# Physical Biology

Bio-322

4 credits, 3h per week

# Physical Biology

- What?
- Why?
- How?

# Course Outline

1. Introduction
2. Molecular Biophysics
3. Cellular biophysics
4. Biophysical techniques
5. *Experiments:* mechanics of DNA, mobility of biomolecules

# Overview

**Course timings:**

Mon 14-1500h

Wed 14-1500h

Fri 12-1300h

**Total time:**

46 lectures (incl. Colloquia)

# Evaluation

Exams (mid and end-semester): 50%

Assignments and internal assessment: 50%

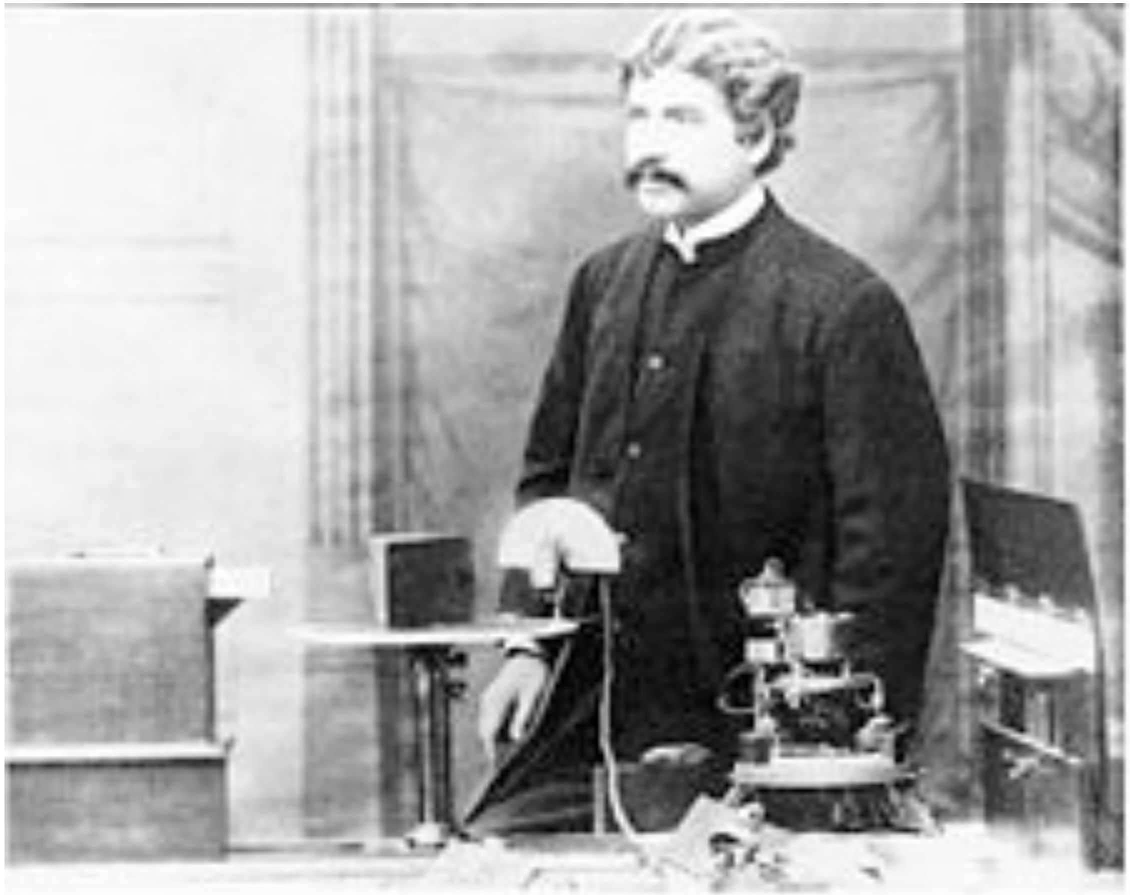
# Instructors

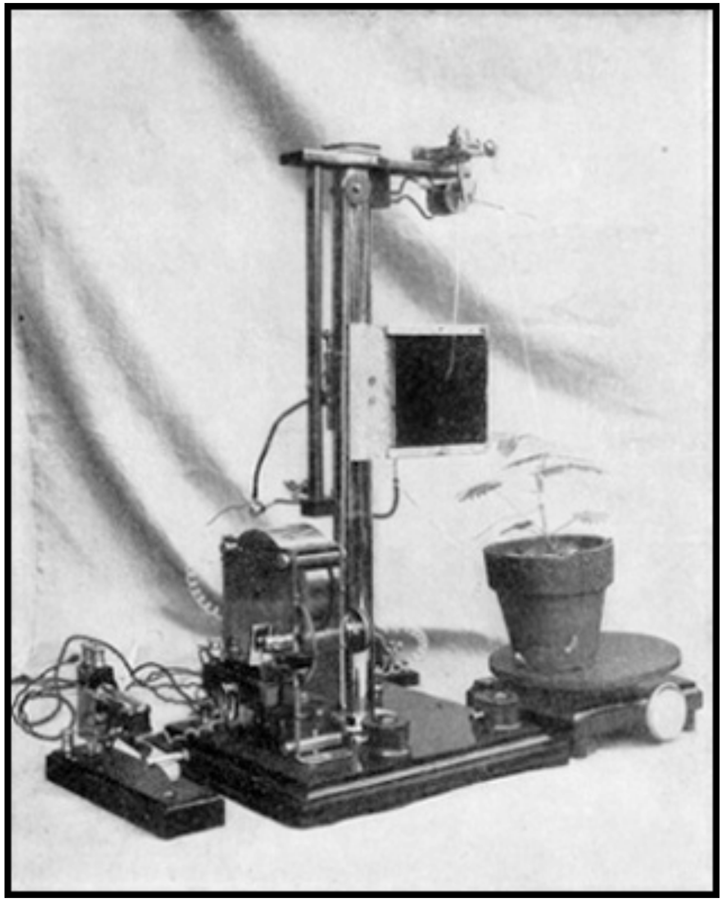
- Chaitanya Athale
- G. Pavan Kumar
- Shiva Patil
- Saikrishna Kayarat

# Plan

**Time line:**

| Time period | Instructor | Topics | No. of lectures |
|---|---|---|---|
| 2-6 Aug | Chaitanya | Introduction | 3 |
| 9-27 Aug | Pavan | Molecular biophysics | 9 |
| 30 Aug- 1 Sept | Shiva | Experimental bio-molecular mechanics | 2 |
| 2-8 Sept | Sai | Molecular structure | 2 |
| 10-24 Sept | Pavan | Biophysical Methods: Light, NMR, Raman | 7 |
| 27 Sept- 15 Nov | Chaitanya | Cellular Biophysics | 22 |
| 17-22 Nov | Shiva | Measuring diffusion in cells- FCR, FRAP | 3 |



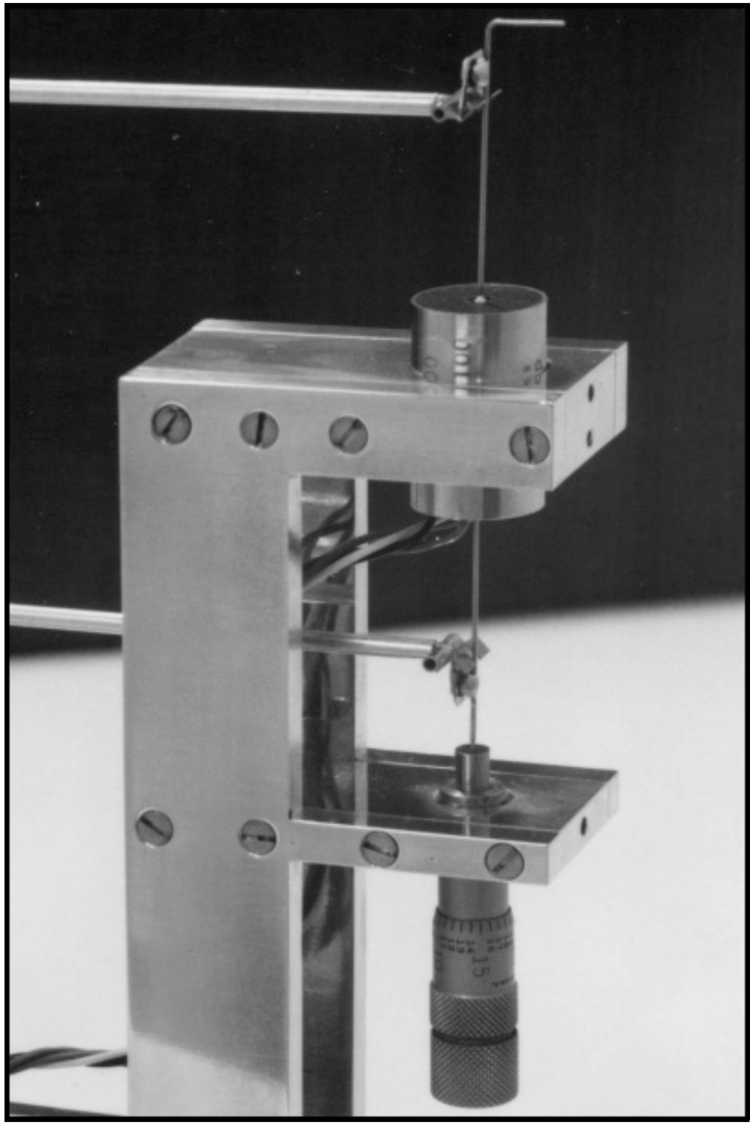


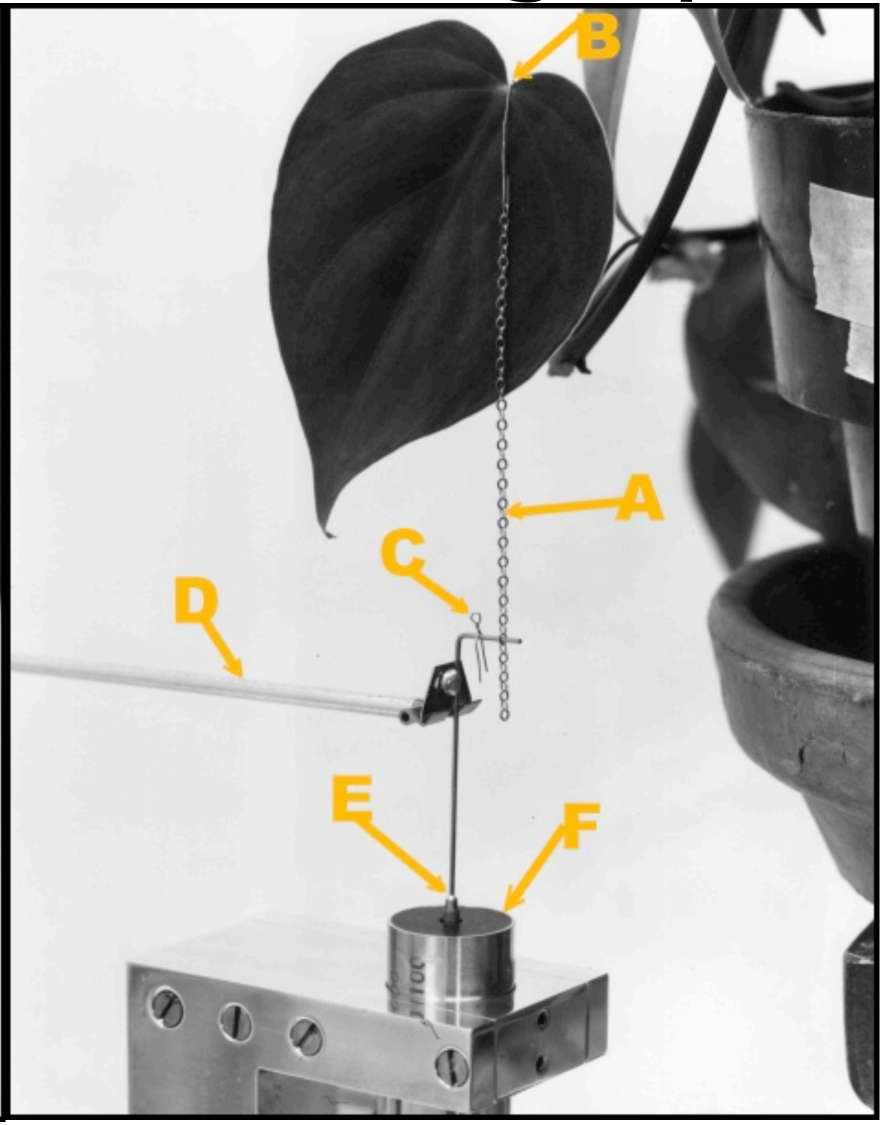
Crescograph

# J.C. Bose (1858-1937)

- Wireless communication (1894/5)
- Plant growth measurement by Crescograph (1919)
- Electric nature of plant sensory conduction (Bose, J. C., Researches on Irritability of Plants, 1913.)
- Cell membrane potential measurements

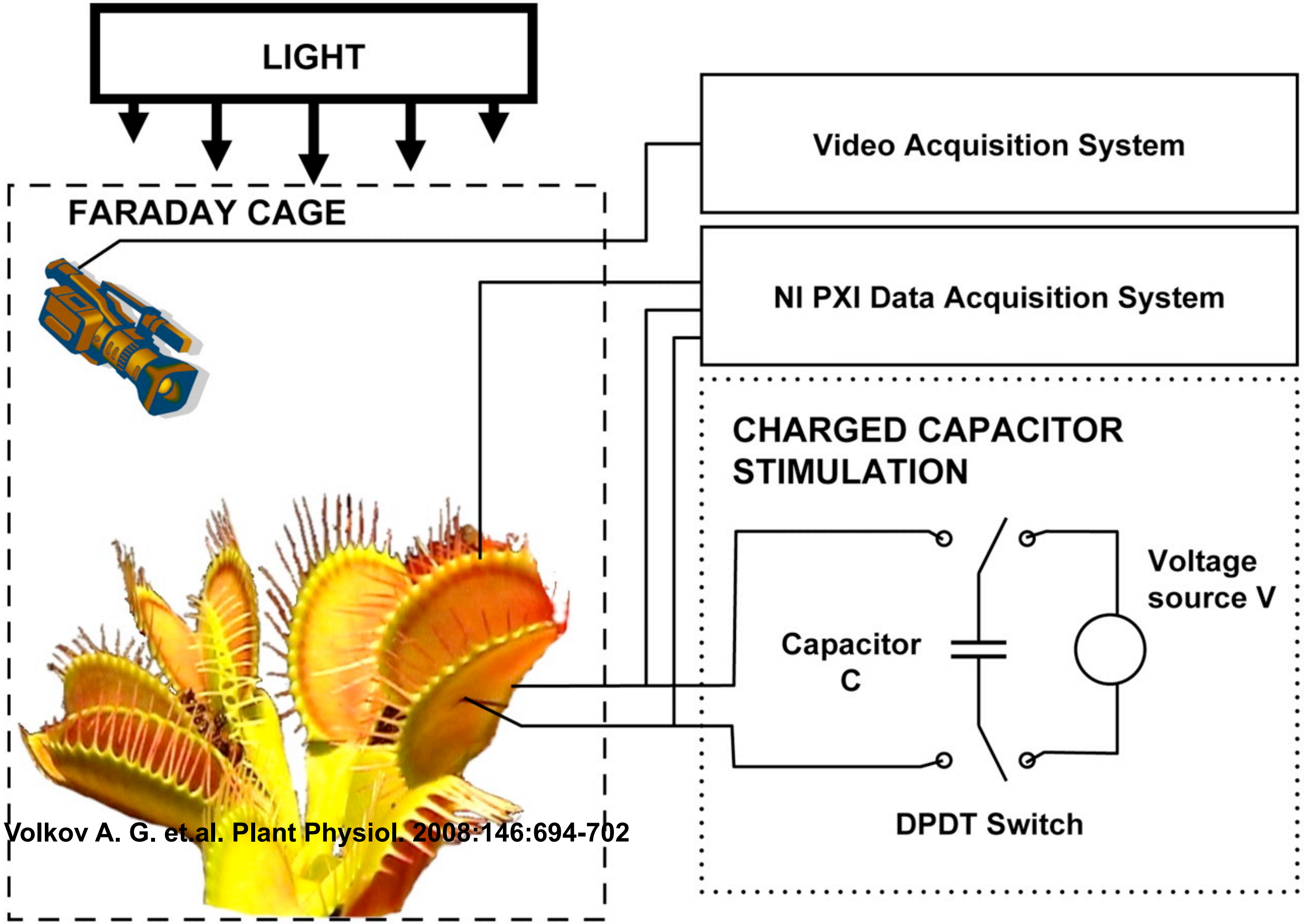
# Modern Crescograph



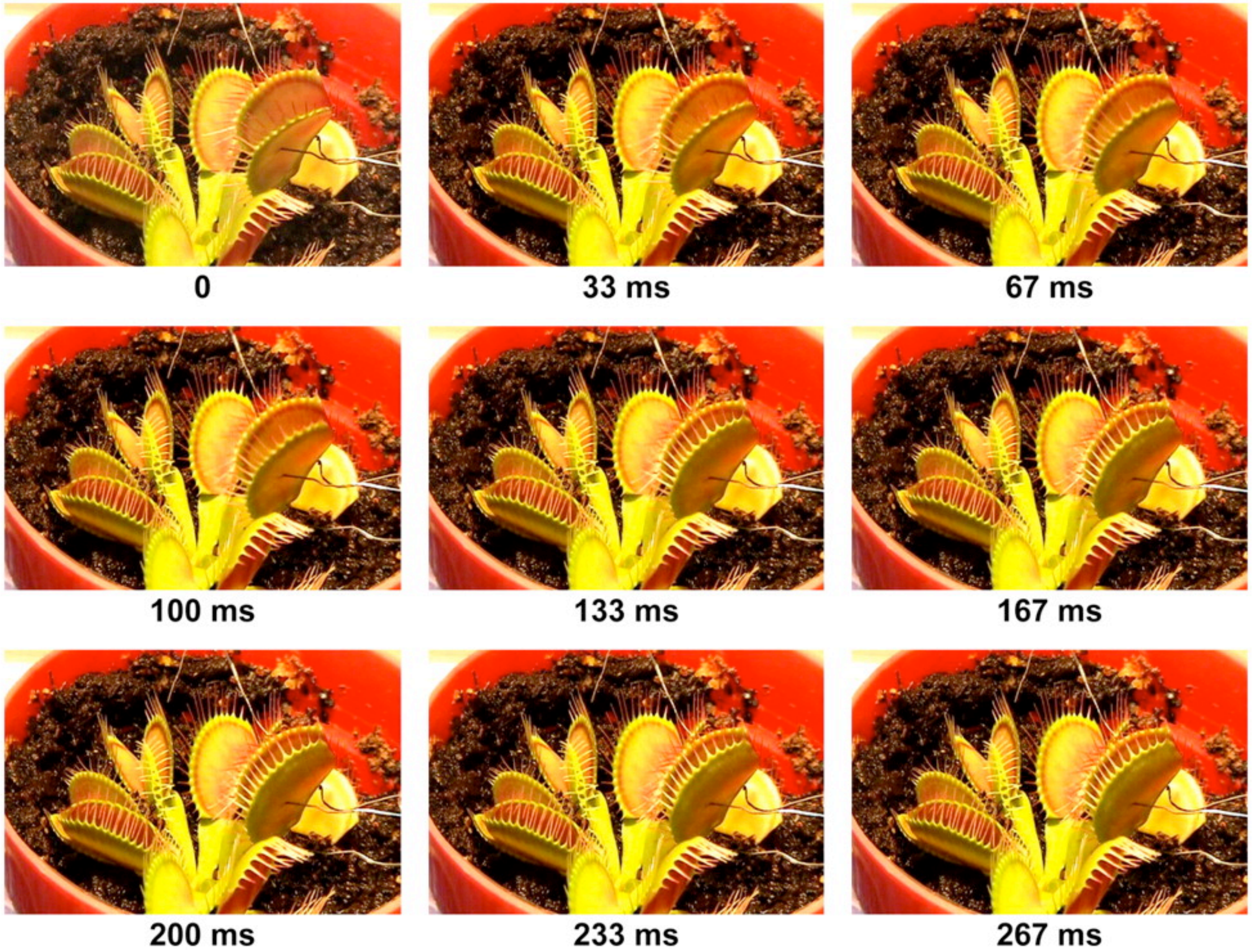



A: gold chain
B: hook
C: 5mg counter weight
D: lever arm
E: transformer core
F: micrometer

# Plants Response to Electrical Stimulus



# Closing of the trap with a 14-μC electrical stimulus.




**Volkov A. G. et.al. Plant Physiol. 2008:146:694-702**

# Biological Physics

Mechanics
Equilibrium
Steady state
Entropy
Electrostatics
Beams and structures
Water
Biological dynamics
Molecular motors
Electricity

# Contributors to Biological Physics

- Francis Crick (DNA structure)
- Alan Turing (theory of periodic biological structures)
- Max Delbrück (replication of viruses)
- Linus Pauling (structure of Hemoglobin)
- G.N. Ramachandran (protein conformations)

# Biological Model Building

- Physical and Chemical Principles
- Quantitative experiments
- Facts
  - Observations (eg. no. of proteins)
  - Mechanisms (eg.  DNA->RNA->Protein)
  - Hypotheses (eg. Bacterial origin of mitochondria)

# Common Strand?




# Molecules

(A) Nucleic acids
(B) Proteins
(C) Lipids
(D) Sugars

Water

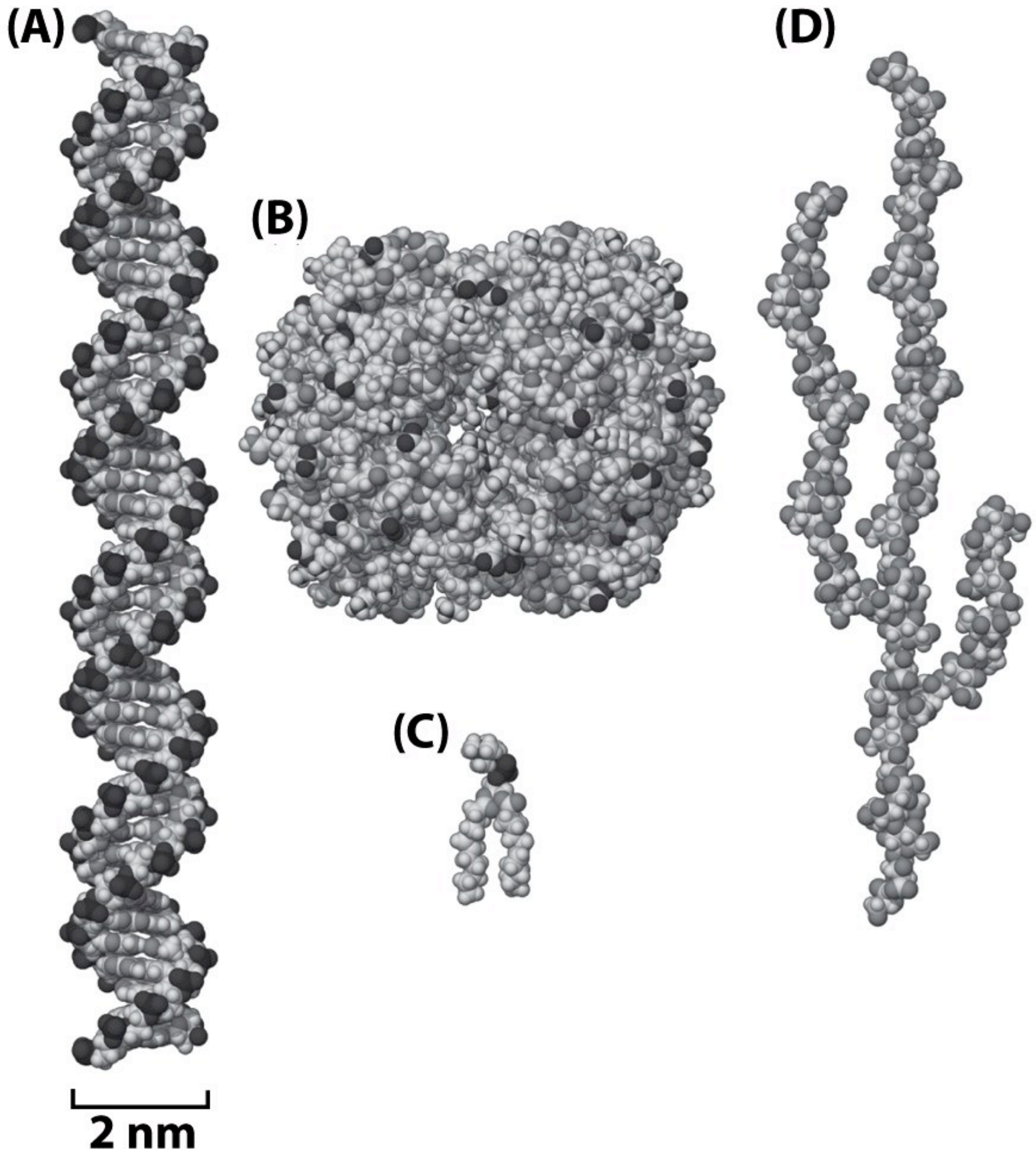



Figure 1.1 Physical Biology of the Cell (© Garland Science 2009)

# Polymers: Nucleic Acids and Proteins

- DNA sequence <-> Protein sequence
- 2 Polymer languages
- DNA: codons (3 base pairs)
- Protein: protein folds α-helix, β-sheet (combinations of amino acids)

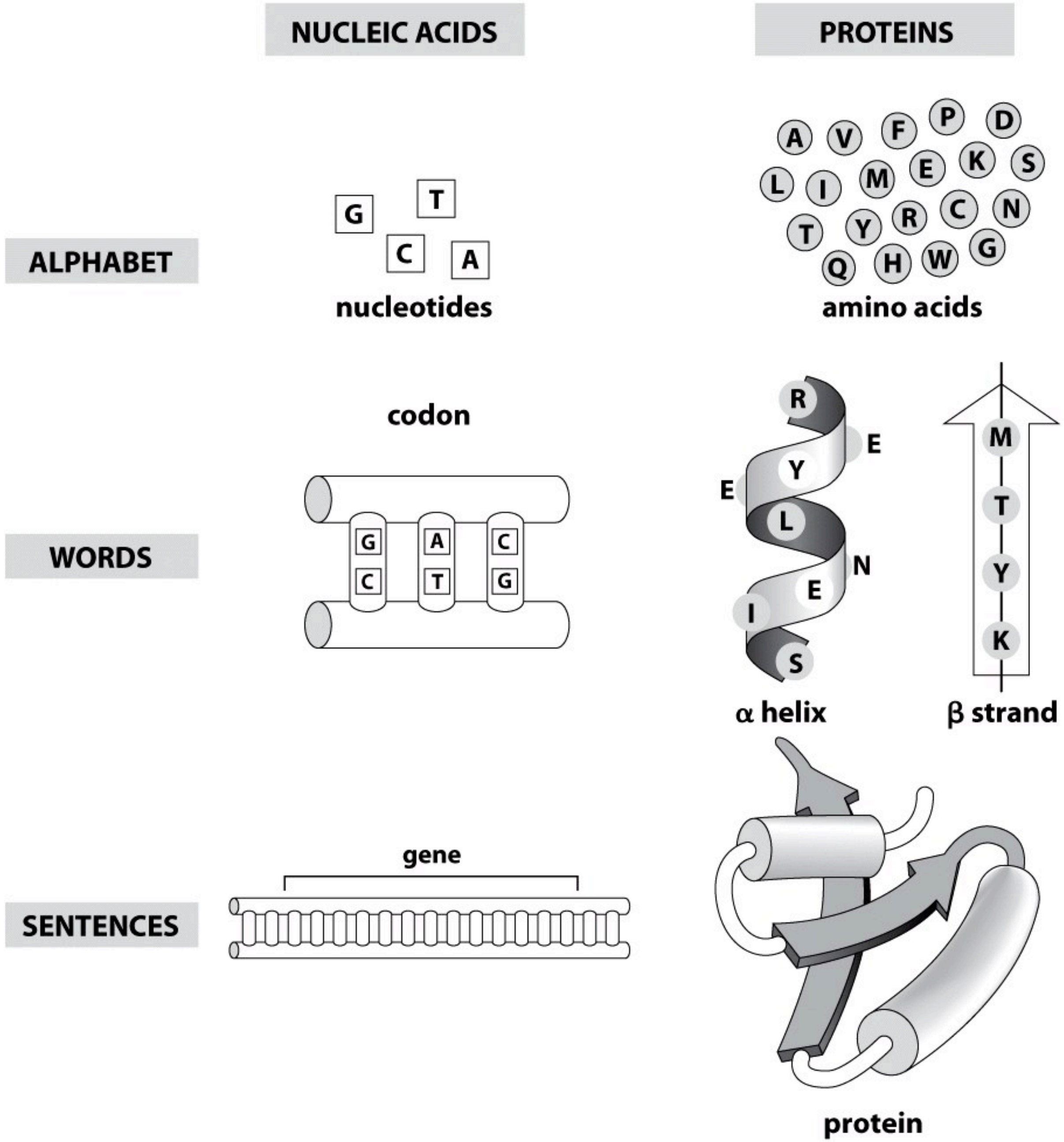



Figure 1.2 Physical Biology of the Cell (© Garland Science 2009)

Purines Pyrimidines

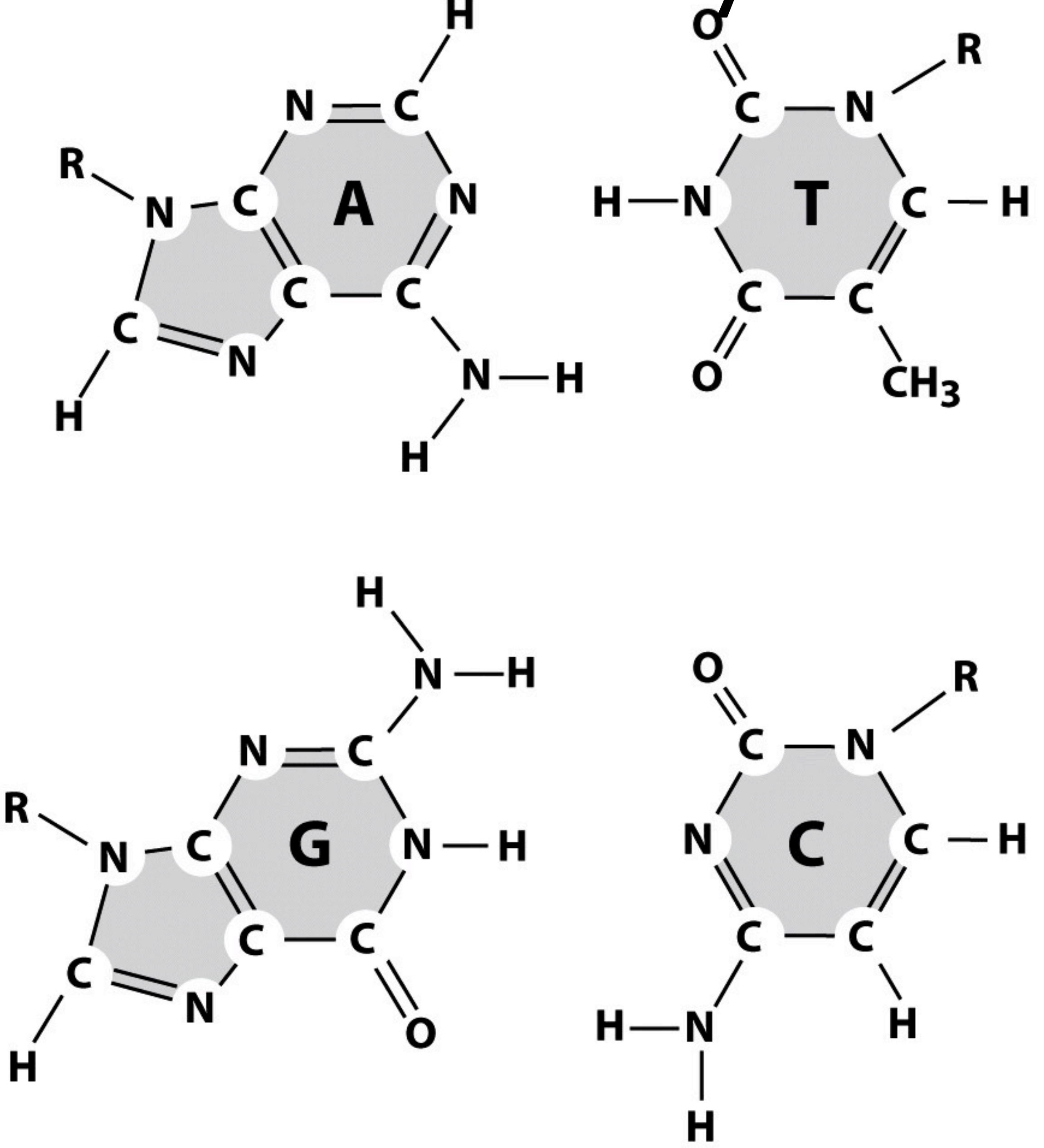



Figure 1.3a Physical Biology of the Cell (© Garland Science 2009)

# DNA Strand

Anti-parallel strands

Complementary

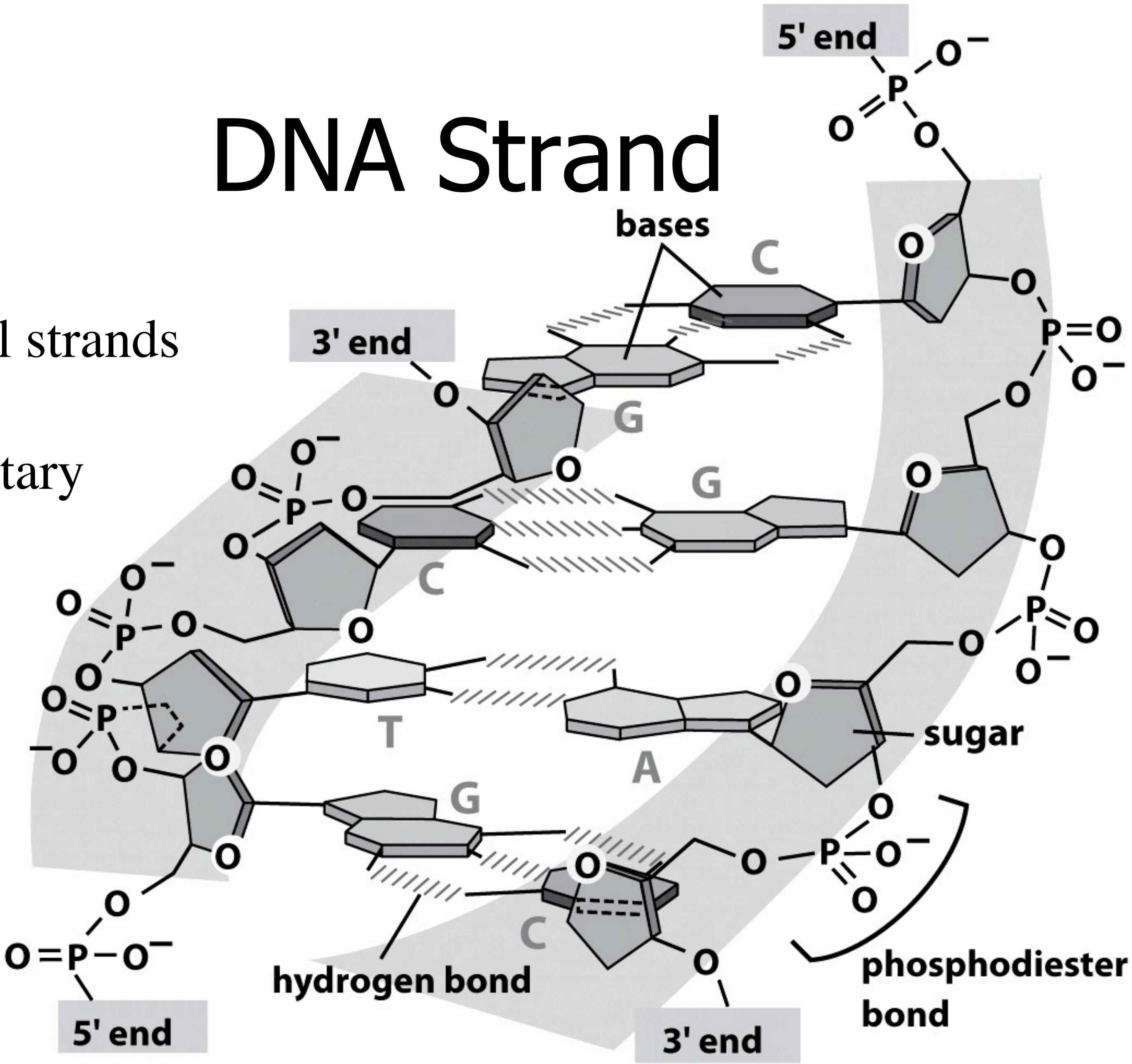



Figure 1.3b Physical Biology of the Cell (© Garland Science 2009)

# DNA Structure

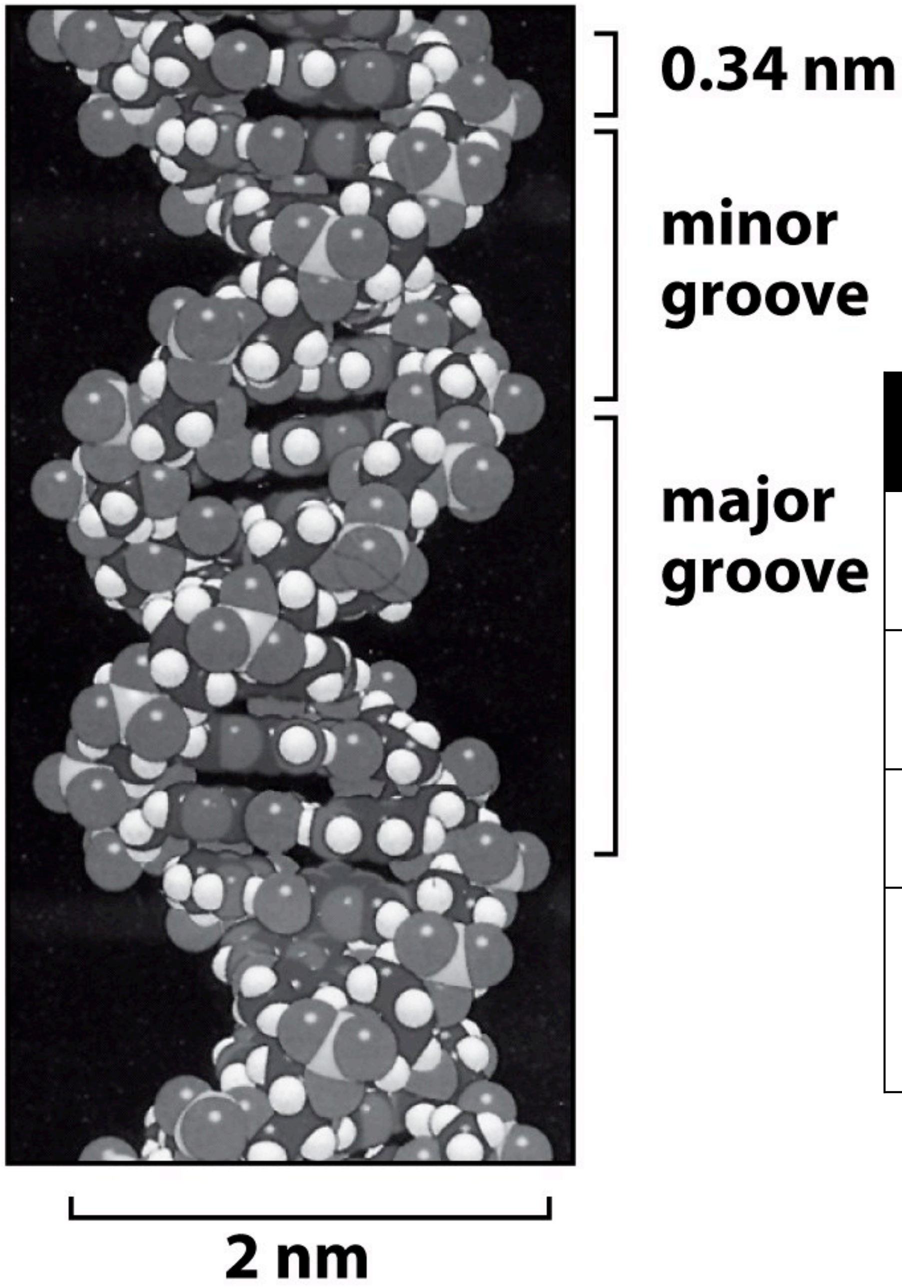



Figure 1.3c Physical Biology of the Cell (© Garland Science 2009)

| | B-DNA | A-DNA | Z-DNA |
|---|---|---|---|
| **Helix** | Right-handed | Right-handed | Left-handed |
| **Rise/bp [nm]** | 0.34 | 0.23 | 0.38 |
| **Bp/turn** | 10.5 | 11 | 12 |
| **Diameter [nm]** | 2 | | |

# Genetic Code

Crick, Brenner et al.
3 bps = 1 codon

Nirenberg, Matthai, Ochoa, Leder, Holley, Khorana
Deciphering the code

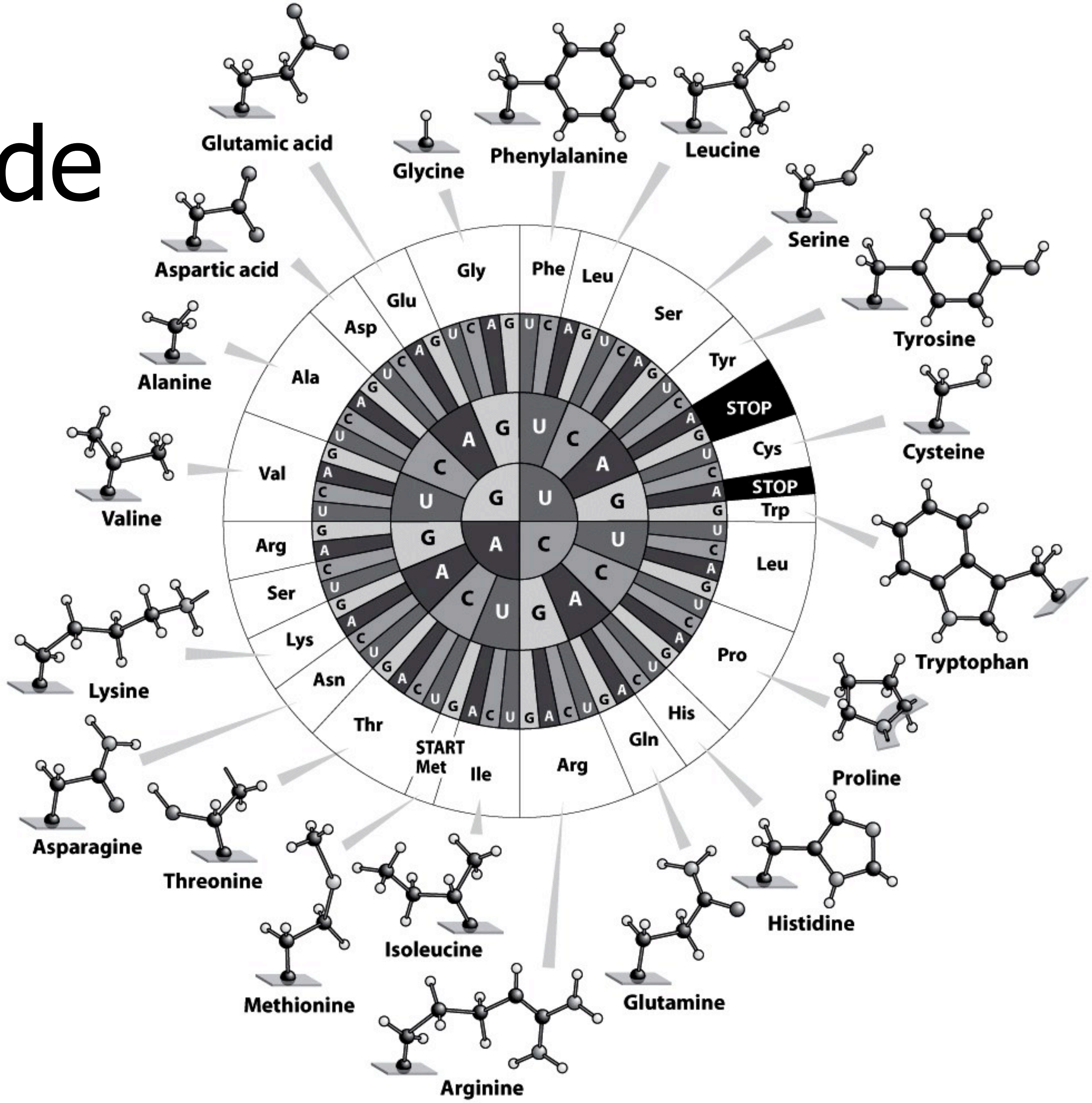
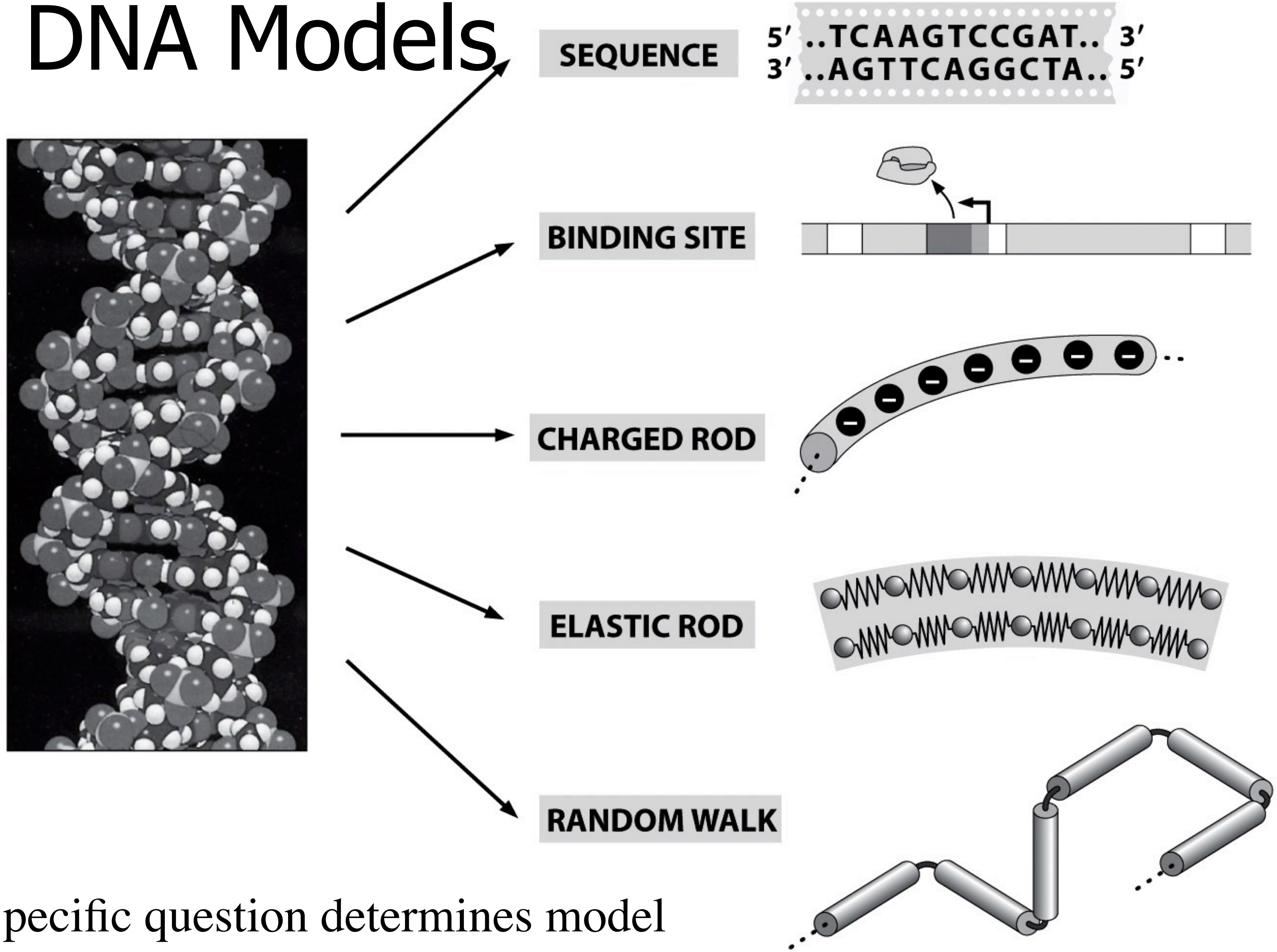



Figure 1.4 Physical Biology of the Cell (© Garland Science 2009)

# Model Building

- Abstraction and simplification
- Analytical models of predictive value
- Collection of models

# DNA Models




Specific question determines model type

# Protein Models

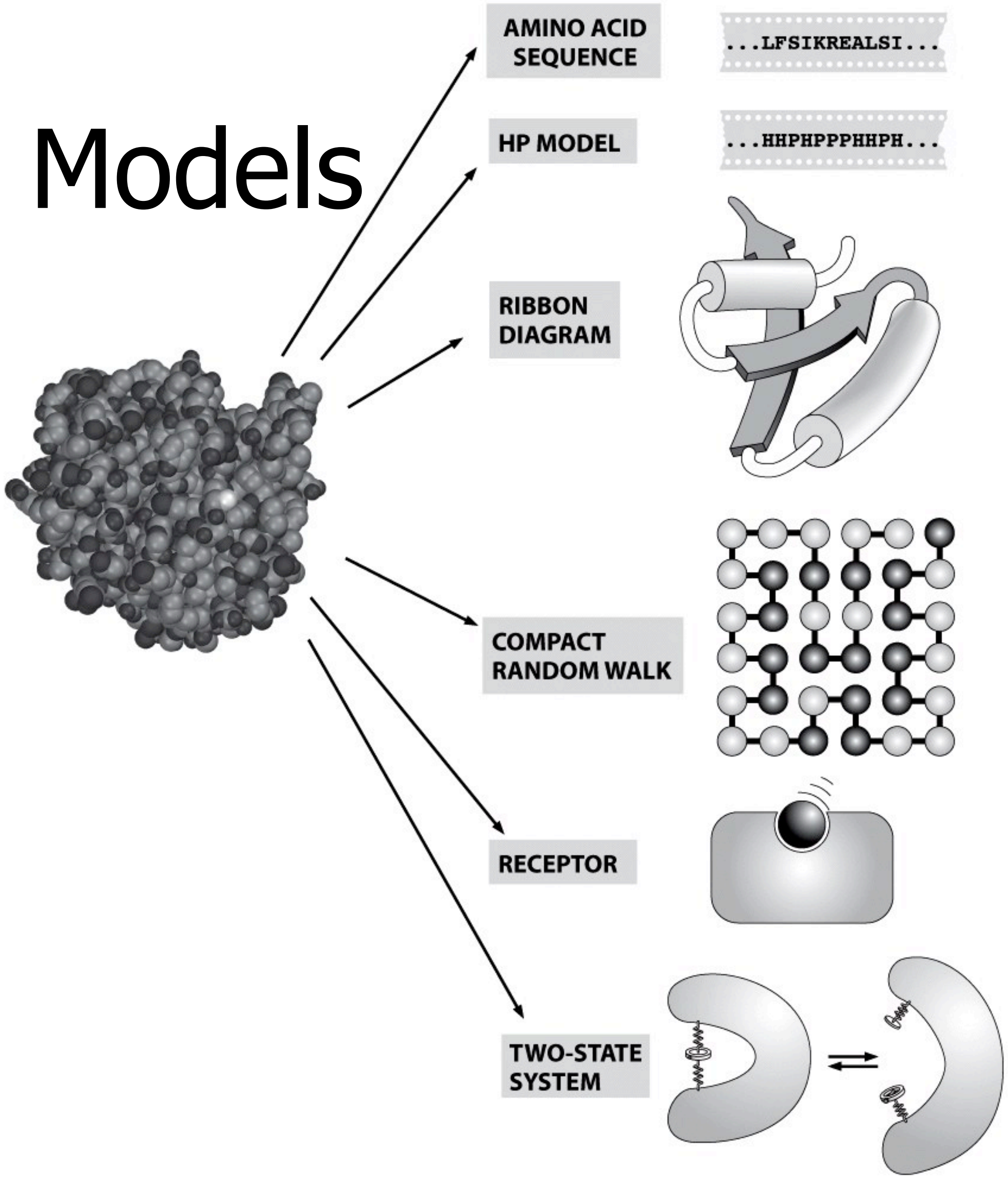



Figure 1.6 Physical Biology of the Cell (© Garland Science 2009)

# Lipid Membrane Models

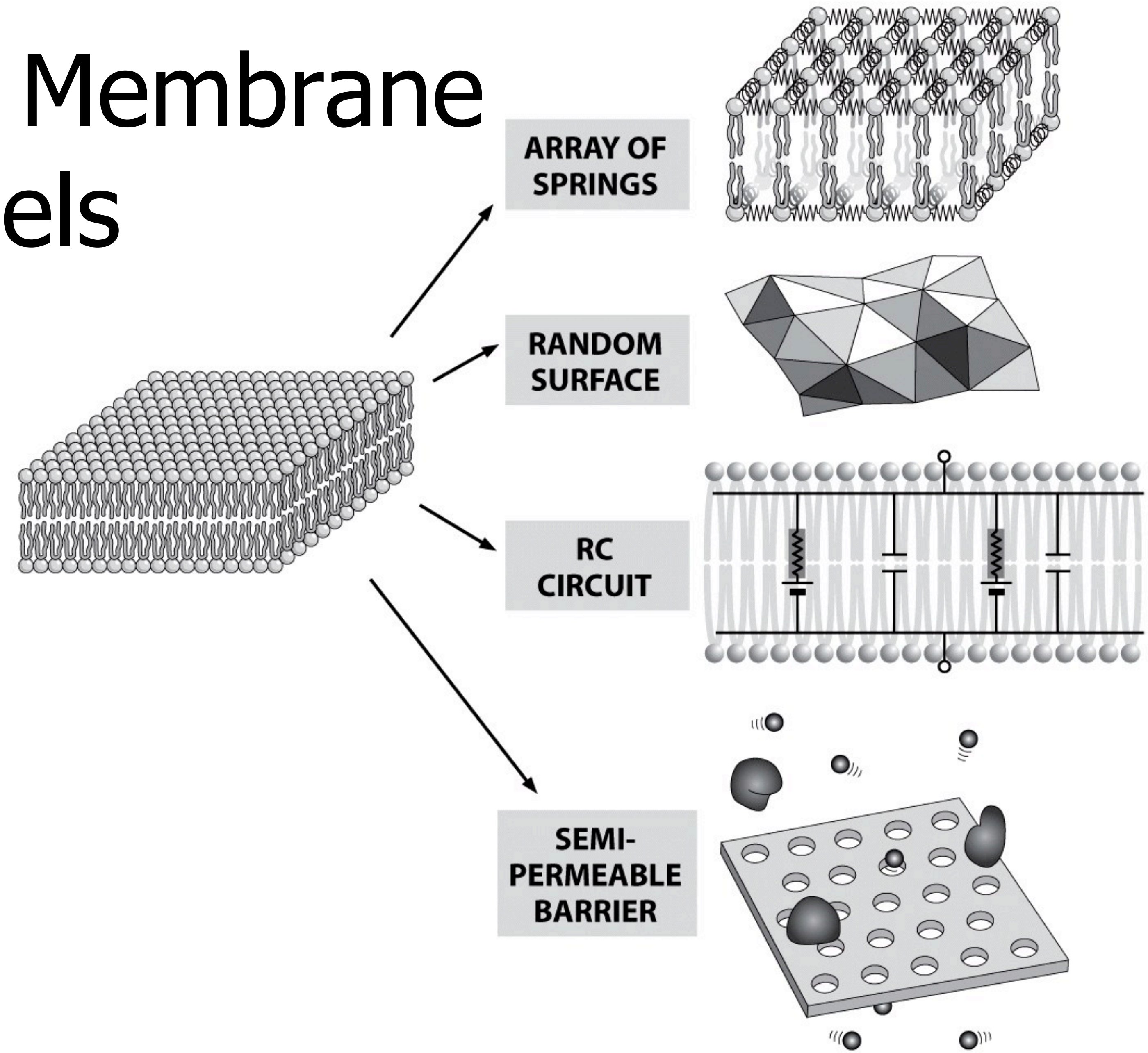



**Figure 1.7 Physical Biology of the Cell (© Garland Science 2009)**

# Cellular Models

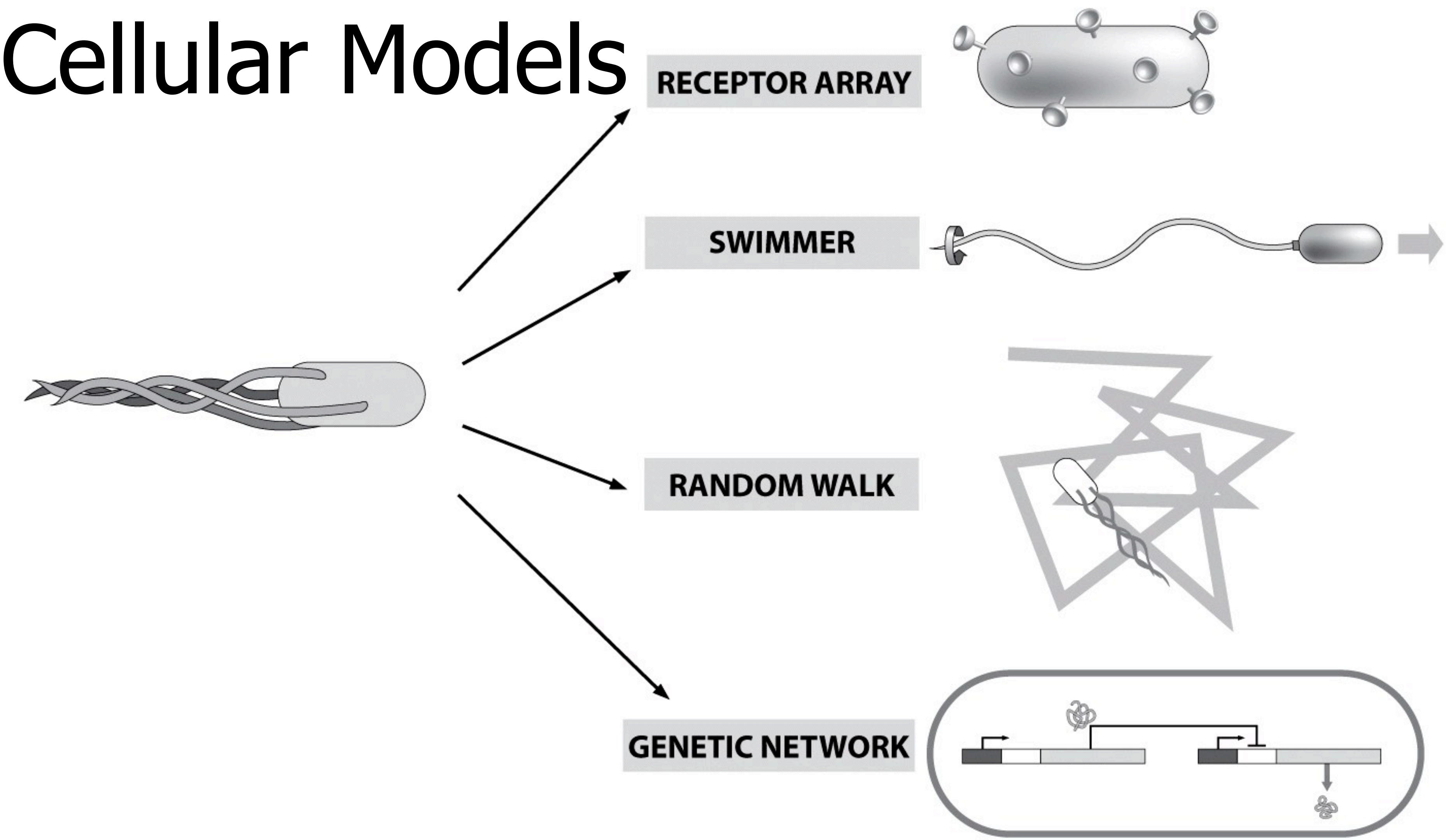



**Figure 1.8 Physical Biology of the Cell (© Garland Science 2009)**

# Models of Water

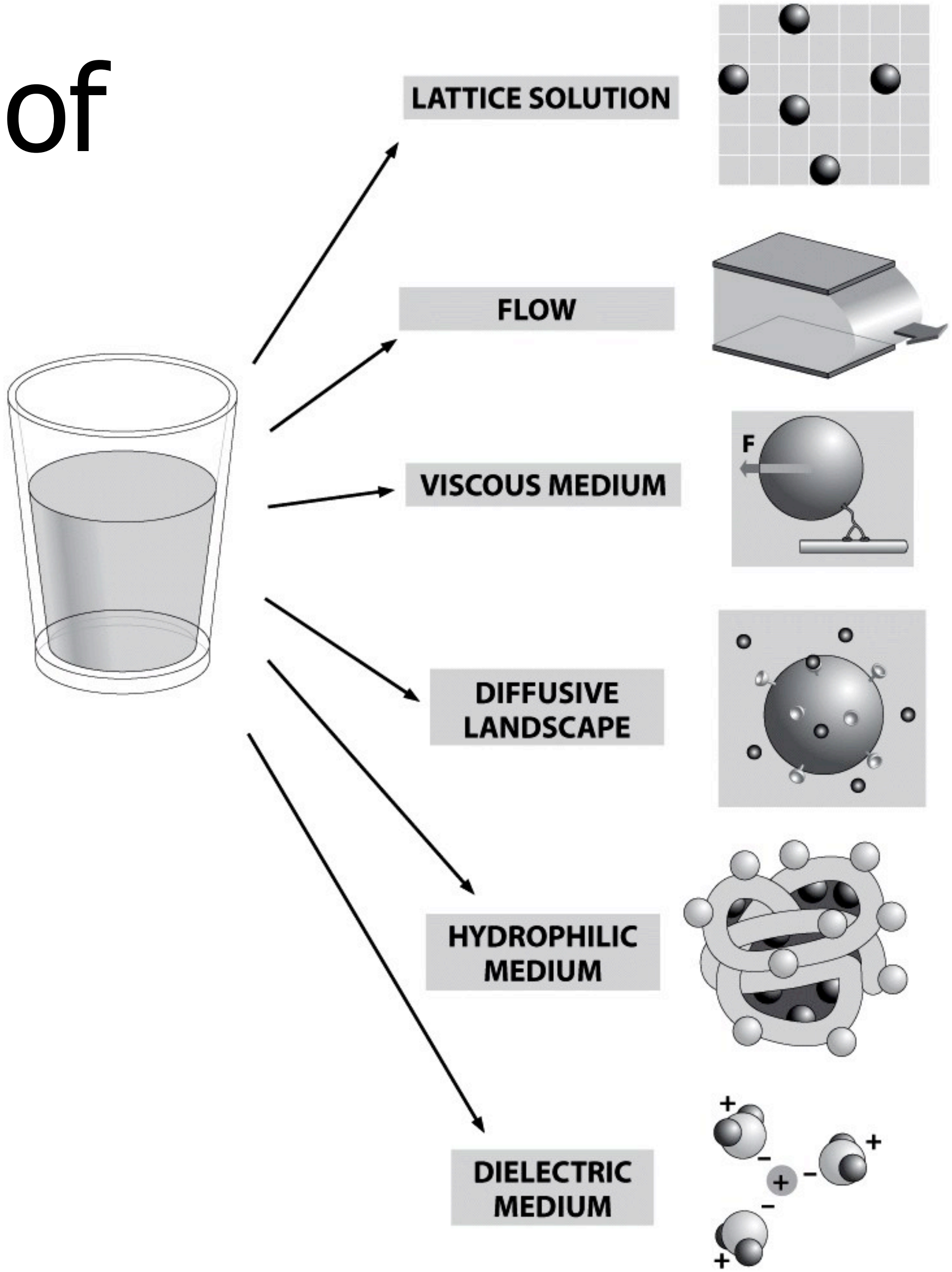
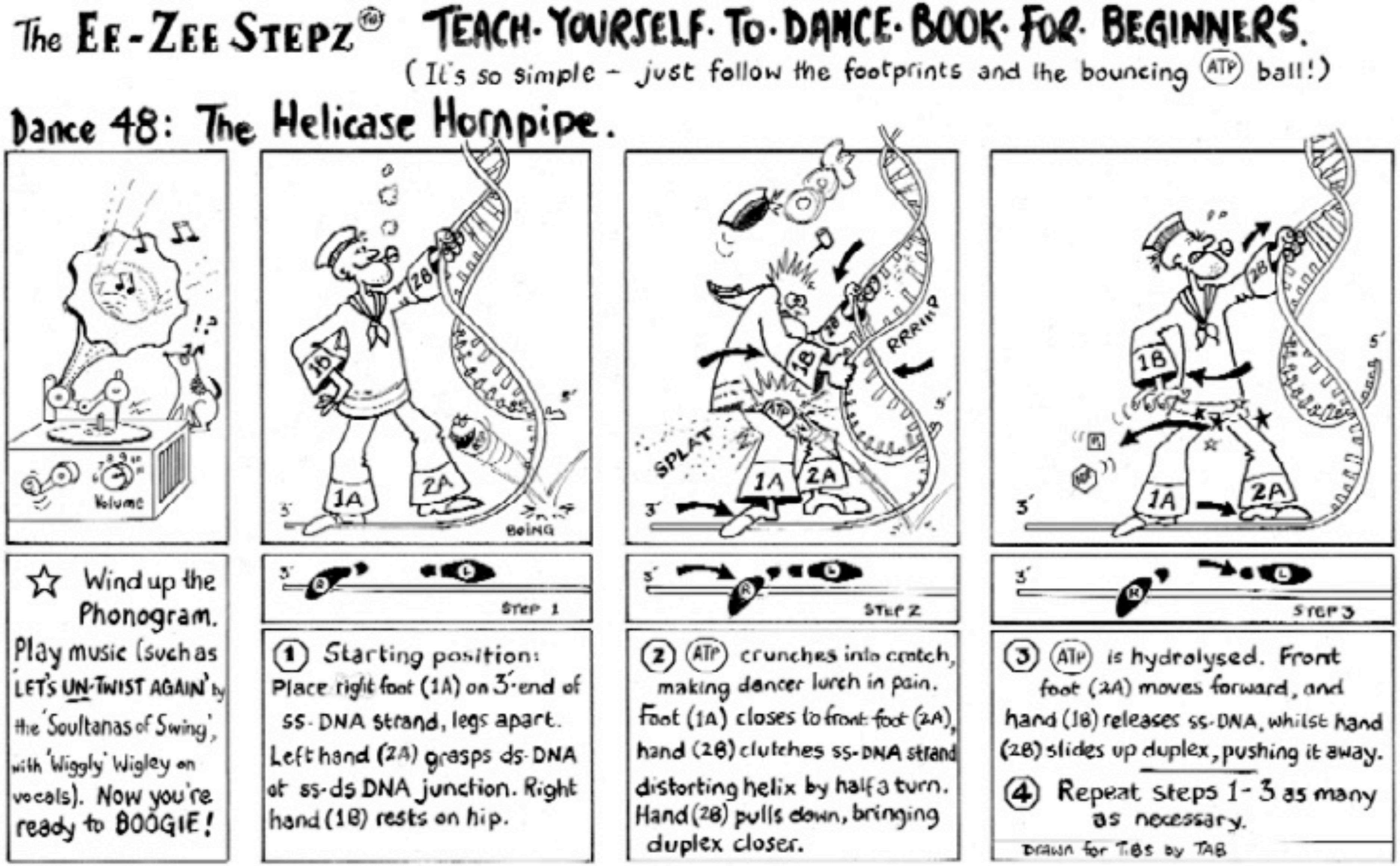



Figure 1.9 Physical Biology of the Cell (© Garland Science 2009)

# Models and Cartoons




Drawn for 'Unwinding the "Gordian knot" of helicase action' by Panos Soultanas and Dale B. Wigley, *TiBS* 26, January 2001, 47–54.


Figure 1.10a Physical Biology of the Cell (© Garland Science 2009)

# Membrane Structures of Mitochondria

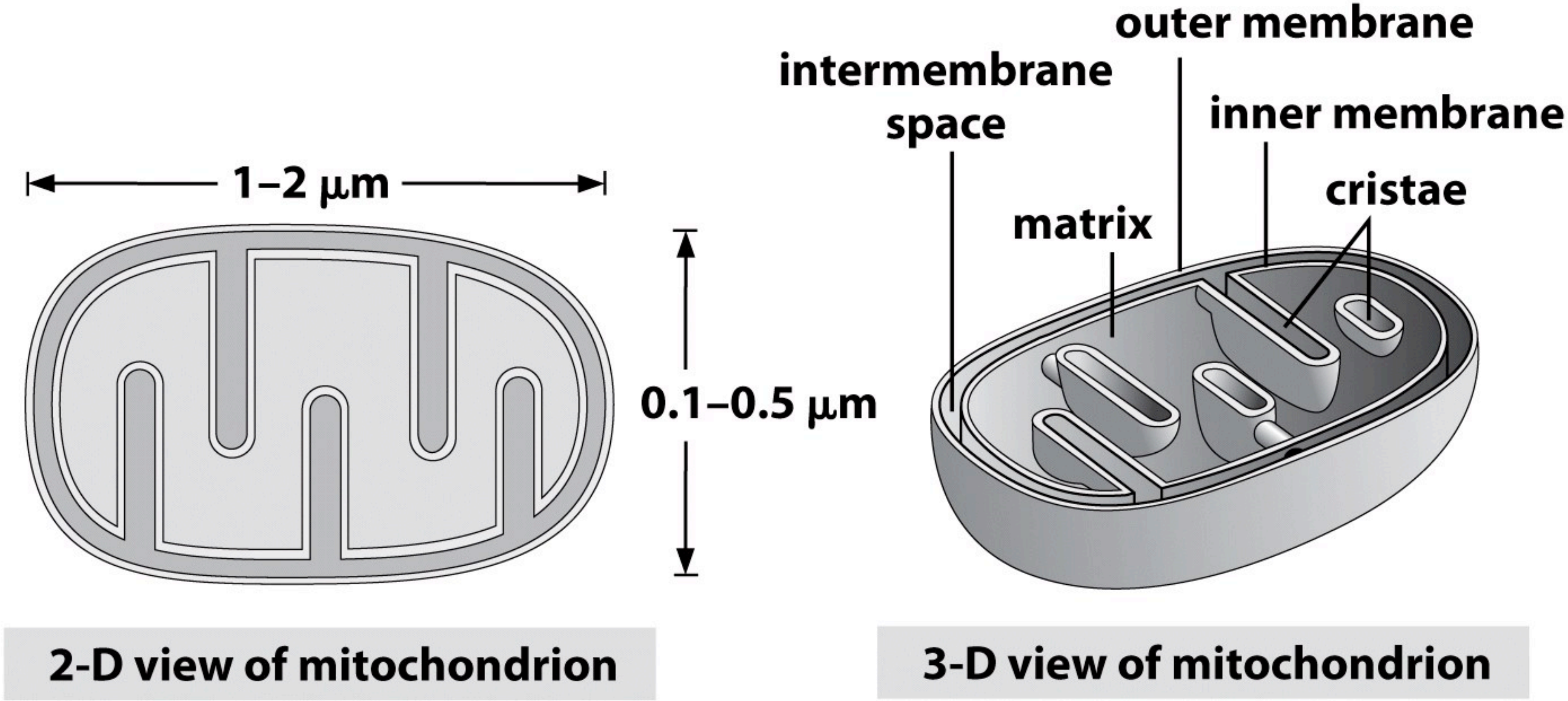



Figure 1.10b Physical Biology of the Cell (© Garland Science 2009)

# Electron Transport Chain

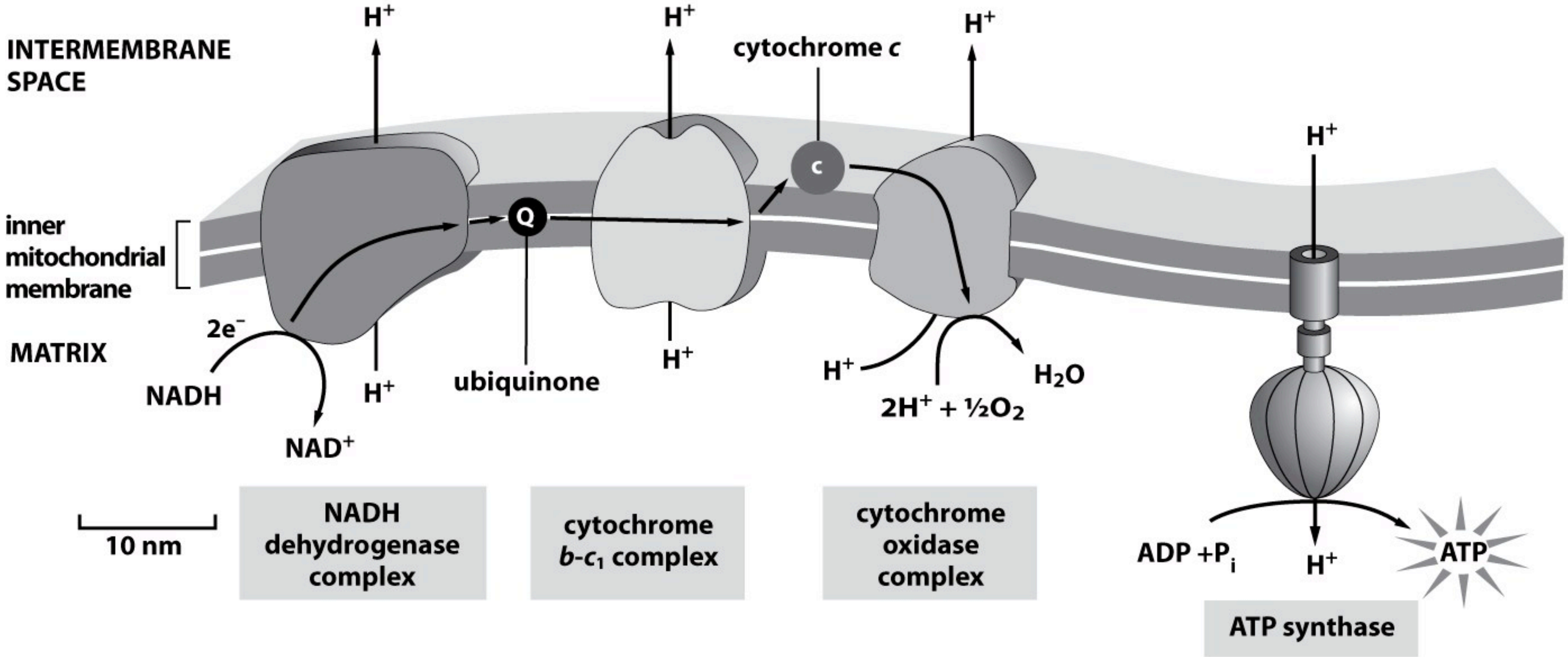



Figure 1.10c Physical Biology of the Cell (© Garland Science 2009)

# Mitochondrial Division

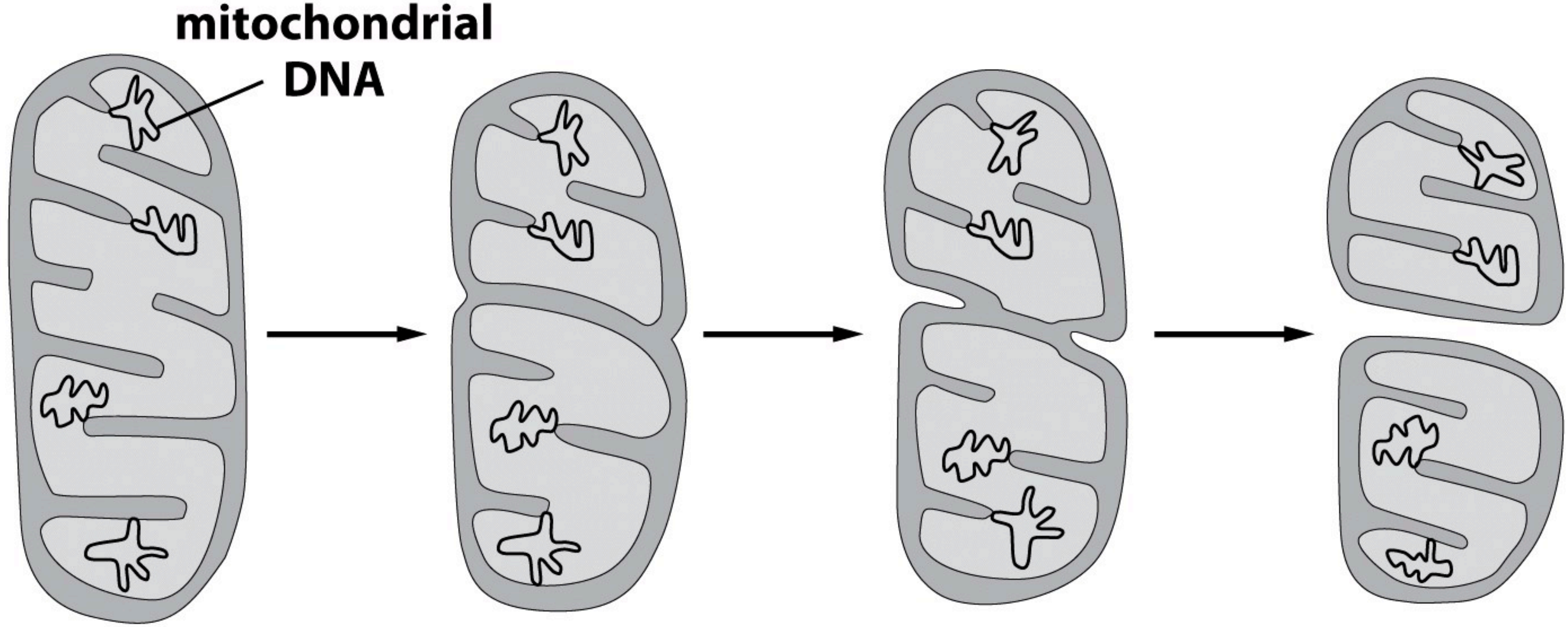



Figure 1.10d Physical Biology of the Cell (© Garland Science 2009)

# Gene Expression: Qualitative

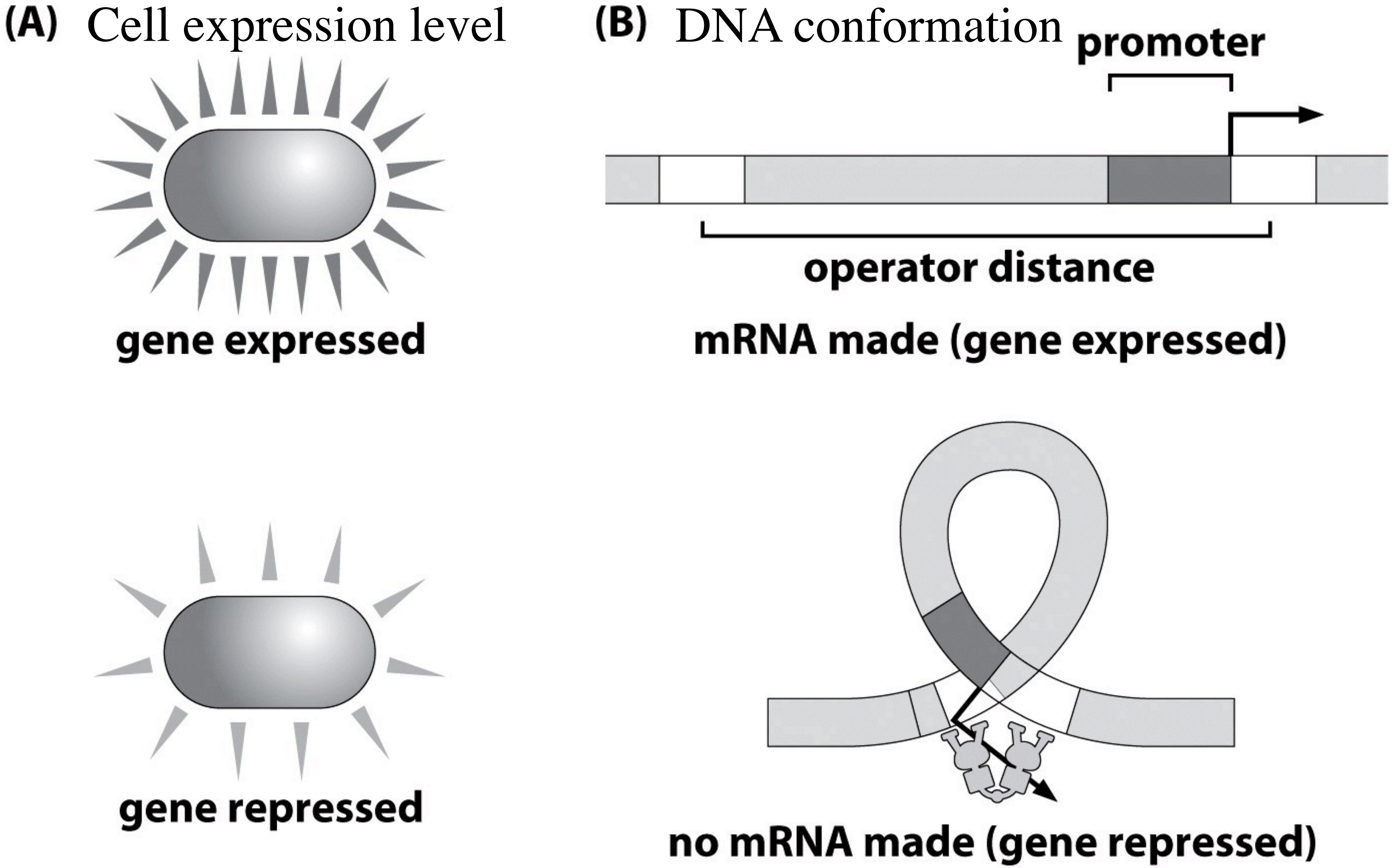
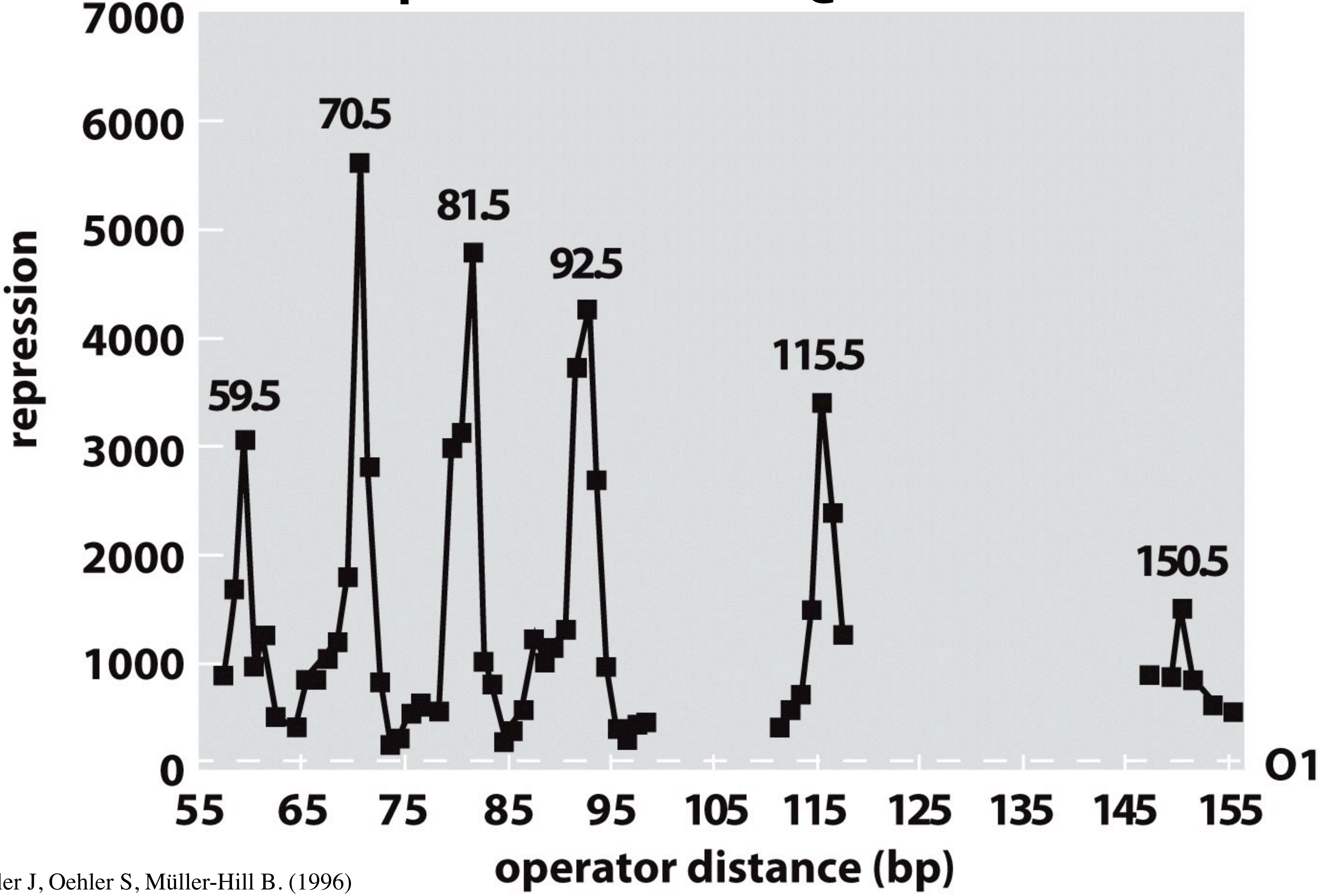



Figure 1.11ab Physical Biology of the Cell (© Garland Science 2009)

# Gene Expression: Quantitative




Müller J, Oehler S, Müller-Hill B. (1996)

Figure 1.11c Physical Biology of the Cell (© Garland Science 2009)

# Models

# Simple Models

- Spring (harmonic oscillator)
- Hooke's law

Potential energy $$energy = \frac{1}{2} k \cdot x^2$$

Restoring force $$F = -k \cdot x$$

# Spring

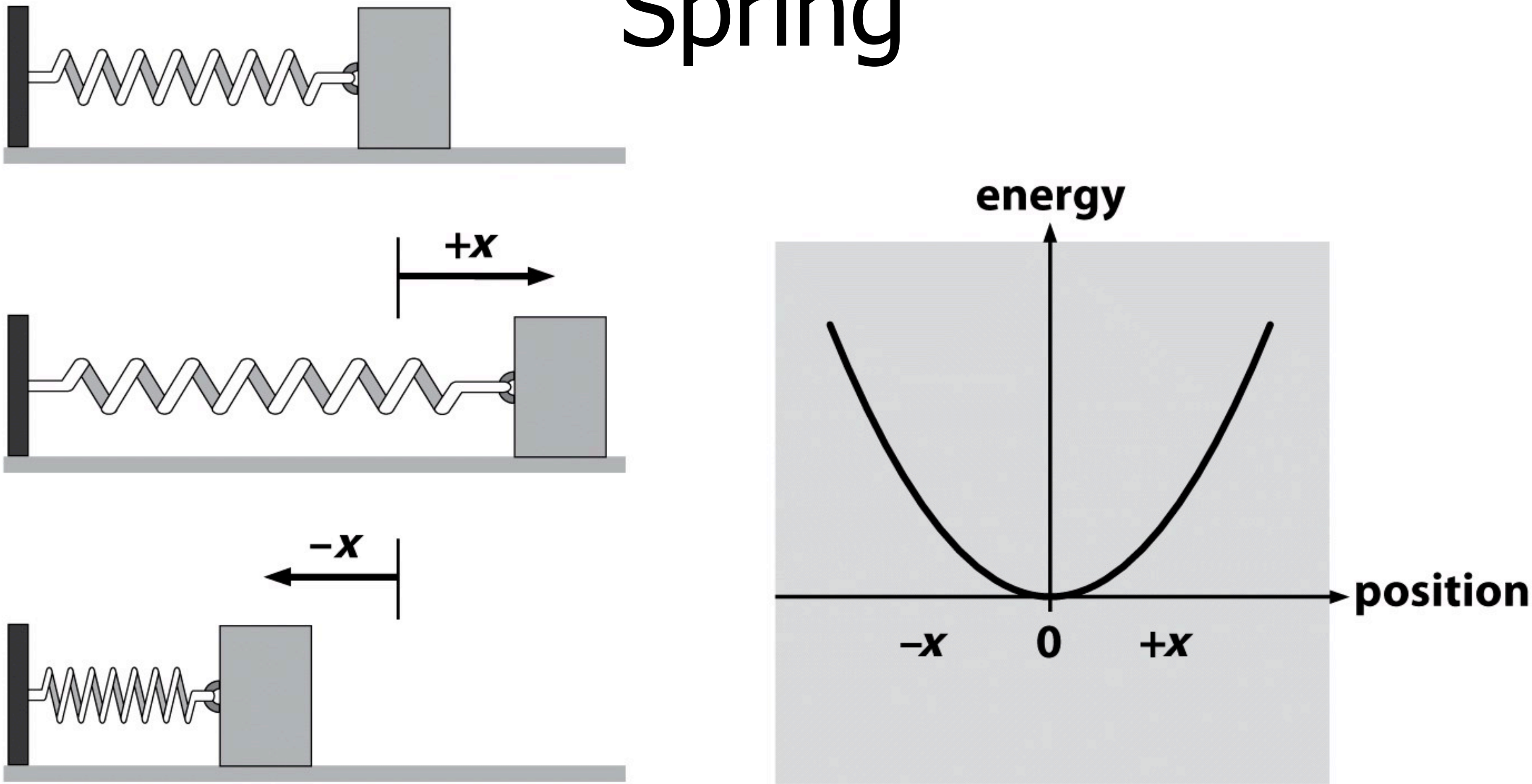



Figure 1.12a Physical Biology of the Cell (© Garland Science 2009)

# Biological Instances of a Simple Harmonic Oscillator

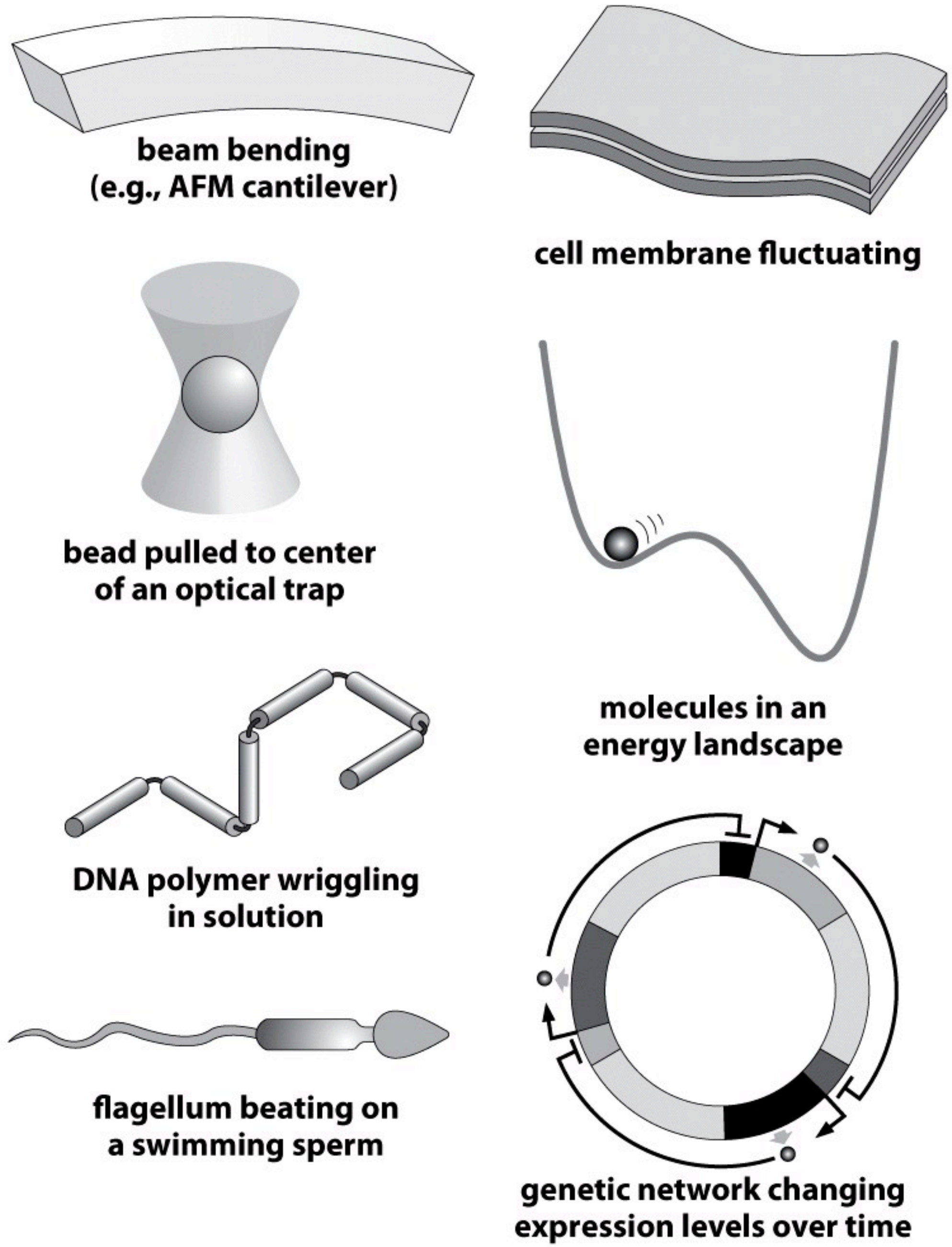



Figure 1.12b Physical Biology of the Cell (© Garland Science 2009)

# Classes of Physical Models

- Simple harmonic oscillator
- Ideal gas
- Two-level systems and Ising model
- Ramdom walks, entropy etc.
- Poisson-Boltzmann model of charge
- Newtonian fluids and Navier-Stokes equation
- Diffusion and random walks
- Rate equation models of chemical kinetics

# Estimates and Models

Estimating genome size in bp from image of bacteriophage genome

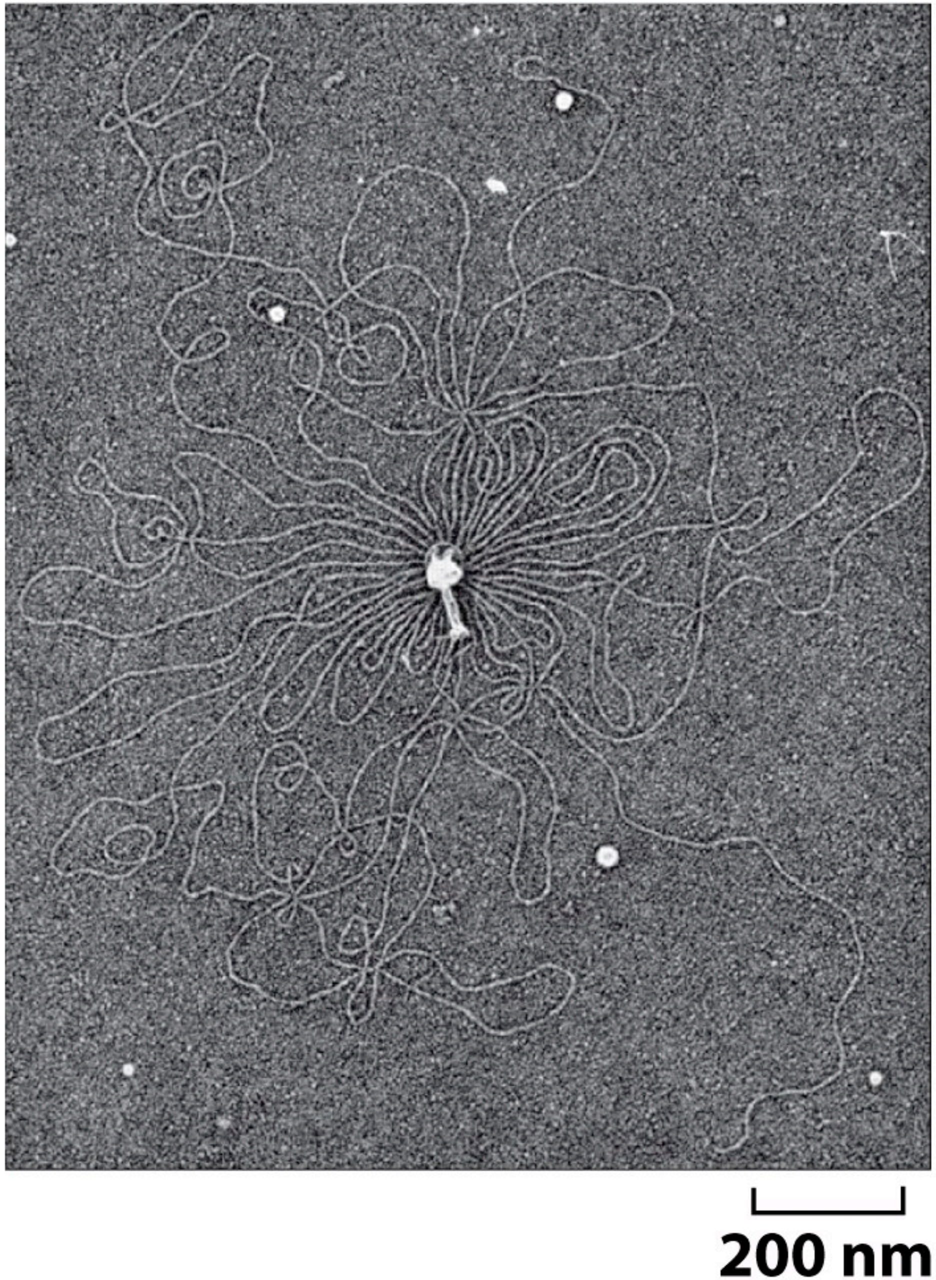



Figure 1.13 Physical Biology of the Cell (© Garland Science 2009)

# Wrong Models are Good

- Inappropriate model (e.g. Incorrect dimensions)
- Lacking detail (e.g. Incomplete)
- Importance of different considerations (e.g. E. coli movement and Brownian motion vs. viscous drag vs. inertia)
- Introduce correct physical model and parameters and compare with experiment

The Best

# Biological Estimates-1

| **Scale** | **Quantity** | **Symbol** | **Rule of thumb** |
|---|---|---|---|
| E. coli | Cell volume | $V_{Ecoli}$ | $\approx 1\ \mu m^3$ |
| | Cell mass | $m_{Ecoli}$ | $\approx 1$ pg |
| | Cell cycle time | $t_{Ecoli}$ | $\approx 3000 s$ |
| | Cell surface area | $A_{Ecoli}$ | $\approx 6\ \mu m^2$ |
| | Swimming speed | $v_{Ecoli}$ | $\approx 20\ \mu m/s$ |
| | Genome length | $N_{bp}^{Ecoli}$ | $\approx 5 \times 10^6$ bp |
| Yeast | Volume of the cell | $V_{yeast}$ | $\approx 60\ \mu m^3$ |
| | Cell mass | $m_{yeast}$ | $\approx 60$ pg |
| | Cell diameter | $d_{yeast}$ | $\approx 5\ \mu m$ |
| | Cell cycle time | $t_{yeast}$ | $\approx 1.2 \times 10^4$ min |
| | Genome length | $N_{bp}^{yeast}$ | $\approx 10^7$ bp |

# Biological Estimates-2

| Scale | Quantity | Symbol | Rule of thumb |
|---|---|---|---|
| Organelles | Diameter of nucleus | $d_{nucleus}$ | ≈5 μm |
| | Length of mitochondrion | $l_{mito}$ | ≈2 μm |
| | Diameter of transport vescicles | $d_{vescicle}$ | ≈50 nm |
| Water | Volume of molecule | $V_{H2O}$ | $\approx 10^{-2}$ nm$^3$ |
| | Density of water | ϱ | 1 g/cm$^3$ |
| | Viscosity of water | η | 1 centipoise ($10^{-2}$ g/(cm-s)) |
| | Hydrophobic embedding energy | $\approx E_{hydr}$ | 25 cal/mol-Å$^2$ |

$k_B T \approx 4$ pN-nm (at room temperature in K)

# Book List

1. Microbe hunters- Paul de Kruif
2. What is life- Erwin Schroedinger