# …NAPOLEON IS IN EQUILIBRIUM

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BIOPH18_L18 From chapter 6, Physical Biology of the cell

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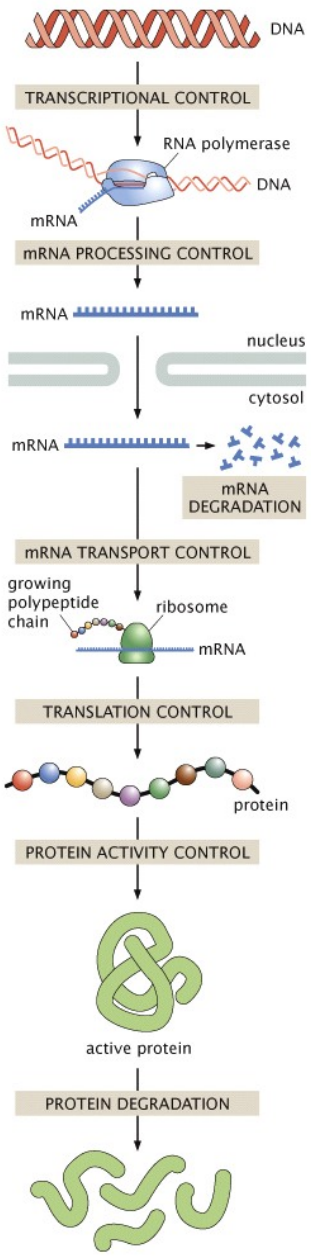



Figure 6.7 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# Statistical mechanics of gene expression

- Gene expression can be measured at the mRNA level: Transcriptome
- CONTROLED BY TRANSCRIPTION FACTORS

- Gene expression can be measured at the protein level: proteome
- CONTROLLED By various mechanisms at the ribosome

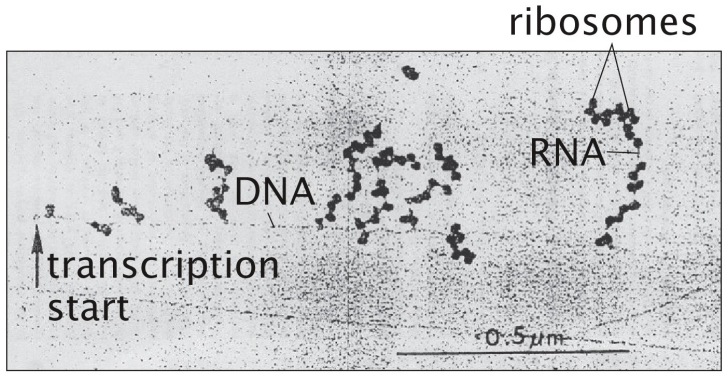



Figure 3.13 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

**Figure 3.9** Electron microscopy image of simultaneous transcription and translation. The image shows bacterial DNA and its associated mRNA transcripts, each of which is occupied by ribosomes. (Adapted from O. L. Miller et al., *Science* 169:392, 1970.)

# Heterogeneity of phenotypes: noise

Pictoresquely, originating from cellular "decisions"

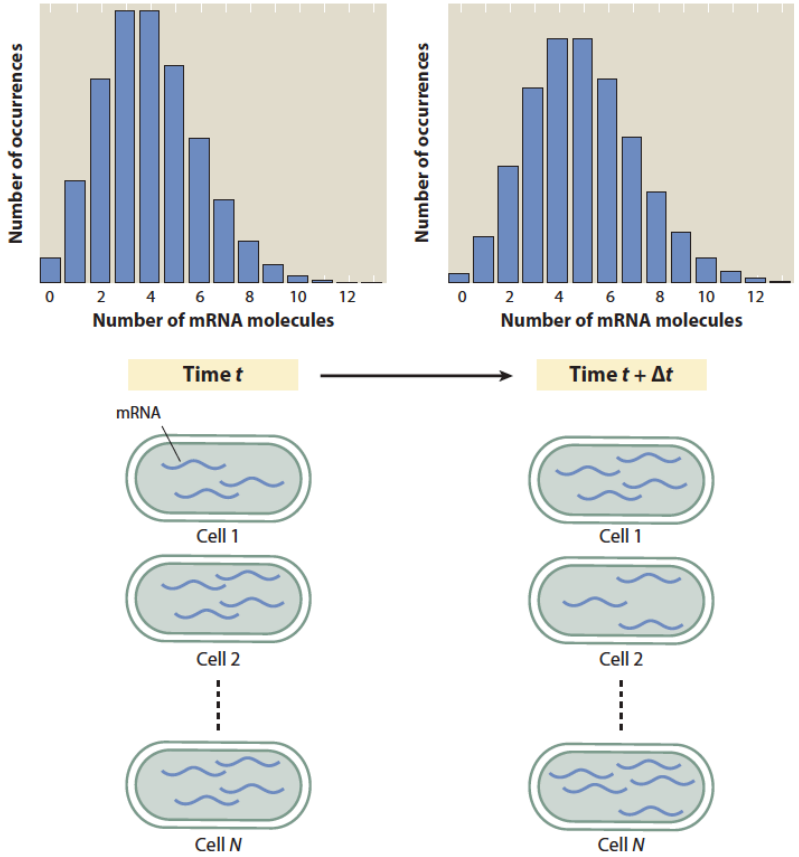



**Figure 2**

Transcription process resulting in change in mRNA census between times $t$ and $t + \Delta t$. The schematic histogram shows the distribution of the number of mRNA molecules found per cell. We refer to the average number of mRNA at time $t$ as $m(t)$; it is found by adding up the total number of mRNA over all cells and dividing by the number of cells. The number of mRNA per cell increases because of transcription and decreases because of mRNA degradation.

From Phillips2015

# Focus on trascriptional control

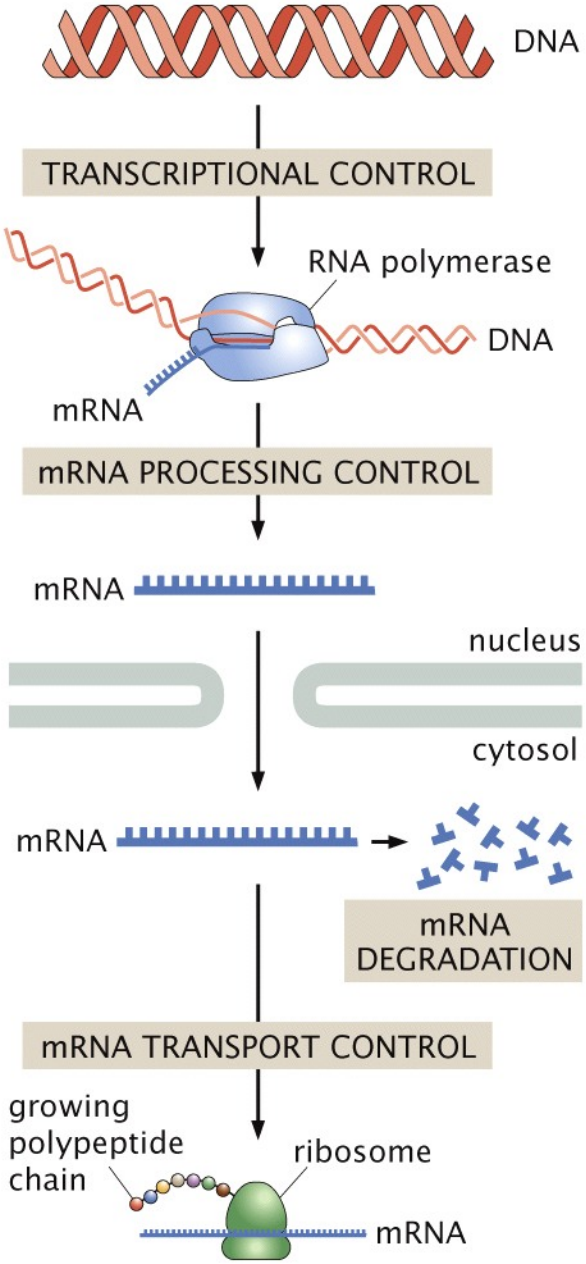



Figure 6.7 (part 1 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

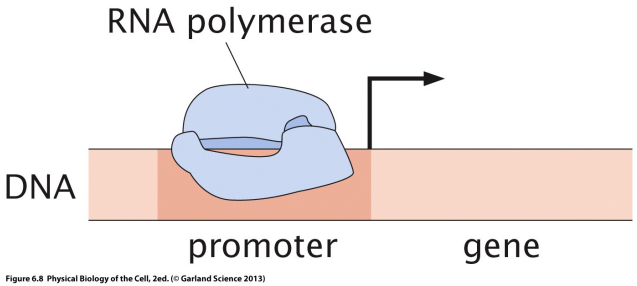



Figure 6.8 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

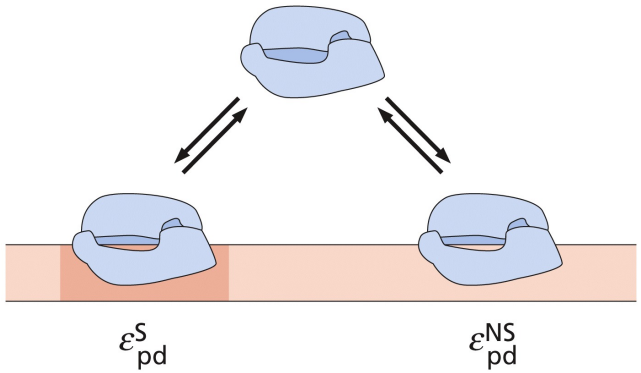



Figure 6.10 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

**Figure 6.10** Polymerase binding energies. Illustration of the difference in binding energy for RNA polymerase when it is bound specifically ($\varepsilon^{S}_{pd}$) and nonspecifically ($\varepsilon^{NS}_{pd}$).

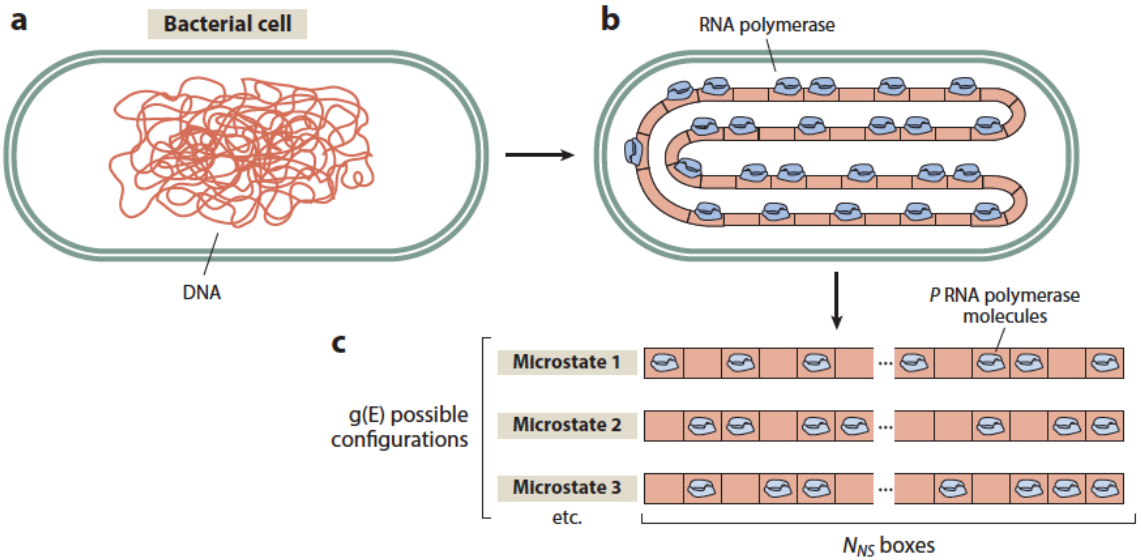



Figure 4

The Boltzmann genome. (*a*) Schematic of a bacterial cell showing the complicated internal arrangement of the genome. (*b*) Abstraction of the genomic landscape of a bacterium into a one-dimensional lattice of binding sites. (*c*) There are many microstates [g(E) of them] of the *P* RNA polymerase molecules on the genomic DNA, and this can be evaluated combinatorially by thinking of the genome as consisting of $N_{NS}$ nonspecific binding sites upon which the *P* RNA polymerases can be arranged.

**Figure 6.9** The RNA polymerase reservoir. Schematic of the ways in which RNA polymerase can be distributed throughout a bacterial cell. These molecules can be bound at any of the $N_{NS}$ nonspecific sites on the DNA, at promoters, or be distributed throughout the cytoplasm. Each microstate corresponds to a different arrangement of the polymerase molecules on these nonspecific binding sites. We consider a model in which RNA polymerase is bound exclusively on the DNA since the cytoplasmic contribution is negligible.

# SCHEME OF STATES AND WEIGHTS

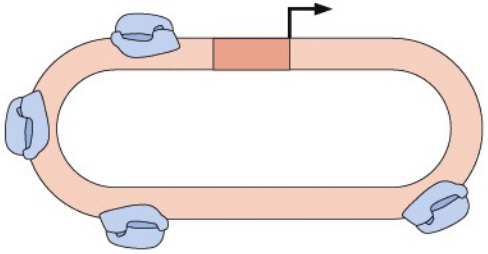
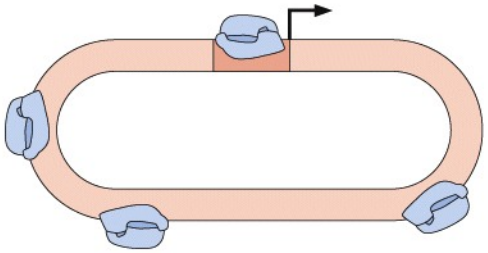
| STATE | ENERGY | MULTIPLICITY | WEIGHT (MULTIPLICITY x BOLTZMANN WEIGHT) |
|---|---|---|---|
|  | $P\varepsilon_{pd}^{NS}$ | $\frac{N_{NS}!}{P!\,(N_{NS}-P)!} \approx \frac{(N_{NS})^P}{P!}$ | $\frac{(N_{NS})^P}{P!}\, e^{-P\varepsilon_{pd}^{NS}/k_BT}$ |
|  | $(P-1)\varepsilon_{pd}^{NS} + \varepsilon_{pd}^{S}$ | $\frac{N_{NS}!}{(P-1)!\,[N_{NS}-(P-1)]!} \approx \frac{(N_{NS})^{P-1}}{(P-1)!}$ | $\frac{(N_{NS})^{P-1}}{(P-1)!}\, e^{-(P-1)\varepsilon_{pd}^{NS}/k_BT}\, e^{-\varepsilon_{pd}^{S}/k_BT}$ |

**Figure 6.11 Physical Biology of the Cell, 2ed. (© Garland Science 2013)**

This is the total partition function

$$Z(P, N_{NS}) = \underbrace{Z_{NS}(P, N_{NS})}_{\text{no RNAP on promoter}} + \underbrace{Z_{NS}(P-1, N_{NS}) e^{-\beta\varepsilon_{pd}^{S}}}_{\text{one RNAP on promoter}}.$$

where:

$$Z_{NS}(P, N_{NS}) = \underbrace{\frac{N_{NS}!}{P!(N_{NS}-P)!}}_{\text{multiplicity}} \times \underbrace{e^{-\beta P\varepsilon_{pd}^{NS}}}_{\text{Boltzmann factor}}.$$

# Calculation scheme for $p_{bound}$

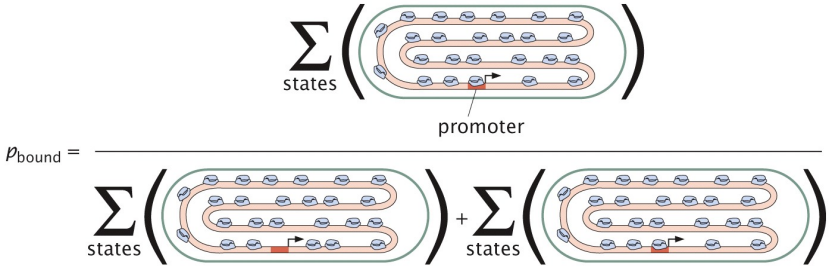



Figure 6.12 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

$$p_{bound} = \frac{\frac{N_{NS}!}{(P-1)!(N_{NS}-(P-1))!} e^{-\beta \varepsilon_{pd}^{S}} e^{-\beta(P-1)\varepsilon_{pd}^{NS}}}{\frac{N_{NS}!}{P!(N_{NS}-P)!} e^{-\beta P \varepsilon_{pd}^{NS}} + \frac{N_{NS}!}{(P-1)!(N_{NS}-(P-1))!} e^{-\beta \varepsilon_{pd}^{S}} e^{-\beta(P-1)\varepsilon_{pd}^{NS}}}.$$

$$p_{bound} = \frac{\frac{P}{N_{NS}} e^{-\beta \Delta \varepsilon_{pd}}}{1 + \frac{P}{N_{NS}} e^{-\beta \Delta \varepsilon_{pd}}} = \frac{1}{1 + \frac{N_{NS}}{P} e^{\beta \Delta \varepsilon_{pd}}},$$

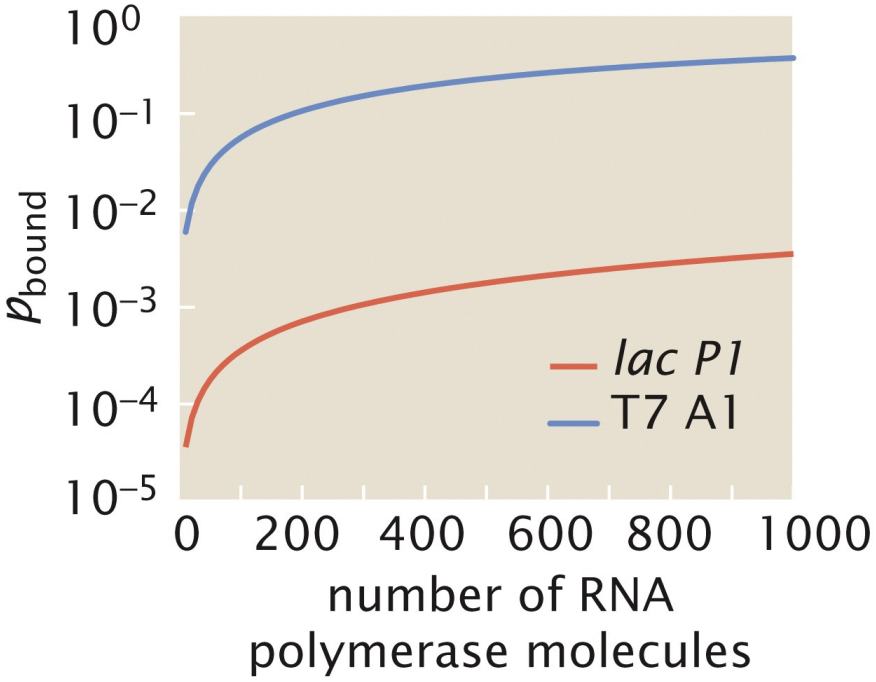



Figure 6.13 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

**Figure 6.13** Probability of promoter occupancy as a function of the number of RNA polymerase molecules. $p_{bound}$ is computed using values for the specific and nonspecific binding obtained *in vitro* and corresponding to the *lac* promoter (solid line), and the A1 promoter from the phage T7.

$$\Delta\varepsilon_{pd} = -2.9\, k_B T$$ E.Coli *lac*promoter

$$\Delta\varepsilon_{pd} = -8.1\, k_B T$$