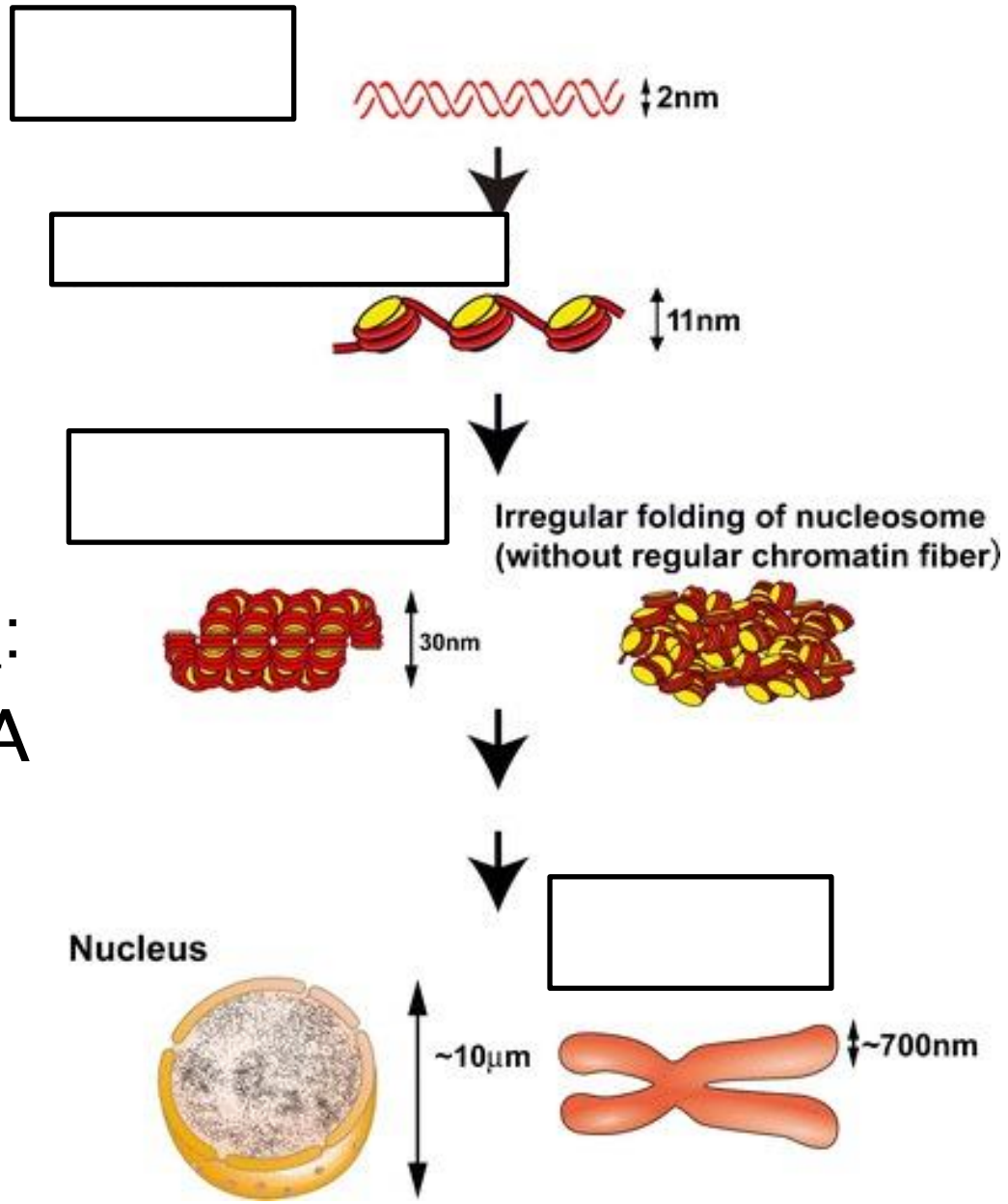
Principles of Transcriptional Regulation

- **Gene expression controlled by extracellular signals**
- **In Prokaryotes, these signals (eg lactose presence) might be in the medium and communicated to the cell by some proteins**
- **There are two types of proteins: activators and repressors**
- **Both are DNA binding proteins (DNBs), have specific binding sites near the genes**
- **Activator increases the rate of transcription, repressor reduces it**
- **Most of the repressors and activators act at the level of transcription initiation**
- **Why synthesize an mRNA if protein is not be synthesized! Energy conservation!**
- **Though, genes can be regulated later after transcription has been initiated, it gives choice of more than one steps where gene expression can be regulated, and also can reduce the response time**
- **In Prok: Holoenzyme RNA pol is generally active and needs repressors to regulate its activity**
- **While in Euk, the promoter is generally wrapped in the nucleosomes hence RNA pol II and needs specific transcriptional factors to become active**
- **The essence of transcription in Prok: activity**
- **The essence of transcription in Euk: inactivity**

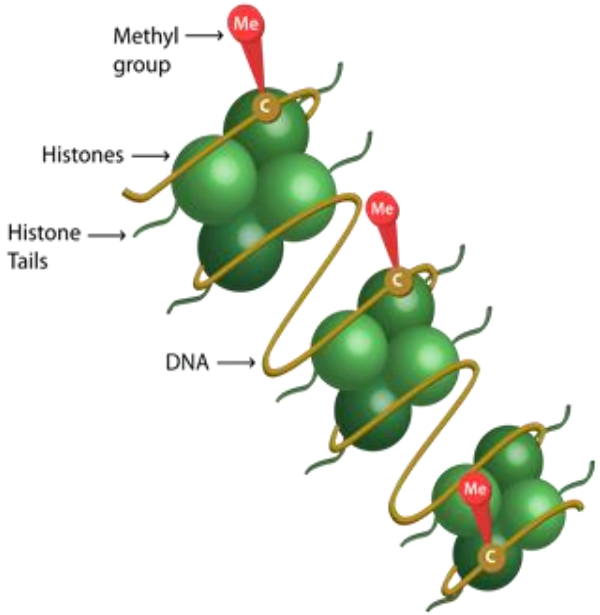
First stage: At the DNA level

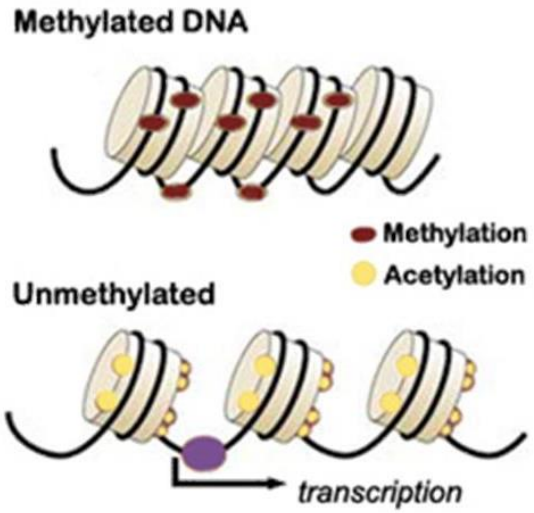


Chromatin Structure:

- Tightly bound DNA → less accessible for transcription

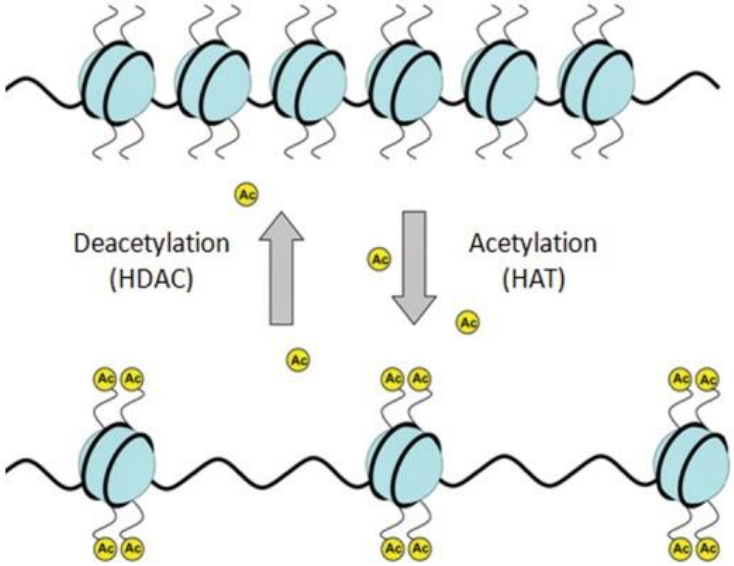
First stage: At the DNA level



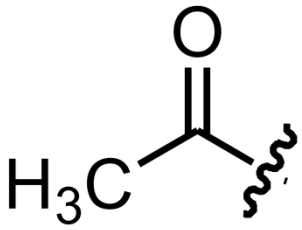


- DNA methylation:
  - Methyl groups are added to the DNA molecule
  - Changes the activity of a DNA segment without changing the sequence
  - When located in a gene promoter, it typically acts to repress gene transcription

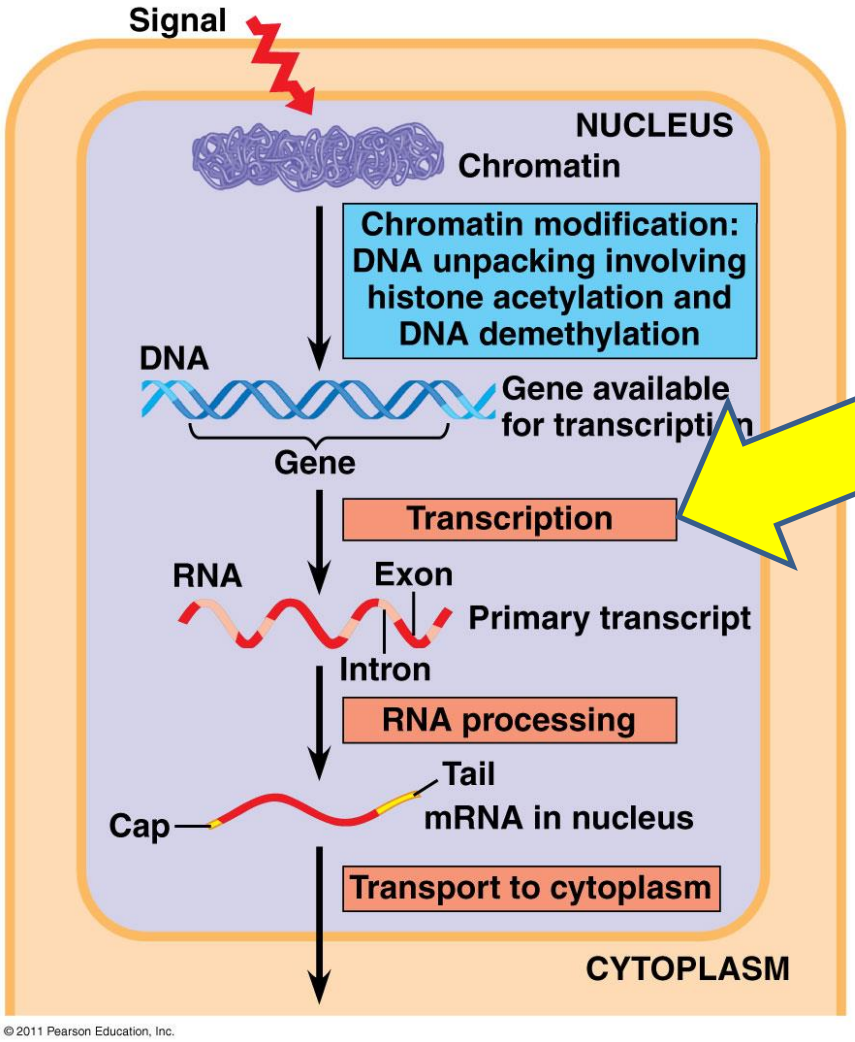
First stage: At the DNA level



- **Histone acetylation**:
  - acetyl groups added to histones;
  - Chromatin loosened; ↑ transcription



Second stage: At the transcription level



Transcription Initiation:

- Specific transcription factors (activators or repressors) bind to control elements (enhancer region)
- Activators: increase transcription
- Repressors: decrease transcription

Regulatory proteins: Mechanisms

Regulatory proteins can work with gene regulation in two conditions

a) **When they are present at adjascent sites to the genes/RNA polymerase**
b) **When they are present at distance**

a) **When present at adjascent sites: the following two are the mechanisms**

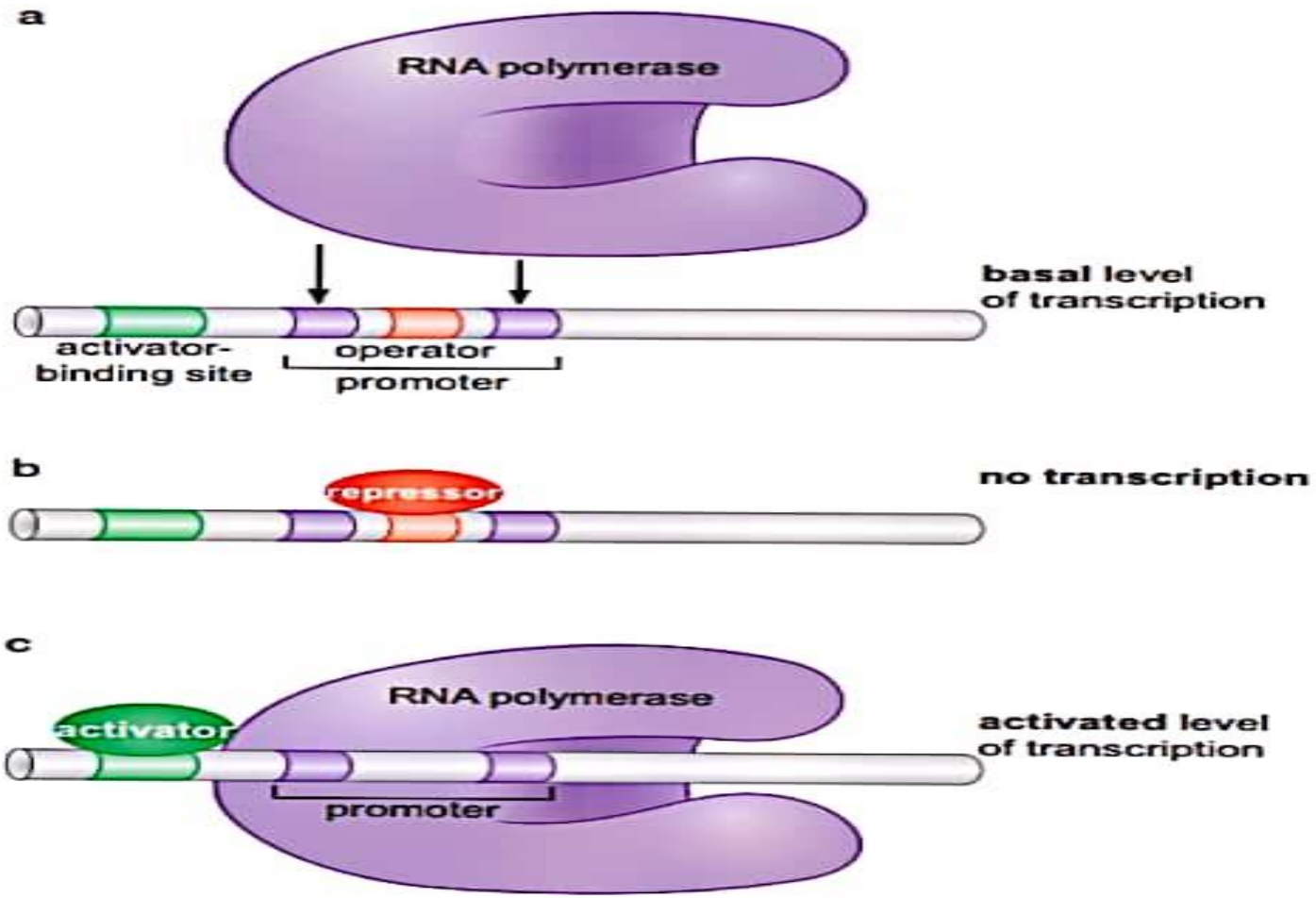
1. **Co-operative Binding/Tighter binding**
2. **Allostery**

Regulatory Proteins:Mechanisms

1. Tighter binding/co-operative binding of RNA pol to promoter by activators

- Regulatory proteins: If regulatory proteins are not bound, then promoters show weak expression k/a constitutive expression and express a basal level of gene products
- If u can recall, in Lac operon also, a repressor protein when bound to the operator preventing the binding of RNA polymerase
- So, binding of RNA polymerase, loosely or tightly defines the speed of transcription
- Activators b/a a close, tighter binding of RNA polymerase to the promoter
- **This is k/a Cooperative Binding and can bring together multiple signals that are required for activity of many genes**

Co-operative Binding: Activation by recruitment of RNA polymerase



Regulatory Proteins:Mechanisms

2. ALLOSTERY: b/a conformational change for

a) To regulate transition from a closed promoter complex to open promoter complex

- With certain promoters, transition from closed to open promoter complex is a rate limiting step.
- Activators help overcoming this by bringing in a **conformational change. This is known as ALLOSTERY**

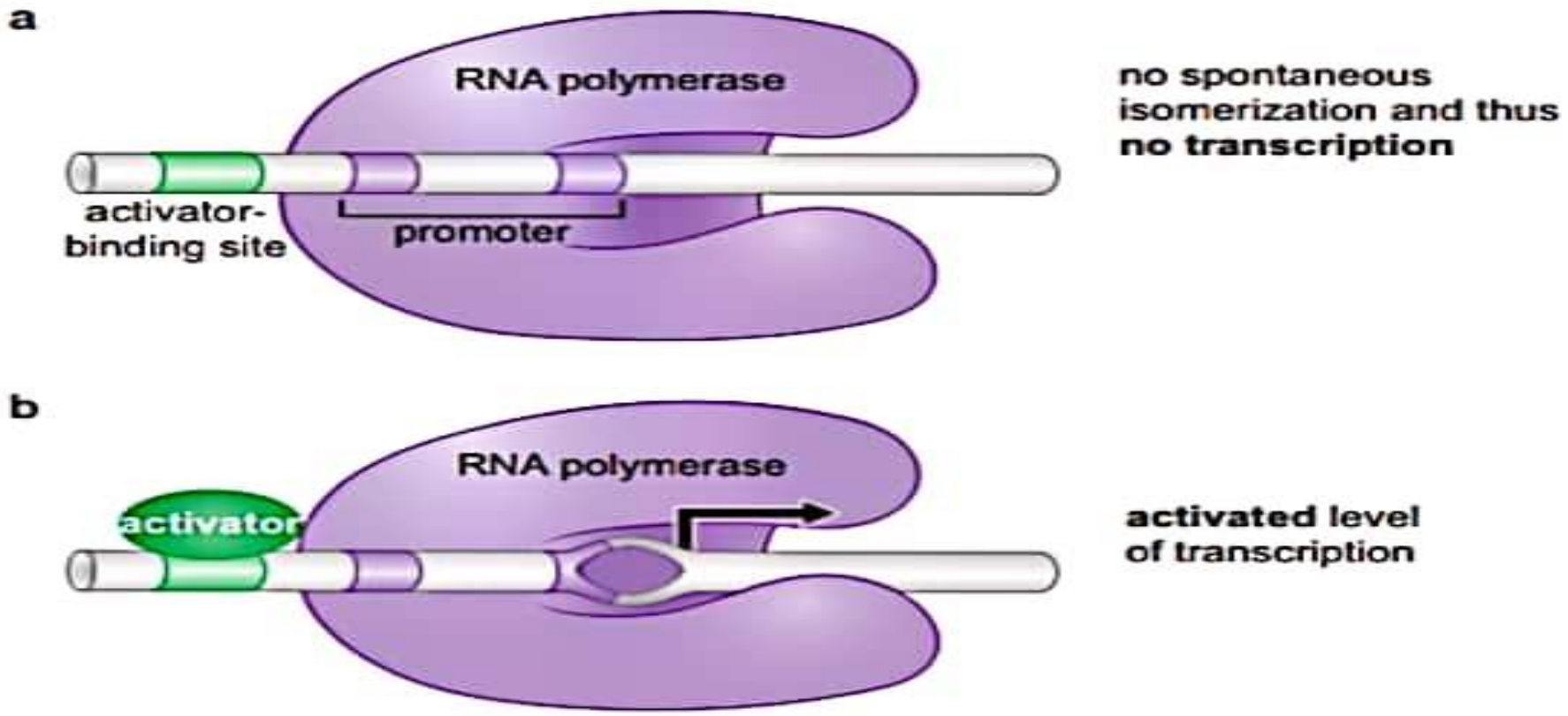
b) Promoter Escape:

- Certain promoters undergo abortive initiation and are **unable to escape the promoter,** activators in such cases help in **promoter escape**
- **Transition from closed to open promoter complex and promoter escape are examples of Allostery**

Allosteric Activation of RNA Polymerase:

a): stable closed complex

b): activator mediated transition to open promoter complex



Regulatory Proteins:Mechanisms

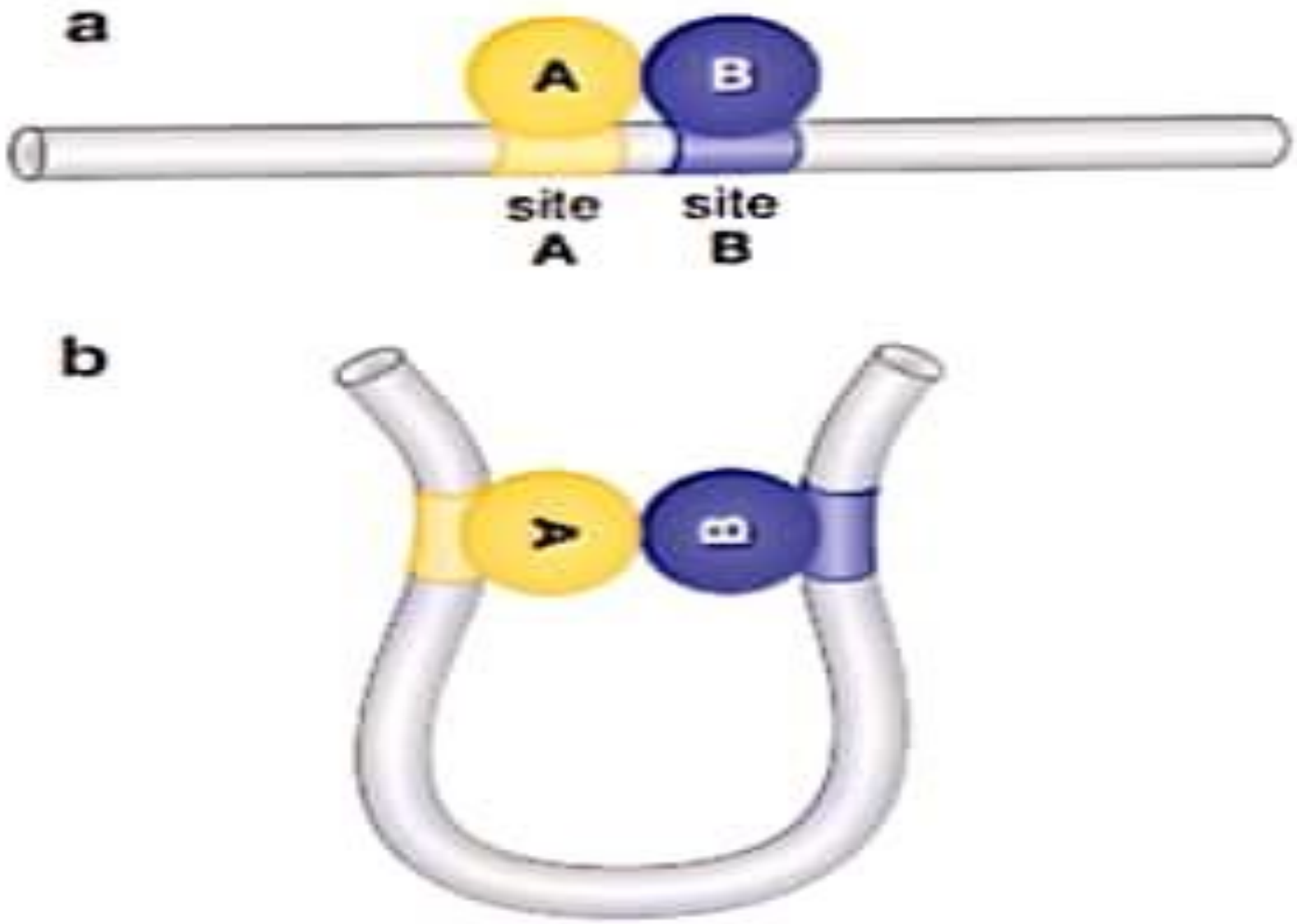
B) When regulatory proteins are present at distance to the genes/RNA polymerase

- Gene regulation is achieved, in such cases by **DNA Looping**. Activators interact to create DNA loops and bring activators and gene and polymerase together, Like wise repressors can also be brought close to the gene by way of looping
- Binding of **DNA Bending Proteins** stabilize such loops

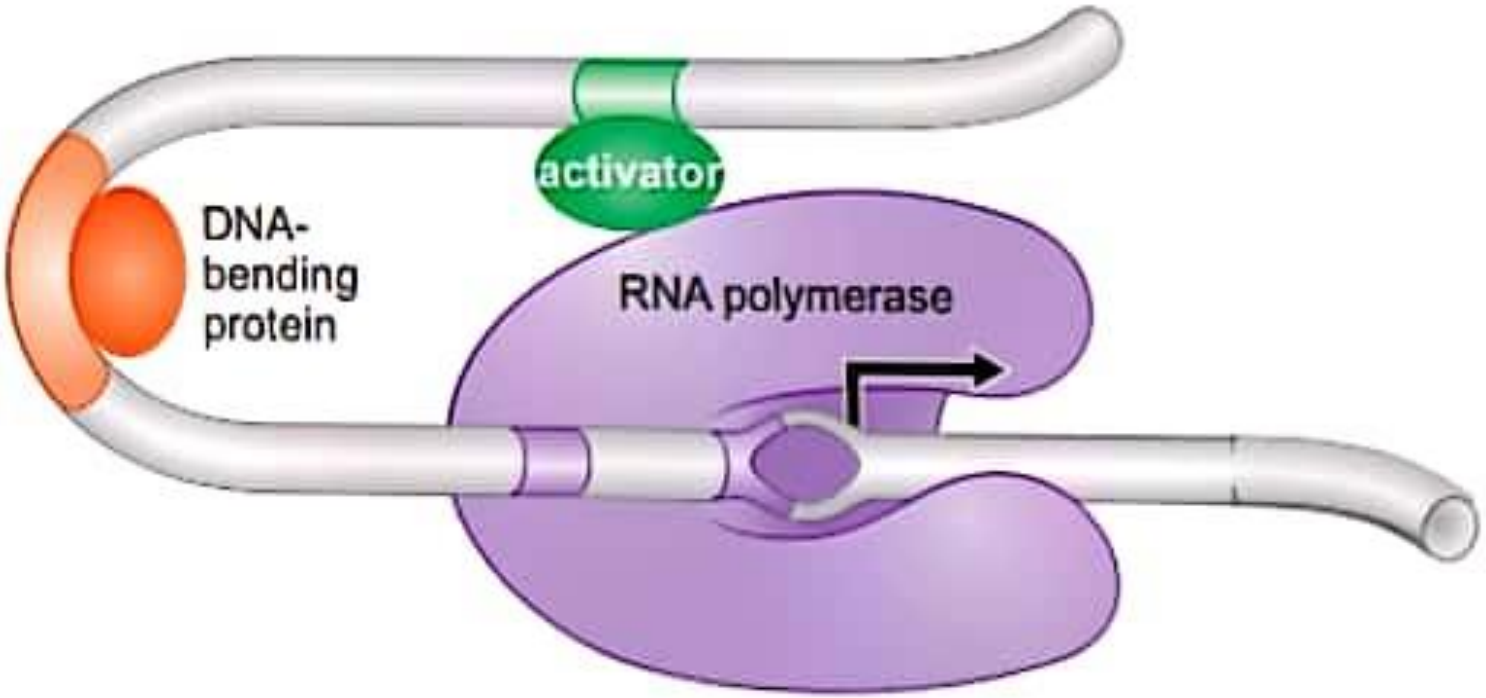
Co-operative Binding/DNA Looping

Interaction between proteins bound to DNA

a) adjascent sites b) distant sites

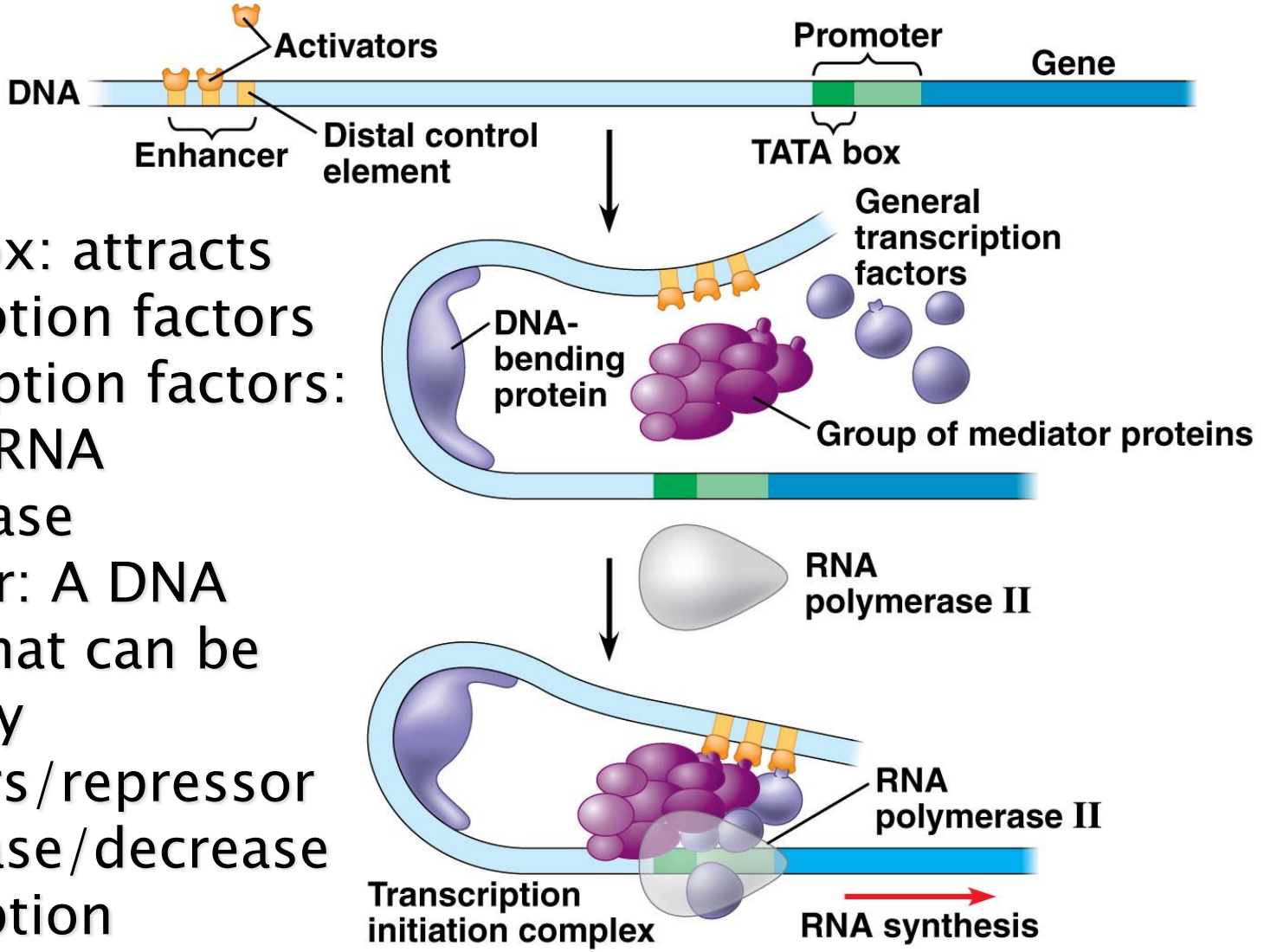


DNA Bending Protein: To facilitate interaction between distant activators and RNA polymerase



Transcription Initiation Complex

- TATA box: attracts transcription factors
- Transcription factors: attracts RNA Polymerase
- Enhancer: A DNA region that can be bound by activators/repressor to increase/decrease transcription



Regulatory Proteins:Mechanisms

Regulation of gene expression at translation

- Though, most of the gene activity is regulated at the level of transcription, there are mechanisms to regulate it at the level of translation as well
- E.g, are
- Attenuation
- Riboswitches
- Small RNAs

Cell type-specific transcription

- A particular combination of control elements can activate transcription only when the appropriate activator proteins are present