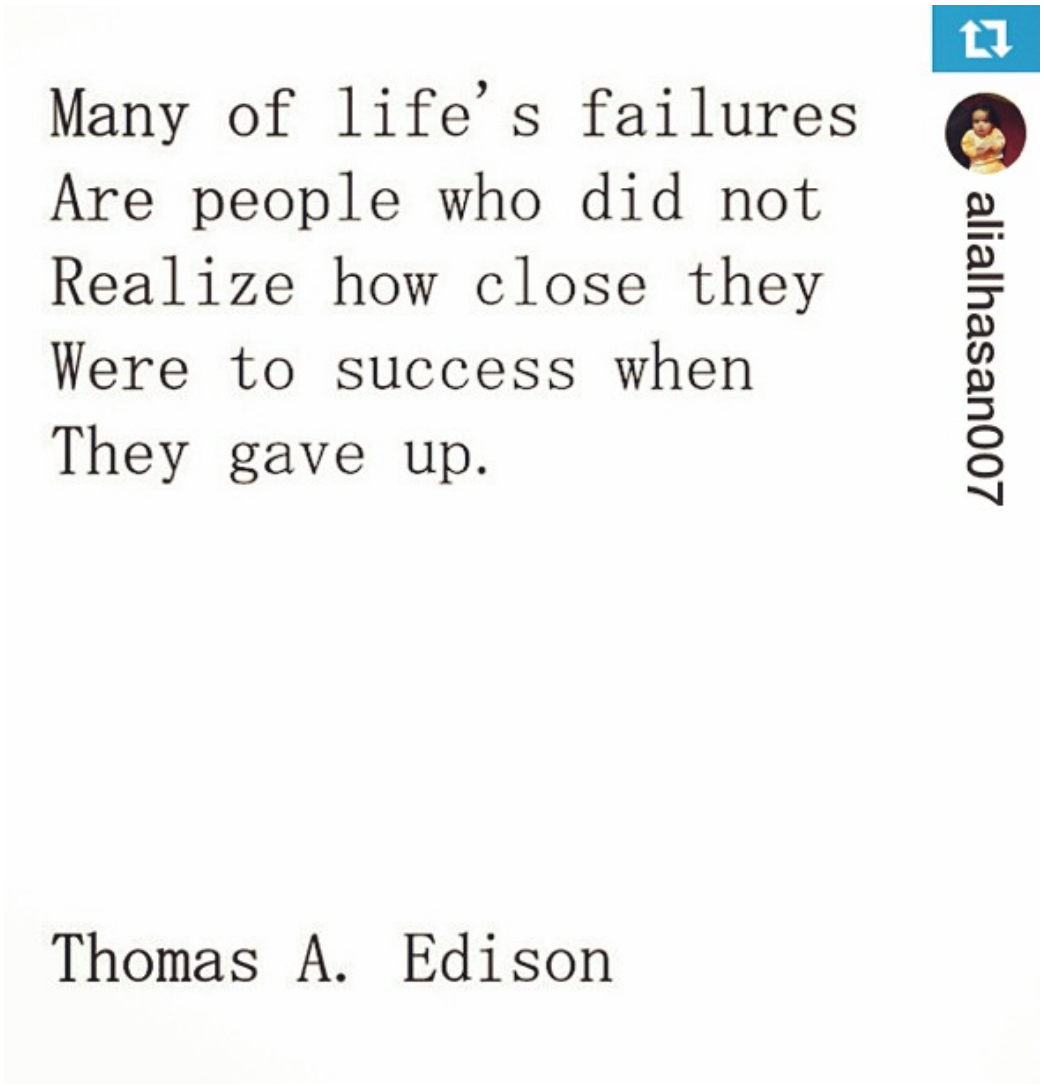
Lecture 22:

Regulation of gene expression

IV. Eukaryotes (part 1)

Course 281

Lessons for life

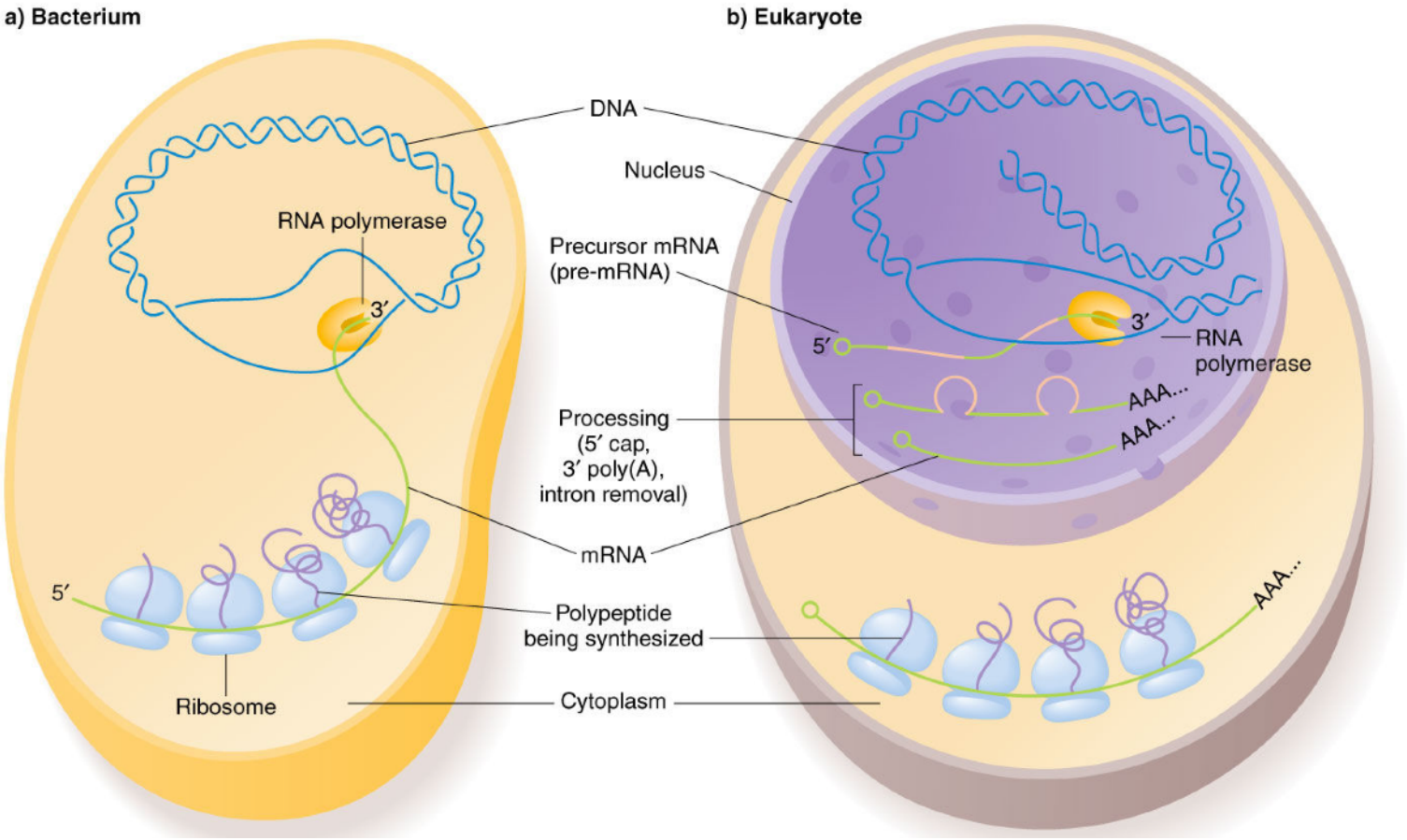


AIMS

- Understand the **general** complexity of transcription regulation in eukaryotes.
- Understand in a broad sense how regulatory proteins (activators, co-activators, repressors, co-repressors) influence transcription in eukaryotes.
- Understand the difference between prokaryotic and eukaryotic repressors.
- Understand how **generally** gene expression is regulated at the transcription initiation level in eukaryotes.

Eukaryotic transcription regulation

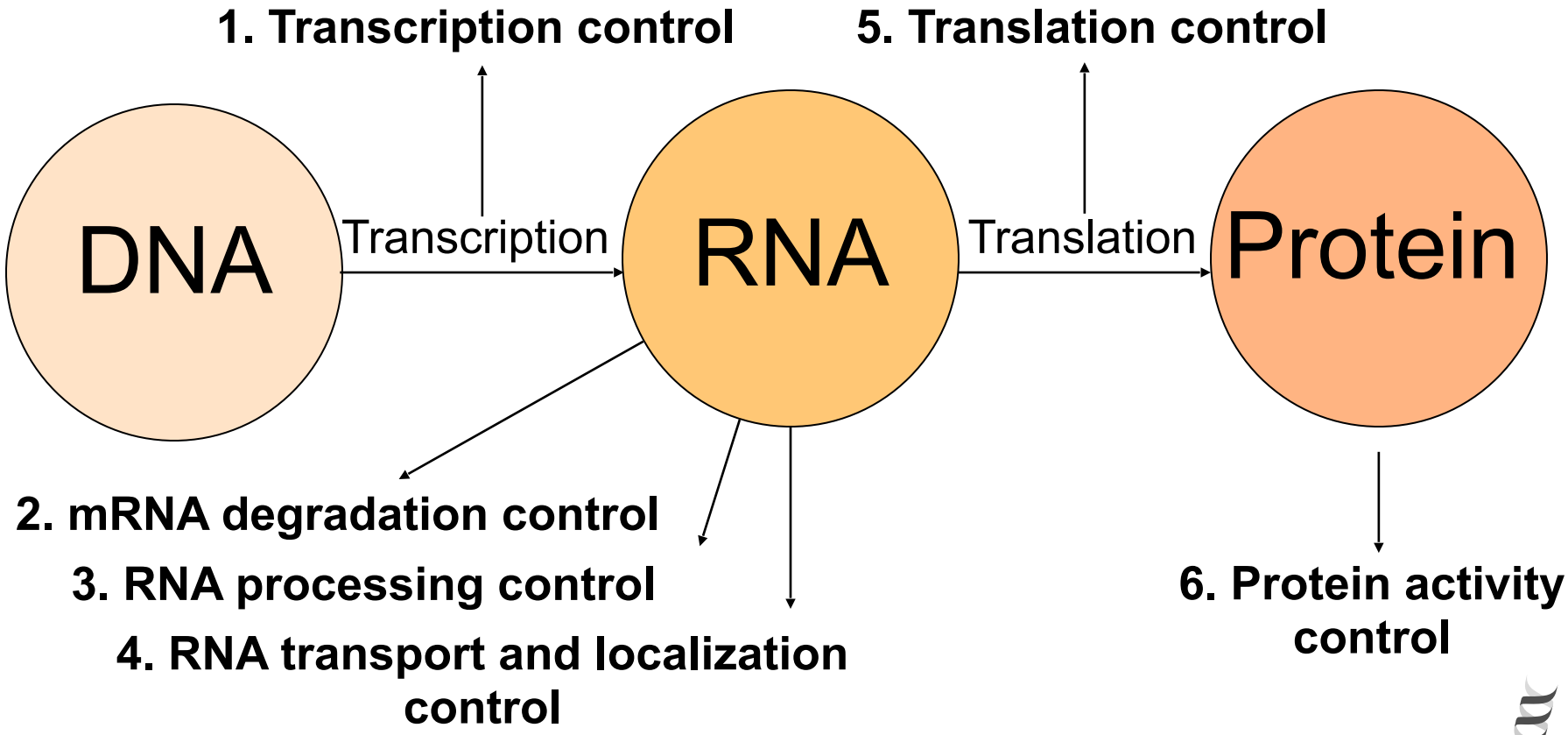
Eukaryotic gene expression is more complicated than in prokaryotes and as a result regulation is also complicated



What is unique in eukaryotic cells that make regulation more complicated?

Regulation of Gene expression

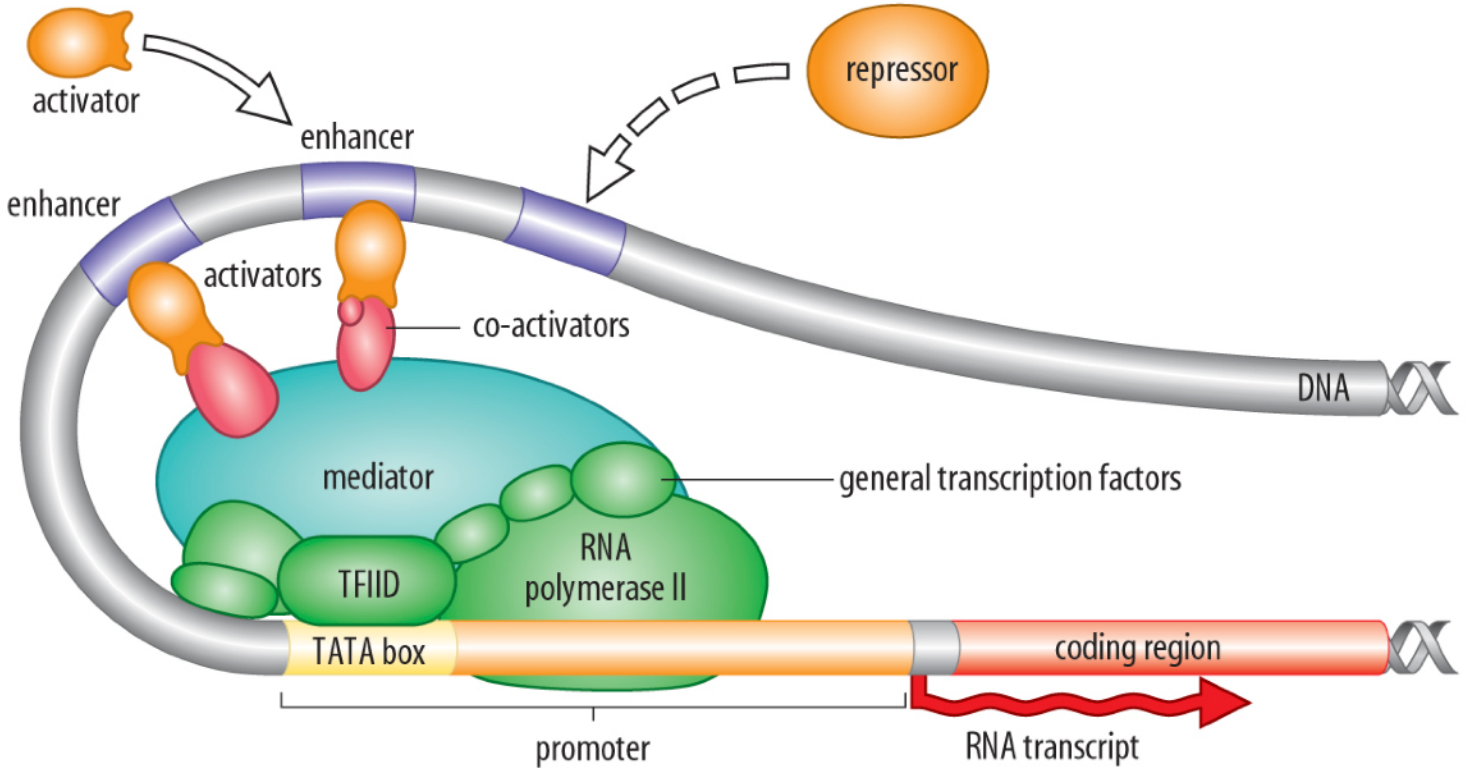
Eukaryotic: regulation of gene expression can take place at multiple stages during the transcription/ translation process.



Regulation of transcription initiation

What happens during transcription initiation?

The assembly of the initiation complex at the promoter site of a gene.



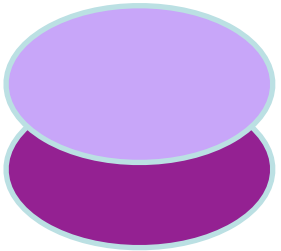
Regulation of transcription initiation

Enhancer/Activator

- **An Enhancer :** is a DNA sequence motif located upstream or downstream of the promoter region.
- **An activator:** is a regulatory protein that binds to enhancer sequence.

Regulation of transcription initiation

Enhancer/Activator

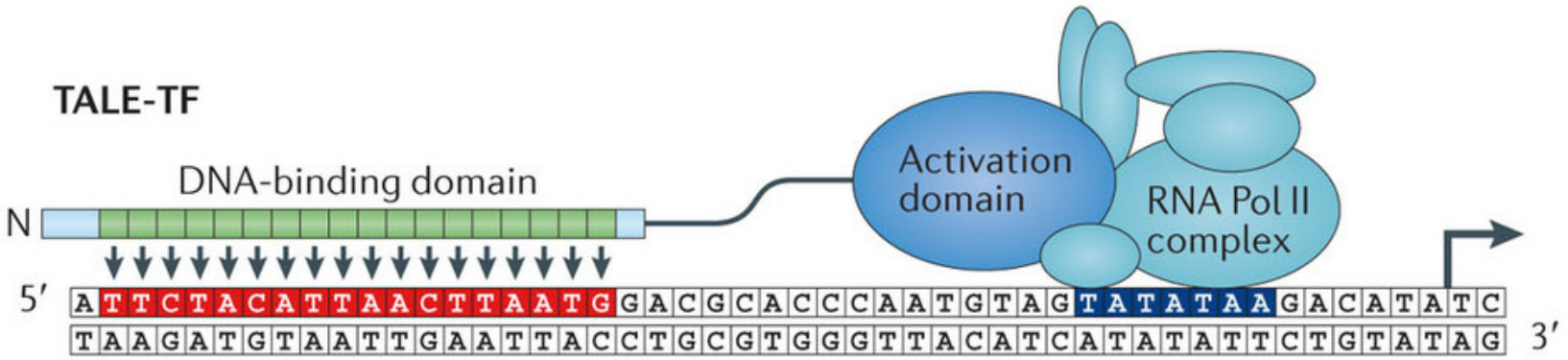


- **Activators contain:**
  - **A DNA binding domain:** a location in the protein binds to DNA (enhancer sequence).
  - **A protein binding domain:** a location in the protein that binds to the transcription initiation complex.

Regulation of transcription initiation

Enhancer/Activator

DNA binding domain and protein binding domain



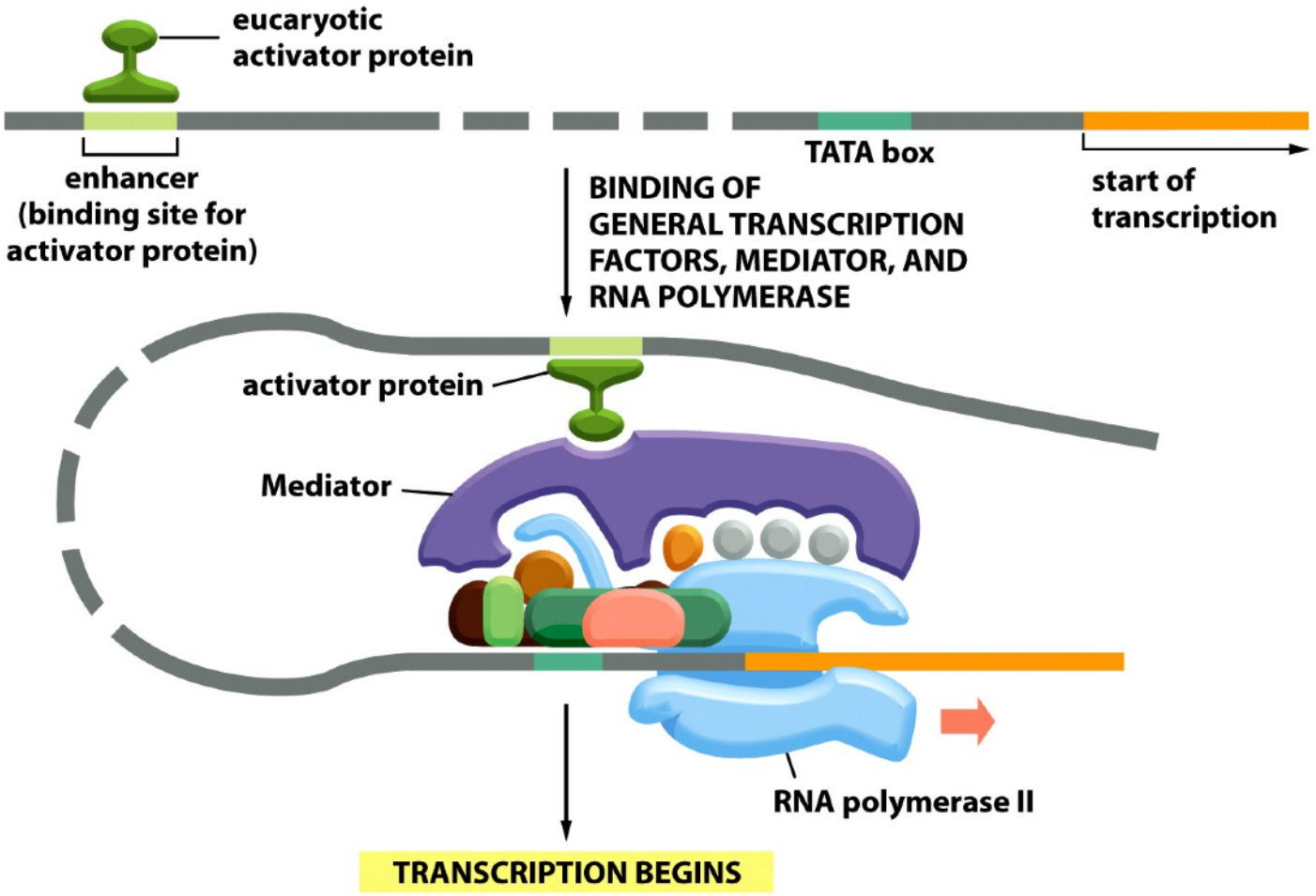
Regulation of transcription initiation

Enhancer/Activator

- When an activator binds to the enhancer sequence away from the promoter, DNA loops so that the activator is in contact with the initiation complex.
- The activator interacts with the transcription initiation complex and facilitates the recruitment of RNA polymerase to start transcription.
- Gene is turned ON and mRNA is made.

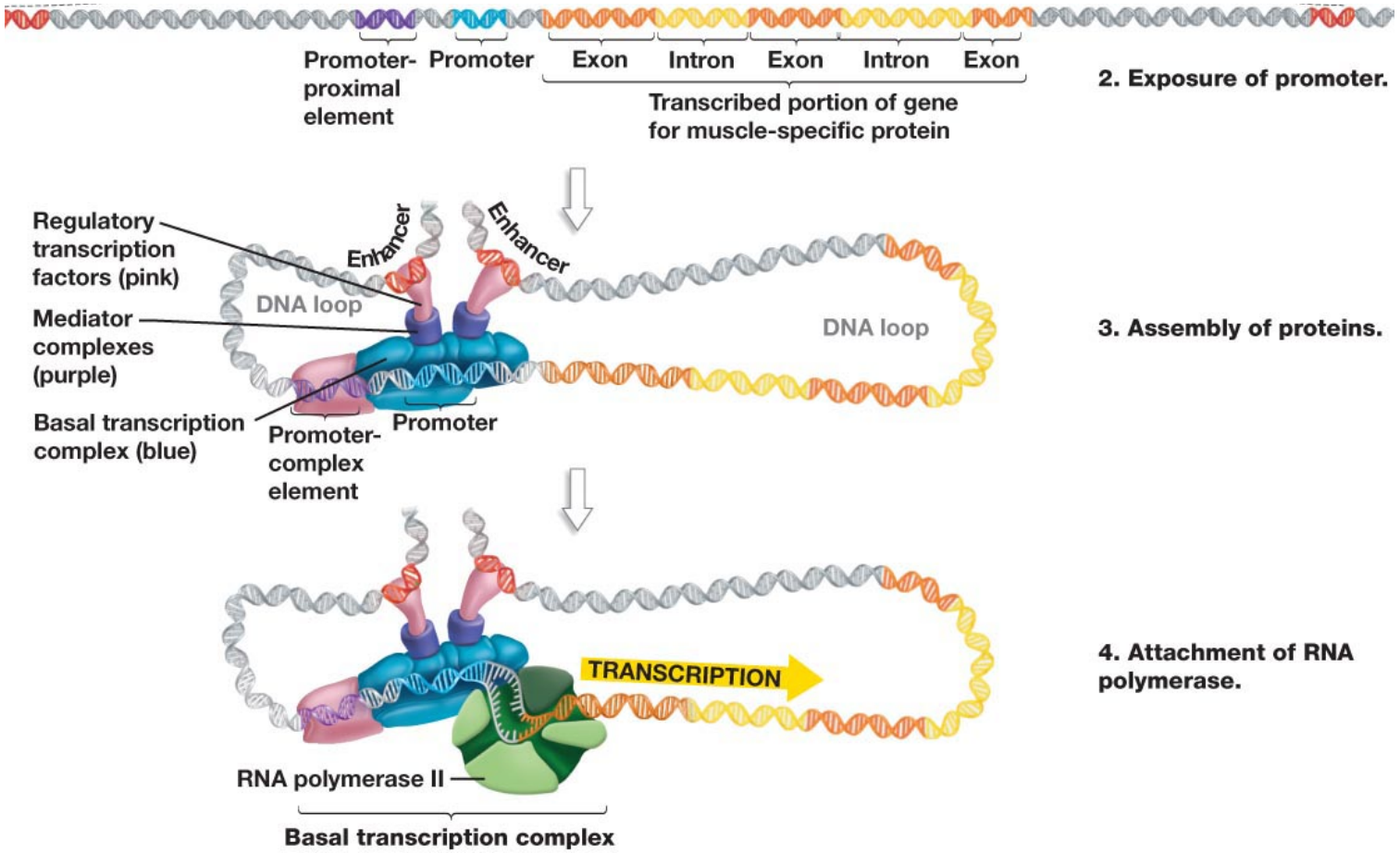
Regulation of transcription initiation

Enhancer/Activator regulates the initiation of transcription by turning genes ON



Regulation of transcription initiation

What are the possible locations of eukaryotic enhancer sequence?



If we consider the transcription machinery of a eukaryotic gene a nice car, what does activators act as?

(1) Breaks

(2) Gas pedal

Regulation of transcription initiation

Silencer/Repressor

- **A silencer:** is a DNA sequence motif located upstream or downstream of the promoter region.
- **A repressor:** is a regulatory protein that binds to silencer sequence.

Regulation of transcription initiation

Silencer/Repressor

- **Repressors contain:**
  - **A DNA binding domain:** a location in the protein binds to DNA (silencer sequence).
  - **A protein binding domain:** a location in the protein that binds to the transcription initiation complex.

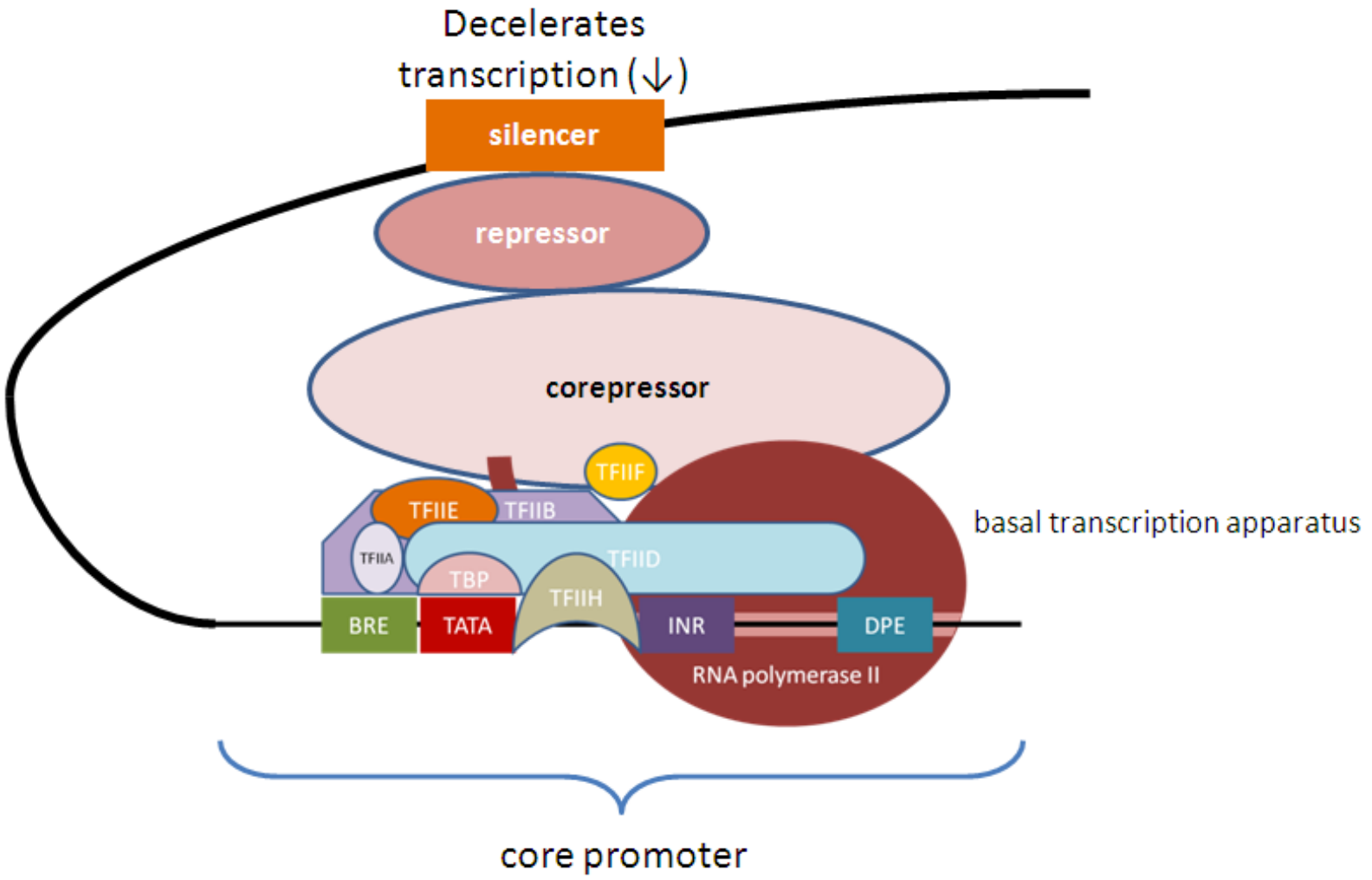
Regulation of transcription initiation

Silencer/Repressor

- When a repressor binds to silencer sequence away from the promoter, DNA loops so that the repressor is in contact with the initiation complex.
- The repressor interacts with the transcription initiation complex and **prevents** the initiation of transcription.
- No mRNA is made.

Regulation of transcription initiation

Silencer/Repressor



If we consider the transcription machinery of a eukaryotic gene a nice car, what does repressors act as?

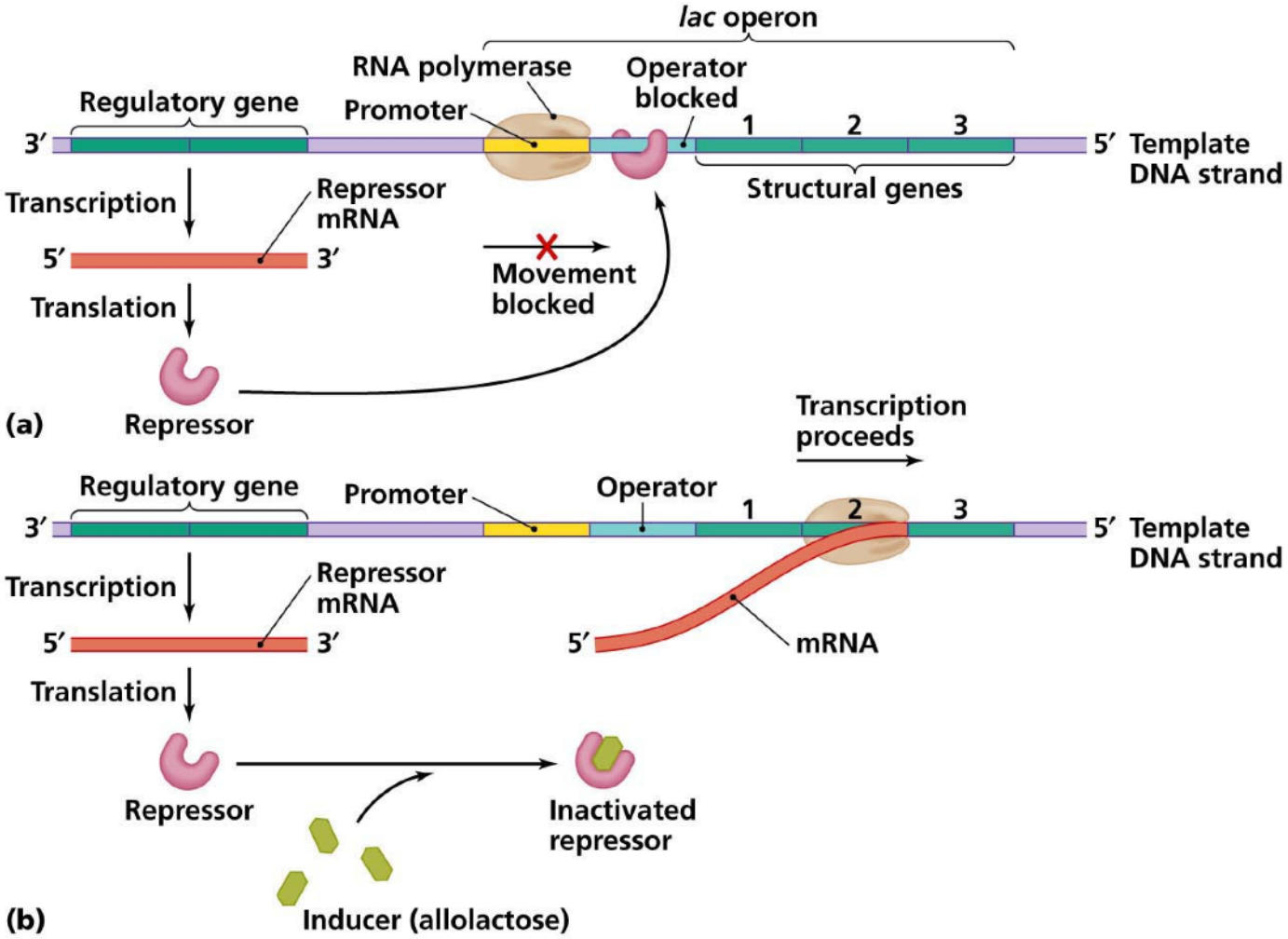
(1) Breaks

(2) Gas pedal

What are the differences between eukaryotic and prokaryotic repressor regulation?

Regulation of transcription initiation

Silencer/Repressor



Regulation of transcription initiation

Silencer/Repressor

- Prokaryotic repressors bind to DNA motifs (operators) located downstream of the promoter of the operon (**WITHIN**).
- Binding to a sequence downstream blocks the movement of RNA polymerase.

Regulation of transcription initiation

Silencer/Repressor

- Eukaryotic repressors bind to DNA motifs (silencers) located away from the gene (**NOT WITHIN**).
- The repressor bound to silencer sequence then interact with the transcription initiation complex **PREVENTING** RNA polymerase normal function.

Let’s complicate things 1

What is the binding site of activators?

What is the binding site of repressors?

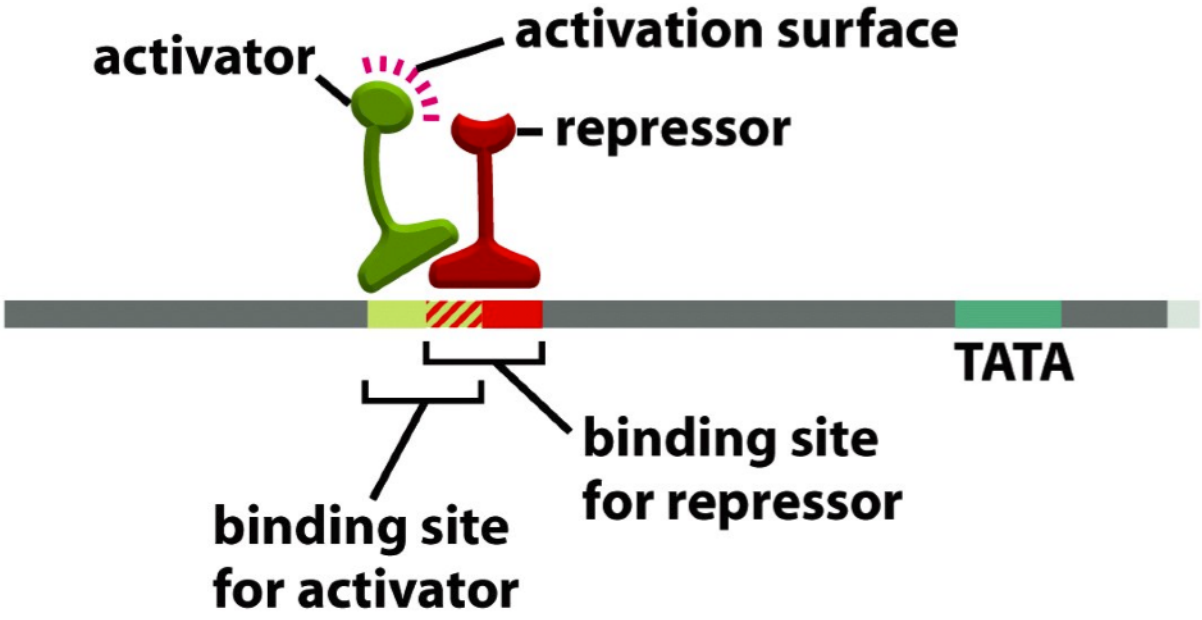
Do binding sites overlap?

Let's complicate things 1

- When enhancer and silencer sequences overlap, the get into a competition called **competitive DNA binding.**

- If repressor binds first, **gene is OFF.**
- If activator binds first, **gene is ON.**

competitive DNA binding

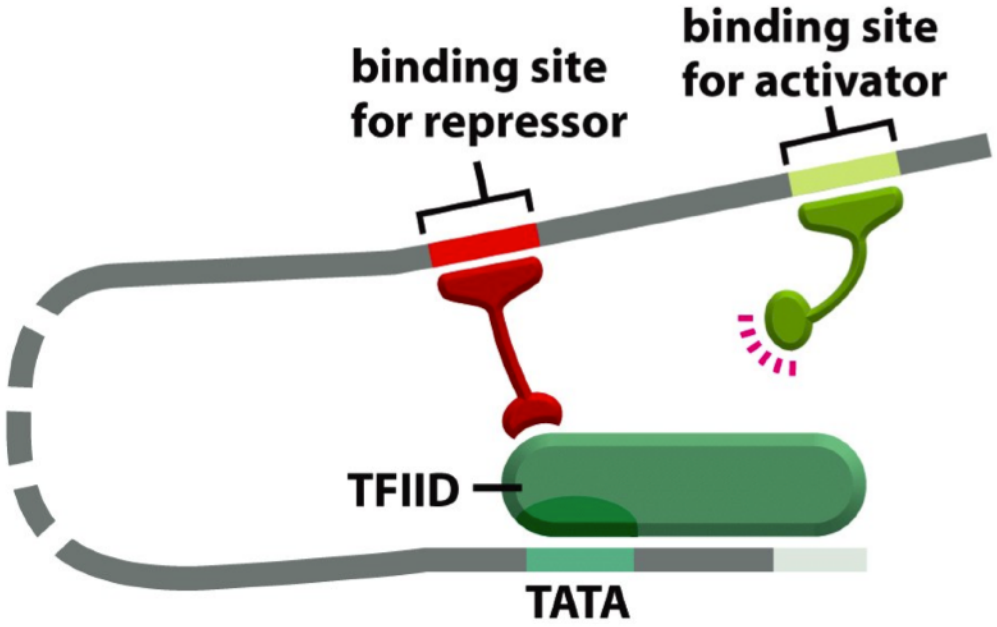


Let's complicate things 2

- Direct or indirect interaction with general transcription factors.

- If direct, binding and repressing or activating is faster.
- If indirect, need **co-activator or co-repressor.**

direct interaction with the general transcription factors

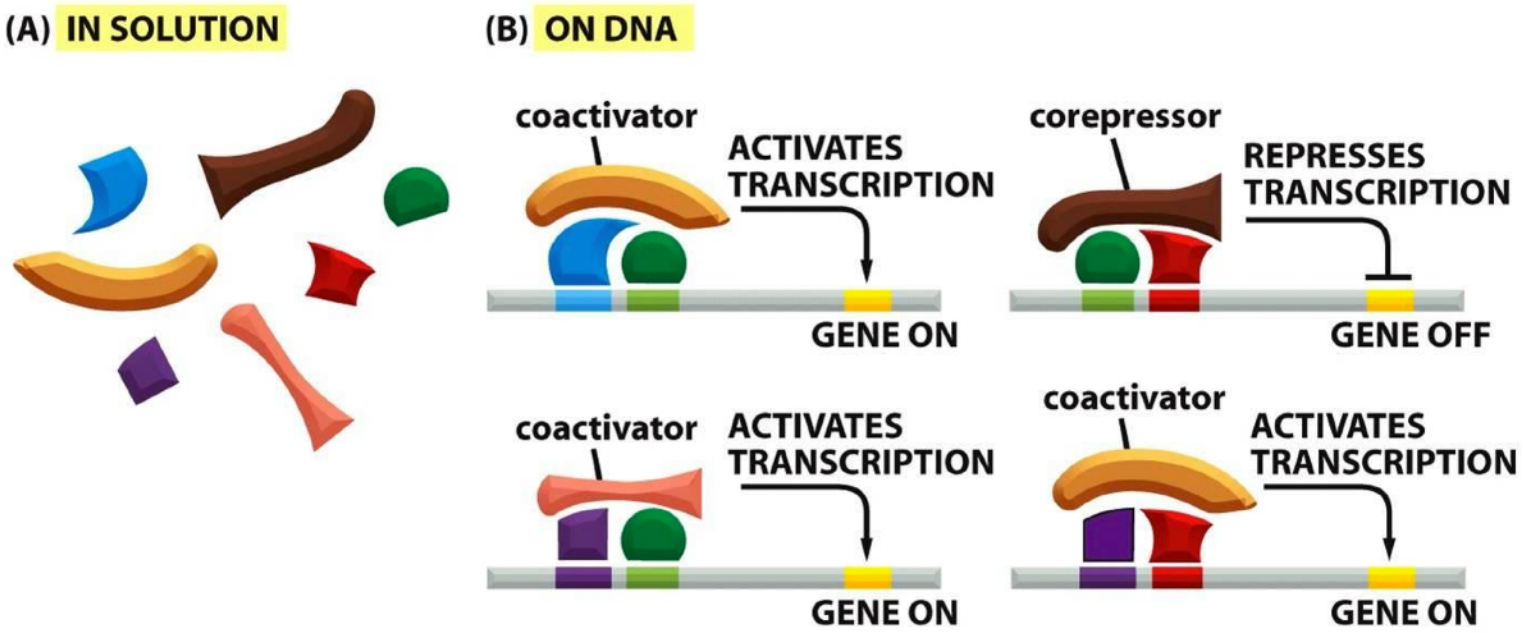


Let's complicate things 2

Co-activator / Co-repressor.

Co-activators and co-repressors provide an additional layer of regulation

How? Why?



Where do activators, co-activators, repressors, co-repressors come from?

Regulatory or housekeeping genes?

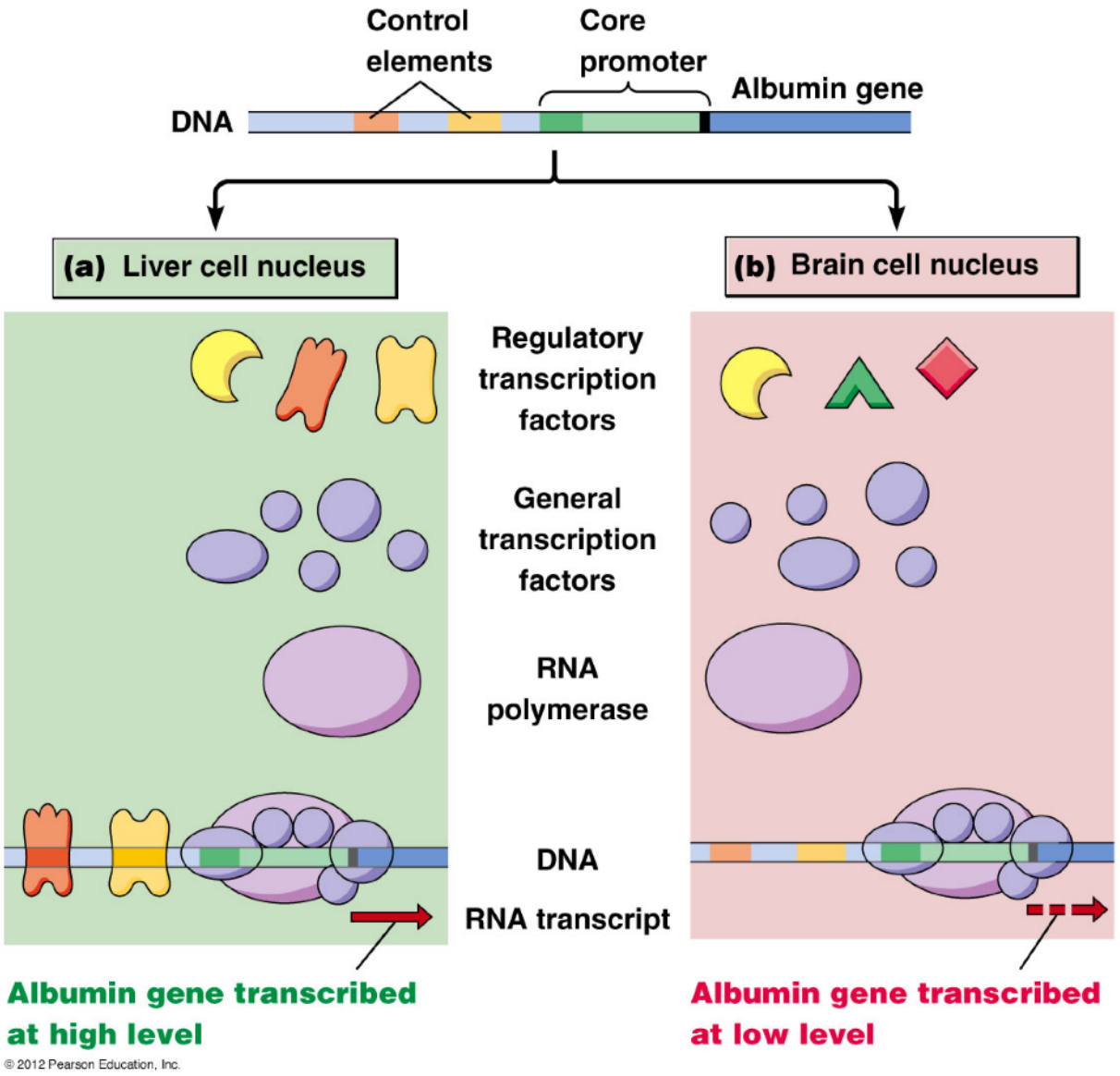
Do co-activator and co-repressors have DNA binding domain?

How many protein binding domains a co-activator contains (hypothetically)?

How it works?

The presence of activators, co-activators, repressors, co-repressors in a specific differentiated cells influence much of the gene is expressed

How it works?


Control elements
Core promoter
Albumin gene
DNA
(a) Liver cell nucleus
(b) Brain cell nucleus
Regulatory transcription factors
General transcription factors
RNA polymerase
DNA
RNA transcript
Albumin gene transcribed at high level
Albumin gene transcribed at low level
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How it works?

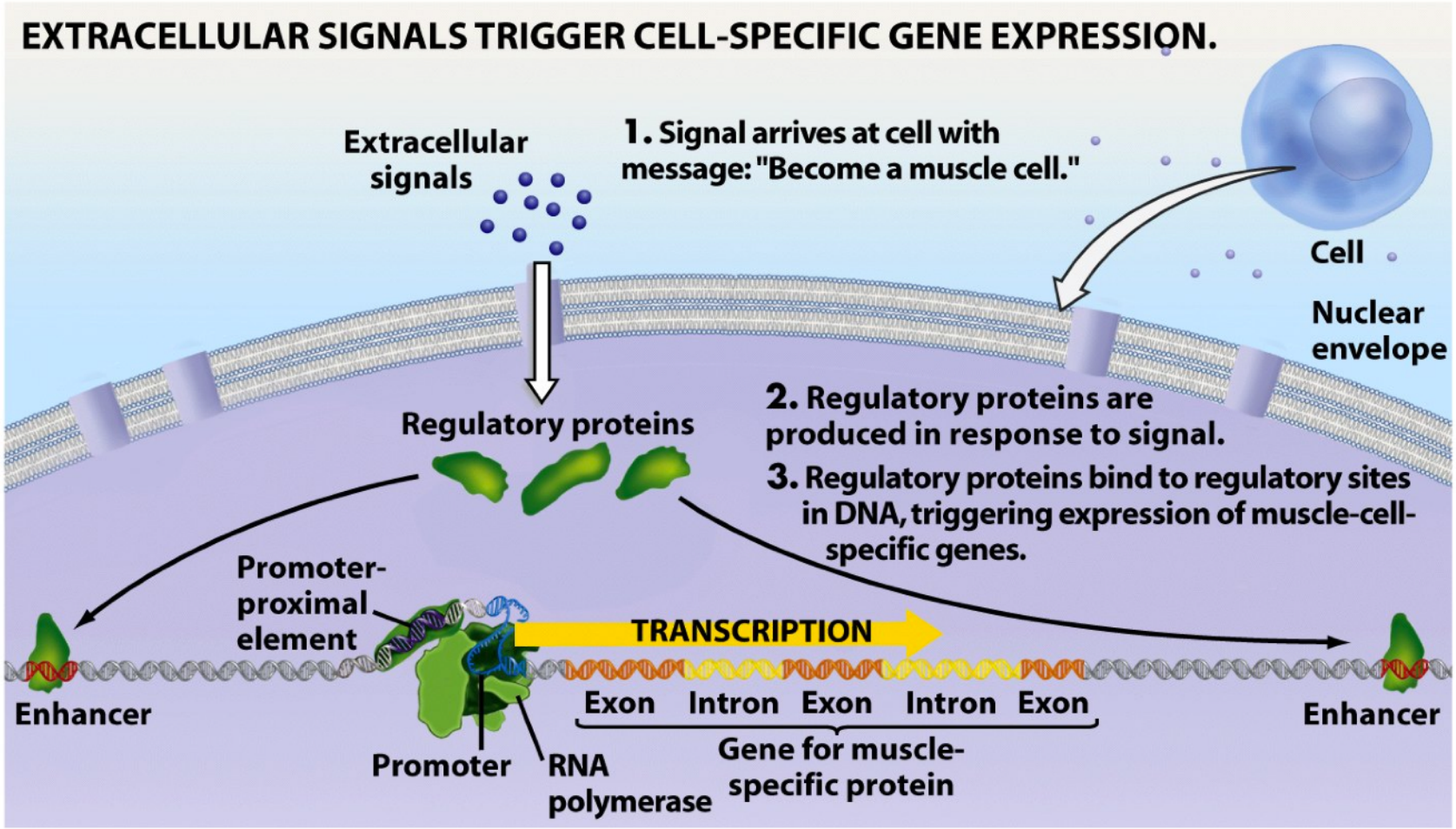
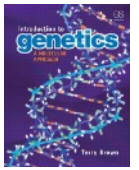
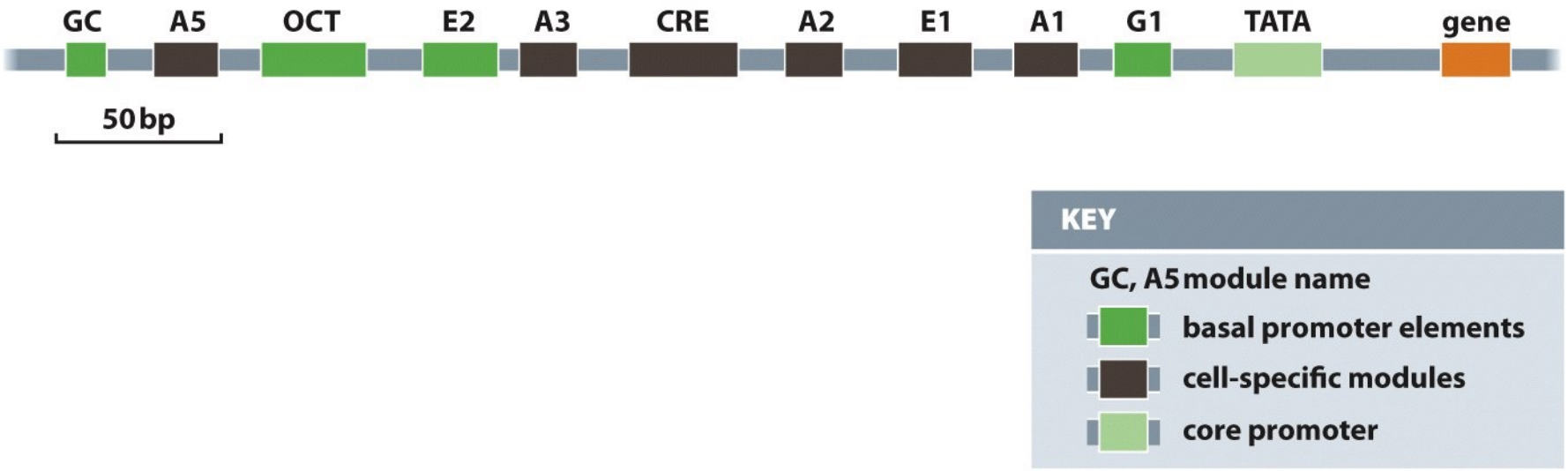


Figure 18-9 Biological Science, 2/e

9.3 REGULATION OF TRANSCRIPTION INITIATION IN EUKARYOTES

- RNA polymerase II promoters are controlled by a variety of regulatory sequences
- Signals from outside the cell must be transmitted to the nucleus in order to influence gene expression
- The RNA polymerase II initiation complex is activated via a mediator protein





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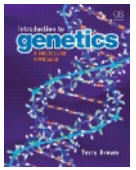

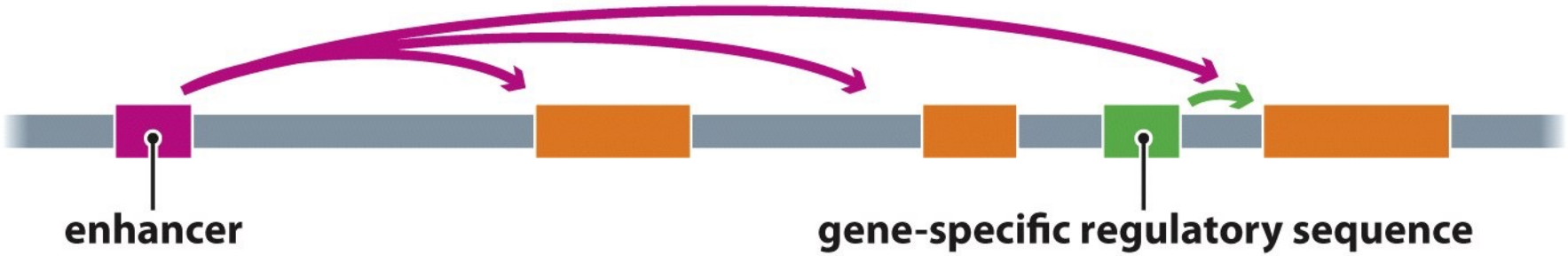

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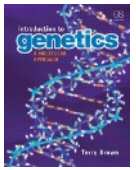

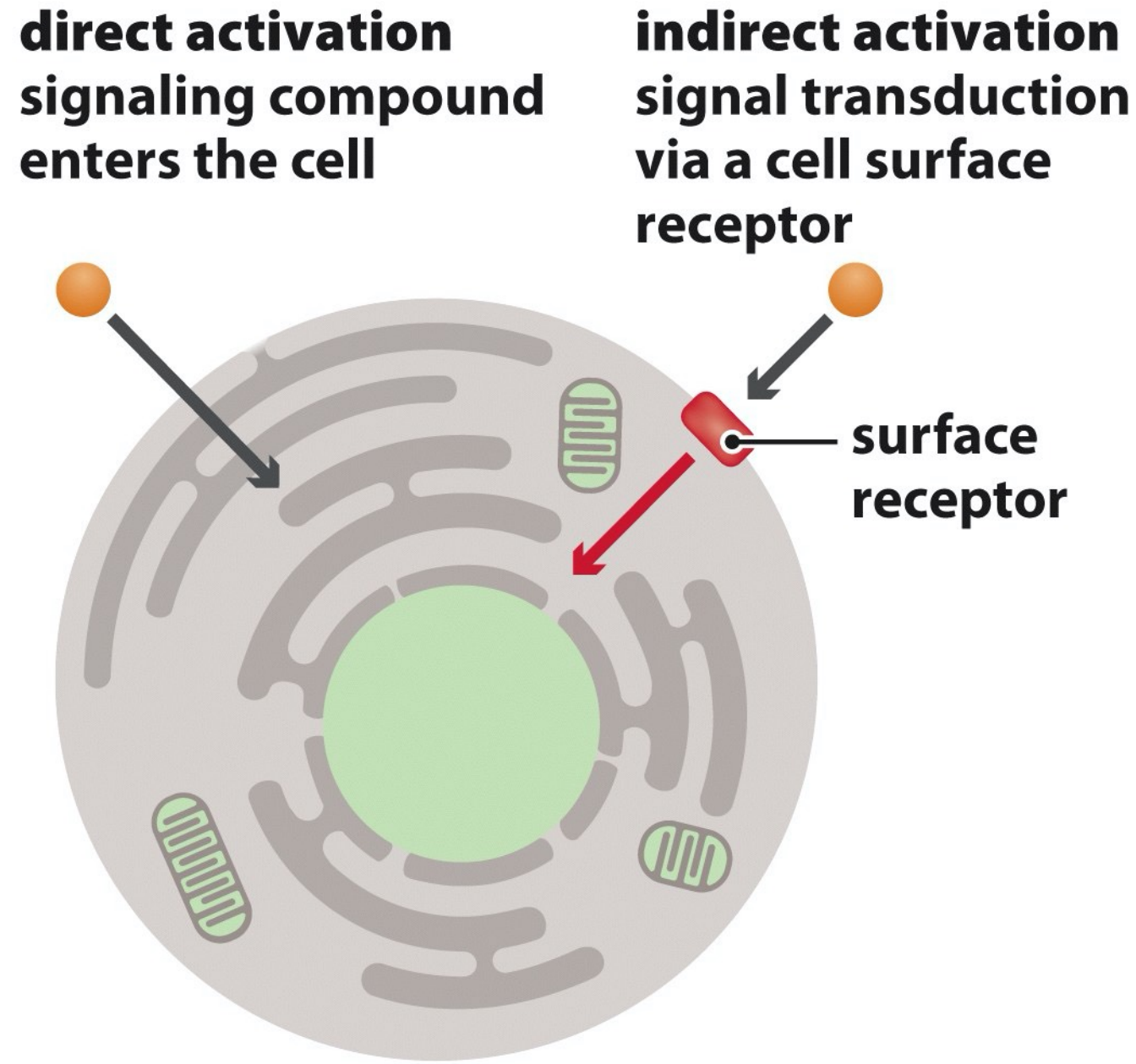

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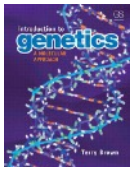

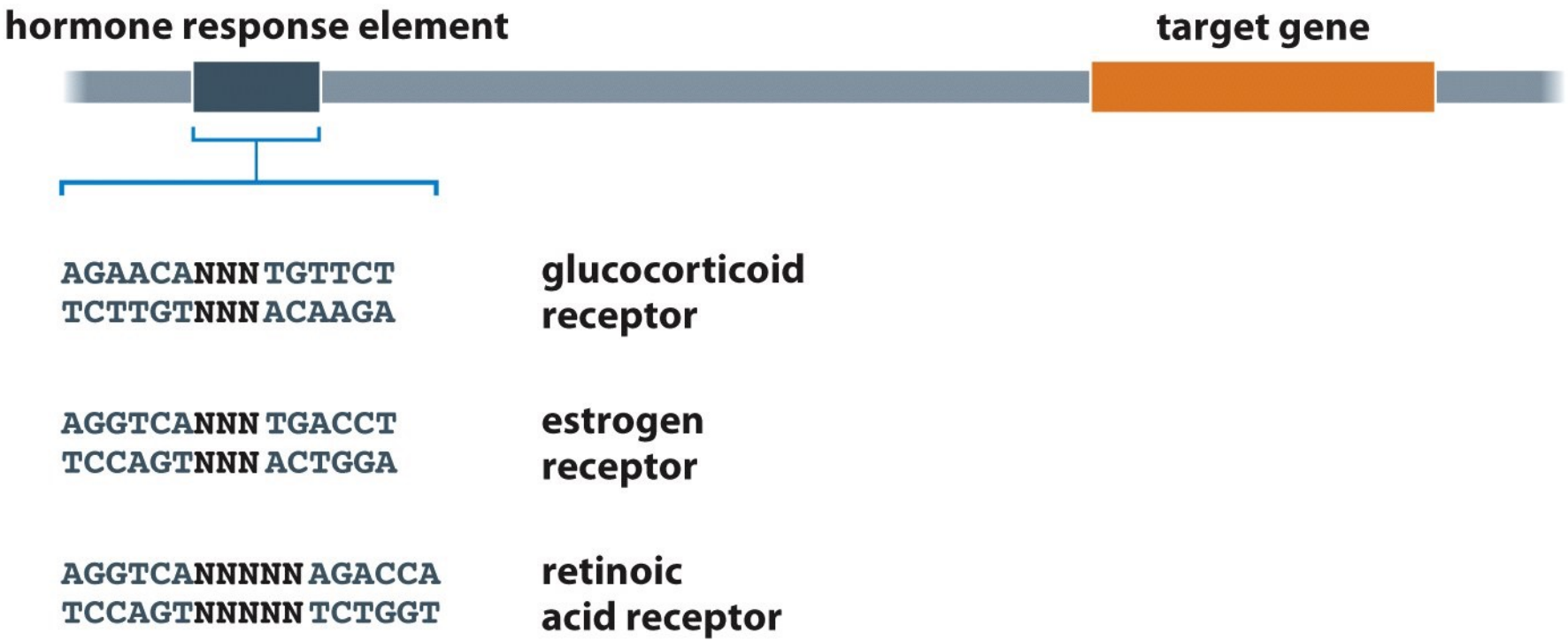

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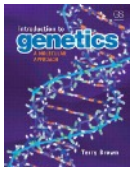

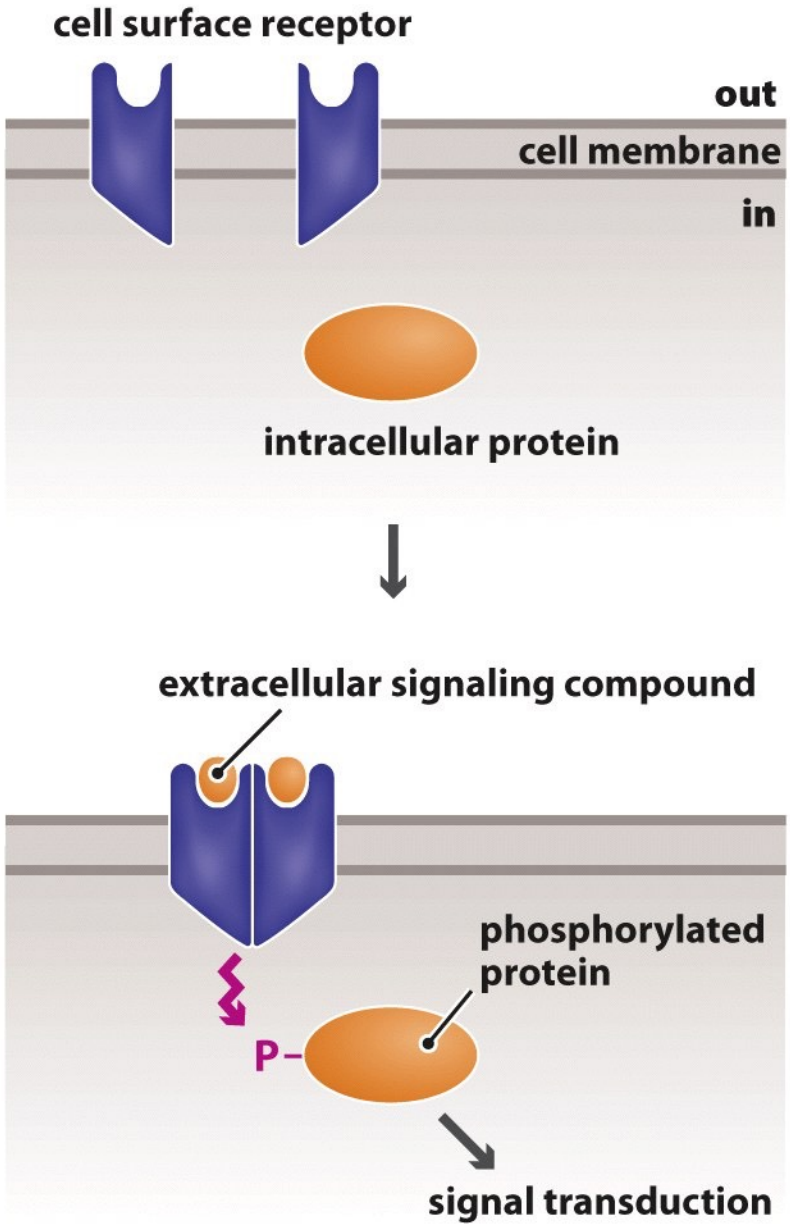

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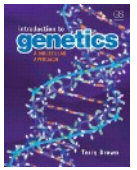

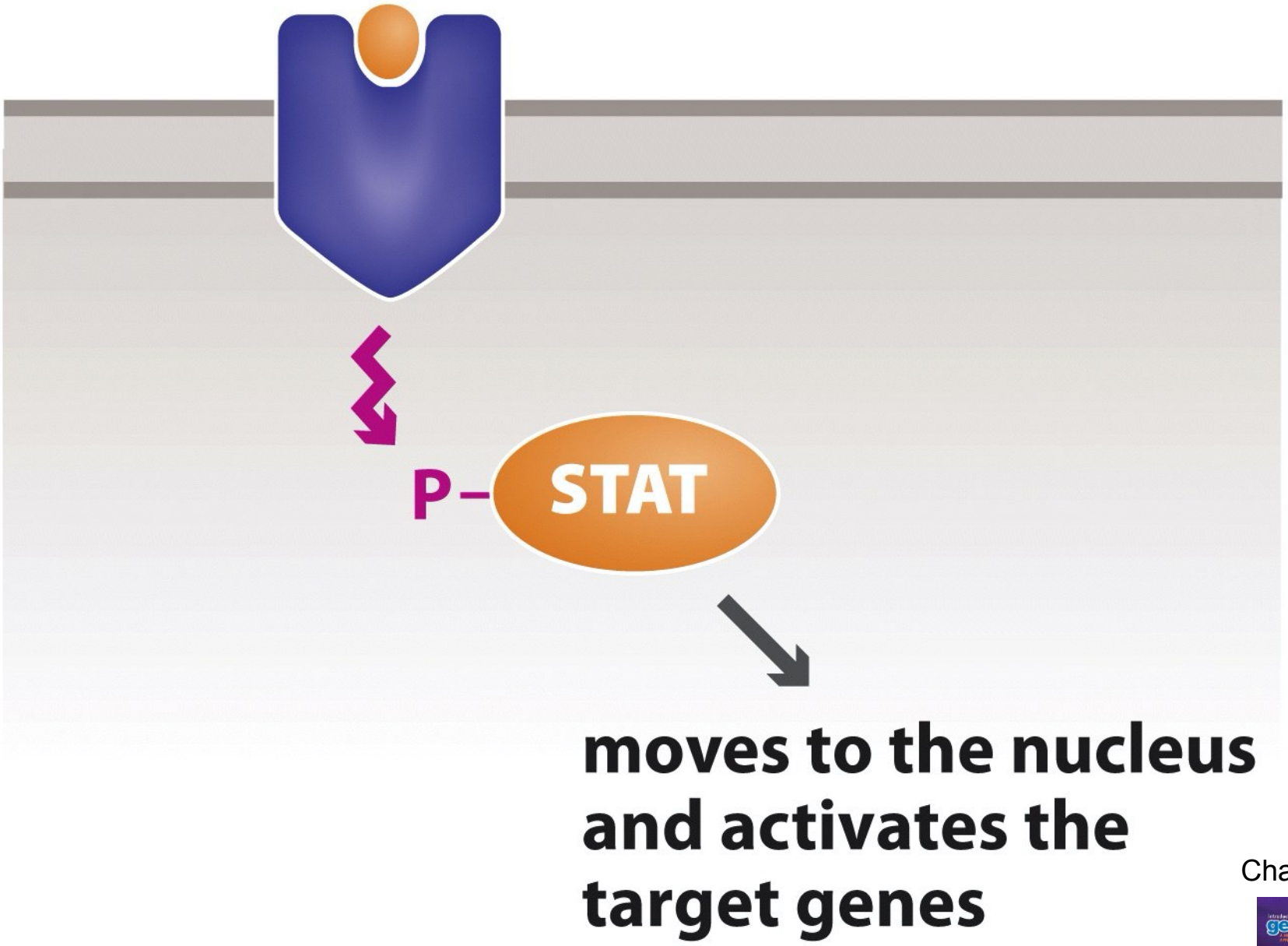

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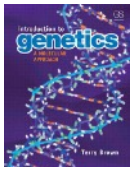

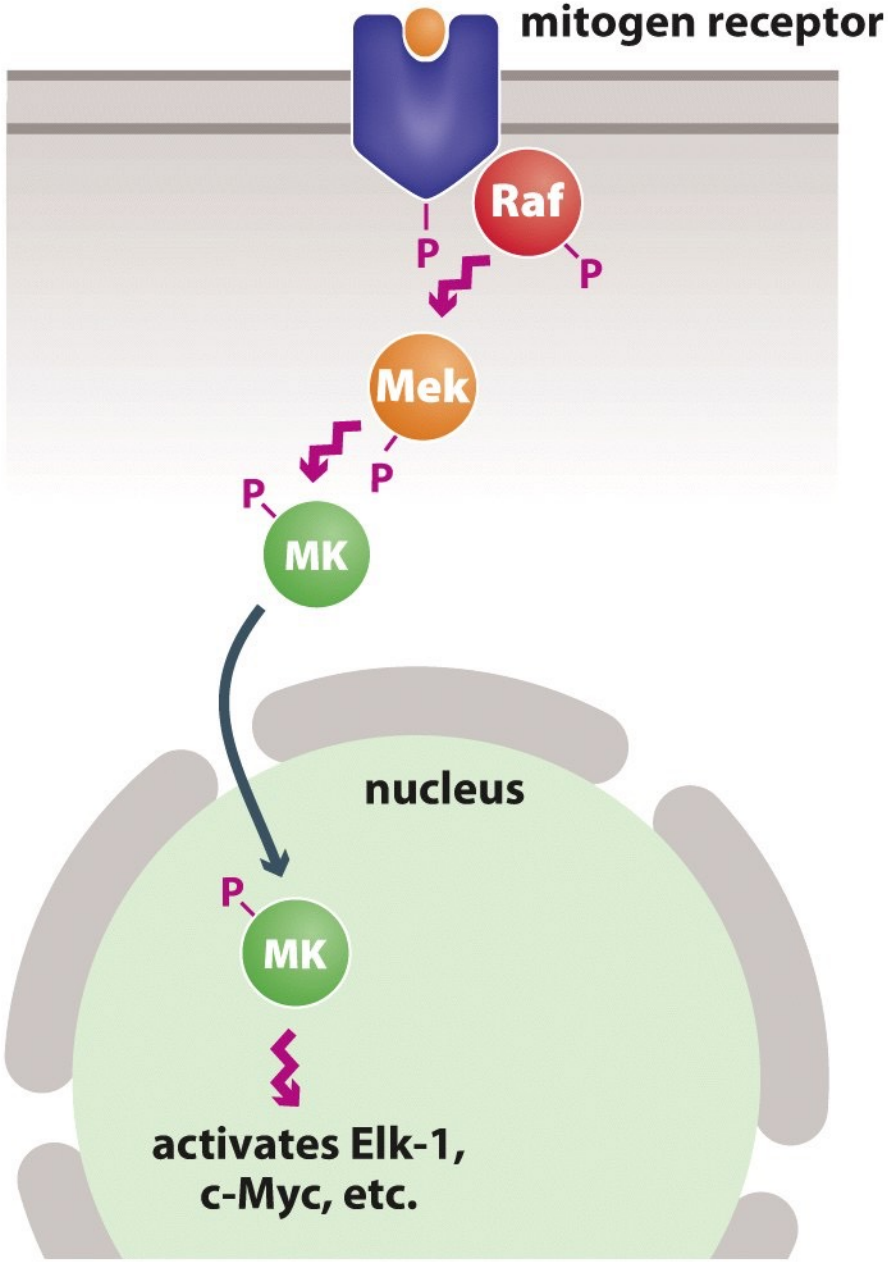

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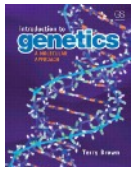

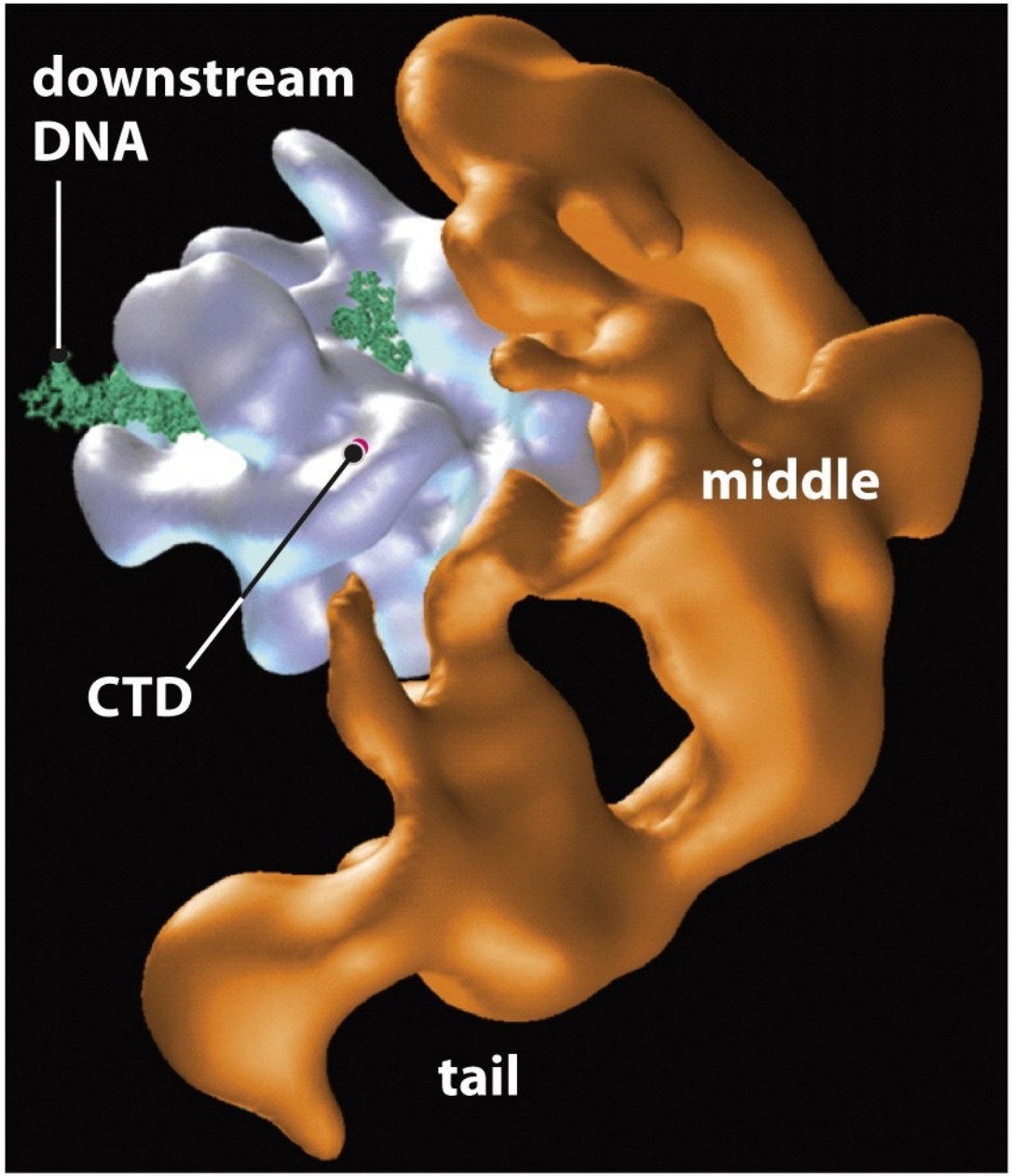

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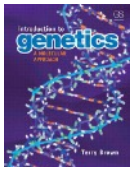

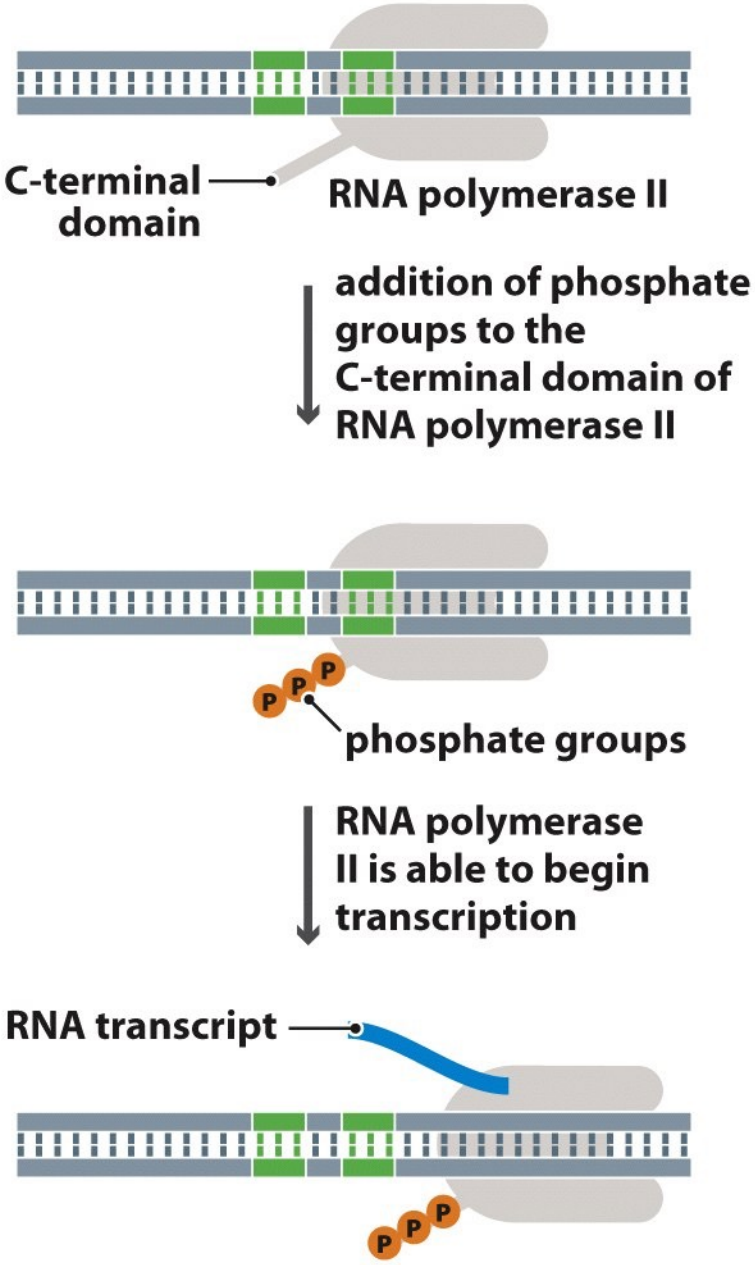

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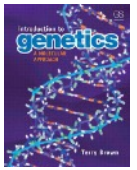
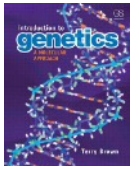
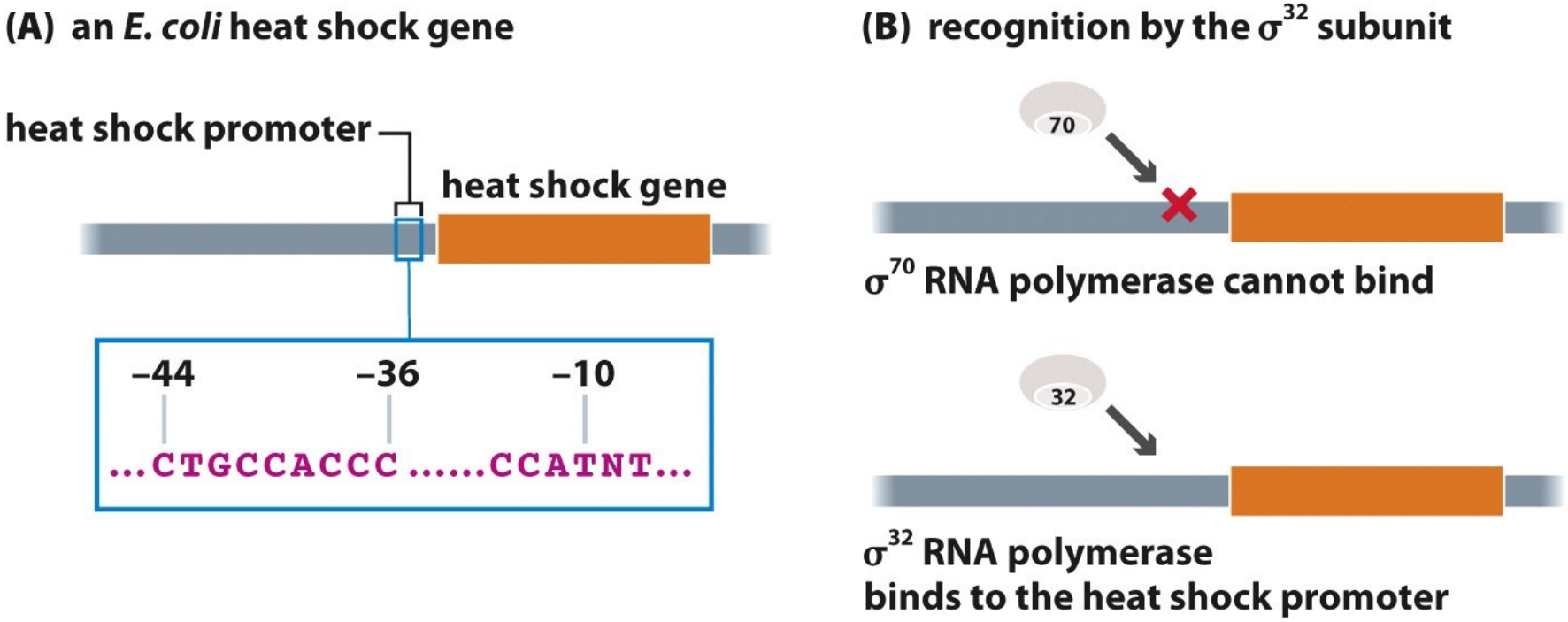


9.4 OTHER STRATEGIES FOR REGULATING GENE EXPRESSION

- Modification of the bacterial RNA polymerase enables different sets of genes to be expressed
- Transcription termination signals are sometimes ignored
- Attenuation is a second control strategy targeting transcription termination
- Bacteria and eukaryotes are both able to regulate the initiation of translation





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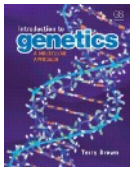
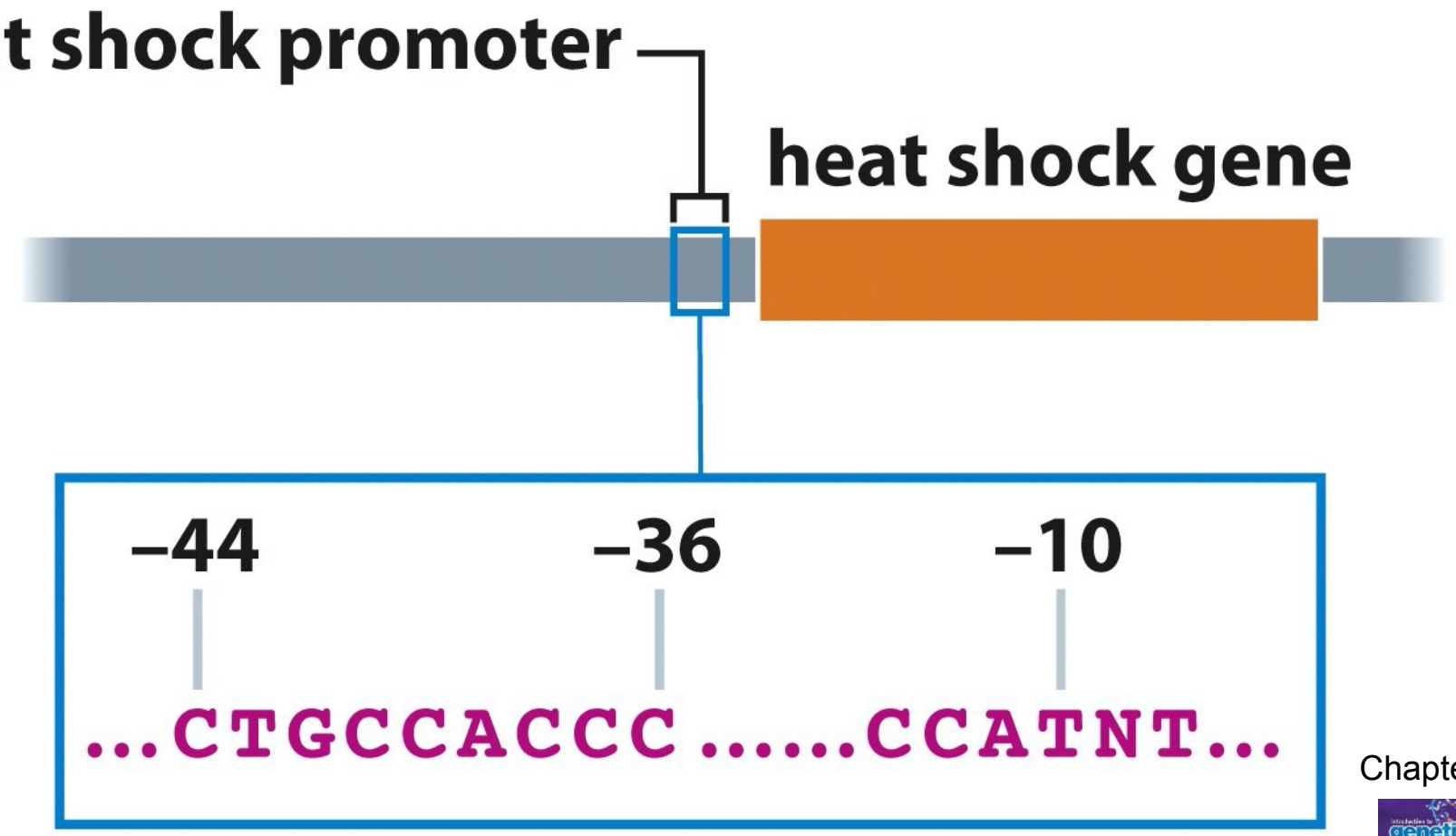


an *E. coli* heat shock gene



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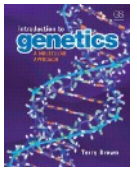
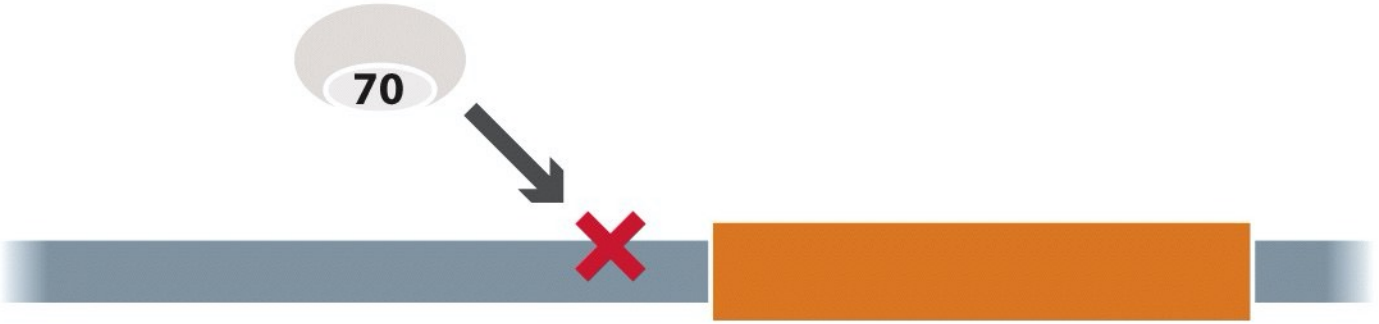


recognition by the σ^{32} subunit



σ^{70} RNA polymerase cannot bind

σ^{32} RNA polymerase
binds to the heat shock promoter

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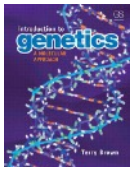
Chapter 9



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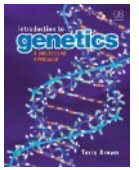

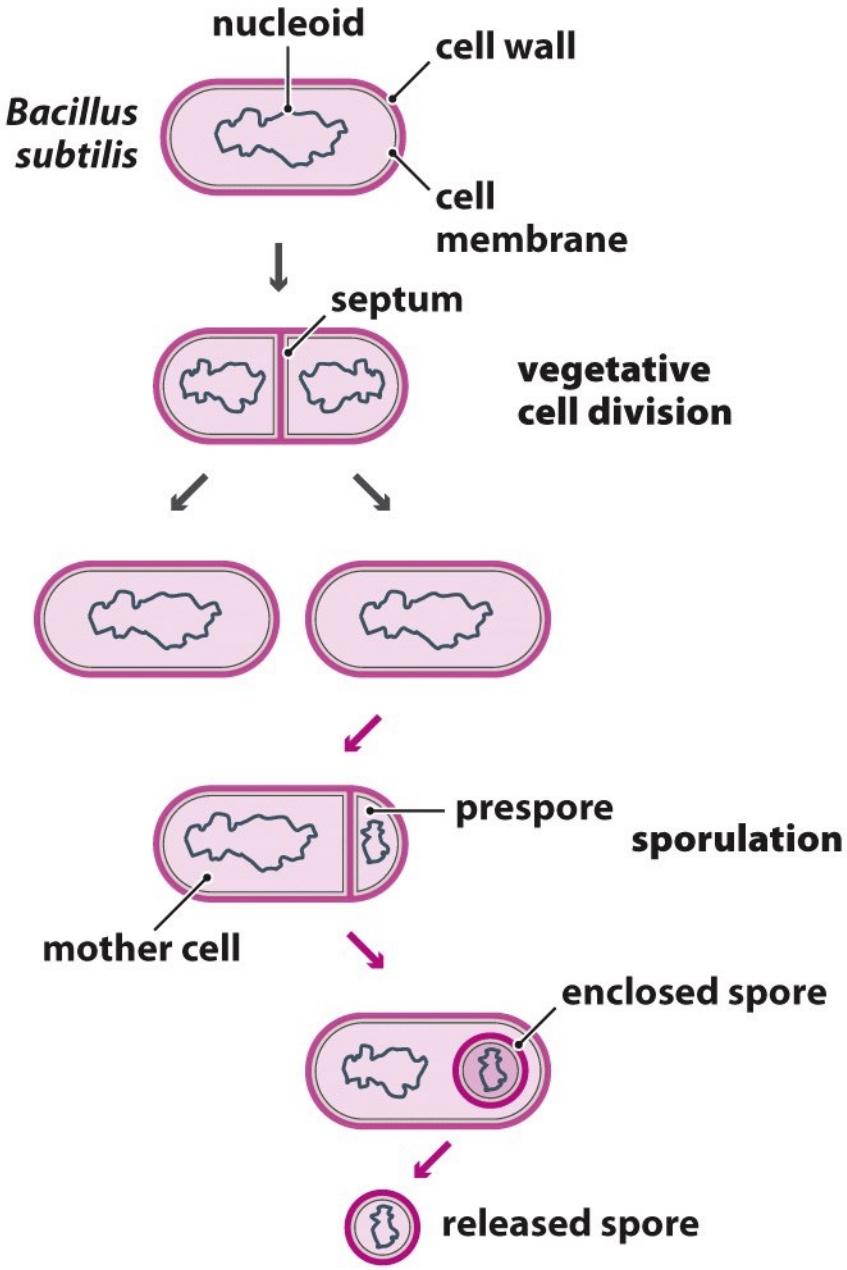

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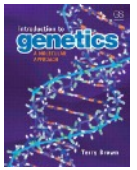

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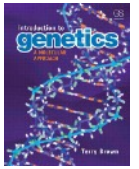

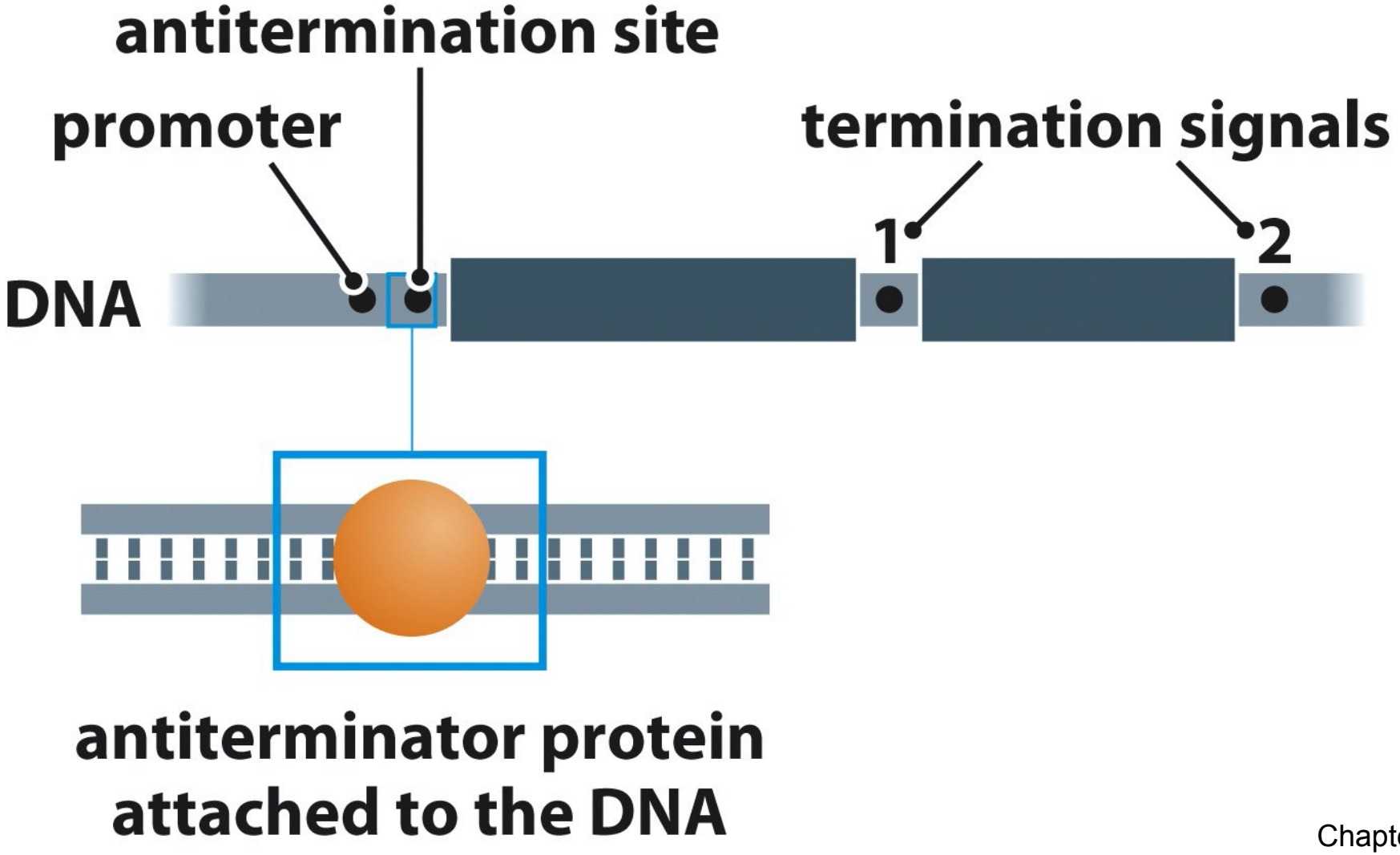

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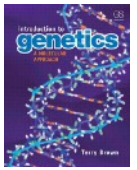

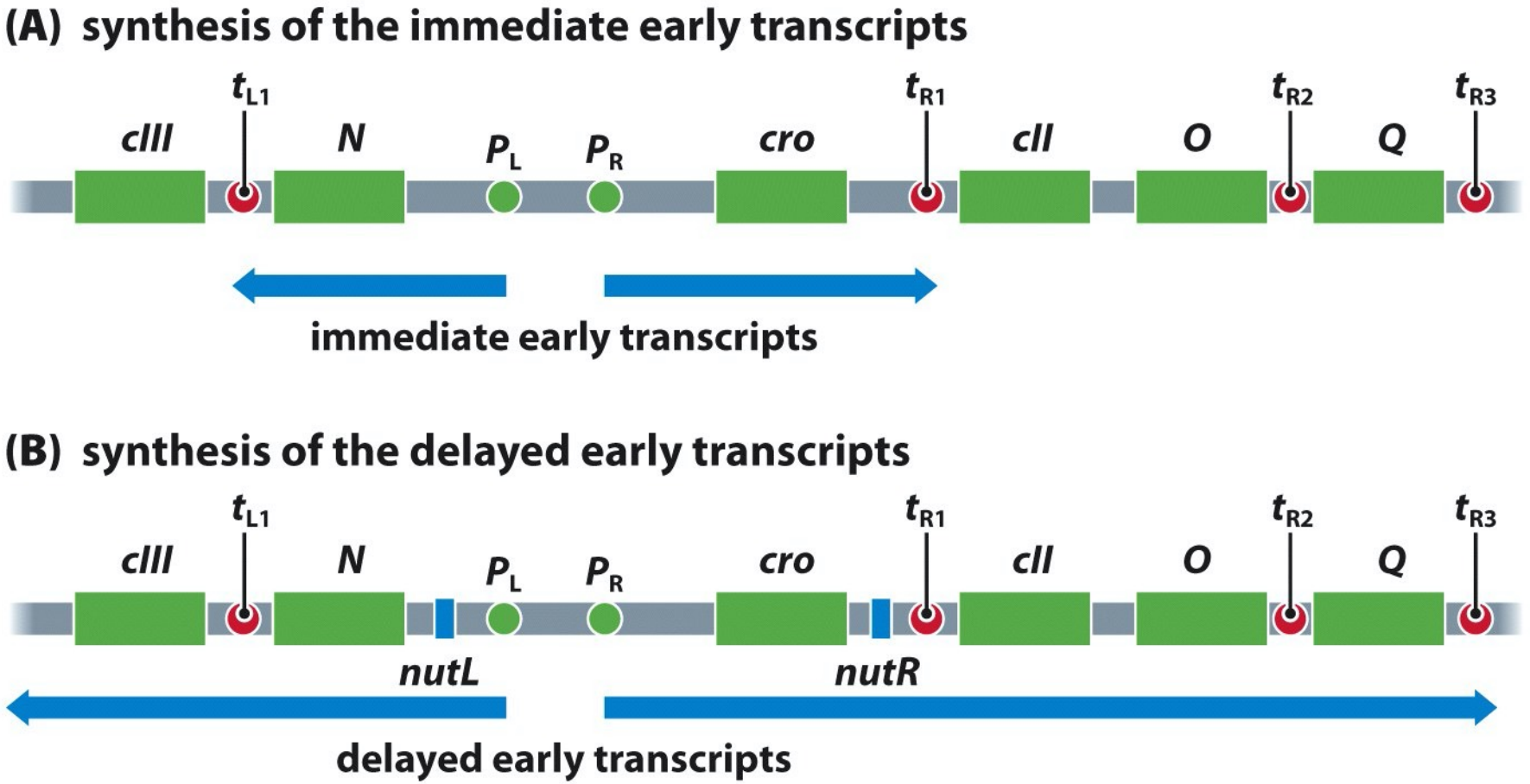

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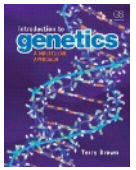


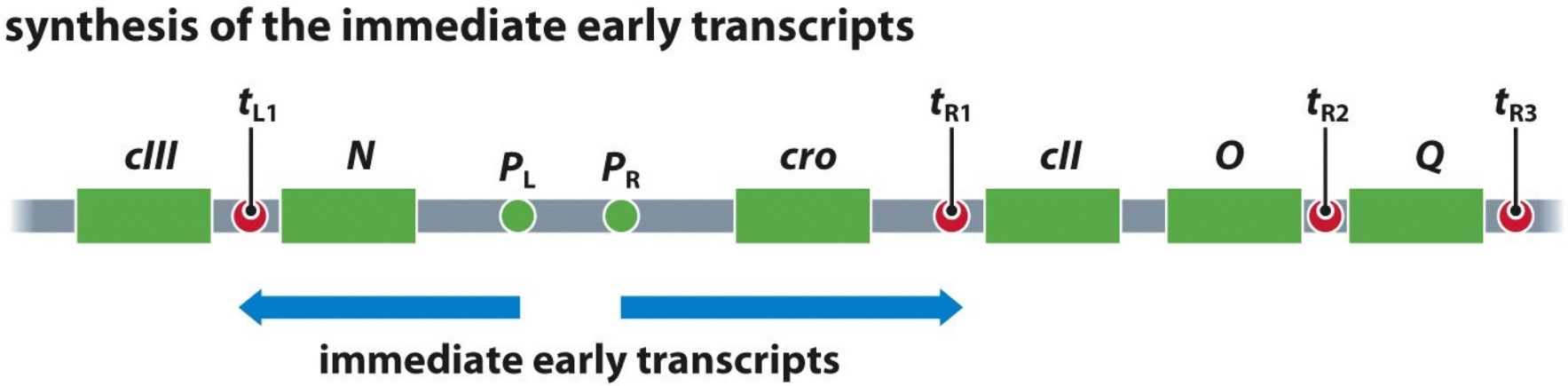
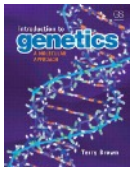


Figure 9.31a Introduction to Genetics (© Garland Science 2012)



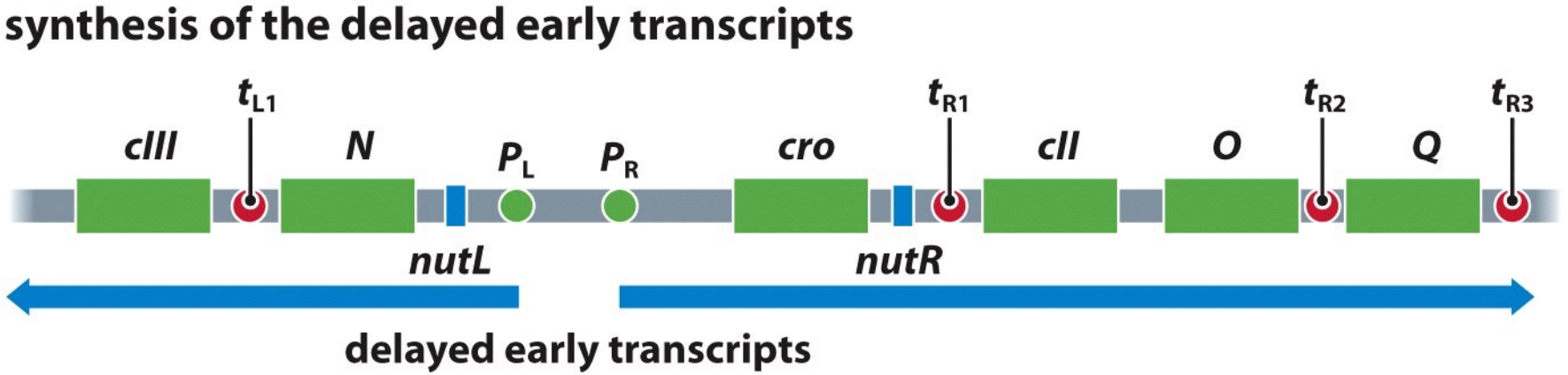
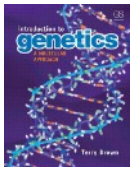
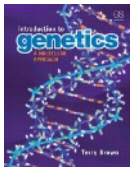


Figure 9.31b Introduction to Genetics (© Garland Science 2012)



9.4 OTHER STRATEGIES FOR REGULATING GENE EXPRESSION

- Modification of the bacterial RNA polymerase enables different sets of genes to be expressed
- Transcription termination signals are sometimes ignored
- Attenuation is a second control strategy targeting transcription termination
- Bacteria and eukaryotes are both able to regulate the initiation of translation



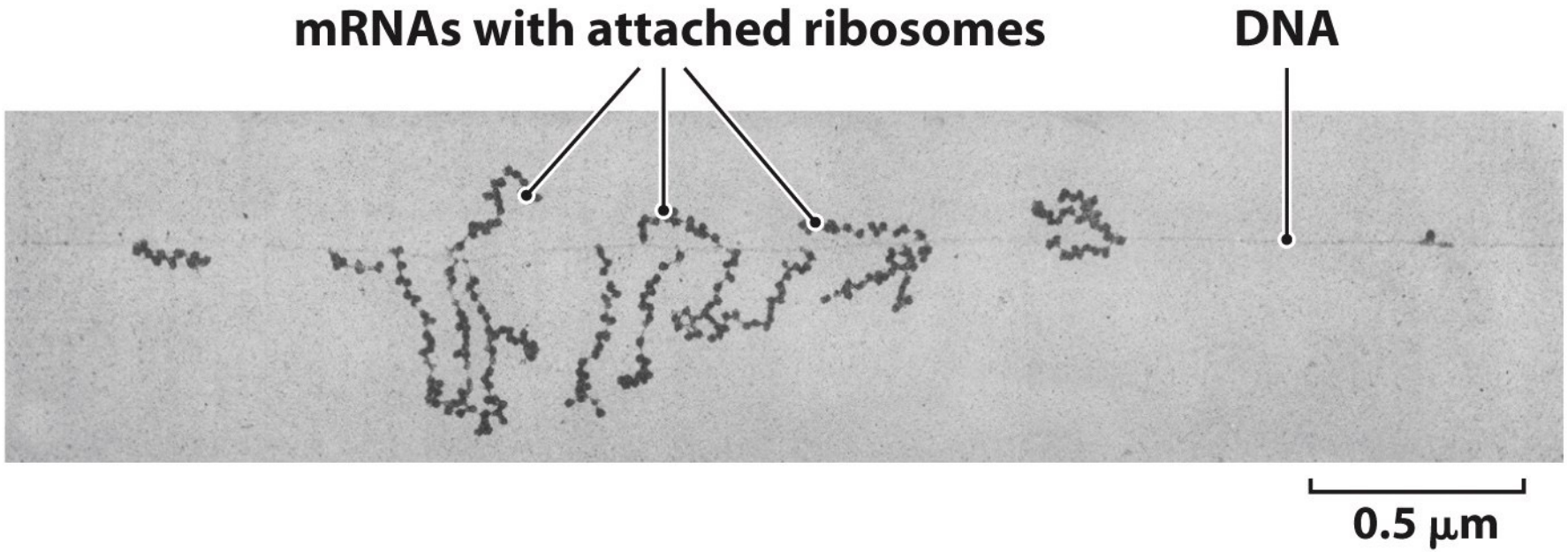
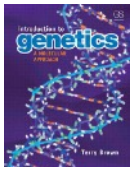
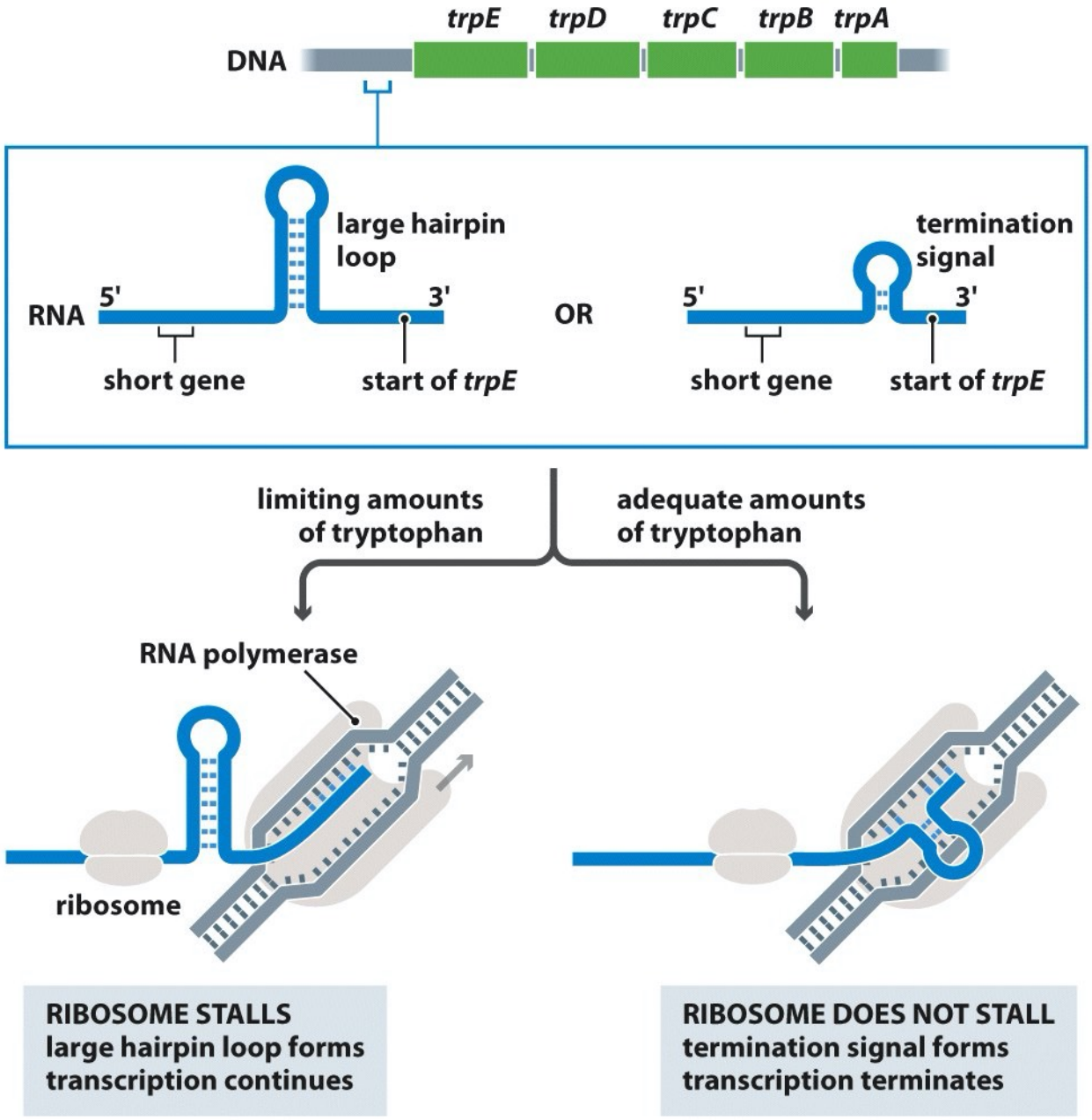


Figure 9.32 Introduction to Genetics (© Garland Science 2012)





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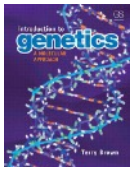

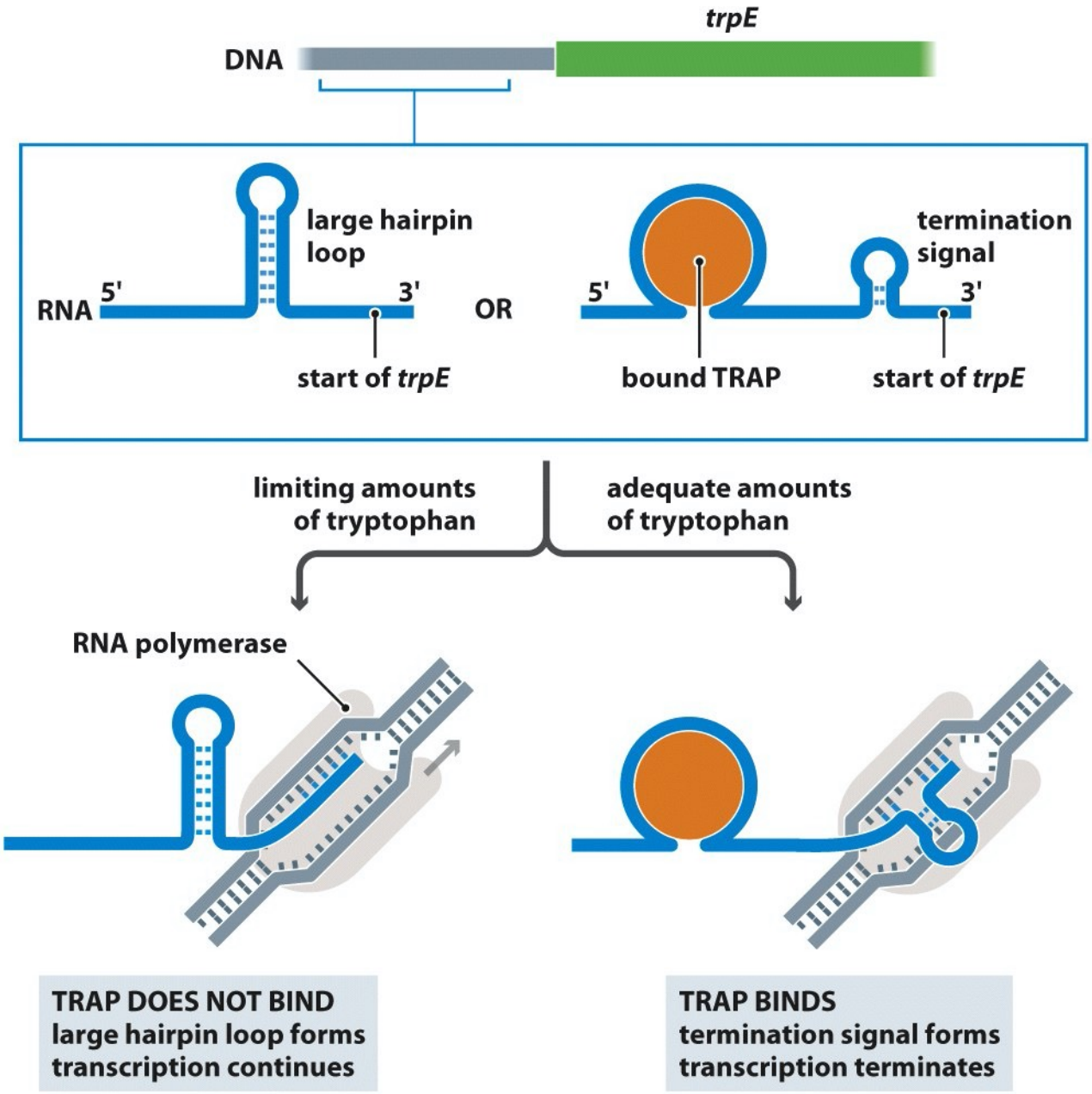

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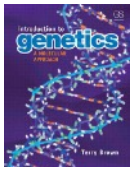

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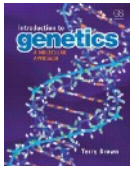


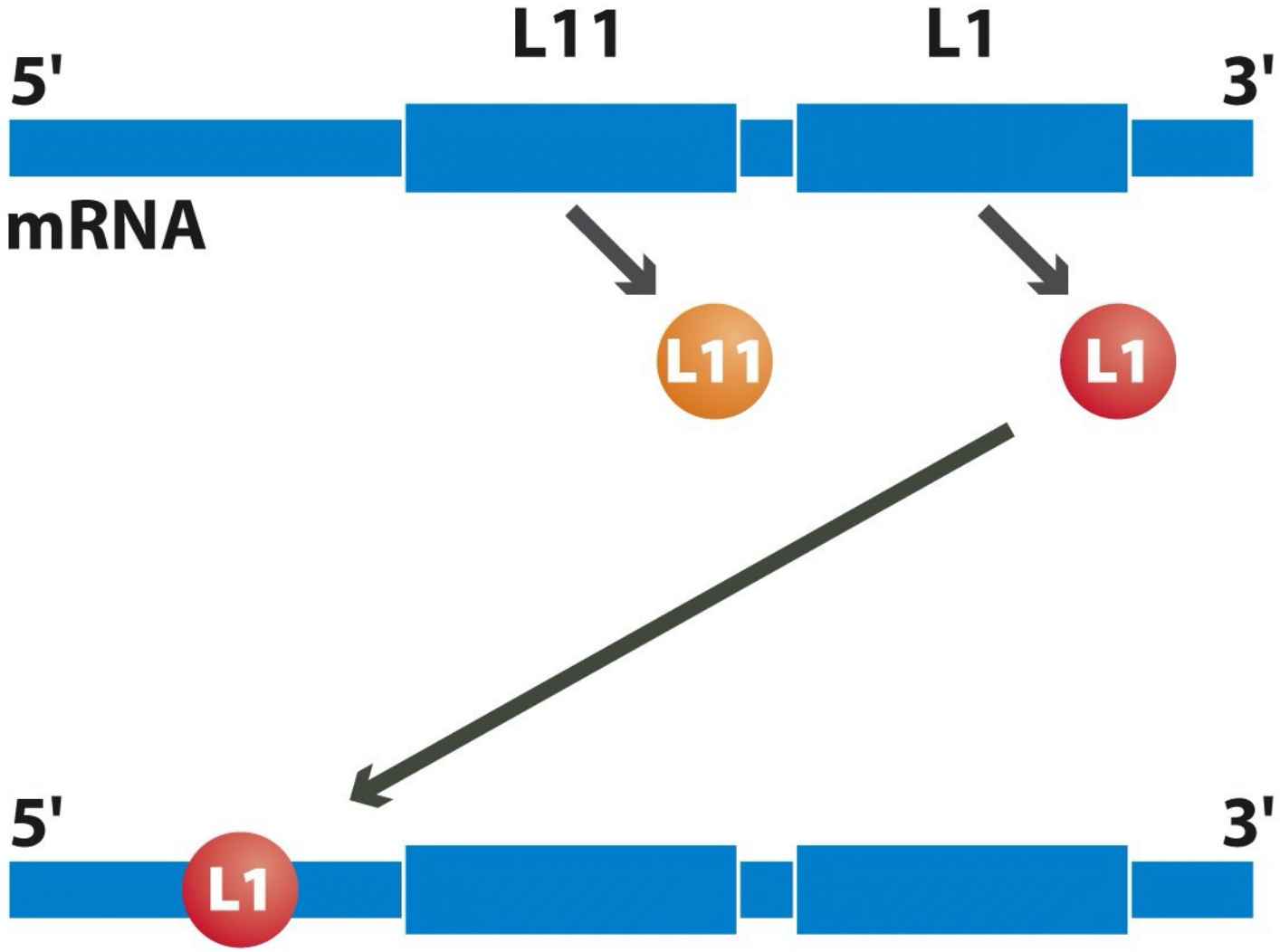
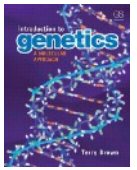
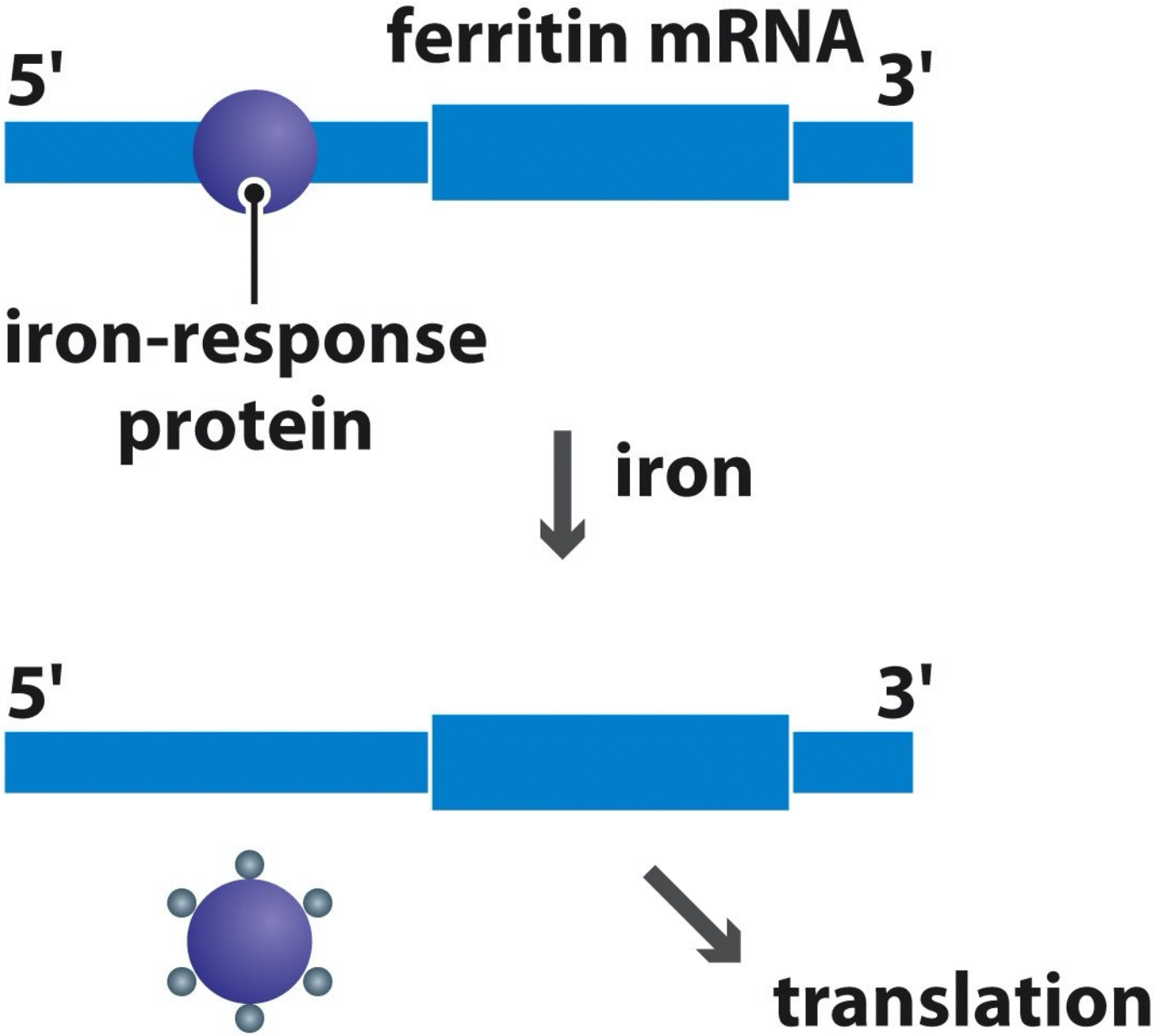


Figure 9.35 Introduction to Genetics (© Garland Science 2012)





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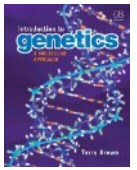


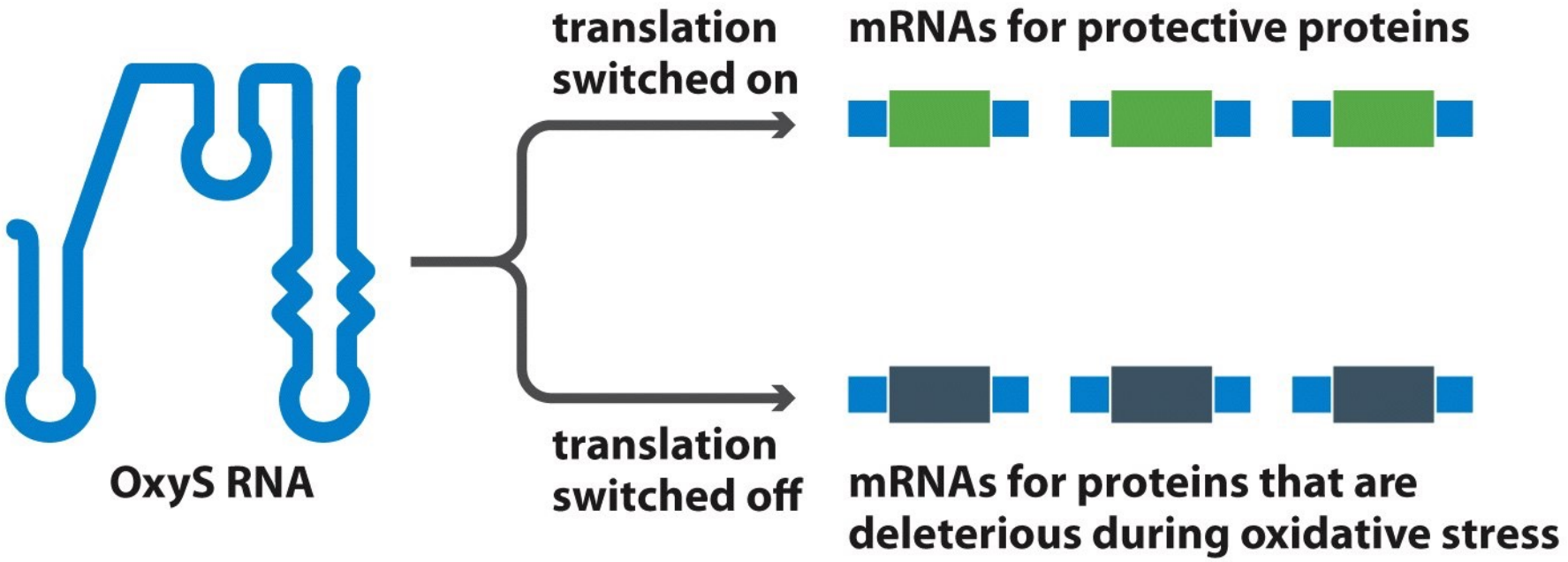
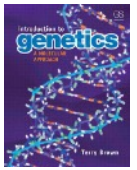


Figure 9.37 Introduction to Genetics (© Garland Science 2012)



To know

Co-repressor

Silencer

Enhancer

Prokaryotic vs. eukaryotic repressors

Co-activator

Activator

repressor

Competitive DNA binding

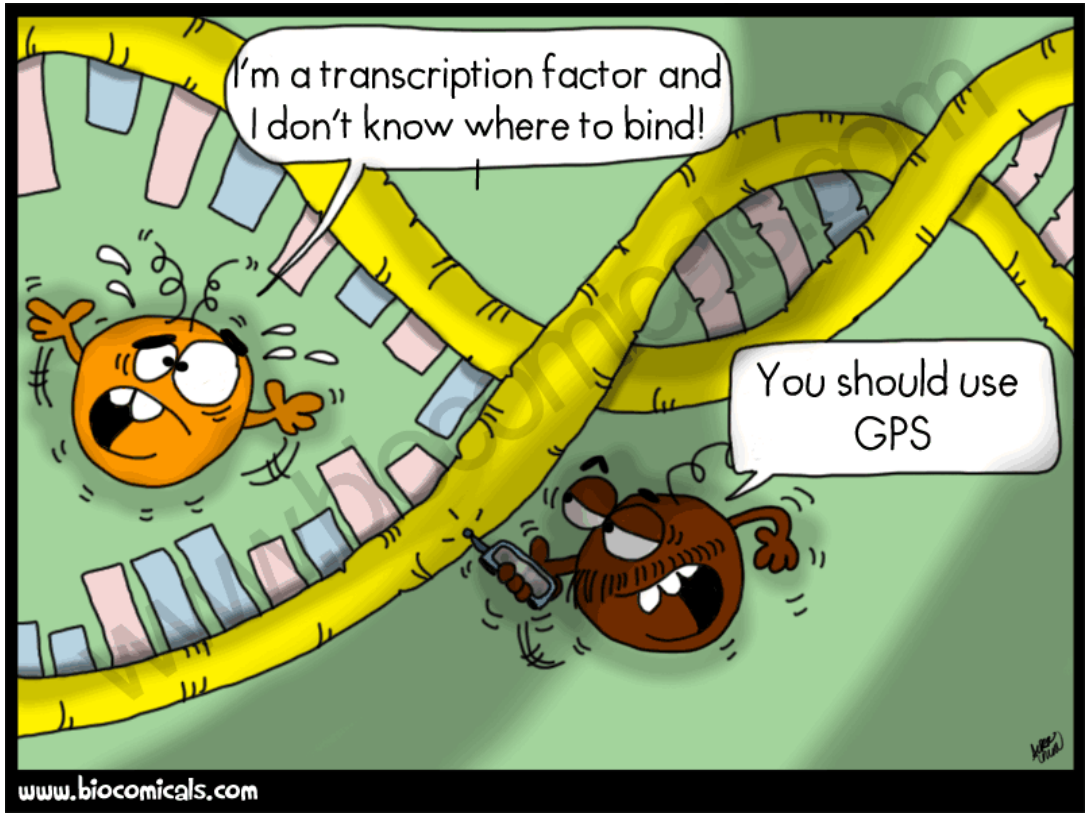
DNA binding domain

Protein binding domain

Expectations

- You know the regulation mechanisms of gene expression in eukaryotes at transcription initiation phase.
- You know the complexity in the mechanisms allows great variation in regulation mechanisms.
- You know the roles of regulatory proteins such as (activators, co-activators, repressors, co-repressors).
- You know the differences between prokaryotic and eukaryotic repressors.

For a smile


I'm a transcription factor and I don't know where to bind!
You should use GPS
www.biocomicals.com