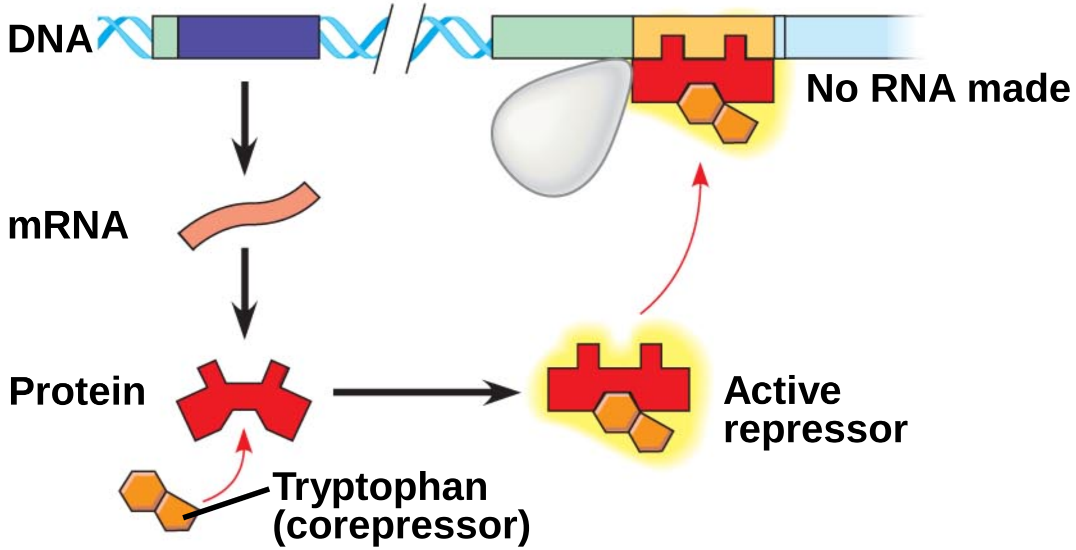
- The repressor can be in an active or inactive form, depending on the presence of other molecules
- A **corepressor** is a molecule that cooperates with a repressor protein to switch an operon off
- For example, *E. coli* can synthesize the amino acid tryptophan

- By default the *trp* operon is on and the genes for tryptophan synthesis are transcribed
- When tryptophan is present, it binds to the *trp* repressor protein, which turns the operon off
- The repressor is active only in the presence of its corepressor tryptophan; thus the *trp* operon is turned off (repressed) if tryptophan levels are high

Fig. 18-3

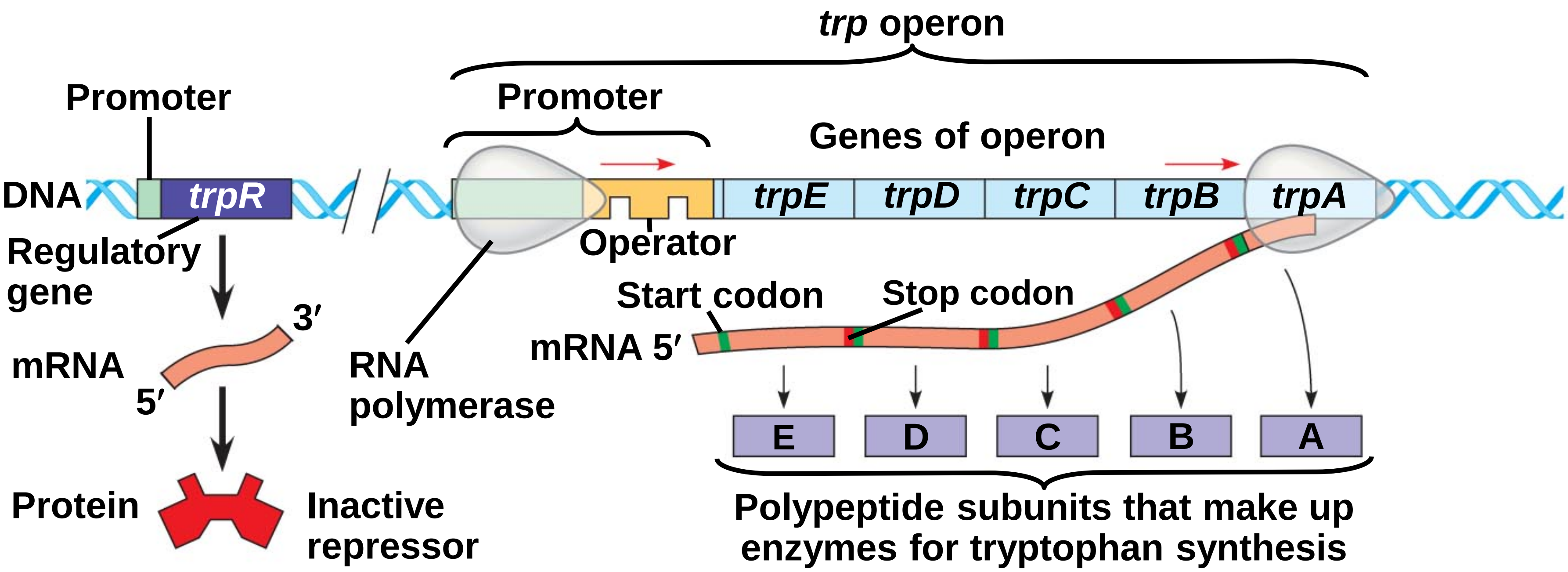


(a) Tryptophan absent, repressor inactive, operon on



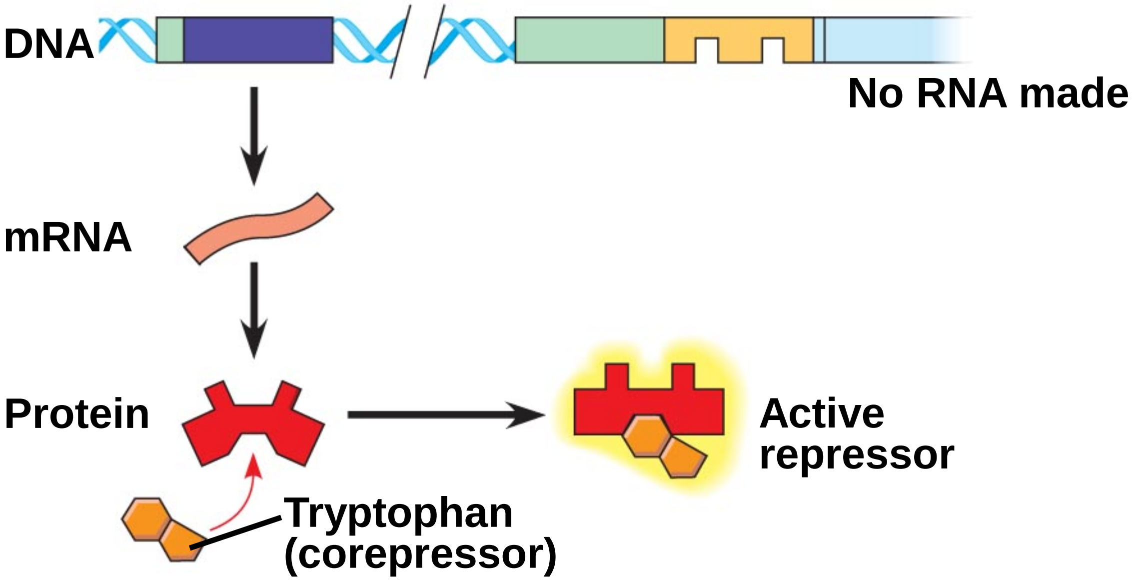
(b) Tryptophan present, repressor active, operon off

Fig. 18-3a



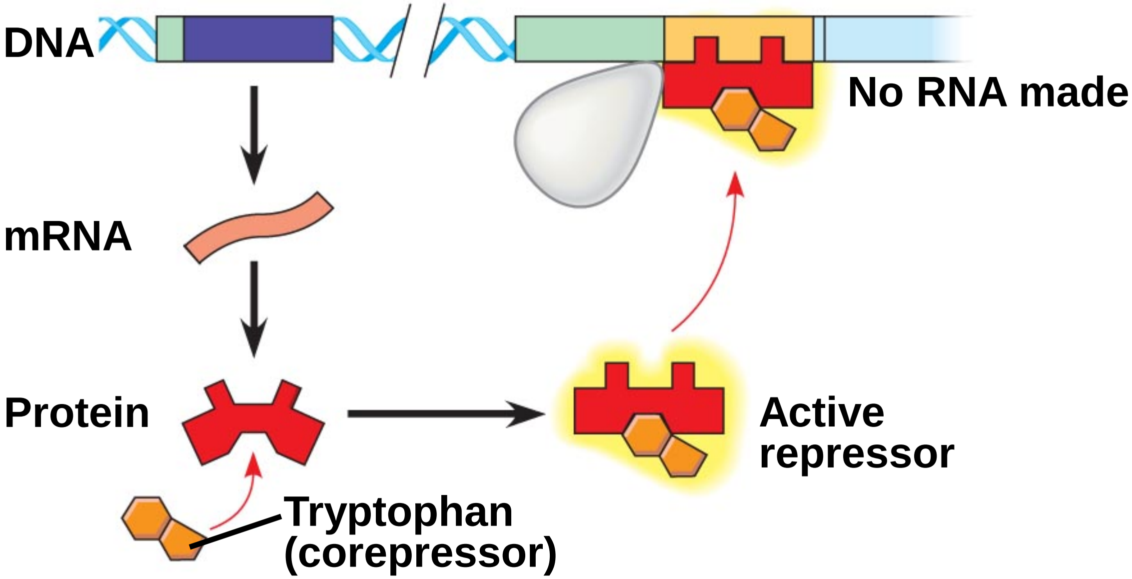
(a) Tryptophan absent, repressor inactive, operon on

Fig. 18-3b-1



(b) Tryptophan present, repressor active, operon off

Fig. 18-3b-2



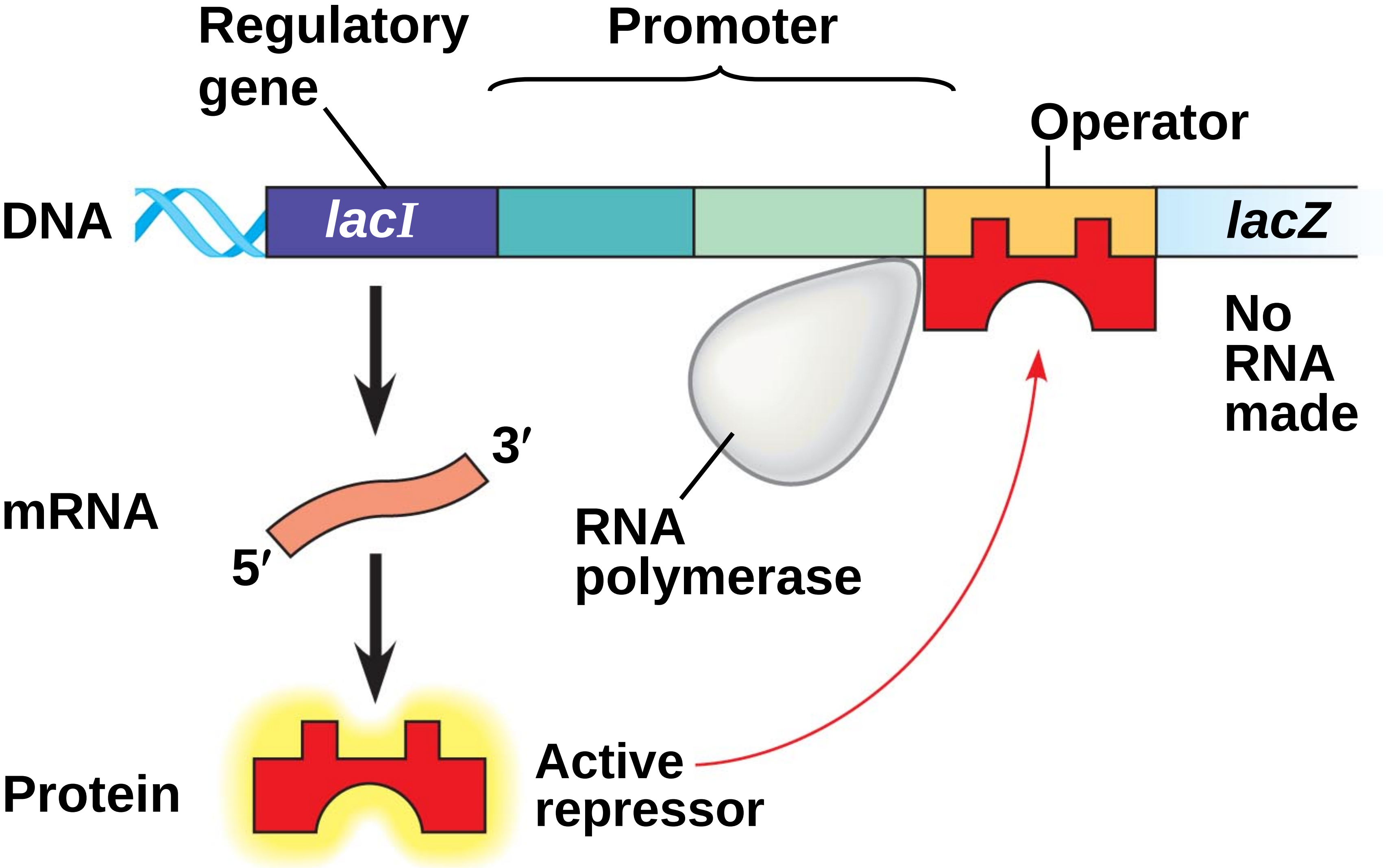
(b) Tryptophan present, repressor active, operon off

Repressible and Inducible Operons: Two Types of Negative Gene Regulation

- A repressible operon is one that is usually on; binding of a repressor to the operator shuts off transcription
- The *trp* operon is a repressible operon
- An inducible operon is one that is usually off; a molecule called an inducer inactivates the repressor and turns on transcription

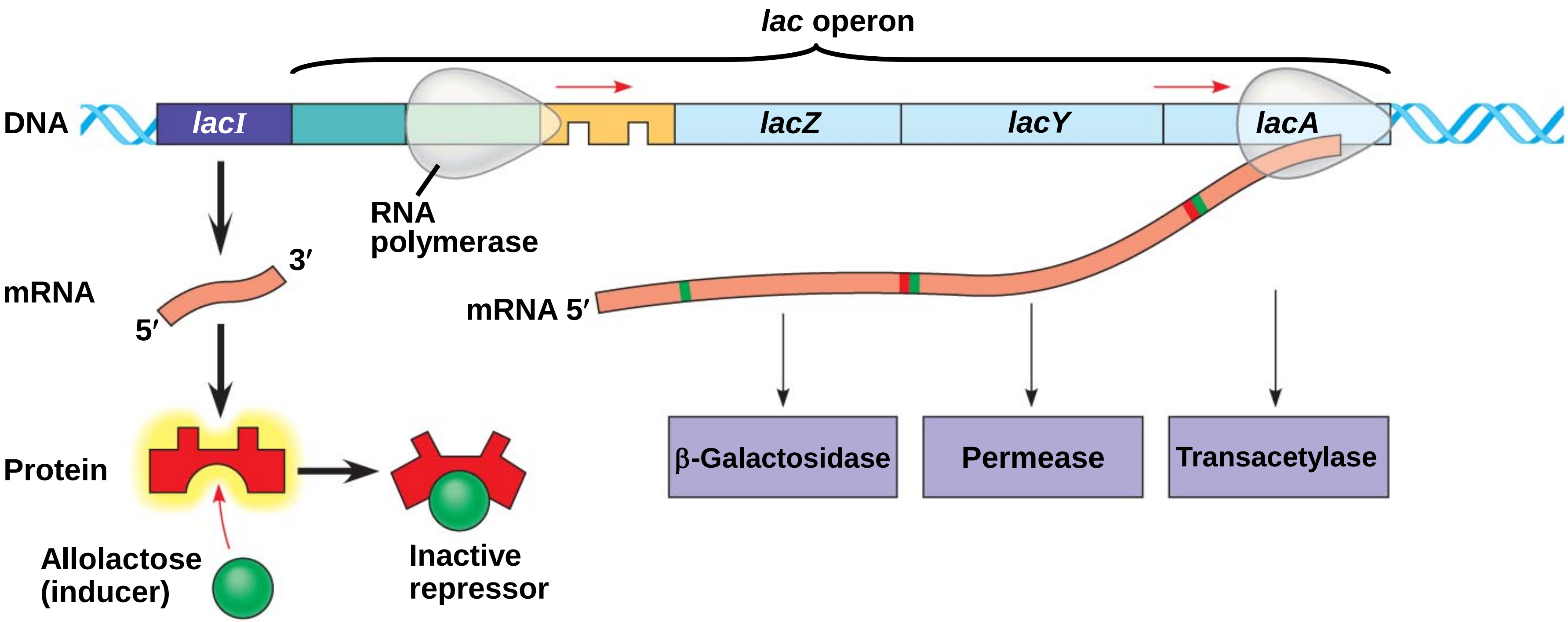
- The *lac* operon is an inducible operon and contains genes that code for enzymes used in the hydrolysis and metabolism of lactose
- By itself, the *lac* repressor is active and switches the *lac* operon off
- A molecule called an **inducer** inactivates the repressor to turn the *lac* operon on

Fig. 18-4a



(a) Lactose absent, repressor active, operon off

Fig. 18-4b



(b) Lactose present, repressor inactive, operon on

Lac Operon Animation

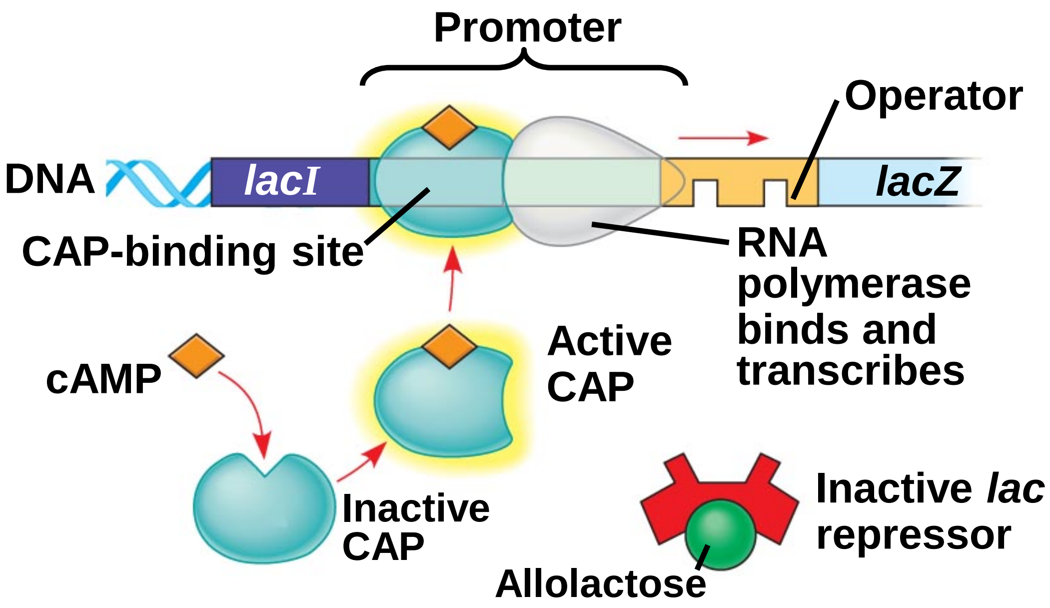
- Inducible enzymes usually function in catabolic pathways; their synthesis is induced by a chemical signal
- Repressible enzymes usually function in anabolic pathways; their synthesis is repressed by high levels of the end product
- Regulation of the *trp* and *lac* operons involves negative control of genes because operons are switched off by the active form of the repressor

Positive Gene Regulation

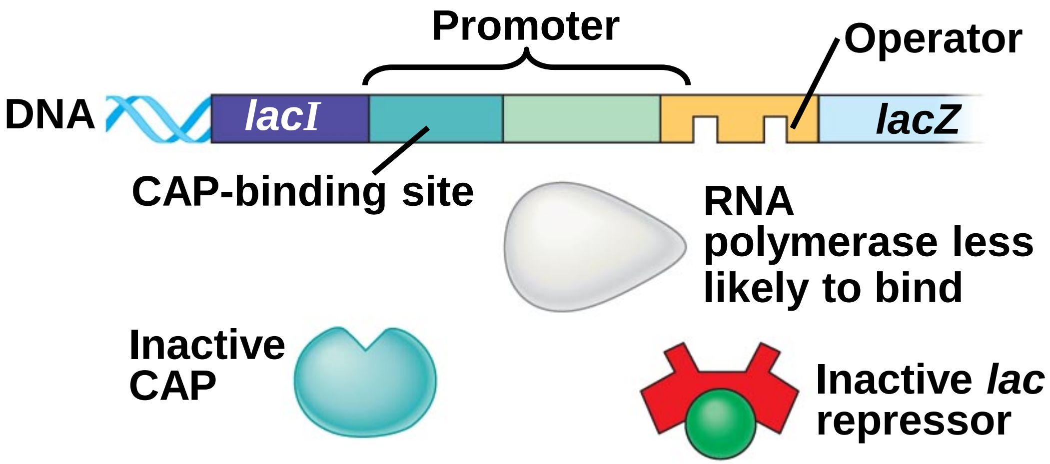
- Some operons are also subject to positive control through a stimulatory protein, such as catabolite activator protein (CAP), an **activator** of transcription
- When glucose (a preferred food source of *E. coli*) is scarce, CAP is activated by binding with **cyclic AMP**
- Activated CAP attaches to the promoter of the *lac* operon and increases the affinity of RNA polymerase, thus accelerating transcription

- When glucose levels increase, CAP detaches from the *lac* operon, and transcription returns to a normal rate
- CAP helps regulate other operons that encode enzymes used in catabolic pathways

Fig. 18-5



(a) Lactose present, glucose scarce (cAMP level high): abundant *lac* mRNA synthesized



(b) Lactose present, glucose present (cAMP level low): little *lac* mRNA synthesized

Concept 18.2: Eukaryotic gene expression can be regulated at any stage

- All organisms must regulate which genes are expressed at any given time

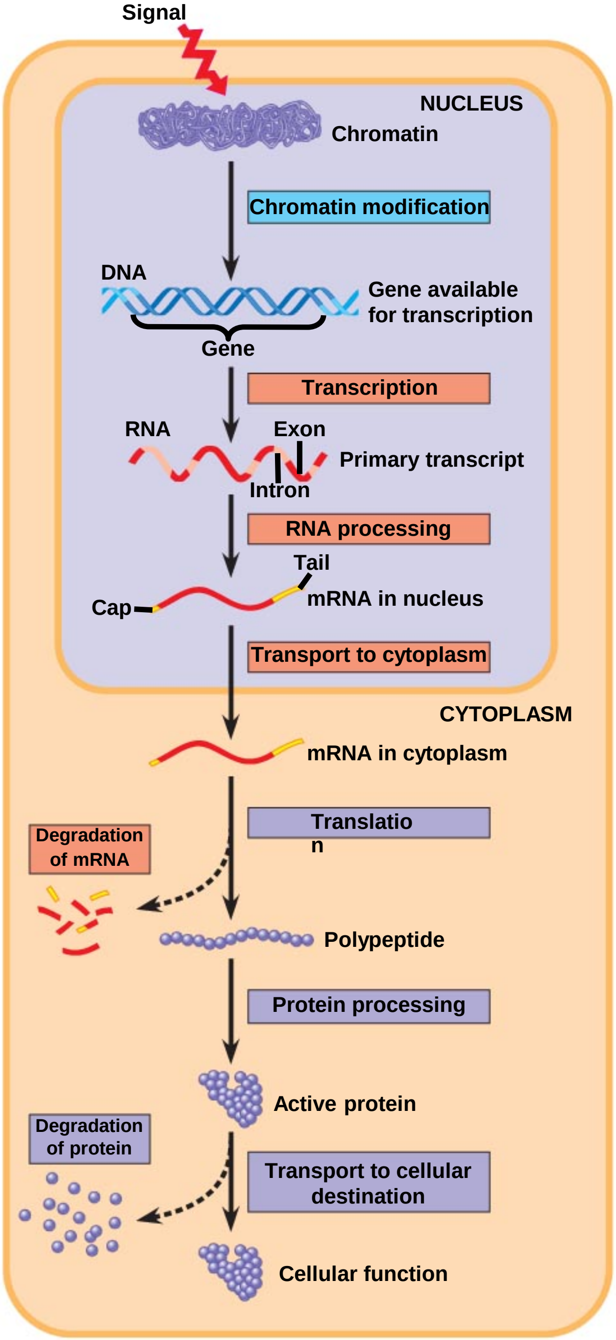
- In multicellular organisms, gene expression is essential for cell specialization

- In single-celled microorganisms, gene expression is essential for survival. Unnecessary genes and enzymes waste energy. Microorganisms cannot afford to be wasteful.

Differential Gene Expression

- Almost all the cells in an organism are genetically identical
- Differences between cell types result from **differential gene expression**, the expression of different genes by cells with the same genome
- Errors in gene expression can lead to diseases including cancer
- Gene expression is regulated at many stages

Fig. 18-6


Signal
NUCLEUS
Chromatin
Chromatin modification
DNA
Gene available for transcription
Gene
Transcription
RNA
Exon
Primary transcript
Intron
RNA processing
Tail
Cap
mRNA in nucleus
Transport to cytoplasm
CYTOPLASM
mRNA in cytoplasm
Translation
Degradation of mRNA
Polypeptide
Protein processing
Active protein
Degradation of protein
Transport to cellular destination
Cellular function

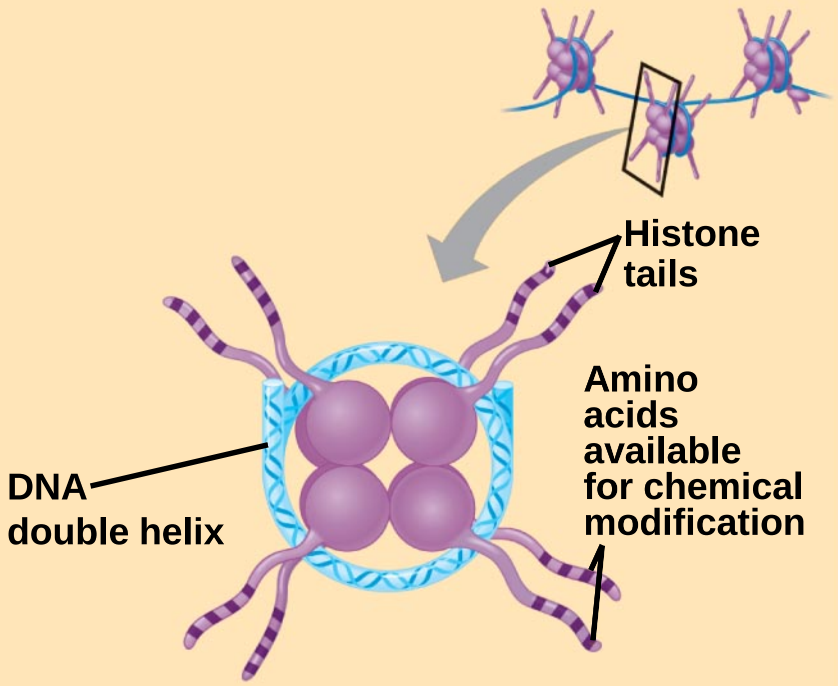
Regulation of Chromatin Structure

- Genes within highly packed heterochromatin are usually not expressed
- Chemical modifications to histones and DNA of chromatin influence both chromatin structure and gene expression

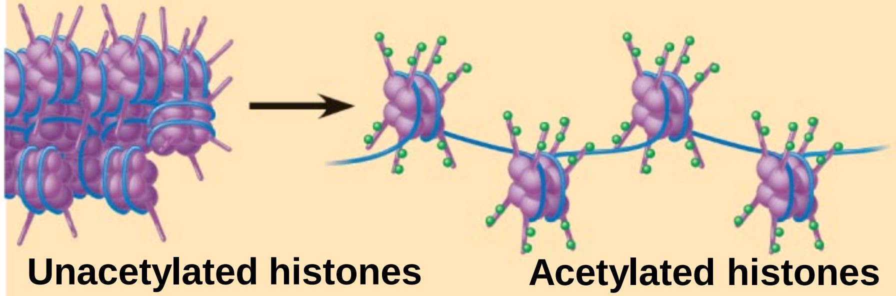
Histone Modifications

- In **histone acetylation**, acetyl groups are attached to positively charged lysines in histone tails (epigenetic)
- This process loosens chromatin structure, thereby promoting the initiation of transcription
- The addition of methyl groups (methylation) can condense chromatin; the addition of phosphate groups (phosphorylation) next to a methylated amino acid can loosen chromatin (both epigenetic modifications)

Fig. 18-7



(a) Histone tails protrude outward from a nucleosome



(b) Acetylation of histone tails promotes loose chromatin structure that permits transcription

- The histone code hypothesis proposes that specific combinations of modifications help determine chromatin configuration and influence transcription

DNA Methylation

- DNA methylation, the addition of methyl groups to certain bases in DNA, is associated with reduced transcription in some species
- DNA methylation can cause long-term inactivation of genes in cellular differentiation
- In **genomic imprinting**, methylation regulates expression of either the maternal or paternal alleles of certain genes at the start of development

Epigenetic Inheritance

- Although the chromatin modifications just discussed do not alter DNA sequence, they may be passed to future generations of cells
- The inheritance of traits transmitted by mechanisms not directly involving the nucleotide sequence is called **epigenetic inheritance**

Regulation of Transcription Initiation

- Chromatin-modifying enzymes provide initial control of gene expression by making a region of DNA either more or less able to bind the transcription machinery

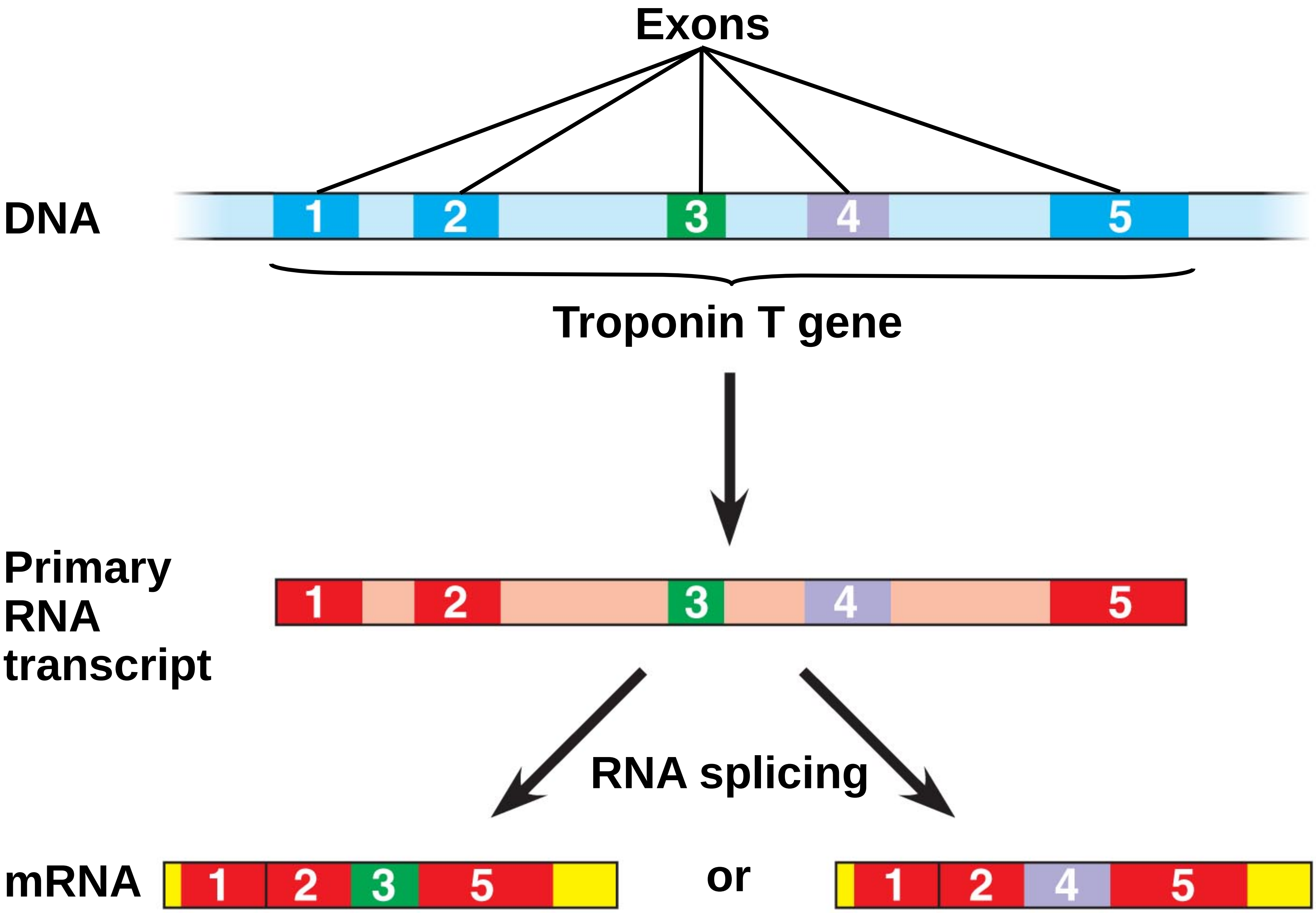
Mechanisms of Post-Transcriptional Regulation

- Transcription alone does not account for gene expression
- Regulatory mechanisms can operate at various stages after transcription
- Such mechanisms allow a cell to fine-tune gene expression rapidly in response to environmental changes

RNA Processing

- In **alternative RNA splicing**, different mRNA molecules are produced from the same primary transcript, depending on which RNA segments are treated as exons and which as introns

Fig. 18-11



Exons

DNA

Troponin T gene

Primary RNA transcript

RNA splicing

mRNA

or

mRNA Degradation

- The life span of mRNA molecules in the cytoplasm is a key to determining protein synthesis
- Eukaryotic mRNA is more long lived than prokaryotic mRNA
- The mRNA life span is determined in part by sequences in the leader and trailer regions

Concept 18.3: Noncoding RNAs play multiple roles in controlling gene expression

- Only a small fraction of DNA codes for proteins, rRNA, and tRNA
- A significant amount of the genome may be transcribed into noncoding RNAs
- Noncoding RNAs regulate gene expression at two points: mRNA translation and chromatin configuration

Effects on mRNAs by MicroRNAs and Small Interfering RNAs

- **MicroRNAs (miRNAs)** are small single-stranded RNA molecules that can bind to mRNA
- These can degrade mRNA or block its translation

- The phenomenon of inhibition of gene expression by RNA molecules is called **RNA interference** (**RNAi**)

- RNAi is caused by **small interfering RNAs (siRNAs)**

- siRNAs and miRNAs (**mi**cro) are similar but form from different RNA precursors

- Both are created by Dicer enzyme

Chromatin Remodeling and Silencing of Transcription by Small RNAs

- siRNAs play a role in heterochromatin formation and can block large regions of the chromosome
- Small RNAs may also block transcription of specific genes

You should now be able to:

1. Explain the concept of an operon and the function of the operator, repressor, and corepressor
2. Explain the adaptive advantage of grouping bacterial genes into an operon
3. Explain how repressible and inducible operons differ and how those differences reflect differences in the pathways they control

4. Explain how DNA methylation and histone acetylation affect chromatin structure and the regulation of transcription

5. Define control elements and explain how they influence transcription

6. Explain the role of promoters, enhancers, activators, and repressors in transcription control

7. Explain how eukaryotic genes can be coordinately expressed

8. Describe the roles played by small RNAs on gene expression