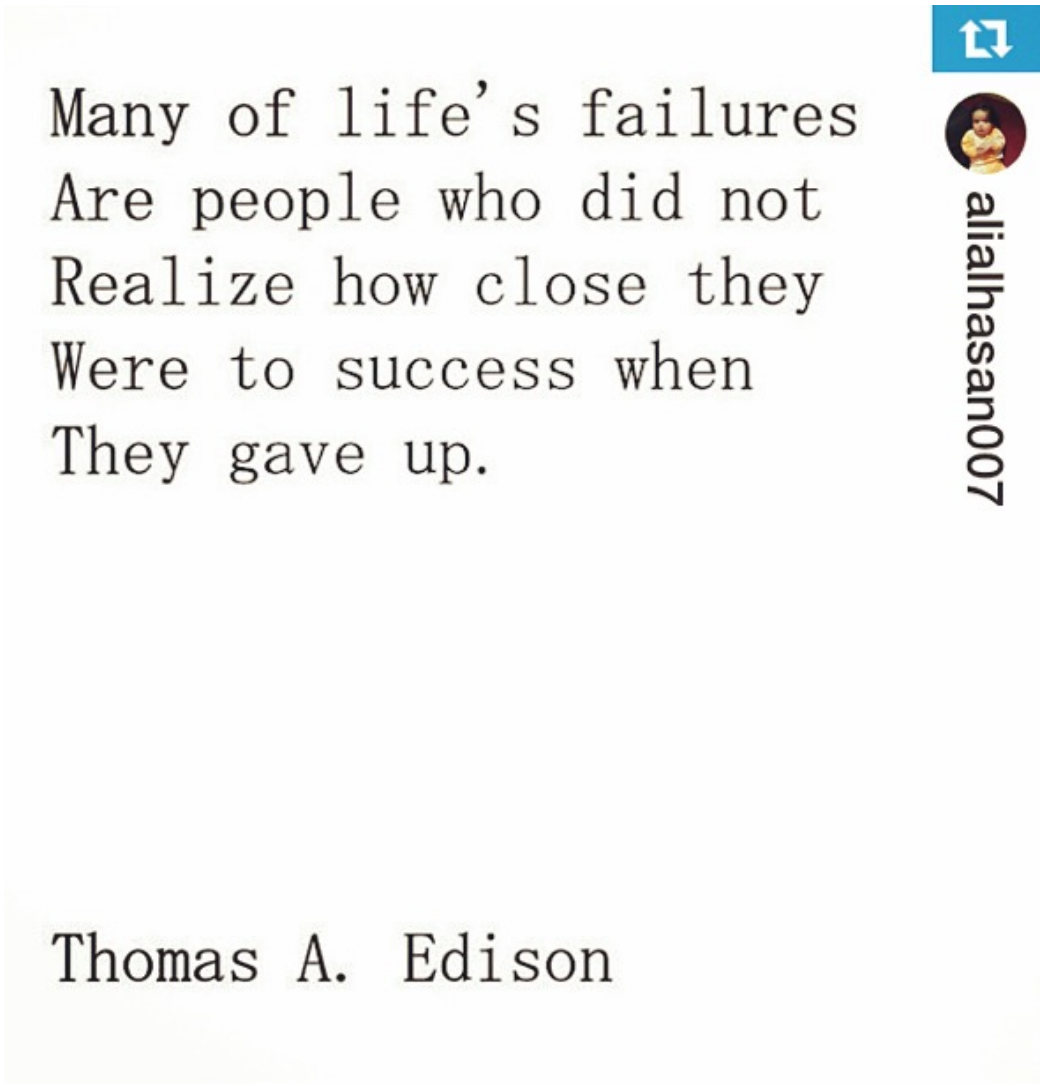
Lecture 27:

Regulation of gene expression

IV. Eukaryotes (part 1)

Course 371

Lessons for life

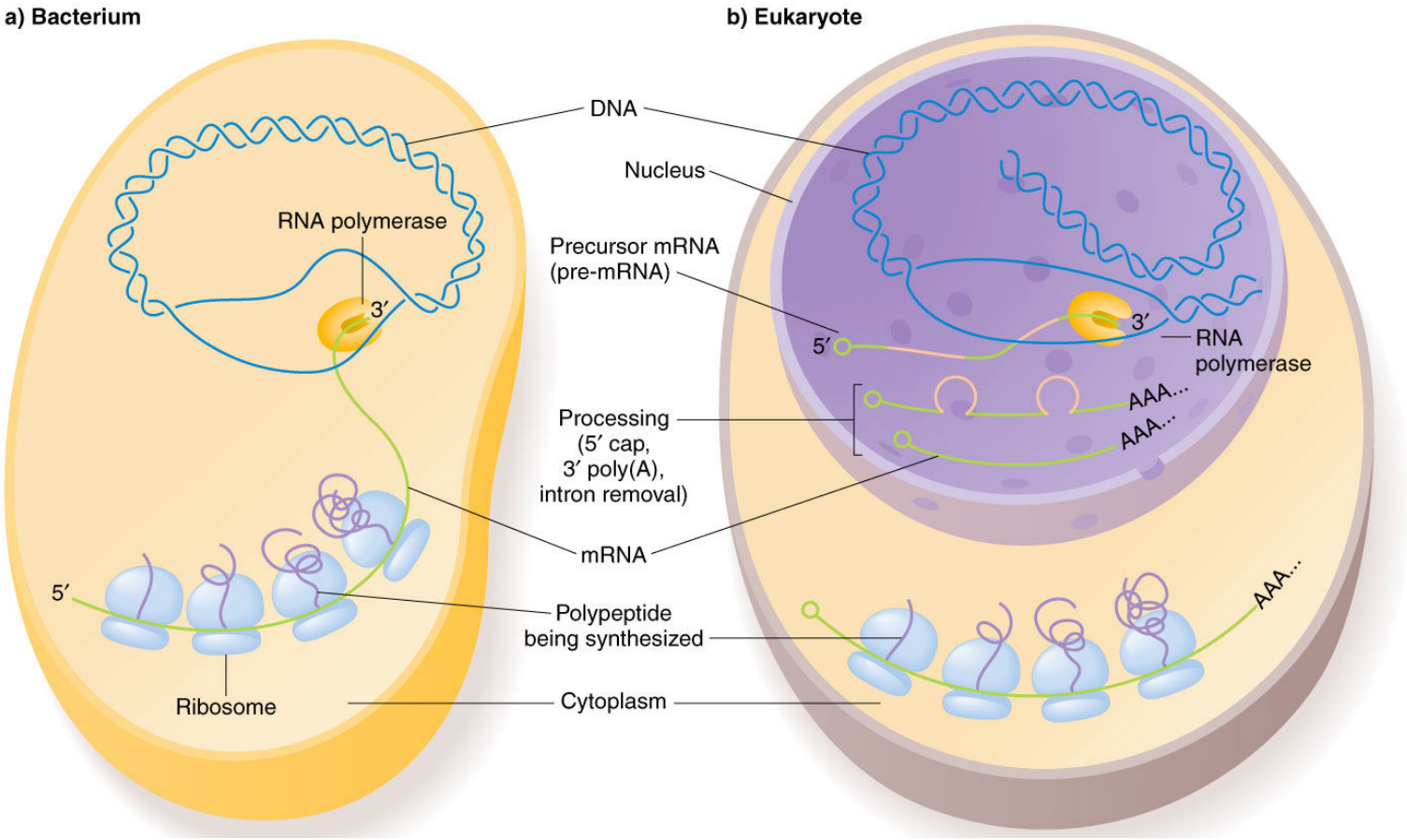


AIMS

- 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

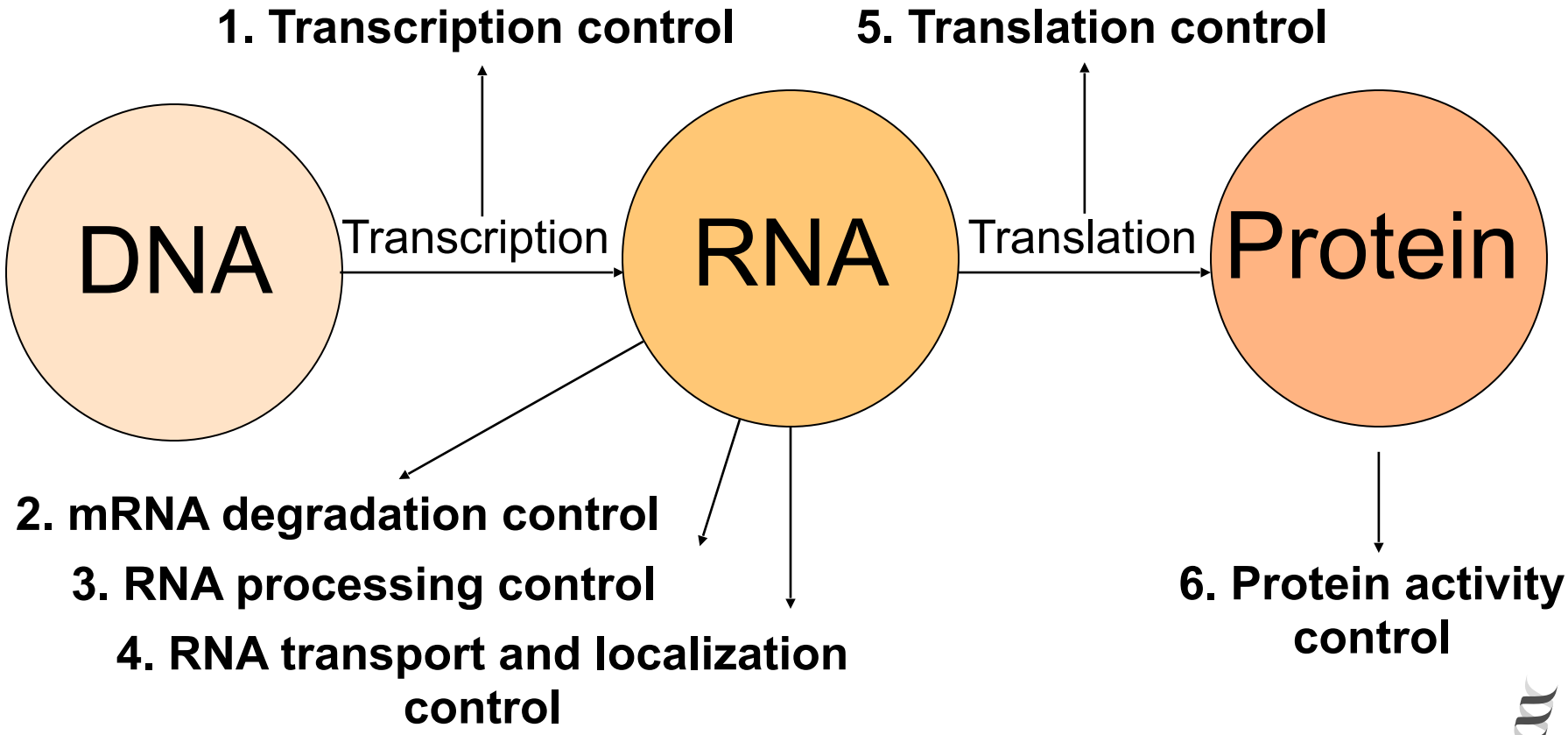
Eukaryotic gene expression is more complicated than in prokaryotes and as a result regulation is also complicated



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

Regulation of Gene expression

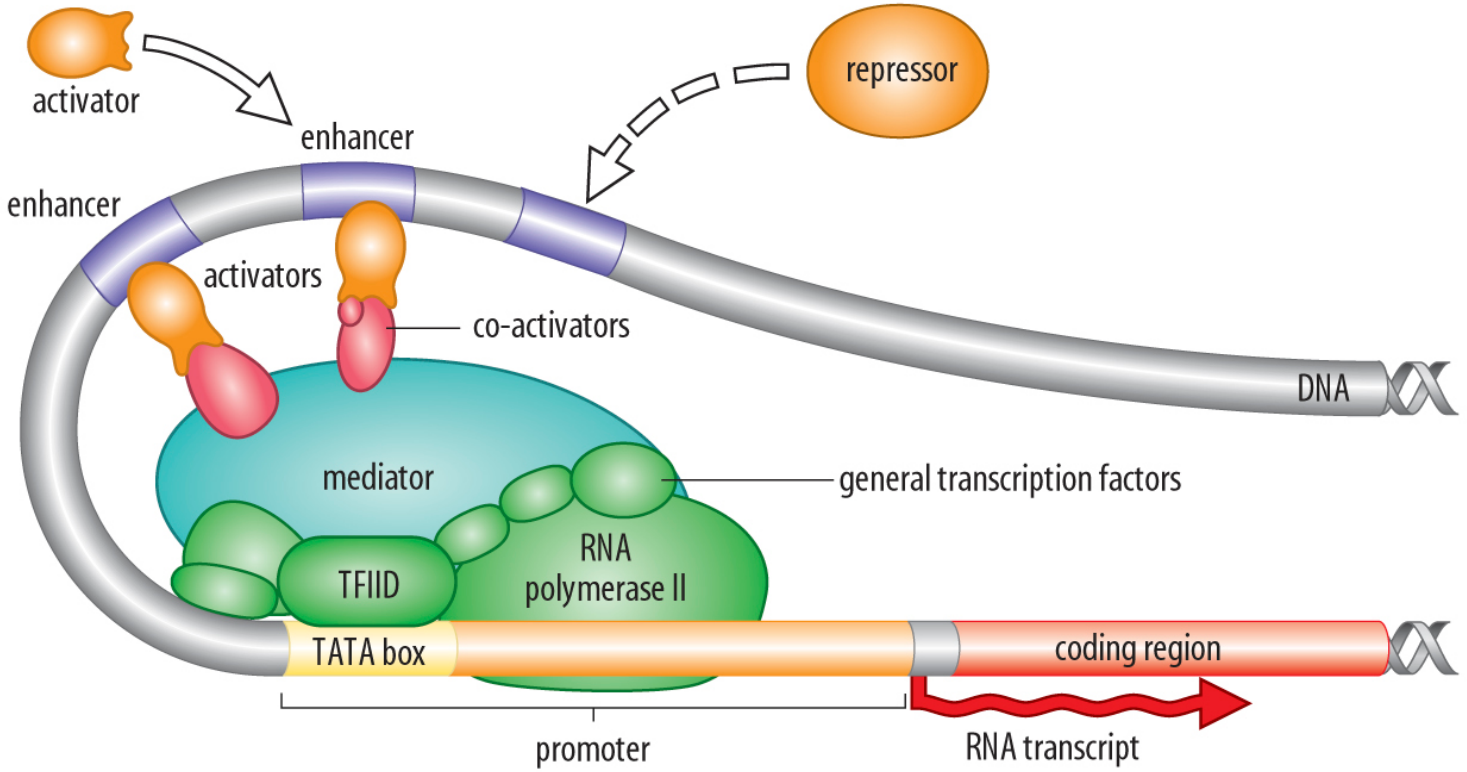
Eukaryotic: regulation of gene expression can take place at multiple stages during the transcription/ translation process.



Regulation of transcription initiation

What happens during transcription initiation?

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



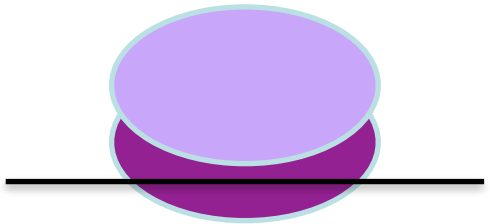
Regulation of transcription initiation

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

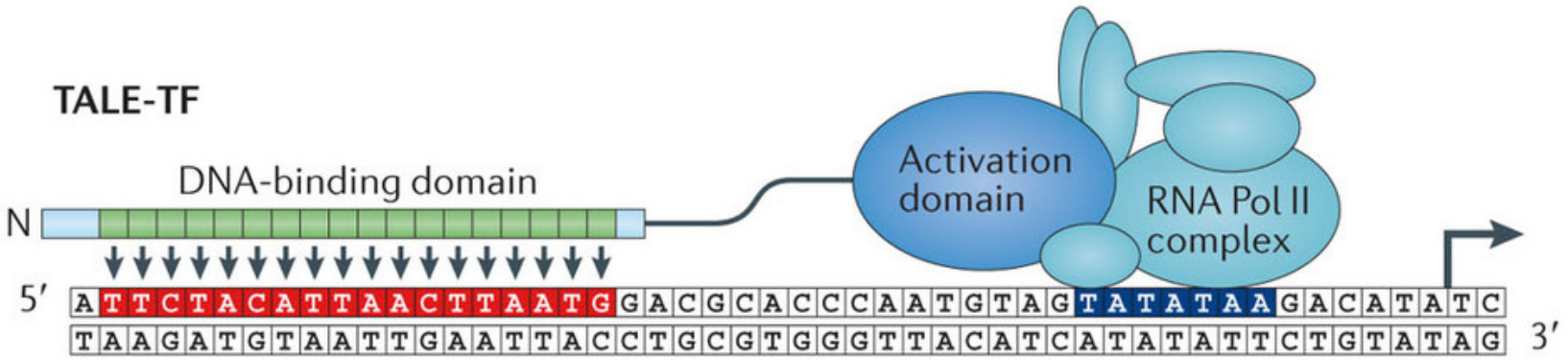


- **Activators contain:**
  - **A DNA binding domain:** a location in the protein binds to DNA (enhancer sequence).
  - **A protein binding domain:** a location in the protein that binds to the transcription initiation complex.

Regulation of transcription initiation

Enhancer/Activator

DNA binding domain and protein binding domain



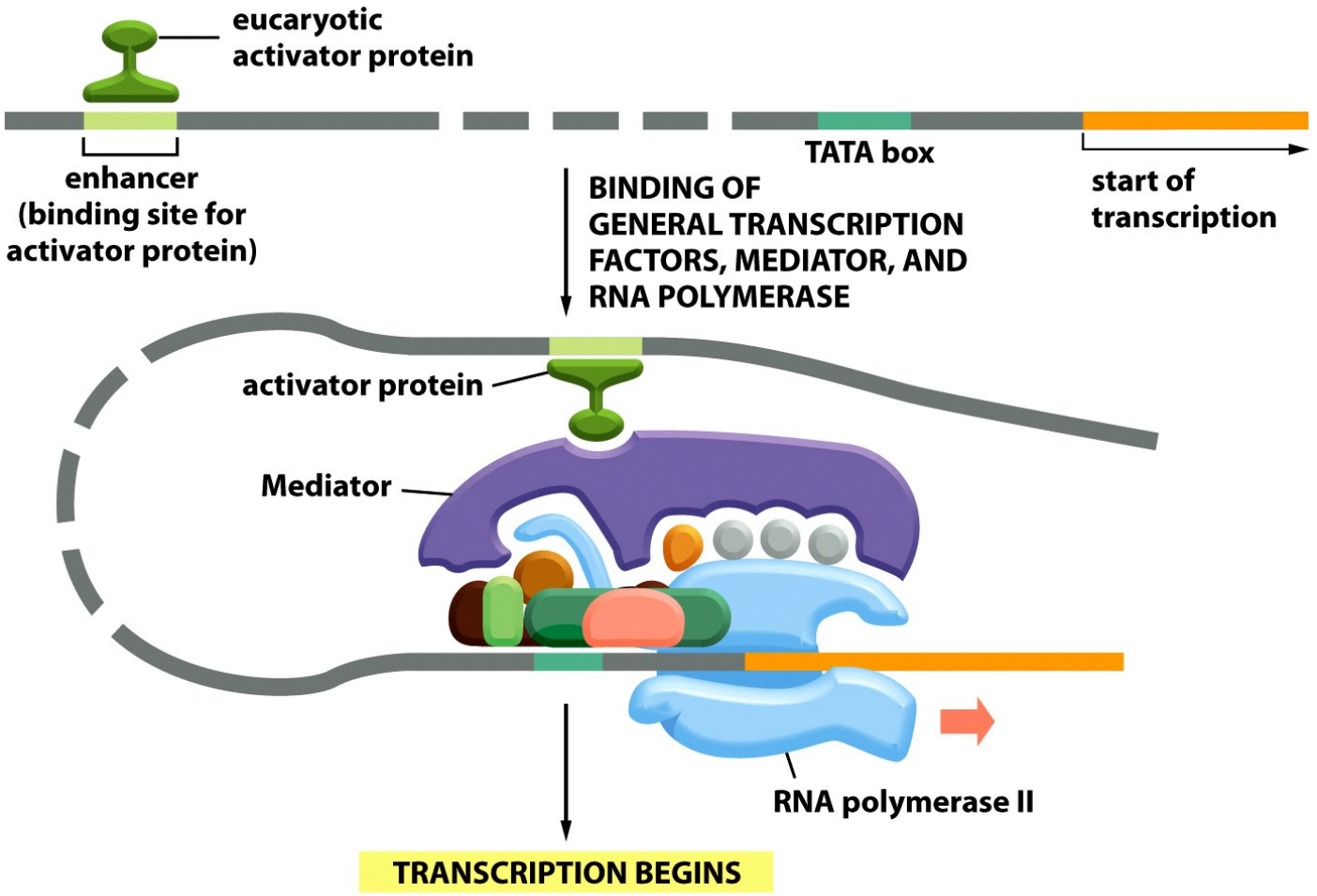
Regulation of transcription initiation

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.

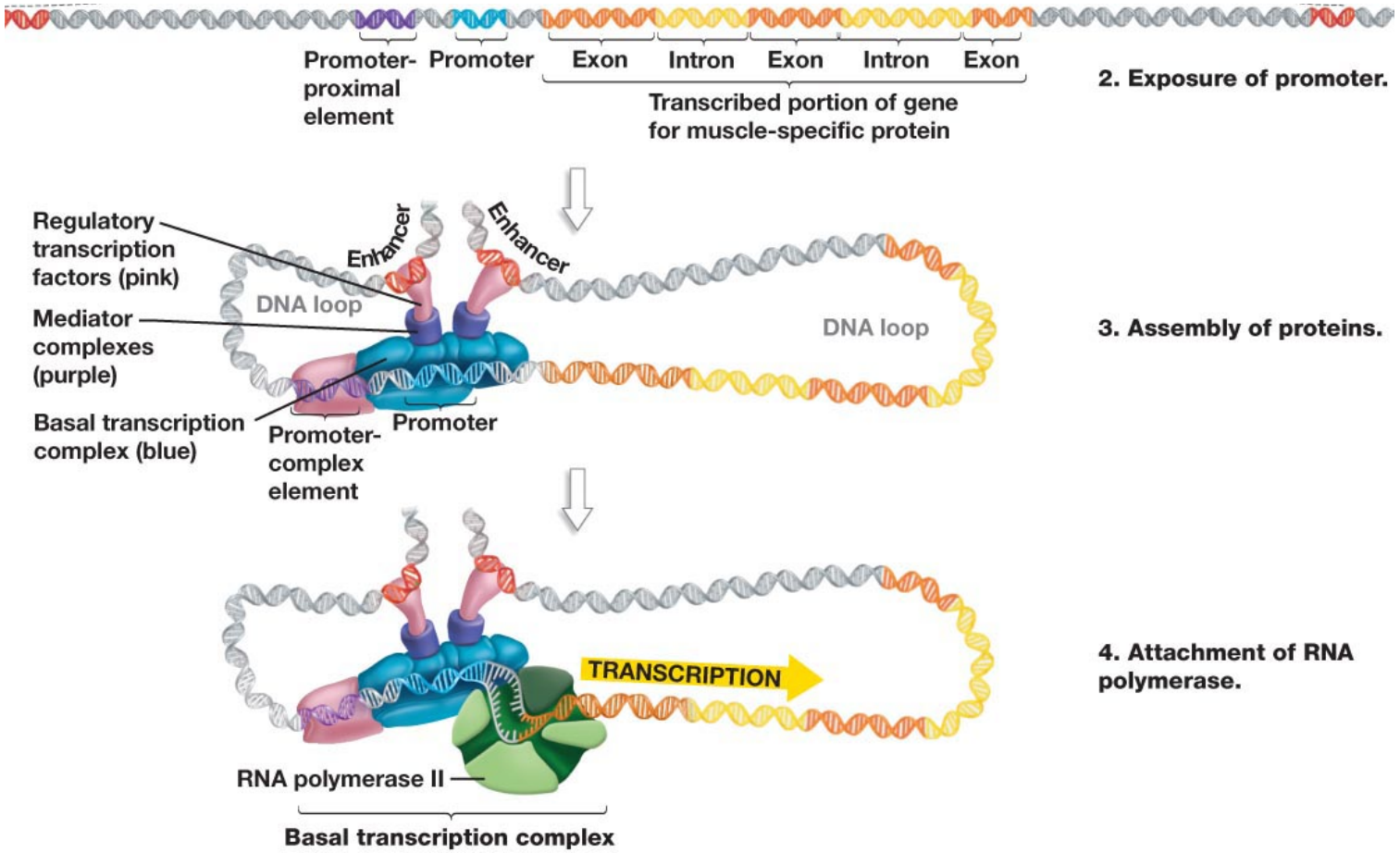
Regulation of transcription initiation

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

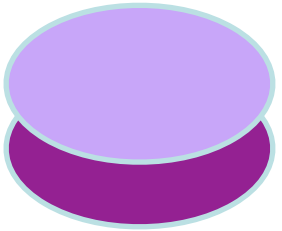
Regulation of transcription initiation

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.

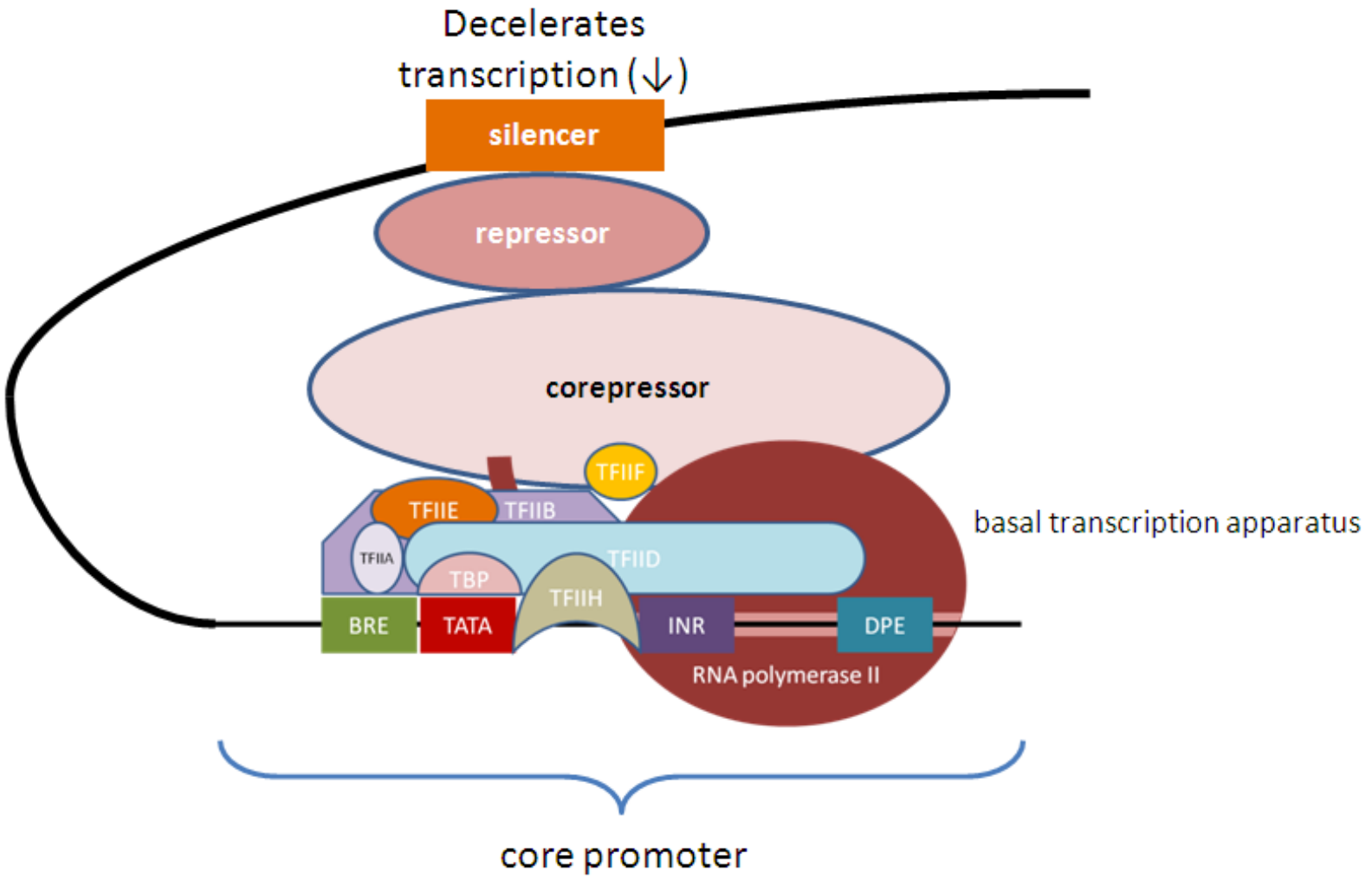
Regulation of transcription initiation

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?

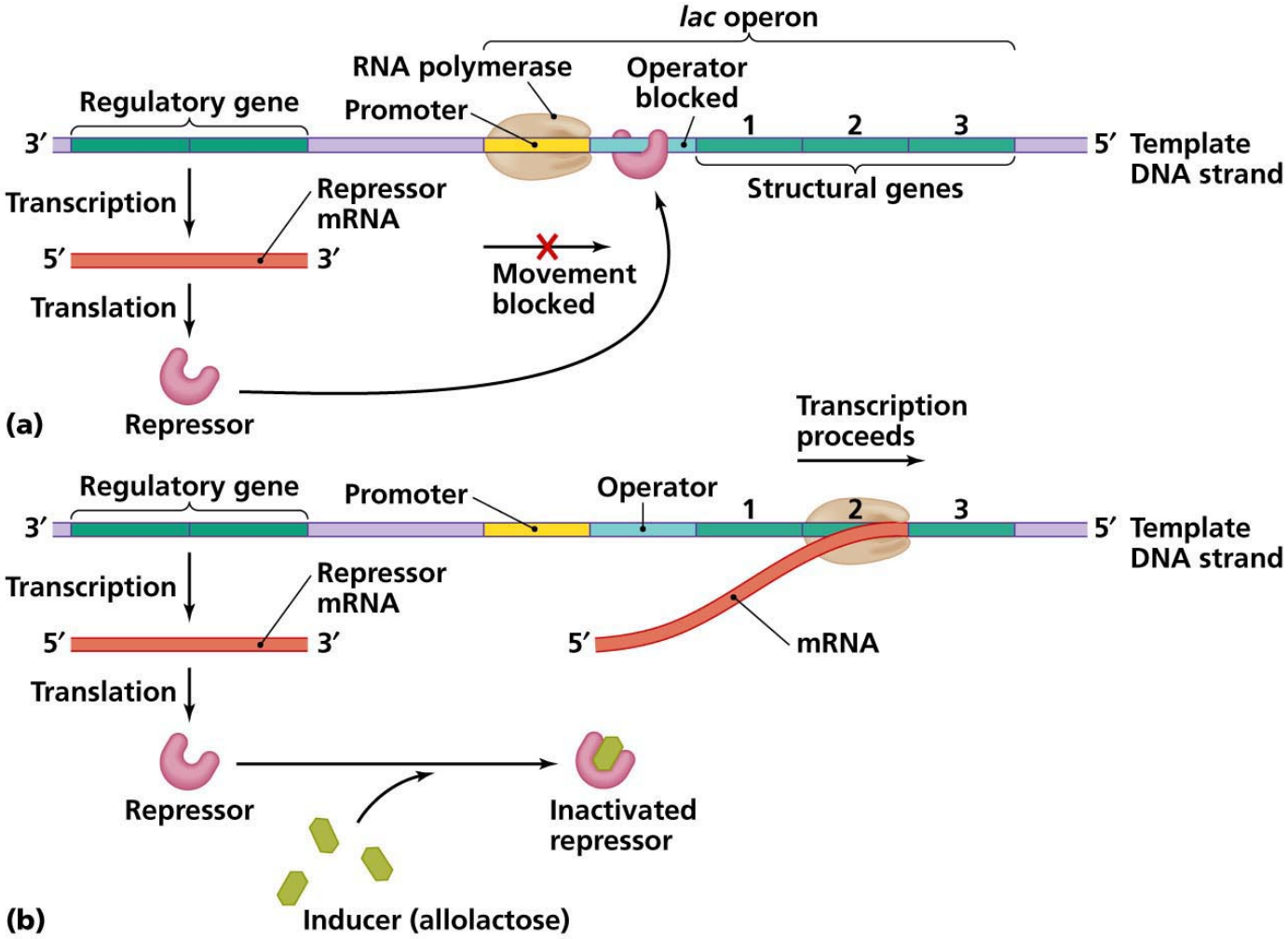
(1) Breaks

(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?

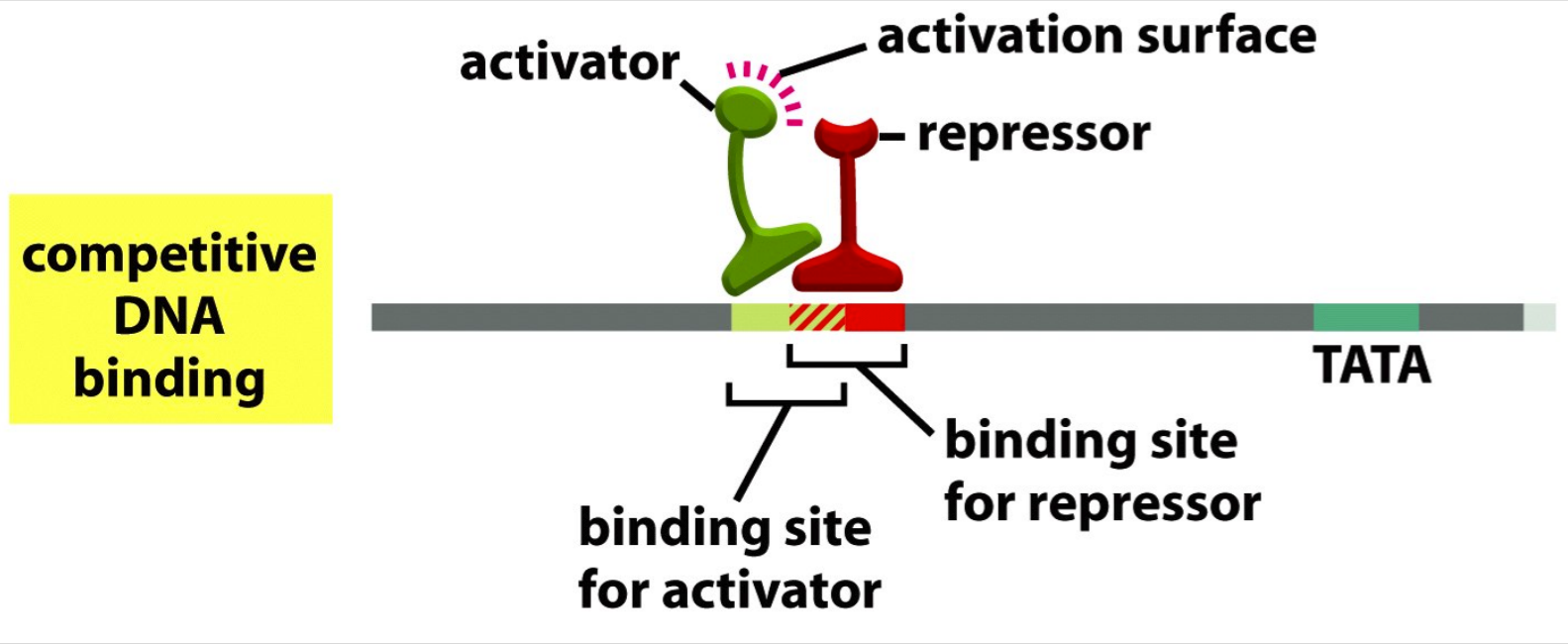
What is the binding site of repressors?

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.**

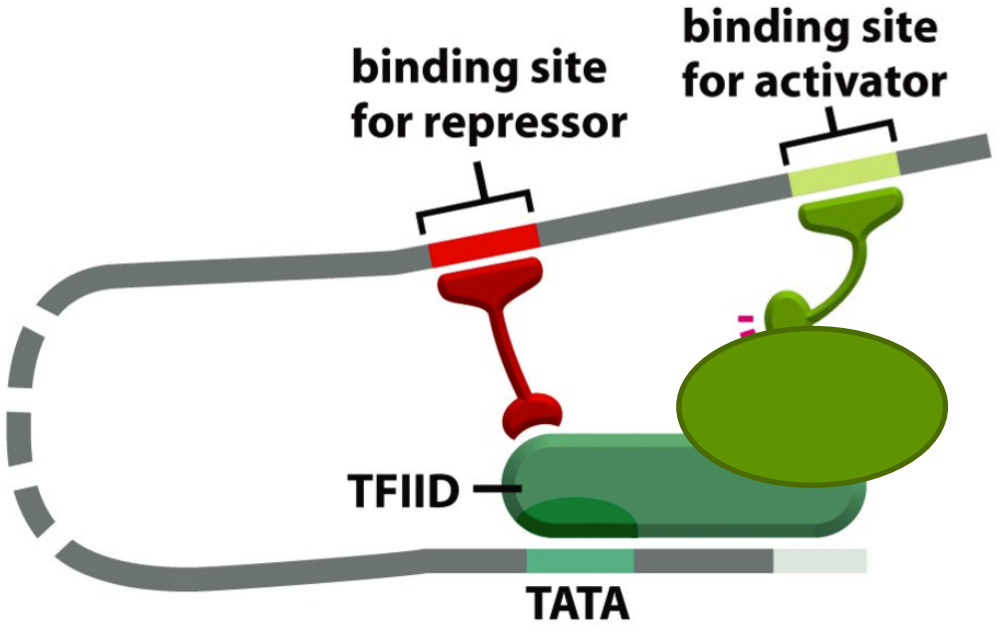


Let's complicate things 2

- 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

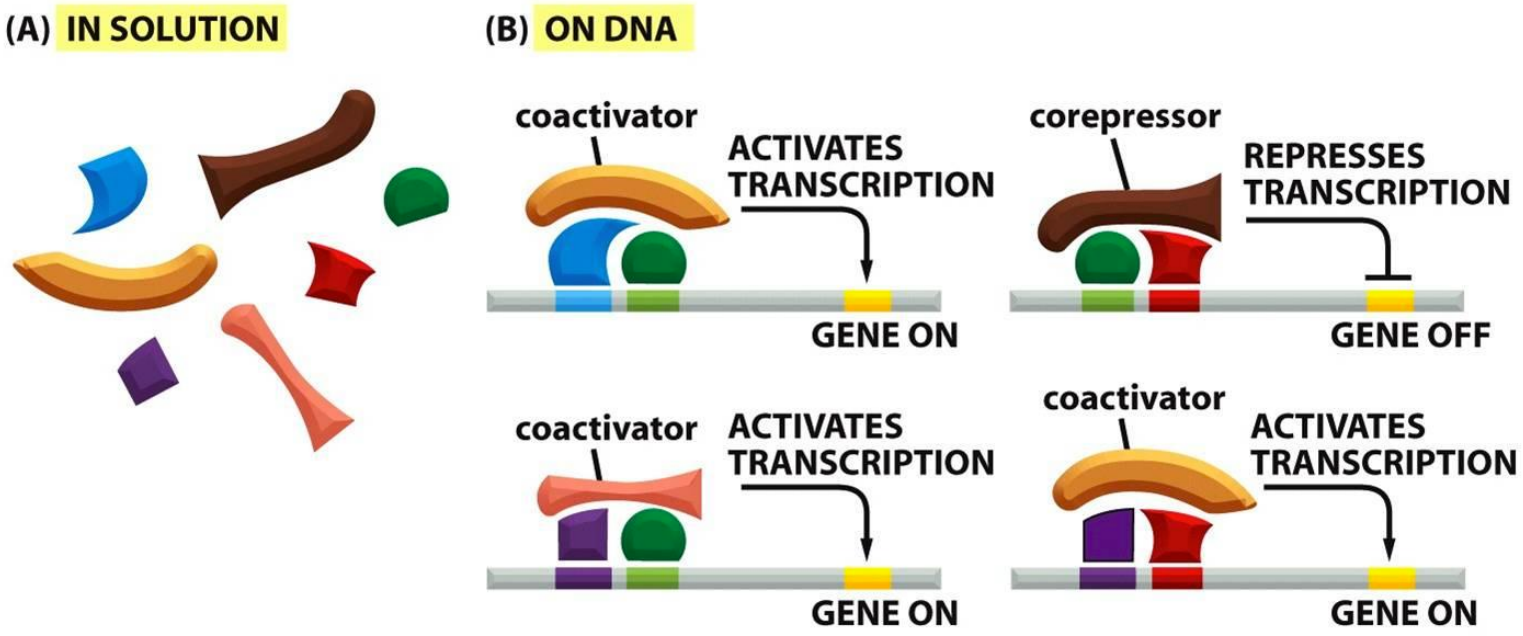


Let's complicate things 2

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?

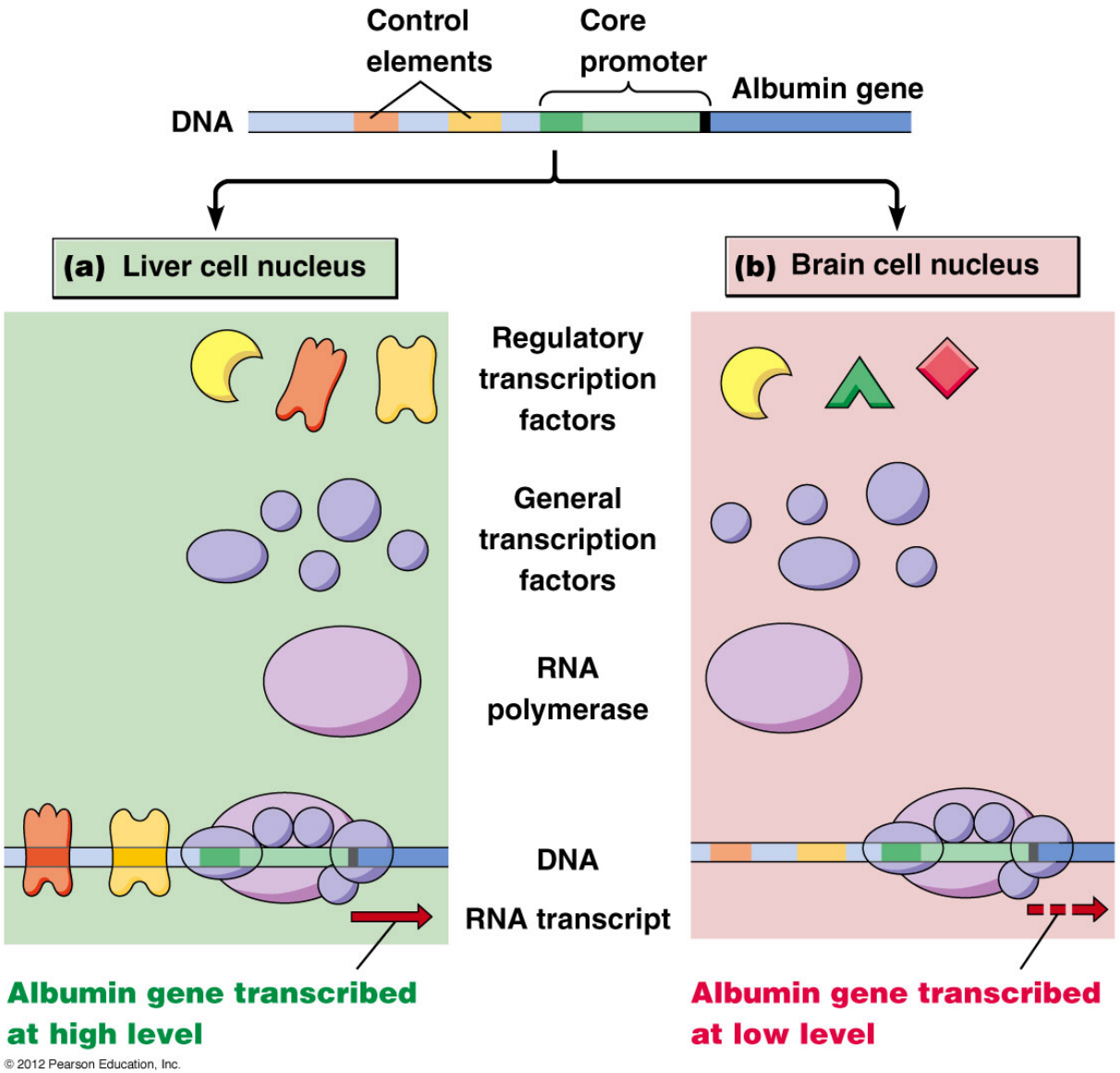
Do co-activator and co-repressors have DNA binding domain?

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?



How it works?

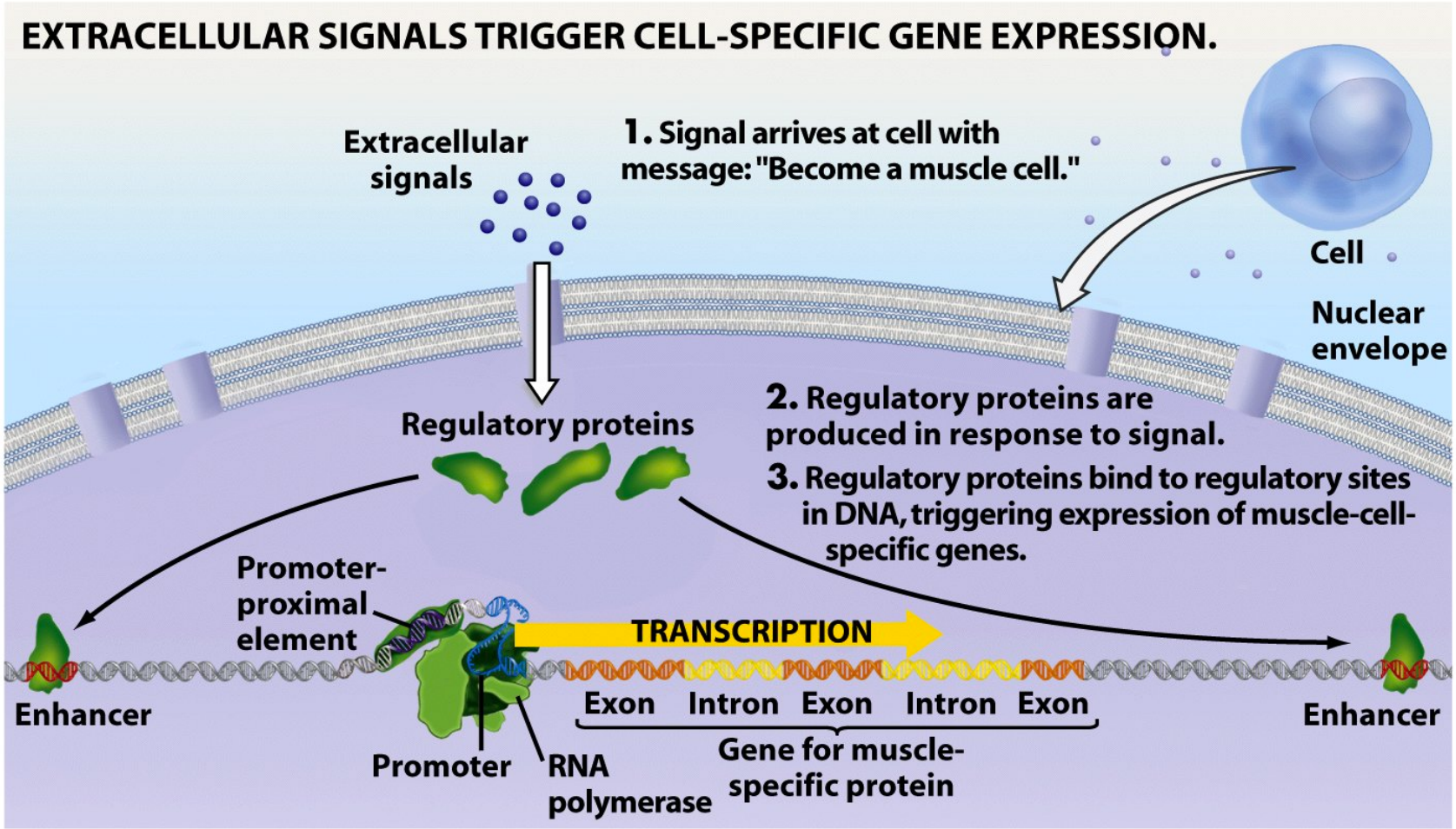


Figure 18-9 Biological Science, 2/e

To know

Co-repressor

Silencer

Enhancer

Prokaryotic vs. eukaryotic repressors

Co-activator

Activator

repressor

Competitive DNA binding

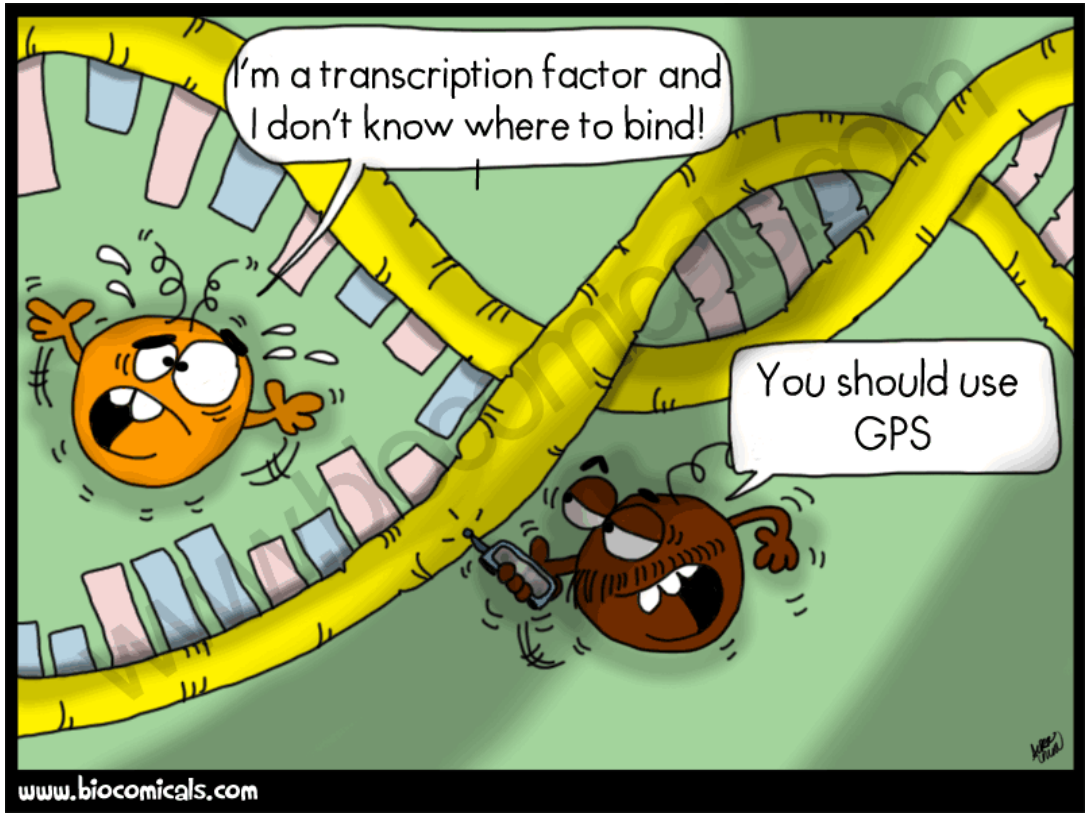
DNA binding domain

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