Lecture of November 12: Chapter 7, Models of Ion Channels and Ligand Binding in the Gibb’s Ensemble

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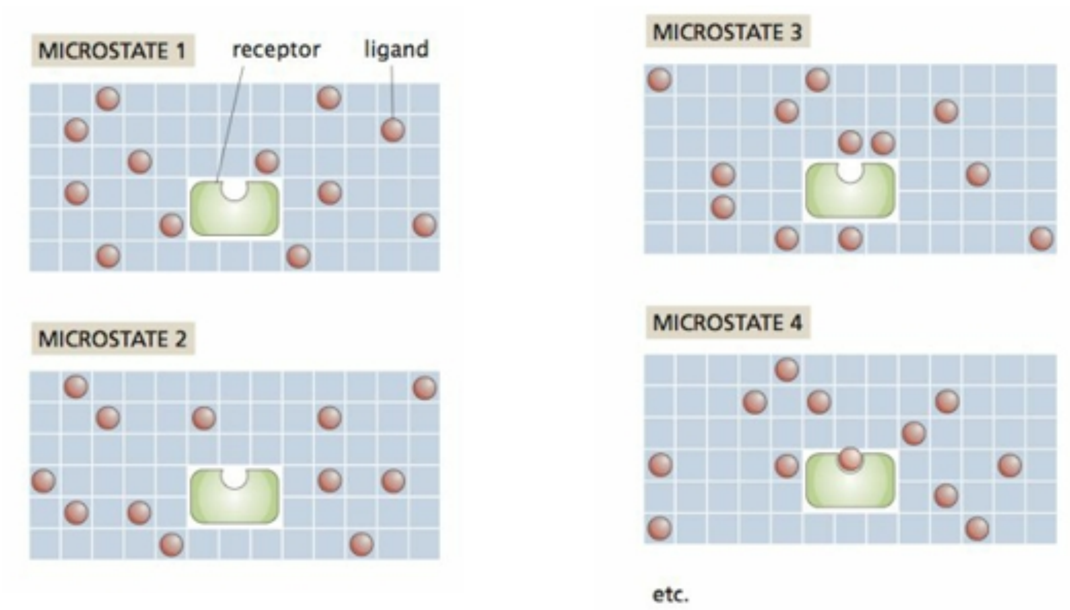
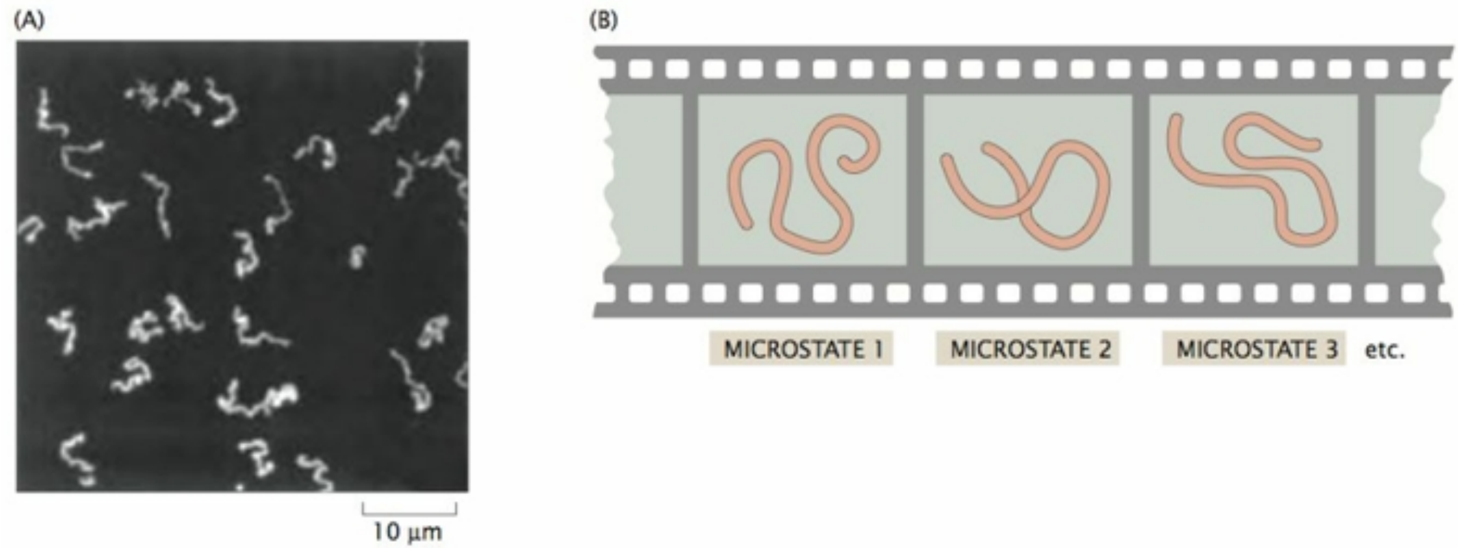
Questions on Lattice Model of Fig 6.1



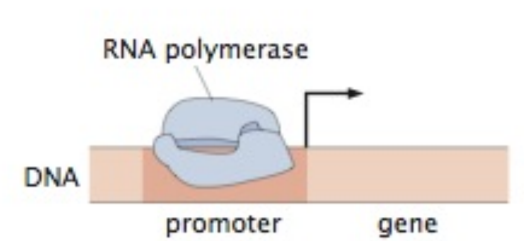
- Can more than one ligand occupy a lattice?
- On page 144 of textbook, it is assumed that the volume of the cubic lattice is 1 nm^3. Is this a reasonable size for the case where the ligand is a protein? What about an ion? What about for an E. Coli?

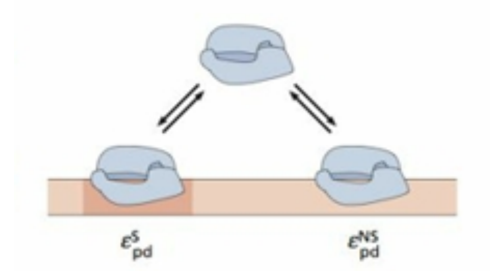
Microstates of a DNA

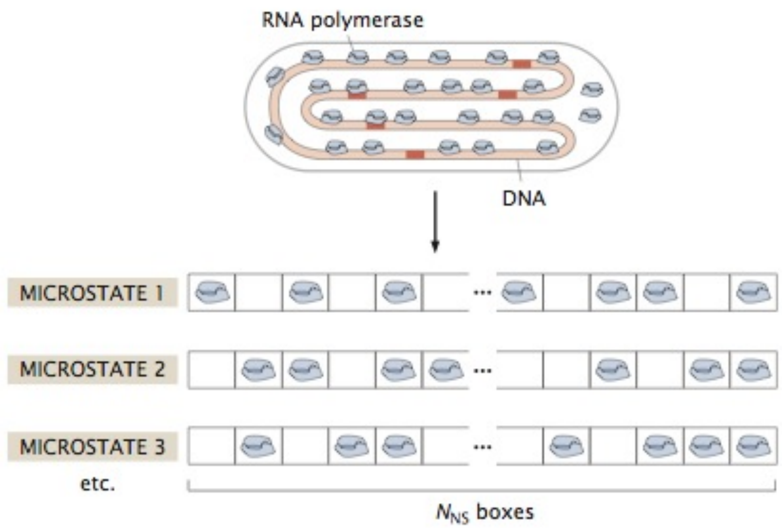


In the case above, what is a microstate? What is a multiplicity?

Binding of RNA polymerase to promoter

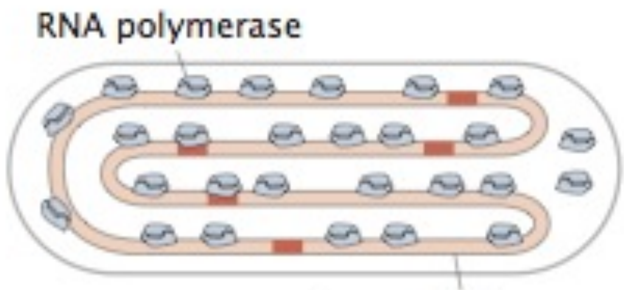


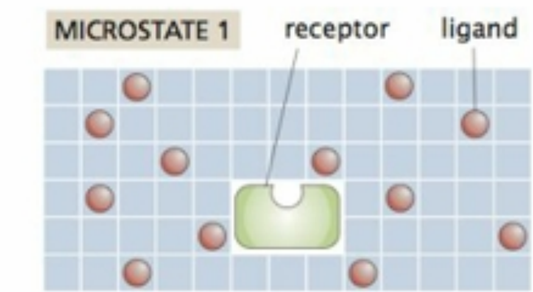




In vivo, are RNA Polymerase are almost always bound on DNA? What about in vitro?

Mathematical Analogy between Ligand-Receptor Model with Binding of RNA polymerase





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

$$p_{\mathrm{bound}} = \frac{(L/\Omega) e^{-\beta \Delta \varepsilon}}{1 + (L/\Omega) e^{-\beta \Delta \varepsilon}},$$

The Canonical (constant temperature) Ensemble: Statistical Weight

For a **microstate labeled** i of energy, E_i, the occupation probability is

$$P_i = \frac{e^{-\frac{E_i}{k_B T}}}{Z}$$

with

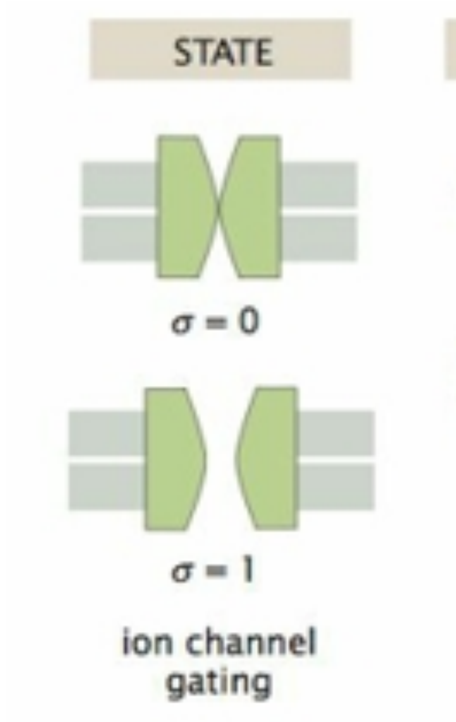
$$Z = \sum_{all\ microstates\ i} e^{-\frac{E_i}{k_B T}}$$

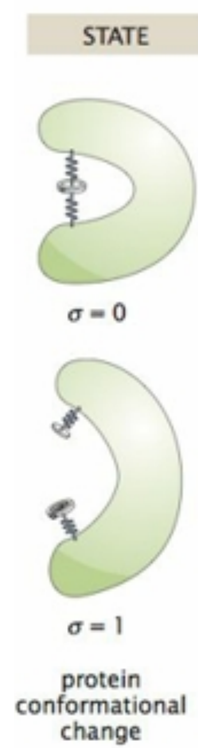
being the **partition function**.

$$e^{-\frac{E_i}{k_B T}}$$

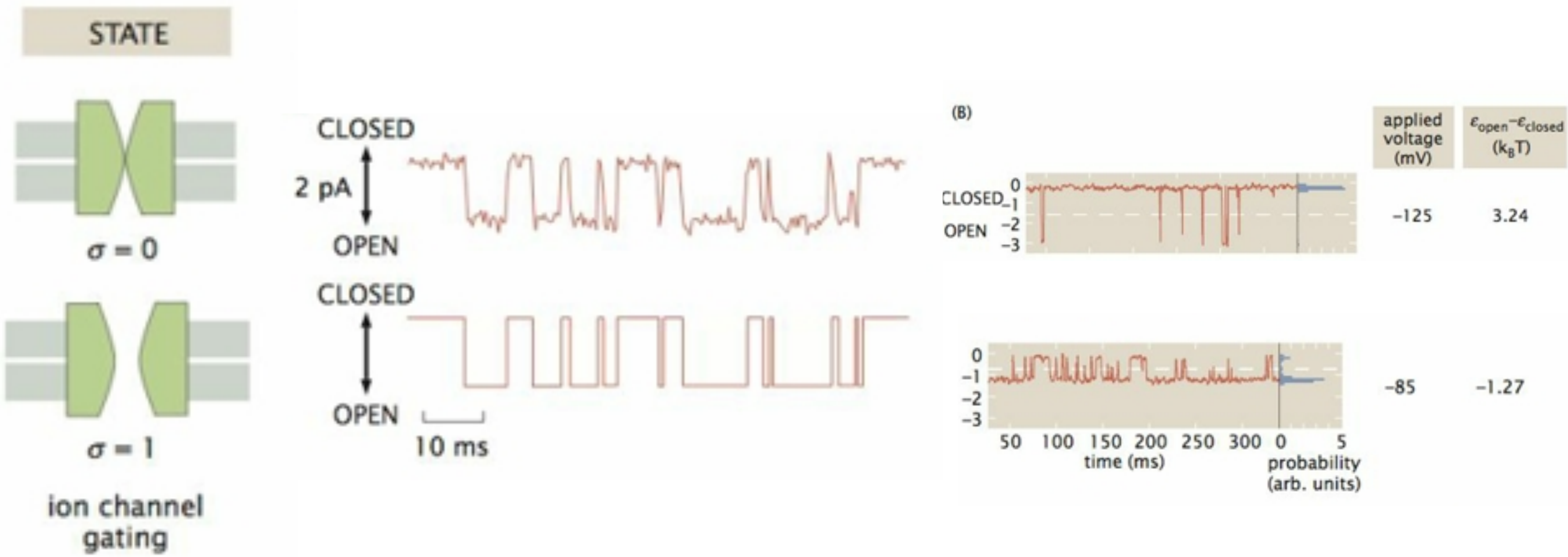
is also known as the **Boltzman Factor**.

Two More Models



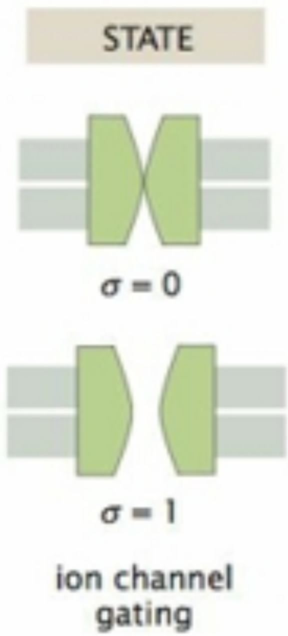


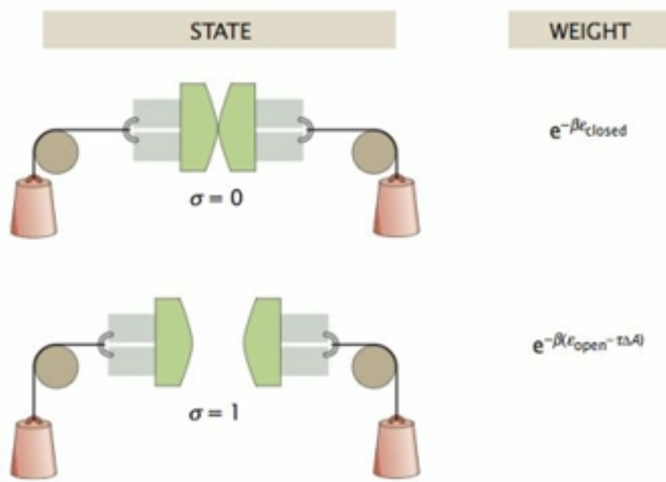
Ion-Channel Gating

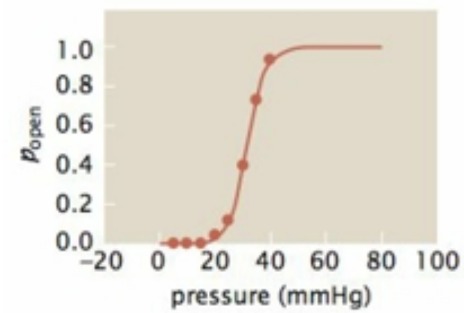


- **Gate** may **open** to reduce **Osmotic Pressure**
- **Two-State (open or closed) Probability**

Ion-Channel Gating



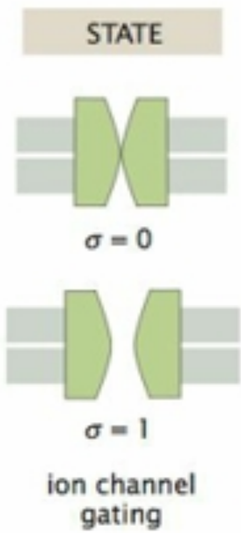


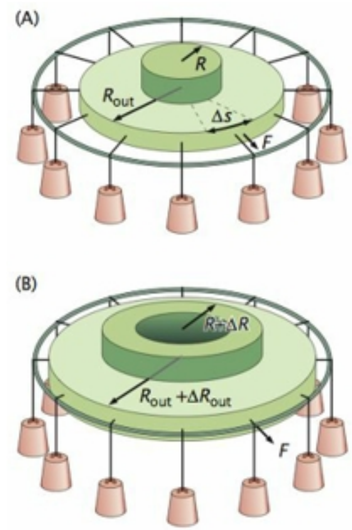


$$E(\sigma) = \sigma\,\varepsilon_{\text{open}} + (1-\sigma)\varepsilon_{\text{closed}} - \sigma\tau\Delta A.$$

- $-\sigma\tau\Delta A$ favors **Open State** in response to **external stress** such as Osmotic Pressure.
- τ is the surface tension in N/m

Ion-Channel Gating





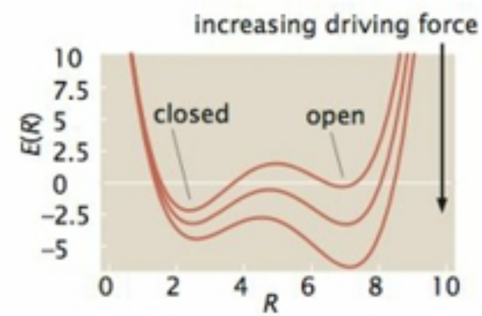
$$\Delta A = 2\pi R \Delta R.$$

$$\Delta G_{\text{tension}} = -\tau 2\pi R \Delta R.$$

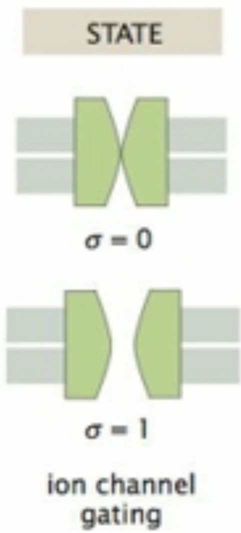
$$\Delta G_{\text{tension}} = -\underbrace{\tau \Delta s}_{\text{force on arc}} \times \underbrace{\frac{R}{R_{\text{out}}}\Delta R}_{\text{displacement of patch}} \times \underbrace{\frac{2\pi R_{\text{out}}}{\Delta s}}_{\text{no. of "patches"}}.$$

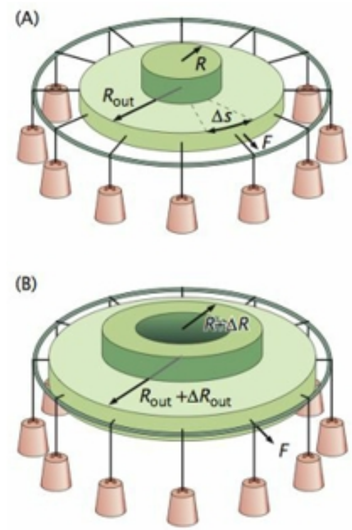
$$p_{\text{open}} = \frac{e^{-\beta(\varepsilon_{\text{open}} - \tau \Delta A)}}{e^{-\beta(\varepsilon_{\text{open}} - \tau \Delta A)} + e^{-\beta \varepsilon_{\text{closed}}}}.$$

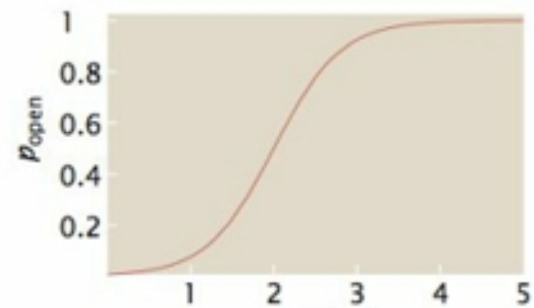
$$\langle \sigma \rangle = \sum_{\sigma=0}^{1} \sigma\, p(\sigma) = p(1) = p_{\text{open}}.$$



Ion-Channel Gating







probability as a function of driving force for gating. The plot shows $p_{\text{open}} = \langle\sigma\rangle$ as a function of the applied tension τ. The parameters used in the plot for a model mechanosensitive channel are $\Delta\varepsilon = -5\,k_B T$ and $\Delta A = 10\,\text{nm}^2$. The plot would have the same functional form if the driving force for gating were voltage rather than tension.

$$p_{\text{open}} = \frac{e^{-\beta(\varepsilon_{\text{open}} - \tau\Delta A)}}{e^{-\beta(\varepsilon_{\text{open}} - \tau\Delta A)} + e^{-\beta\varepsilon_{\text{closed}}}}.$$

$$\langle\sigma\rangle = \sum_{\sigma=0}^{1} \sigma\, p(\sigma) = p(1) = p_{\text{open}}.$$

Section 6.2.2: Solute Chemical Potential

Gibbs Free Energy of Solute (S) in Water (H_2O)

$$G_{tot}(T, p, N_{H_2O}, N_s) = N_{H_2O}\mu^0_{H_2O}(T, p) + N_s\varepsilon_s(T, p) + k_B T\left(N_s \ln\frac{N_s}{N_{H_2O}} - N_s\right). \quad (6.85)$$

Chemical Potential of Solute (S)

$$\mu_s = \partial G/\partial N_s, \qquad \mu_s = \varepsilon_s + k_B T \ln\frac{c}{c_0}. \quad (6.86)$$

Below is the expression of a **general chemical potential** of i^{th} solute, μ_i with reference (0) chemical potential, μ_{i0}, and solute concentration, c, and reference concentration c_0.

$$\mu_i = \mu_{i0} + k_B T \ln\frac{c_i}{c_{i0}},$$

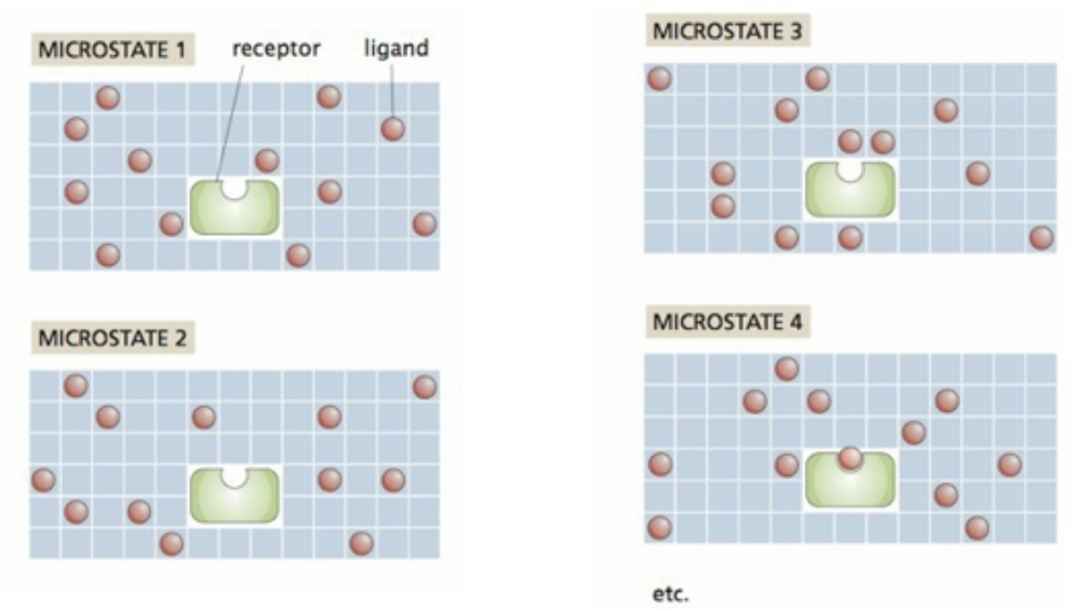
The Gibbs Distribution

$$p(E_s^{(i)}, N_s^{(i)}) = \frac{e^{-\beta(E_s^{(i)} - \mu N_s^{(i)})}}{\mathcal{Z}}, \quad (7.15)$$

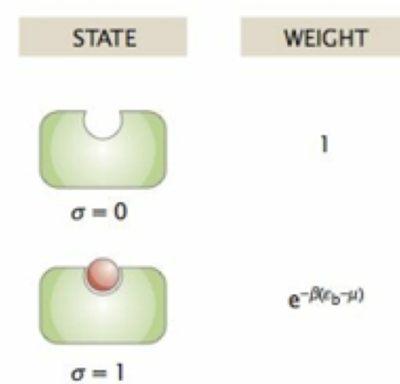
$$\mathcal{Z} = \sum_i e^{-\beta(E_s^{(i)} - N_s^{(i)}\mu)}. \quad (7.16)$$

$$\langle N \rangle = \frac{1}{\mathcal{Z}} \sum_i N_i e^{-\beta(E_i - N_i\mu)}, \quad (7.18)$$

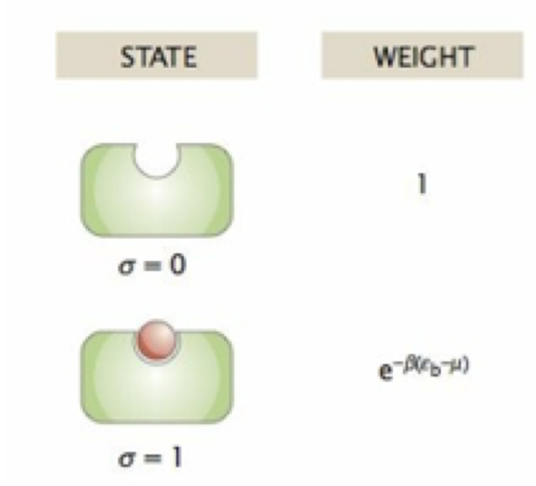
Ligand-Receptor Model in the Gibb's Ensemble



- Ligand binding to receptor is considered to be a chemical process that alter the Gibbs Free Energy by the chemical potential μ.
- The State and weight change to Figure 7.10 on the **right**



Ligand-Receptor Model in the Gibb's Ensemble



$$\mathcal{Z} = \sum_{\text{states}} e^{-\beta(E_{\text{state}} - N_{\text{state}}\mu)},$$

$$\mathcal{Z} = \sum_{\sigma=0}^{1} e^{-\beta(\varepsilon_b \sigma - \mu\sigma)}.$$

$$\mathcal{Z} = 1 + e^{-\beta(\varepsilon_b - \mu)}.$$

Normalized Average Number of Bound Ligand: $$\langle N \rangle = \frac{e^{-\beta(\varepsilon_b - \mu)}}{1 + e^{-\beta(\varepsilon_b - \mu)}}.$$

$$0 < \langle N \rangle < 1$$

$$\mu = \mu_0 + k_B T \ln(c/c_0) \longrightarrow \langle N \rangle = \frac{(c/c_0)e^{-\beta\Delta\varepsilon}}{1 + (c/c_0)e^{-\beta\Delta\varepsilon}},$$