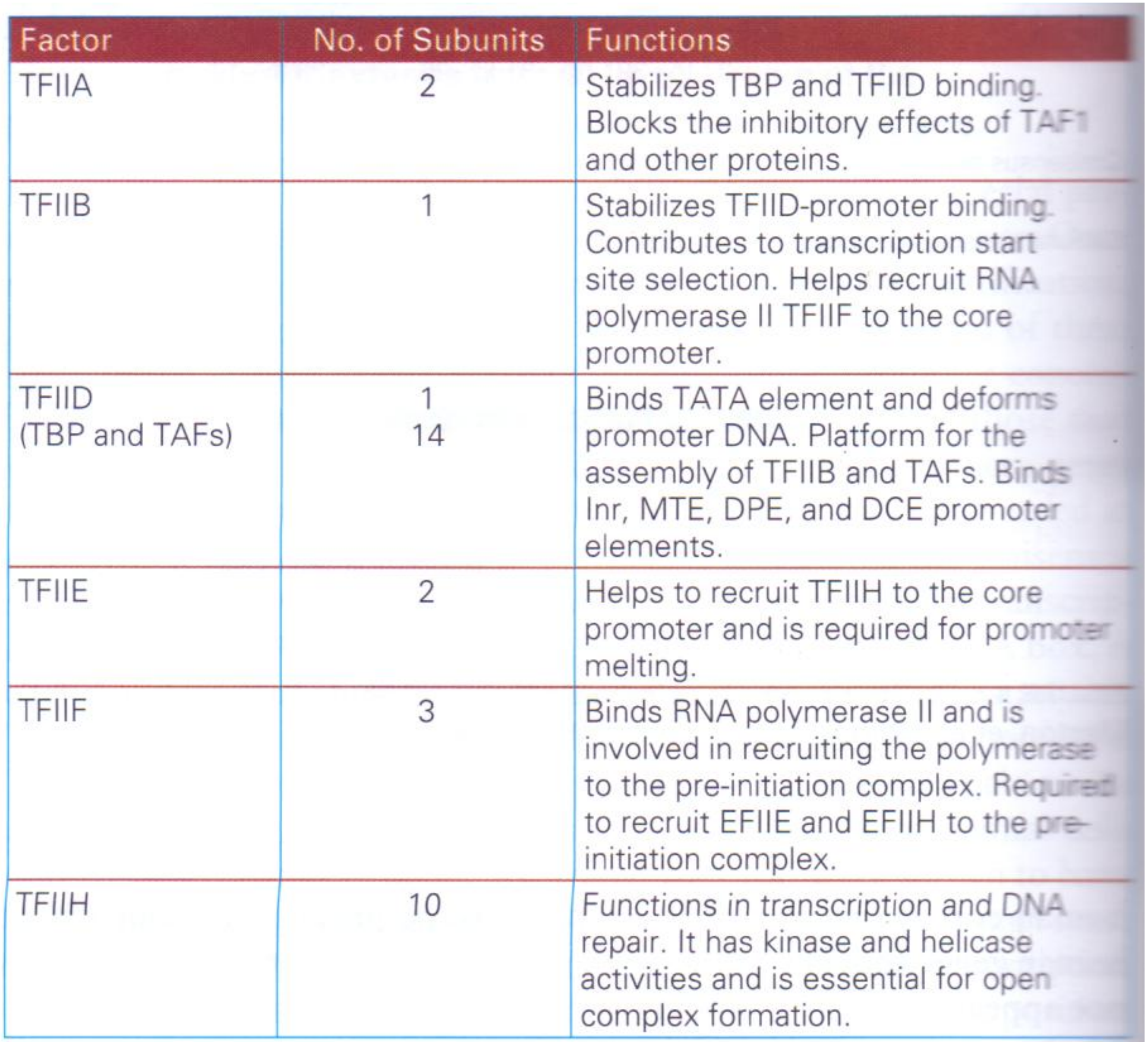
SOS in Biochemistry, Jiwaji University, Gwalior
M.Sc. II Semester (2019-20)
Paper BCH 205: Fundamentals of Molecular Biology (Unit III)

Eukaryotic Transcription - II

General Transcription Factors

General Transcription Factors

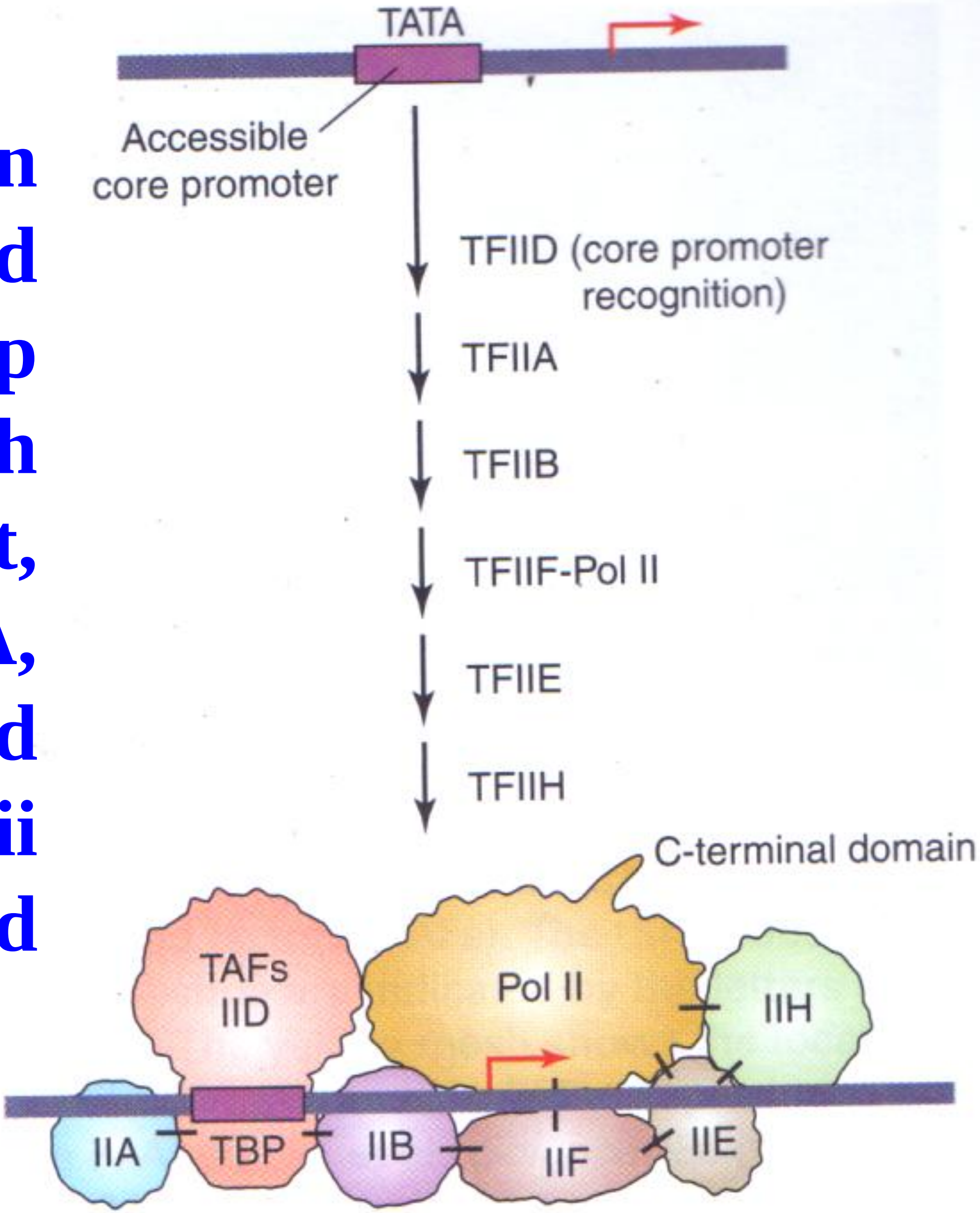


Factor	No. of Subunits	Functions
TFIIA	2	Stabilizes TBP and TFIID binding. Blocks the inhibitory effects of TAF1 and other proteins.
TFIIB	1	Stabilizes TFIID-promoter binding. Contributes to transcription start site selection. Helps recruit RNA polymerase II TFIIF to the core promoter.
TFIID (TBP and TAFs)	1 14	Binds TATA element and deforms promoter DNA. Platform for the assembly of TFIIB and TAFs. Binds Inr, MTE, DPE, and DCE promoter elements.
TFIIE	2	Helps to recruit TFIIH to the core promoter and is required for promoter melting.
TFIIF	3	Binds RNA polymerase II and is involved in recruiting the polymerase to the pre-initiation complex. Required to recruit EFIIE and EFIIH to the pre-initiation complex.
TFIIH	10	Functions in transcription and DNA repair. It has kinase and helicase activities and is essential for open complex formation.

General Transcription Factors and Pre-initiation Complex (PIC) Pathway

(for RNA polymerase II promoters with a TATA containing core promoter)

The pre-initiation complex is assembled on DNA in a multistep process in which TFIID binds first, followed by TFIIA, TFIIB, a preformrd complex of RNA pol ii and TFIIF, TFIIE and TFIIH.



Transcription Fidelity

Transcription Fidelity

1. RNA polymerases select correct NTP substrate to prevent transcription errors.
2. Two known proof reading functions to detect and remove misincorporated nucleotides:
   - a. Pyrophosphorylytic Editing
   - b. Hydrolytic Editing

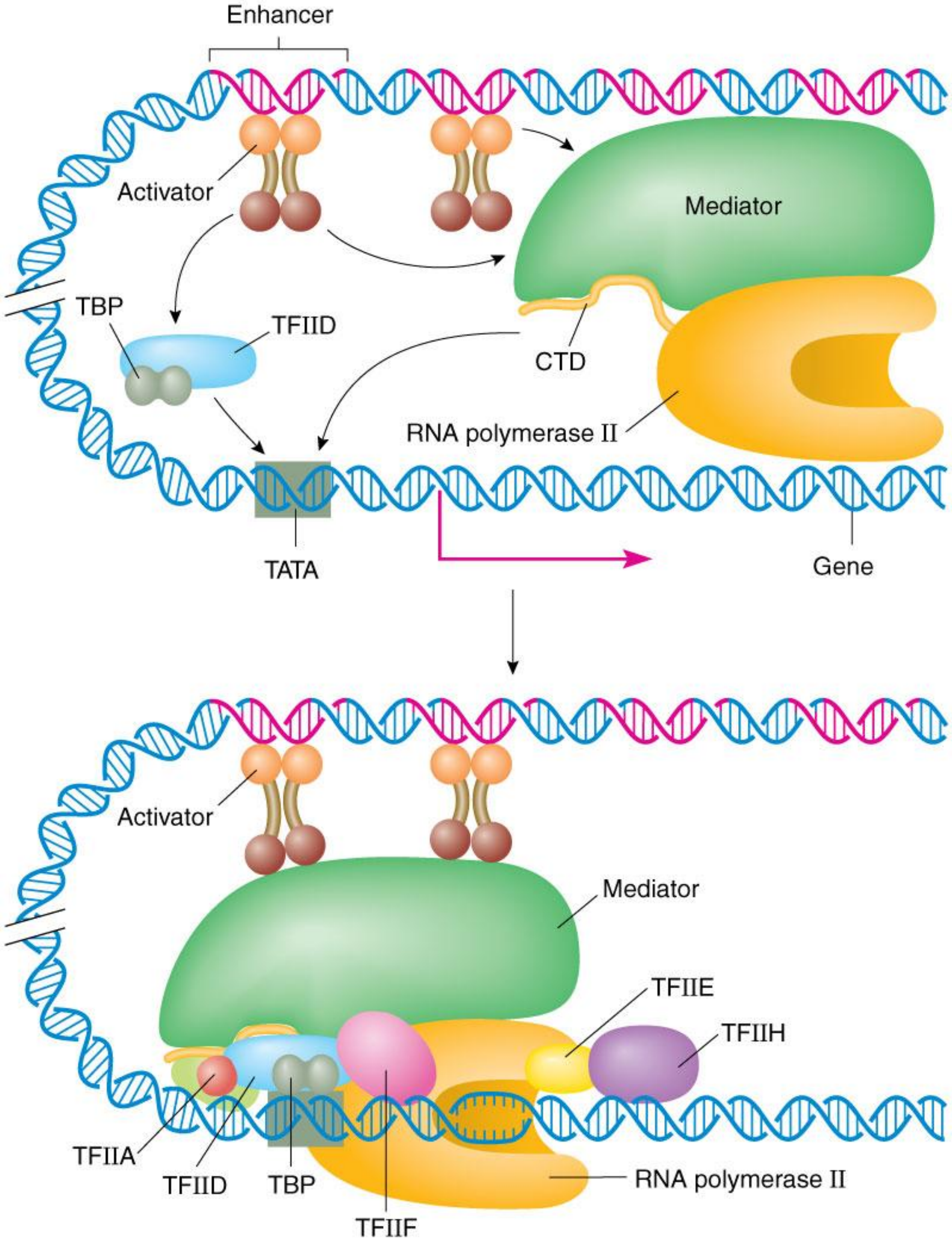
Enhancers

Enhancers

- Occur upstream or downstream of the transcription start site.
- Regulatory proteins bind specific enhancer sequences; binding is determined by the DNA sequence.
- Loops may form in DNA bound to TFs and make contact with upstream enhancer elements.
- Interactions of regulatory proteins determine if transcription is activated or repressed (positively or negatively regulated).

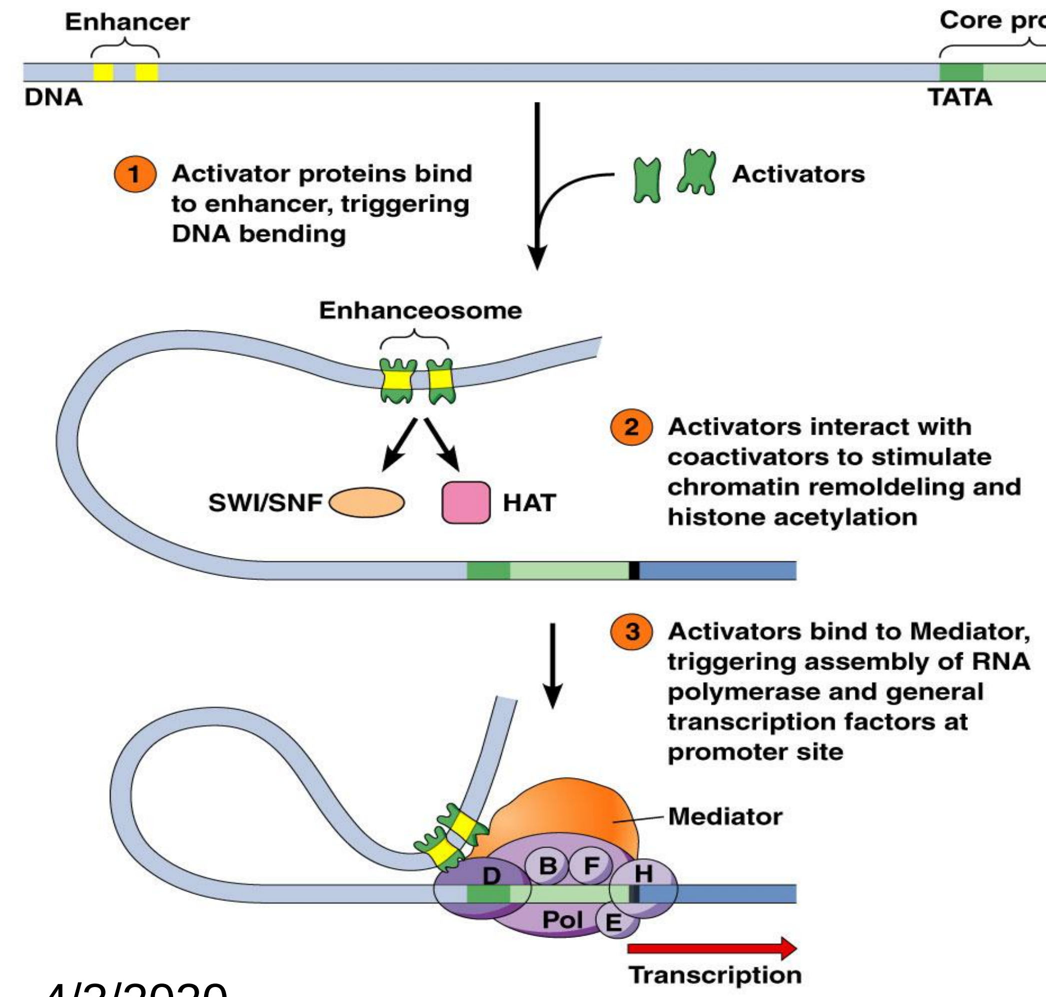
Activation of transcription:

By transcription factors (TFs), activator, and coactivator proteins.



Model for Enhancer Action

Suppressor or silencer



① Activator proteins bind to enhancer, triggering DNA bending

② Activators interact with coactivators to stimulate chromatin remoldeling and histone acetylation

③ Activators bind to Mediator, triggering assembly of RNA polymerase and general transcription factors at promoter site

DHAC: De-acetylase complex
MTC: Methyl transferase complex
Co-repressor

HAT: histone acetyl transferase
Co-activator

Remodeling complex

Little more about promoters and enhancers:

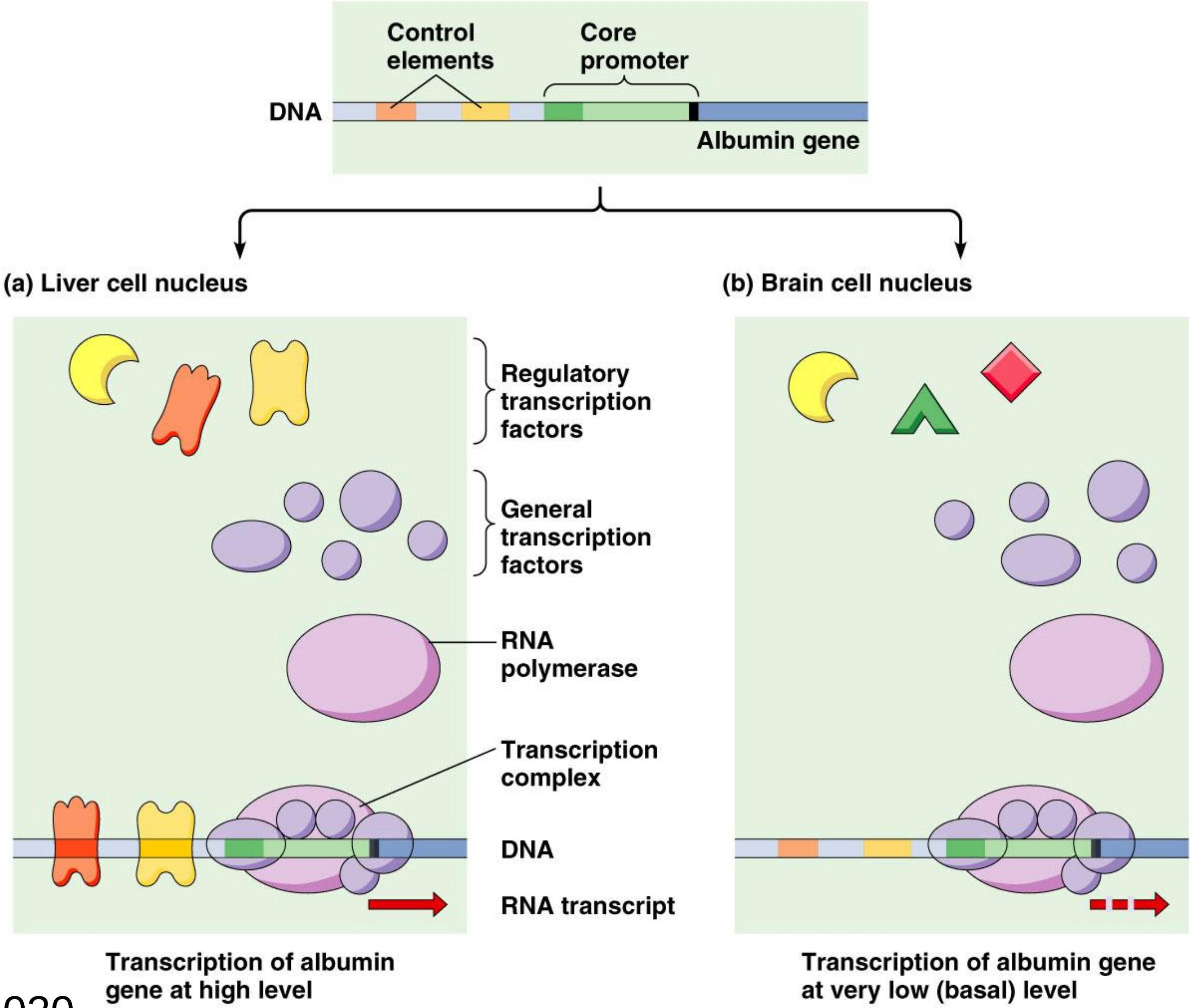
- **Some regulatory proteins are common in all cell types, others are specific.**

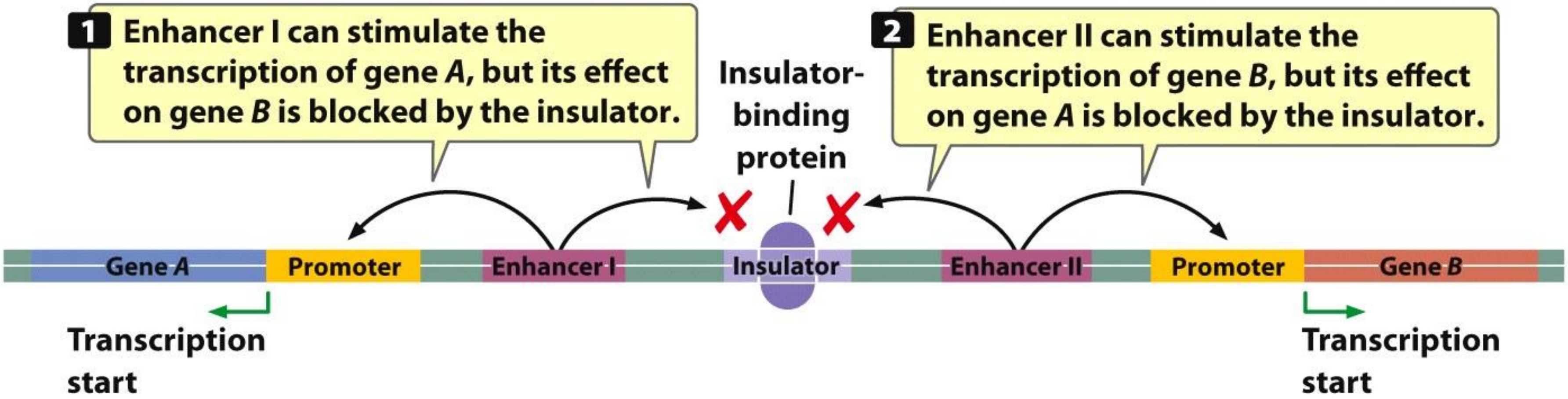
- **Each promoter and enhancer possesses a specific set of proteins (coactivators) that determines expression.**

- **Rate of gene expression is controlled by interaction between positive and negative regulatory proteins.**

- **Combinatorial gene regulation; enhancers and promoters bind many of the same regulatory proteins, implying lots of interaction with fine and coarse levels of control.**

Combinatorial Model for Gene Expression





1 Enhancer I can stimulate the transcription of gene *A*, but its effect on gene *B* is blocked by the insulator.

2 Enhancer II can stimulate the transcription of gene *B*, but its effect on gene *A* is blocked by the insulator.

Figure 12.17

Genetics Essentials: Concepts and Connections, Second Edition

Response Elements

Response Elements

- An element that causes a gene to respond to a regulatory TF is called as response element.
- Promoter modules that uniquely identify particular group of genes are called as response elements.
- Some examples are:
    - HSE (heat shock response element)
    - GRE (Glucocorticoid response element)
    - MRE (Metal response element)
- Response elements are recognized by factors that coordinate the transcription of particular group of genes

Response Elements

- **Response elements have the same general characters as other promoter or enhancer module.**
- **They contain short consensus sequences that can be recognized in the appropriate promoters. The actual module is closely related but not necessarily identical.**
- **In promoters, the modules are not present at the fixed distance from start point but are usually in the region of <200 bp upstream of it.**
- **The presence of single module is usually sufficient to confer the regulatory response, but there may be multiple copies.**

Response Elements

- Response elements may be located in promoters or in enhancers.
- Usually HSE if found in a promoter
  and GRE is found in an enhancer
- All response elements function via same general principle
- The presence of single module is usually sufficient to confer the regulatory response, but there may be multiple copies.

Response Elements

Regulatory Agent	Module	Consensus	DNA Bound	Factor	Size (kd)
Heat shock	HSE	CNNGANNTCCNNG	27 bp	HSTF	93
Glucocorticoid	GRE	TGGTACAAATGTTC	20 bp	Receptor	94
Phorbol ester	TRE	TGACTCA	22 bp	AP1	39
Serum	SRE	CCATATTAGG	20 bp	SRF	52

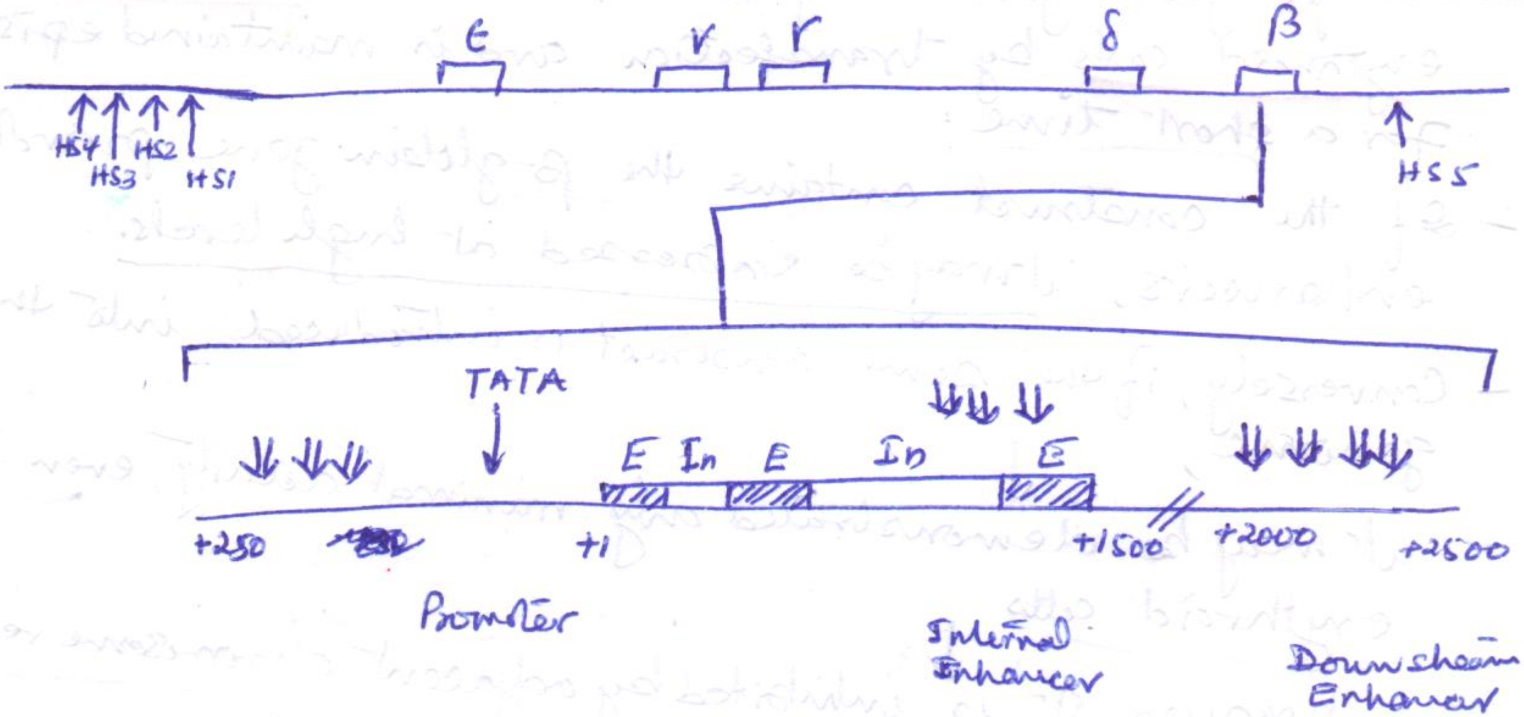
Locus Control Region
(LCR)

LCR

A locus control region (LCR) is an eukaryotic *cis*-acting element, usually located a considerable distance from the gene it regulates, which is essential for transcriptional activity because it establishes an independent chromatin domain.

Human β-globin cluster

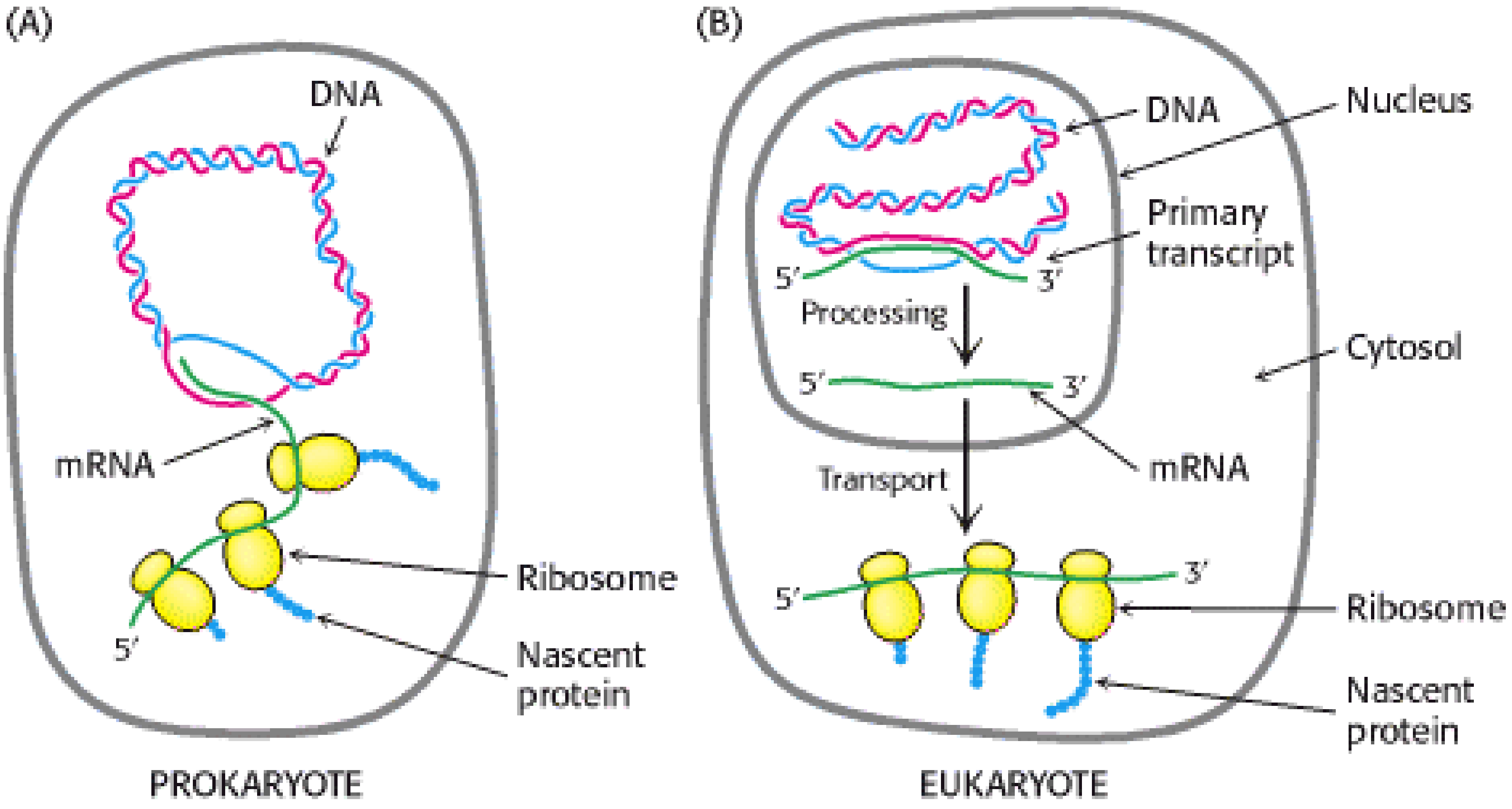
HS1 = Hypersensitive site 1



⇒ Binding sites for erythroid specific transcription factor GATA-1

- There are numerous binding sites for GATA 1 & a second erythroid specific protein NF-E2 in LCR

Comparison between Prokaryotic & Eukaryotic Transcription


(A)
DNA
mRNA
5′
Ribosome
Nascent protein
PROKARYOTE
(B)
DNA
Nucleus
Primary transcript
5′
3′
Processing
5′
3′
Cytosol
mRNA
Transport
3′
5′
Ribosome
Nascent protein
EUKARYOTE