Lecture 6:
Entropy Rules! (contd.)

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Boltzmann distribution (by counting: Textbook, pages 230-231)

Information theory:
based on the constraints (for example the total energy) ***derive the least biased probability distribution***

Shannon entropy:

$$S(p_1, p_2, p_3 ..., p_N) = -\sum_{i=1}^{N} p_i \ln p_i$$

where p_i is the probability of the system to be in the i-th microstate.

For example, if nothing is known about the system except that there is N microstates, then for all $p_i = 1/N$ and $S = \ln N$ (the maximal value).

How do we formally derive this result?

Maximize Shannon entropy S' using Lagrange multiplier method for each constraint:

$$S' = -\sum_{i=1}^{N} p_i \ln p_i - \lambda \left[\sum_{i=1}^{N} p_i - 1 \right]$$

Maximization equations:

$$\partial S'/\partial\lambda = 0 \quad \rightarrow \quad -\sum_{i=1}^{N} p_i + 1 = 0$$

$$\partial S'/\partial p_i = 0 \quad \rightarrow \quad -\ln p_i - 1 - \lambda = 0$$

$$p_i = \exp(-1-\lambda)$$

Note that the probabilities p_i do not depend on i!

$$\sum_{i=1}^{N} p_i = 1 \rightarrow \sum_{i=1}^{N} \exp(-1-\lambda) = 1 \rightarrow \exp(-1-\lambda) = 1/N$$

$$p_i = 1/N$$

Boltzmann distribution is a maximum entropy distribution with a fixed average energy:

$$S' = -\sum_i p_i \ln p_i - \lambda[\sum_i p_i - 1] - \beta[\sum_i p_i E_i - \langle E\rangle]$$

$$-\ln p_i - 1 - \lambda - \beta E_i = 0 \rightarrow p_i = \exp(-1-\lambda)\ \exp(-\beta E_i)$$

$$\sum_i p_i = 1 \rightarrow \exp(1+\lambda) = \sum_i \exp(-\beta E_i) = Z$$

$$p_i = \exp(-\beta E_i) \,/\, \sum_i \exp(-\beta E_i)$$

Ideal gas approximation: the interaction range is small in comparison to the mean spacing between molecules

For a system with N independent variables $(x_1, x_2, \ldots x_N)$ **the probability distribution can be factorized:**

$$P(x_1, x_2, \ldots x_N) = P(x_1)\ P(x_2) \ldots P(x_N)$$

– uniform spatial distribution of ideal gas molecules.

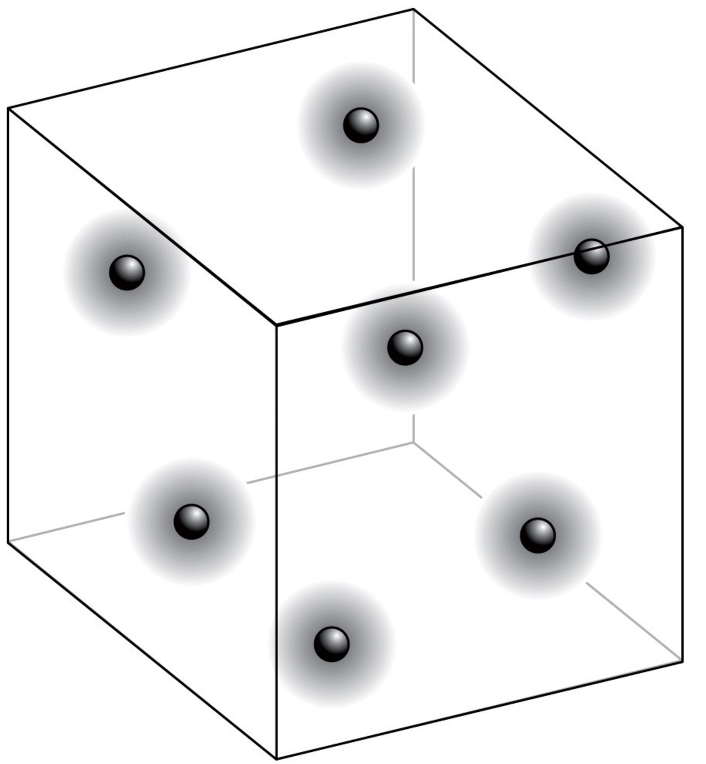


Figure 6.19 Physical Biology of the Cell (© Garland Science 2009)

Microscopic state of the system is described by (x, p_x) **so the key information that we need to derive is** $P(p_x)$ **knowing the kinetic energy of** $E = p_x^2/(2m)$.

Probability distribution for a system with average energy is:

$$P(p_x) = \frac{\exp[-\beta p_x^2/(2m)]}{\sum_{states} \exp[-\beta p_x^2/(2m)]}$$

Instead of a sum, we use an integral over a continuous variable p_x:

$$\sum_{states} \rightarrow \int_{-\infty}^{\infty} dp_x$$

where we will use the integral:

$$\int_{-\infty}^{\infty} \exp(-\alpha p_x^2)\, dp_x = \sqrt{\pi/\alpha}$$

According to the equipartition theorem, each degree of freedom is associated with :

$$\langle E \rangle = \frac{1}{2} k_B T$$

Calculate ⟨E⟩ using the Boltzmann distribution:

$$Z = \int_{-\infty}^{\infty} \exp[-\beta p_x^2/(2m)]\, dp_x = \sqrt{2m\pi/\beta}$$

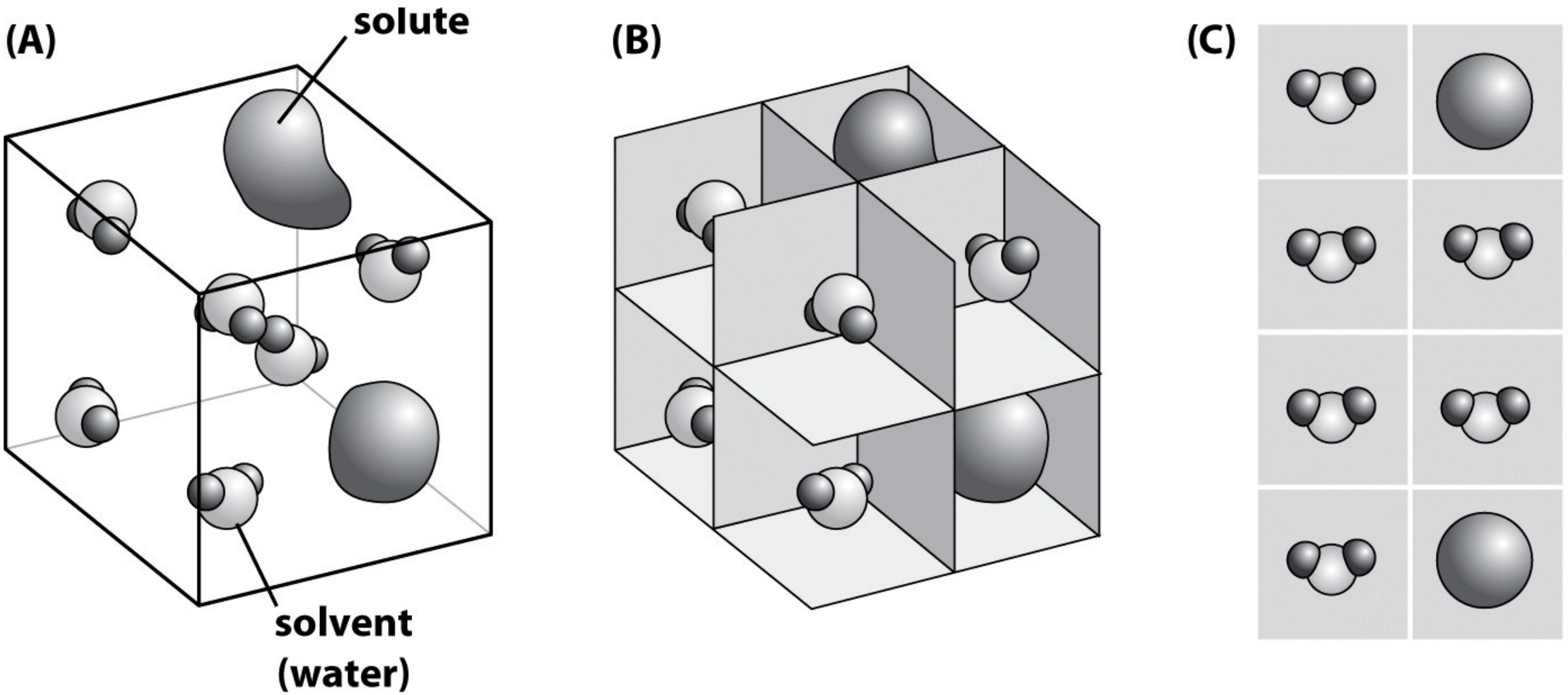
$$\langle E \rangle = \int_{-\infty}^{\infty} p_x^2/(2m) \exp[-\beta p_x^2/(2m)]\, dp_x$$

We use the following trick:

$$\langle E \rangle = - Z^{-1} \, \partial Z/\partial \beta = \frac{1}{2} \beta^{-1}$$

so we showed that the Lagrange multiplier $\beta = (k_B T)^{-1}$ **.**

Free energy and chemical potential of a *dilute solution*: Application of a lattice model (and ideal gas approx.)



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Configurational entropy of N objects placed into W available spots:

$$W(N,\Omega) = \frac{\Omega!}{N!\,(\Omega - N)!} \qquad S = k_B \ln W$$

How to calculate the chemical potential of a dilute solutions?

$$\mu_{SOLUTE} = (\partial G_{TOT} / \partial N_S)_{T,p}$$

$$G_{TOT} = N_W\, \mu^0_W + N_S\, \varepsilon_S - T\, S_{MIX}$$

water G + solute energy + mixing entropy contribution

Mixing entropy contribution:

-independent solute molecules (ideal gas)

-lattice model: $N_W + N_S$ is a total number of lattice sites

$$W(N_W,N_S) = (N_W + N_S)! / (N_W!\, N_S!)$$

$$S = k_B \ln W = \ln[(N_W + N_S)! / (N_W!\, N_S!)] \approx$$

$$-\, k_B \{N_W \ln[N_W/(N_W + N_S)] + N_S \ln[N_S/(N_W + N_S)]\} =$$

$$-\, k_B [N_W \ln(1 - N_S/N_W) + N_S \ln(N_S/N_W)]$$

Taking into account the Taylor expansion of ln(1+x) ≈ x, we get:

$$S_{MX} = -\, k_B [N_S \ln(N_S/N_W) - N_S]$$

$$G_{TOT}(T,p,N_W,N_S) = N_W \mu_W^0 + N_S \varepsilon_S(T,p) + k_B T(N_S \ln(N_S/N_W) - N_S)$$

$$\mu_S(T,p) = \varepsilon_S(T,p) + k_B T \ln(c/c_0)$$

or in a general form expressed in concentration c=N/V:

$$\mu_i = \mu_{i0} + k_B T \ln(c_i/c_{i0})$$

Osmotic pressure Is an Entropic Effect

- consider a cell in an aqueous environment exchanging material with a solution (intake of food, excretion of waste)

- chemical potential difference proportional to ΔG:

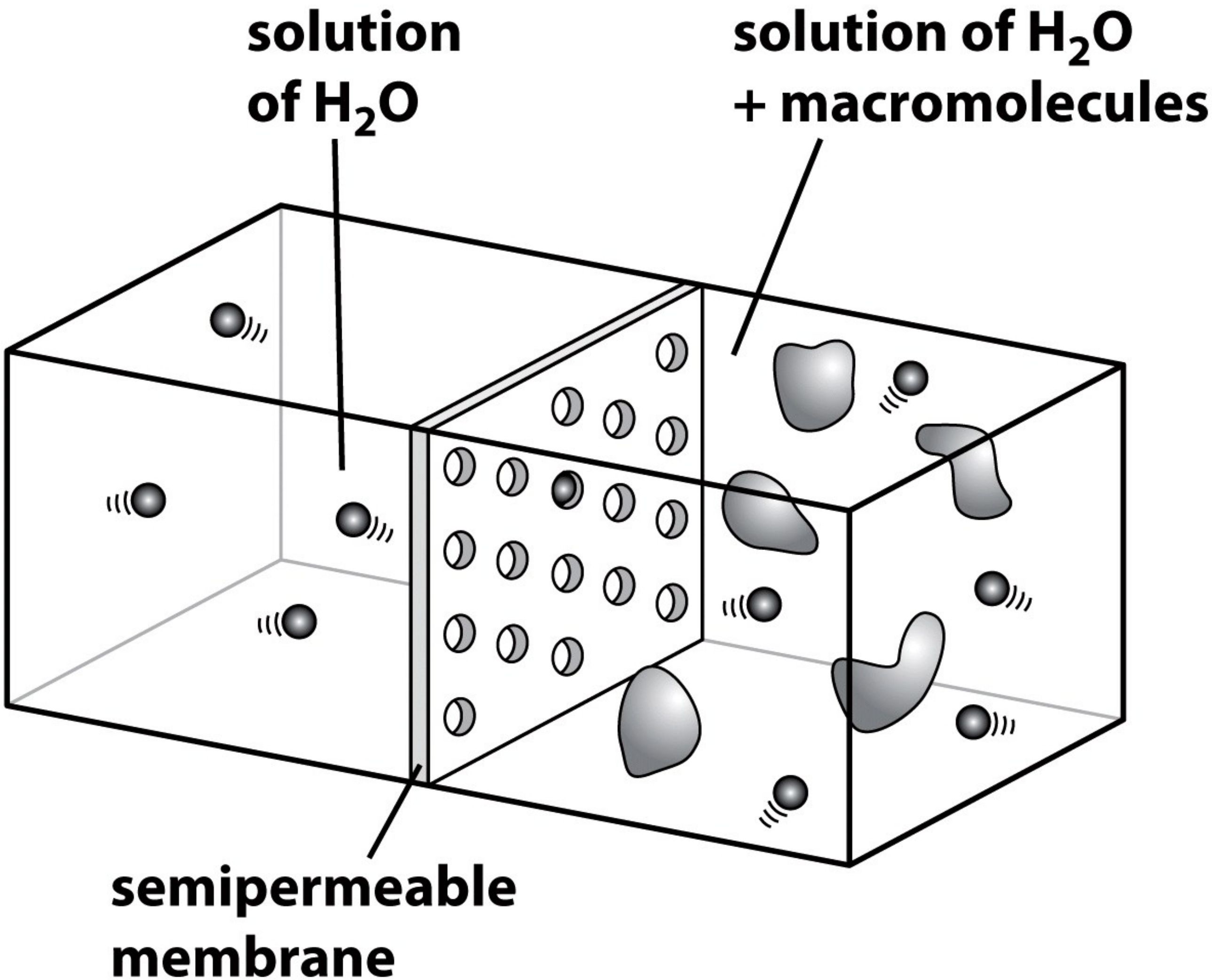
$$\Delta G = (\mu_1 - \mu_2)\, dN \leq 0 \text{ (spontaneous)}$$

- cell with a crowded environment of biomolecules: tendency of almost all components to move out causes a mechanical pressure called *osmotic pressure*

- lipid membranes with ion channels to regulate ion concentration

- calculate osmotic pressure due to a dilute solution of N_S molecules

Osmotic pressure on a semipermeable membrane, which only allows water molecules through



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$$\mu_W(T,p) = (\partial G_{TOT} / \partial N_W)_{T,p} =$$

$$\mu_W^0(T,p) - k_B T \, N_S/N_W$$

For both sides of the membrane in equilibrium:

$$\mu_W^0(T,p_1) = \mu_W^0(T,p_2) - k_B T \, N_S/N_W$$

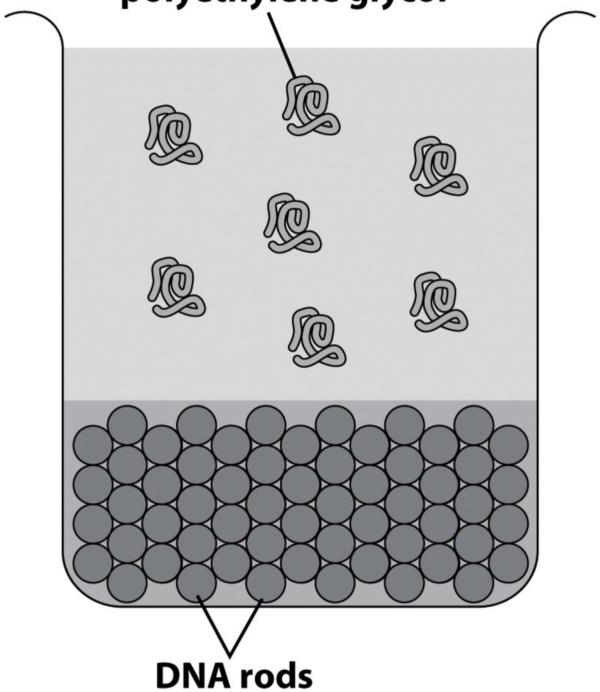
Expand the chemical potential at p_2 around the p_1 value:

$$\mu_W^0(T,p_2) \approx \mu_W^0(T,p_1) + (\partial \mu_W^0/\partial p)\,(p_2 - p_1)$$

and consider that $(\partial \mu_W^0/\partial p) = v = N_W/V$ is volume per water molecule so that

$$(p_2 - p_1) = k_B T \, N_S/V$$

Measuring interstrand interactions in DNA using osmotic pressure



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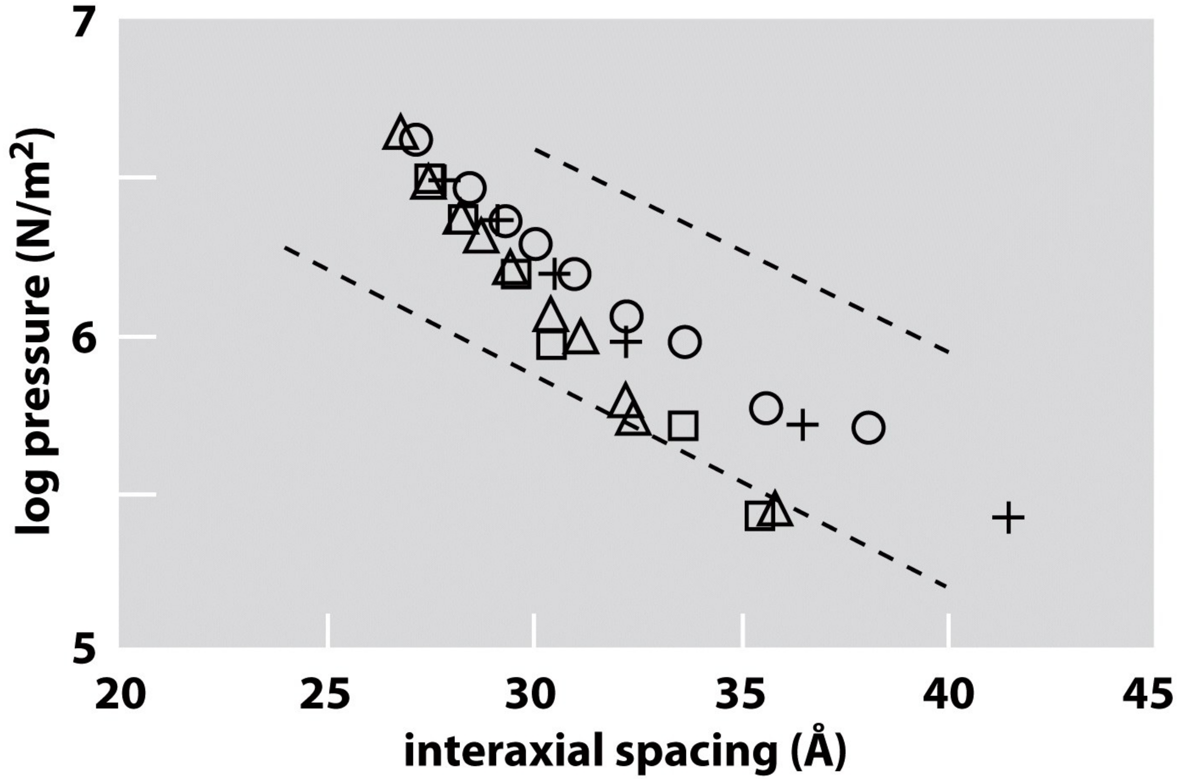

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pressure: $p(d_s) = F_0 \exp(-d_s/c)$

d_s … **interstrand spacing;** F_0 **depends on the ionic solution**

Law of Mass Action and Equilibrium Constants (Chemical Reactions)

- chemical equilibrium between A, B and their complex AB:

$$A + B \leftrightarrow AB$$

- final equilibrium independent of whether we start with only A and B, or with a high concentration of AB and no A or B

- N_A, N_B, N_{AB} … number of A, B, and AB molecules
- In equilibrium: $dG = 0$

$$0 = (\partial G/\partial N_A)\, dN_A + (\partial G/\partial N_B)\, dN_B + (\partial G/\partial N_{AB})\, dN_{AB}$$

- A more convenient and general expression:

$$\sum_{i=1}^{N} \mu_i \, dN_i = 0$$

Stoichiometric coefficients for each of the reactants are defined as:

$$\nu_i = \pm 1$$

depending on whether the number of particles of the i-th type increases or decreases during the reaction:

$$\sum_{i=1}^{N} \mu_i \nu_i = 0$$

$$\sum_{i=1}^{N} \mu_{i0} \nu_i = -k_B T \sum_{i=1}^{N} \ln(c_i/c_{i0})^{\nu i}$$

or

$$-\beta \sum_{i=1}^{N} \mu_{i0} \nu_i = \ln[\prod_{i=1}^{N} (c_i/c_{i0})^{\nu i}]$$

or

$$\prod_{i=1}^{N} c_i^{\nu i} = (\prod_{i=1}^{N} c_{i0}^{\nu i}) \exp(-\beta \sum_{i=1}^{N} \mu_{i0} \nu_i)$$

where we define *the equilibrium constant* K_{eq}:

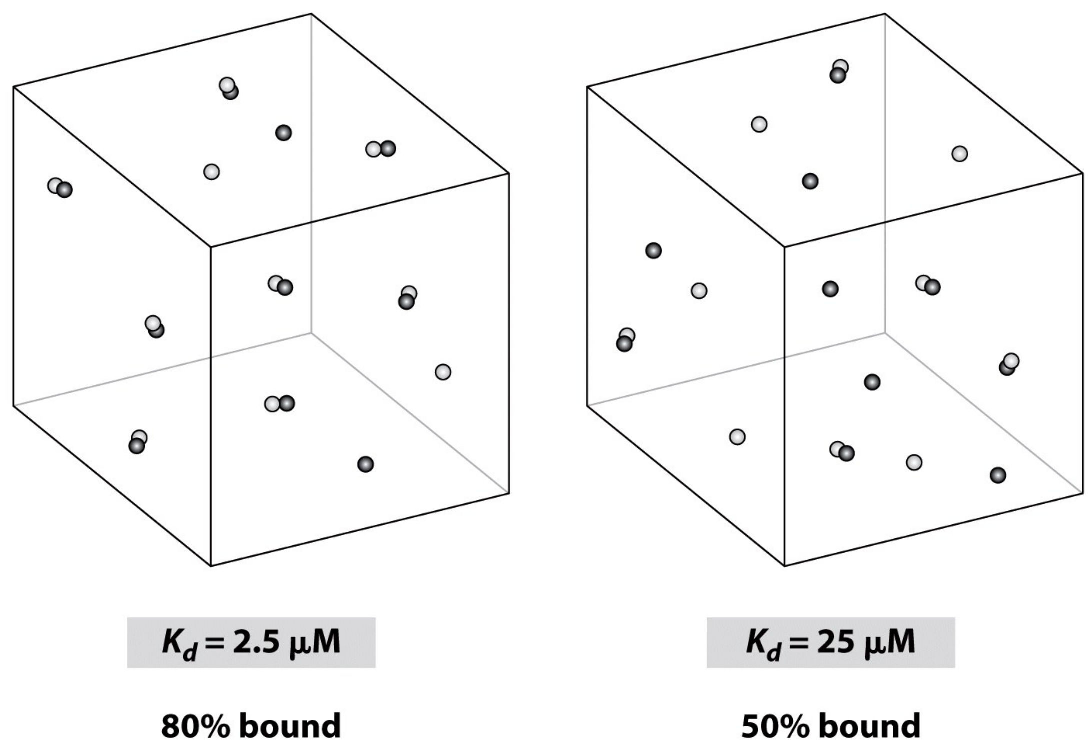
$$K_{eq} = (\prod_{i=1}^{N} c_{i0}^{\nu i}) \exp(-\beta \sum_{i=1}^{N} \mu_{i0} \nu_i)$$

$K_d = 1/K_{eq}$ … dissociation constant

In our case of the reaction $A + B \leftrightarrow AB$, we can express K_d as:

$$K_d = \prod_{i=1}^{N} c_i^{-\nu_i} = c_A \, c_B / c_{AB}$$

Example: total concentration: 50 μM



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Application to Ligand-Receptor Binding:

$$L + R \leftrightarrow LR$$

$$K_d = [L][R]/[LR] \text{ or } [LR] = [L]\,[R]/K_d$$

Binding probability:

$$p_{bound} = \frac{[LR]}{[LR] + [R]} = \frac{[L]/K_d}{1 + [L]/K_d}$$

A natural interpretation of K_d: K_d is the concentration at which the receptor has a probability of ½ of being occupied by a ligand. Based on out prior result, we can express it in terms of lattice model parameters as: $K_d = \nu^{-1}\ \exp(\beta\Delta\varepsilon)$

Important: K_d depends on the concentration of *free* ligands not their *total* concentration!

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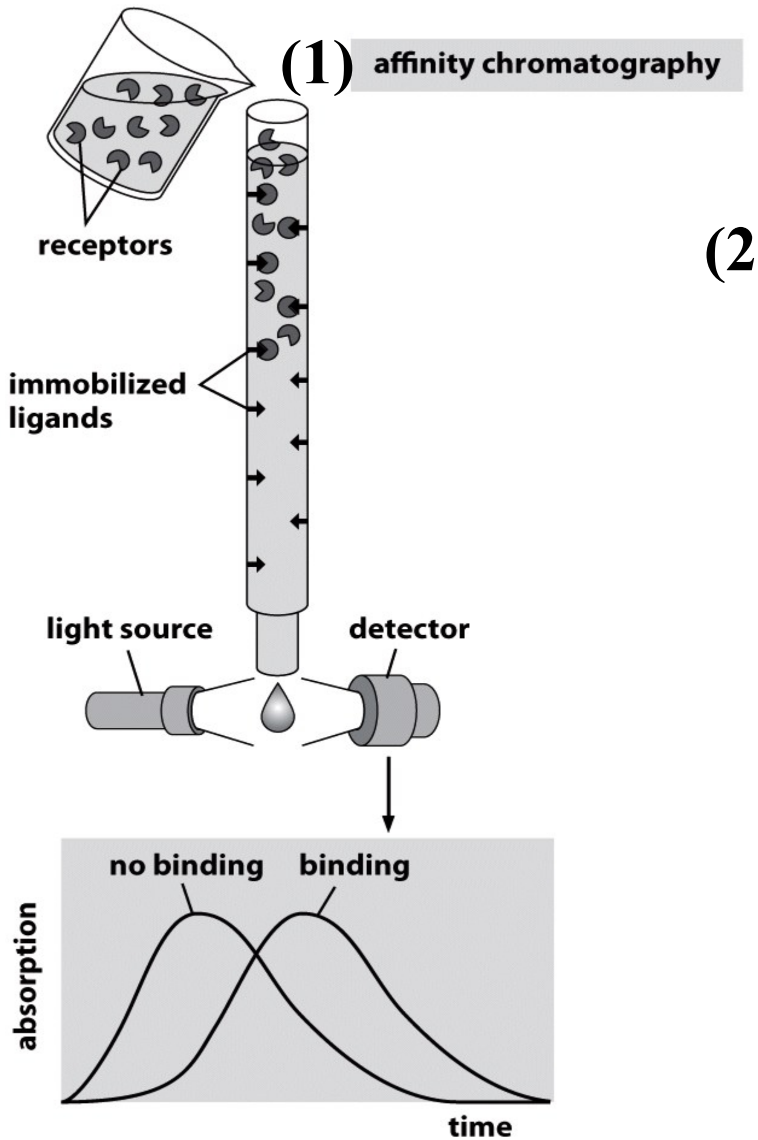

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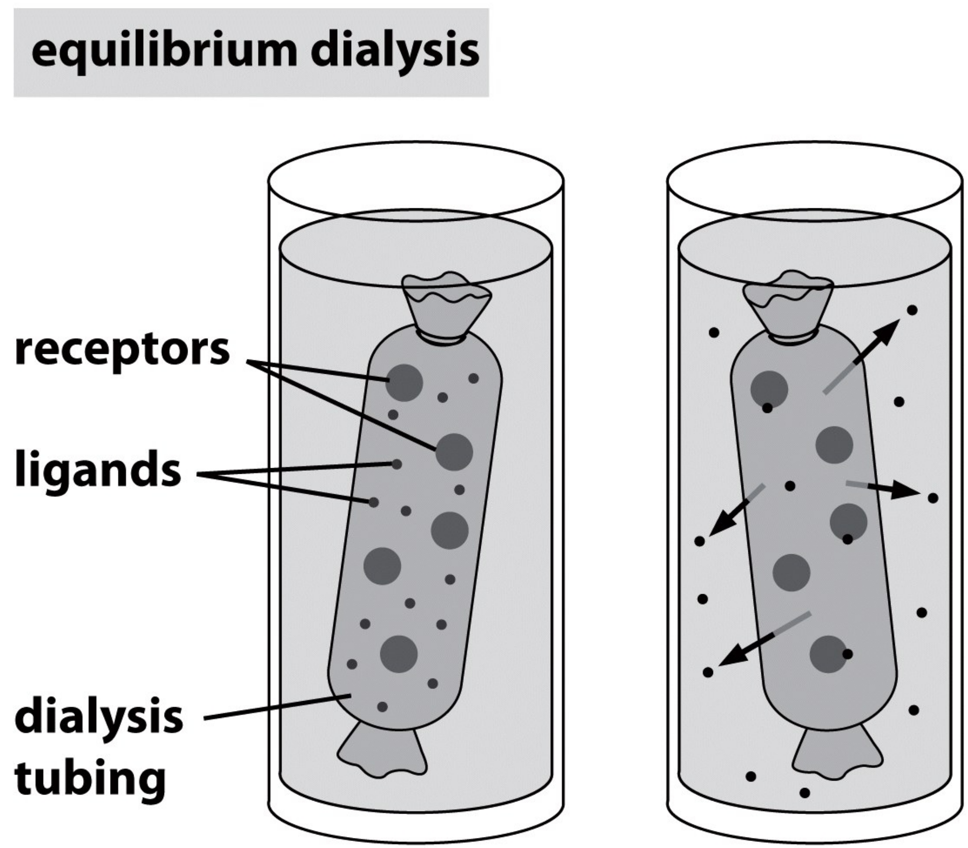

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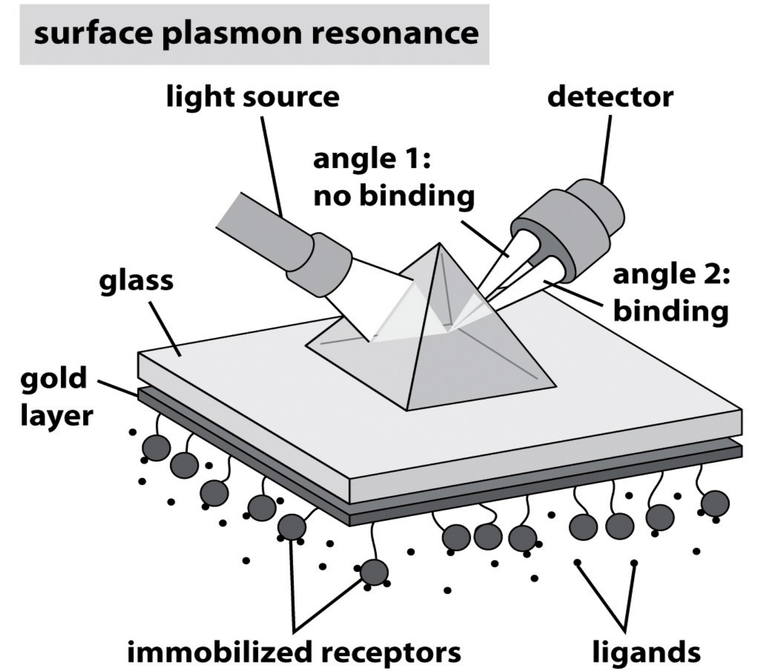

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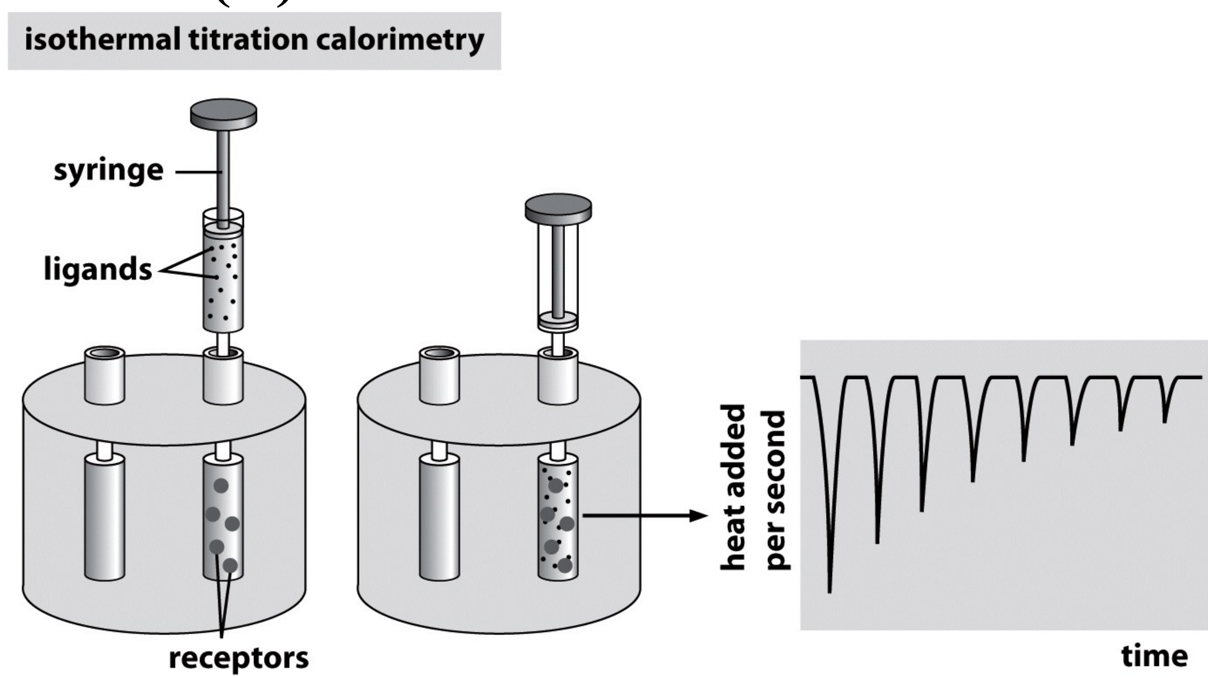

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Cooperative Ligand-Receptor Binding: The Hill Function

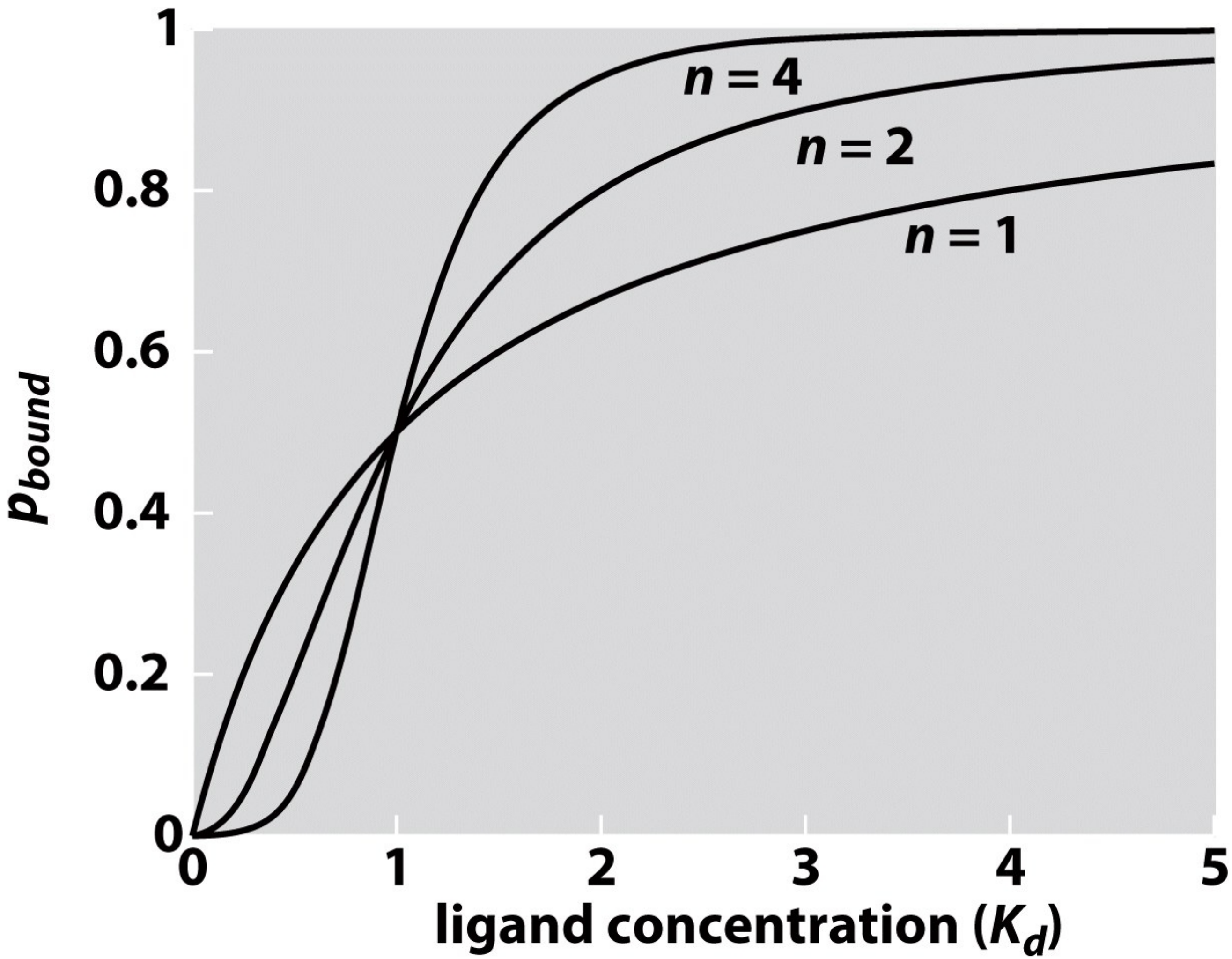
Biological function: an on-off switch behavior triggered by Binding of a ligand to a receptor involves a cooperative (all-or-none) mechanism:

$$L + L + R \leftrightarrow L_2R$$

$$K_d^{\,2} = [L]^2[R]/[L_2R]$$

$$p_{bound} = \frac{([L]/K_d)^2}{1 + ([L]/K_d)^2} = \frac{([L]/K_d)^n}{1 + ([L]/K_d)^n}$$

The larger the n, the sharper the binding curve (probability of binding versus ligand concentration)



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