

# **Molecular Biophysics**

## **Entropy, Boltzmann and Gibbs**

Physical Biology of the Cell, chapters 5 and 6

# Free energy

## Helmholtz free energy

For a process that takes place at constant T

$$F = U - TS$$

## Gibbs free energy

For a process that takes place at constant T and P

$$G = U - TS + PV$$

During a process the changes are:

$$\Delta F = \Delta U - T\Delta S$$

$$\Delta G = \Delta U - T\Delta S + P\Delta V$$

But  $\Delta V \approx 0$ , so  $\Delta F \approx \Delta G$  and therefore it doesn't matter whether we use  $F$  or  $G$ .

# The natural direction of processes

As a system approaches equilibrium:

$$\Delta G \leq 0$$

So  $G \approx U - TS$  is **minimised** at equilibrium.

This implies *decreasing*  $U$  or *increasing*  $S$  or both.

N.B. Entropic term becomes more significant at high temperature.

Maximising  $S$  involves finding the macrostate with the largest number of corresponding microstates

# Possible models of macromolecules

## (1) DNA

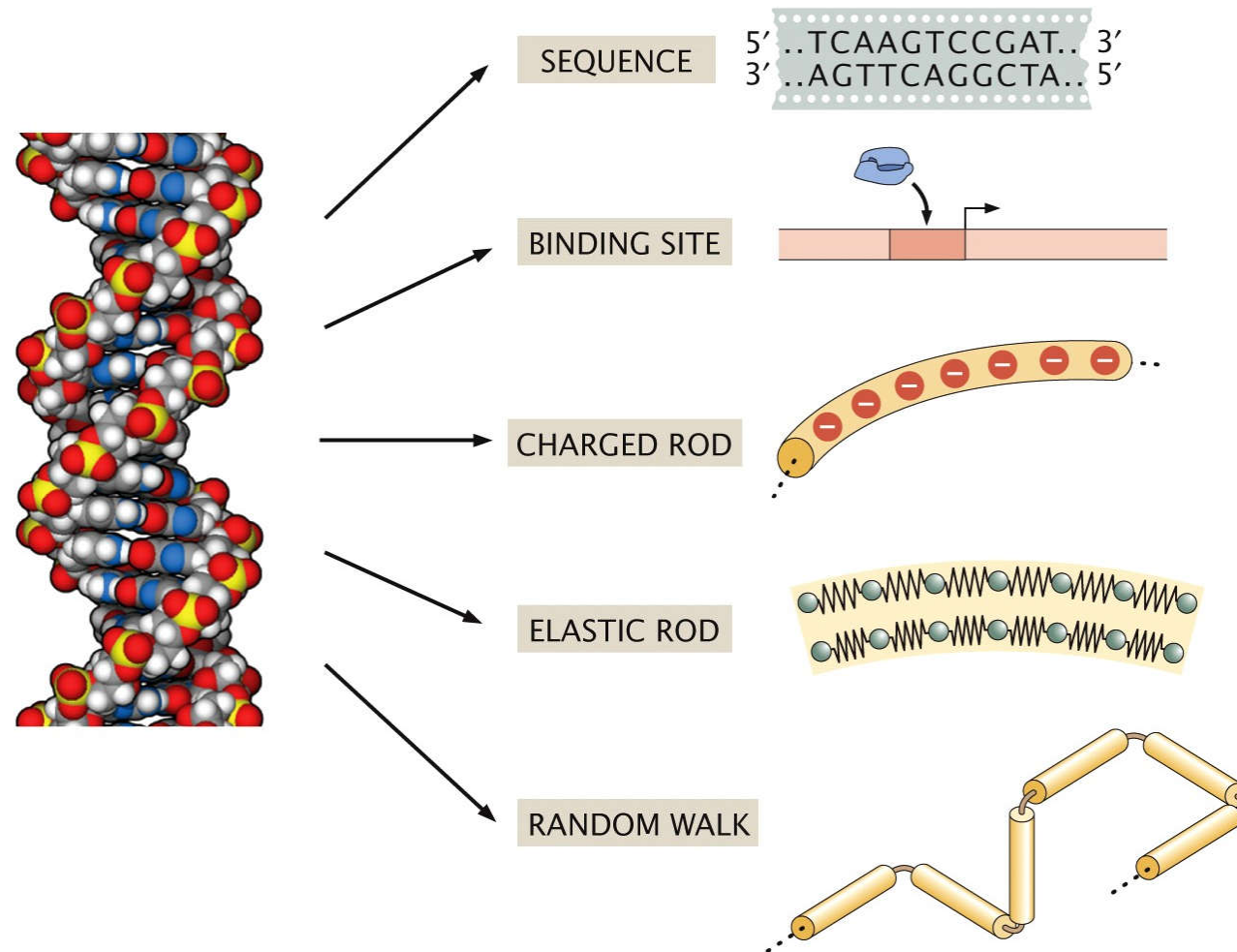


Figure 1.5 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# Possible models of macromolecules

## (2) Proteins

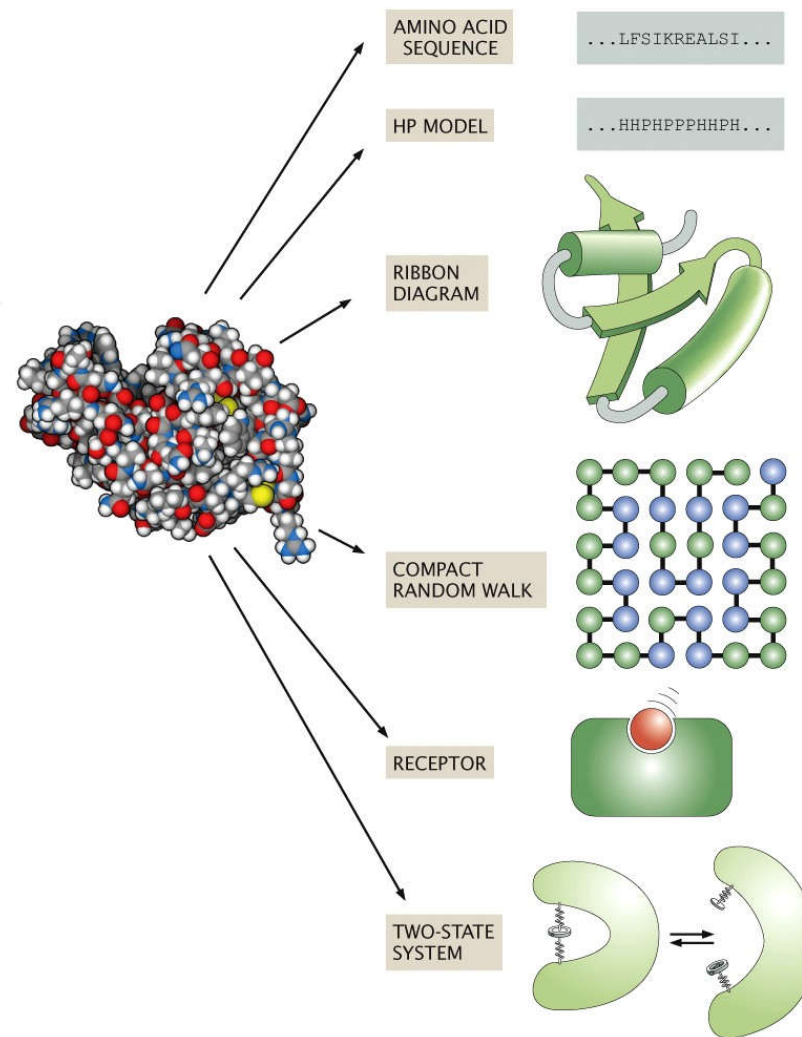


Figure 1.6 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# Possible contributions to U in biological systems

As an illustrative example, consider a polymer...

## (i) *...as a uniform rod*

U depends on the degree of stretching and bending

## (ii) *...as a collection of atoms*

U depends on

- covalent bonds – e.g. stretching
- electrostatic interactions
- van der Waals interactions
- hydrogen bonds

## (iii) *...binding to another molecule (ligand)*

U depends on the same as above plus the energy of interaction

# Energy as a function of length scale

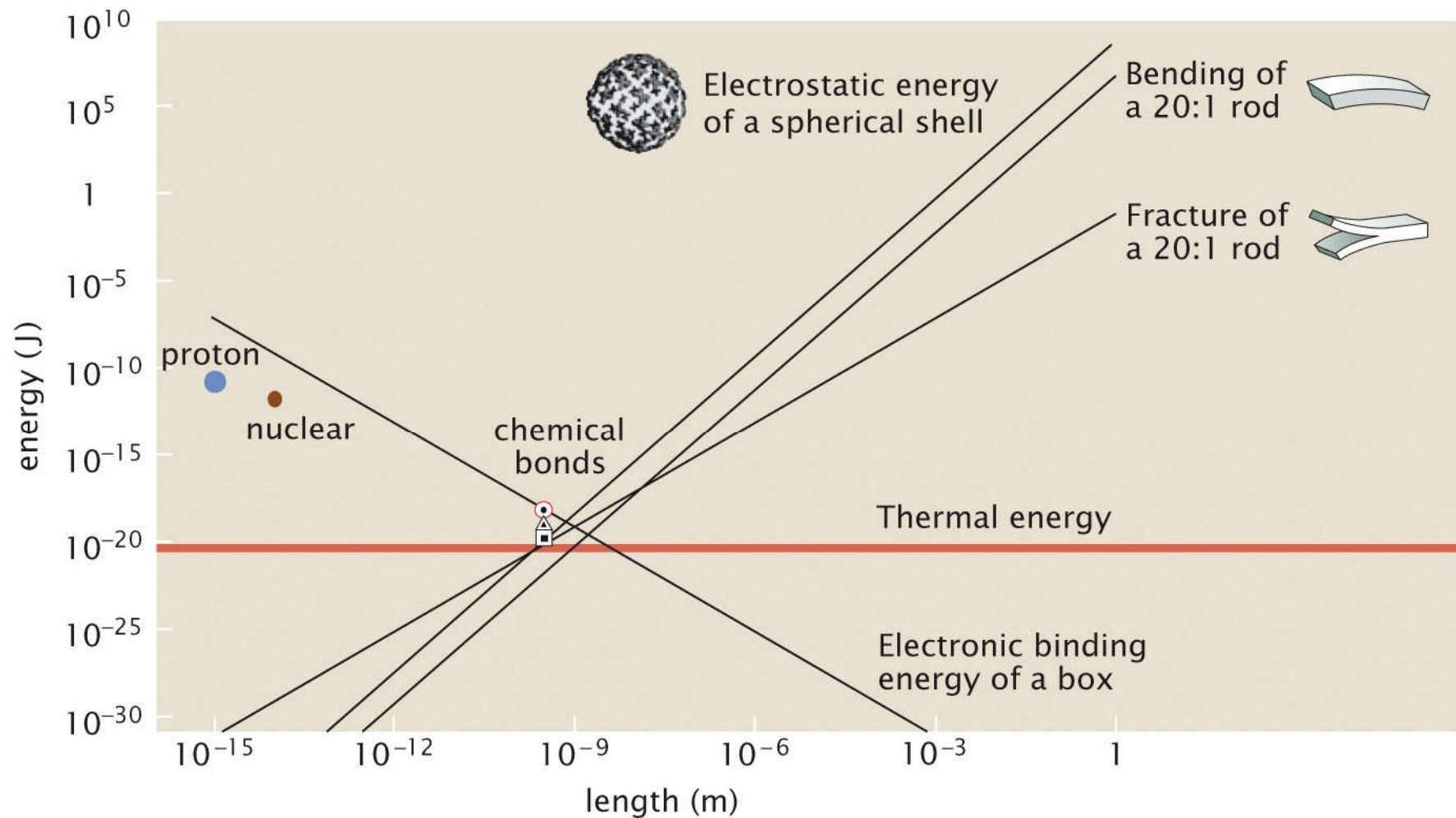


Figure 5.1 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# Schematic representation of an isolated system with sub-compartments separated by a barrier

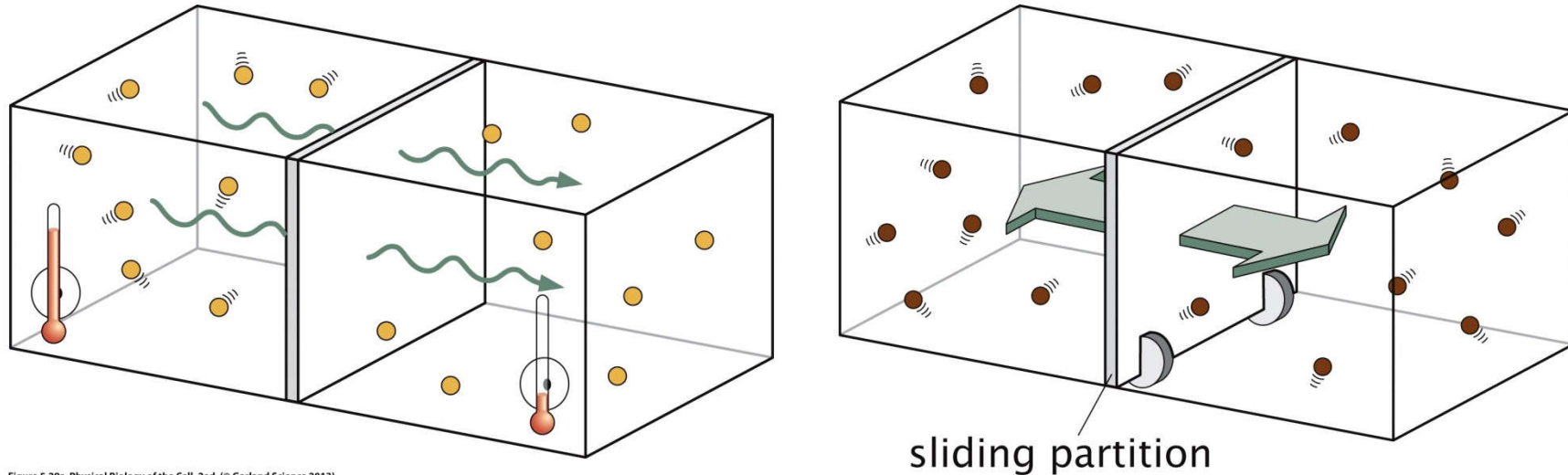


Figure 5.29a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

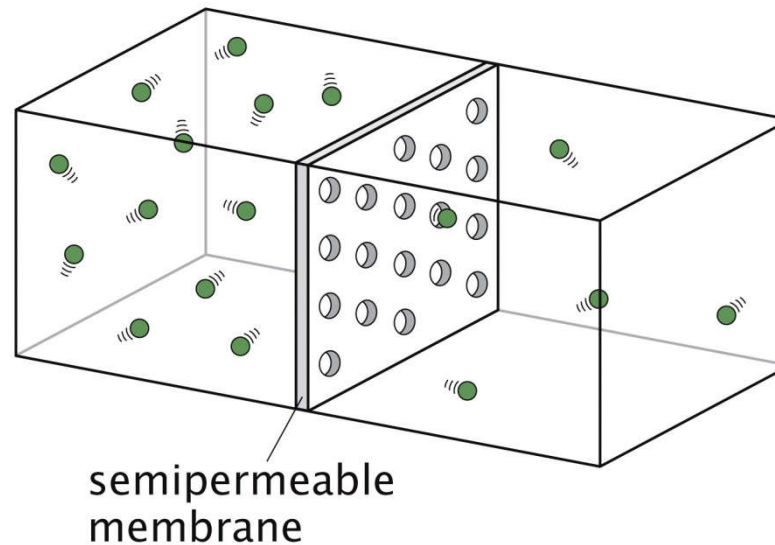


Figure 5.29c Physical Biology of the Cell, 2ed. (© Garland Science 2013)



# Possible arrangements of proteins on a DNA molecule

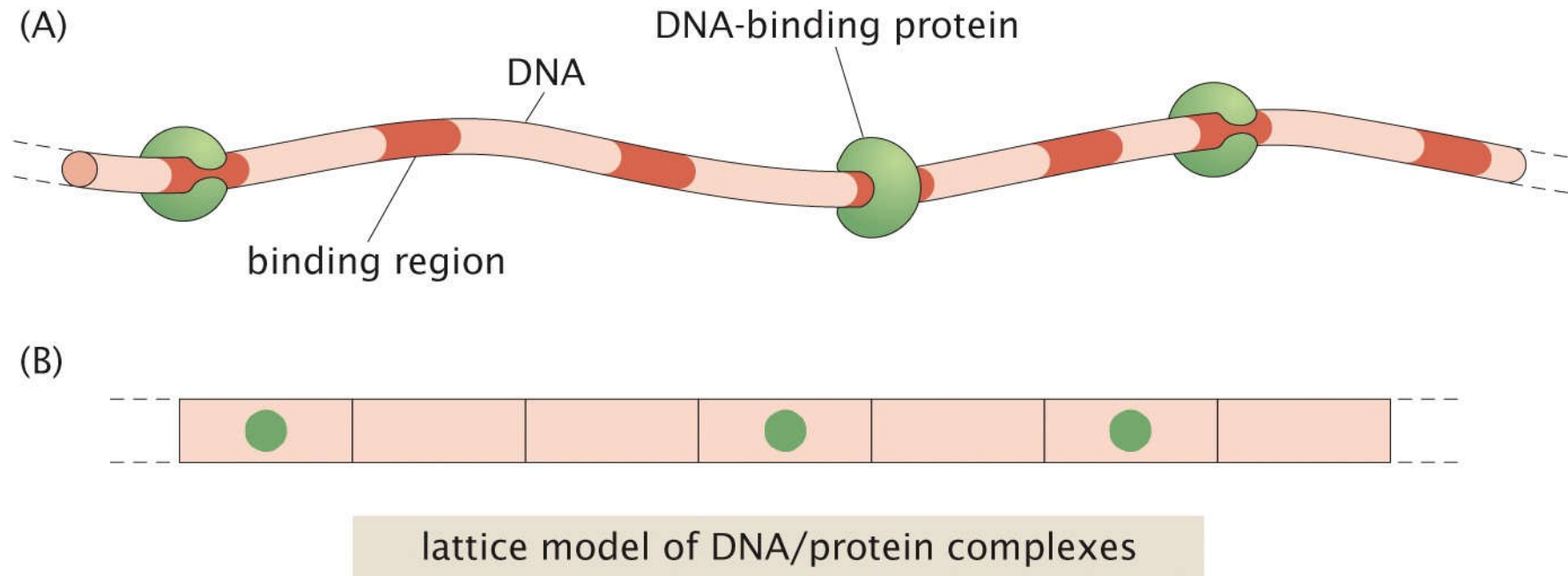


Figure 5.25 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Assume:  $N$  binding sites on DNA  
 $N_p$  of them are occupied by a protein  
Binding energy is the same at all sites

# Entropy as a function of protein concentration

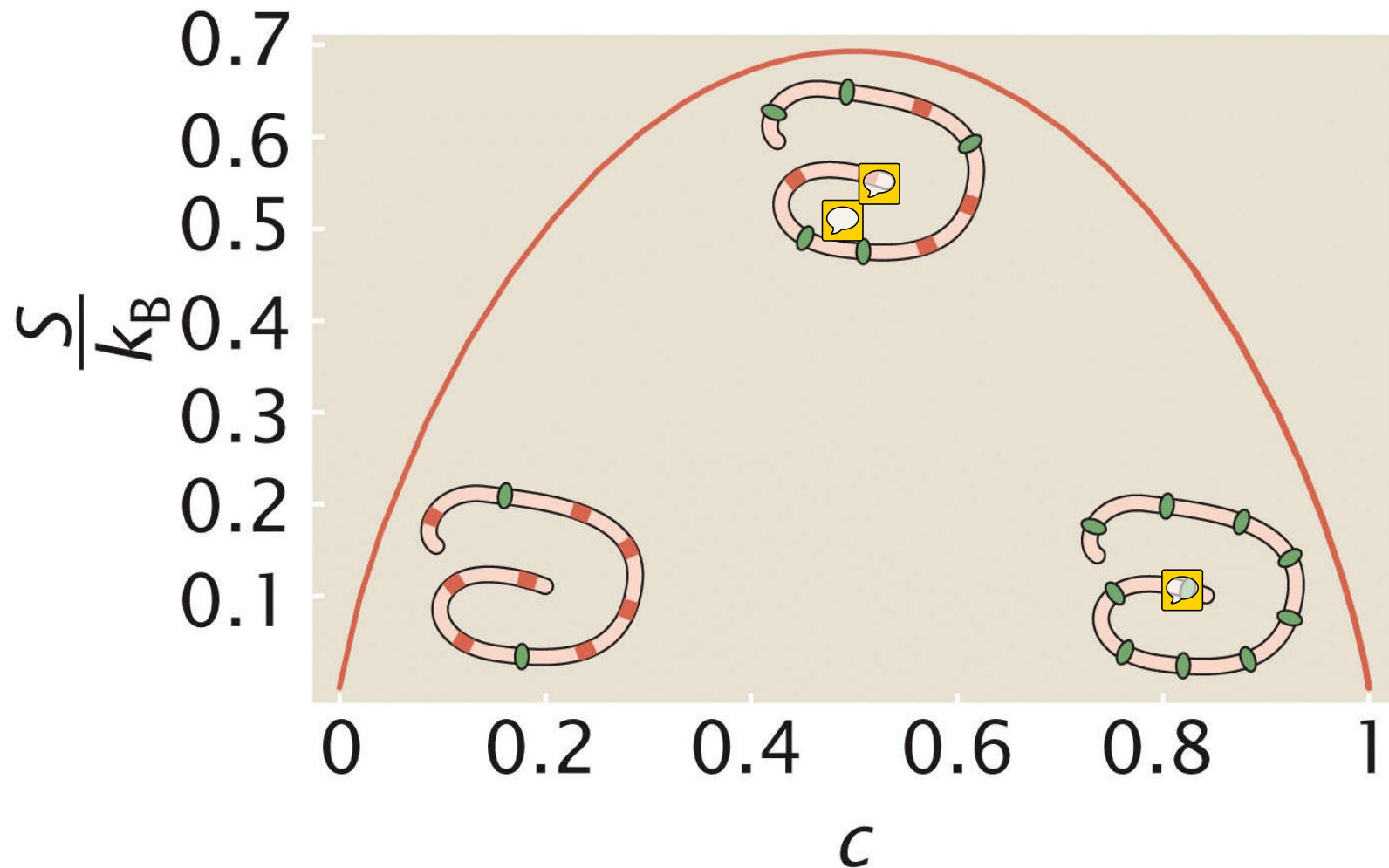


Figure 5.26 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# Isolated and closed systems

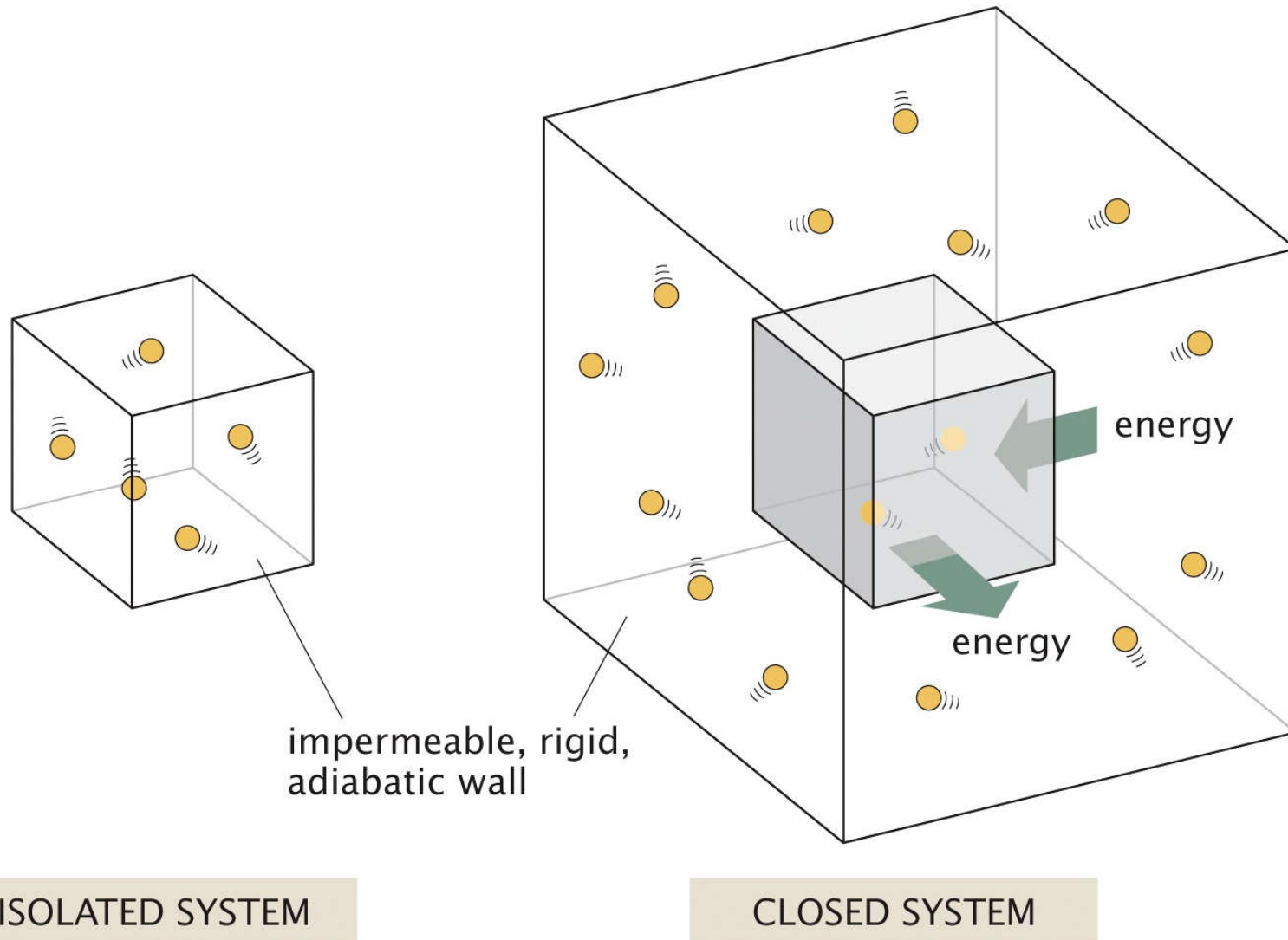
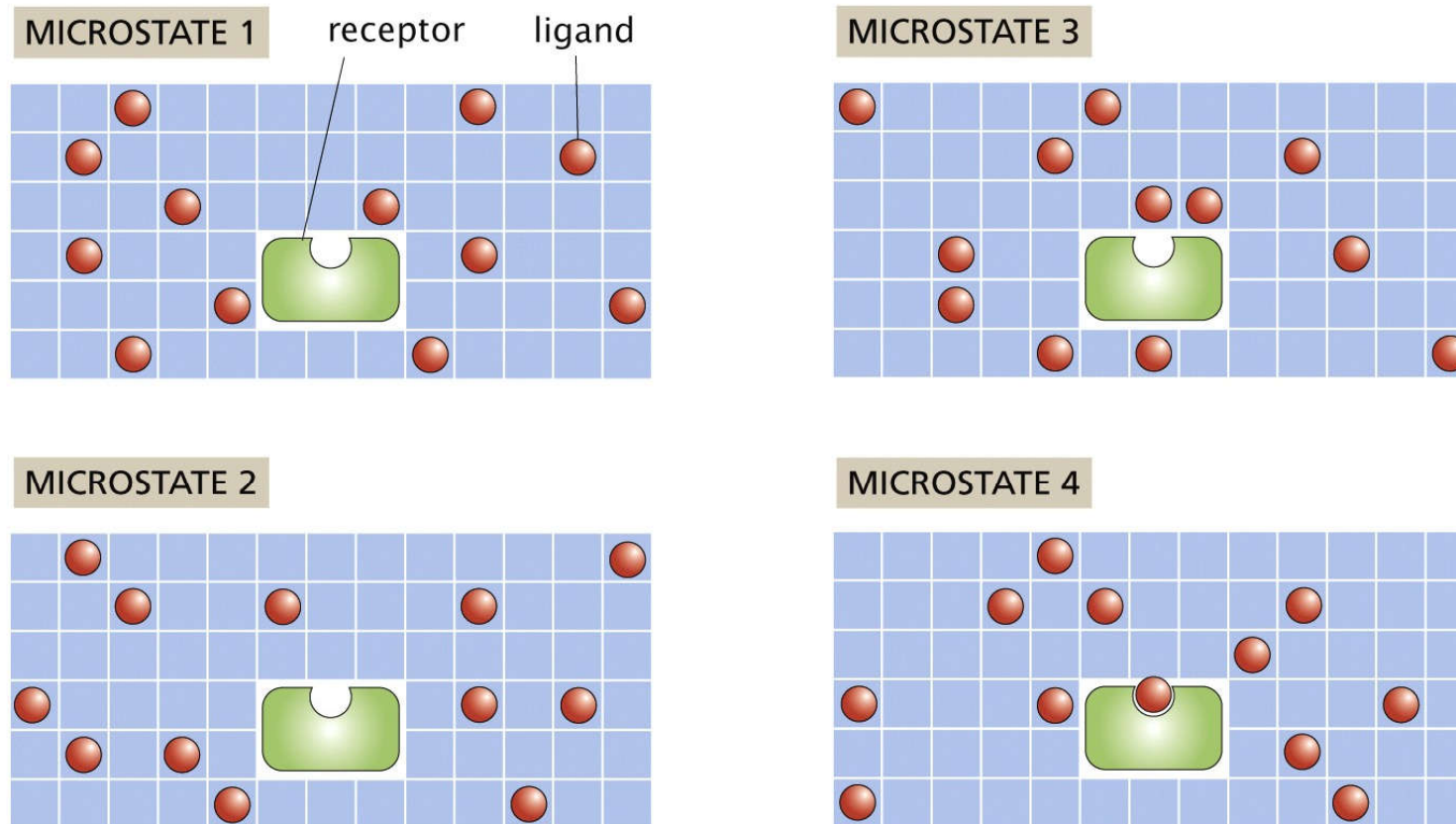


Figure 5.30 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# Microstates: Simple lattice model of ligand-receptor binding



etc.

Figure 6.1 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# States and weights diagram for receptor-ligand binding

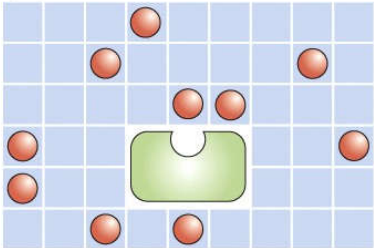
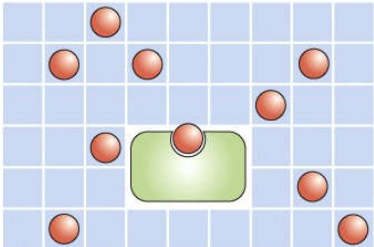
STATE	ENERGY	MULTIPLICITY	WEIGHT
<p>(A)</p> 	$L\varepsilon_{\text{sol}}$	$\frac{\Omega!}{L!(\Omega-L)!} \approx \frac{\Omega^L}{L!}$	$\frac{\Omega^L}{L!} e^{-\beta L\varepsilon_{\text{sol}}}$
<p>(B)</p> 	$(L-1)\varepsilon_{\text{sol}} + \varepsilon_b$	$\frac{\Omega!}{(L-1)!(\Omega-L+1)!} \approx \frac{\Omega^{L-1}}{(L-1)!}$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

Figure 6.4 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Assume:  $L$  ligands on  $\Omega$  lattice sites  
 1 receptor with 1 binding site  
 $\varepsilon_b$  = binding energy  
 $\varepsilon_{\text{sol}}$  = energy of ligand in solution

# Probability of receptor occupancy

$$p_{\text{bound}} = \frac{\sum_{\text{states}} \left( \text{Diagram 1} \right)}{\sum_{\text{states}} \left( \text{Diagram 2} \right) + \sum_{\text{states}} \left( \text{Diagram 3} \right)}$$

The diagram illustrates the probability of a receptor being occupied by a ligand. The numerator represents the sum of all states where the receptor is occupied (bound). The denominator represents the sum of all states where the receptor is either occupied or unoccupied (free). Each diagram shows a 5x5 grid of blue squares representing possible positions for a red spherical ligand. A green rectangular receptor is located in the bottom-center of the grid. In the first diagram (numerator), the ligand is bound to the receptor. In the second and third diagrams (denominator), the ligand is unbound and occupies one of the 24 other positions in the grid.

Figure 6.5 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# Average occupancy as a function of ligand concentration and binding energy

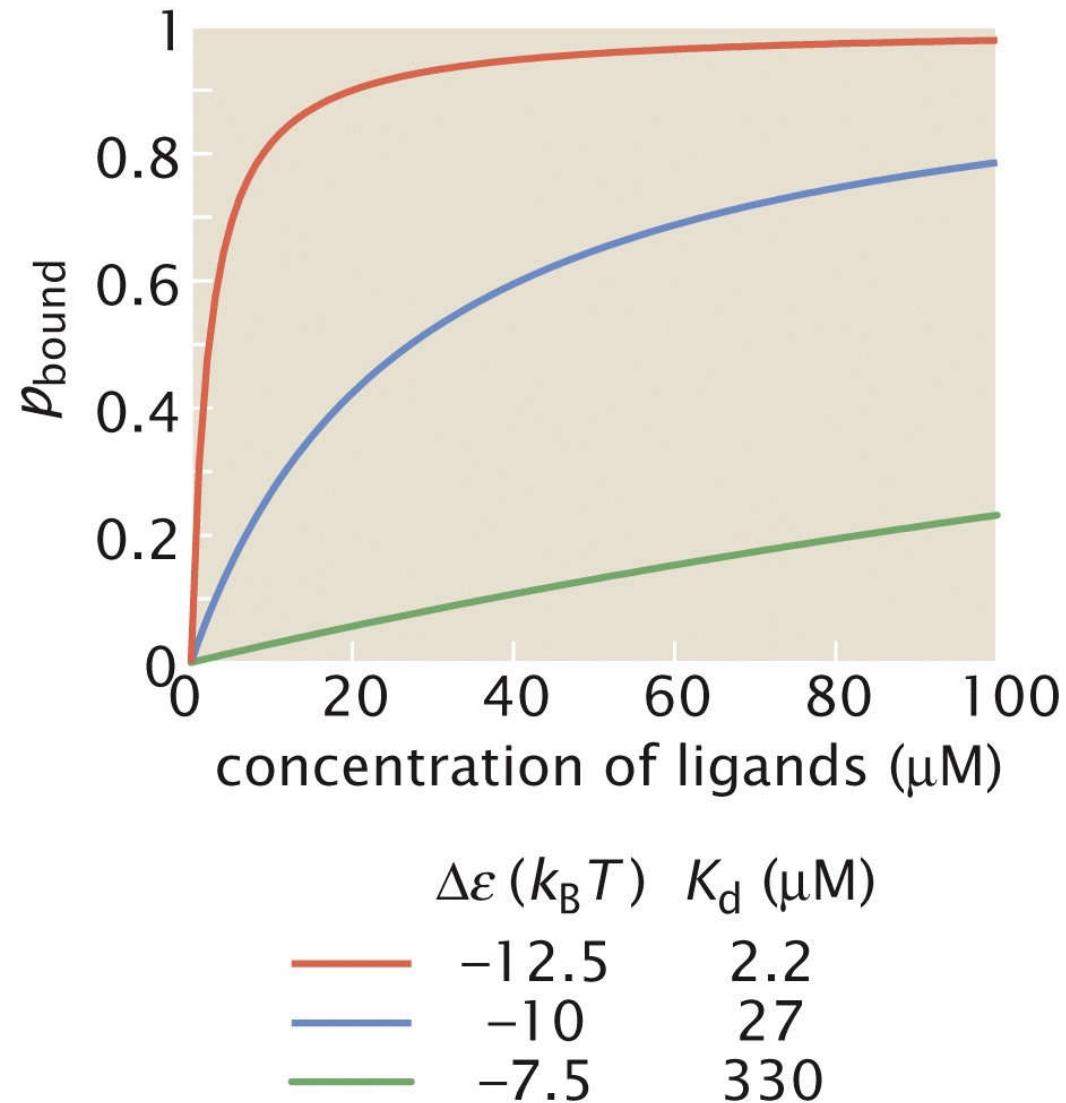


Figure 6.6 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

# Hydrogen bonding network in water

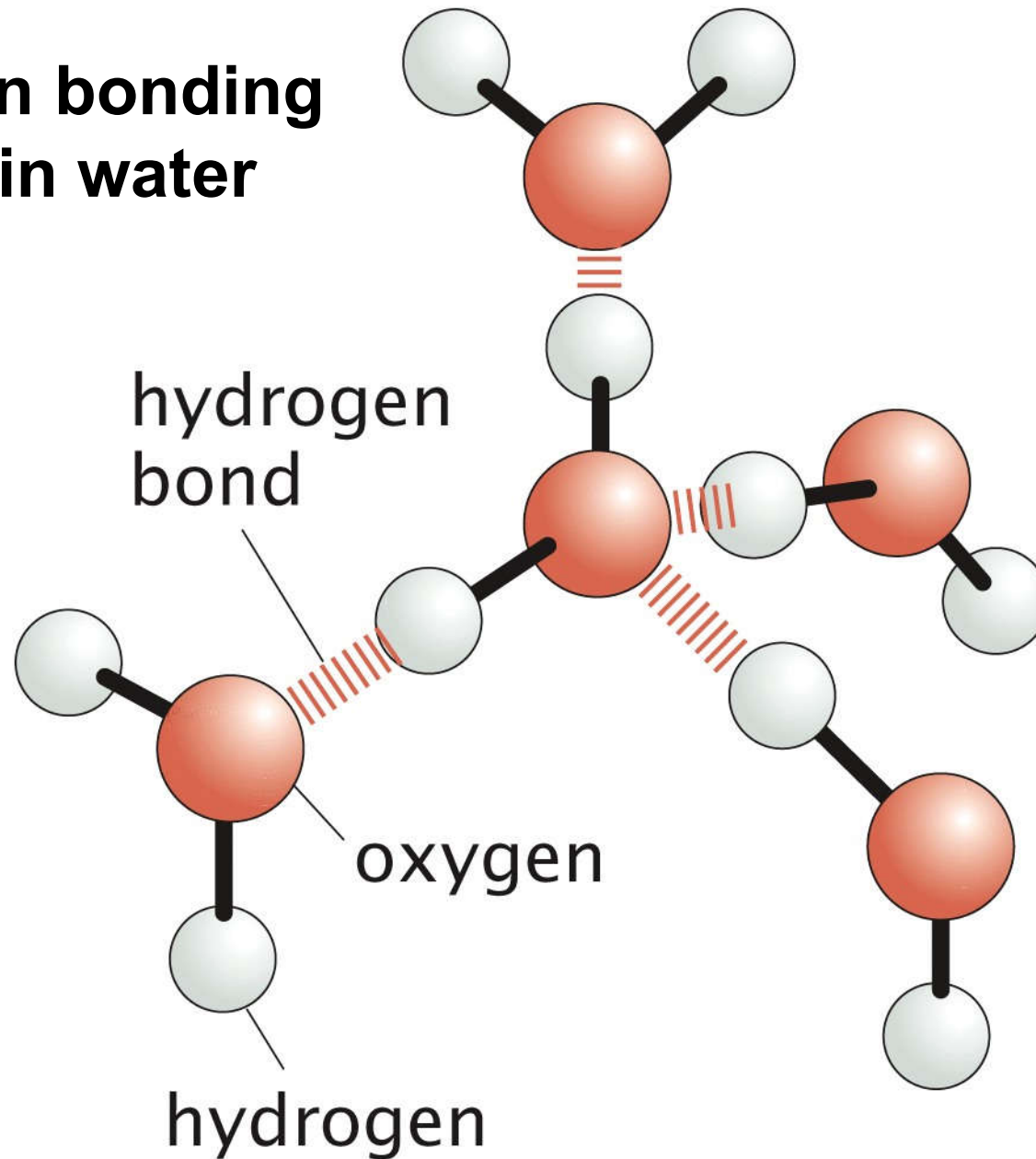


Figure 5.27 Physical Biology of the Cell, 2ed. (© Garland Science 2013)



# Orientation of water molecules in a tetrahedral network

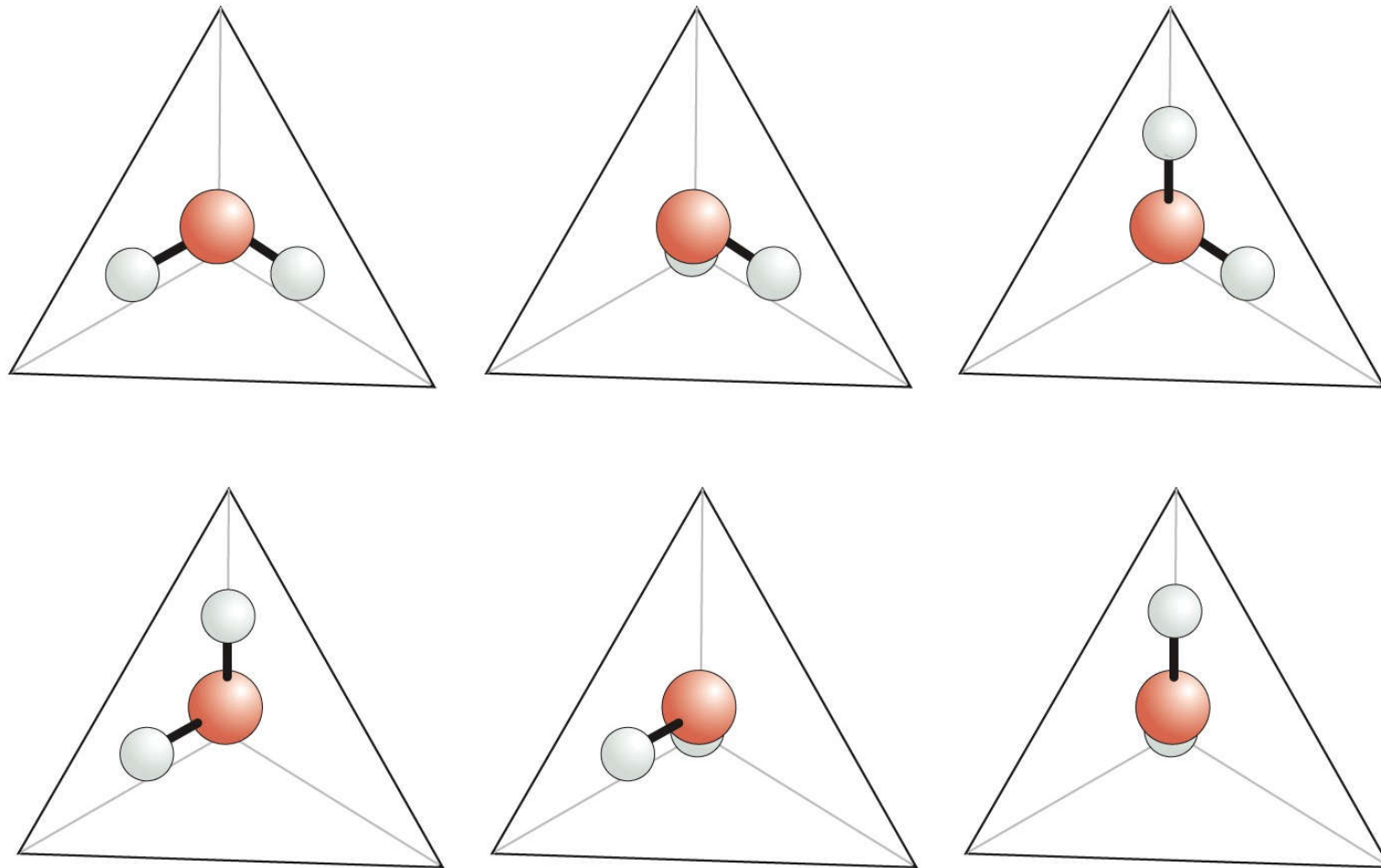


Figure 5.28 Physical Biology of the Cell, 2ed. (© Garland Science 2013)