Lecture 10: Genomes

Goal: Model to obtain insights into how the same DNA sequence can result in a diversity of gene expression profiles

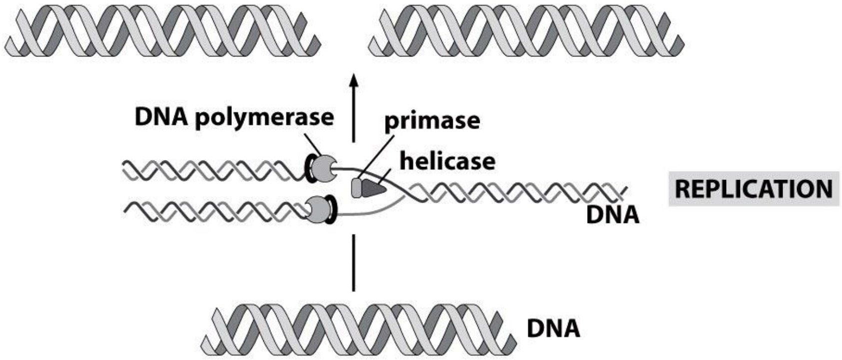
- Central dogma of molecular biology
- Genome regulation
- Genetic networks

PBOC Chapter 3.2.1, 6.1.2 (refresh Lecture 06), 19.2 (except 19.2.5)

Central dogma of molecular biology

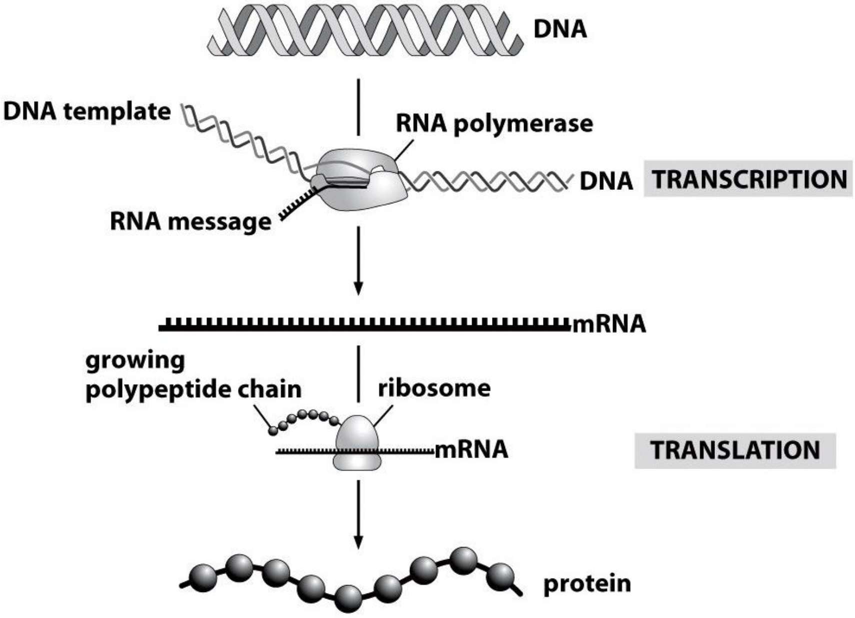
Recall (Lecture 1, 6)

Processes of the central dogma



DNA → DNA

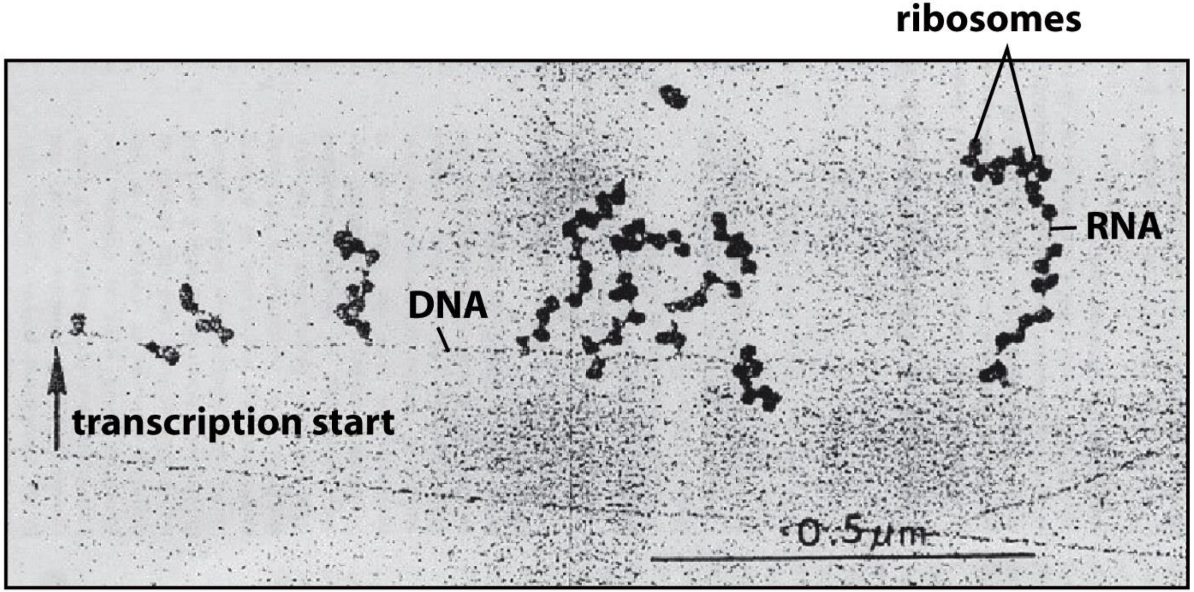
replisome: DNA polymerase
+ primase + helicase



DNA → mRNA → protein

Central dogma of molecular biology

Processes of the central dogma



In bacteria, ribosomes can bind to RNA even before it has finished being transcribed

Central dogma of molecular biology

Processes of the central dogma

What are the rates of processes involved in the central dogma?

Given replication rate per replisome of 250-1000 bp/s, and *E. coli* genome size of 5×10^6 bp, what range of times should it take to replicate the genome?

Given an average protein molecular weight of 46 kDa, an average amino acid molecular weight of 110 Da, and a transcription rate of 40 nucleotides/s, how long should it take on average to make an mRNA transcript?

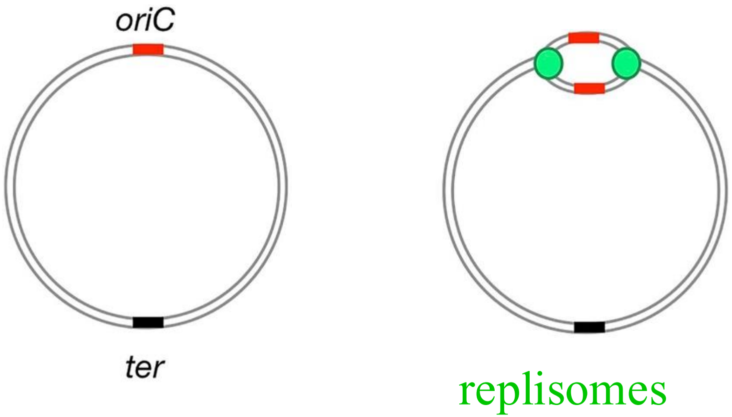
Given an E. coli cell cycle time of 3,000 seconds, and the facts that the number of proteins must double during this time, and that there are ~20,000 ribosomes per cell, what is the rate of translation per ribosome (units aa/second)? If needed, look back at Lecture 2 where we estimated the number of proteins per cell.

Central dogma of molecular biology

Processes of the central dogma: Replication

Given replication rate per replisome of 250-1000 bp/s, and *E. coli* genome size of 5×10^6 bp, what range of times should it take to replicate the genome?

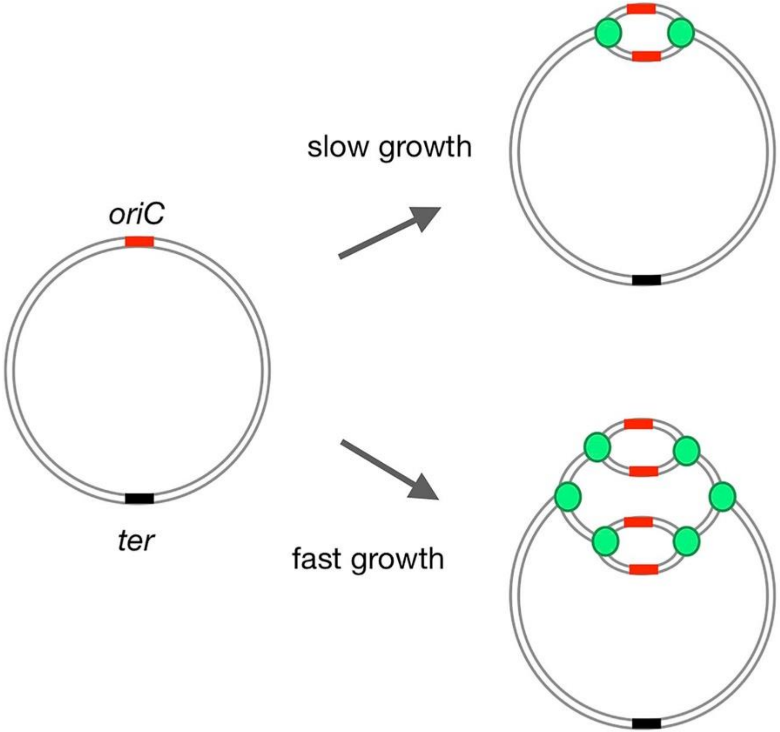
bacteria contain a single circular genome



Central dogma of molecular biology

Processes of the central dogma: Replication

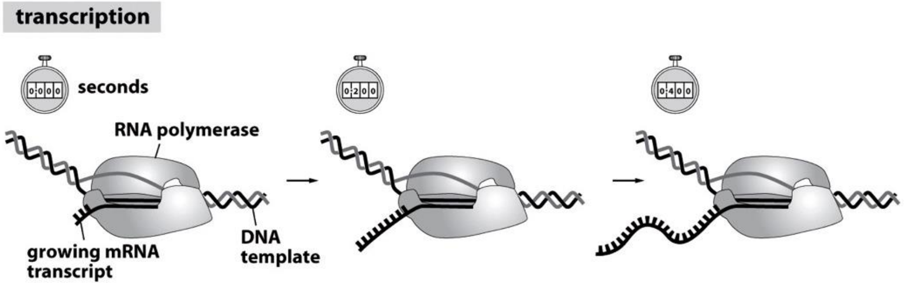
E. coli can divide in much less than 3000 seconds, in fact, as little as 1000 seconds



Central dogma of molecular biology

Processes of the central dogma: Transcription

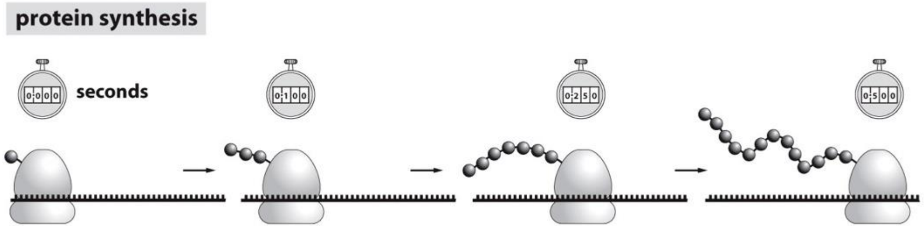
Given an average protein molecular weight of 46 kDa, an average amino acid molecular weight of 110 Da, and a transcription rate of 40 nucleotides/s, how long should it take on average to make an mRNA transcript?



Central dogma of molecular biology

Processes of the central dogma: Translation

Given an E. coli cell cycle time of 3,000 seconds, and the facts that the number of proteins must double during this time, and that there are ~20,000 ribosomes per cell, what is the rate of translation per ribosome (units aa/second)? If needed, look back at Lecture 2 where we estimated the number of proteins per cell.



Genome regulation

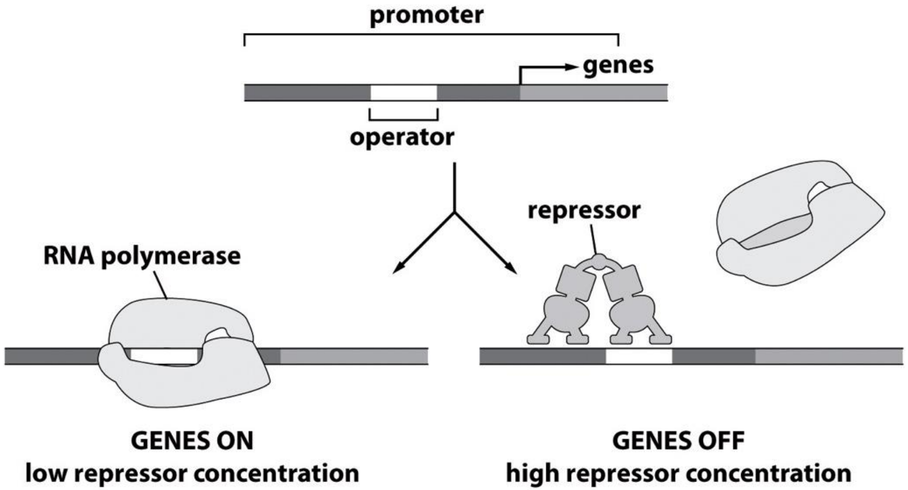
Statistical mechanics of gene expression

Review Lecture 6 annotated slides 13-20, along with PBoC 6.1.2

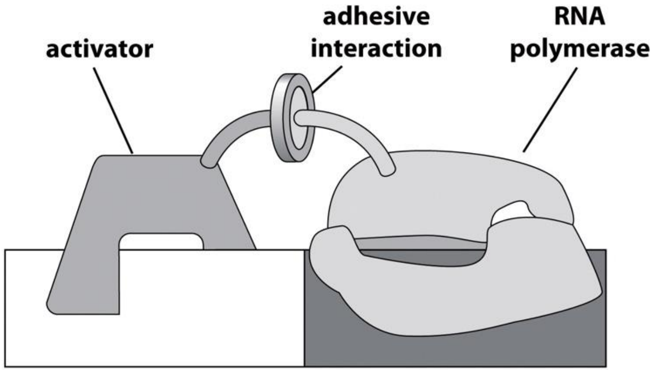
Genome regulation

Genetic networks: Molecules

negative regulation



positive regulation

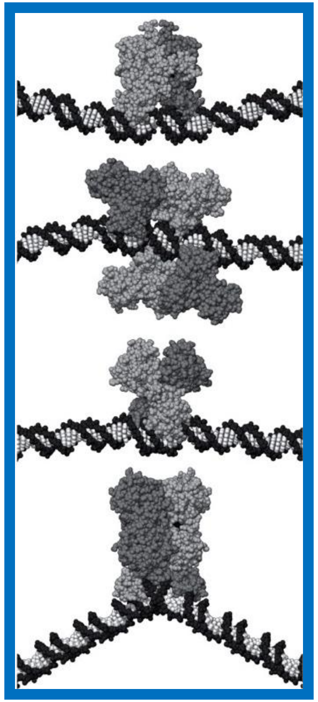


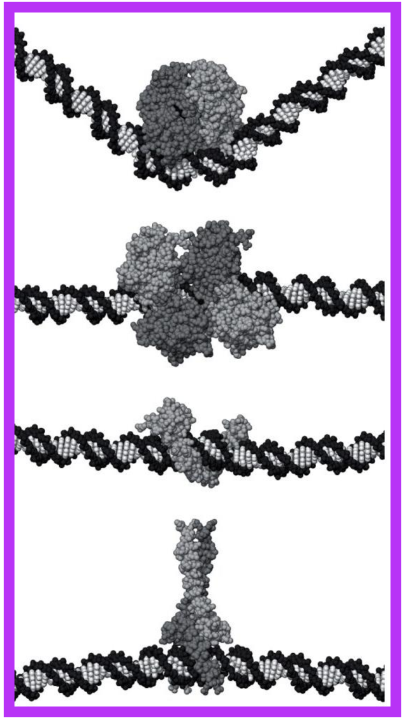
Repressors and activators change the probability of RNA polymerase binding to the promoter of a gene

Genome regulation

Genetic networks: Molecules

Repressors and activators can both bind to DNA and deform it in the promoter region of a gene.



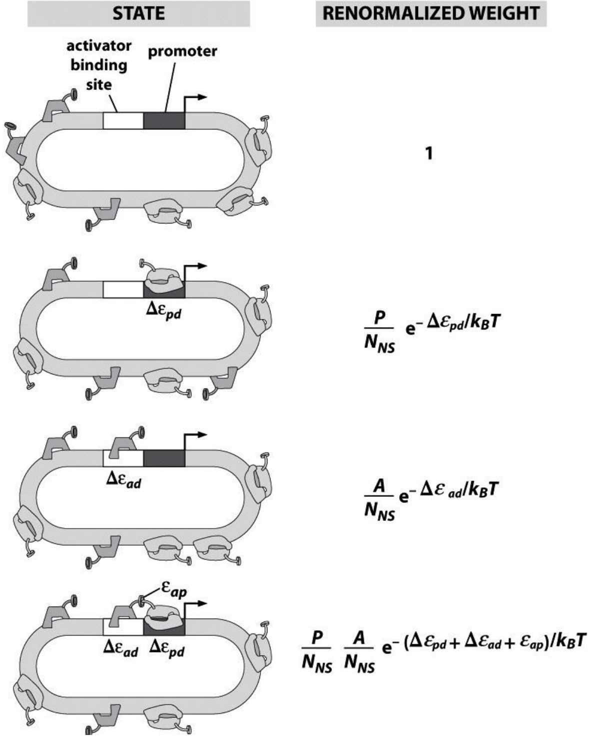


Repressors bind to the promoter site, to block RNA polymerase from binding

Activators bind upstream of the promoter site, to enhance RNA polymerase binding

Genome regulation

Genetic networks: Models (activation)

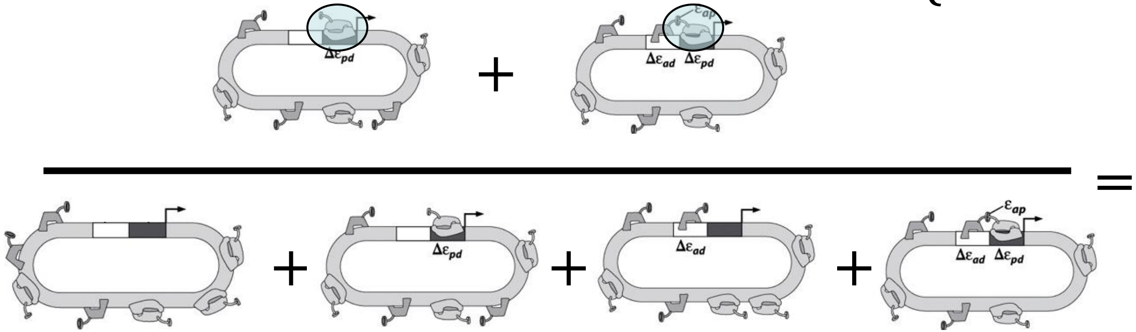


STATE	RENORMALIZED WEIGHT
activator binding site promoter	1
$\Delta\varepsilon_{pd}$	$\frac{P}{N_{NS}} e^{-\Delta\varepsilon_{pd}/k_BT}$
$\Delta\varepsilon_{ad}$	$\frac{A}{N_{NS}} e^{-\Delta\varepsilon_{ad}/k_BT}$
ε_{ap} $\Delta\varepsilon_{ad}$ $\Delta\varepsilon_{pd}$	$\frac{P}{N_{NS}} \frac{A}{N_{NS}} e^{-(\Delta\varepsilon_{pd}+\Delta\varepsilon_{ad}+\varepsilon_{ap})/k_BT}$

Genome regulation

Genetic networks: Models (activation)

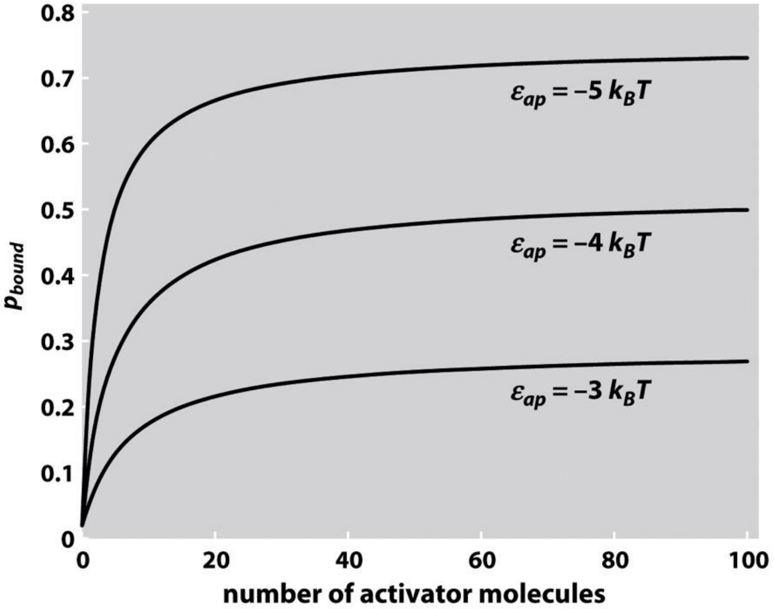
$P_{bound} =$

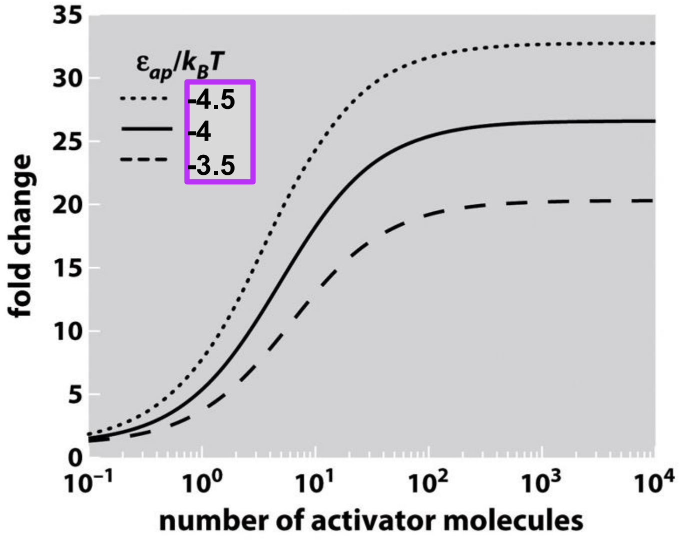


$$= \frac{\text{states with RNAp bound}}{\text{all states}}$$

Genome regulation

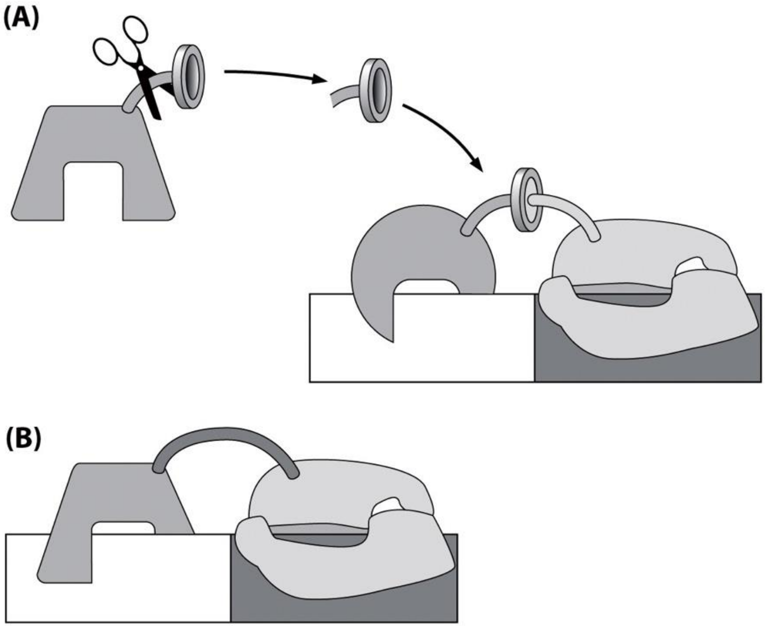
Genetic networks: Models (activation)





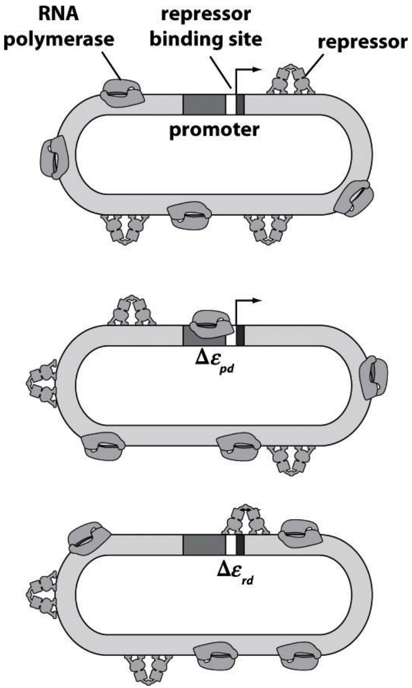
Genome regulation

Genetic networks: Models (activation)



Genome regulation

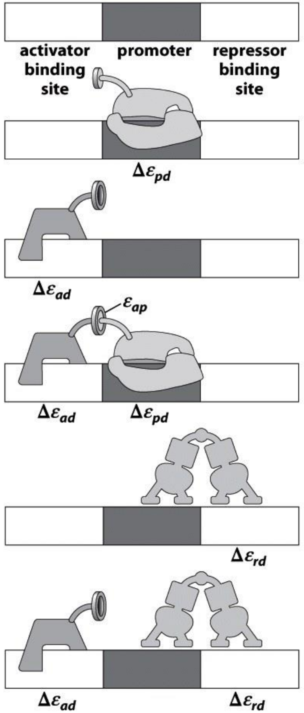
Genetic networks: Models (repression)

STATE	RENORMALIZED WEIGHT
	1 $\frac{P}{N_{NS}} e^{-\Delta\varepsilon_{pd}/k_BT}$ $\frac{R}{N_{NS}} e^{-\Delta\varepsilon_{rd}/k_BT}$

Genome regulation

Genetic networks: Models (activation + repression)

STATE



RENORMALIZED WEIGHT

$$1$$

$$\frac{P}{N_{NS}}\, e^{-\Delta\varepsilon_{pd}/k_BT}$$

$$\frac{A}{N_{NS}}\, e^{-\Delta\varepsilon_{ad}/k_BT}$$

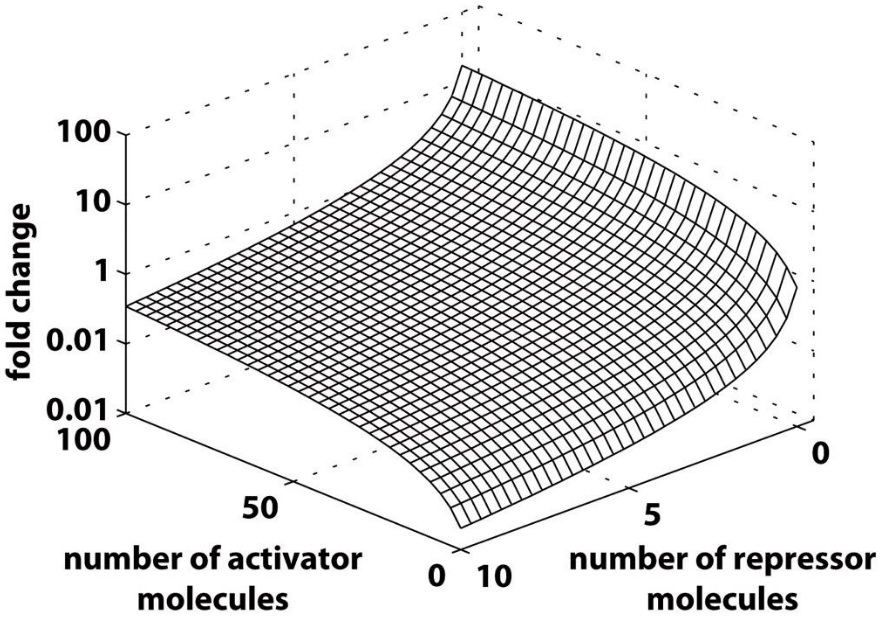
$$\frac{P}{N_{NS}}\,\frac{A}{N_{NS}}\, e^{-(\Delta\varepsilon_{pd}+\Delta\varepsilon_{ad}+\varepsilon_{ap})/k_BT}$$

$$\frac{R}{N_{NS}}\, e^{-\Delta\varepsilon_{rd}/k_BT}$$

$$\frac{A}{N_{NS}}\,\frac{R}{N_{NS}}\, e^{-(\Delta\varepsilon_{pd}+\Delta\varepsilon_{rd})/k_BT}$$

Genome regulation

Genetic networks: Models (activation + repression)



Lecture 10: Genomes

Summary:

Lecture 11: Genomes

Goal: Model interactions between gene regulatory elements, discuss common motifs in genetic circuits

Watch Prof. Uri Alon video before class
Answer guiding questions
In-class small group discussions

Reading support : Alon Network Motifs