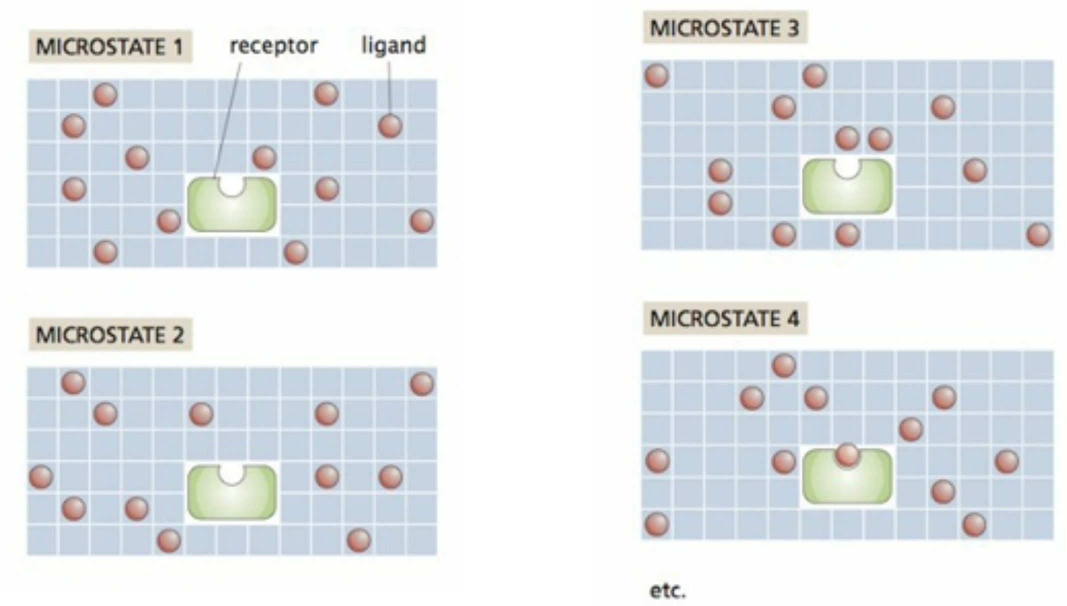
Lecture of November 5 and 7, 2018
Chapter 5 and 6: Models of Biophysical Processes

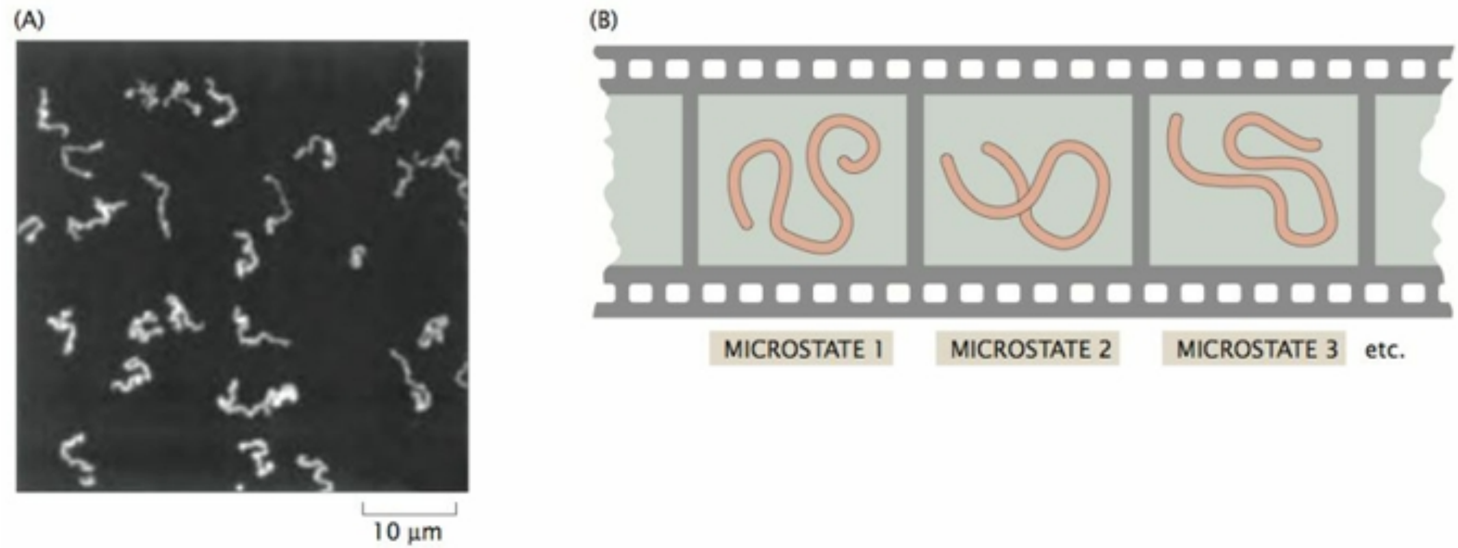
Apichart Linhananta
Department of Physics
Lakehead University

Microstates: Lattice Model of Fig 6.1



- A Microstate is a particular realization of the microscopic arrangement of the constituents for the problem of interest.
- In the above **lattice model** of **Ligand Receptor Binding,** the **ligands** are **spheres** that can occupy a **fix lattice positions** depicted as **squares**. There is **one receptor** (the green object) with a binding site for **one ligand**.
- In the 4 example microstates above, only microstate 4 has a bounded ligand.

Microstates of a DNA



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

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

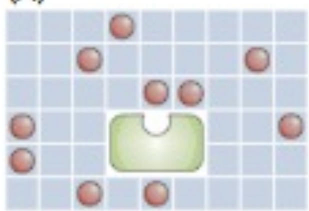
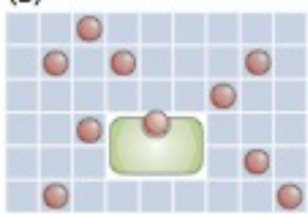
being the **partition function**.

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

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

Example: Ion Channel

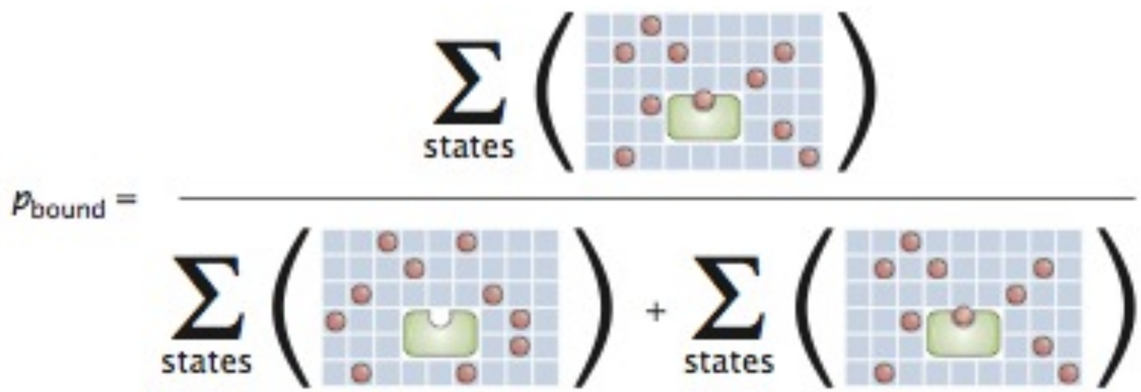
Lattice Model of Ligand-Receptor

STATE	ENERGY	MULTIPLICITY	WEIGHT
(A) 	$L\varepsilon_{sol}$	$\frac{\Omega!}{L!(\Omega-L)!} \approx \frac{\Omega^L}{L!}$	$\frac{\Omega^L}{L!} e^{-\beta L\varepsilon_{sol}}$
(B) 	$(L-1)\varepsilon_{sol} + \varepsilon_b$	$\frac{\Omega!}{(L-1)!(\Omega-L+1)!} \approx \frac{\Omega^{L-1}}{(L-1)!}$	$\frac{\Omega^{L-1}}{(L-1)!} e^{-\beta[(L-1)\varepsilon_{sol} + \varepsilon_b]}$

- **Microstates A:** No bound ligand
- **Microstates B:** One bound ligand
- Note that I used **microstates** since there are many microstates with **no bound ligand**, and many with a bound ligand
- The **multiplicity** is the number of **microstates** with the same **energy**

Probability of Bound State

$$\text{weight when receptor occupied} = \underbrace{e^{-\beta\varepsilon_b}}_{\text{bound ligand}} \times \underbrace{\sum_{\text{solution}} e^{-\beta(L-1)\varepsilon_{\text{sol}}}}_{\text{free ligands}}, \tag{6.10}$$



The denominator is the partition function, Z

The partition function, Z, of the Lattice Model of Ligand-Receptor

$$Z(L,\Omega) = \underbrace{\sum_{\text{solution}} e^{-\beta L \varepsilon_{\text{sol}}}}_{\text{none bound}} + \underbrace{e^{-\beta \varepsilon_{\text{b}}} \sum_{\text{solution}} e^{-\beta (L-1) \varepsilon_{\text{sol}}}}_{\text{ligand bound}}. \tag{6.12}$$

$$Z(L,\Omega) = e^{-\beta L \varepsilon_{\text{sol}}} \frac{\Omega!}{L!(\Omega - L)!} + e^{-\beta \varepsilon_{\text{b}}} e^{-\beta (L-1) \varepsilon_{\text{sol}}} \frac{\Omega!}{(L-1)![\Omega - (L-1)]!}. \tag{6.14}$$

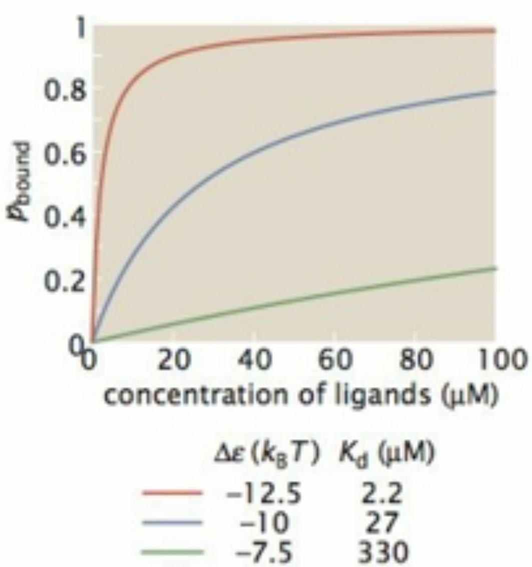
Probability of the bound state of the Lattice Model of Ligand-Receptor

$$p_{\mathrm{bound}} = \frac{e^{-\beta\varepsilon_b}\frac{\Omega^{L-1}}{(L-1)!}e^{-\beta(L-1)\varepsilon_{\mathrm{sol}}}}{\frac{\Omega^L}{L!}e^{-\beta L\varepsilon_{\mathrm{sol}}} + e^{-\beta\varepsilon_b}\frac{\Omega^{L-1}}{(L-1)!}e^{-\beta(L-1)\varepsilon_{\mathrm{sol}}}}. \tag{6.17}$$

$$p_{\mathrm{bound}} = \frac{(L/\Omega)e^{-\beta\Delta\varepsilon}}{1+(L/\Omega)e^{-\beta\Delta\varepsilon}}, \tag{6.18}$$

Probability of the bound state of the Lattice Model of Ligand-Receptor

$$p_{\mathrm{bound}} = \frac{(c/c_0)\mathrm{e}^{-\beta\Delta\varepsilon}}{1+(c/c_0)\mathrm{e}^{-\beta\Delta\varepsilon}}.$$



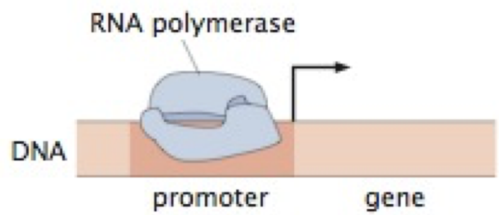
- K_D is the dissociation constant
- $c_0 = \frac{1}{V_{box}}$ is a **reference concentration**, V_{box} is the volume of **one lattice site**.
- Textbook assumes $V_{box} = 1nm^3$, which gives $c_0 \sim 0.6M$

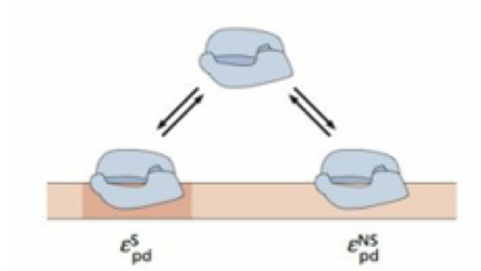
Probability of the bound state of the Lattice Model of Ligand-Receptor

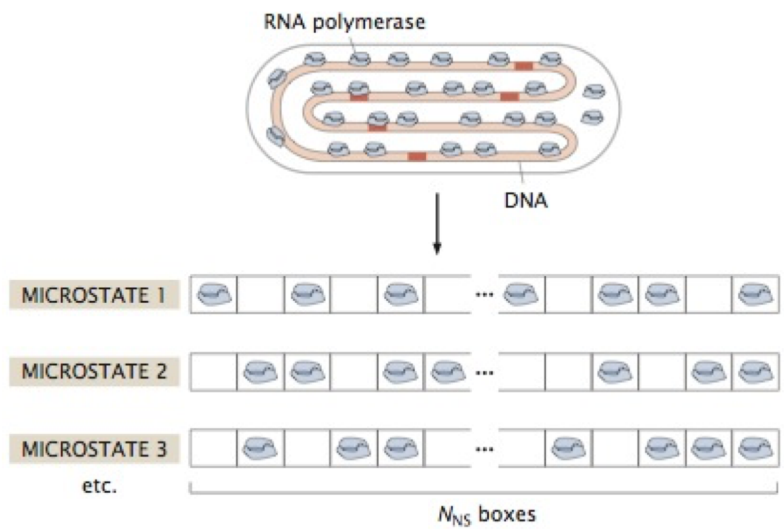
Issues:

- **Indistinguishable** Multiplicity, $\frac{\Omega!}{L!(\Omega-L)!}$
- Or **Distinguishable** Multiplicity, $\frac{\Omega!}{(\Omega-L)!}$
- Problem 6.4 and 6.5 in textbook

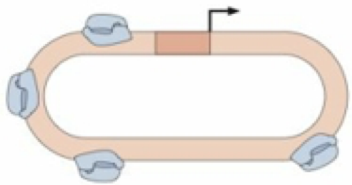
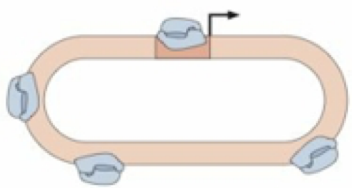
Binding of RNA polymerase to promoter



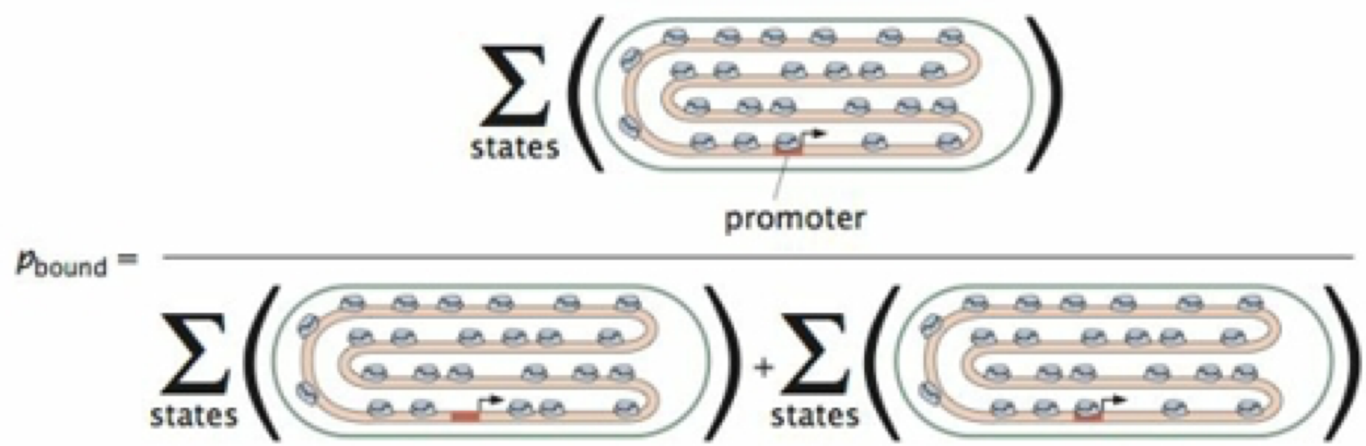




Binding of RNA polymerase to promoter

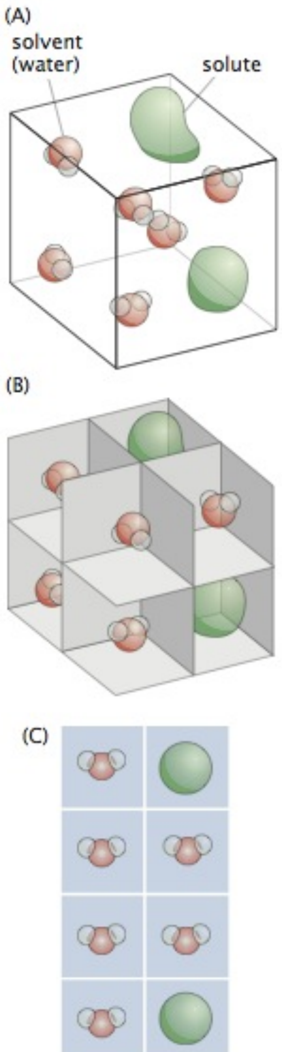
STATE	ENERGY	MULTIPLICITY	WEIGHT (MULTIPLICITY x BOLTZMANN WEIGHT)
	$P\varepsilon_{pd}^{NS}$	$\frac{N_{NS}!}{P!\,(N_{NS}-P)!} \approx \frac{(N_{NS})^P}{P!}$	$\frac{(N_{NS})^P}{P!}\, e^{-P\varepsilon_{pd}^{NS}/k_BT}$
	$(P-1)\varepsilon_{pd}^{NS} + \varepsilon_{pd}^{S}$	$\frac{N_{NS}!}{(P-1)!\,[N_{NS}-(P-1)]!}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

Binding of RNA polymerase to promoter



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

Lattice Model of Solutes in Water H_2O



$$\mu_{\text{solute}} = \left(\frac{\partial G_{\text{tot}}}{\partial N_{\text{s}}}\right)_{T,p}.$$

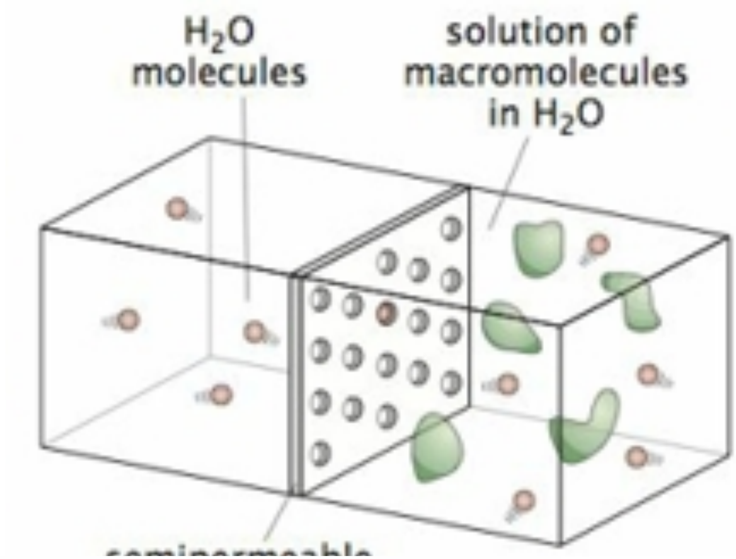
$$\mu_{\text{solute}} = G_{\text{tot}}(N_{\text{s}}+1) - G_{\text{tot}}(N_{\text{s}}).$$

$$G_{\text{tot}} = \underbrace{N_{\text{H}_2\text{O}}\mu^0_{\text{H}_2\text{O}}}_{\text{water free energy}} + \underbrace{N_{\text{s}}\varepsilon_{\text{s}}}_{\text{solute energy}} - \underbrace{TS_{\text{mix}}}_{\text{mixing entropy}}.$$

$$S_{\text{mix}} = -k_{\text{B}}\left(N_{\text{H}_2\text{O}}\ln\frac{N_{\text{H}_2\text{O}}}{N_{\text{H}_2\text{O}}+N_{\text{s}}} + N_{\text{s}}\ln\frac{N_{\text{s}}}{N_{\text{H}_2\text{O}}+N_{\text{s}}}\right).$$

$$\mu_{\text{s}} = \varepsilon_{\text{s}} + k_{\text{B}}T\ln\frac{c}{c_0}.$$

Osmotic Pressure: Derivation of **van**'t **Hoff's** factor



$$\underbrace{\mu_{\mathrm{H_2O}^0}(T, p_1)}_{\text{solute-free side}} = \underbrace{\mu^0_{\mathrm{H_2O}}(T, p_2) - \frac{N_\mathrm{s}}{N_{\mathrm{H_2O}}} k_\mathrm{B} T}_{\text{side with solutes}} .$$

$$p_2 - p_1 = \frac{N_\mathrm{s}}{V} k_\mathrm{B} T,$$

$$\mu^0_{\mathrm{H_2O}}(T, p_2) \approx \mu^0_{\mathrm{H_2O}}(T, p_1) + \left(\frac{\partial \mu^0_{\mathrm{H_2O}}}{\partial p}\right)(p_2 - p_1).$$

Van't Hoff factor for **osmotic pressure**, valid for **dilute solution**