Energy and Equilibrium

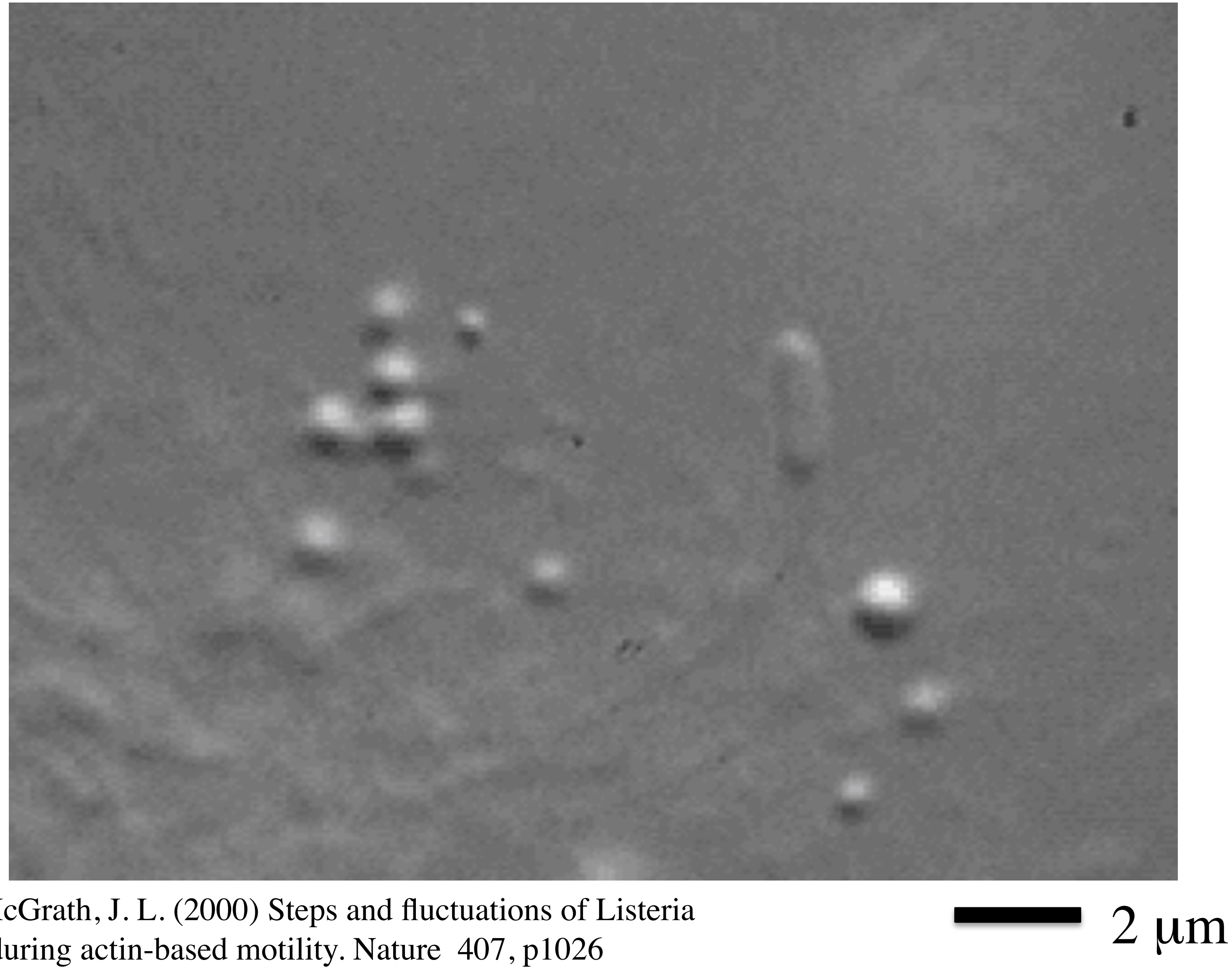
2010-10-18

http://www.iiserpune.ac.in/~cathale/lects/bio322-2010.html

Diffusion and thermal energy

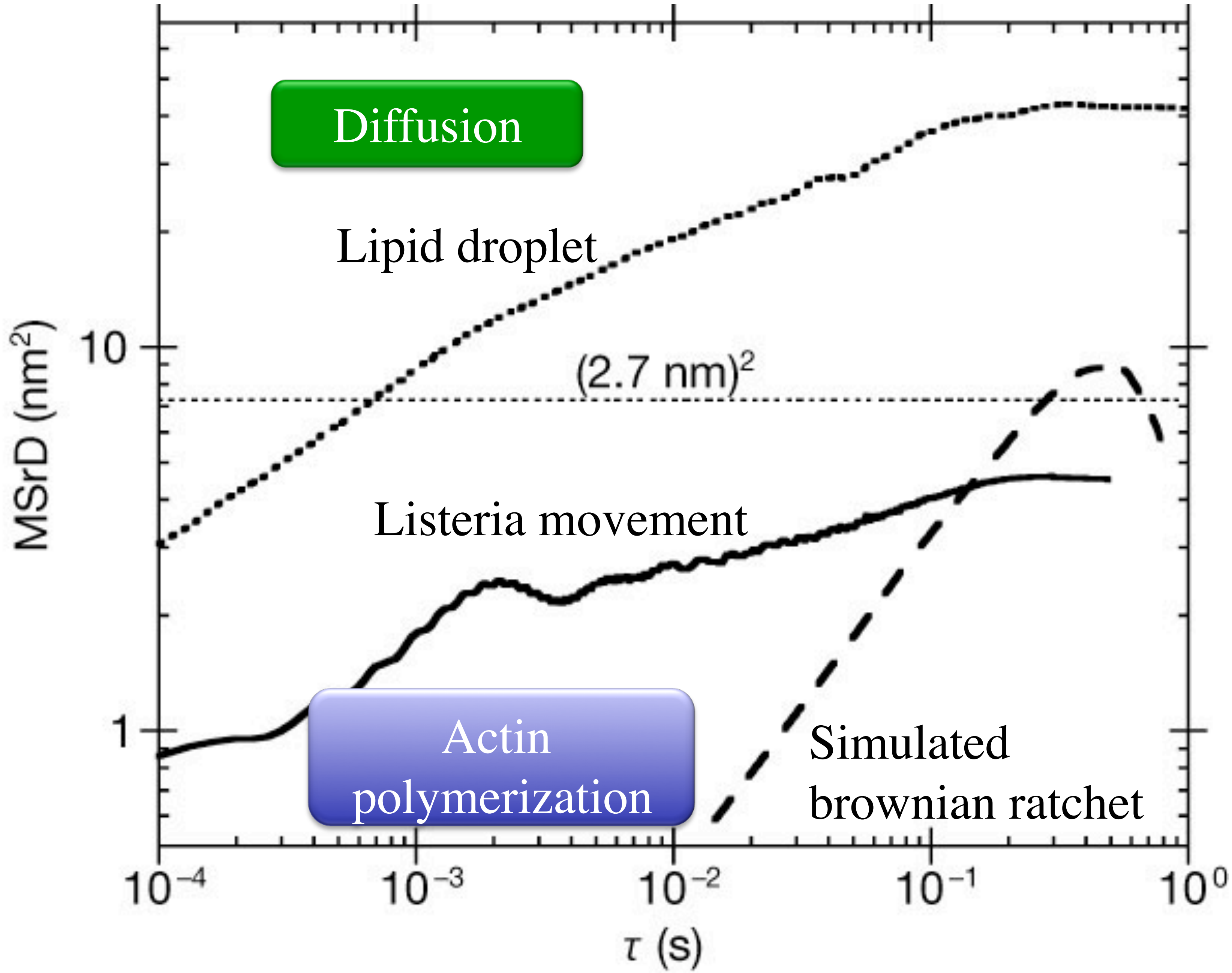
ENERGY

Listeria Inside a Cos7 Cell



Kuo, S.C., and McGrath, J. L. (2000) Steps and fluctuations of Listeria monocytogenes during actin-based motility. Nature 407, p1026

Cellular Movement



Thermal Energy Scale

Time scales and feasibility of reactions determined by energies

Thermal energy available inside living systems

$k_B T = 1.38\text{x}10^{-23}$ J/K x 300 K $\approx 4.1\text{x}10^{-21}$ J = ?? pN-nm

Diffusion Times and Length Scales

For a diffusing particle inside a cell

$t_{diffusion} \approx x^2/D$

Molecules Moving Inside Cells

Stokes-Einstein Relation

$D=k_B T/f$

f = stokes frictional force

$= 6\pi\eta r$ (spherical object)

Diffusion coefficient	D (m/s^2)
Dynamic viscosity	η (Pa-s)
Radius of particle	r (m)

A. Einstein "Über die von der molekularkinetischen Theorie der Wärme geforderte Bewegung von in ruhenden Flüssigkeiten suspendierten Teilchen", Annalen der Physik 17 pp. 549-560 (1905)

Getting Around a Cell

- How long could it take a single protein molecule to traverse the length of E. coli?

$r = 2.5$ nm

$\eta \approx 1\text{x}10^{-3}$ N-s/m^2

D=?

$L_{E.coli}$~1 μm

$t_{e.coli}$=?

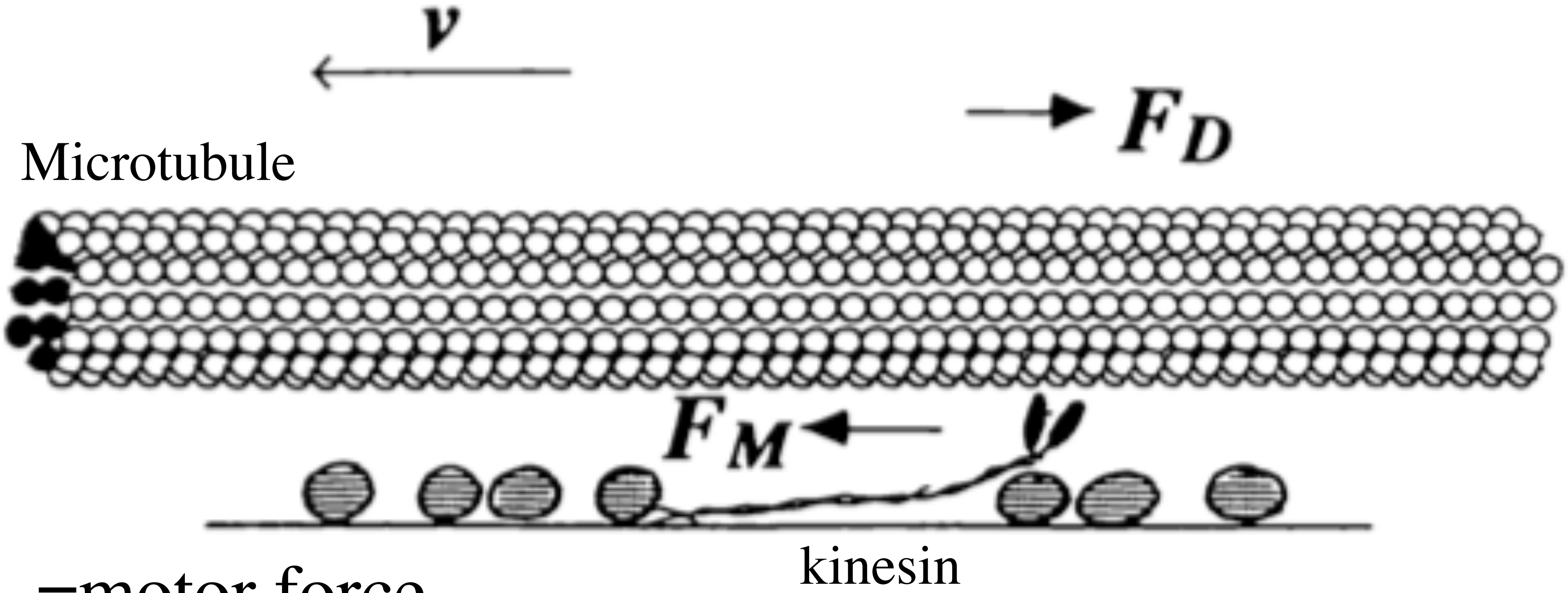
- Squid giant axon length 10 cm. t=?

Molecular Motors

- Kinesin motor speed in cells ~ 1 μm/s
- Measured effective speeds of protein in axon ~ 0.02 μm/s
- Processive vs. Non-processive motion

Estimating Force Exerted by Single Motors

F_M=4.2±0.5 pN



F_M=motor force

F_D=viscous drag force

ν=speed

Hunt et al. (1994) Biophys. J.

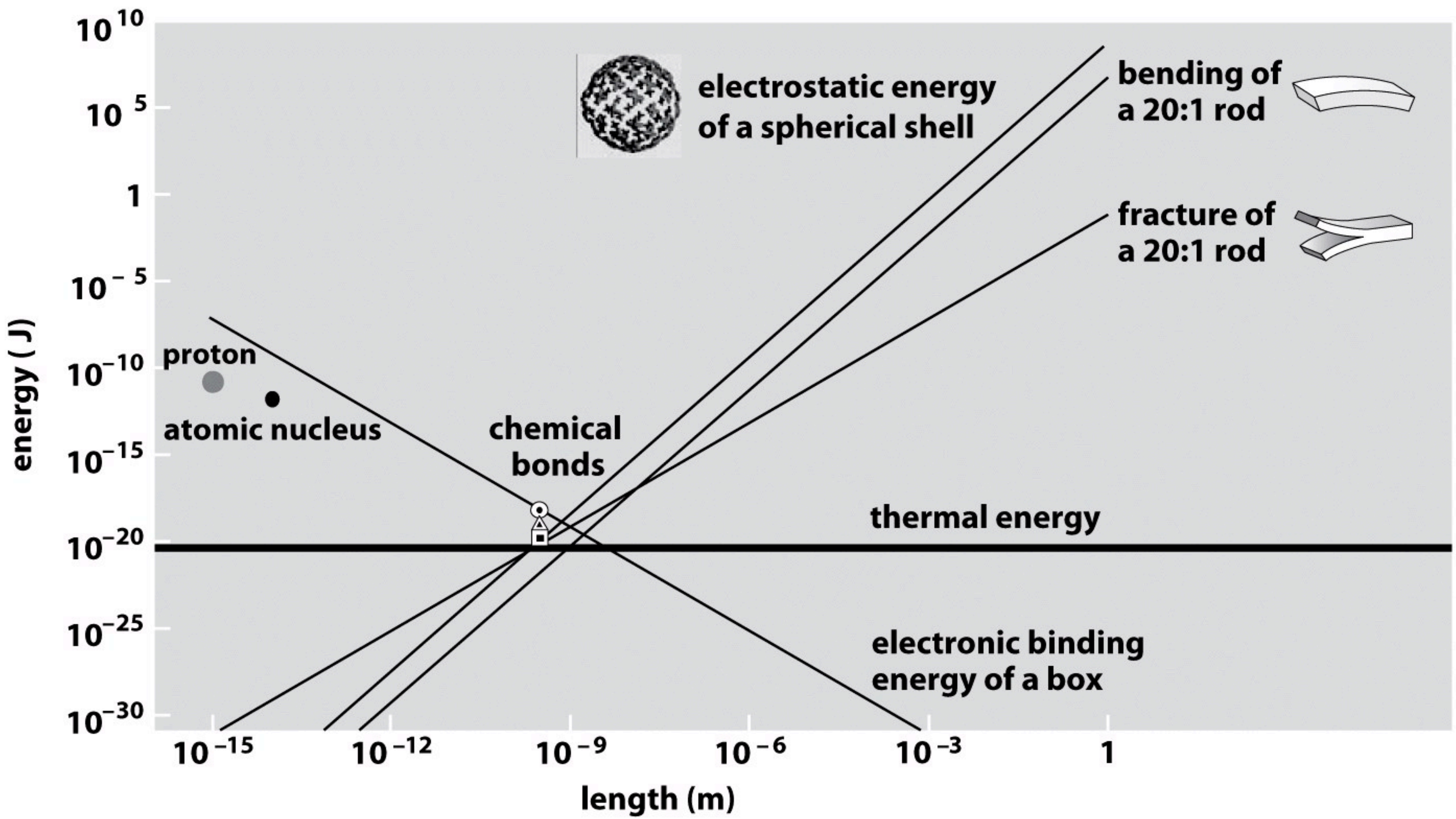


Figure 5.1 Physical Biology of the Cell (© Garland Science 2009)

Biological Minimzation

- Equilibrium
- Out-of-equilibrium
- Fast processes vs. slow processes

Biochemical Equilibrium Assumptions

Enzyme Substrate interactions

$$A \underset{k-}{\overset{k+}{\rightleftharpoons}} B \xrightarrow{r} C$$

Sub-processes and Approach to Equilibrium

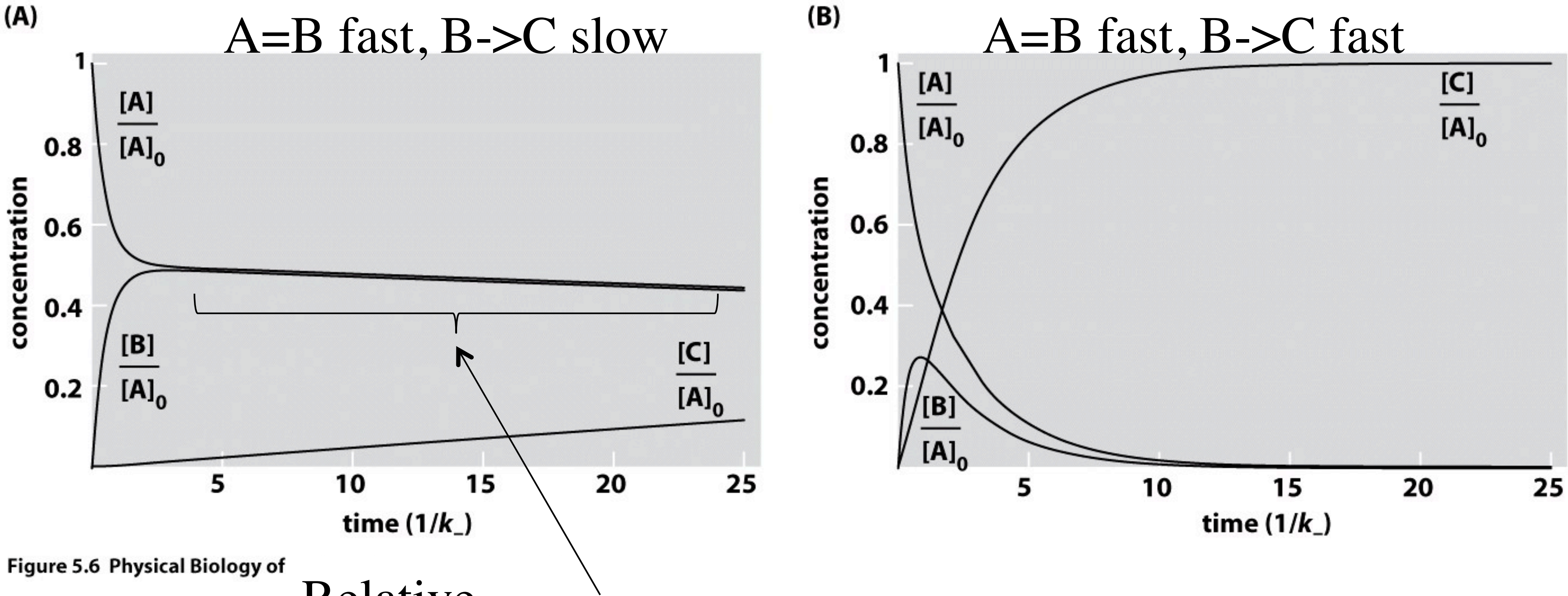


Figure 5.6 Physical Biology of

Relative concentrations of A and B reach equilibrium

If conversion from B->C too rapid, equilibrium assumption not valid

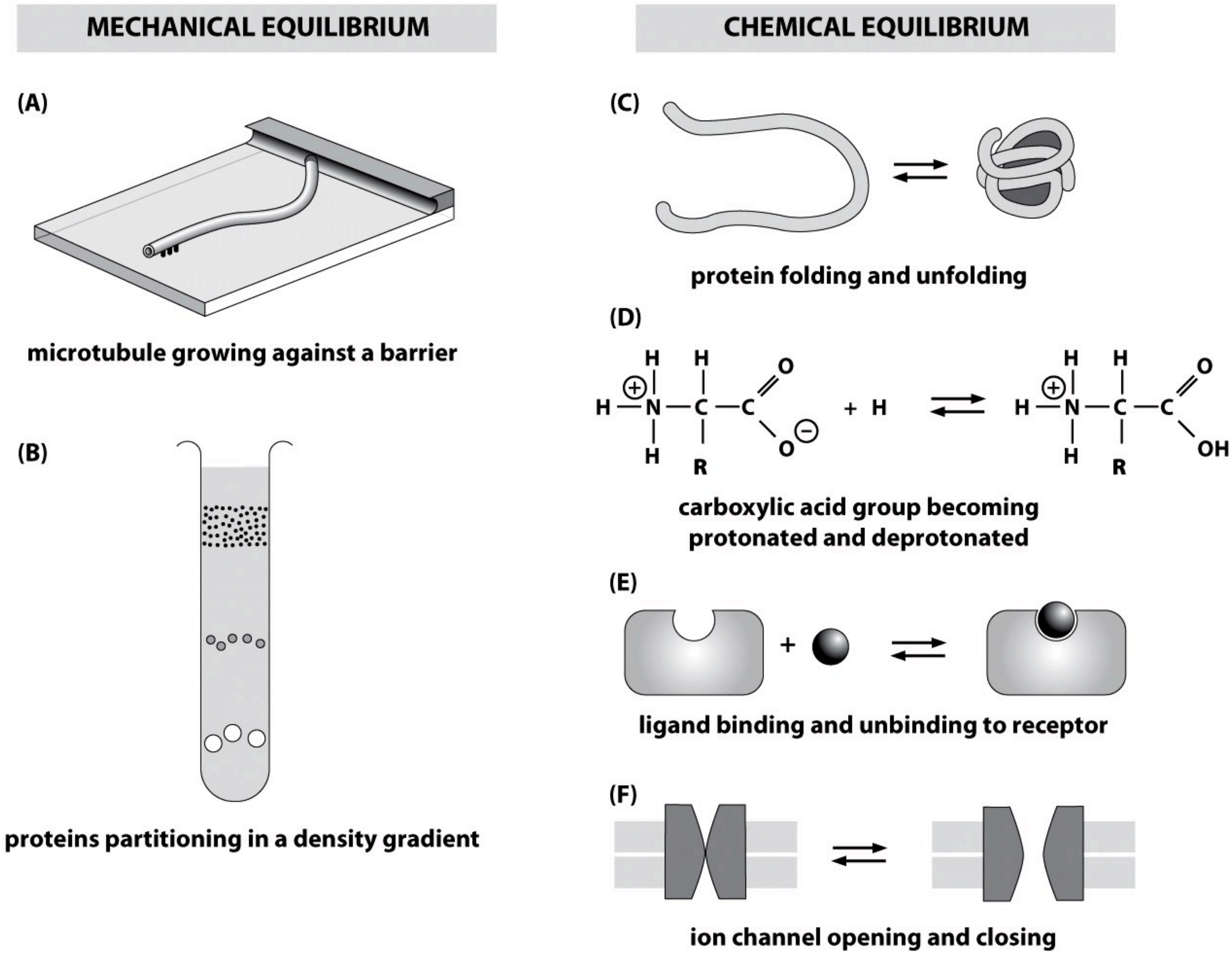


Figure 5.7 Physical Biology of the Cell (© Garland Science 2009)

2010-10-20

Diffusion Coefficient (D)

Derive random walk and diffusion coefficient and msd relation

Derive expression for diffusion coefficient in stokes-einstein formulation

Protein Minimization

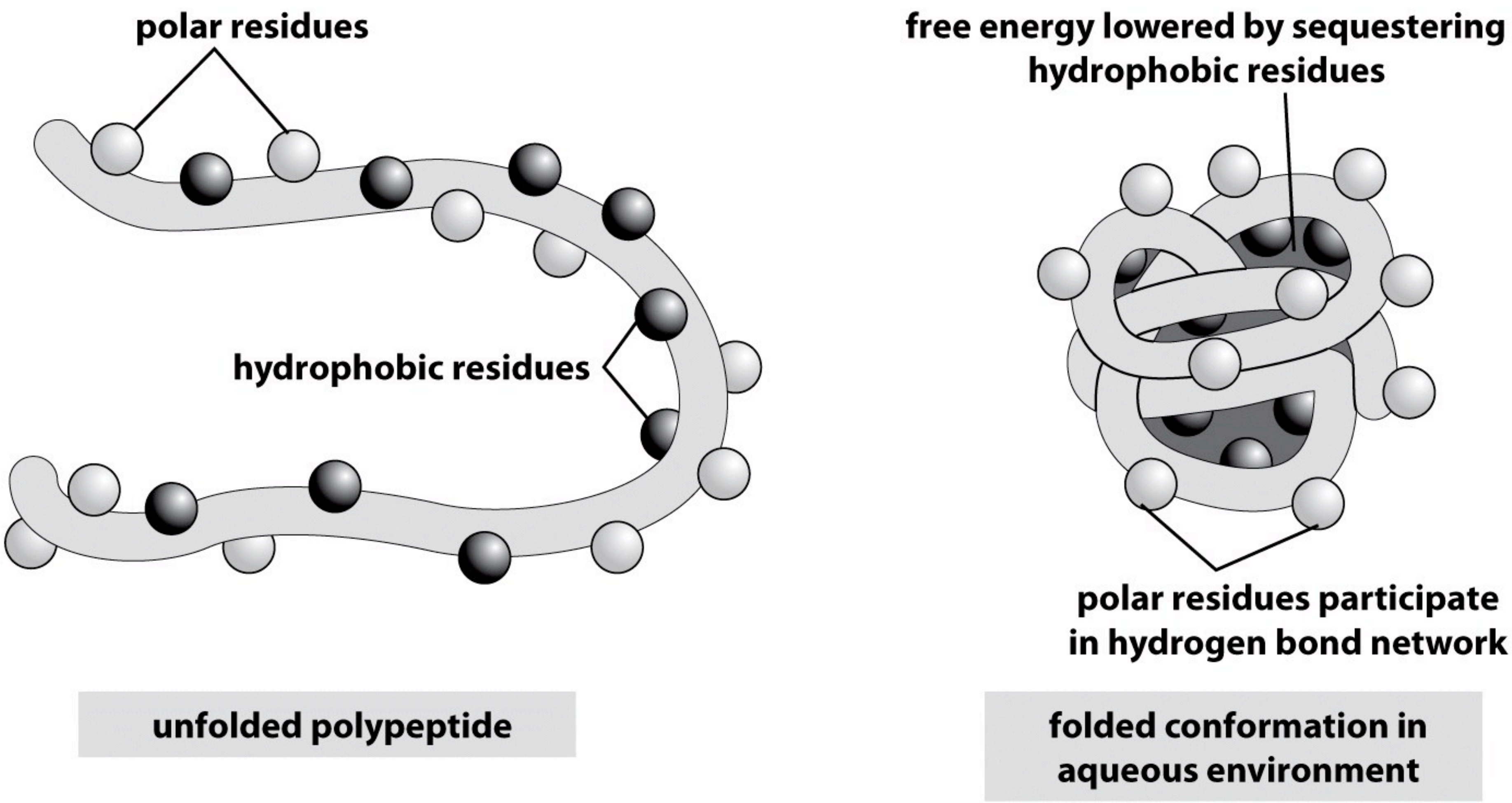
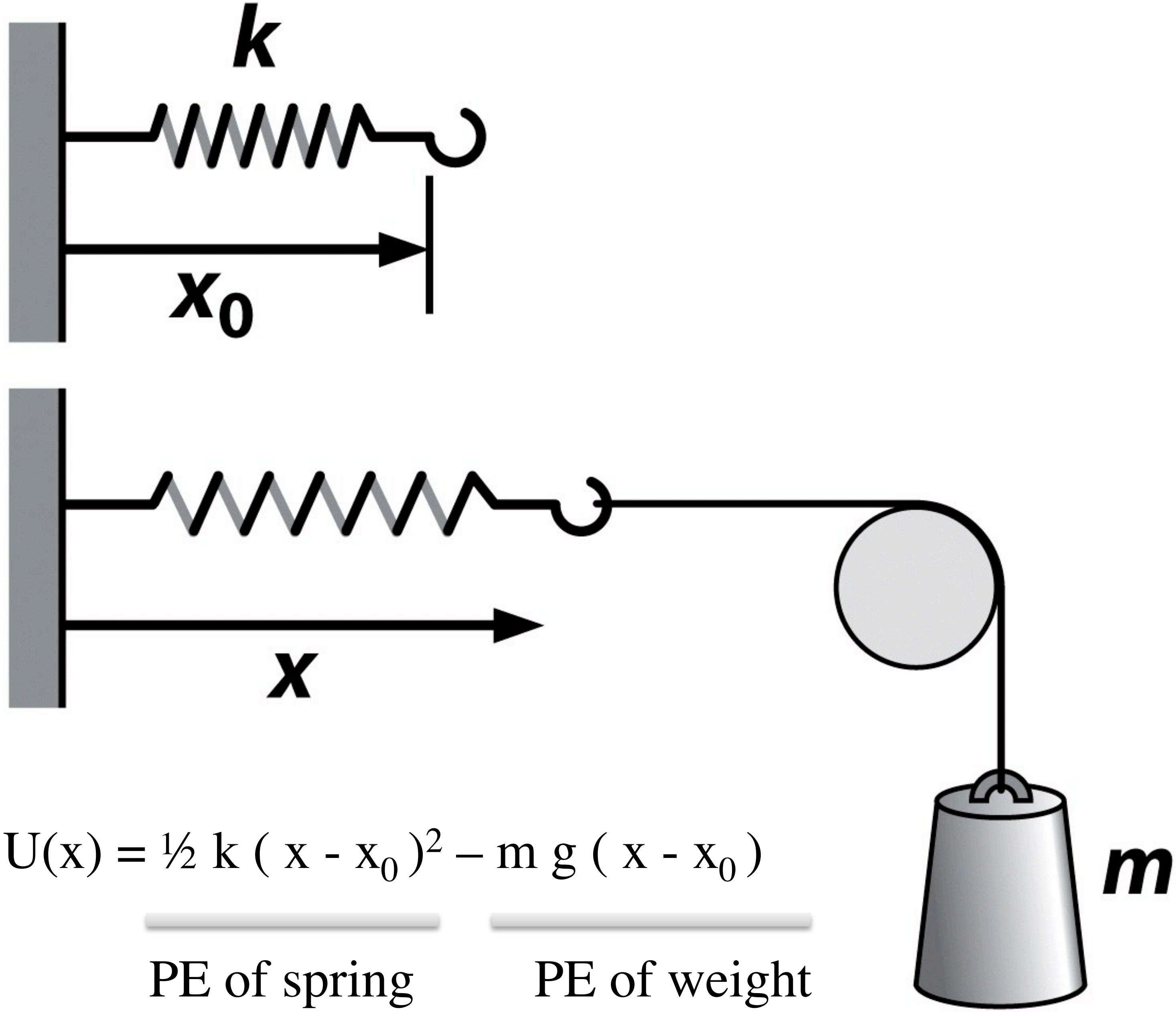


Figure 5.8 Physical Biology of the Cell (© Garland Science 2009)

2010-10-22

ENERGY MINIMIZATION

Spring with Weight



$$U(x) = \tfrac{1}{2}\, k\, (x - x_0)^2 - m\, g\, (x - x_0)$$

PE of spring — PE of weight

Figure 5.11a Physical Biology of the Cell (© Garland Science 2009)

Mechanical Equilibrium as Energy Minimization

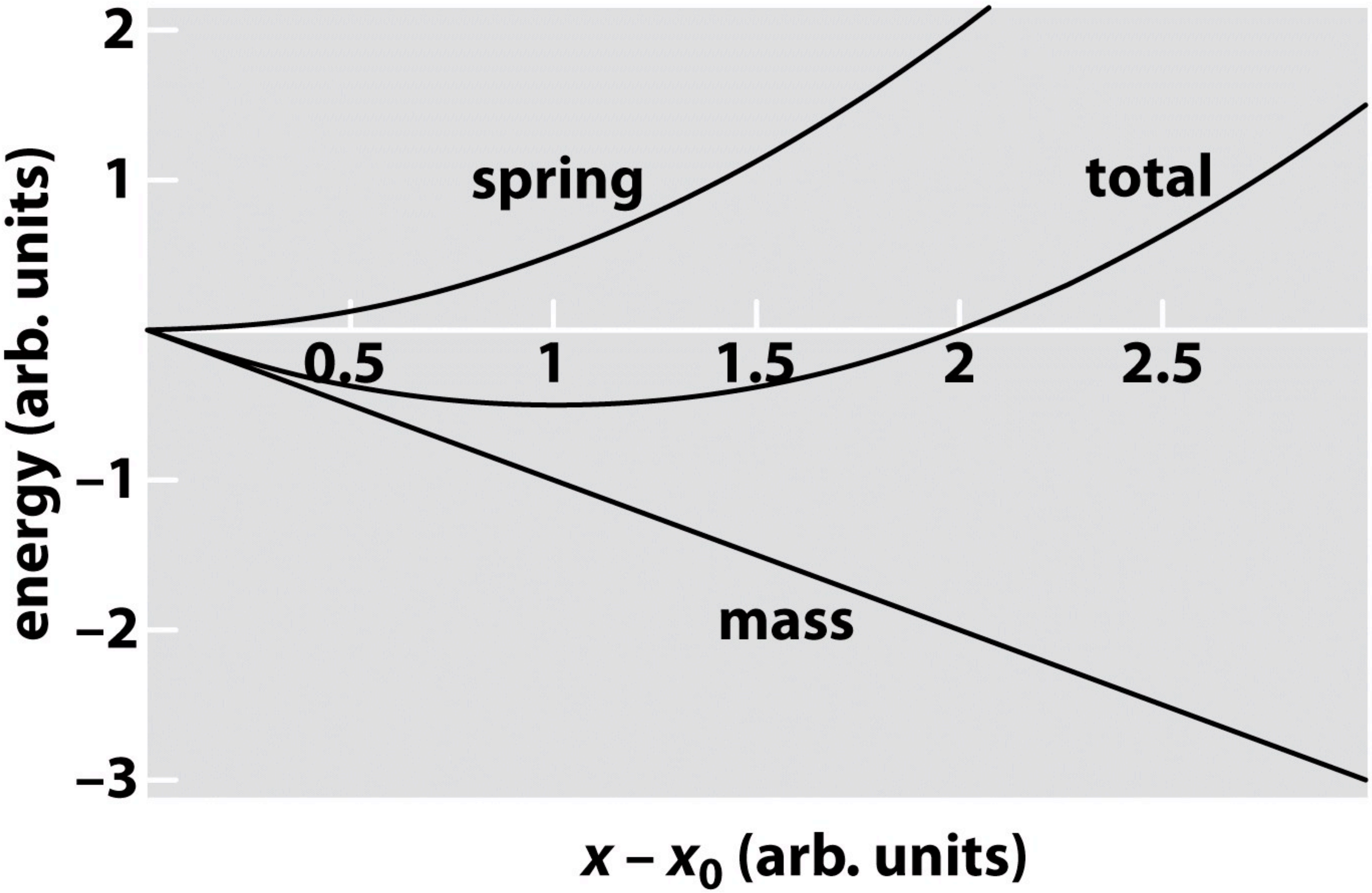


Figure 5.11b Physical Biology of the Cell (© Garland Science 2009)

Equilibrium

$dU/dx = k(x_{eq}-x_0)-mg = 0$

$x_{eq} =$

Springs Everywhere

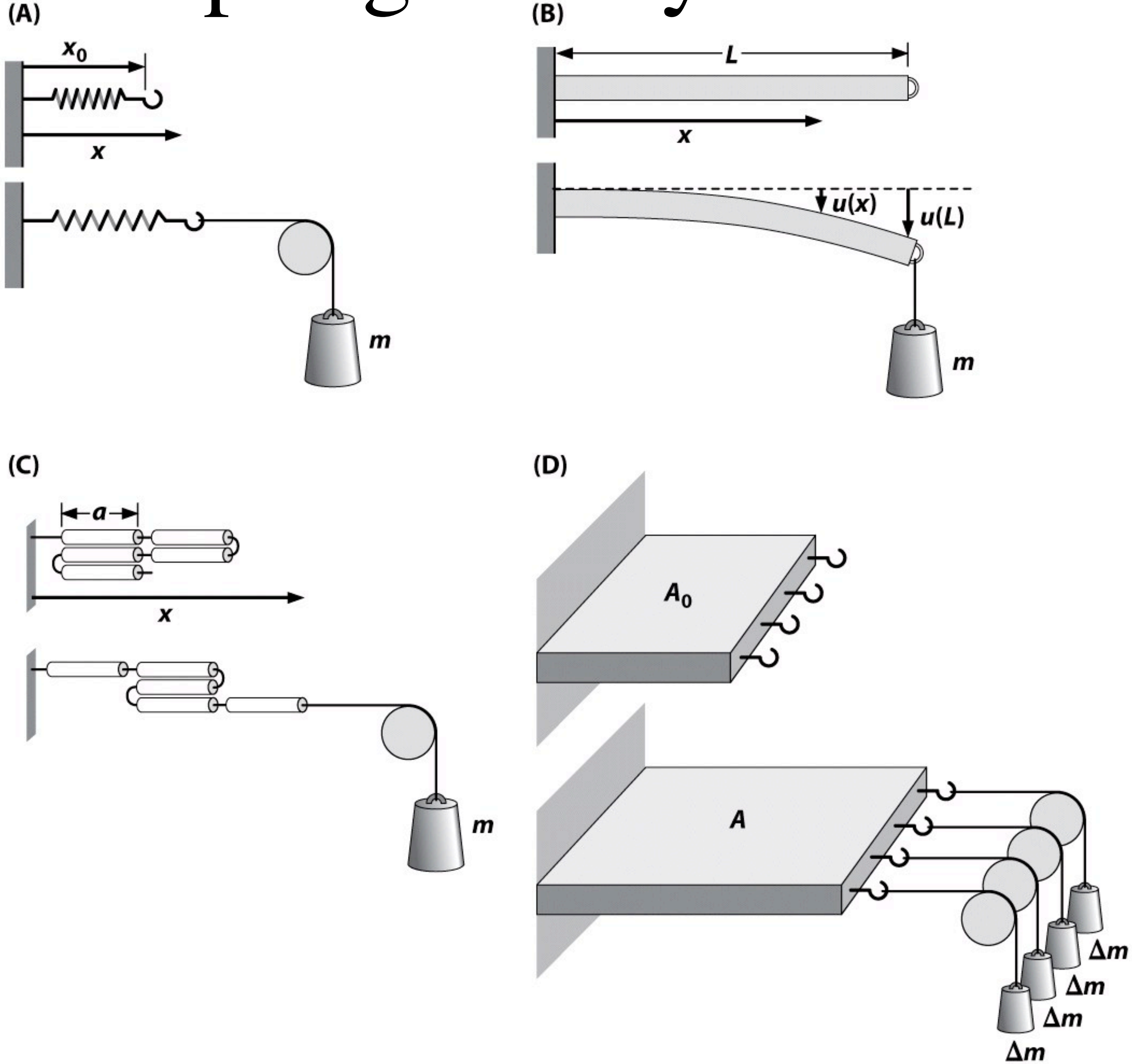


Figure 5.12 Physical Biology of the Cell (© Garland Science 2009)

Optical Trap

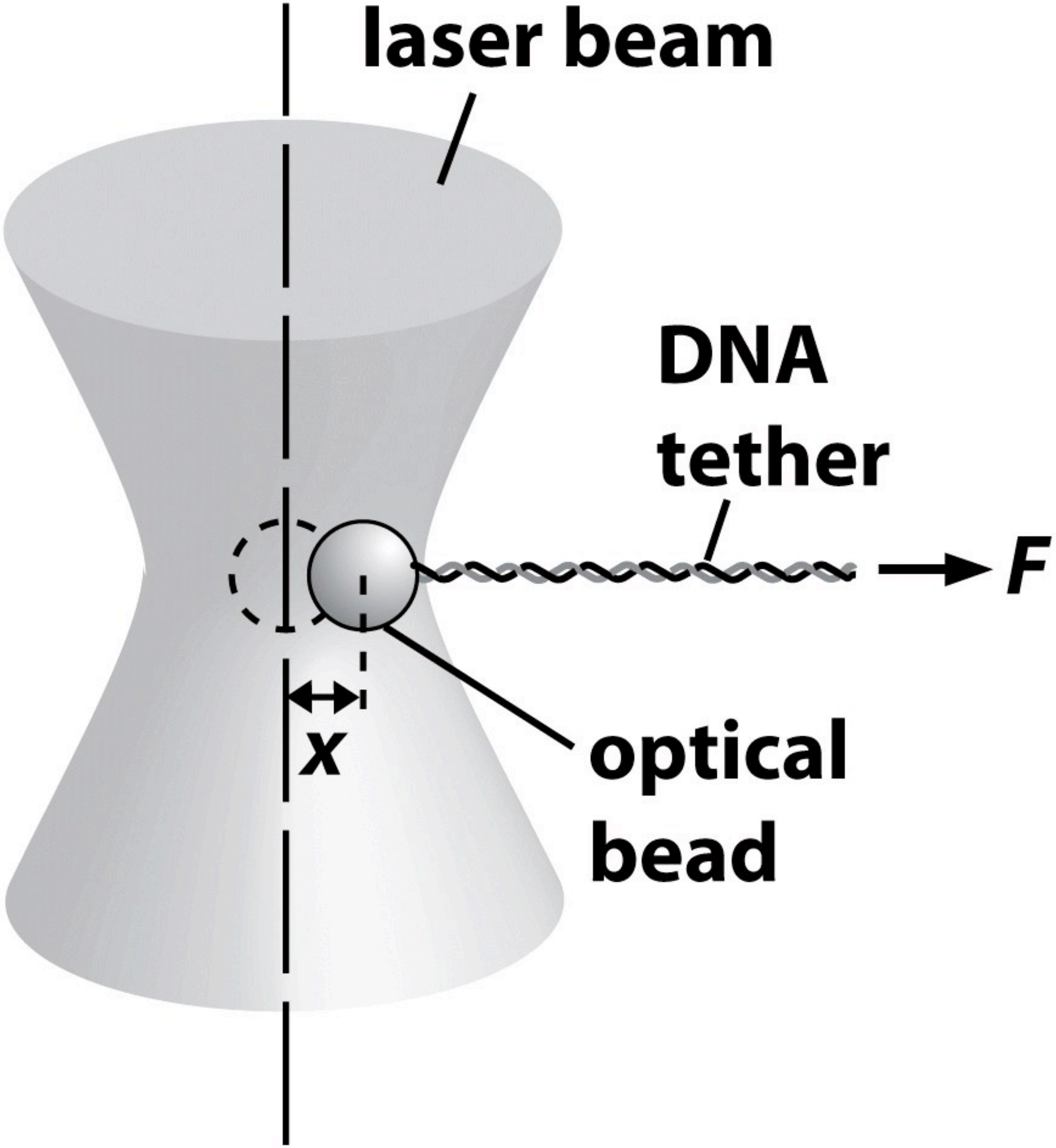


Figure 5.13a Physical Biology of the Cell (© Garland Science 2009)

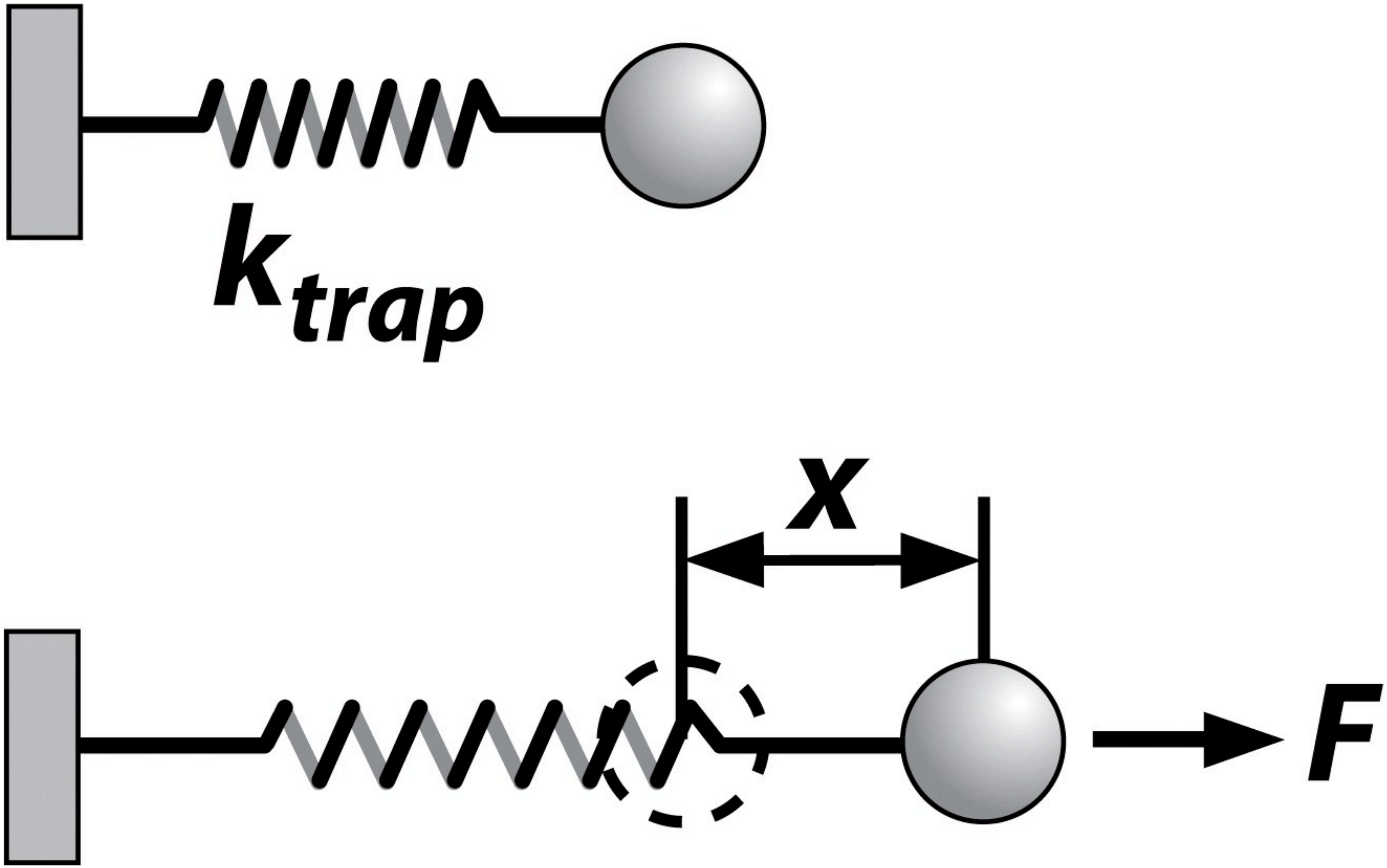
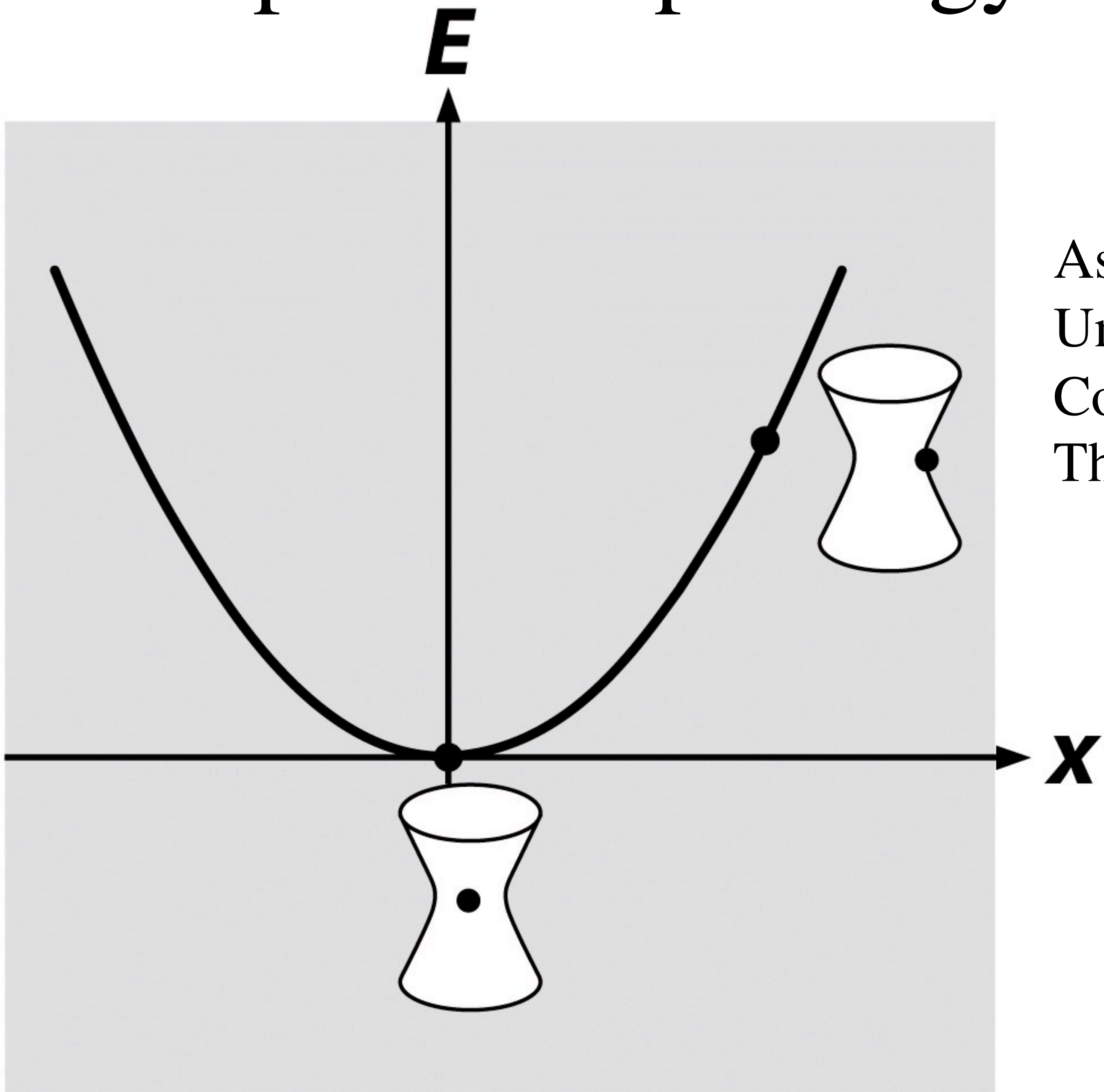


Figure 5.13b Physical Biology of the Cell (© Garland Science 2009)

$$U(x)=(1/2)* k_{trap}*x^2 - F*x$$

Optical Trap Energy

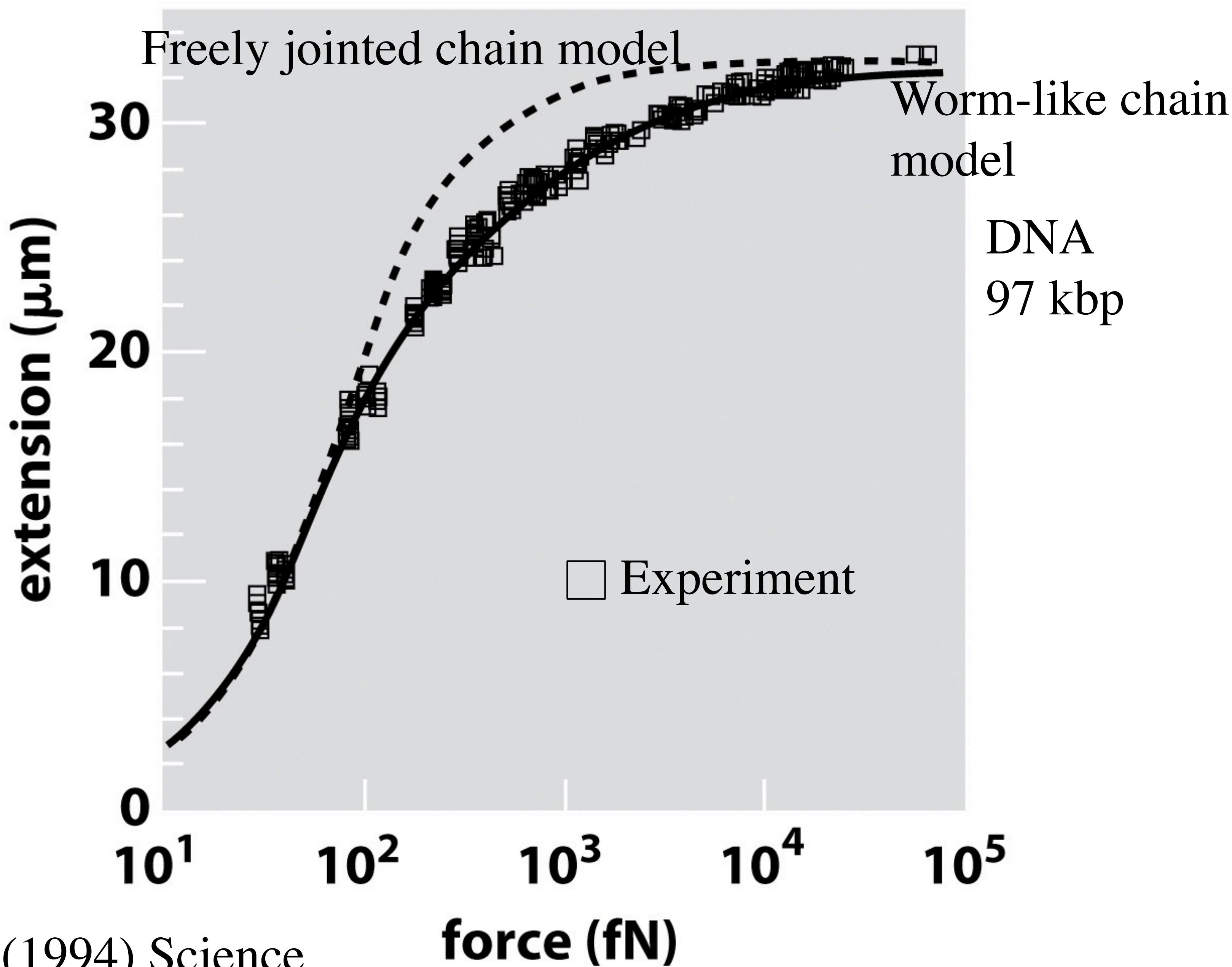


Assignment:
Under what
Conditions does
This curve hold?

x_{eq}=

Figure 5.13c Physical Biology of the Cell (© Garland Science 2009)

DNA Force Extension



Bustamente (1994) Science

Figure 5.14 Physical Biology of the Cell (© Garland Science 2009)

Entropic Elasticity of λ-Phage DNA

DNA is unique among polymers both for its size, and for its long persistence length, $A \approx 50$ nm (*1*). Since A encompasses many base pairs, and thus to a large degree is averaged over sequence, a continuum elastic description of DNA bending is plausible. Recently, S. B. Smith *et al.* made a direct mechanical measurement of the force versus extension $F(x)$ for a 97-kb λ-DNA dimer (*2*). Here we show that these experimental data may be precisely fit by the result of an appropriate elastic theory and thereby provide a quantitative baseline, departures from which will signal effects of more biological interest.

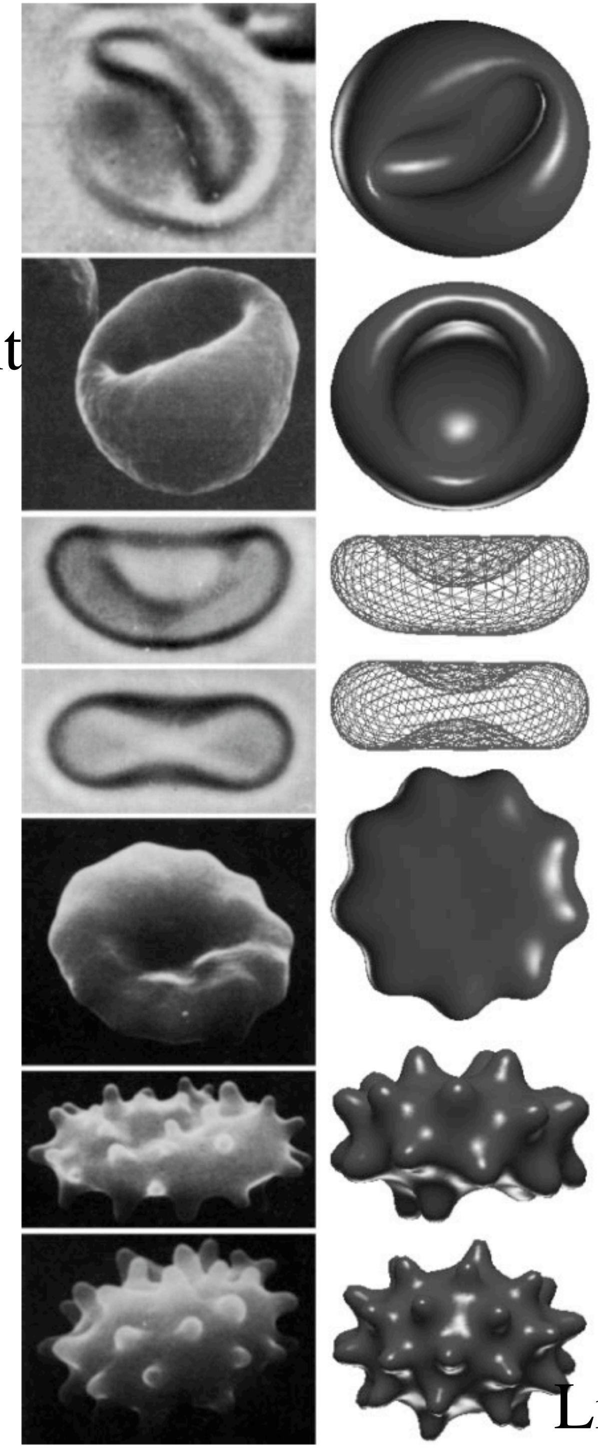
If the force is used as a Lagrange multiplier to fix the extension, the free energy of a stretched worm-like polymer corresponds to the quantum-mechanical ground state energy of a dipolar rotator with moment of inertia A, subject to an electric field F (*3*). Although the quality of the experimental data required us to supply a complete numerical solution, both the large- and small-force limits admit analytical asymptotic solutions that are summarized by the following interpolation formula:

$$FA/kT = \frac{1}{4}(1 - x/L)^{-2} - \frac{1}{4} + x/L$$

where k is Boltzmann's constant, T is temperature, and L is the molecular contour length. For large $F \gg kT/A$, the accessible conformations reduce to quadratic fluctuations around a straight line, while for $F \ll kT/A$ the polymer conformation becomes a directed random walk. The force needed to extend a freely jointed chain model diverges less strongly as $x \rightarrow L$ [$F \propto (1 - x/L)^{-1}$] as fluctuations inside each segment are suppressed.

A nonlinear least-squares fit of the exact $F(x)$ to experimental data (Fig. 1) gives $L = 32.80 \pm 0.10$ μm and $A = 53.4 \pm 2.3$ nm (90% confidence level errors; $\chi^2/n = 1.04$ for $n = 303$ data points). This L is close to the crystallographic value of 32.7 μm, while A is in good agreement with the results of cyclization studies (*1*). Refinements of the present technique may well become the most accu-

RBC Shapes



Experiment

Minimum-energy shapes calculated from model

Stomatocyte-Discocyte-Echinocyte sequence of human RBCs

Lim, Wortis, Mukhopadhya (2002) PNAS

Energy Model

$$F_{ADE}[S] = \frac{\kappa_b}{2}\oint_S d\mathcal{A}(2H - C_0)^2 + \frac{\bar{\kappa}}{2}\frac{\pi}{\mathcal{A}D^2}(\Delta\mathcal{A} - \Delta\mathcal{A}_0)^2, \quad [1]$$

D = membrane thickness

A = membrane area

$\kappa_B, \bar{\kappa}$ = bending elastic moduli

S= surface of closed vescicle

H=local mean curvature

C_0=spontaneous curvature

Area-difference elasticity model

Helfrich (1973) Naturforsch., Lim, Wortis, Mukhopadhya (2002)

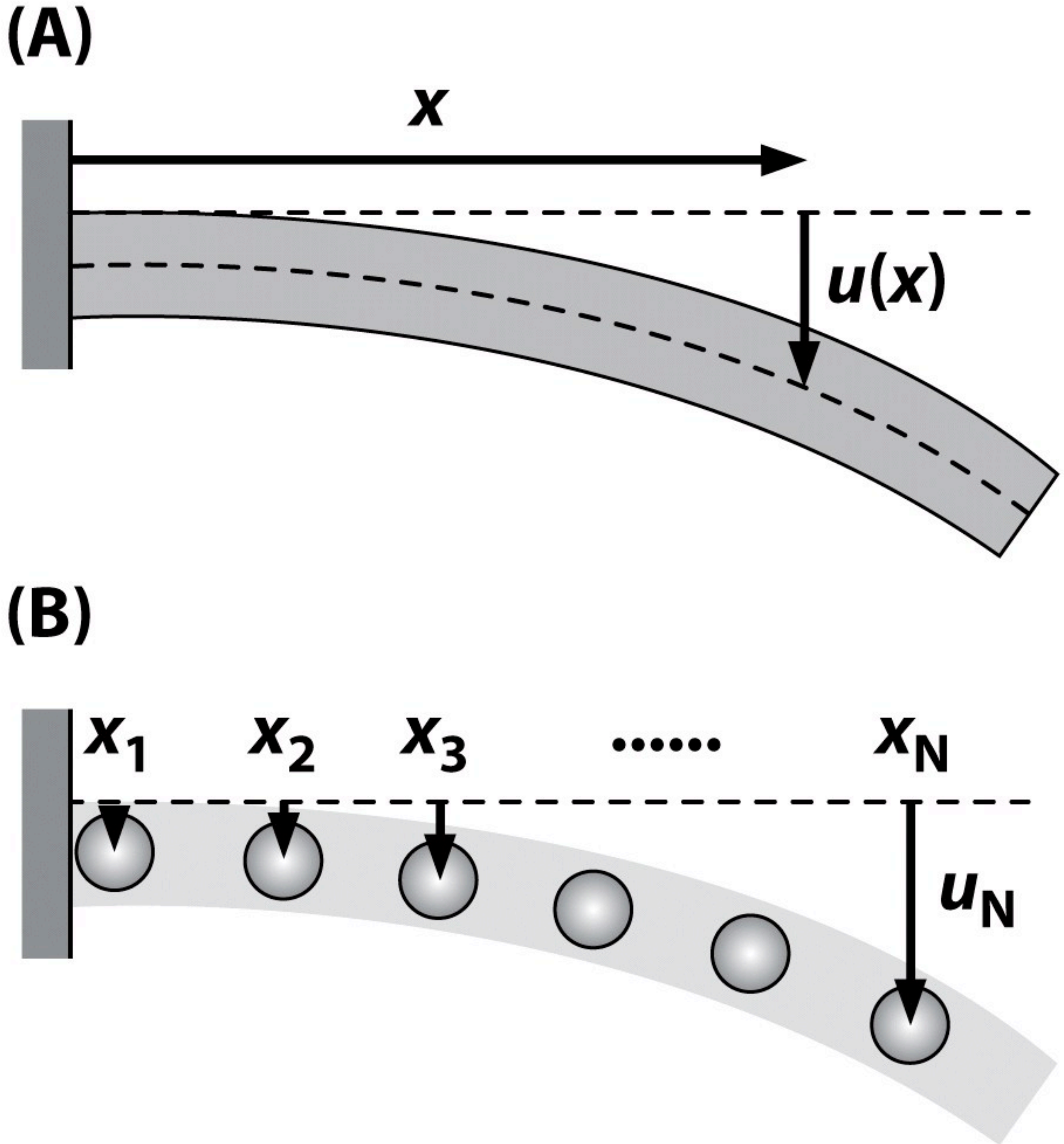


Figure 5.15 Physical Biology of the Cell (© Garland Science 2009)

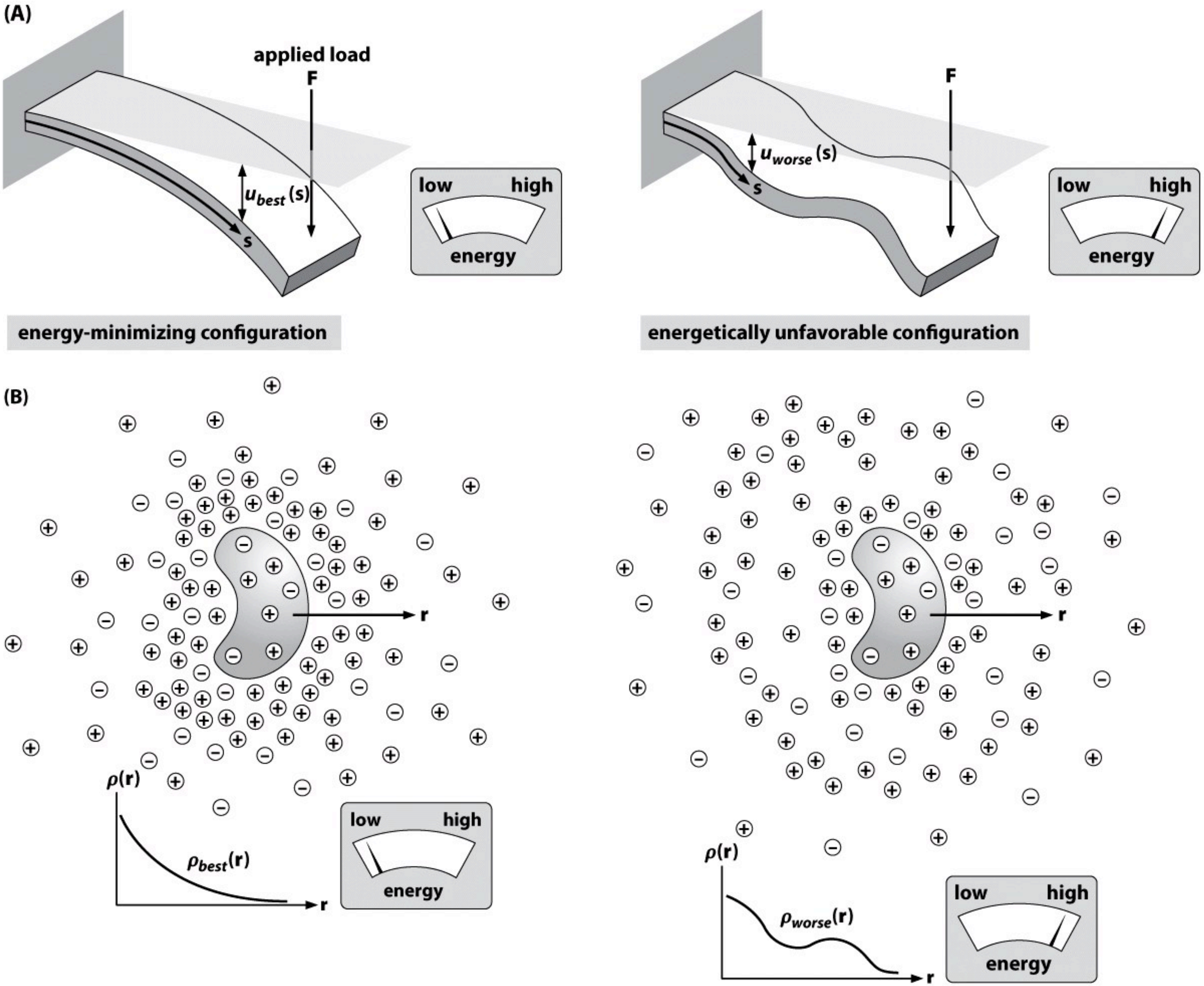


Figure 5.16 Physical Biology of the Cell (© Garland Science 2009)

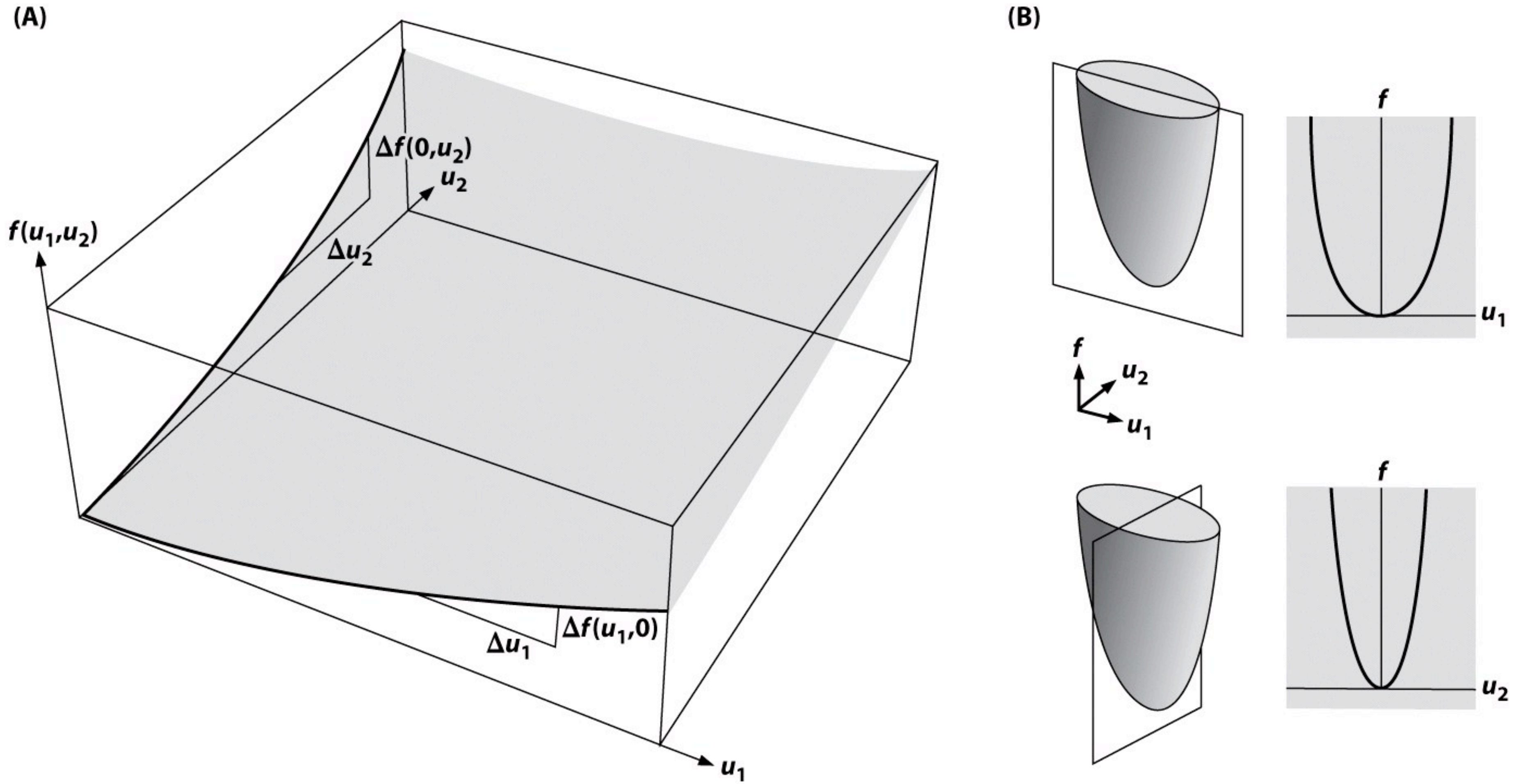


Figure 5.17 Physical Biology of the Cell (© Garland Science 2009)

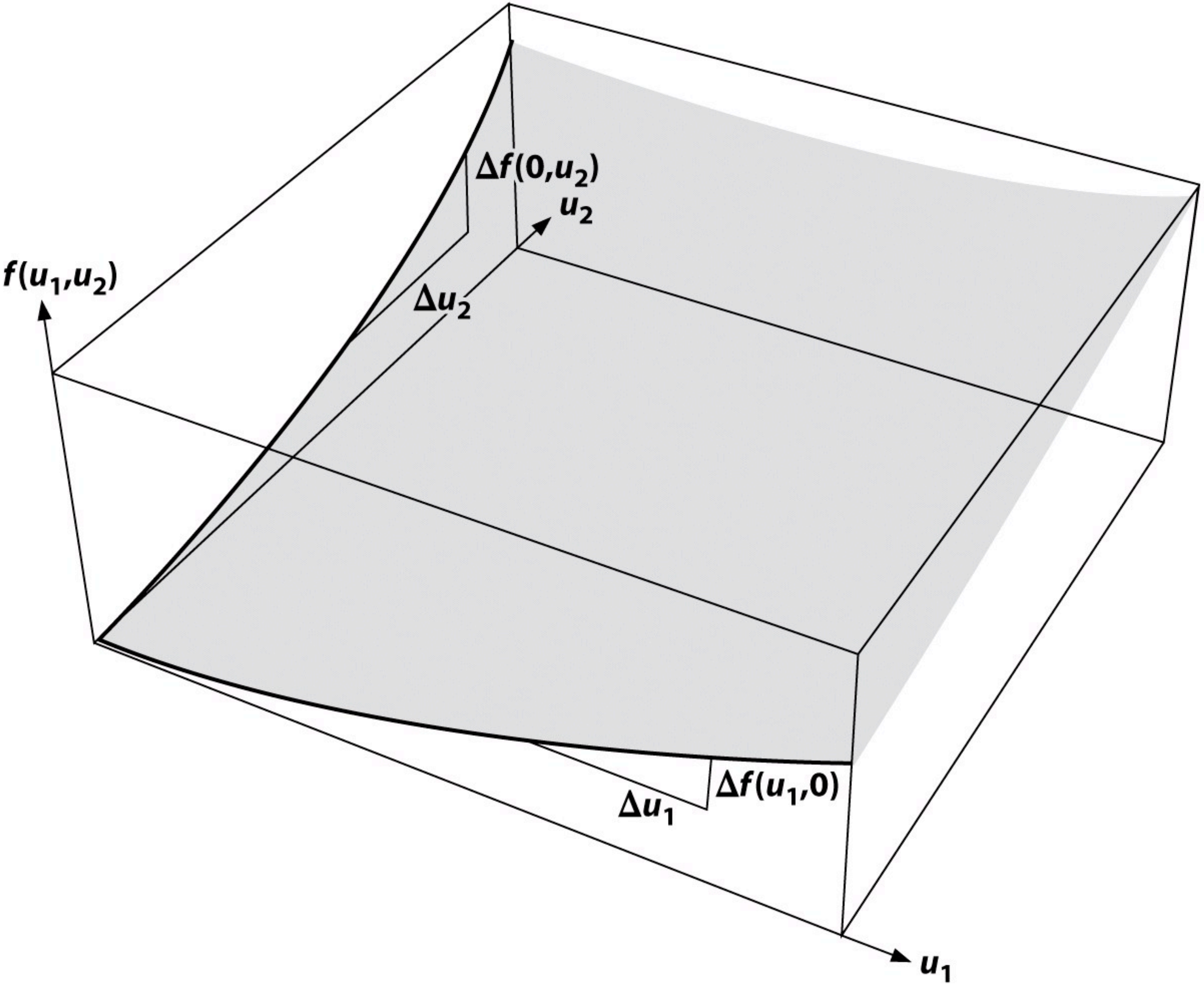


Figure 5.17a Physical Biology of the Cell (© Garland Science 2009)

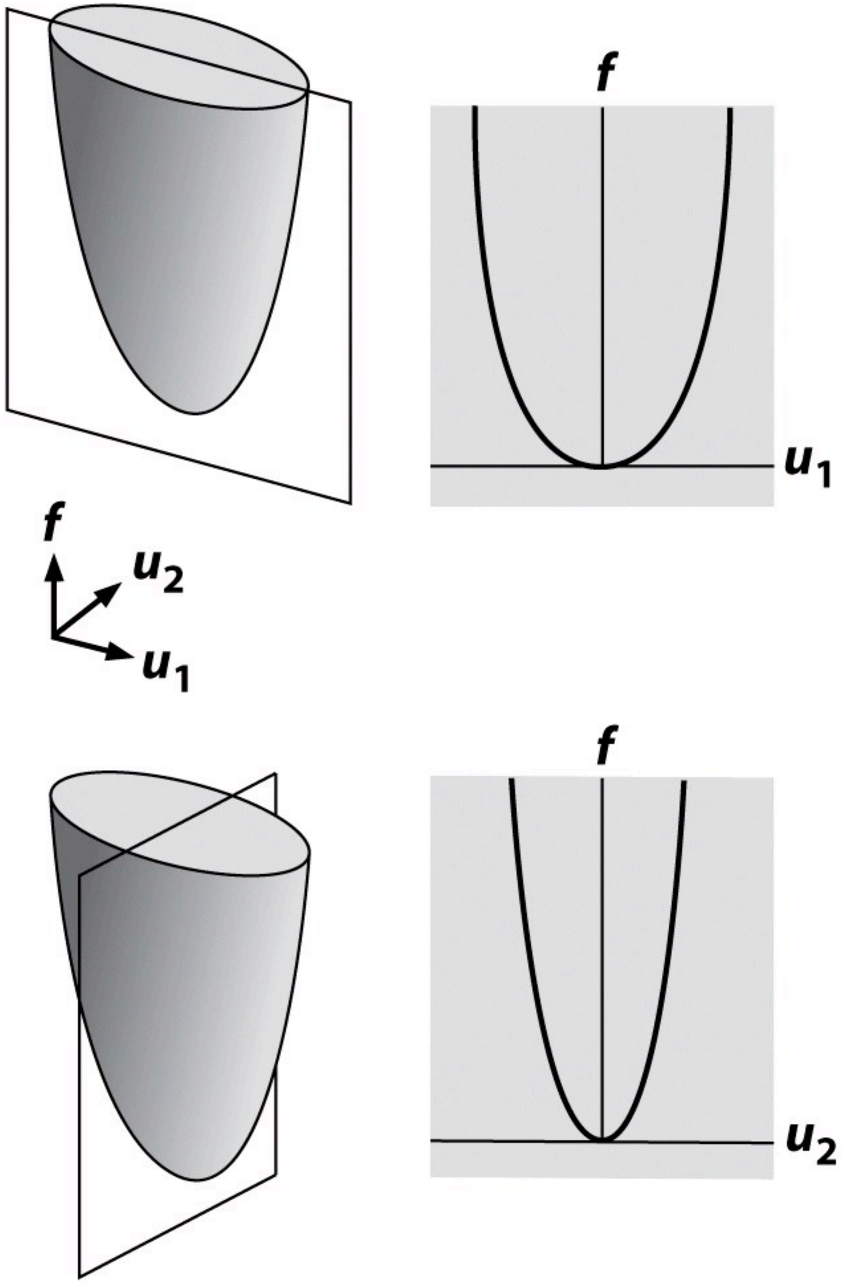


Figure 5.17b Physical Biology of the Cell (© Garland Science 2009)

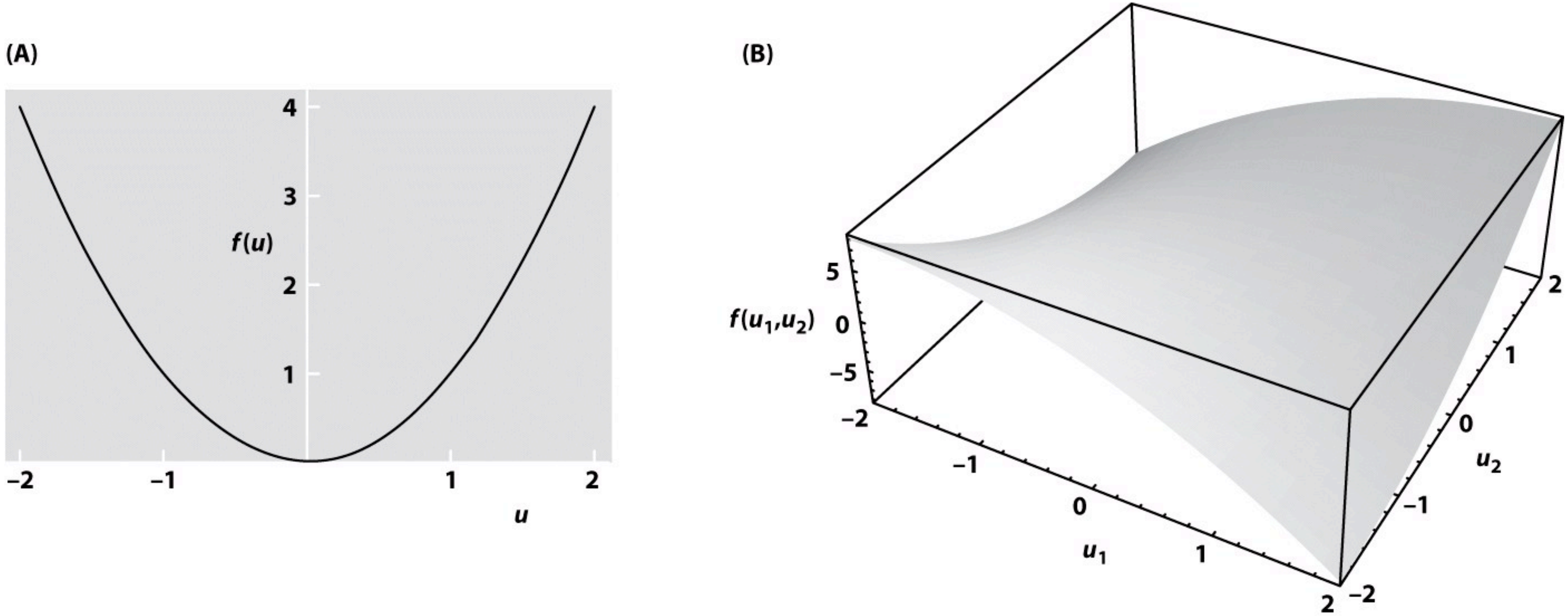


Figure 5.18 Physical Biology of the Cell (© Garland Science 2009)

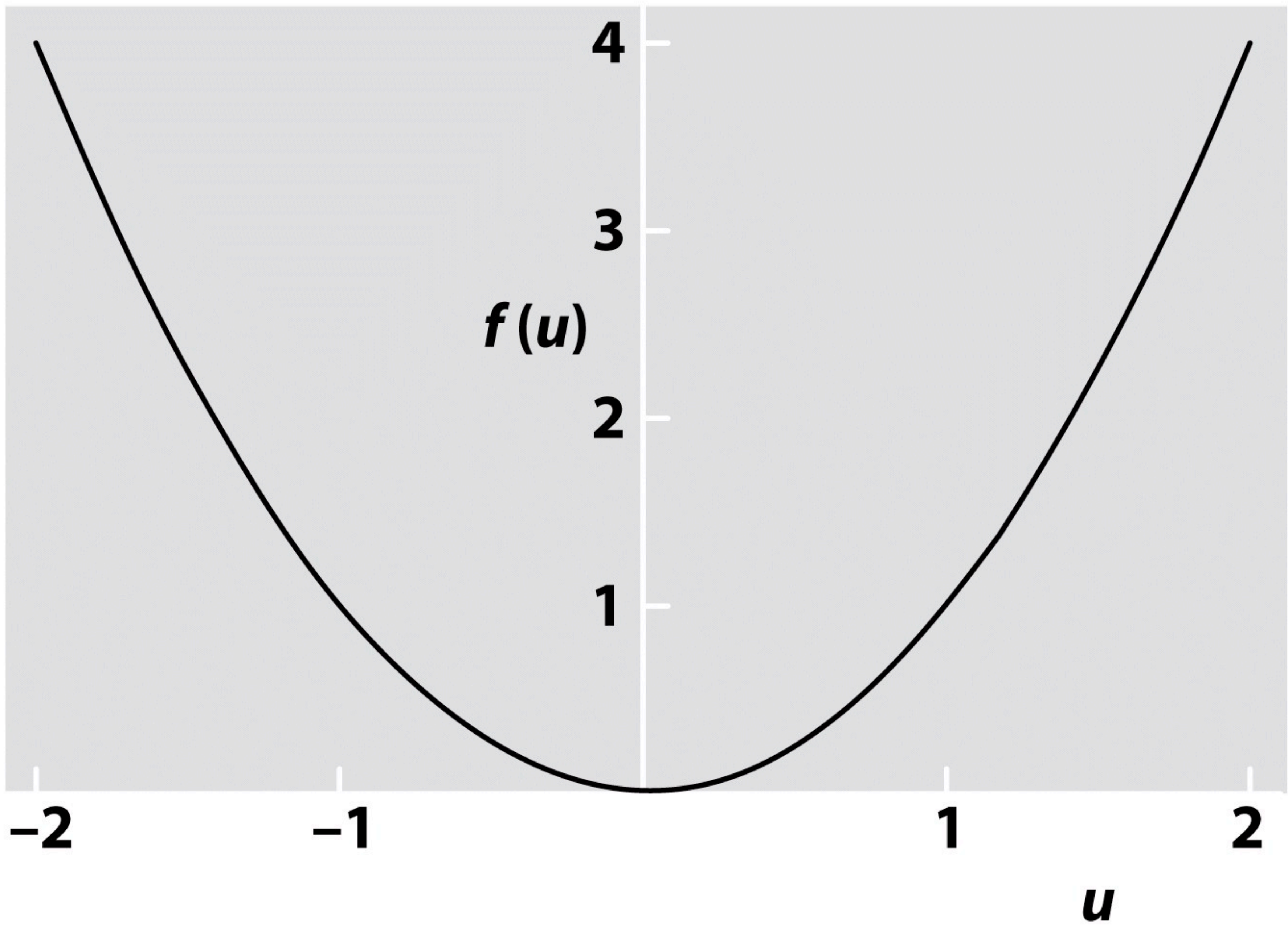


Figure 5.18a Physical Biology of the Cell (© Garland Science 2009)

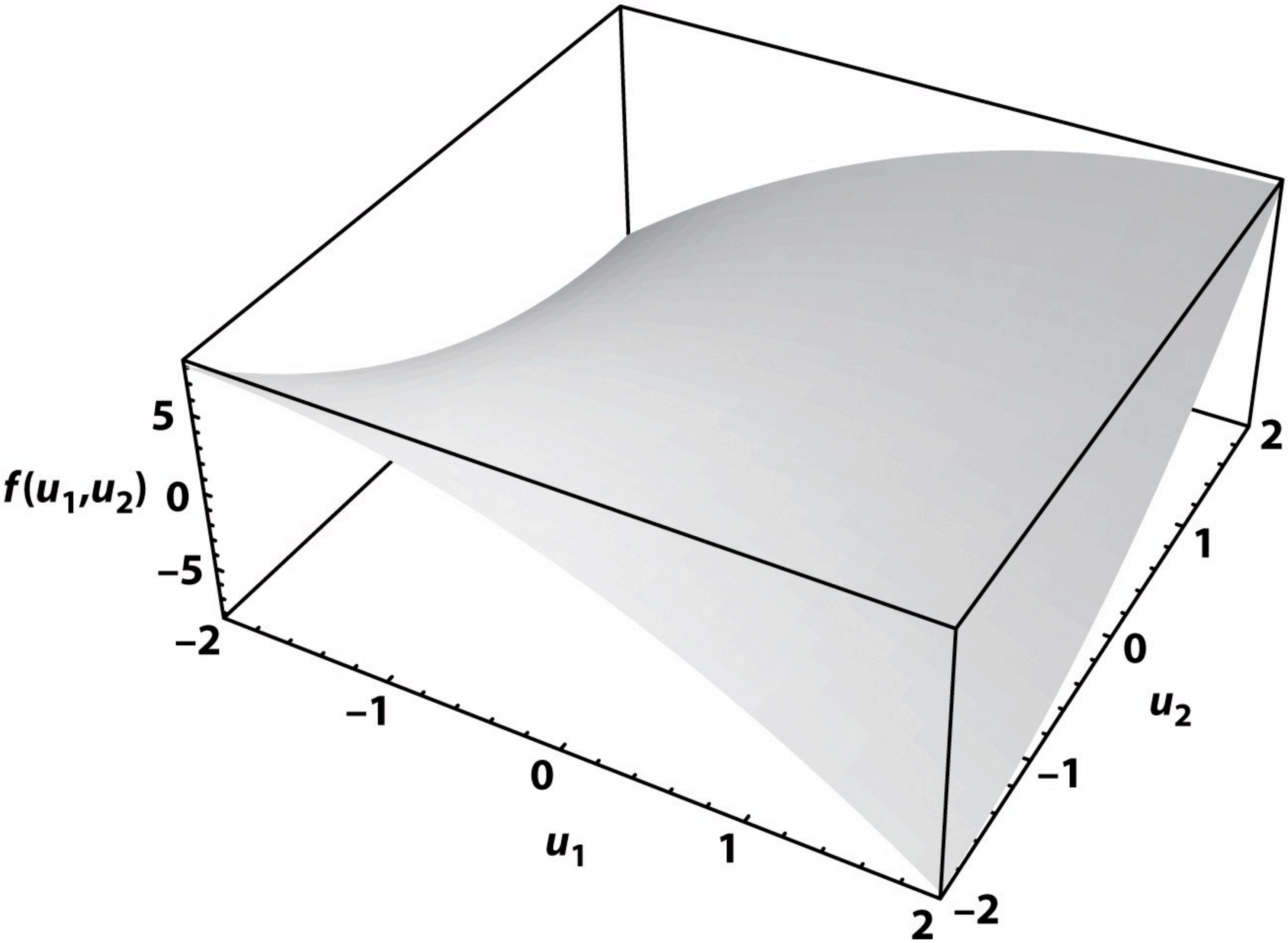


Figure 5.18b Physical Biology of the Cell (© Garland Science 2009)

Mechanical and Energy Equilibrium

2010-10-25

Potential Energy

$$U(x) = U(x_{eq} + \Delta x) \approx U(x_{eq}) + \left.\frac{dU}{dx}\right|_{eq} \Delta x + \frac{1}{2}\left.\frac{d^2U}{dx^2}\right|_{eq} \Delta x^2$$

Δx = excursion around the equilibrium point

Configurational Energy

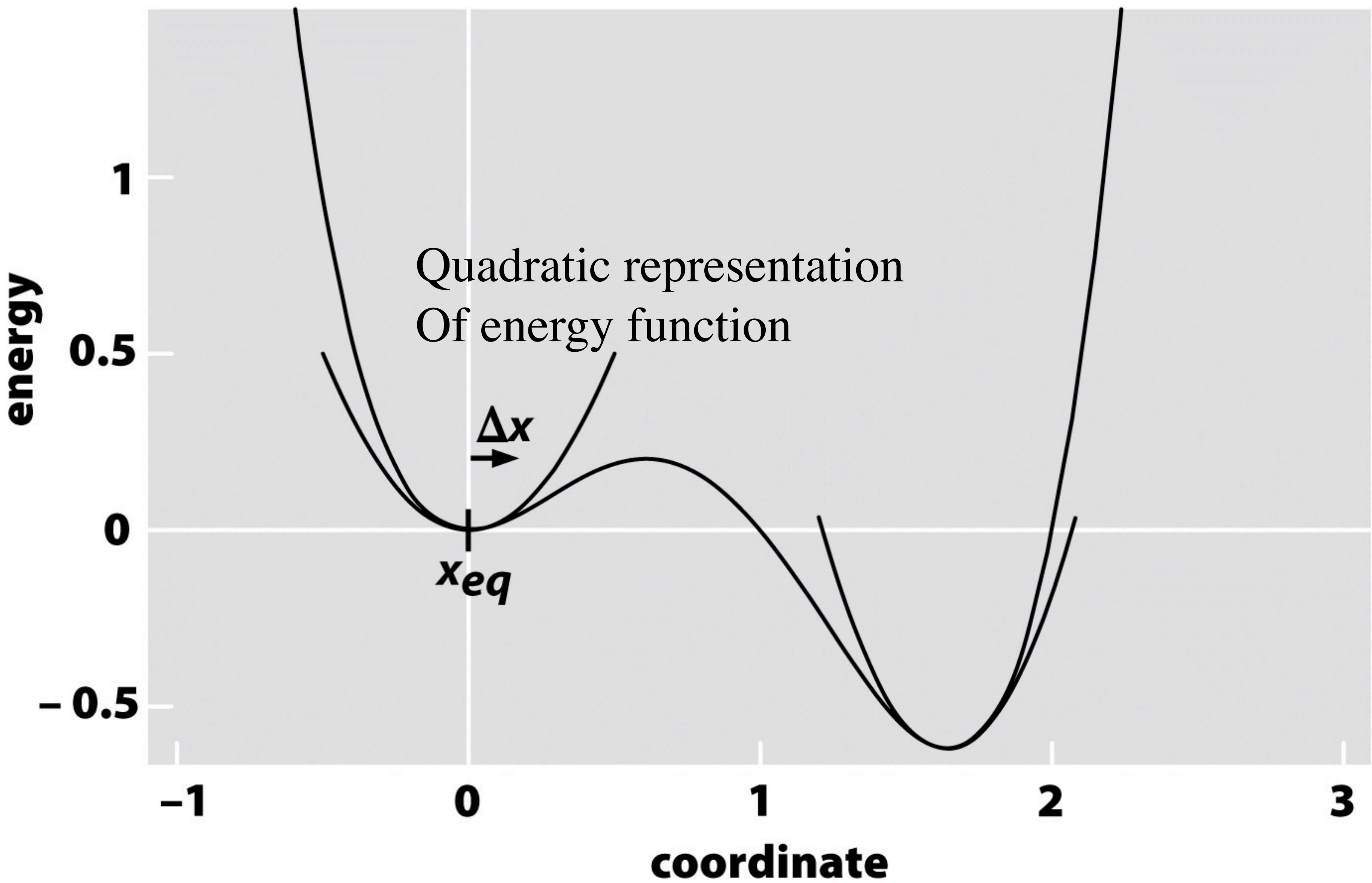


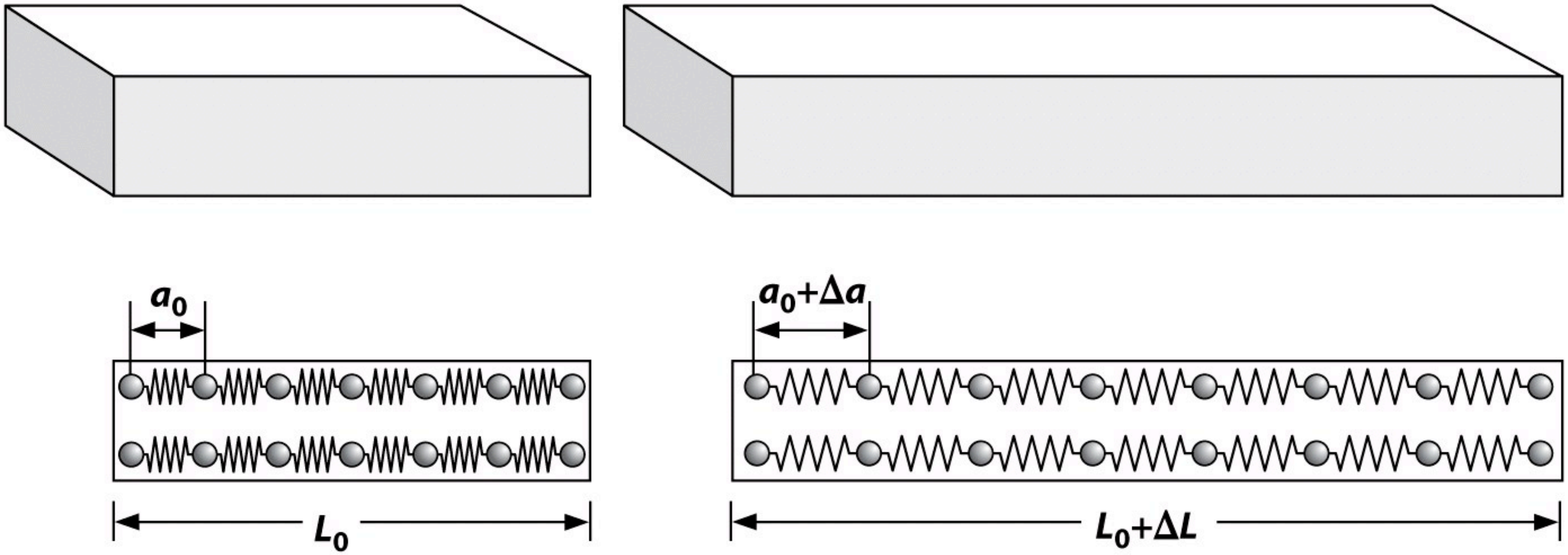
Figure 5.19 Physical Biology of the Cell (© Garland Science 2009)

Since equilibrium demands the first derivative be zero,

$$U(x_{eq} + \Delta x) \approx U(x_{eq}) + \frac{1}{2} \left. \frac{d^2U}{dx^2} \right|_{eq} \Delta x^2$$

This is of the form $U(x) = kx^2$

Stretching of a Rod



Stress

Strain

Microscopic basis

Energy of Deformation

Strain energy

Integration of effect due to small springs

F-actin Stretching by Axial Force

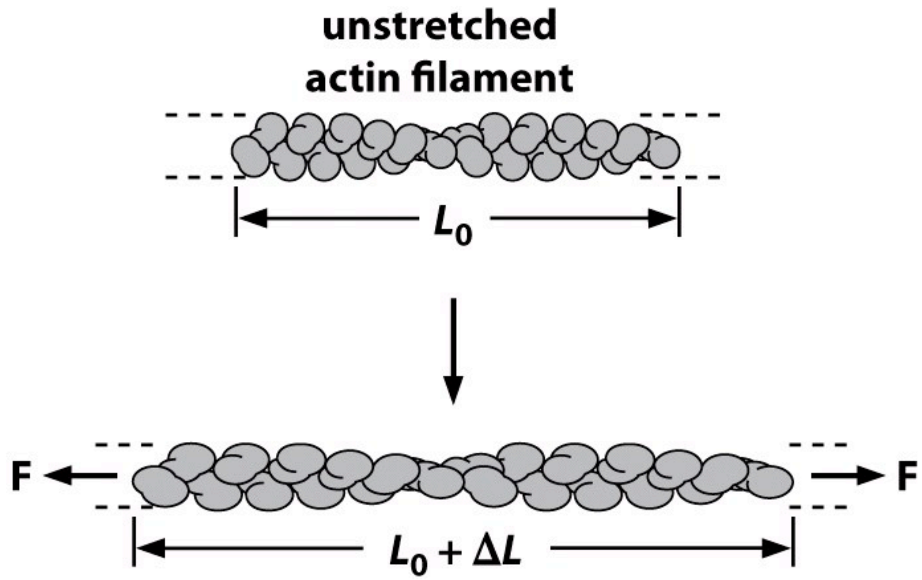
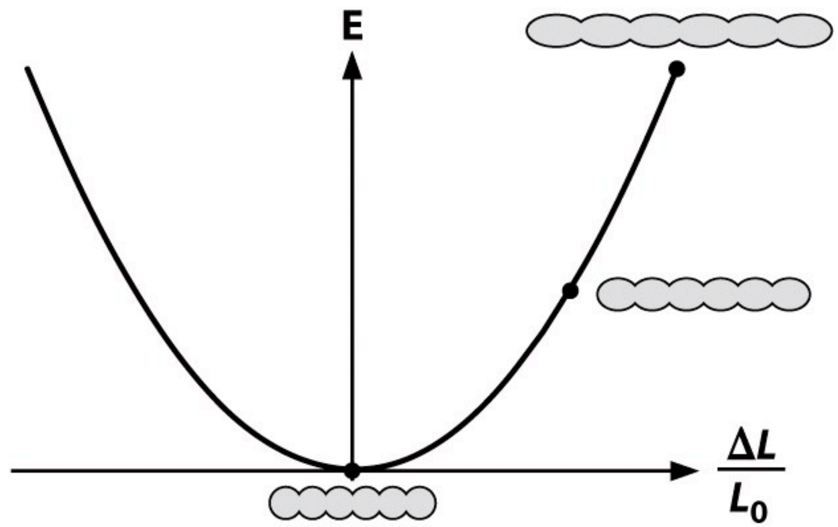


Figure 5.22a Physical Biology of the Cell (© Garland Science 2009)



Lipid Membrane Thickness Change

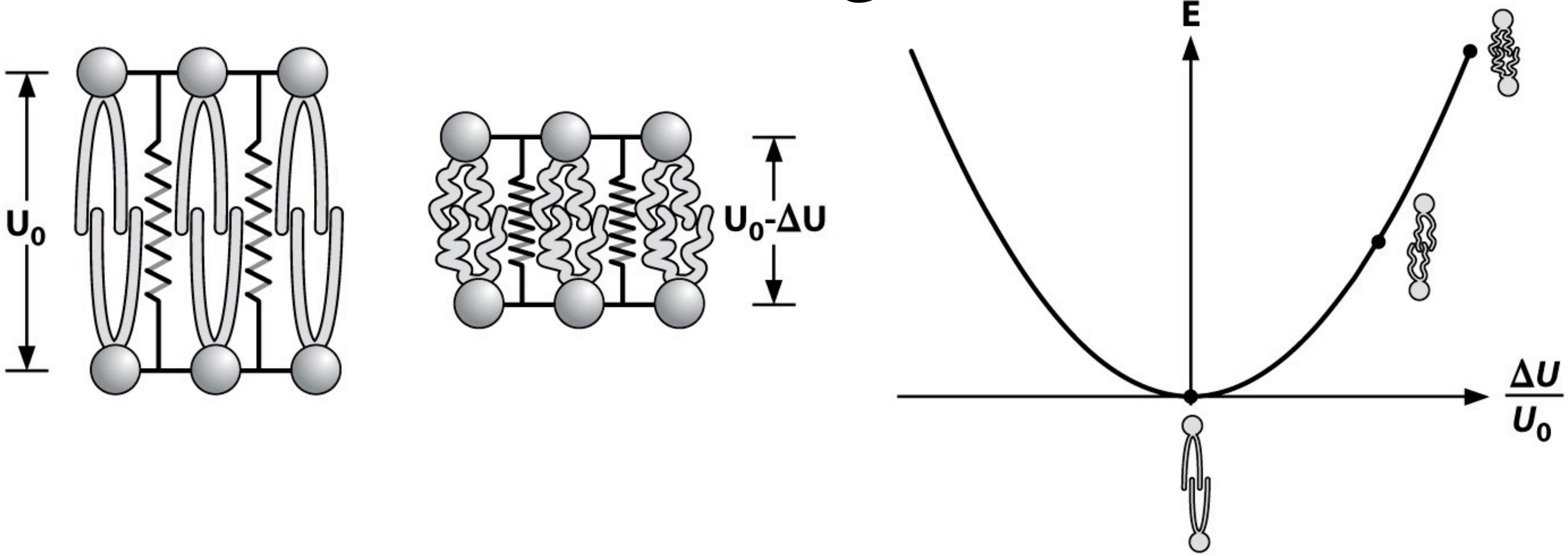


Figure 5.22b Physical Biology of the Cell (© Garland Science 2009)

Free Energy

- Equilibrium configuration of systems in terms of mechanics
- Thermal fluctuations dictate equilibria
- Energy minimization
- Entropy maximization

Opposing tendencies. Need to understand entropy

Free Energy Minimization

Free energy = energy – temperature*entropy

entropy = measure of no. of different ways of organizing the system

Equilibrium state corresponds to the minimal free energy state of a system

Entropy

$S = k_B * \ln W$

W = no. of microstates compatible with macrostate

k_B= Boltzmann constant

Protein Binding Sites on DNA

N = total no. of binding sites

Np = sites occupied by protein of interest

Energy of non-specific binding uniform

Possible Arrangement of Proteins on DNA

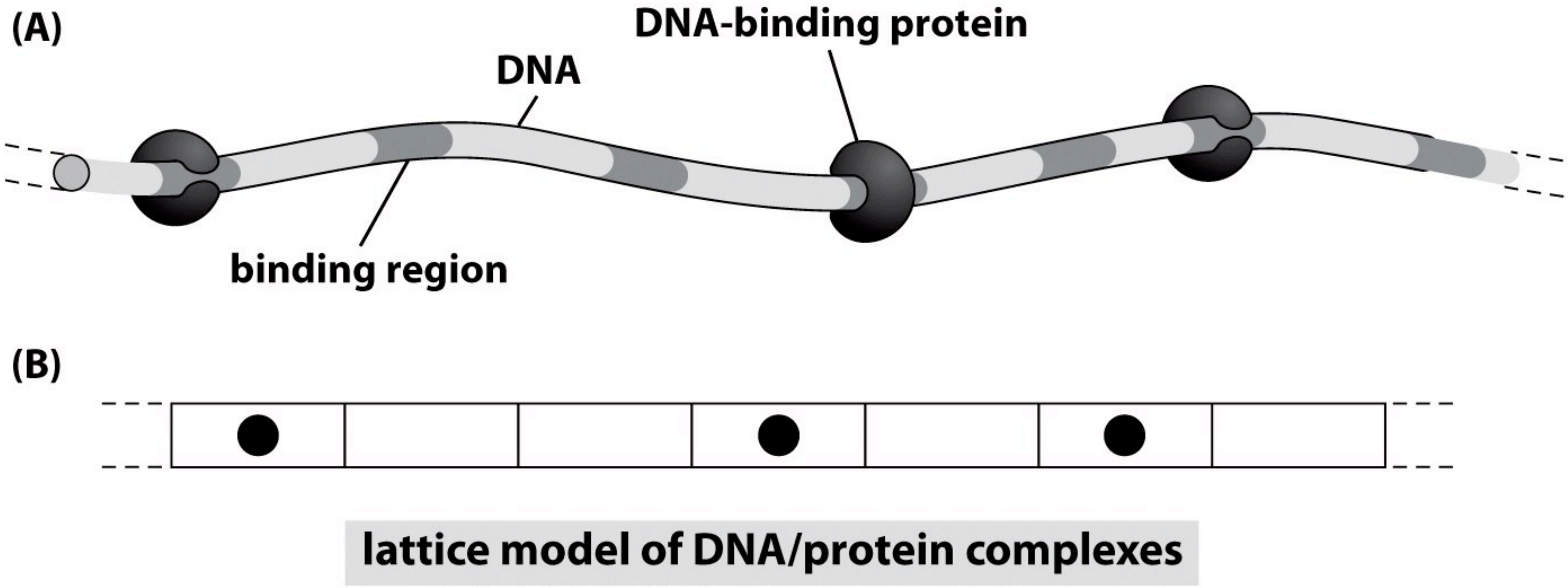


Figure 5.23 Physical Biology of the Cell (© Garland Science 2009)

Entropy of DNA-Protein System

$S = k_B \ln W(N_p;N)$

S = entropy

$W(N_p;N)$ = No. of ways of re-arranging N_p proteins on N binding sites

Total no. of ways of laying down N_p proteins

$N x (N-1) x (N-2) x \ldots (N-N_p+1)$

Independent of arrangement…

Thus

$$W(Np;N) = \frac{N*(N-1)*(N-2)\ldots*(N-N_P+1)}{N_P*(N_P-1)\ldots*1}$$

Multiply and divide by $(N - N_P)!$

$$W\left(N;N_P\right) = \frac{N!}{N_P!(N - N_P)!}$$

Lac Repressor

- No. of proteins (N_P) ~ 10
- E. coli genome (no. of binding sites N) ~ 5×10^6 bps

- $W \sim 3 \times 10^{60}$

Entropy

$$S = k_B \ln \frac{N!}{N_P!(N - N_P)!}$$

By Stirling approximation

$$\ln N! \approx N \ln N - N$$

$S = -k_B N[c*\ln c + (1-c)*\ln(1-c)]$

Where

$c = N_p/N$

Entropy of DNA Binding Proteins

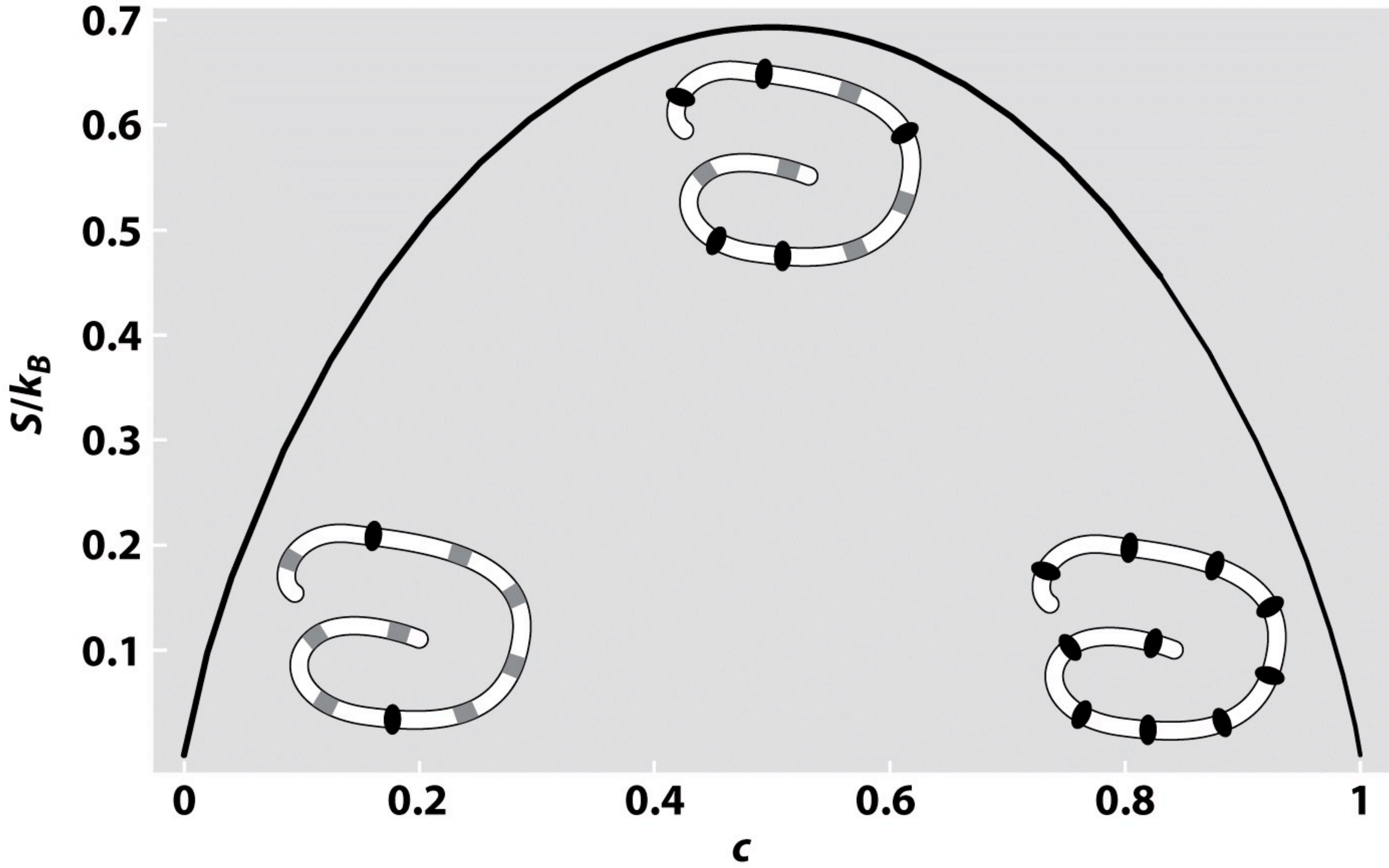


Figure 5.24 Physical Biology of the Cell (© Garland Science 2009)

Hydrogen Bonding Network of Water

Hydrophobicity:
Reducing the
H-bond network
of
water
by molecule

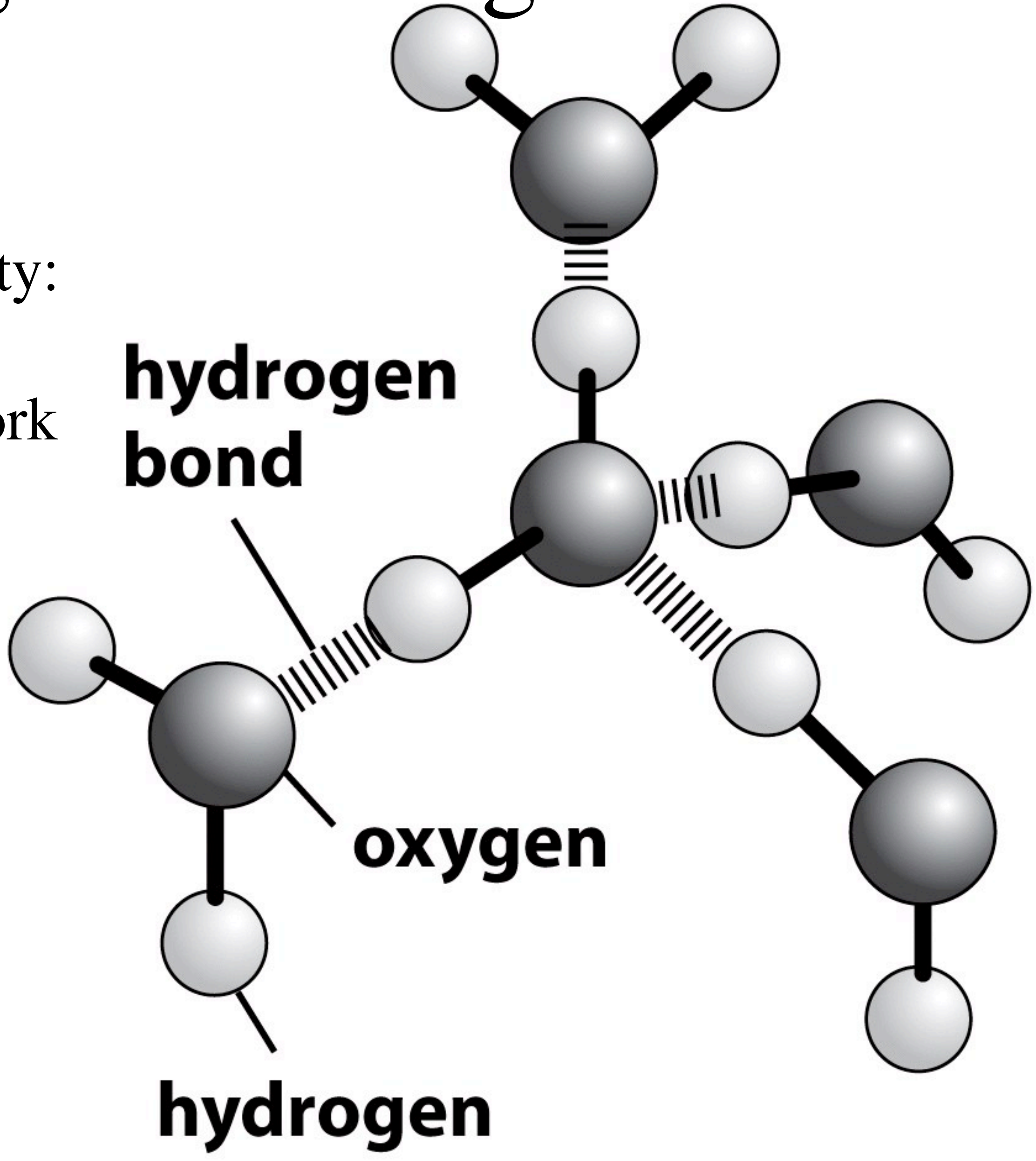


Figure 5.25 Physical Biology of the Cell (© Garland Science 2009)

Tetrahedral Arrangement of Water

Coarse grained approximation

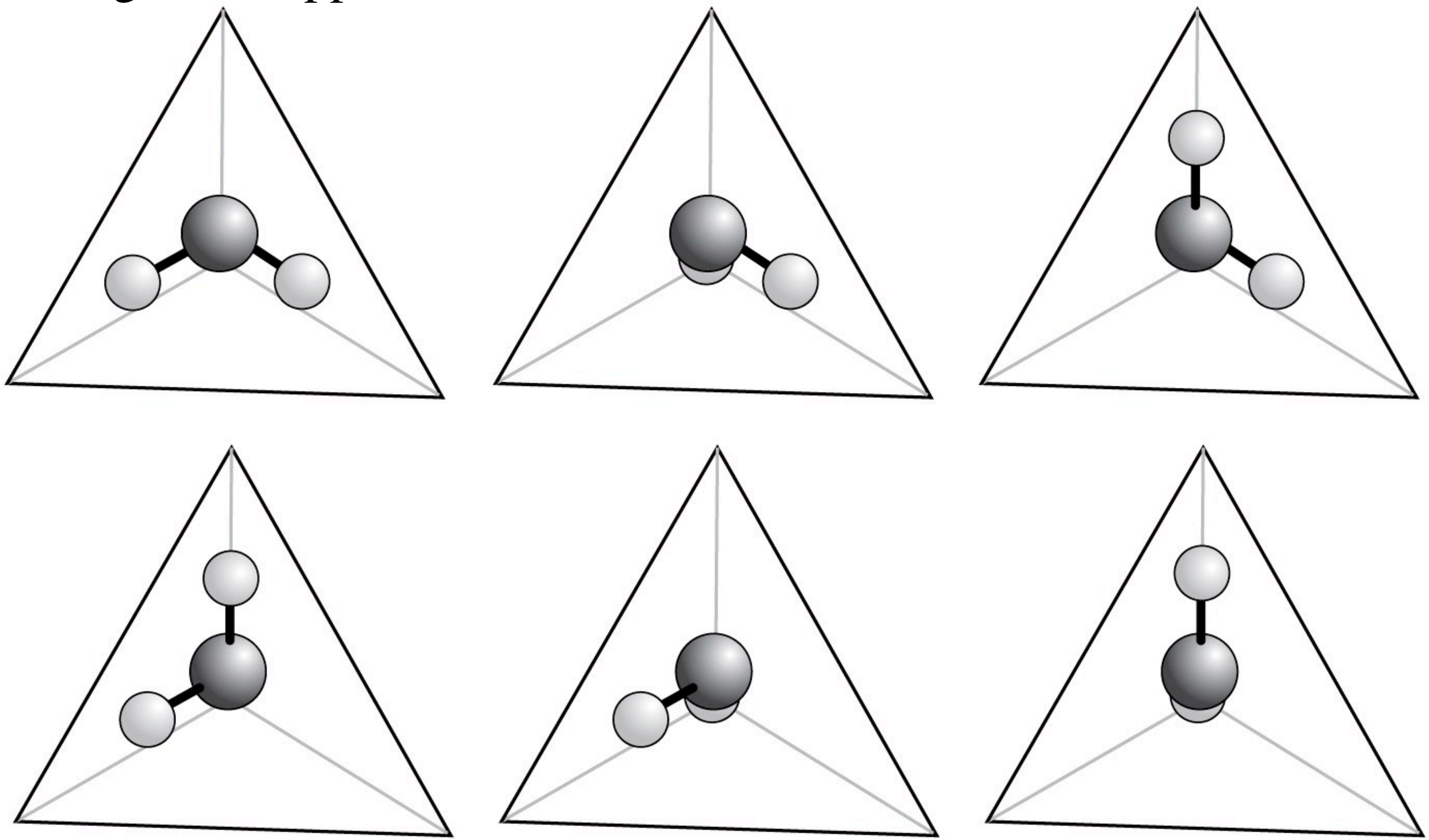


Figure 5.26 Physical Biology of the Cell (© Garland Science 2009)

Addition of Polar Element

If one vertex occupied by non-polar molecule,

3 configurations available

Entropy change:

$$\Delta S_{hydrophobic} = k_B \ln 3 - k_B \ln 6 = -k_B \ln 2$$

Free Energy Cost:

$$\Delta G_{hydrophobic}(n) = n k_B T \ln 2$$

Free Energy Cost

γ = free enegy cost per unit area

A = effective area of interface between hydrophobic molecule and water

$$\Delta G_{hydrophobic} = \gamma A$$

Area/water-molecule

Area 10 water molecules ~ 1 nm^2

ln 2 = 0.7

γ= $7k_BT/nm^2$

Oxygen $\gamma \sim 1k_BT$

Octane $\gamma \sim 15k_BT$

Entropy Maximization

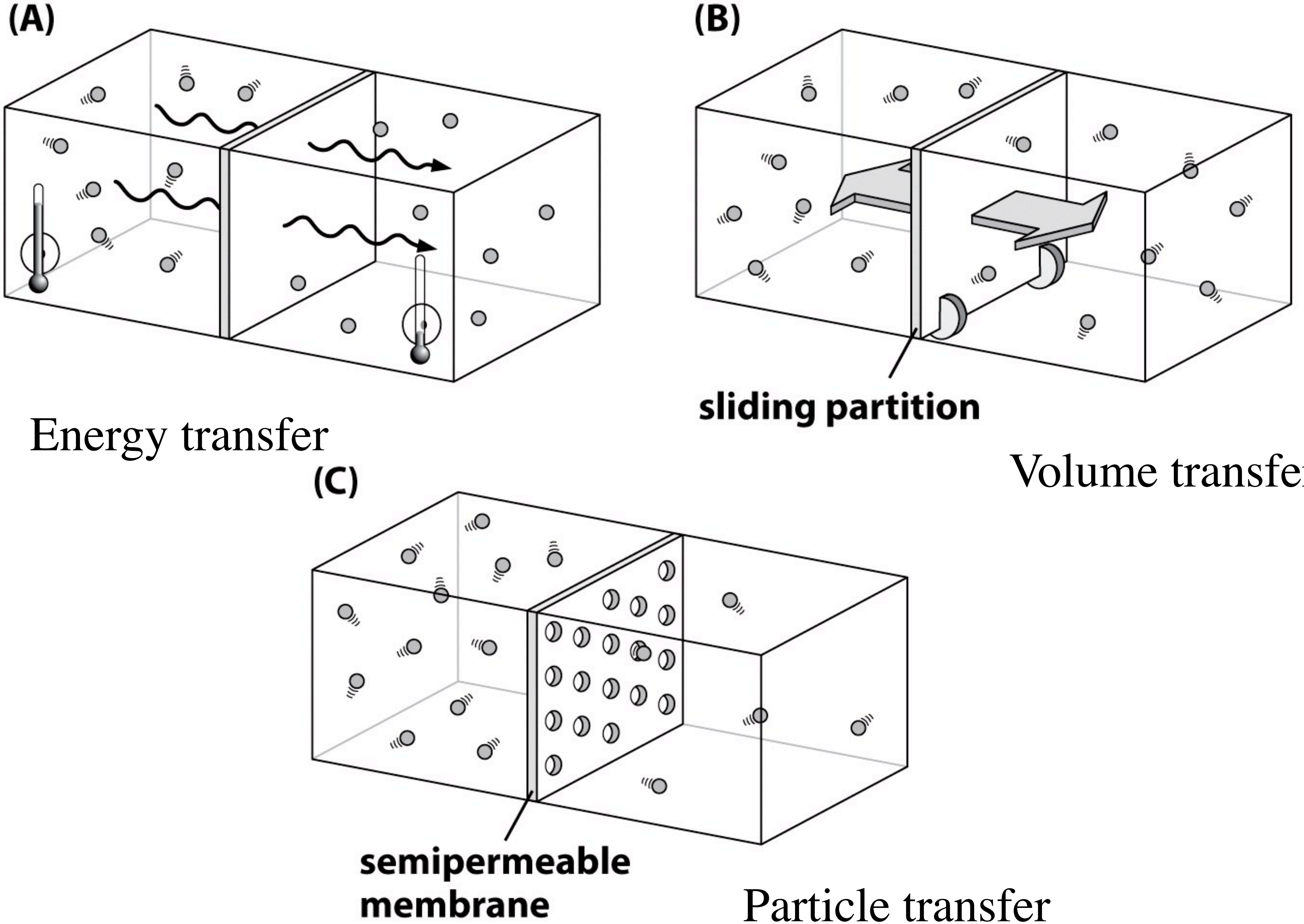
Isolated system

Constraints

If constraints removed, entropy maximal

$S_{total} = S1(E1,V1,N1) + S2(E2,V2,N2)$

Isolated System



Energy transfer

Volume transfer

Particle transfer

Figure 5.27 Physical Biology of the Cell (© Garland Science 2009)

Examples

- Force-extension characteristics of DNA
- Depletion of forces between macromolecular assemblies
- Osmotic pressure

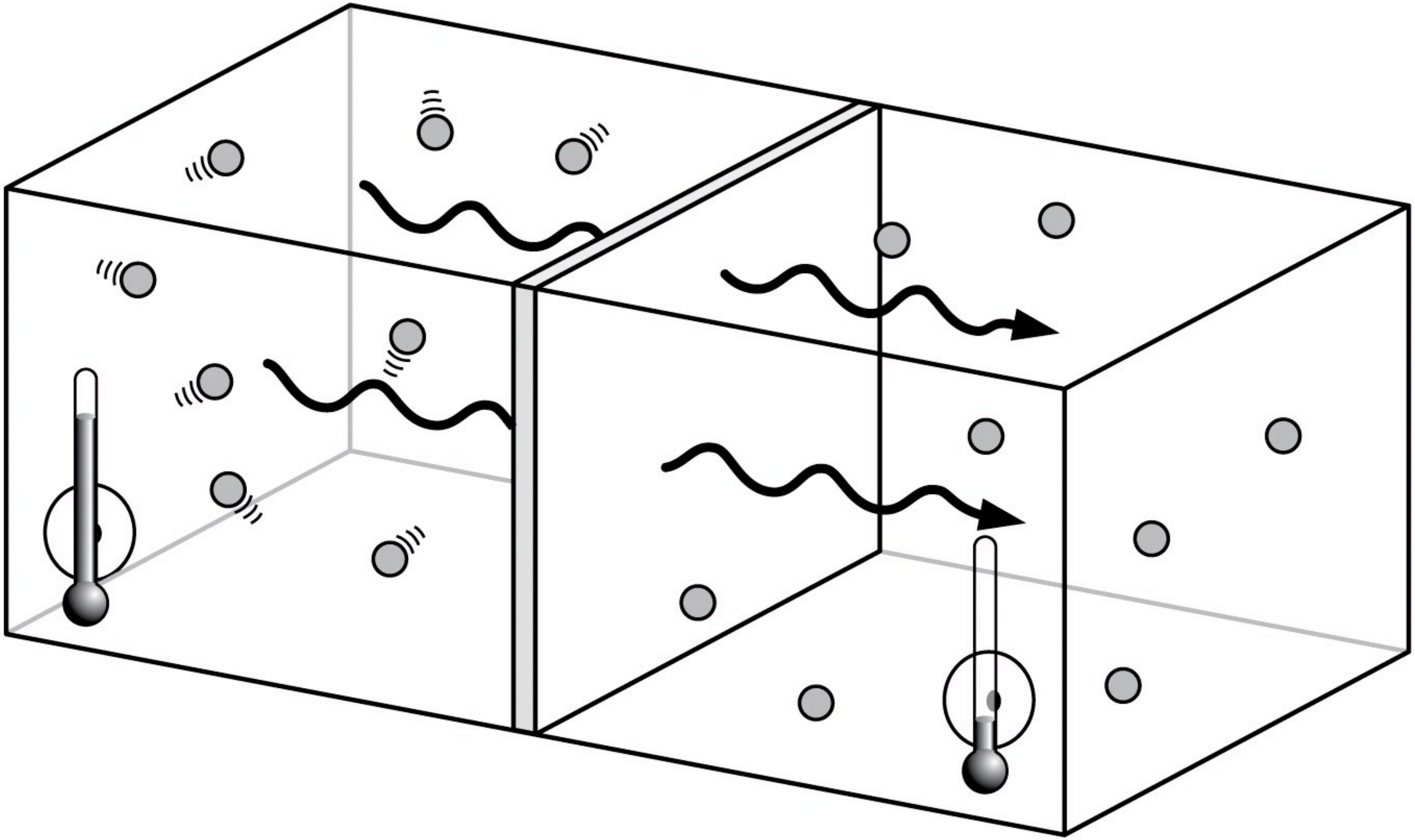


Figure 5.27a Physical Biology of the Cell (© Garland Science 2009)

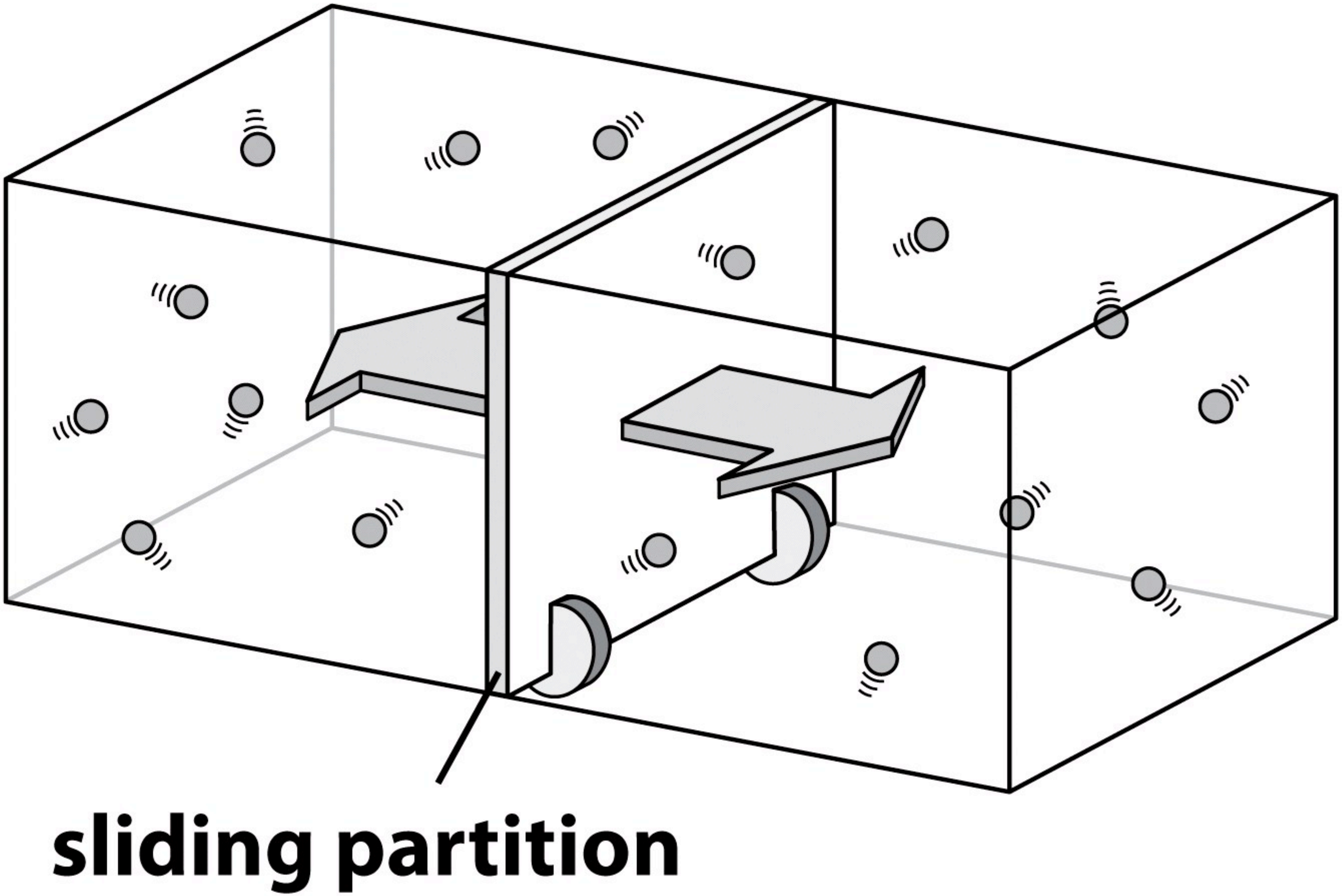


Figure 5.27b Physical Biology of the Cell (© Garland Science 2009)

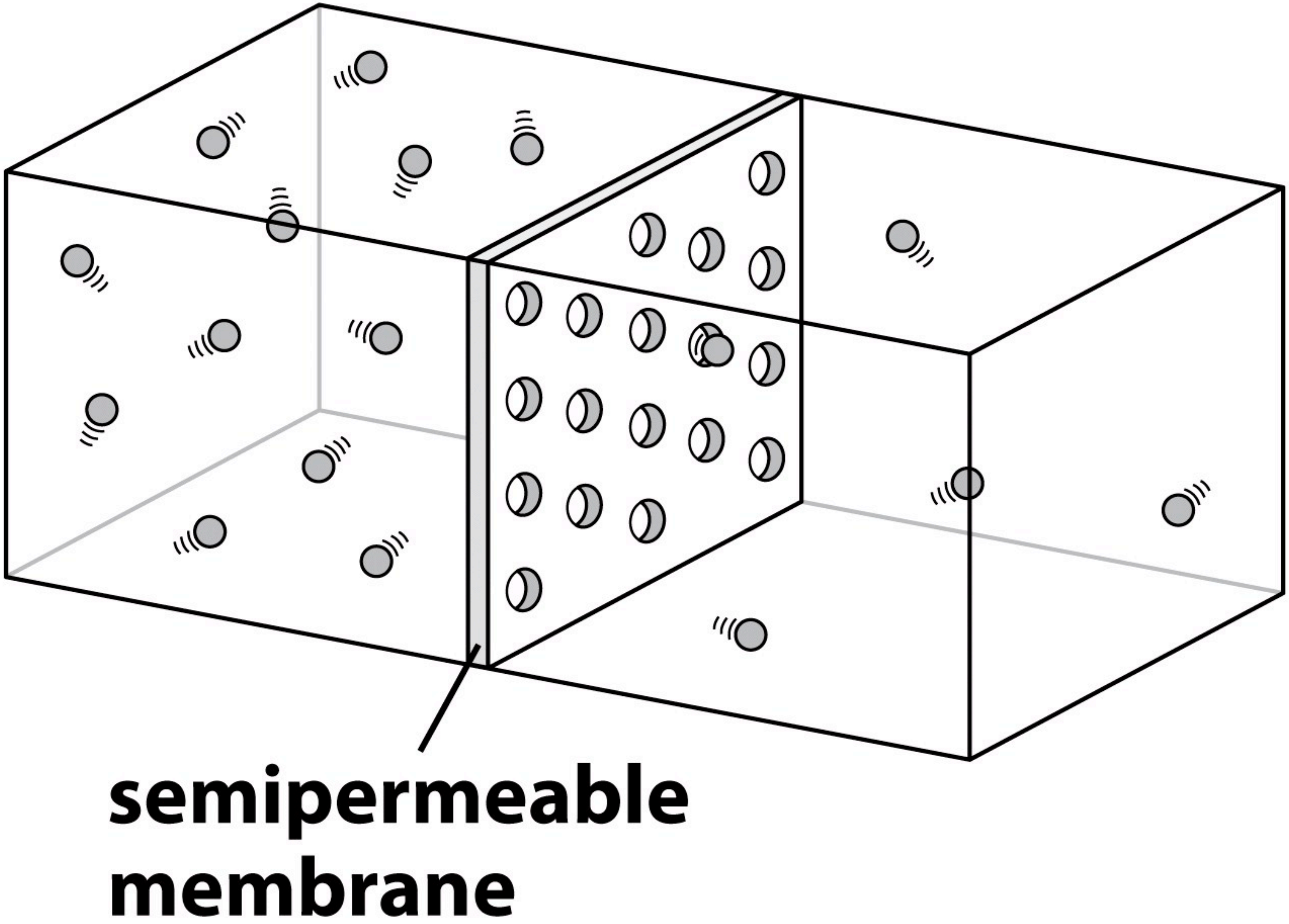


Figure 5.27c Physical Biology of the Cell (© Garland Science 2009)

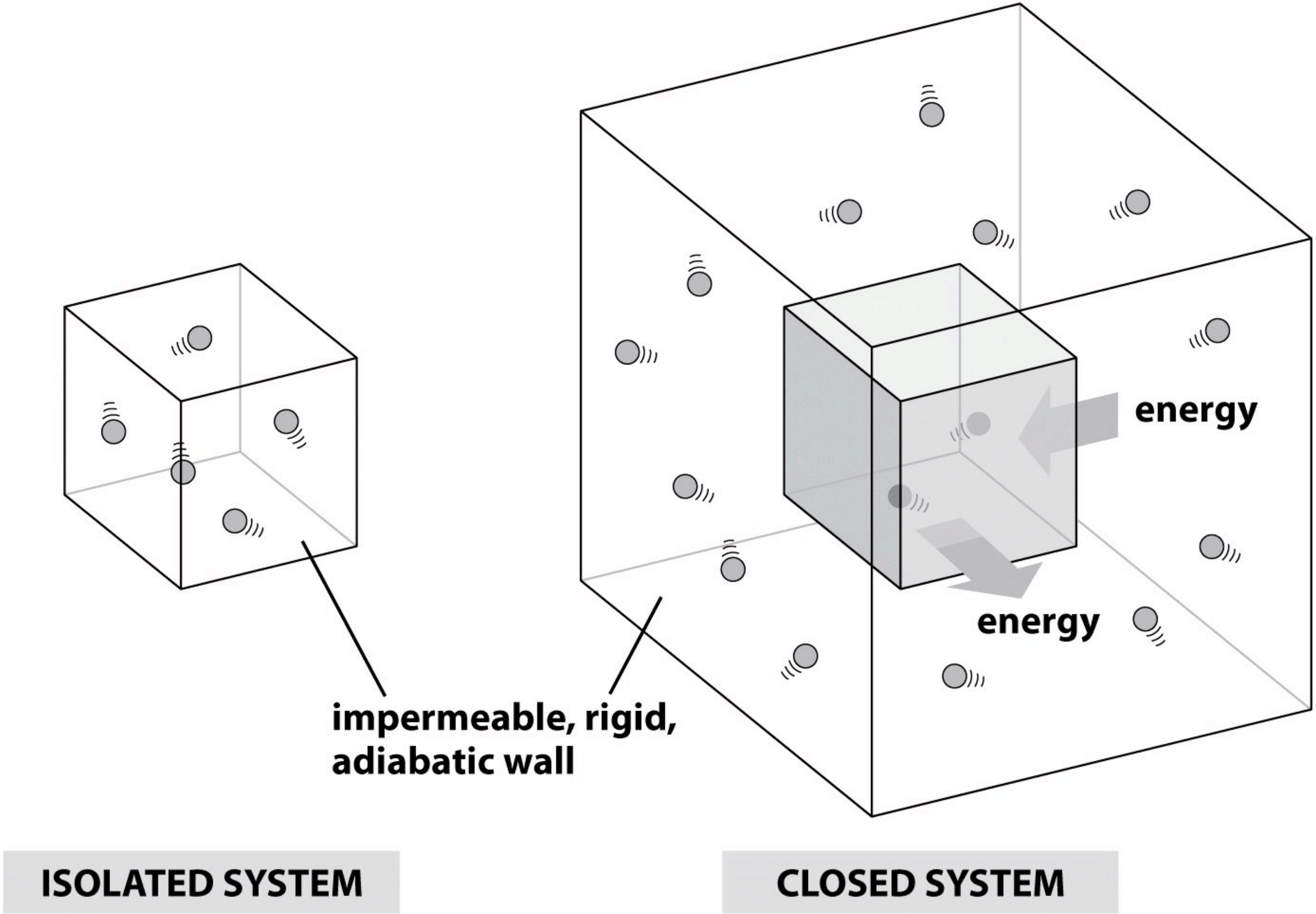
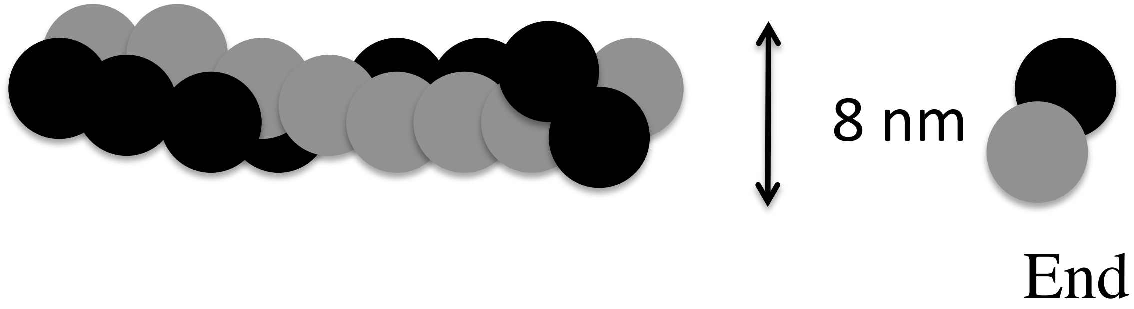


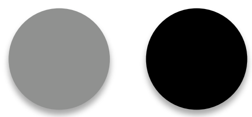
Figure 5.28 Physical Biology of the Cell (© Garland Science 2009)

Actin

f-actin (filamentous)



g-actin (globular)

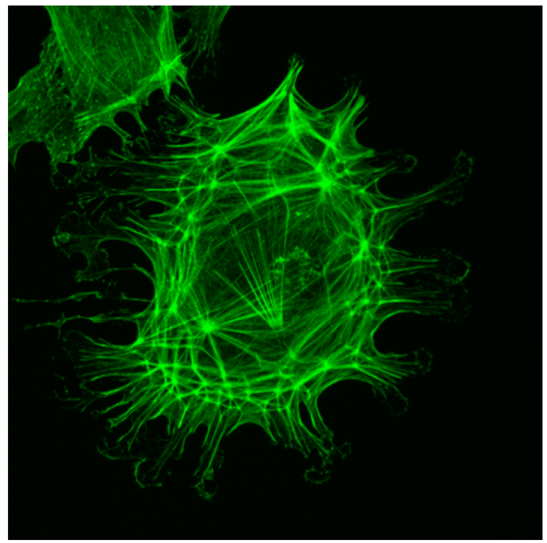


α, β, γ isoforms

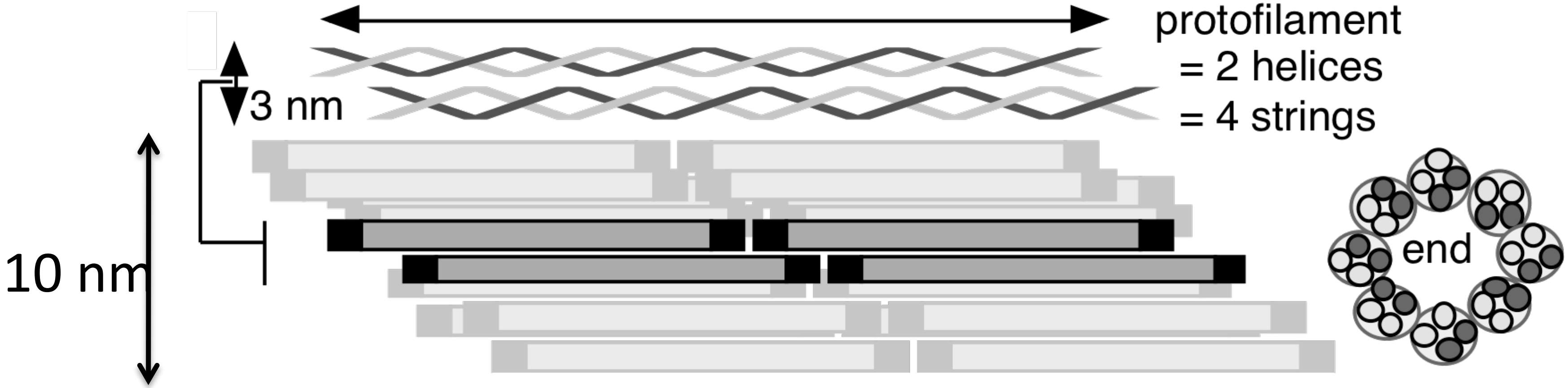
Monomer

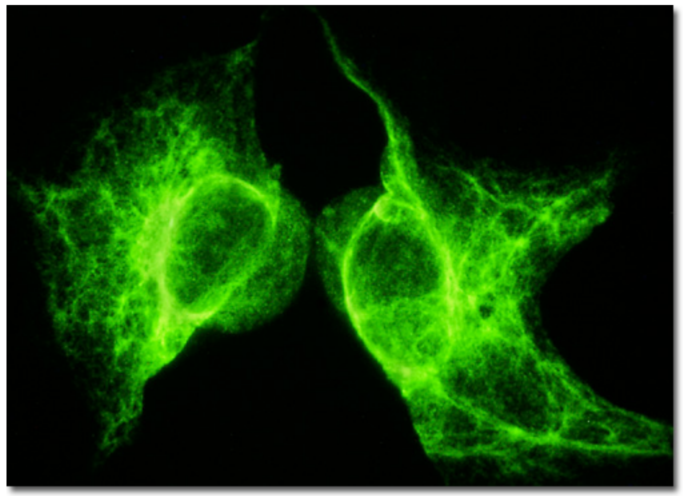
375 a.a.

42 kDa



Intermediate Filament





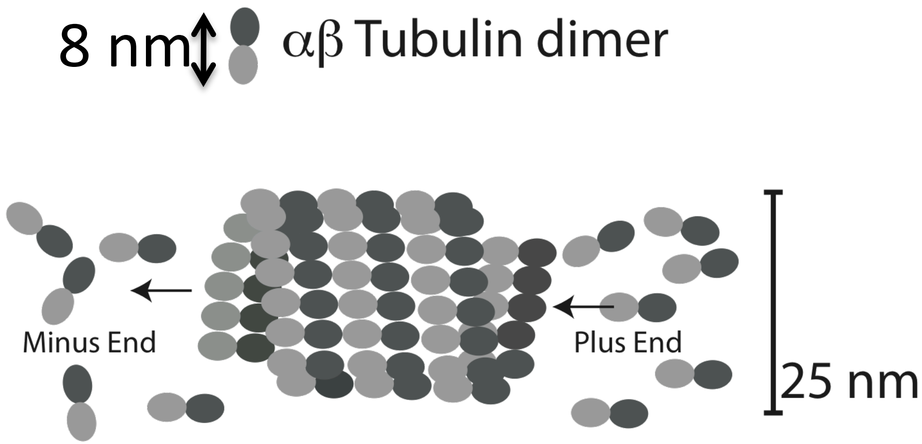
Monomer

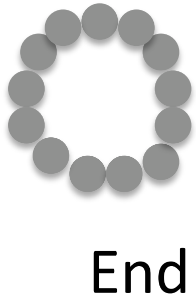
466 a.a. (vimentin)

57 kDa (usu. 40-70 kDa)

Keratin, Vimentin, Lamin, GFAP

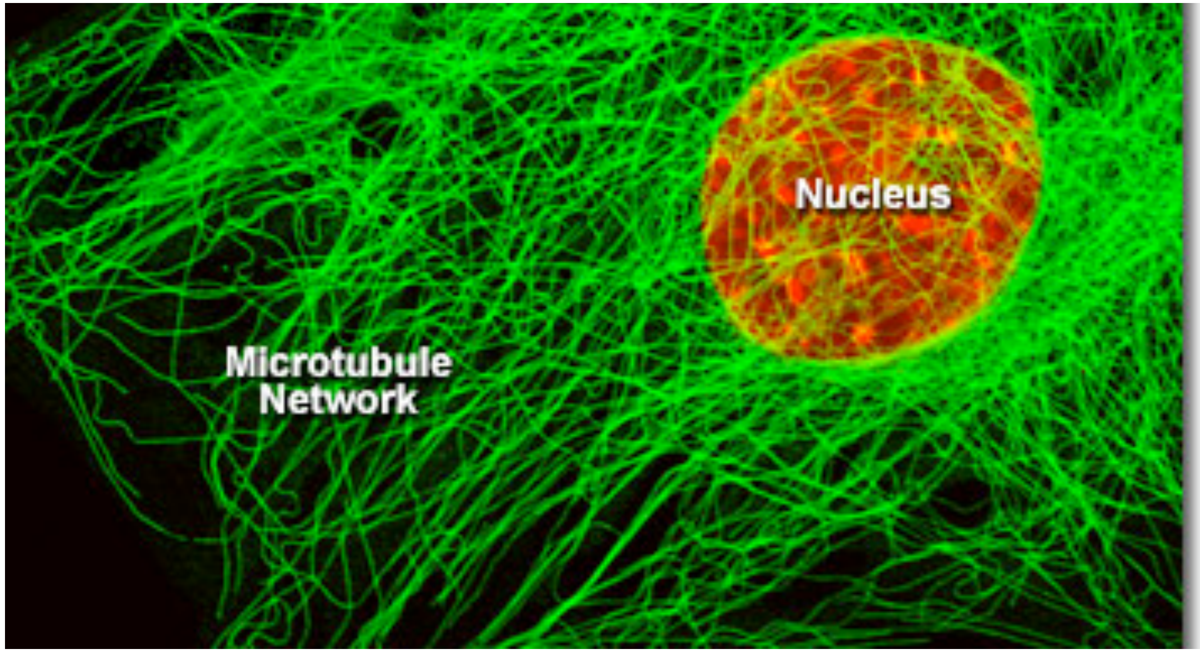
Microtubule





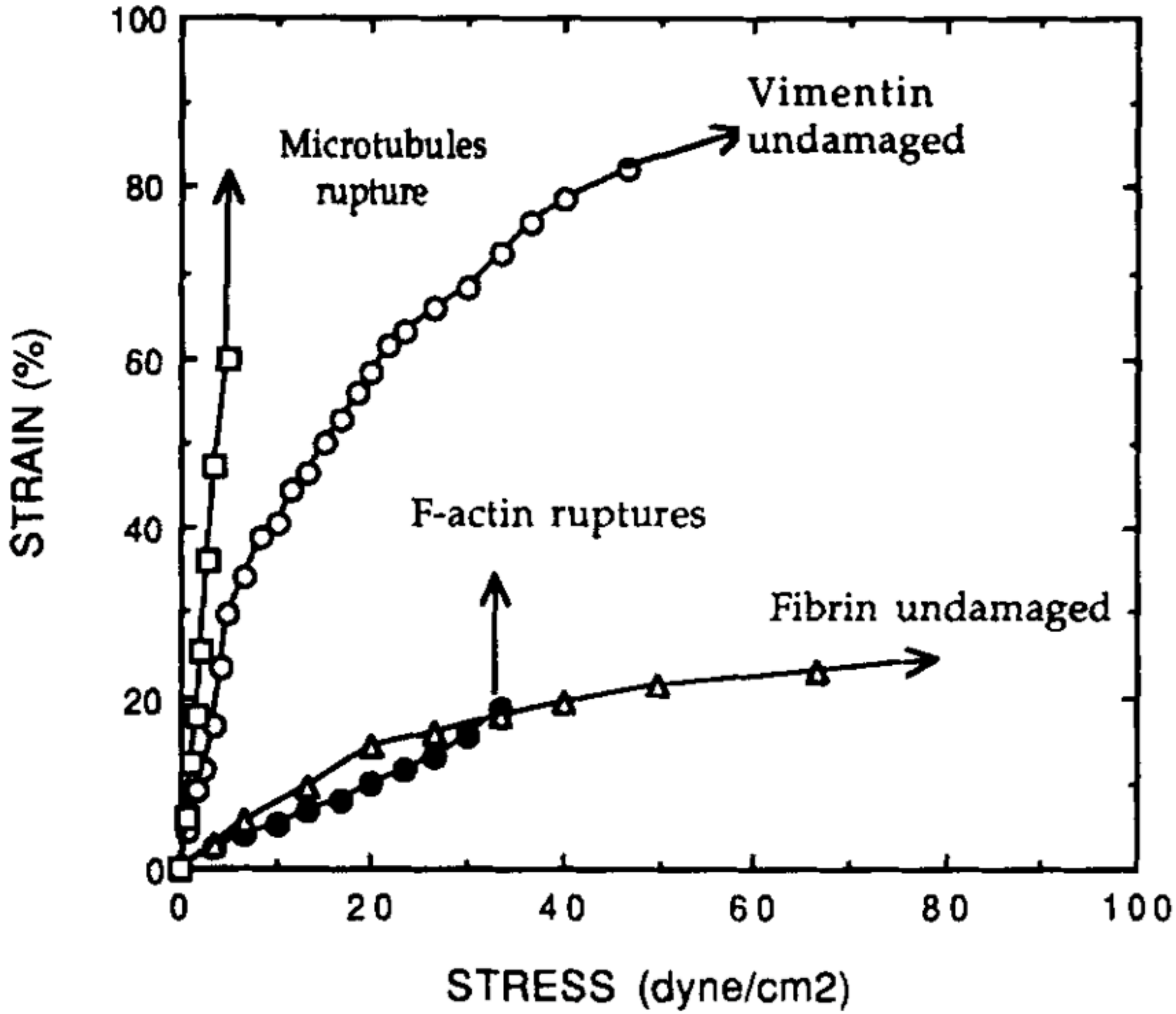
Monomer: α and β tubulin

451 a.a.
50 kDa



Stretching the Cytoskeleton

- Actin filamen
  (microfilamen
- Microtubules
- Intermediate
  filaments



Janmey et al. (1991) JCB

Stirling Approximation

Stirling approximation

ln N! = ln[N(N-1)(N-2)…x1]

But

ln(ab) = ln(a) + ln(b)

So, $\ln N! = \sum_{n=1}^{N} \ln n$

$$\sum_{n=1}^{N} \ln n \approx \int_{n=1}^{N} (\ln x) dx = N \ln N - N$$

Taylor Expansion Series

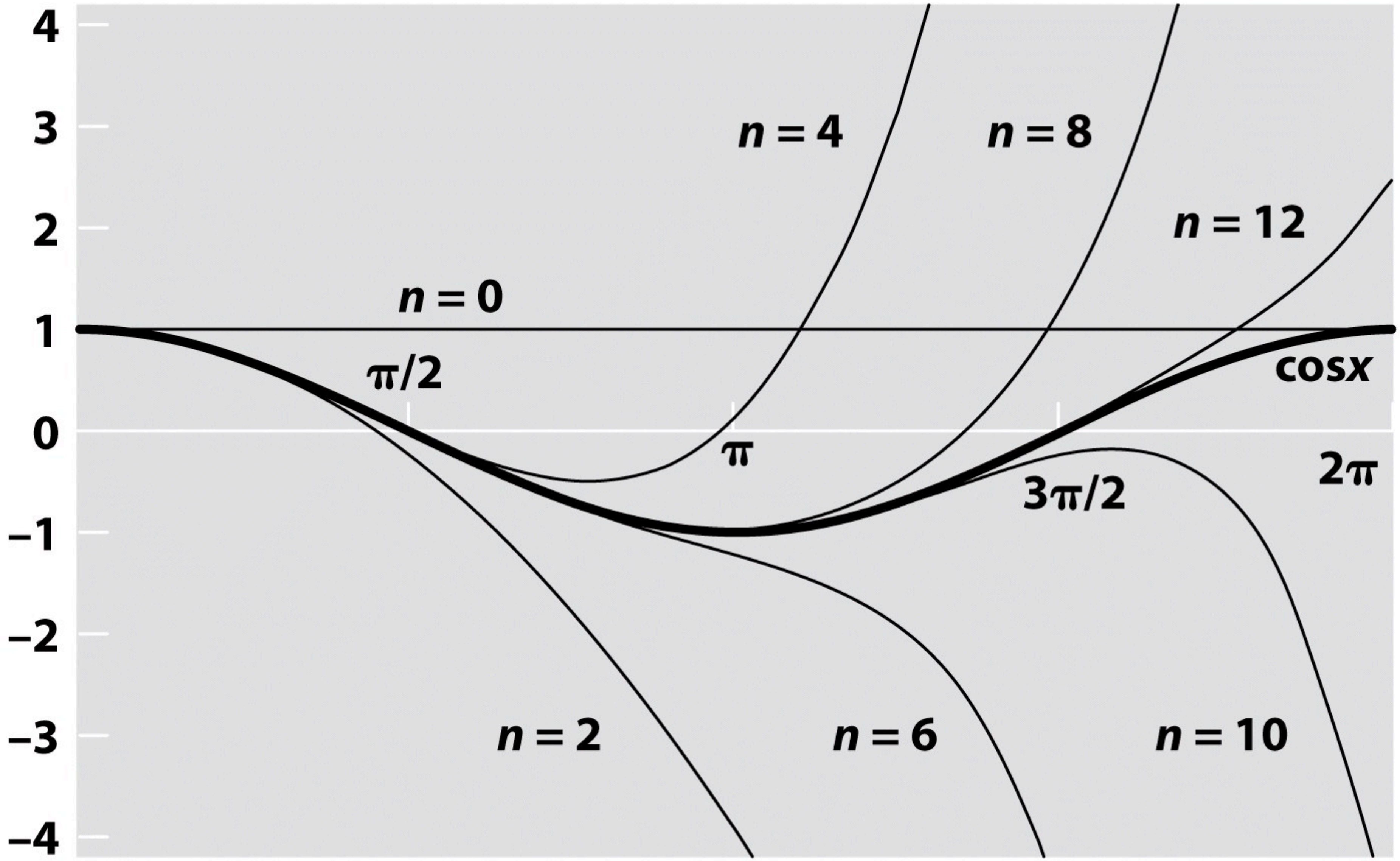


Figure 5.20 Physical Biology of the Cell (© Garland Science 2009)