Physical Biology

Bio322

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

Construction Plans

- Organelles
- Cells
- Organisms
- Estimates of size

Fundamental Unit of Life

- Cell
- Energy consumption, structure formation
- Replication
- Hooke (1665) using cork and compound microscope
- Leewenhoek (1674) first living cell- Spirogyra

Origin of the Cell

Primeval Soup
Self-replicating molecules (RNA?)
Peptide formation
Carbohydrates
Clay
Genes first or metabolism first
Lipid layers
Primitive cellular compartments

Astrobiology, Artificial Life, Prebiotic Life, PNA's, Replicating vescicles

Search for the Minimal Cell

Mycoplasma genitalium

Genome size: 5.8 x 10^5 basepairs

482 protein-coding genes

~100 dispensible genes

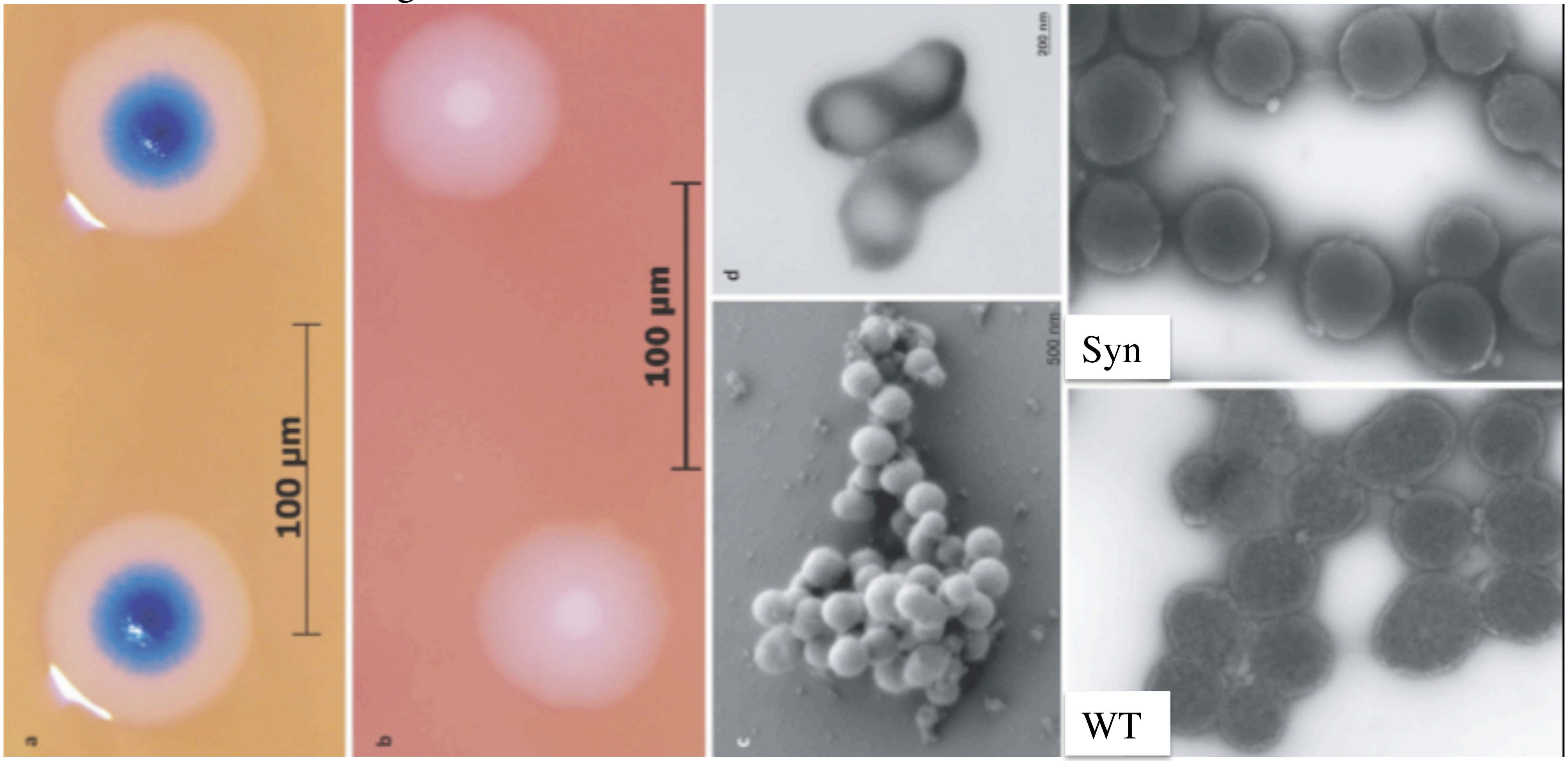
http://cmr.jcvi.org

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

M. mycoides JCV1-syn1.0 Xgal test

M. mycoides W.T. Xgal test

E.M of synthetic strains



Synthetic genome

Phenotype

Replication

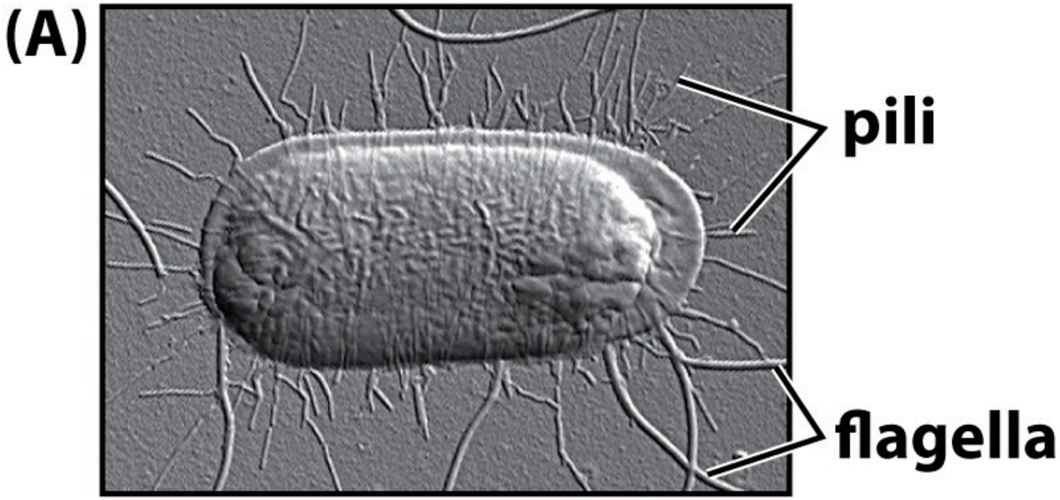
Gibson et al. (May 2010)

Model Organism: *E. coli*

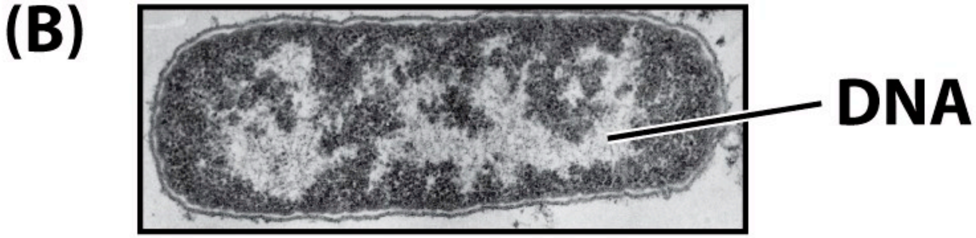
- Easy to isolate (gut bacterium found in fecal matter)
- Growth in anaerobic and anaerobic conditions
- Mutagenesis easy: e.g. nucleotide synthesis mutants
- Experiments showing insight

Sizes

AFM image



EM



Schematic

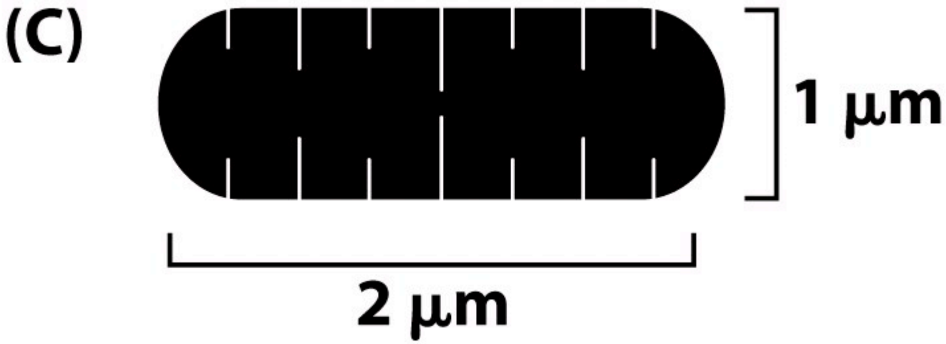
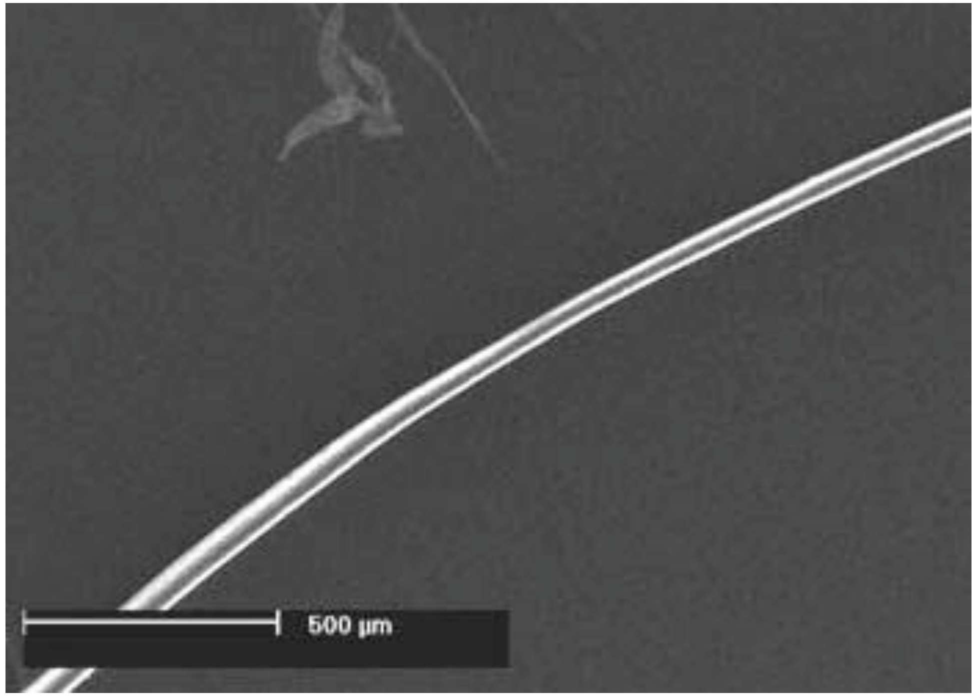


Figure 2.1 Physical Biology of the Cell (© Garland Science 2009)

Human hair



>How many end-on cells will give diameter of human hair?

> What is the fold relation between DNA and E. coli diameters?

Ribosome Census

- 20% protein component of cell is ribosomal
- Assume all ribosomal protein bound
- What is the number of ribosomes in an E. coli cell?
- Mass of single Ribosome ~ 2.5 Mda
- Ribosome contains 1/3 protein, 2/3 RNA

Ribosomes in Cell: Relative Volume

- Ribosome diameter ~ 20 nm
- Total volume?
- What is the percent volume occupied by ribosomes relative to cell volume?

No. of Lipid Molecules/cell

- Shape of cell gives surface area.
- $N_{lipid} = ?$
- Area per lipid ~ 0.5 nm^2

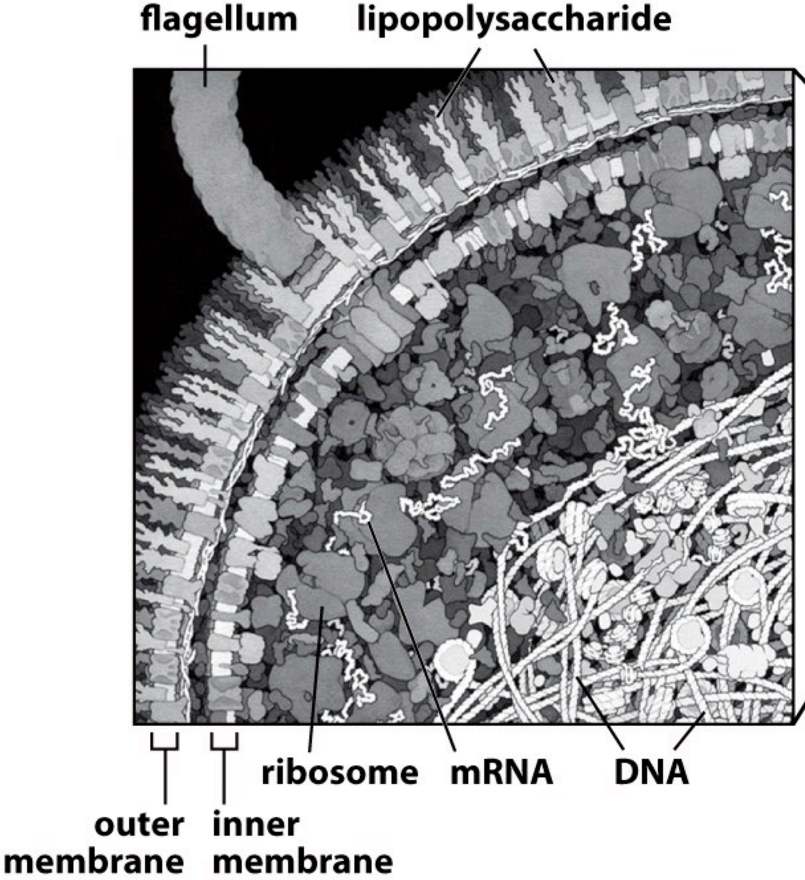
Water Molecules

- 70% cell mass is water
- N_{H2O}=?

Inorganic Ions

- [K] ~ 100 mM
-

Macromolecular Census



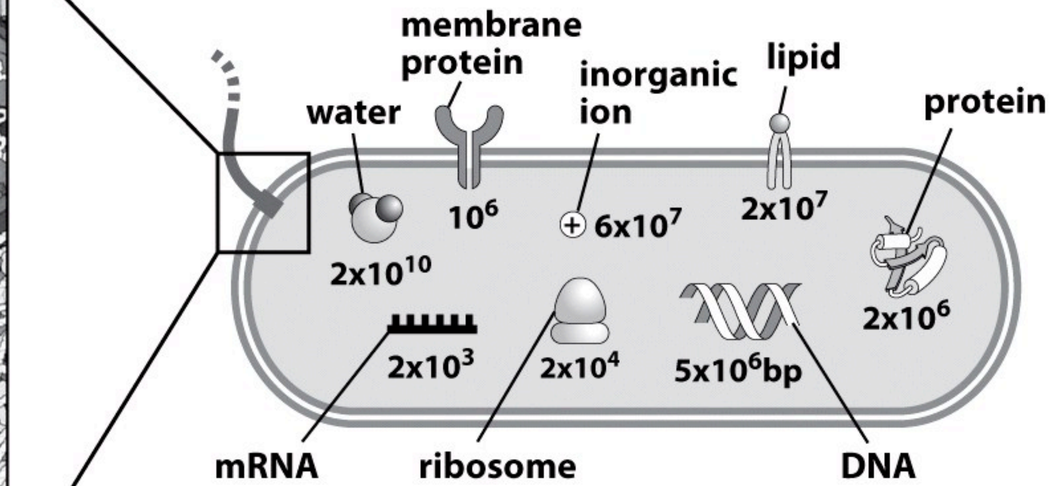


Figure 2.2 Physical Biology of the Cell (© Garland Science 2009)

- Volume of E. coli in femtolitres?
- Mass of single E. coli cell?
- How many proteins per E. coli?
- Dry mass of E. coli 30% of wet weight.
- 50% dry-mass is protein.

Why?

Abundance vs. Scarcity.

Bulk vs. Stochastic.

Observed Census Results

Substance	% of total dry weight	Number of molecules
Macromolecule		
Protein	55.0	2.4×10^6
RNA	20.4	
23S RNA	10.6	19,000
16S RNA	5.5	19,000
5S RNA	0.4	19,000
Transfer RNA (4S)	2.9	200,000
Messenger RNA	0.8	1,400
Phospholipid	9.1	22×10^6
Lipopolysaccharide	3.4	1.2×10^6
DNA	3.1	2
Murein	2.5	1
Glycogen	2.5	4,360
Total macromolecules	**96.1**	
Small molecules		
Metabolites, building blocks, etc.	2.9	
Inorganic ions	1.0	
Total small molecules	**3.9**	

Table 2.1 Physical Biology of the Cell (© Garland Science 2009)

How to Make a Molecular Census

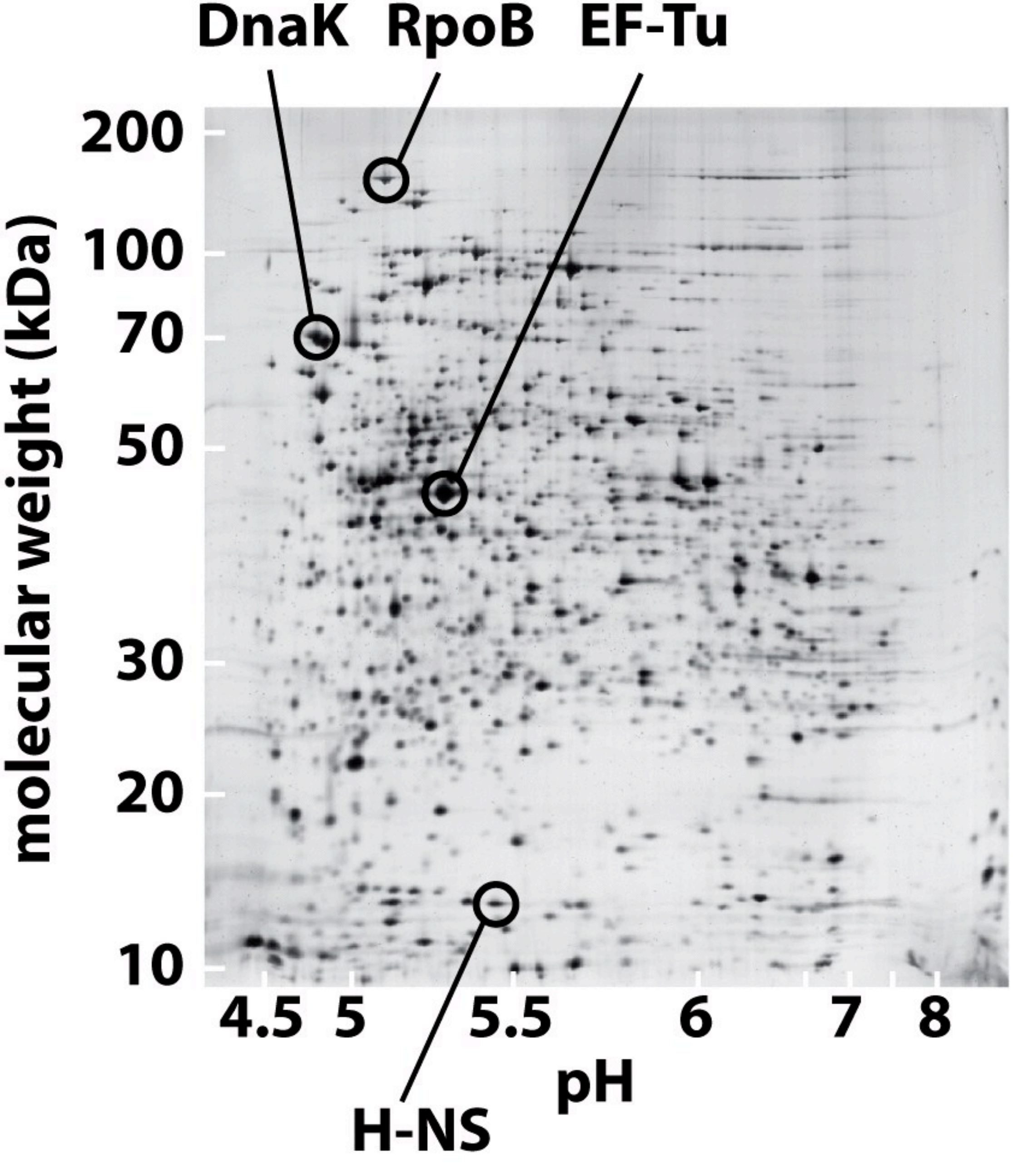


Figure 2.3 Physical Biology of the Cell (© Garland Science 2009)

Concentrations and Spacing

If there is only 1 copy of a molecule in an E. coli cell, what is its concentration in Molarity?

What is the inter-molecular spacing for a given concentration?

Concentrations and Spacing

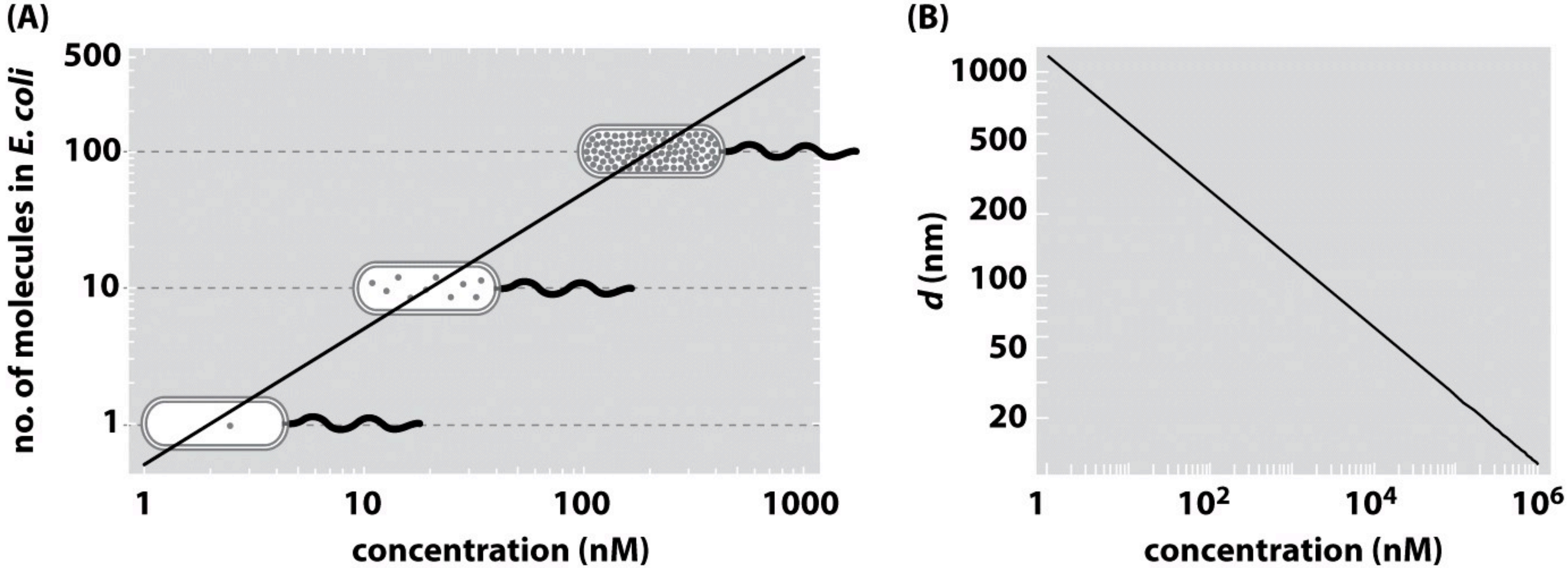


Figure 2.4 Physical Biology of the Cell (© Garland Science 2009)

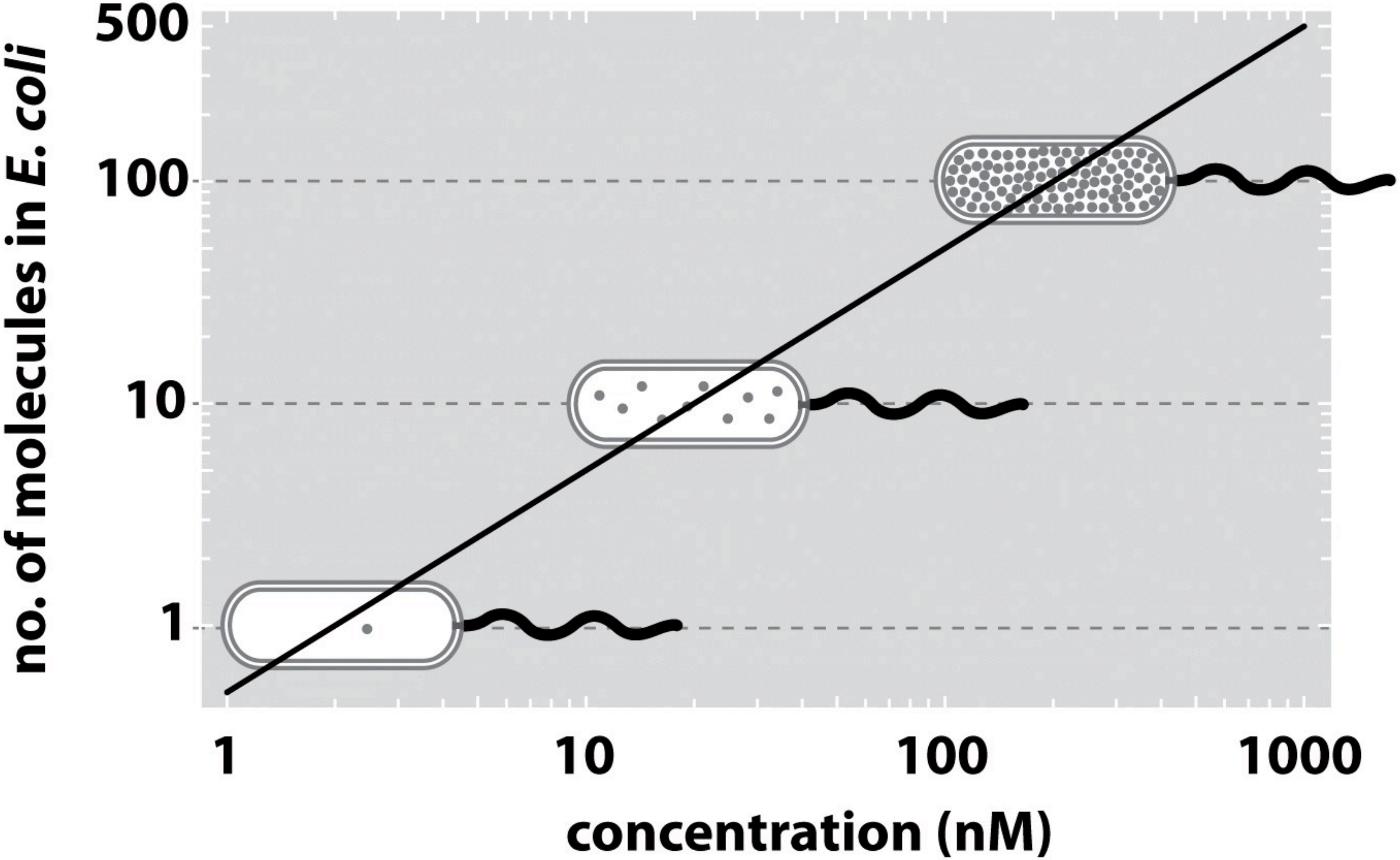


Figure 2.4a Physical Biology of the Cell (© Garland Science 2009)

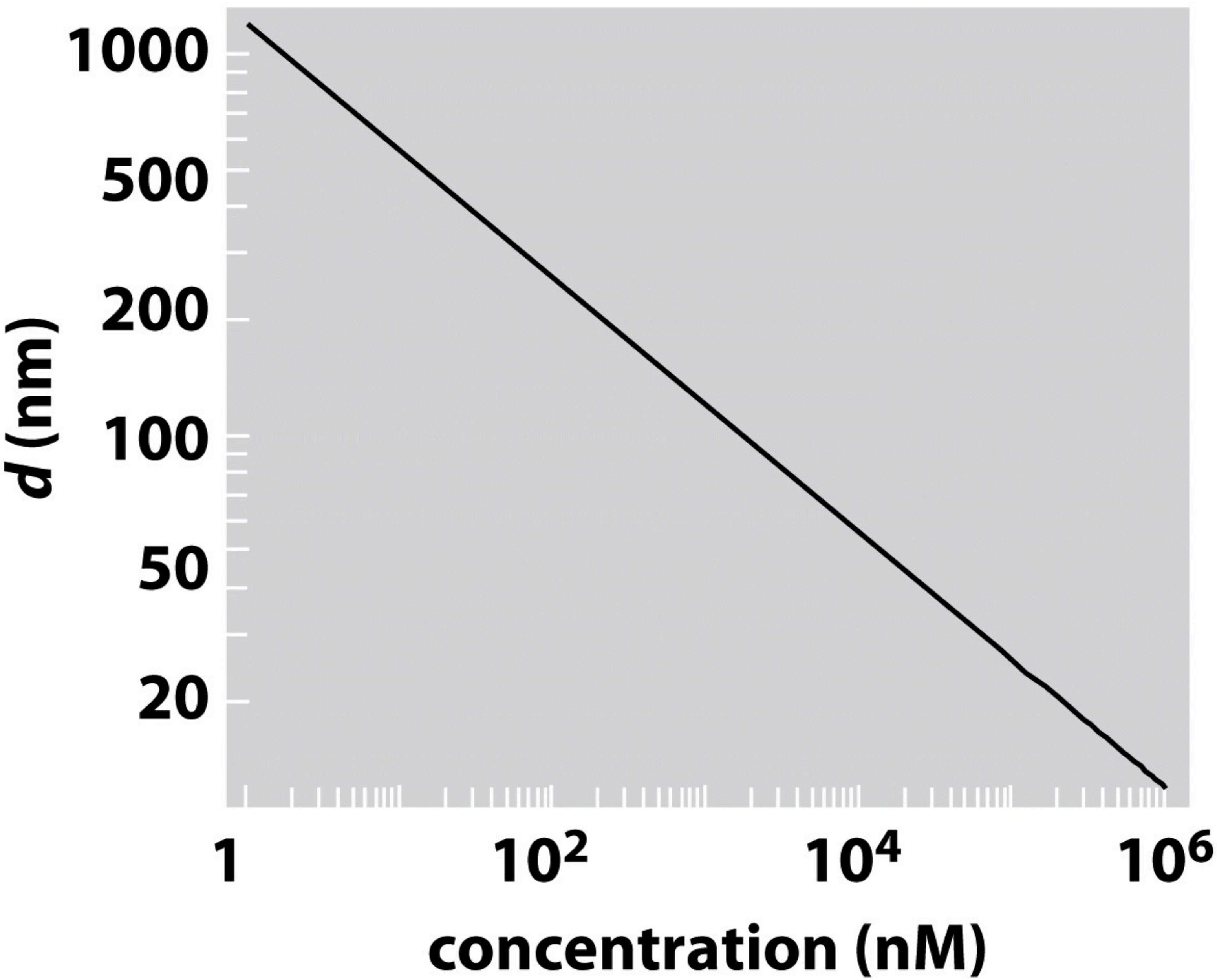


Figure 2.4b Physical Biology of the Cell (© Garland Science 2009)

Next

- Experimental tools to look inside cells
- Spatial scales of biological structure
- DNA
- Organelles
- Membrane
- Assemblies
- Viruses
- Tissues

Probing Biological Structure

- Radiation
- Forces

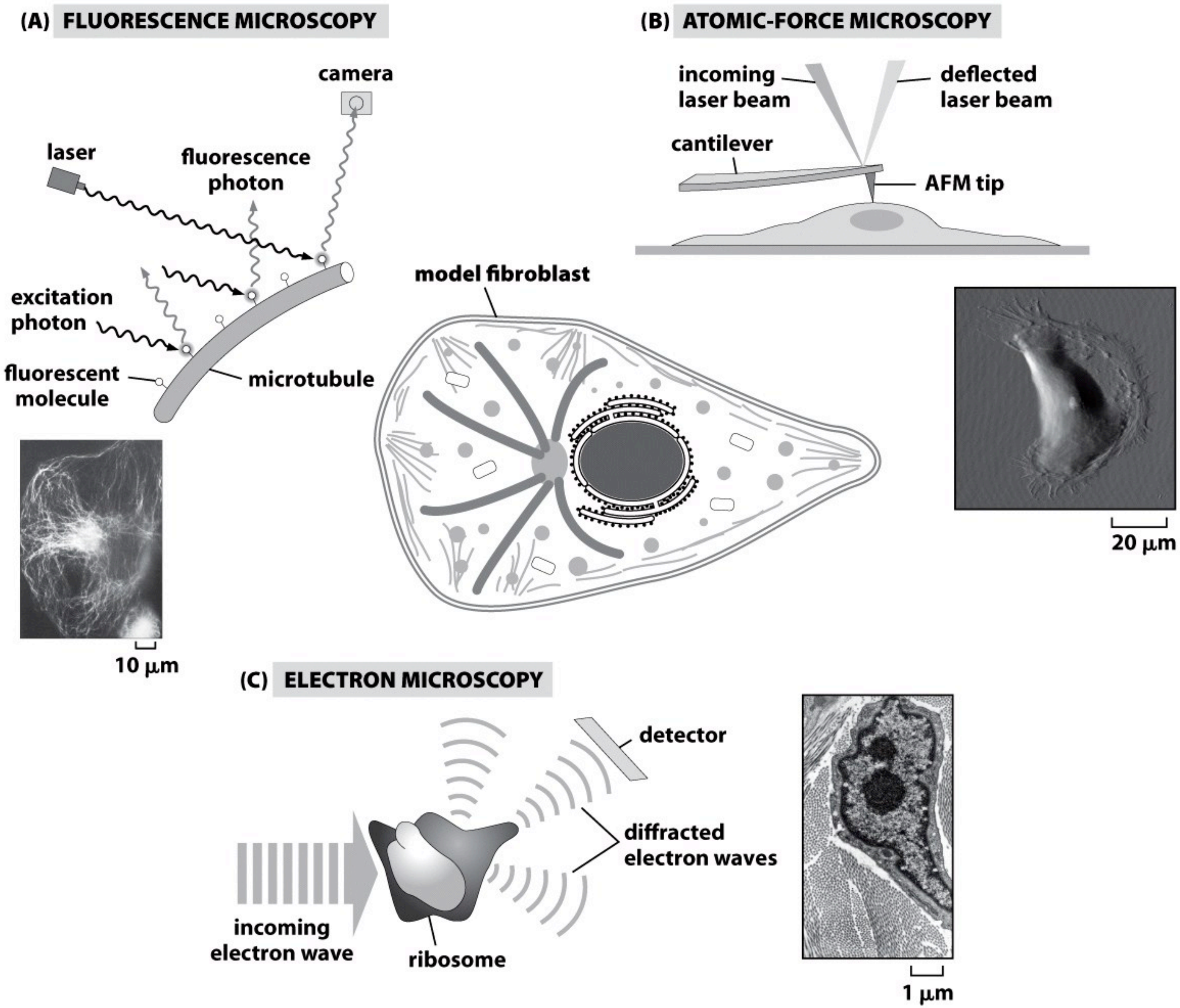


Figure 2.5 Physical Biology of the Cell (© Garland Science 2009)

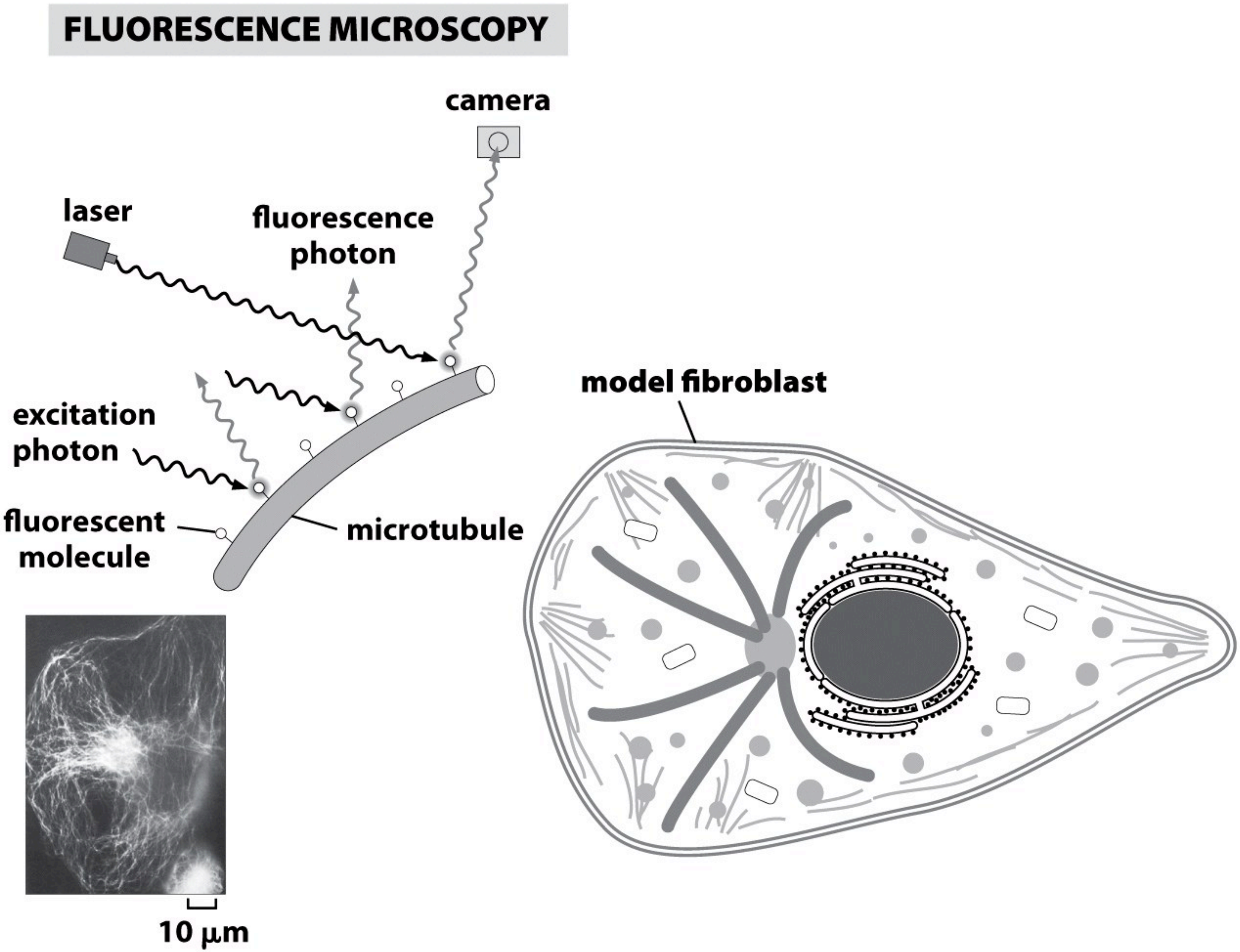


Figure 2.5a Physical Biology of the Cell (© Garland Science 2009)

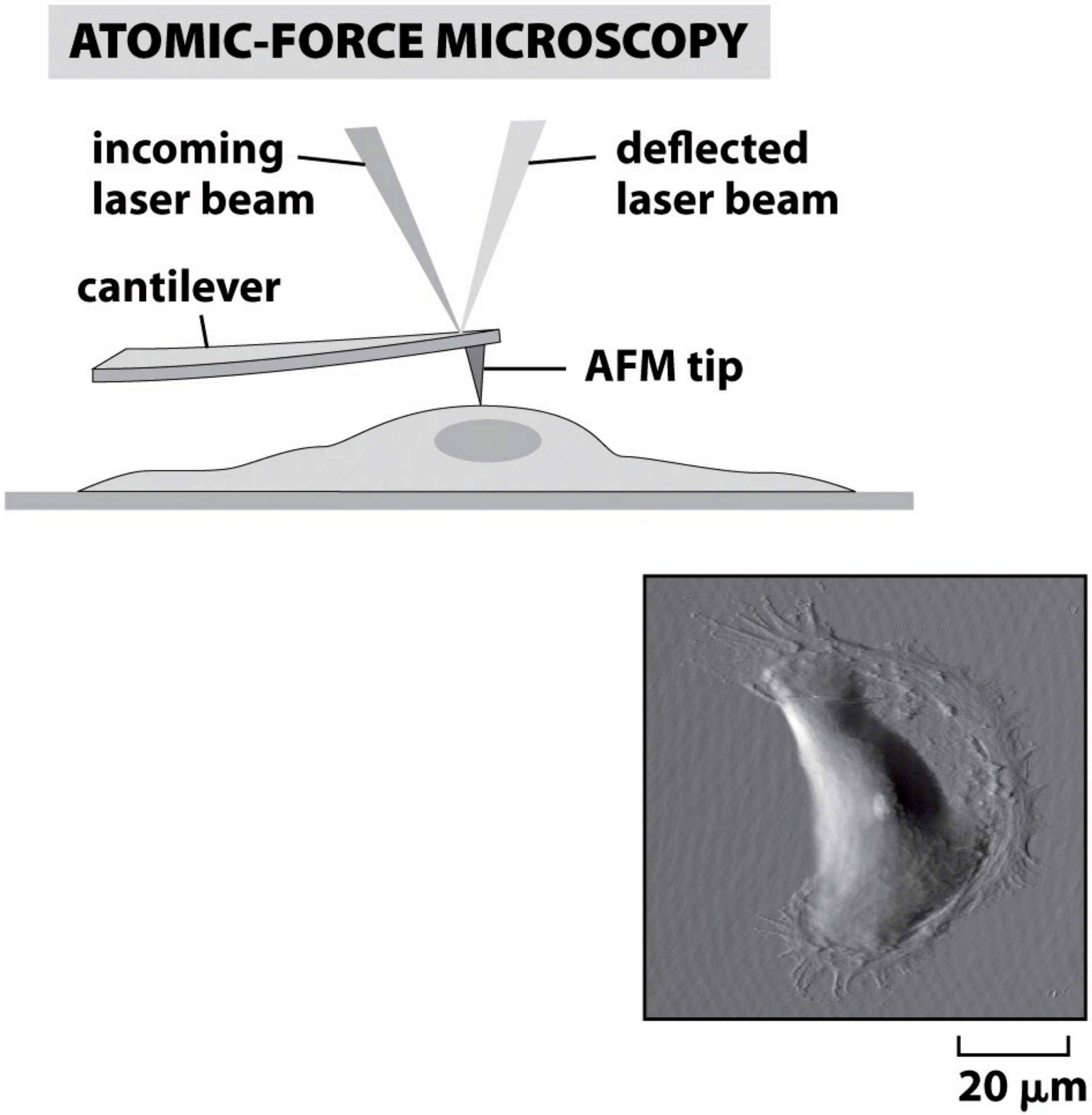


Figure 2.5b Physical Biology of the Cell (© Garland Science 2009)

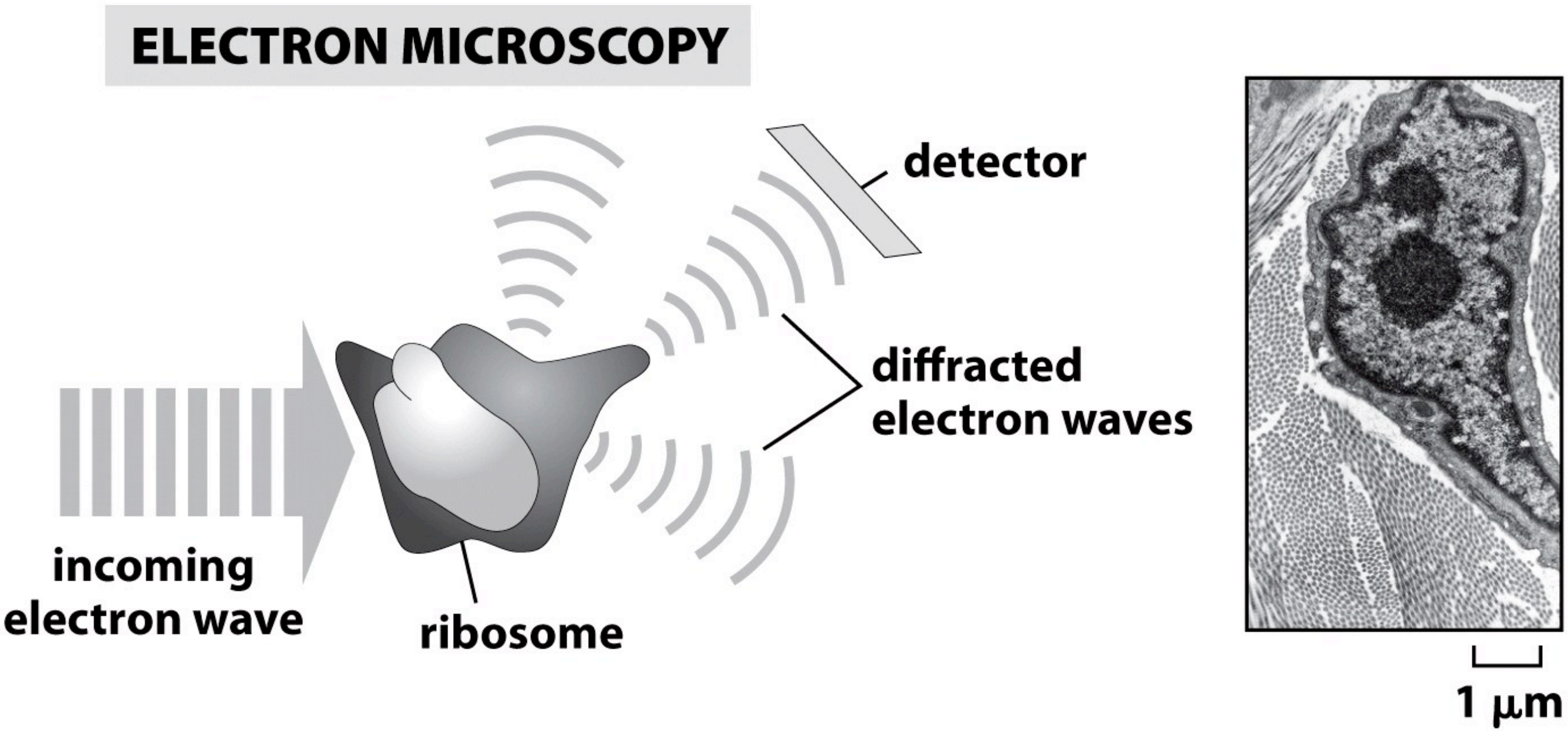


Figure 2.5c Physical Biology of the Cell (© Garland Science 2009)

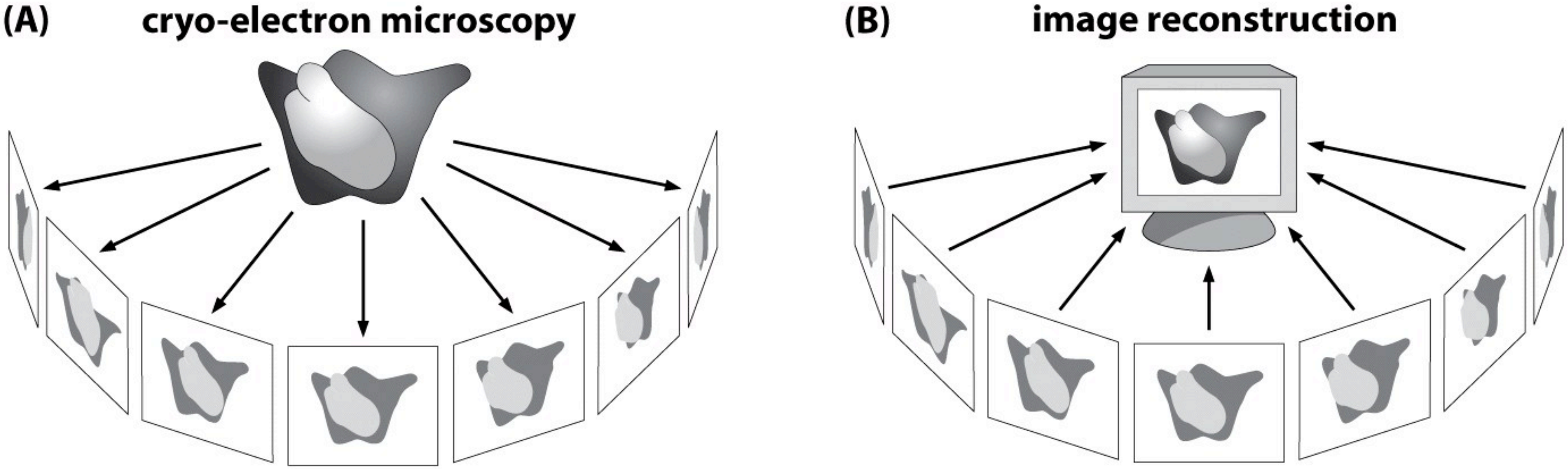


Figure 2.6 Physical Biology of the Cell (© Garland Science 2009)

cryo-electron microscopy

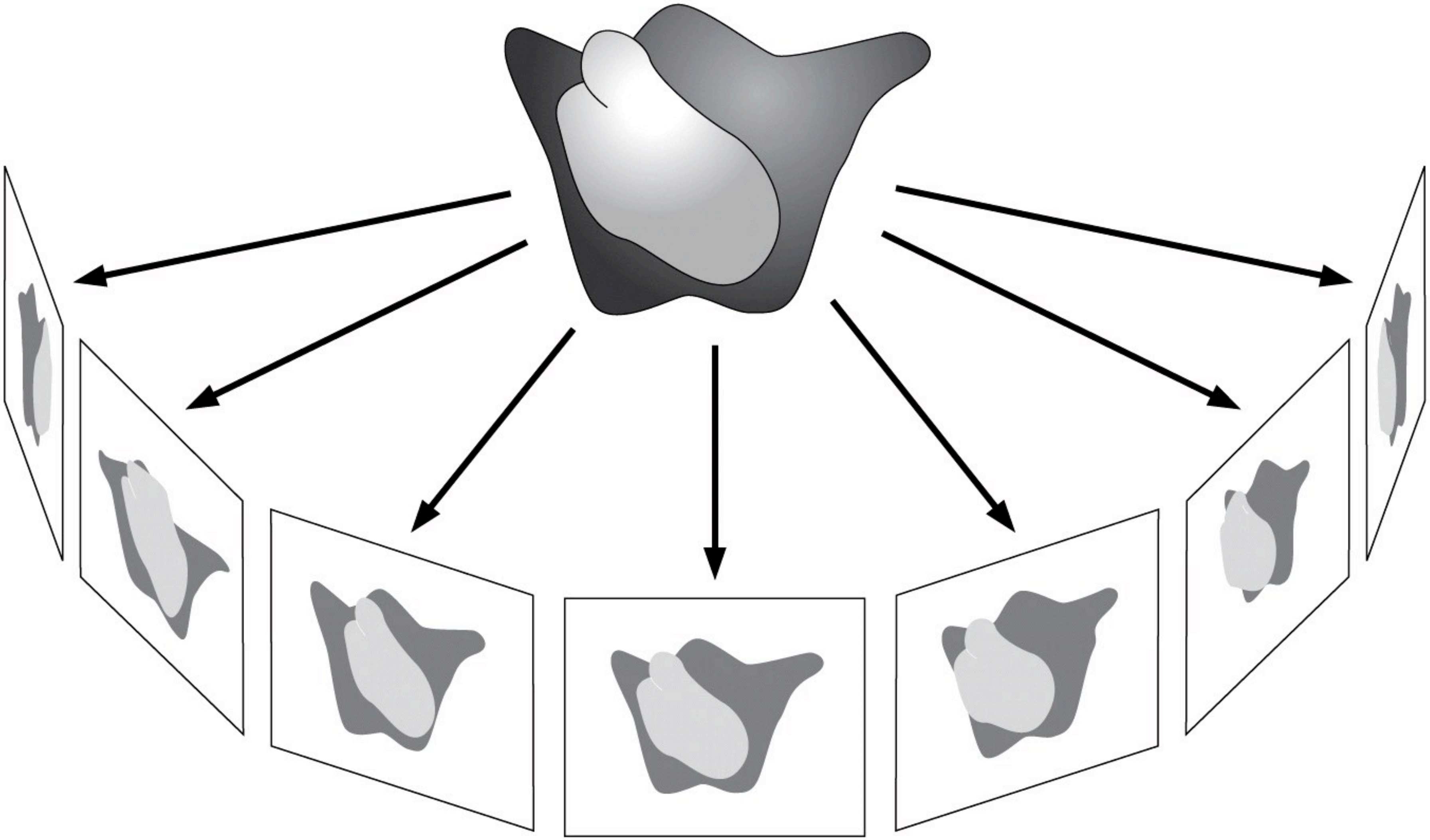


Figure 2.6a Physical Biology of the Cell (© Garland Science 2009)

image reconstruction

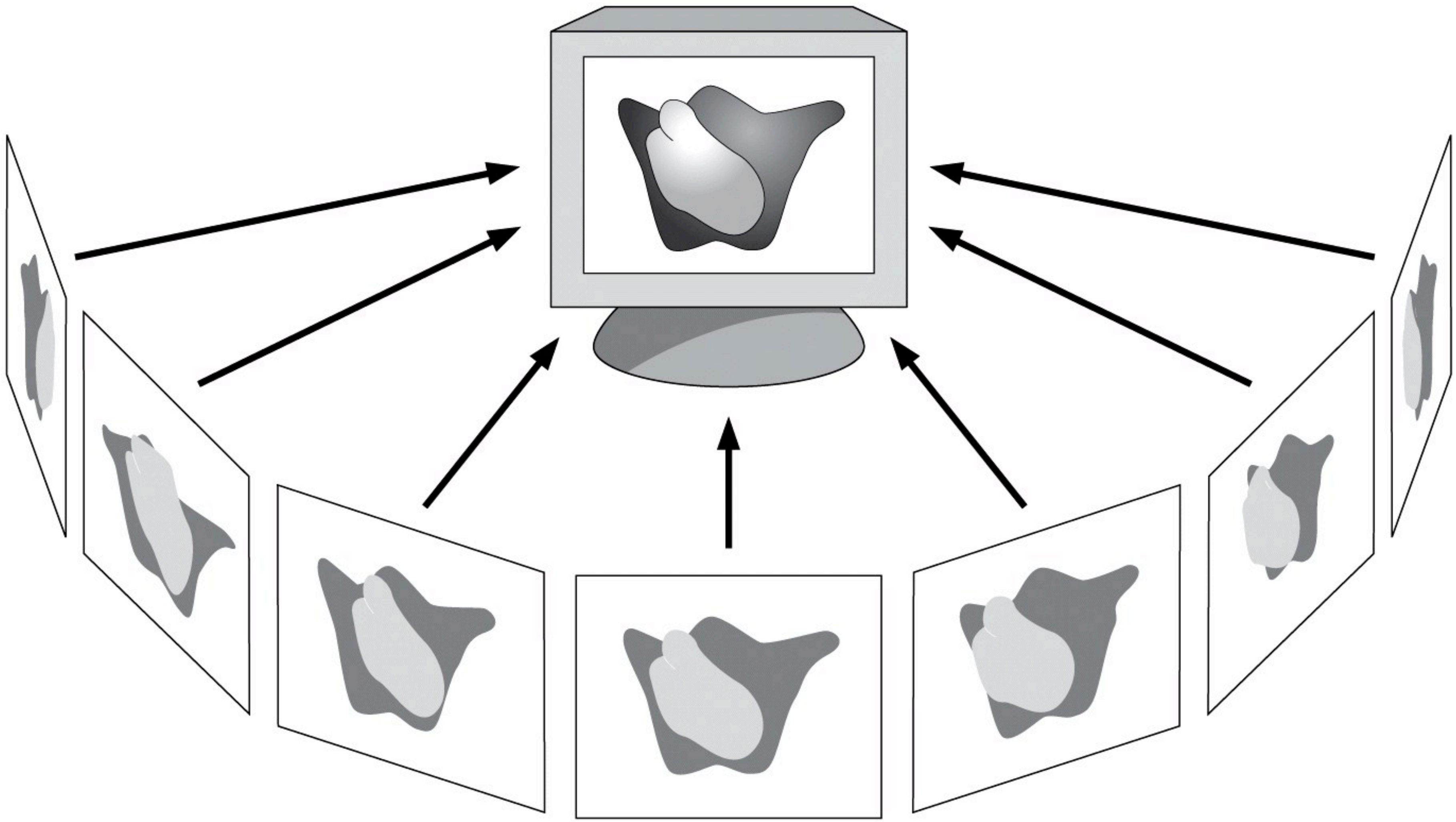


Figure 2.6b Physical Biology of the Cell (© Garland Science 2009)

Powers of 10

Spatial scale with relation to E. coli

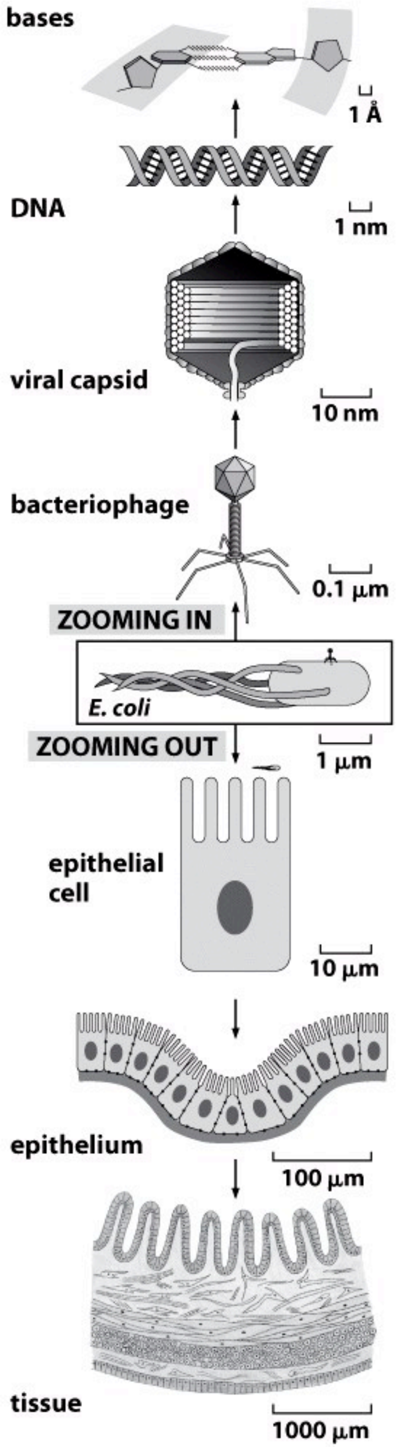


Figure 2.7 Physical Biology of the Cell (© Garland Science 2009)

Smaller than E. coli

Molecules, assemblies, cells

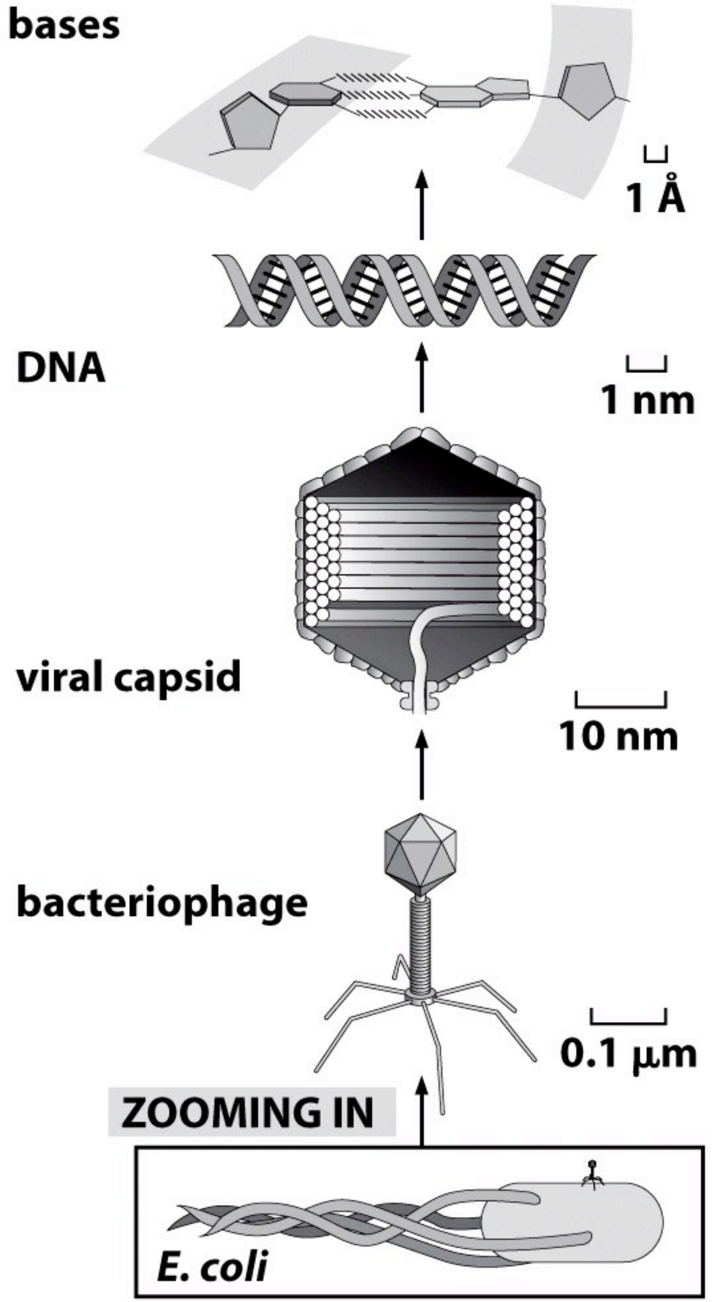


Figure 2.7 (part 1) Physical Biology of the Cell (© Garland Science 2009)

Higher Scales

Origin of multi-cellularity

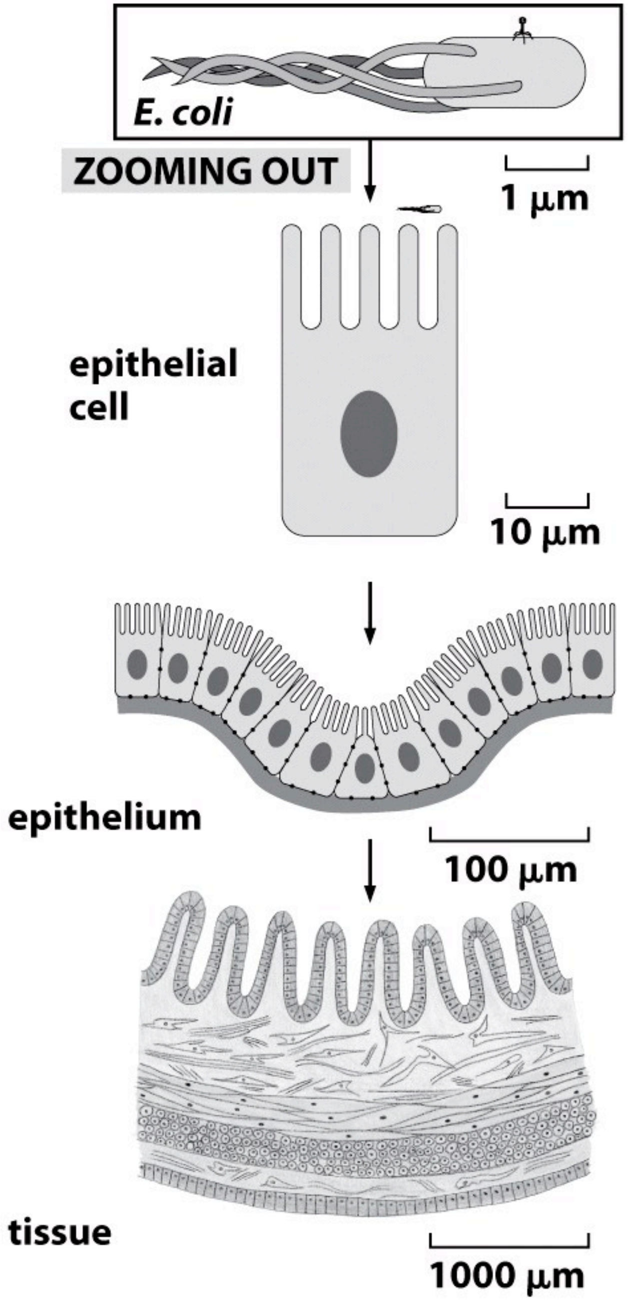


Figure 2.7 (part 2) Physical Biology of the Cell (© Garland Science 2009)

Diversity

Unity of governing principles

Diversity of form

Model cell types

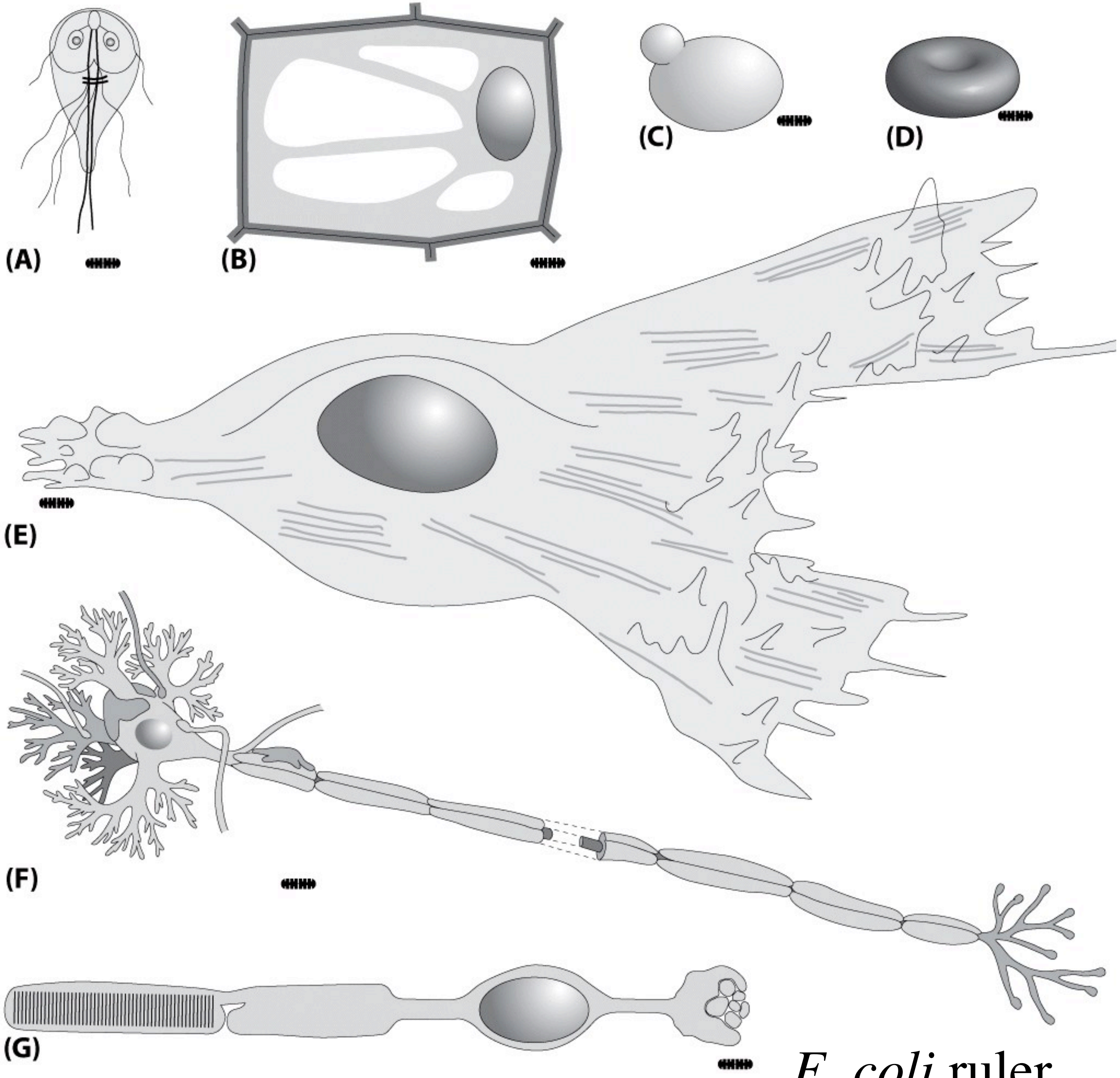
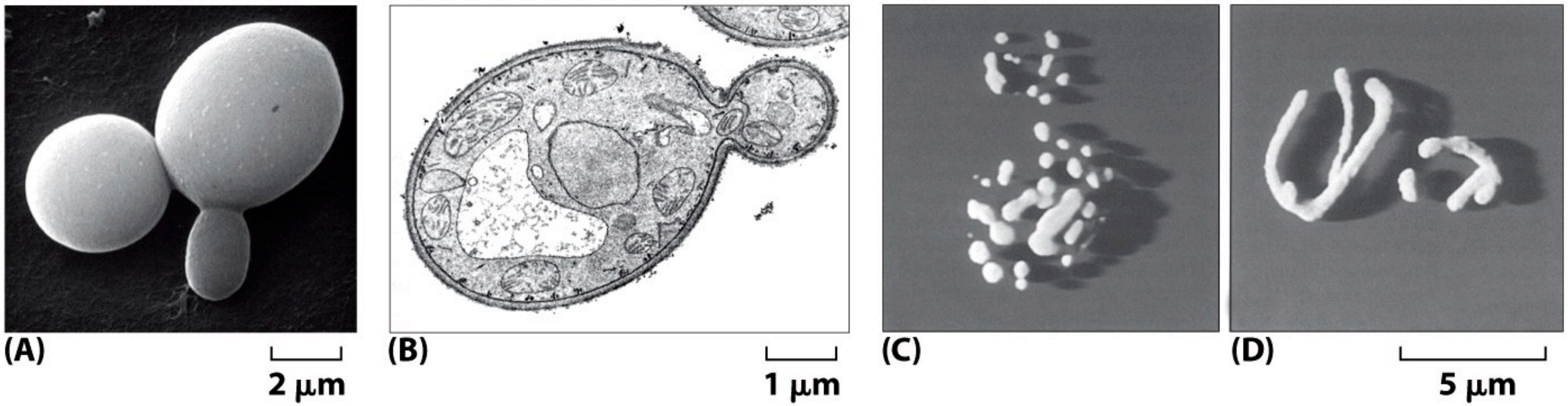


Figure 2.8 Physical Biology of the Cell (© Garland Science 2009)

E. coli ruler

Yeasts



- Candida albicans

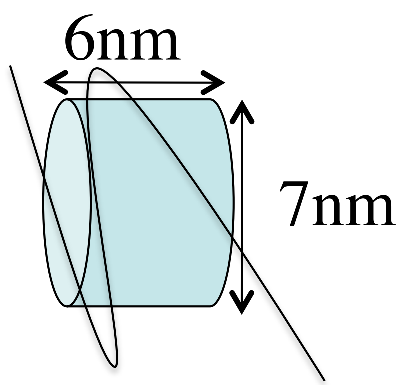
Saccharomyces cerevisae mitochondria in different growth conditions

Why study yeasts?

Eukaryotic Cell: Size Scale

Yeast
diameter ~ 5 μm
Volume
Area
Nucleus diameter ~
Genome 1.2 x 10^7 bps
Histones
Nucleosome:
How many nucleosomes?
150 bps per nucleosome, 50 bps spacer
Vol per histone octamer: 230 nm^3
Volume of base-pair?
Packing fraction = Vol genome/ Vol nucleus = ?

Nucleosome



Proteins and Lipids

Yeast $N_{proteins}$=?

Density similar to E. coli

E. coli $N_{protein}$ = total protein mass/mass per protein

$15*10^{-14}$ g/$5*10^{-20}$ g ~ 3 x 10^6

Yeast N_{lipids} = ?

Estimating Protein Copy Numbers

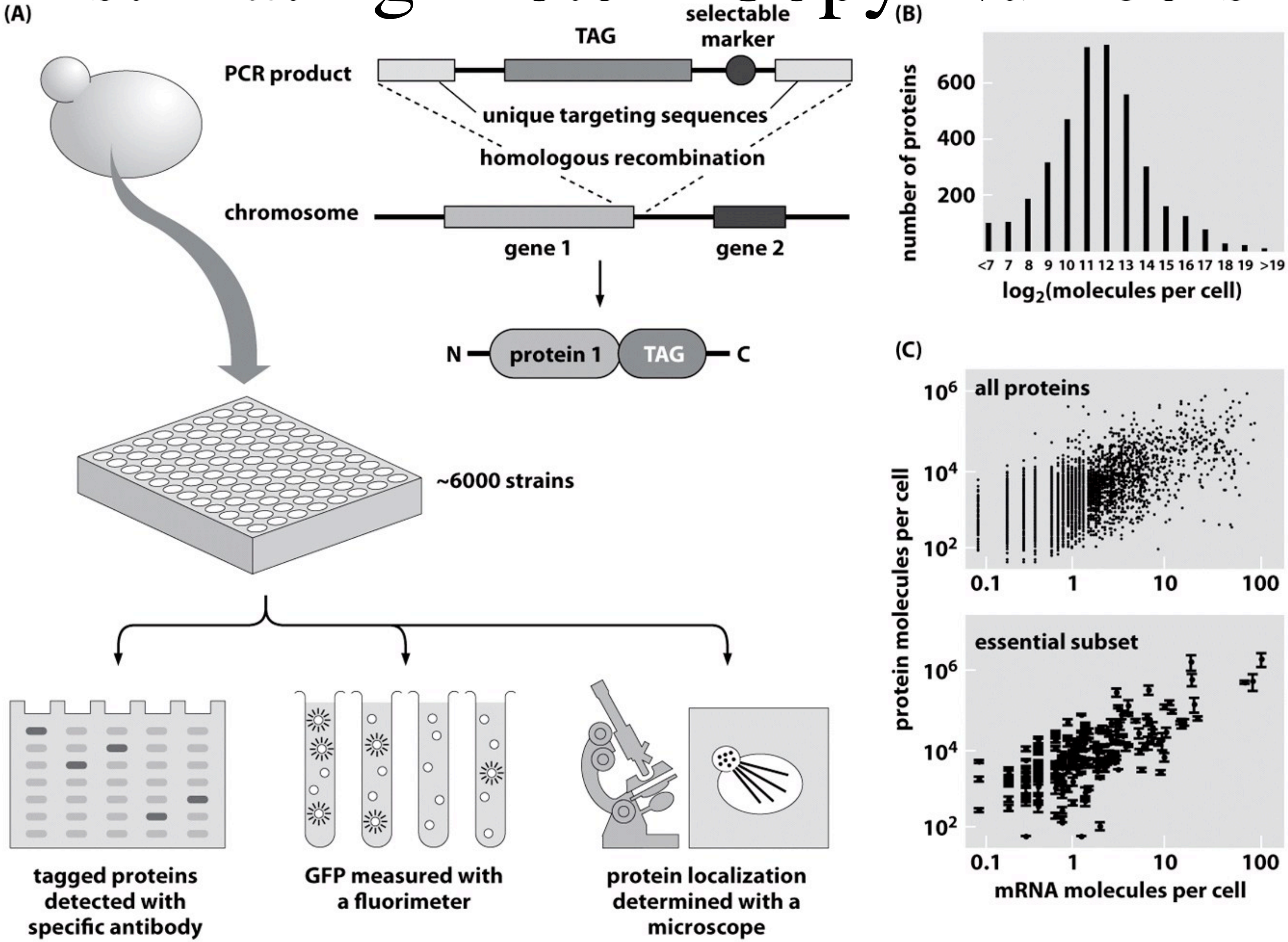


Figure 2.10 Physical Biology of the Cell (© Garland Science 2009)

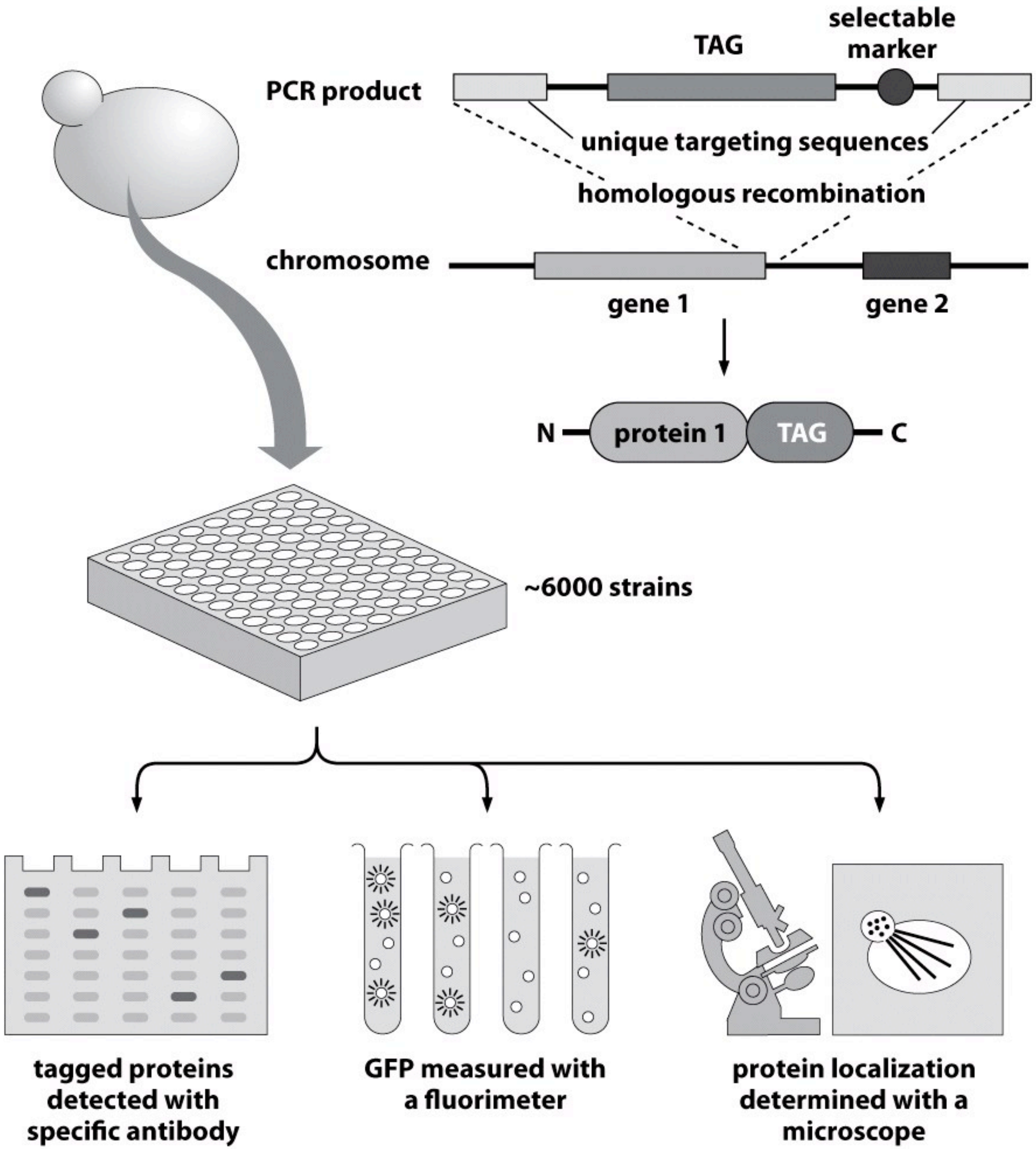


Figure 2.10a Physical Biology of the Cell (© Garland Science 2009)

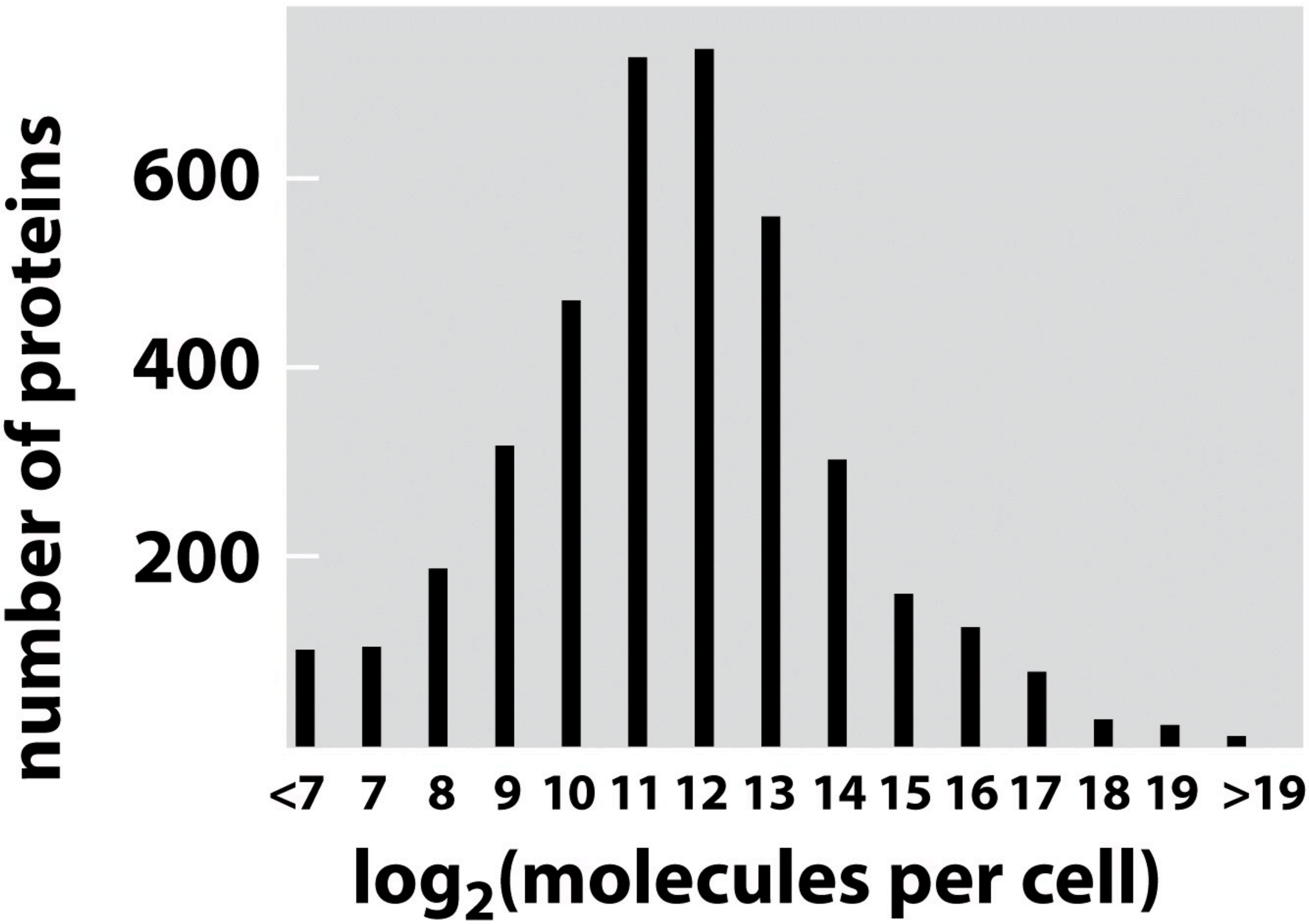


Figure 2.10b Physical Biology of the Cell (© Garland Science 2009)

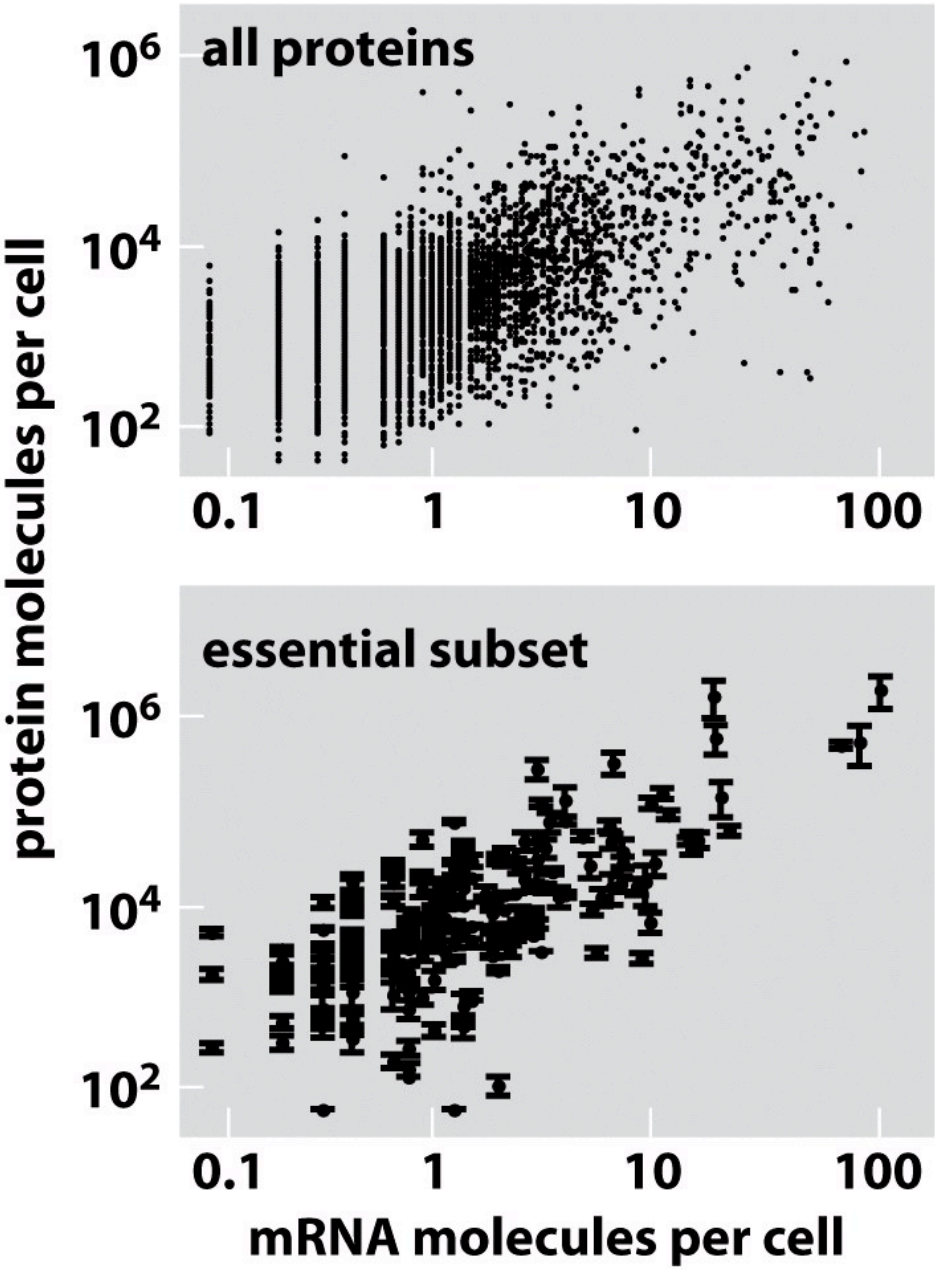


Figure 2.10c Physical Biology of the Cell (© Garland Science 2009)

Deformation in Cells

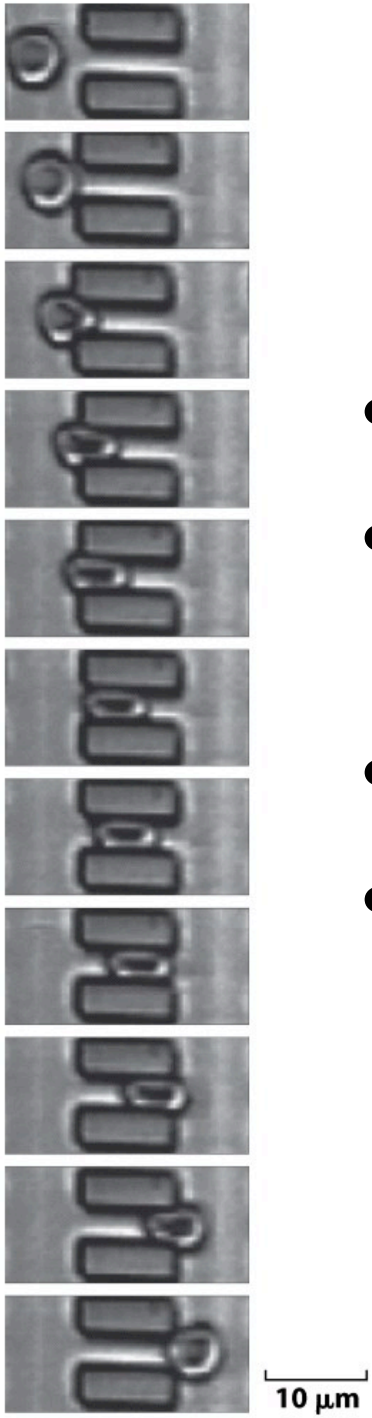


Figure 2.11 Physical Biology of the Cell (© Garland Science 2009)

- Dilute suspension of RBCs
- Microfabrication of silicon wafer capillary
- 2-4 micron wide capillaries
- Mobility is active (Ca^{2+} dependent)

Human Fibroblasts

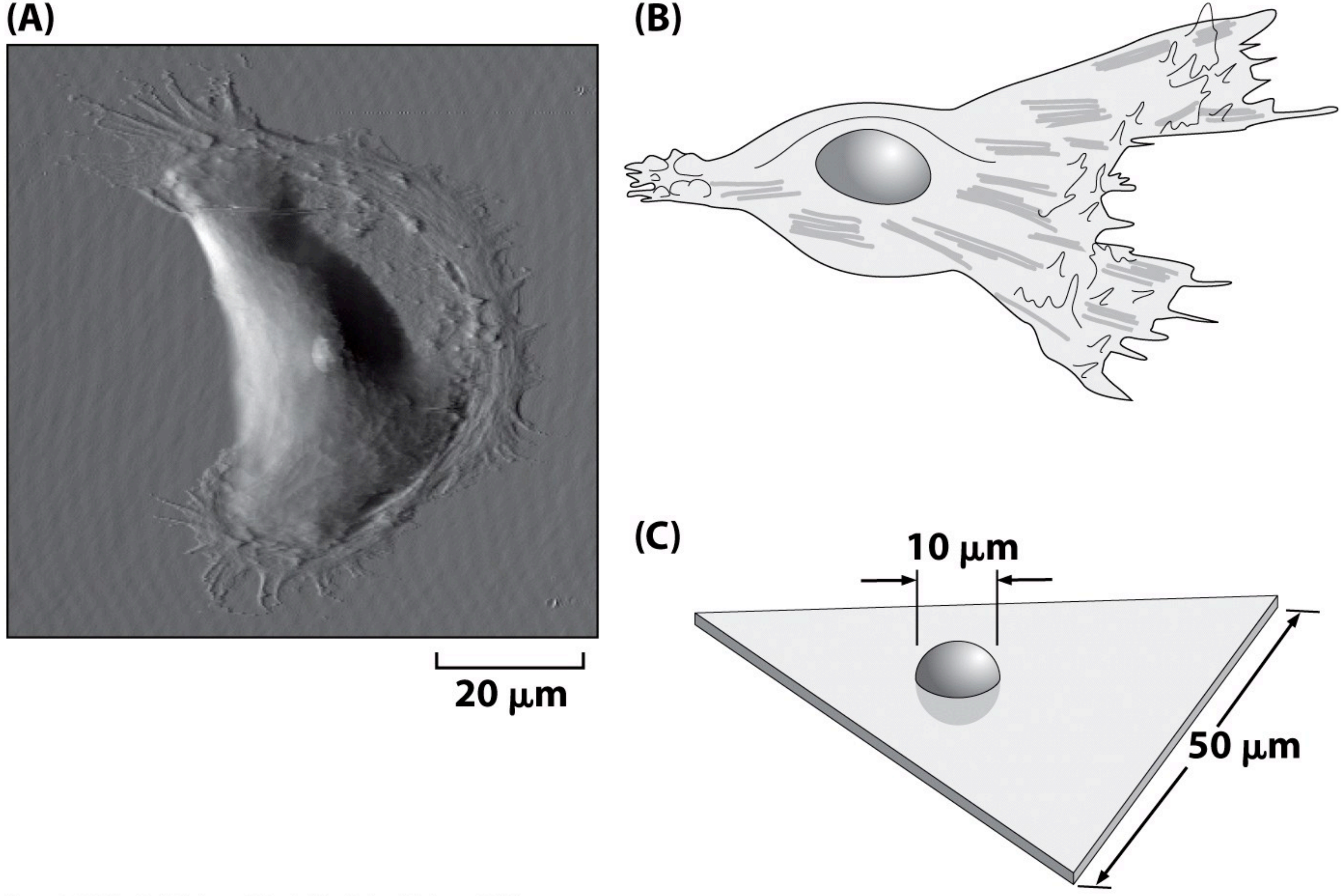


Figure 2.12 Physical Biology of the Cell (© Garland Science 2009)

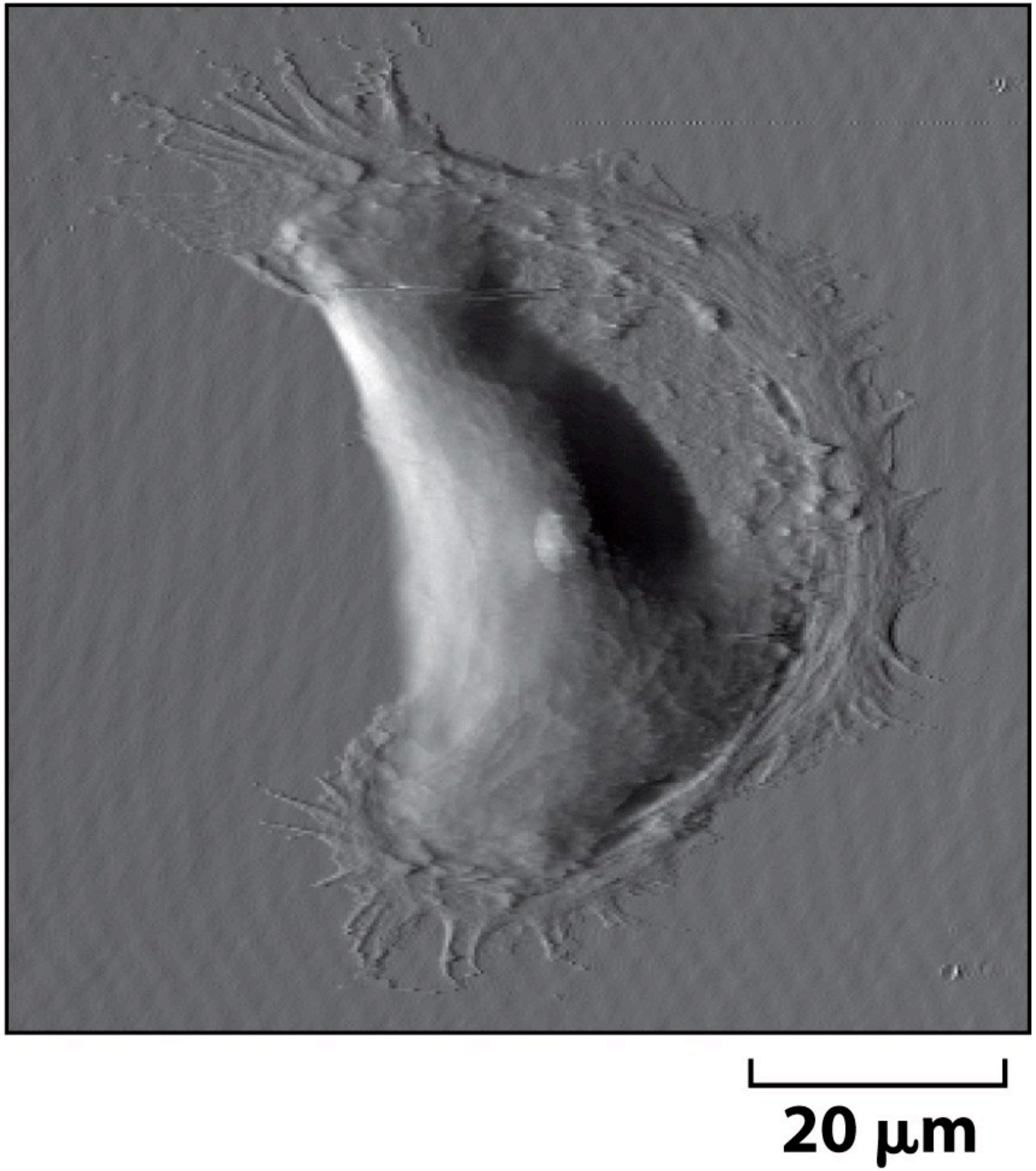


Figure 2.12a Physical Biology of the Cell (© Garland Science 2009)

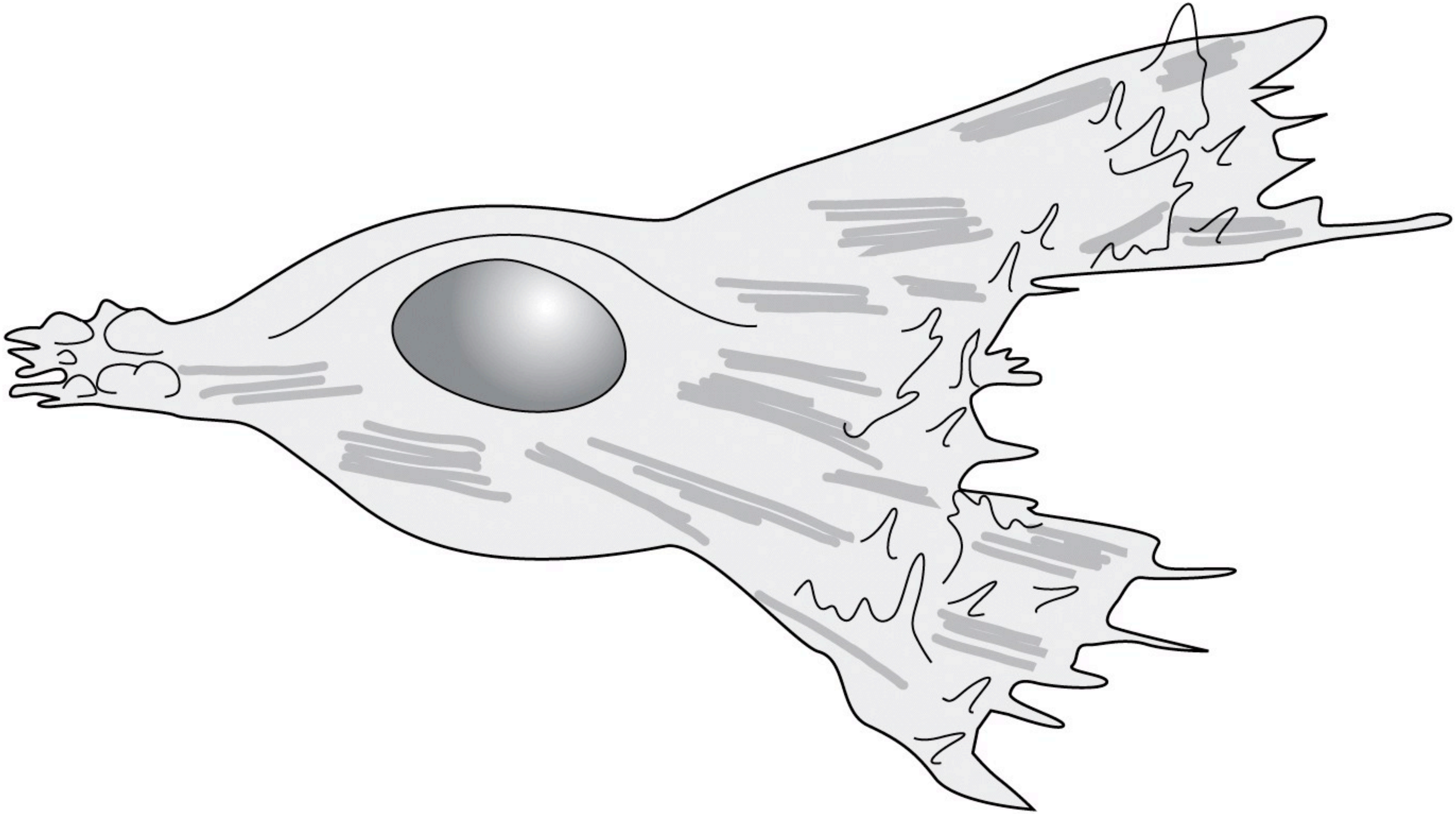


Figure 2.12b Physical Biology of the Cell (© Garland Science 2009)

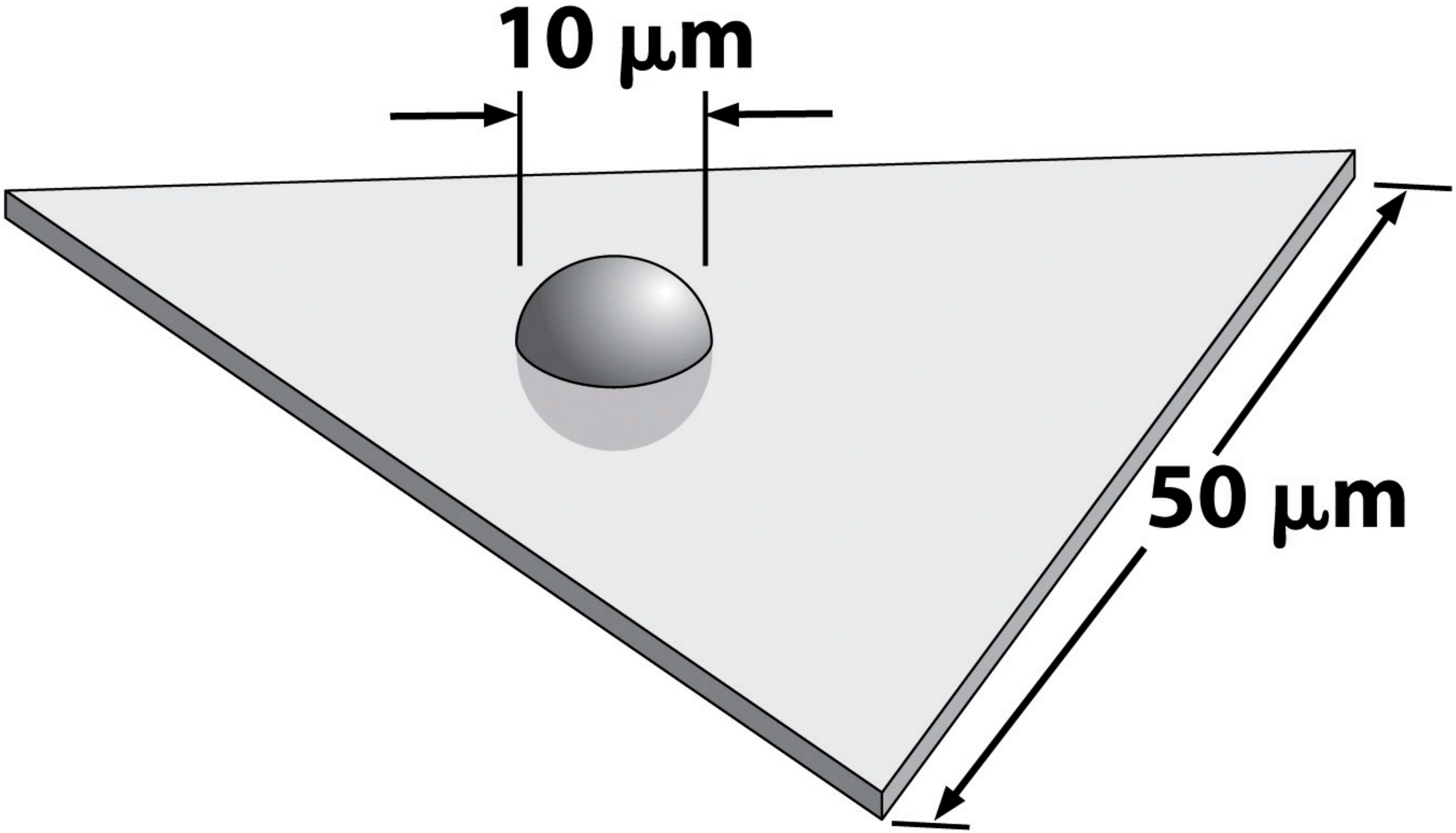
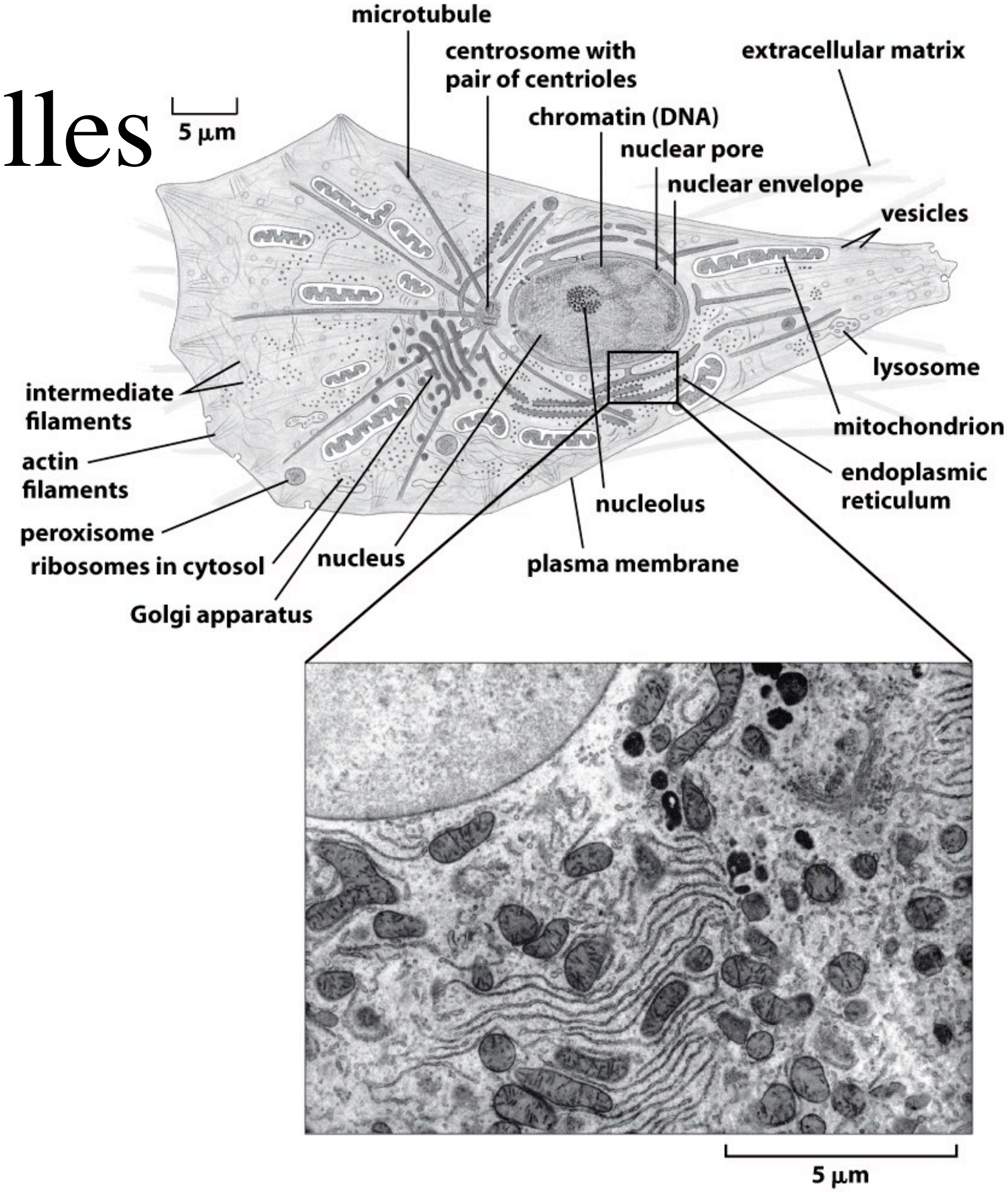


Figure 2.12c Physical Biology of the Cell (© Garland Science 2009)

Cellular Organelles



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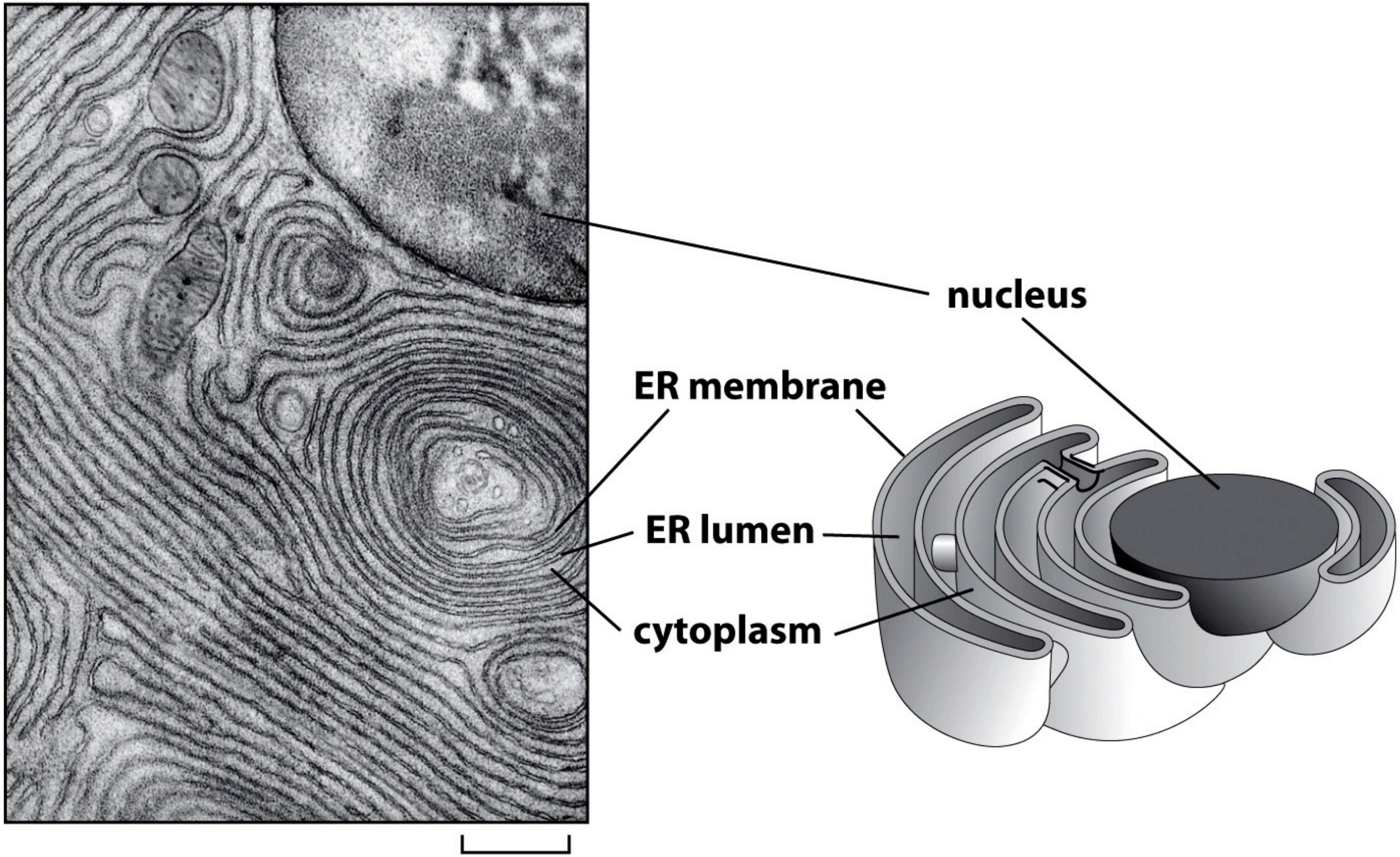
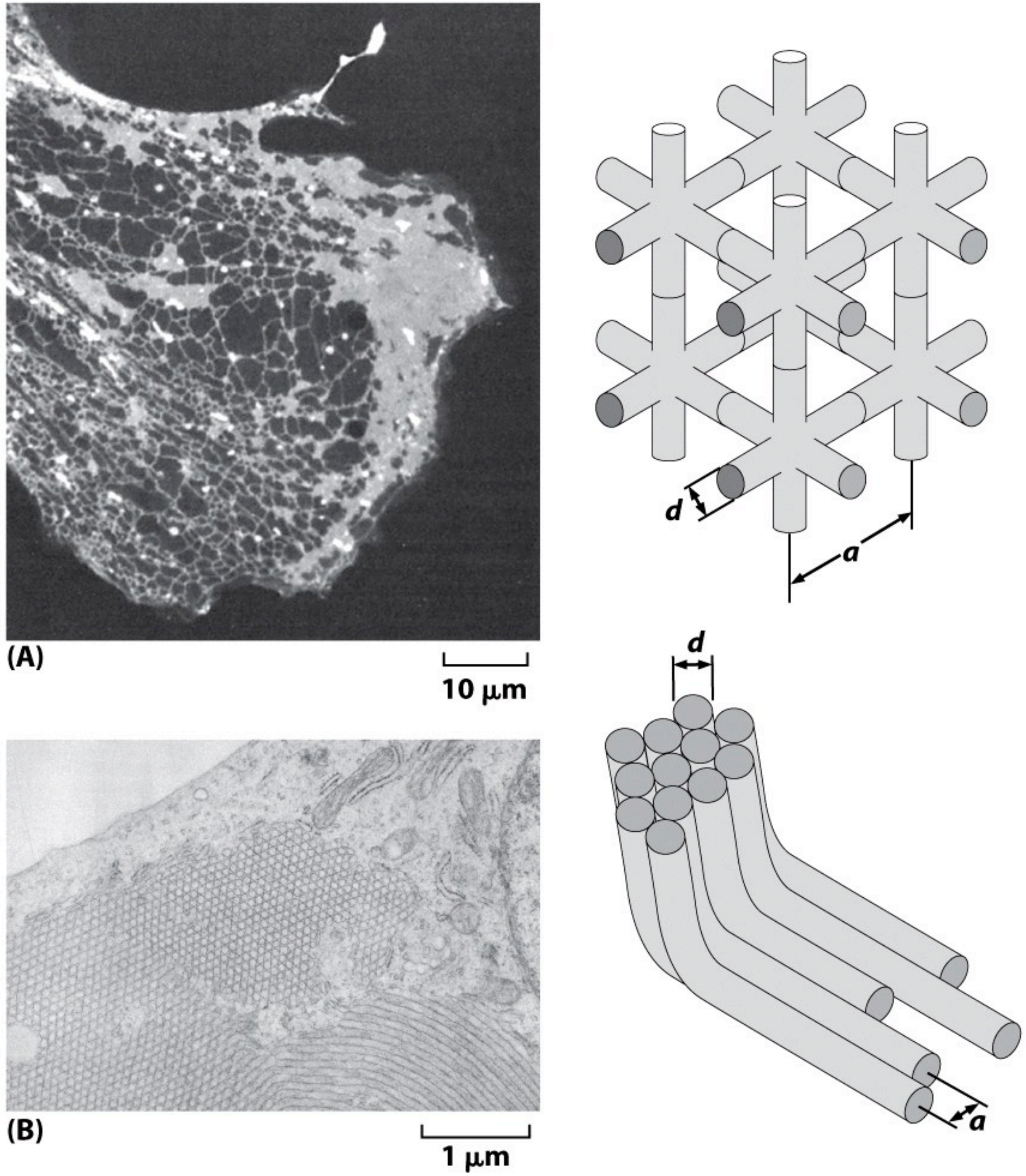
Endoplasmic Reticulum



Pancreatic cell dominated by E.R.

Endoplasmic Reticulum

DiOC6 membrane label



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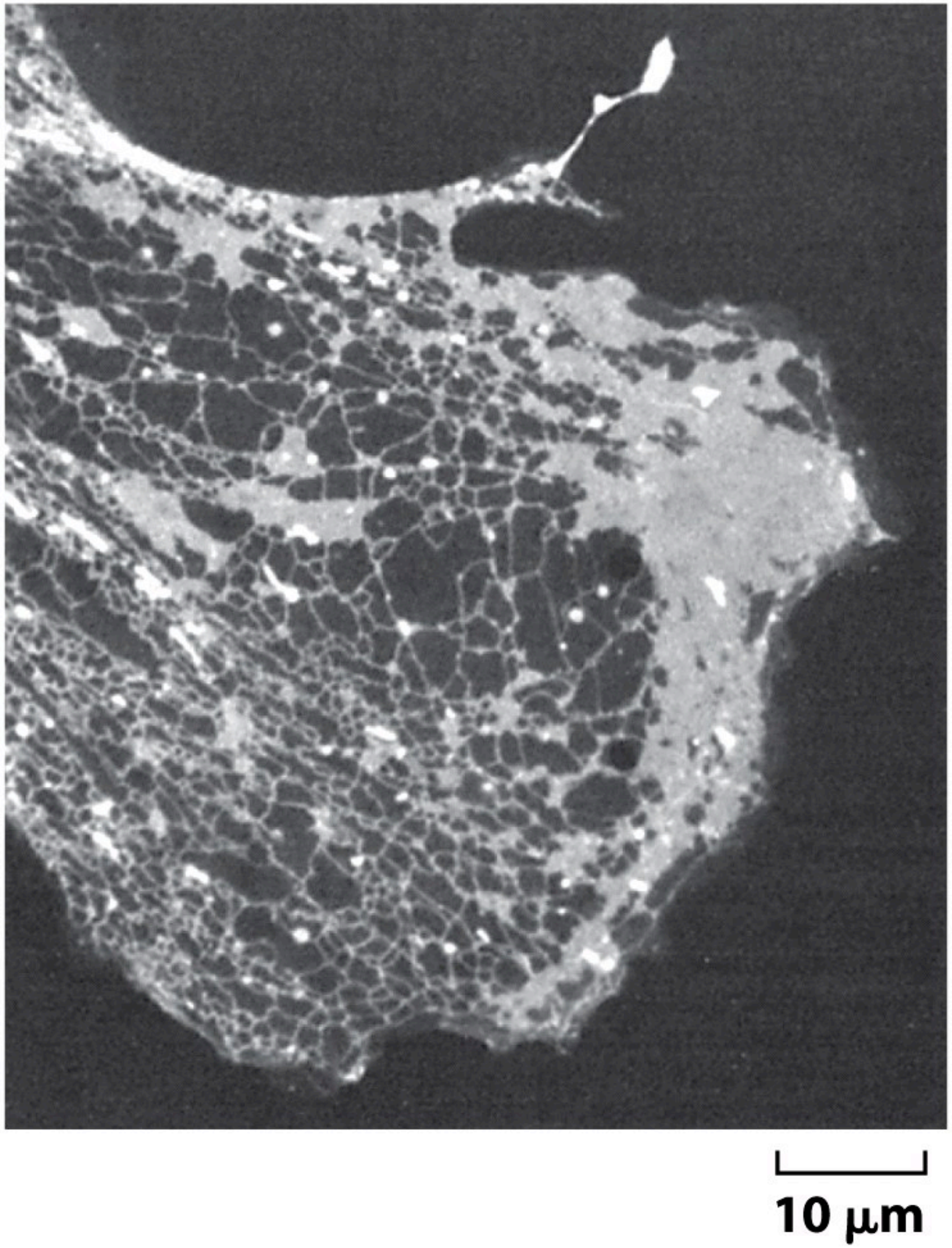

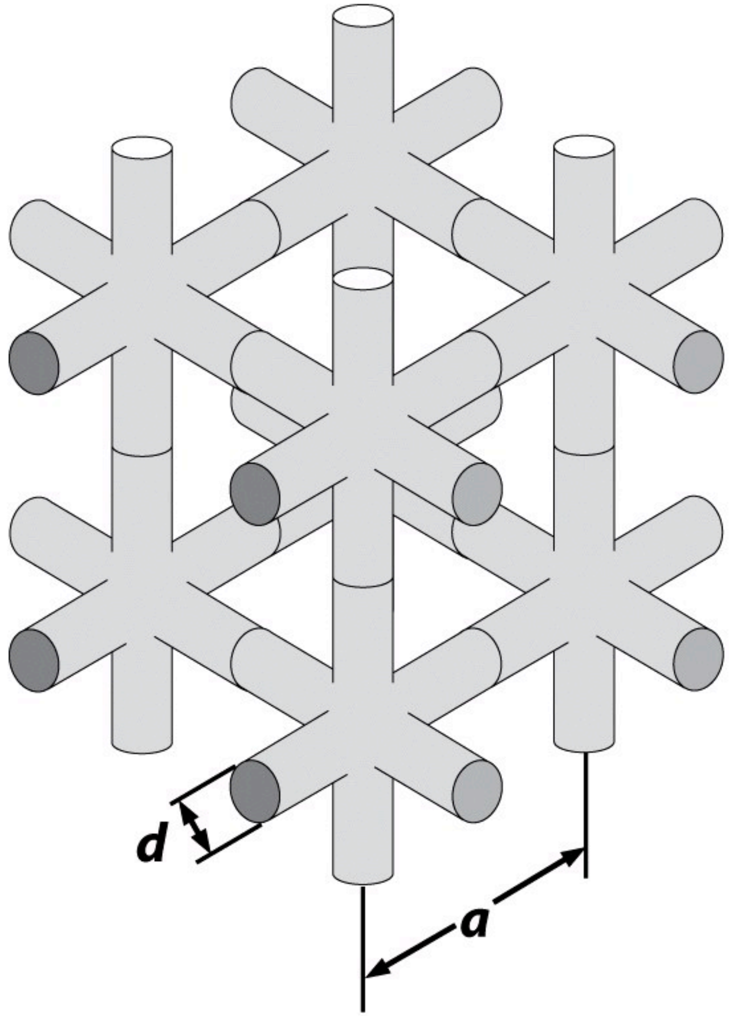

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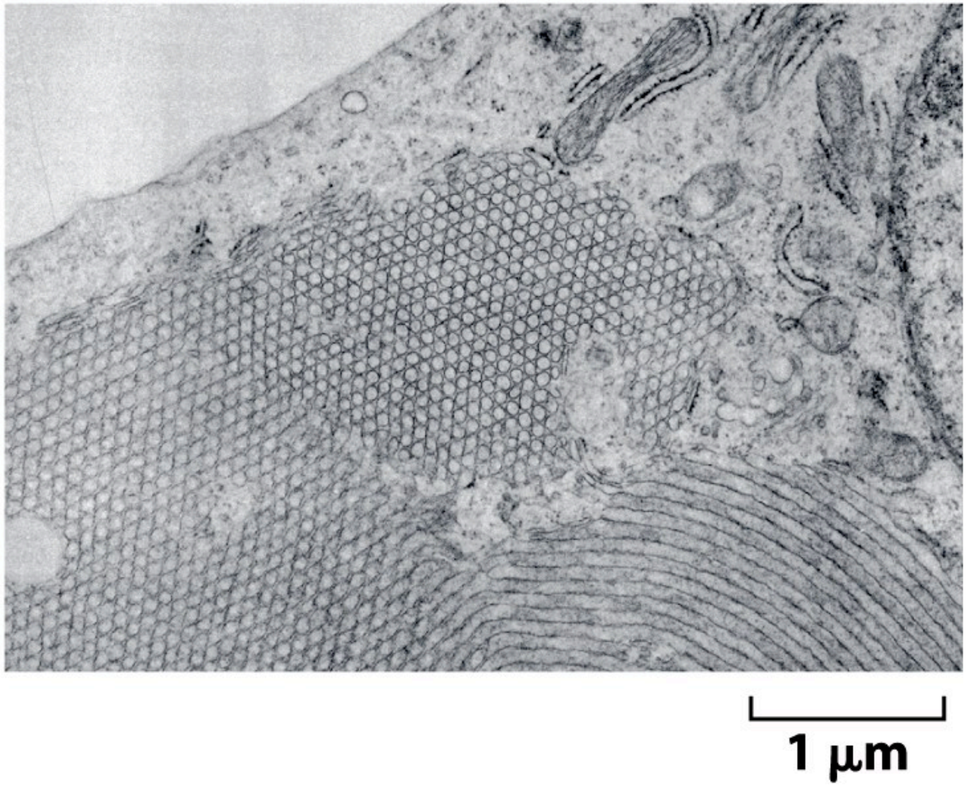


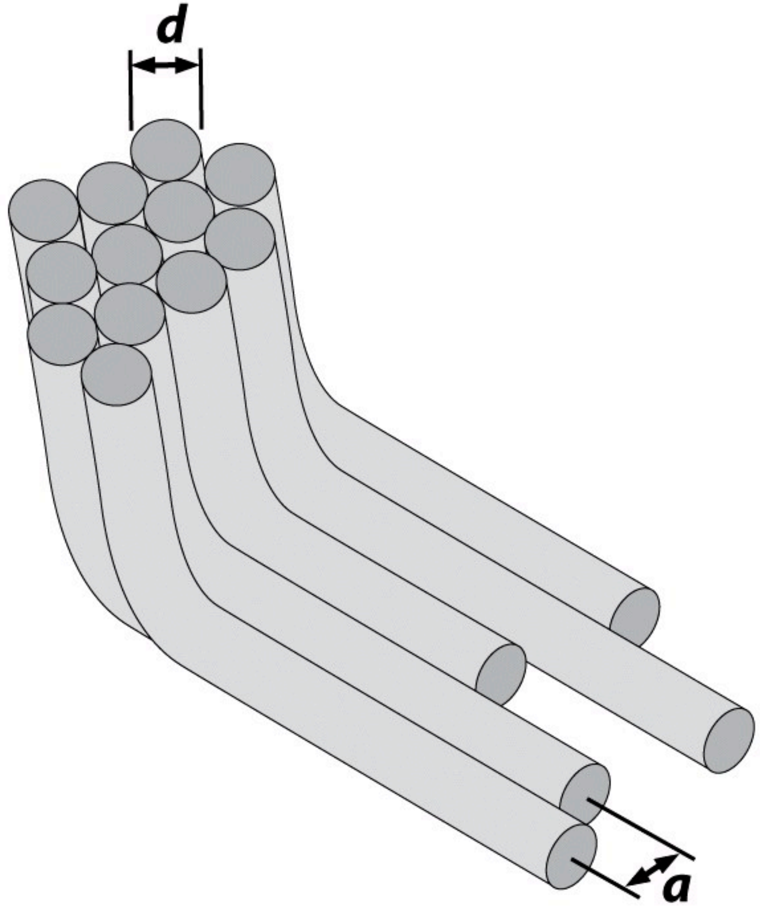
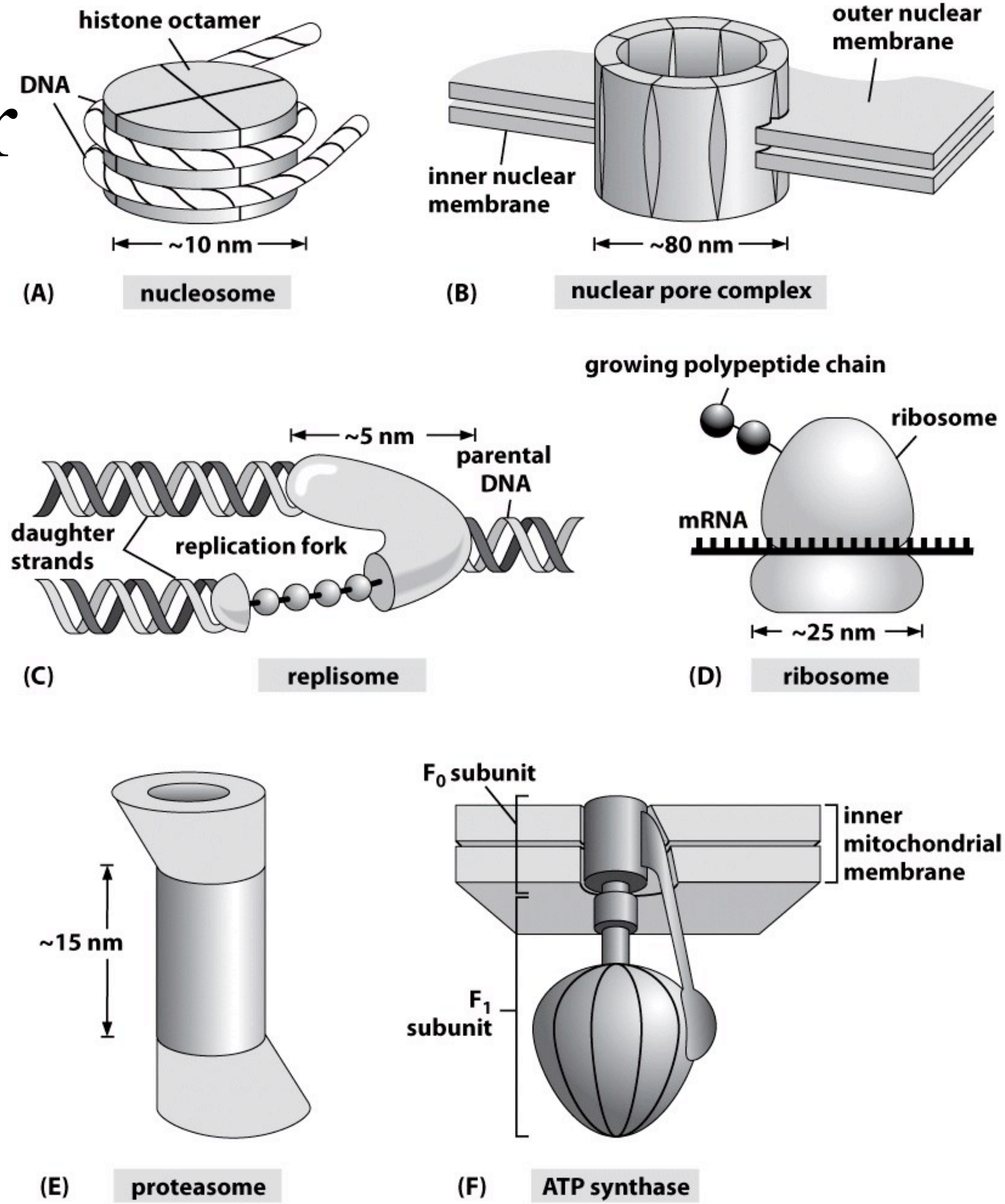


Figure 2.15b Physical Biology of the Cell (© Garland Science 2009)

Macromolecular Assemblies



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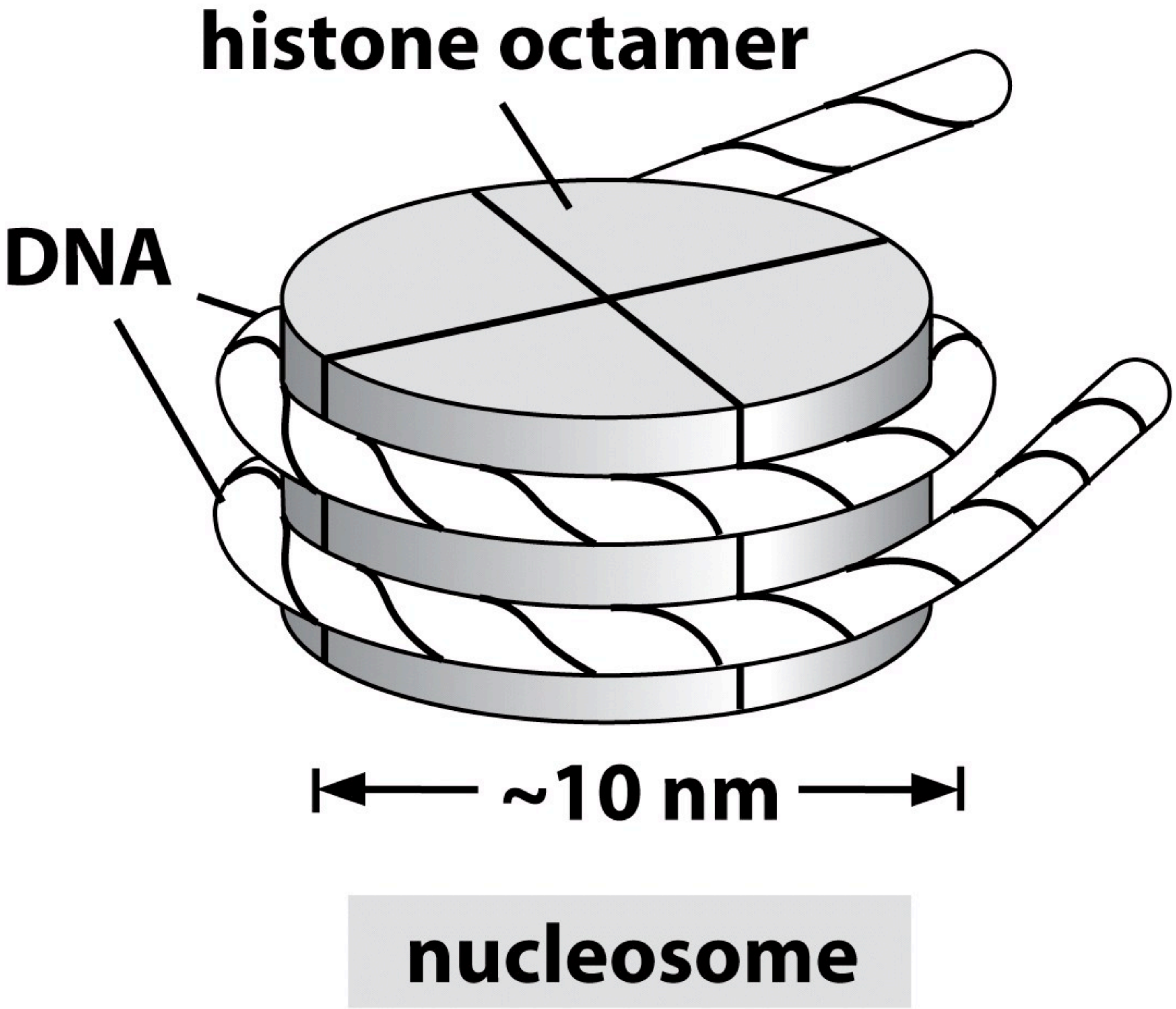
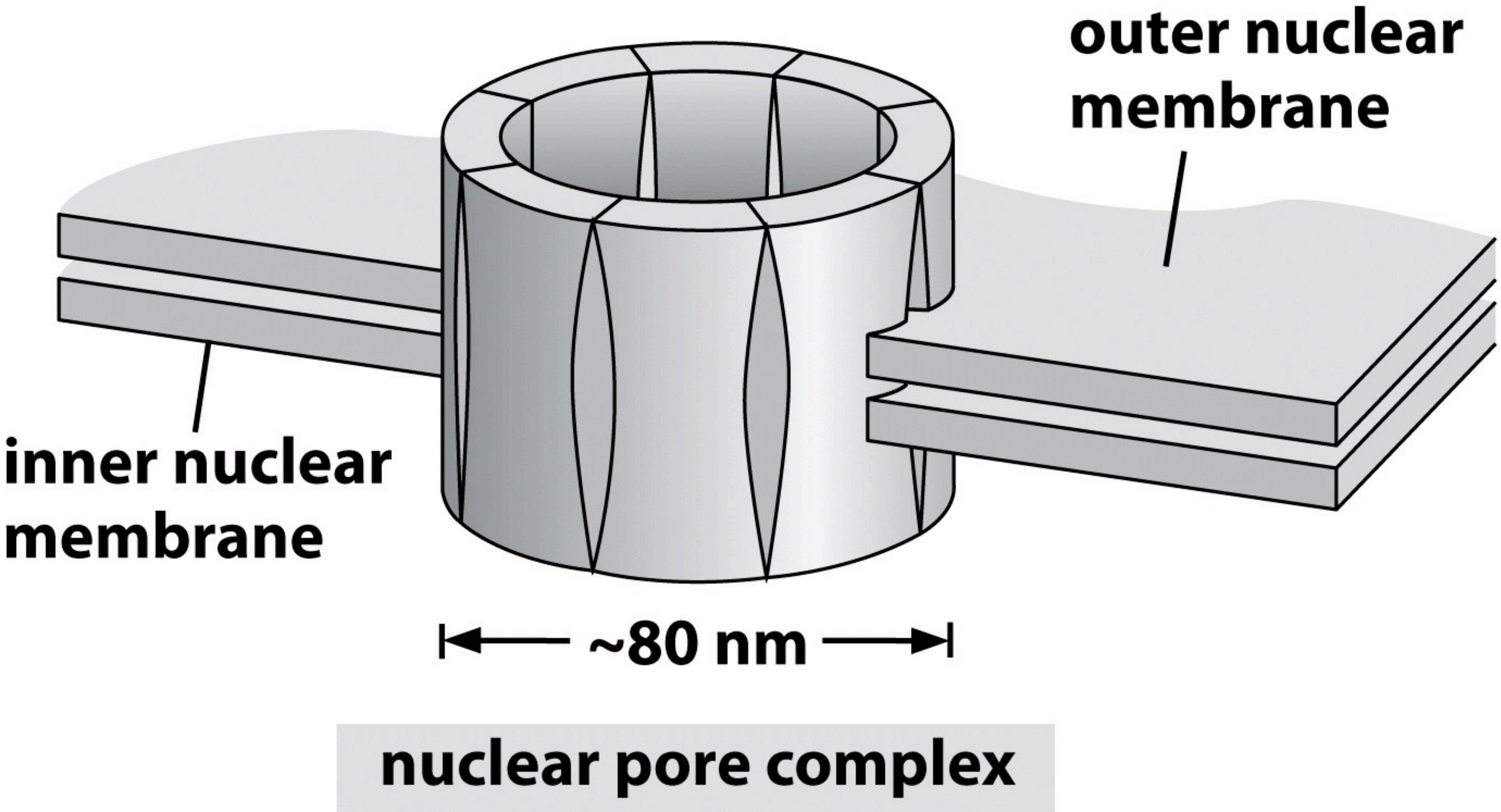


Figure 2.16a Physical Biology of the Cell (© Garland Science 2009)



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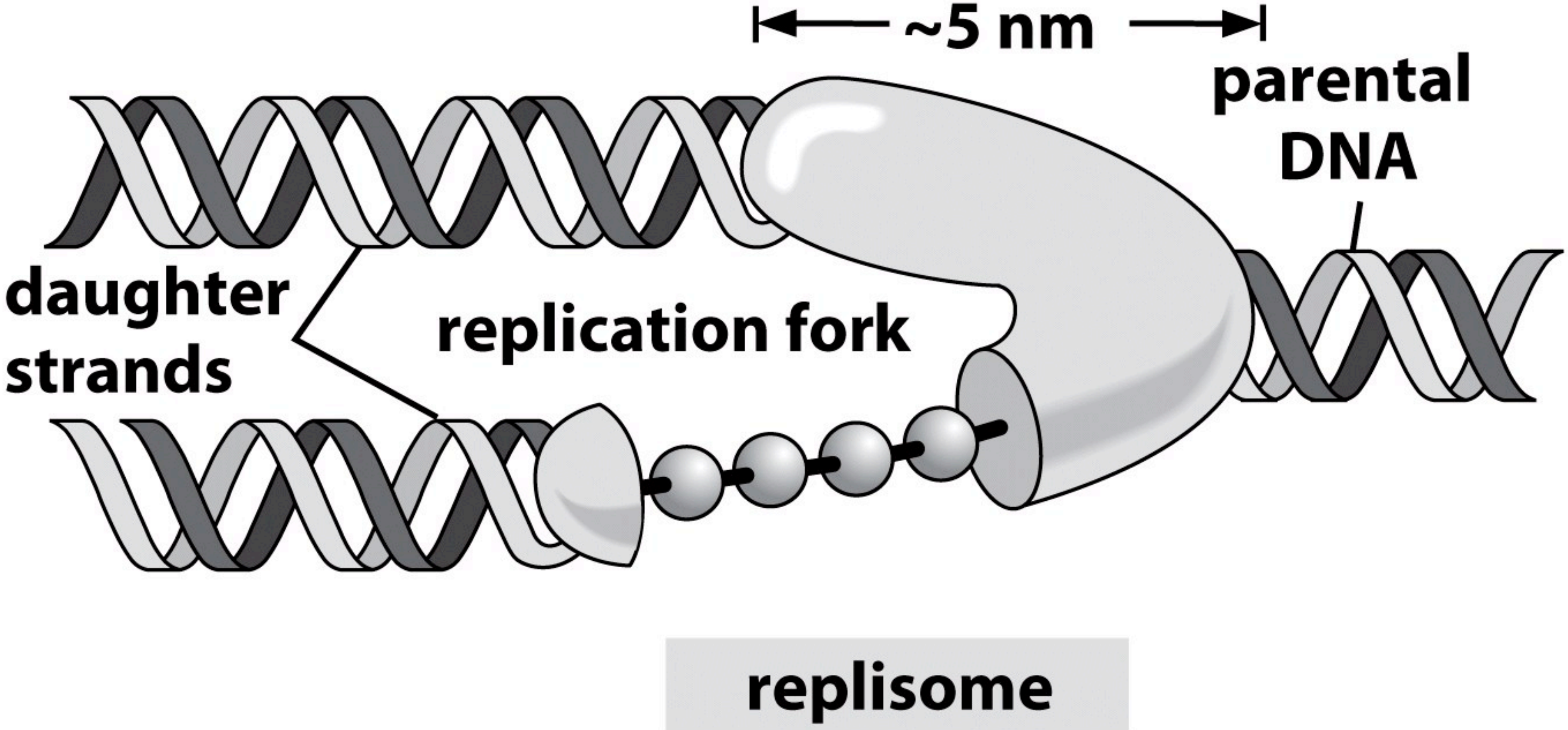

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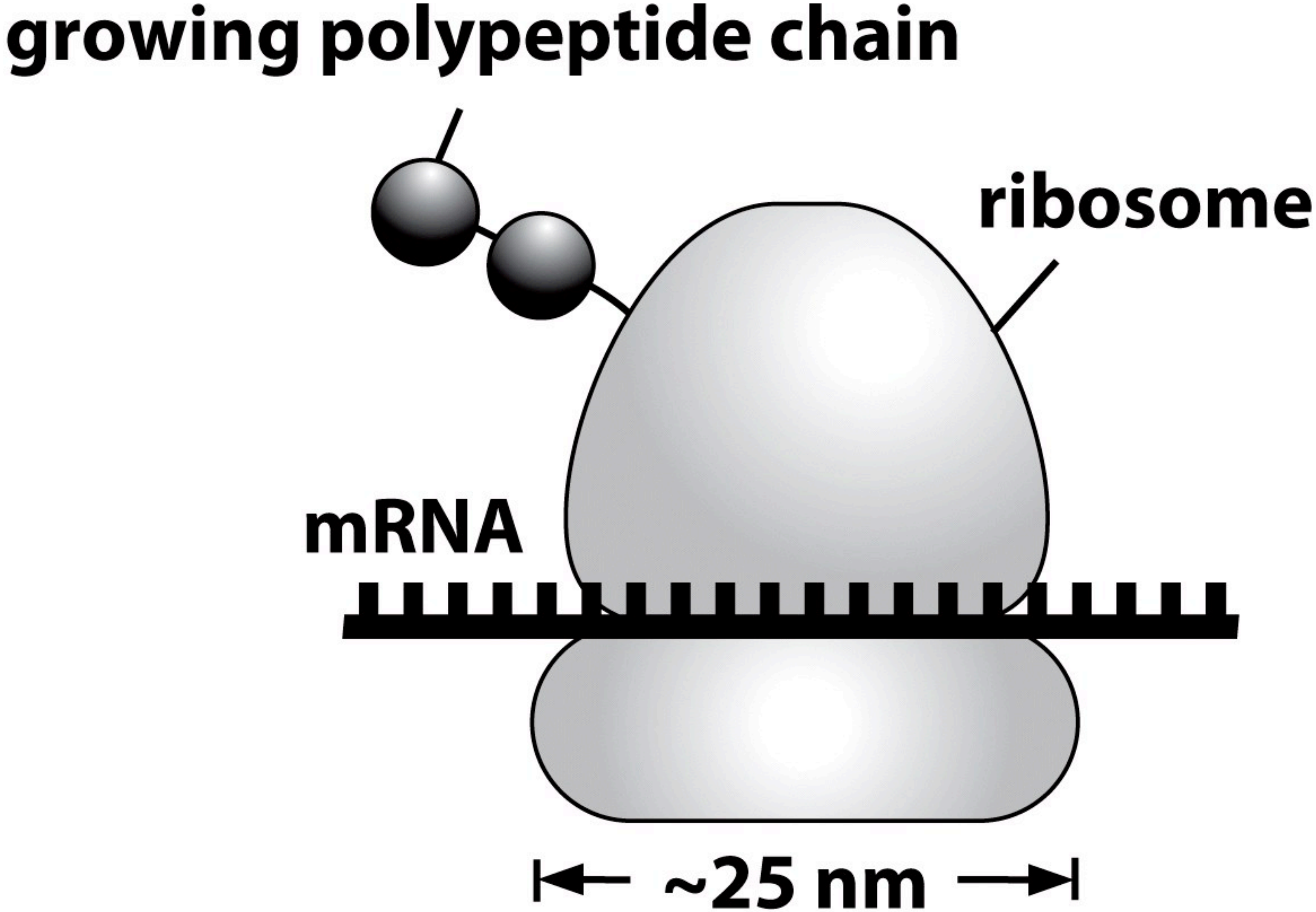


ribosome

Figure 2.16d Physical Biology of the Cell (© Garland Science 2009)

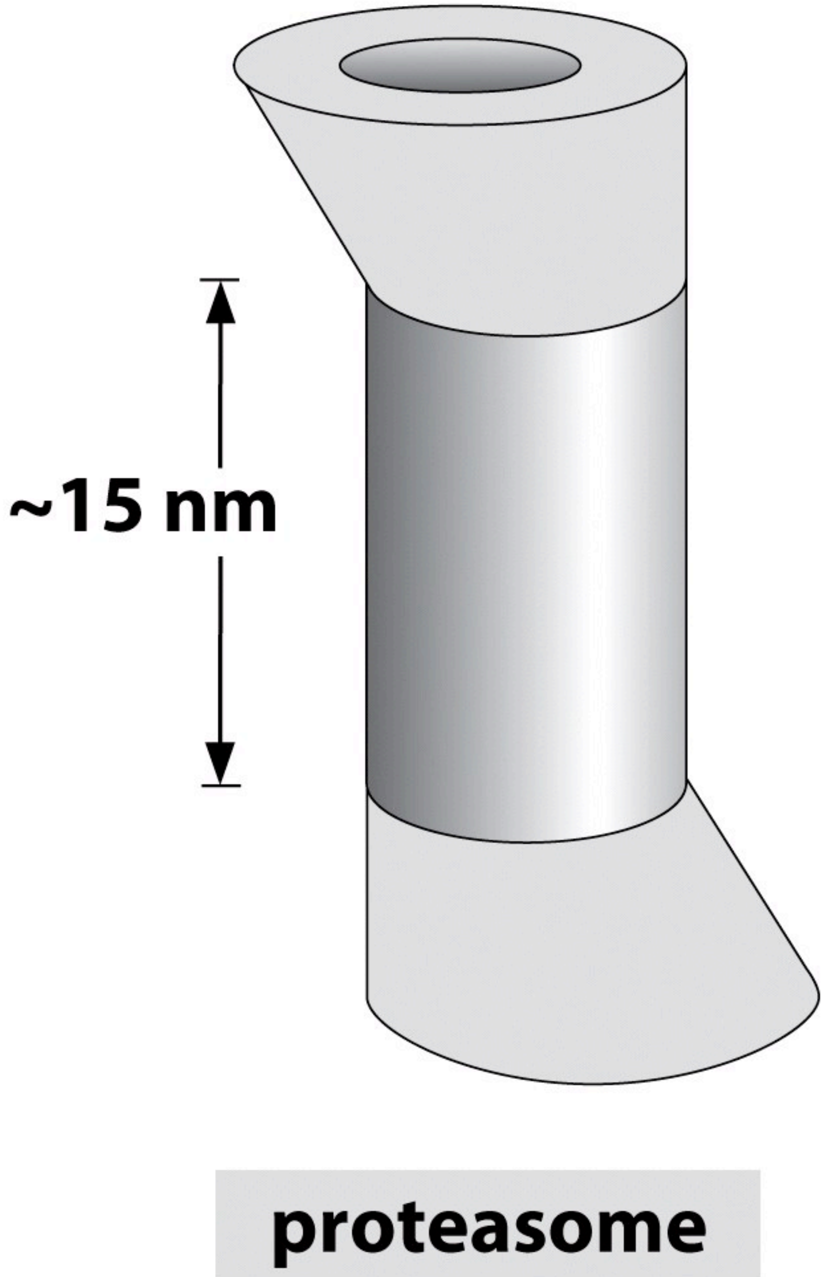


Figure 2.16e Physical Biology of the Cell (© Garland Science 2009)

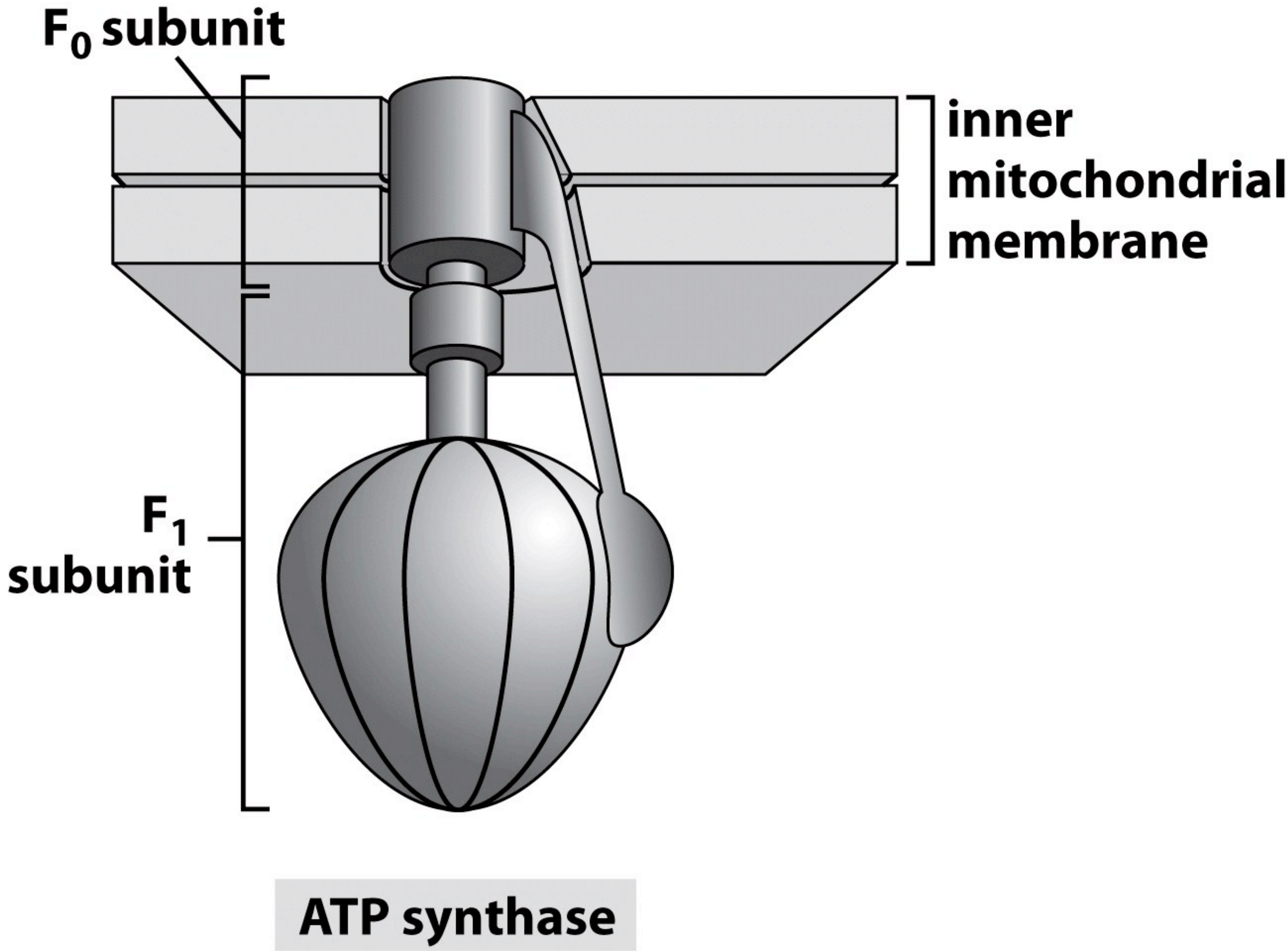


Figure 2.16f Physical Biology of the Cell (© Garland Science 2009)

Helical Assemblies

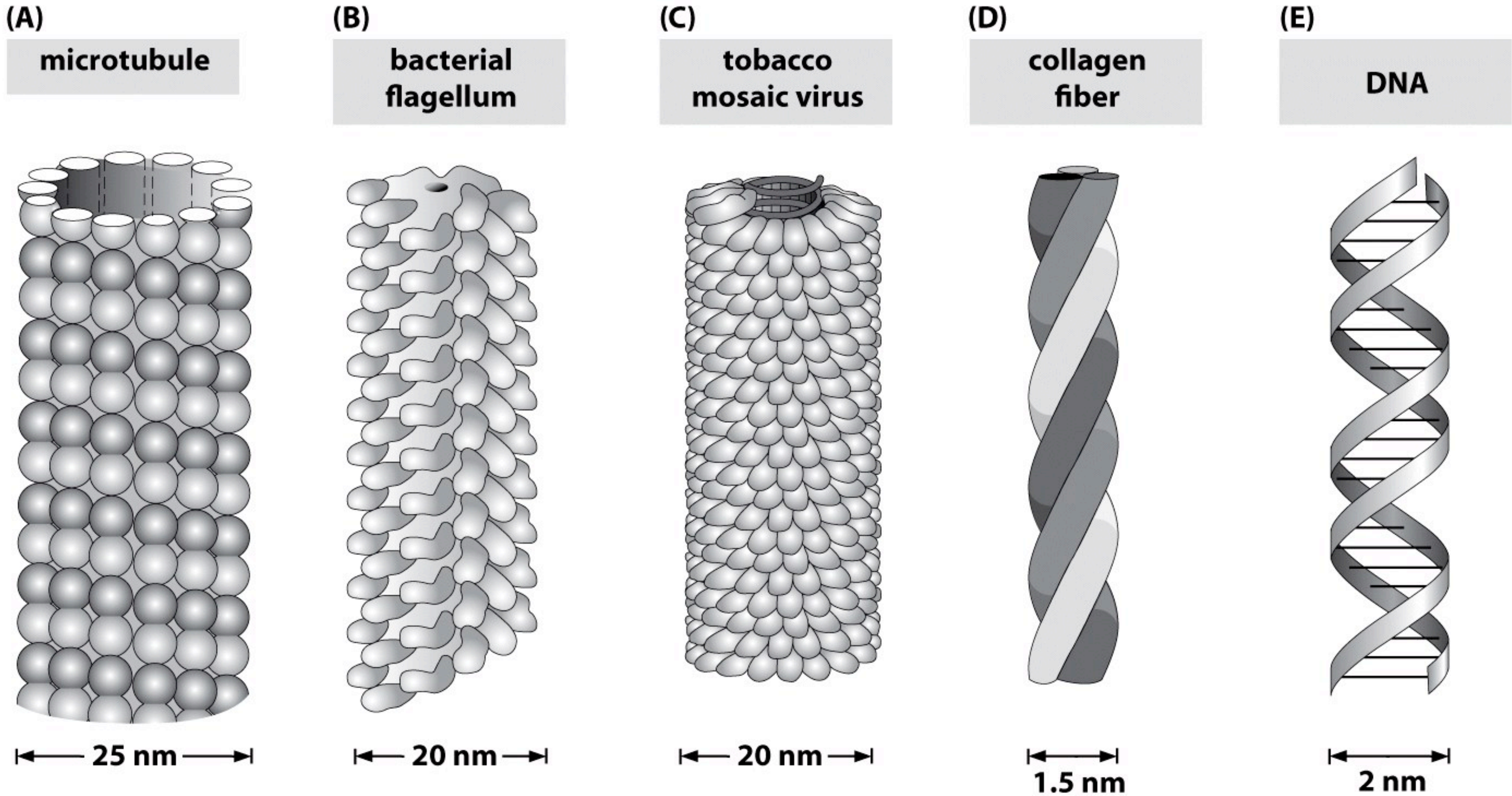


Figure 2.17 Physical Biology of the Cell (© Garland Science 2009)

Superstructures

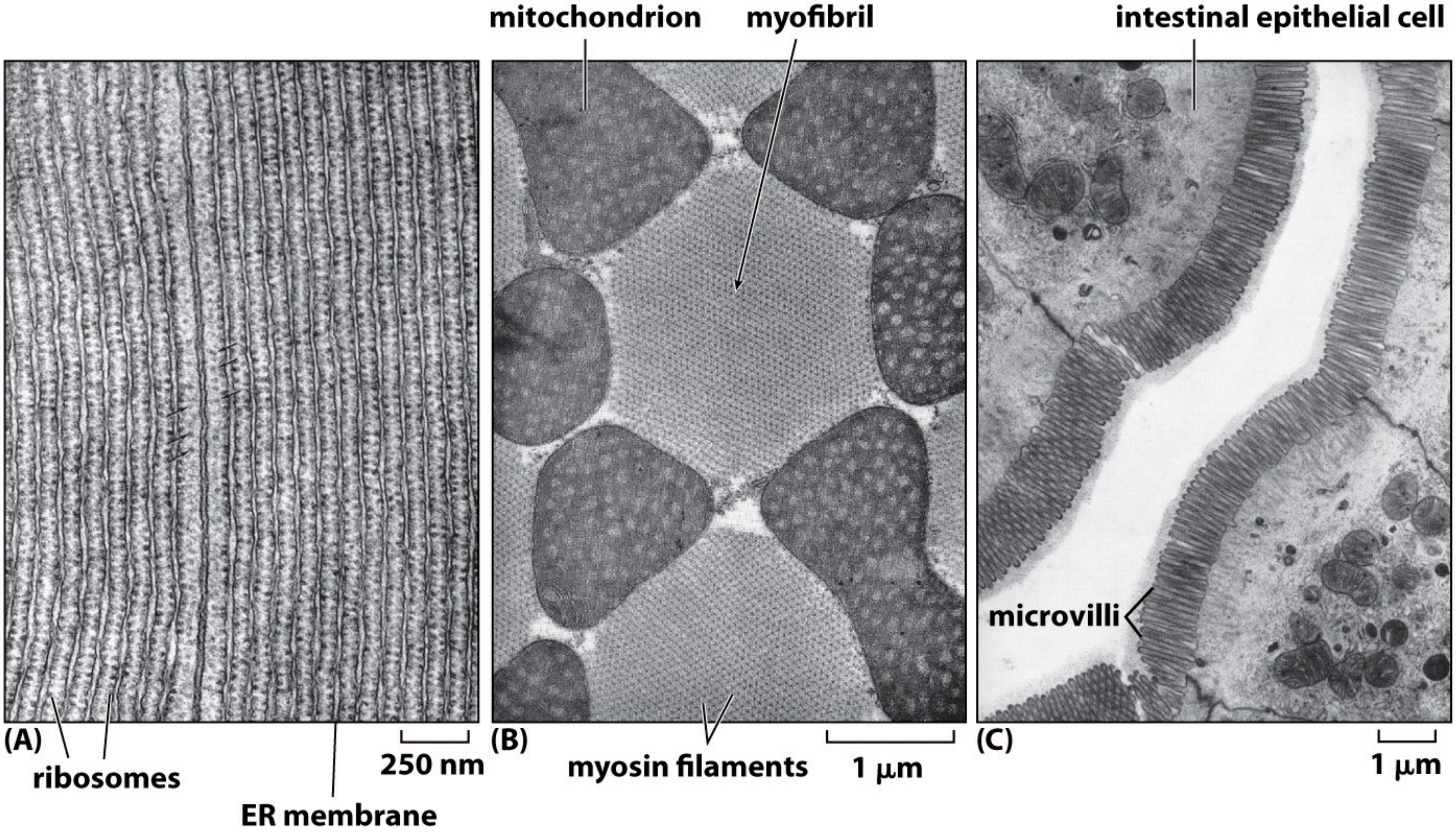


Figure 2.18 Physical Biology of the Cell (© Garland Science 2009)

Viral Capsids

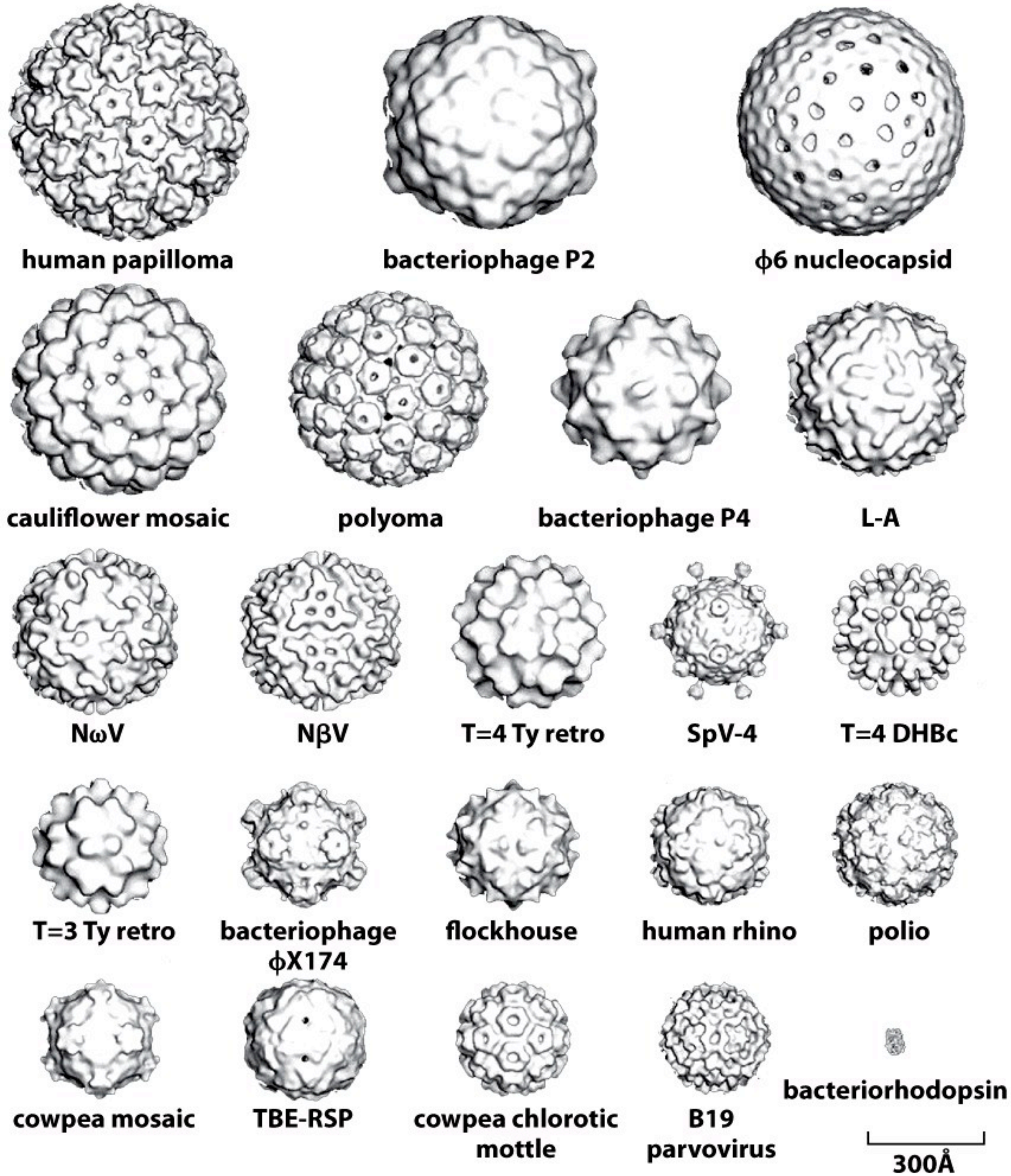
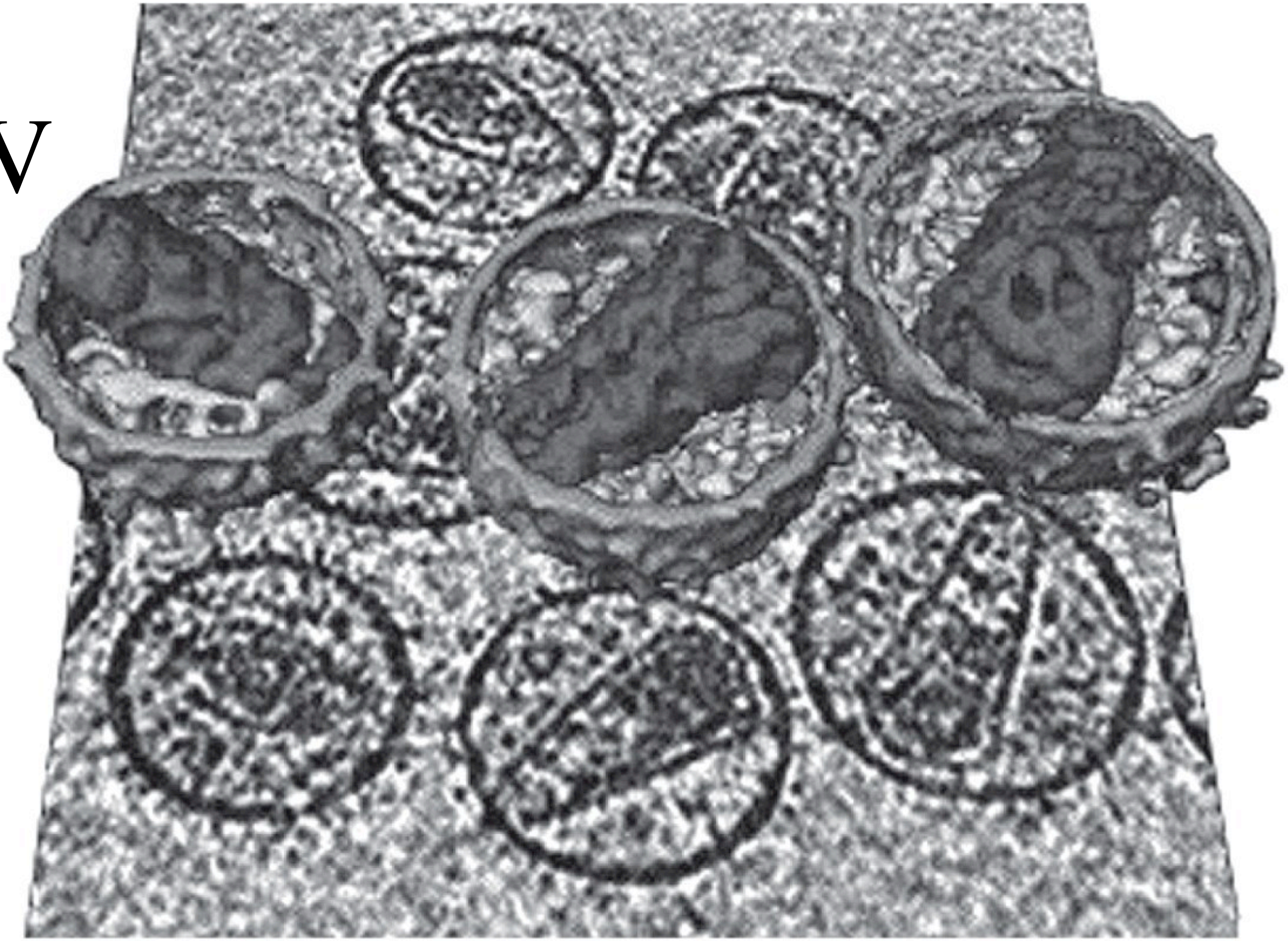


Figure 2.19 Physical Biology of the Cell (© Garland Science 2009)

HIV



Genome 10 kb

100 nm

Electron microscopy tilt series

Architecture of HIV

Diameter ~ 120-150 nm

Lipid bilayer radius ~ 5nm

Gag protein radius ~ 2 nm

N_{Gag} = ?

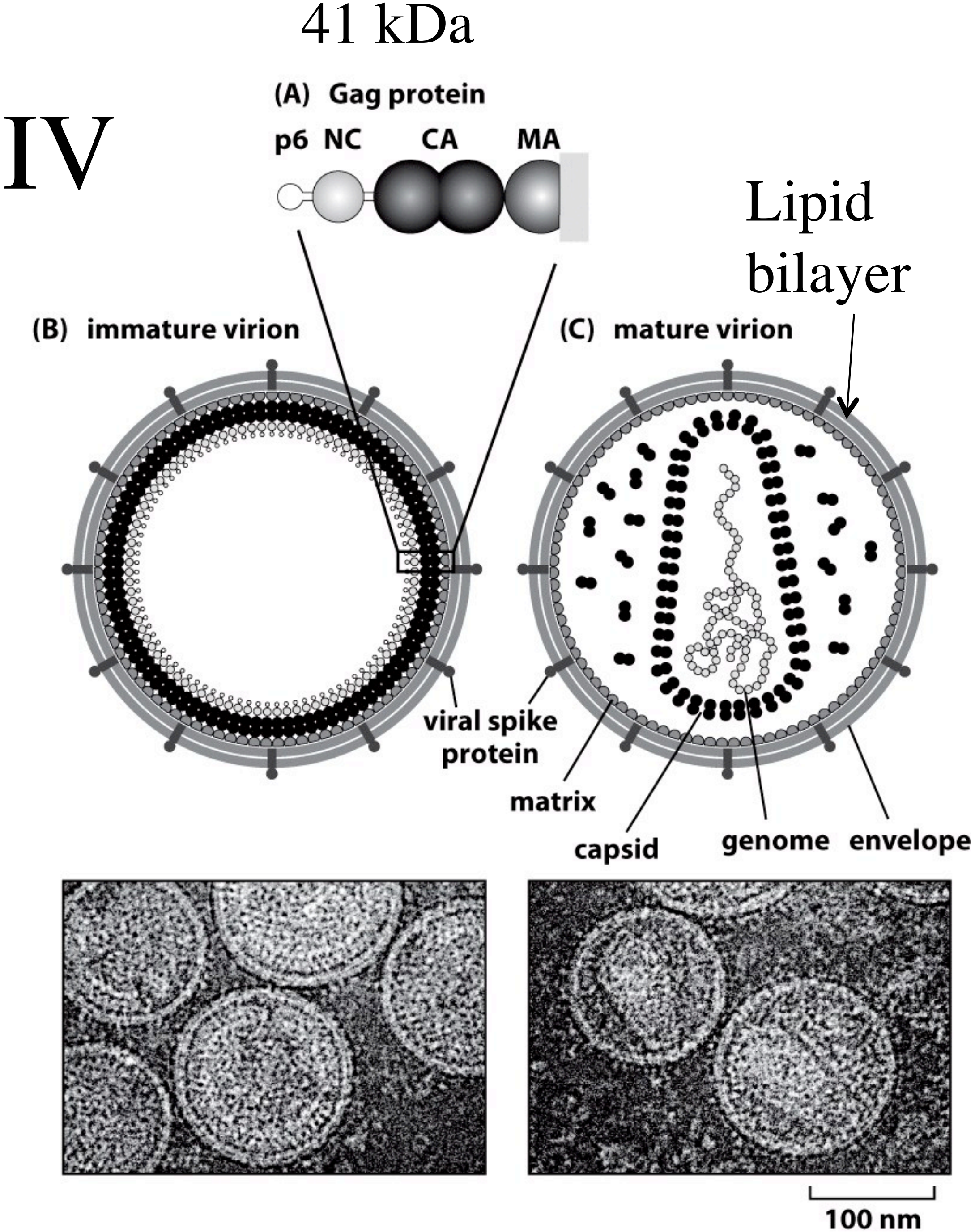


Figure 2.21 Physical Biology of the Cell (© Garland Science 2009)

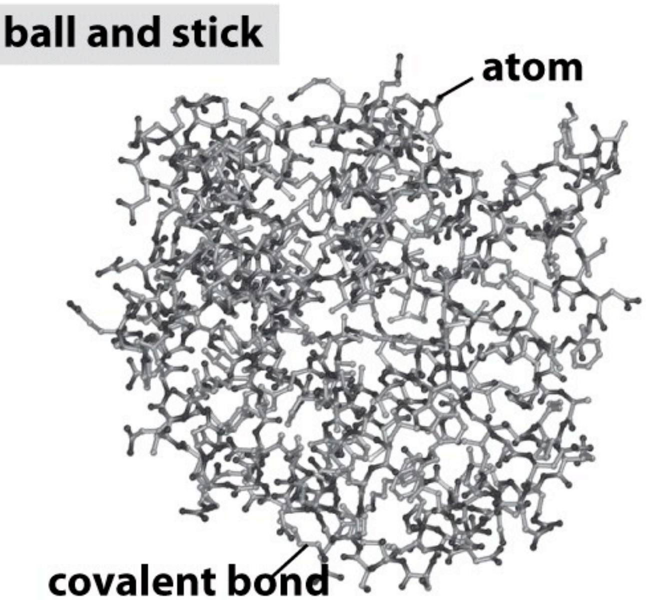
Molecular Architecture

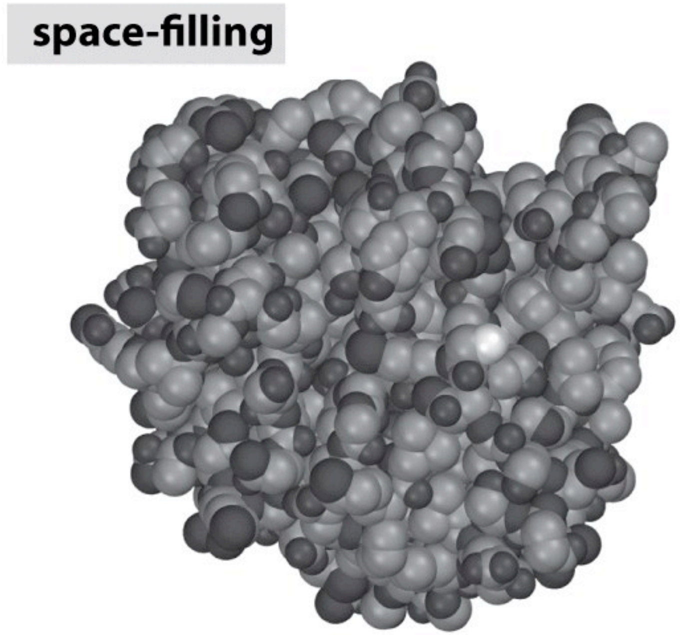
Structure of atoms

$r_i(t) = x_i(t)\mathbf{i} + y_i(t)\mathbf{j} + z_i(t)\mathbf{k}$

$<r_i(t)>_{time}$

*www.**pdb**.org/*





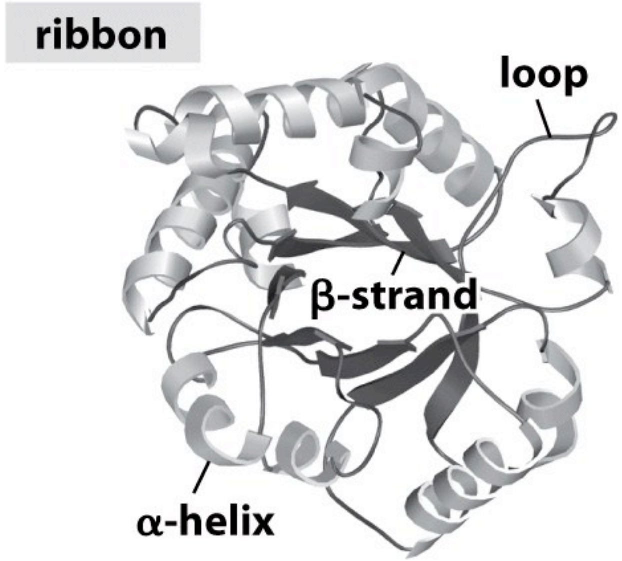


Figure 2.22 Physical Biology of the Cell (© Garland Science 2009)

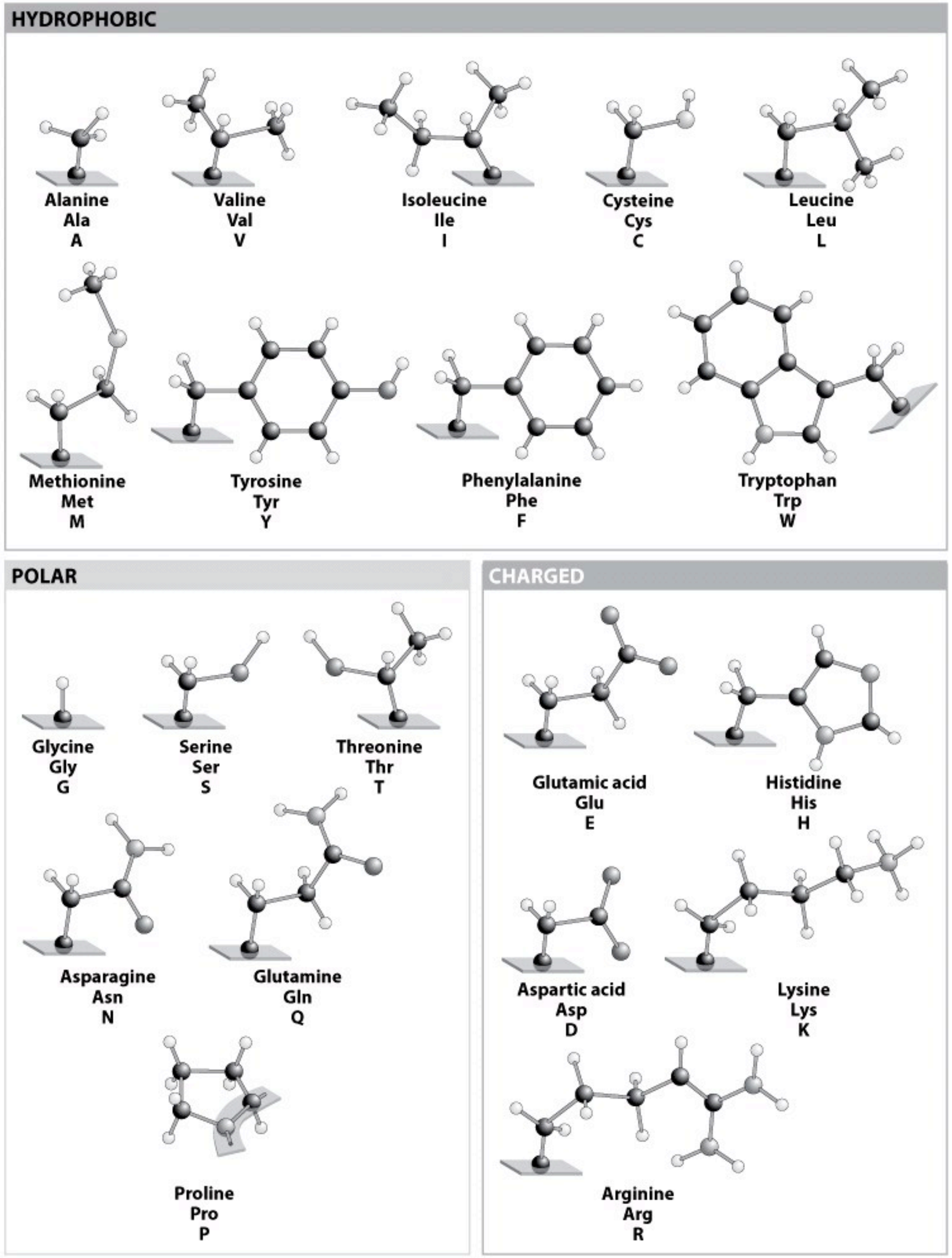


Figure 2.23 Physical Biology of the Cell (© Garland Science 2009)

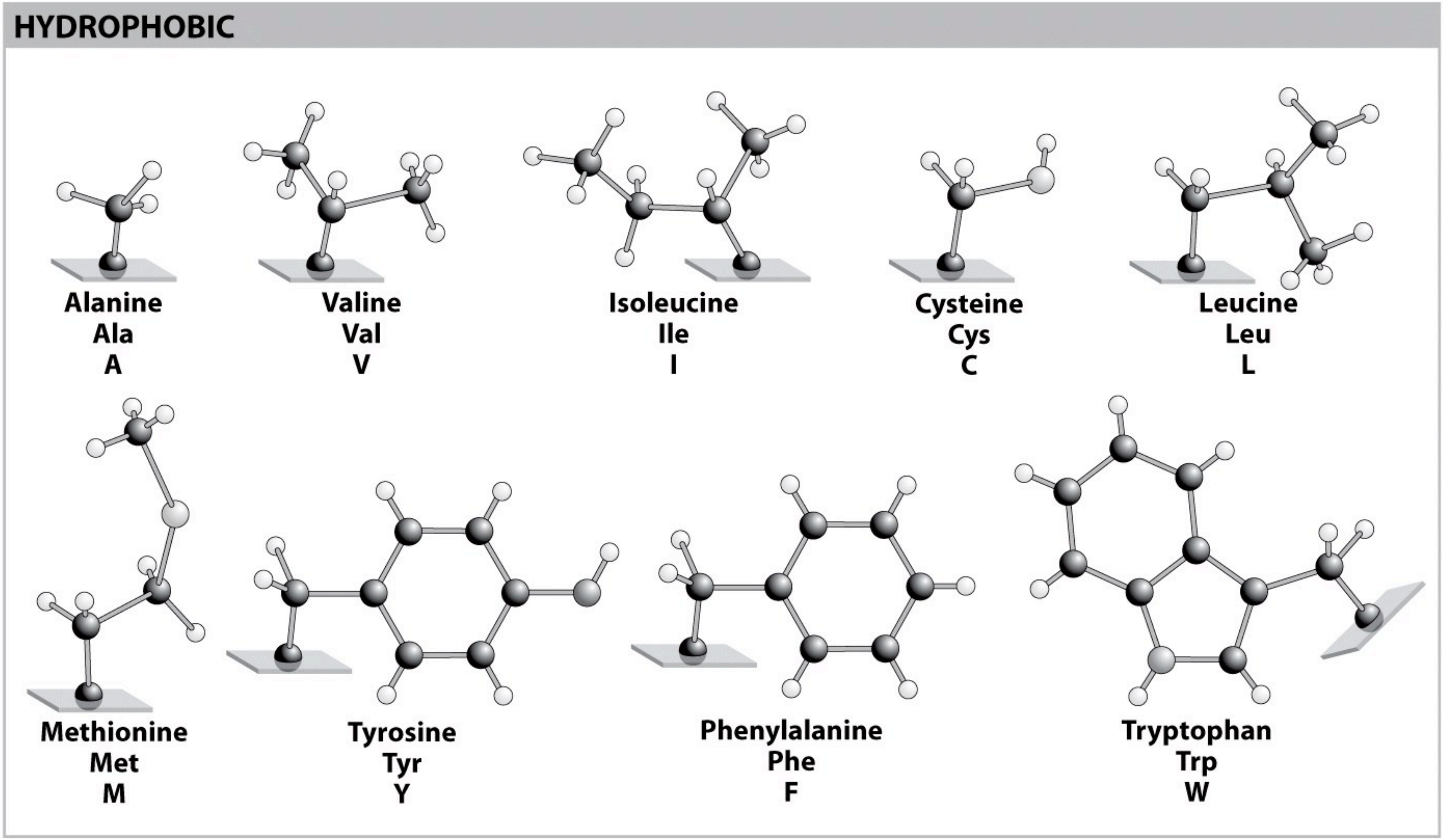


Figure 2.23 (part 1) Physical Biology of the Cell (© Garland Science 2009)

POLAR

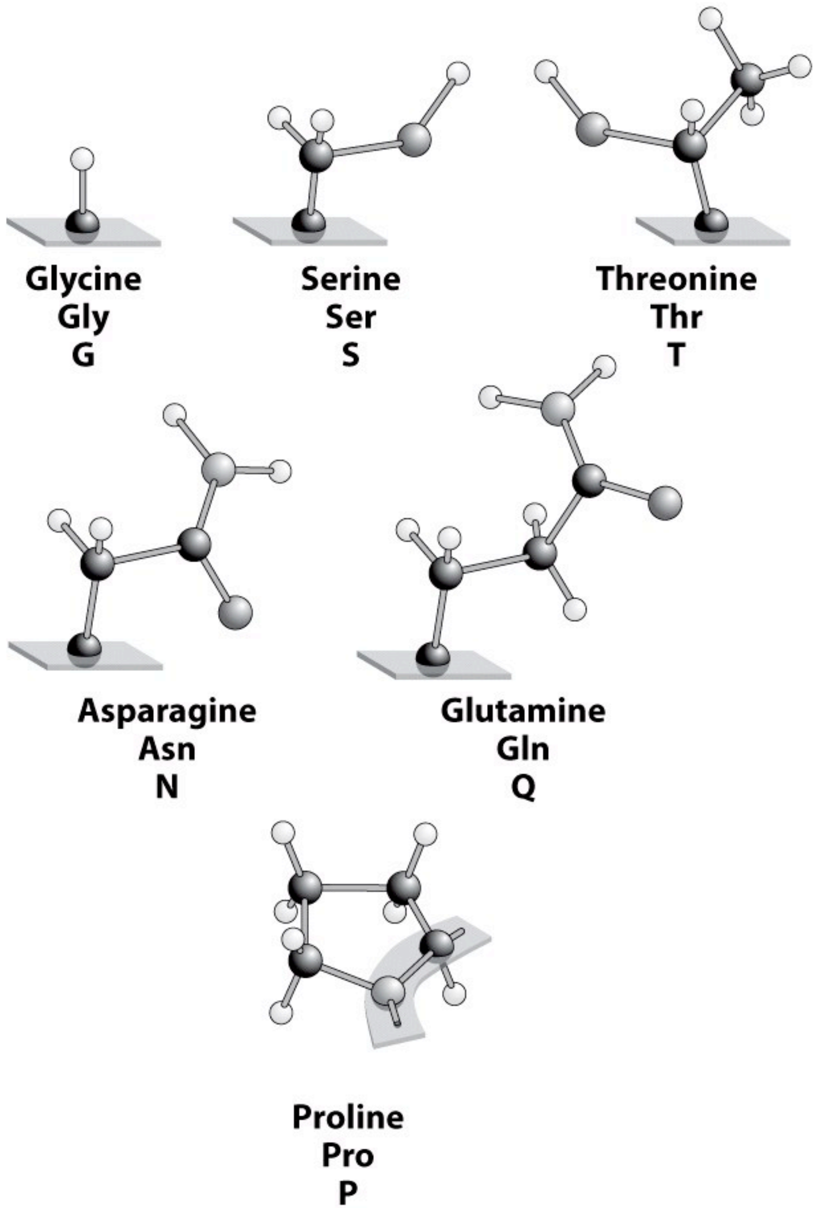


Figure 2.23 (part 2) Physical Biology of the Cell (© Garland Science 2009)

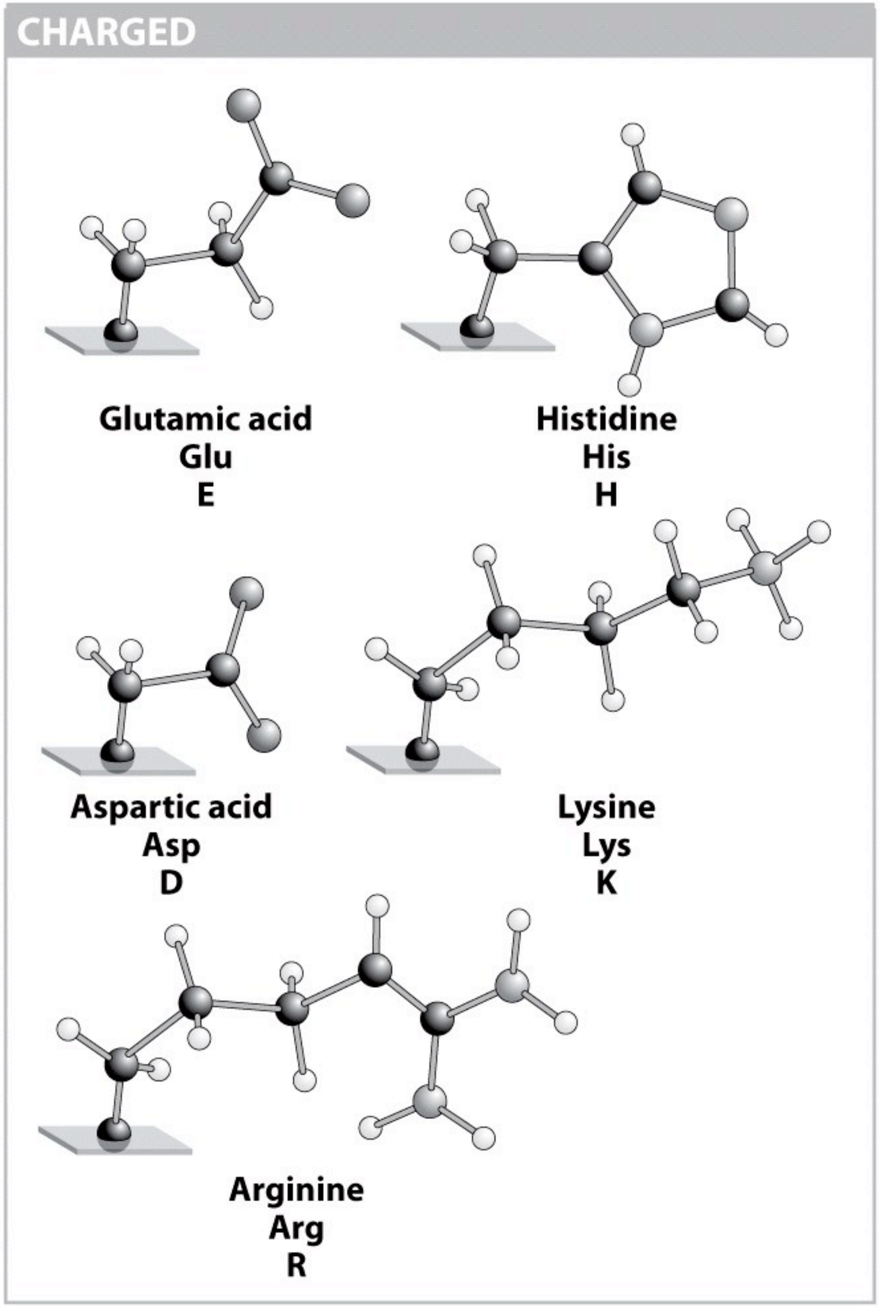


Figure 2.23 (part 3) Physical Biology of the Cell (© Garland Science 2009)

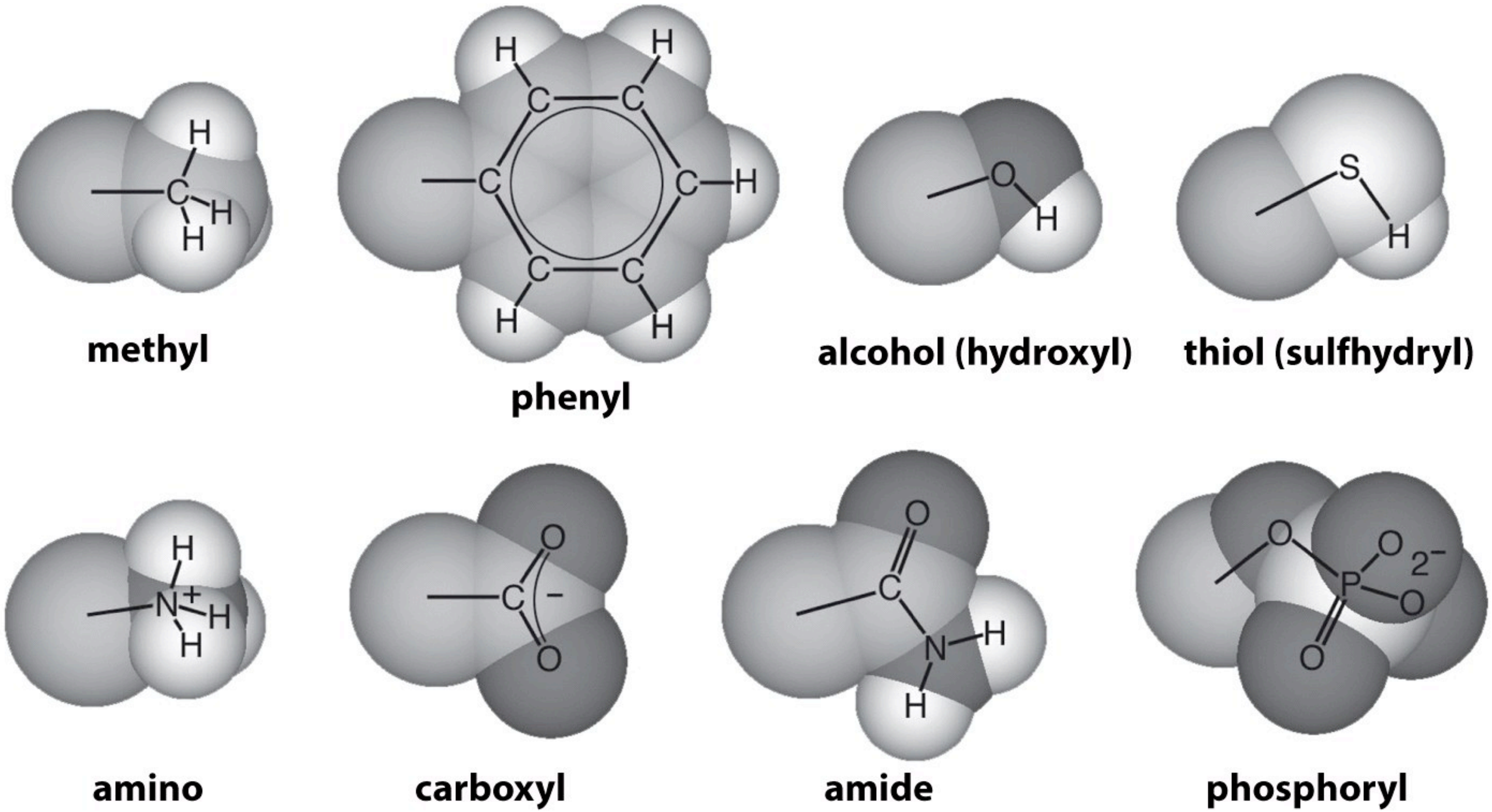
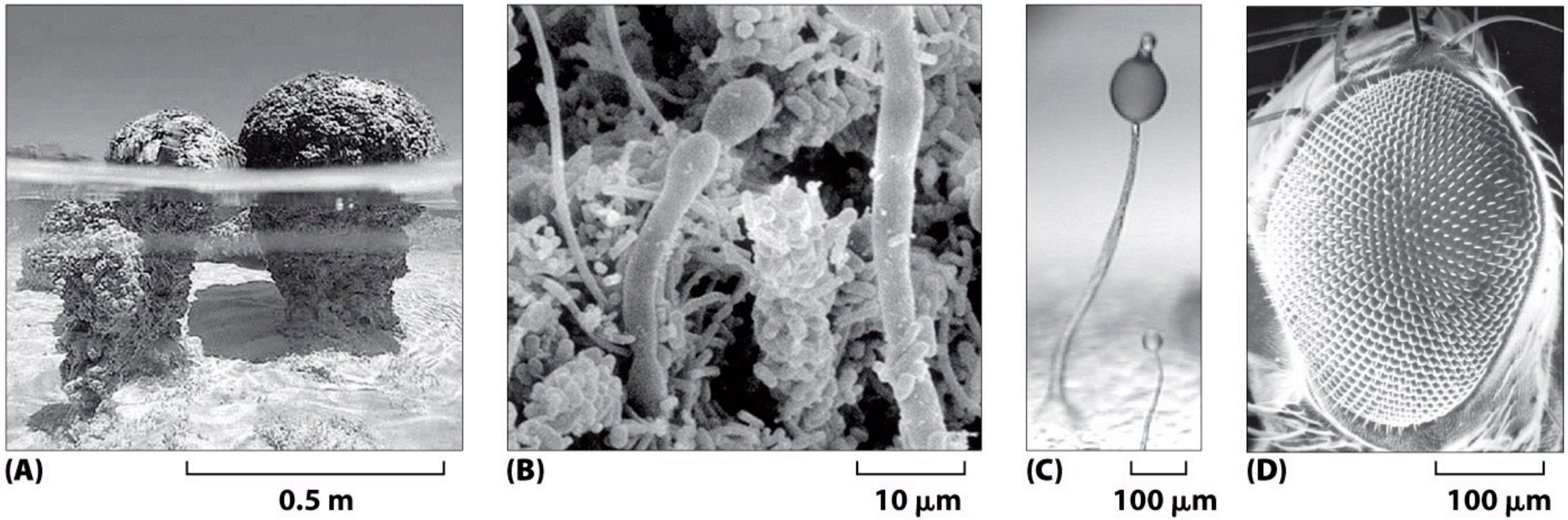


Figure 2.24 Physical Biology of the Cell (© Garland Science 2009)

Communities of Cells



Stromatolites Bacterial biofilm Amoeba Drosophila eye

Biofilm Formation

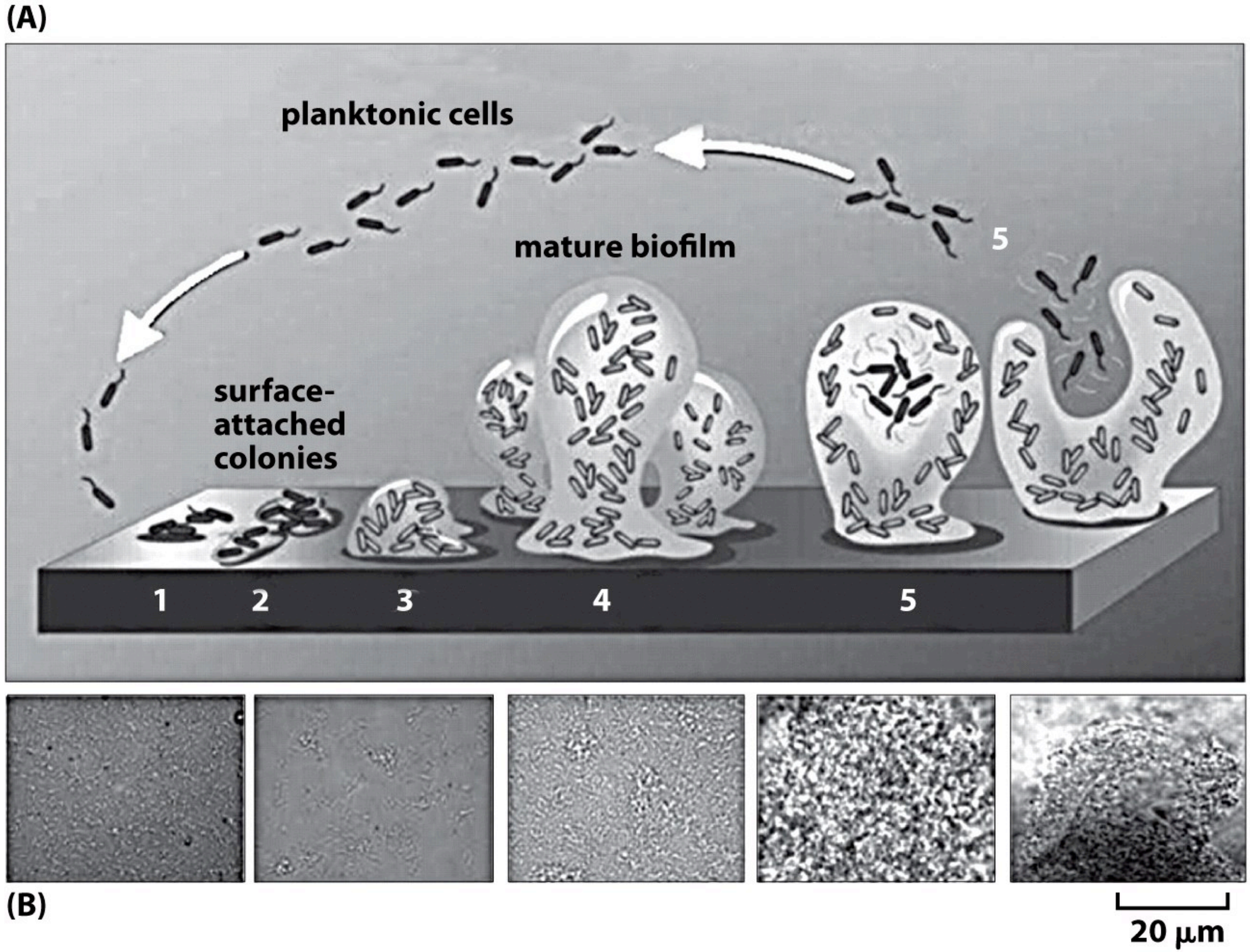


Figure 2.26 Physical Biology of the Cell (© Garland Science 2009)

Multicellularity in Dicytostelium

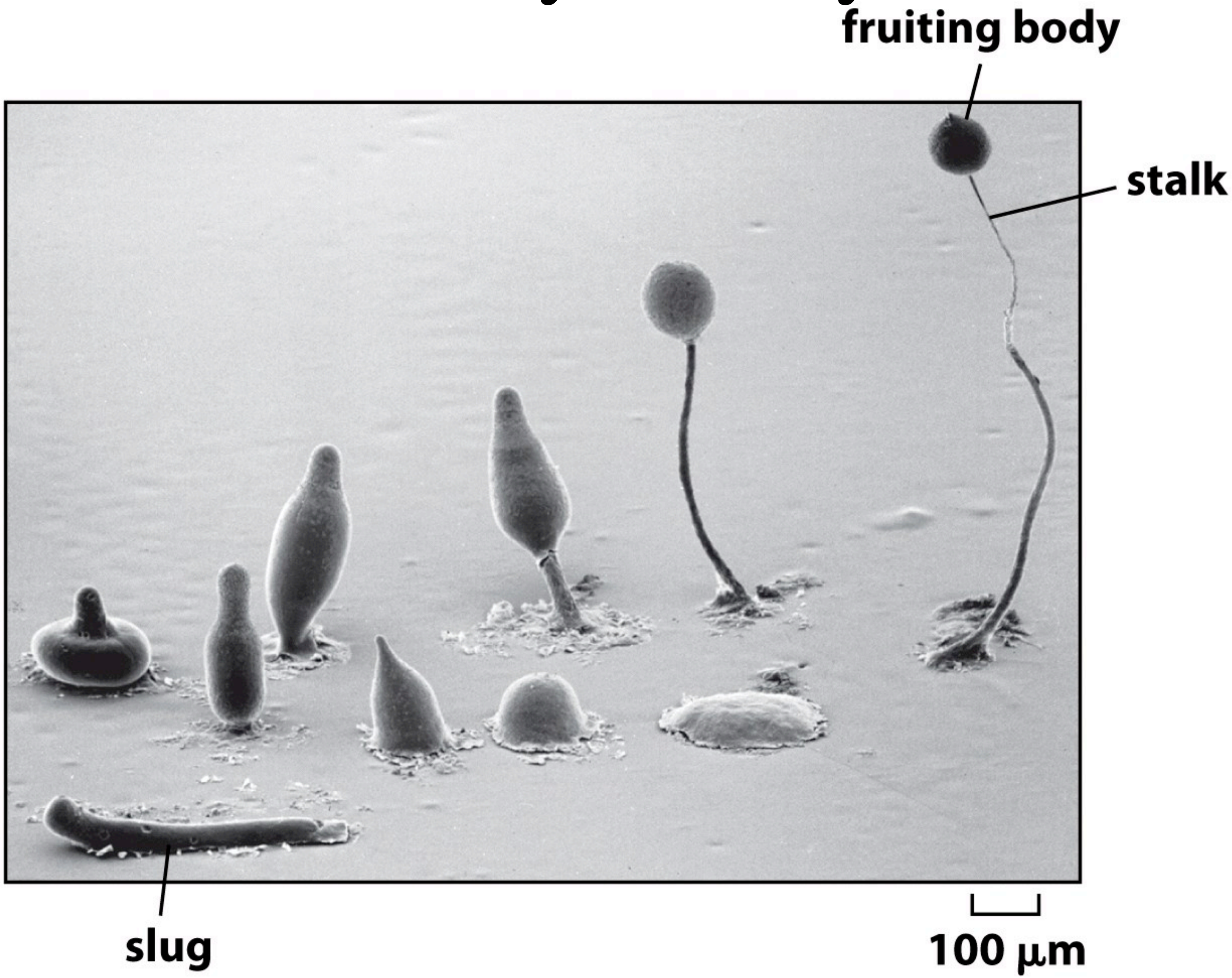


Figure 2.27 Physical Biology of the Cell (© Garland Science 2009)

Dicytostelium Slug Size

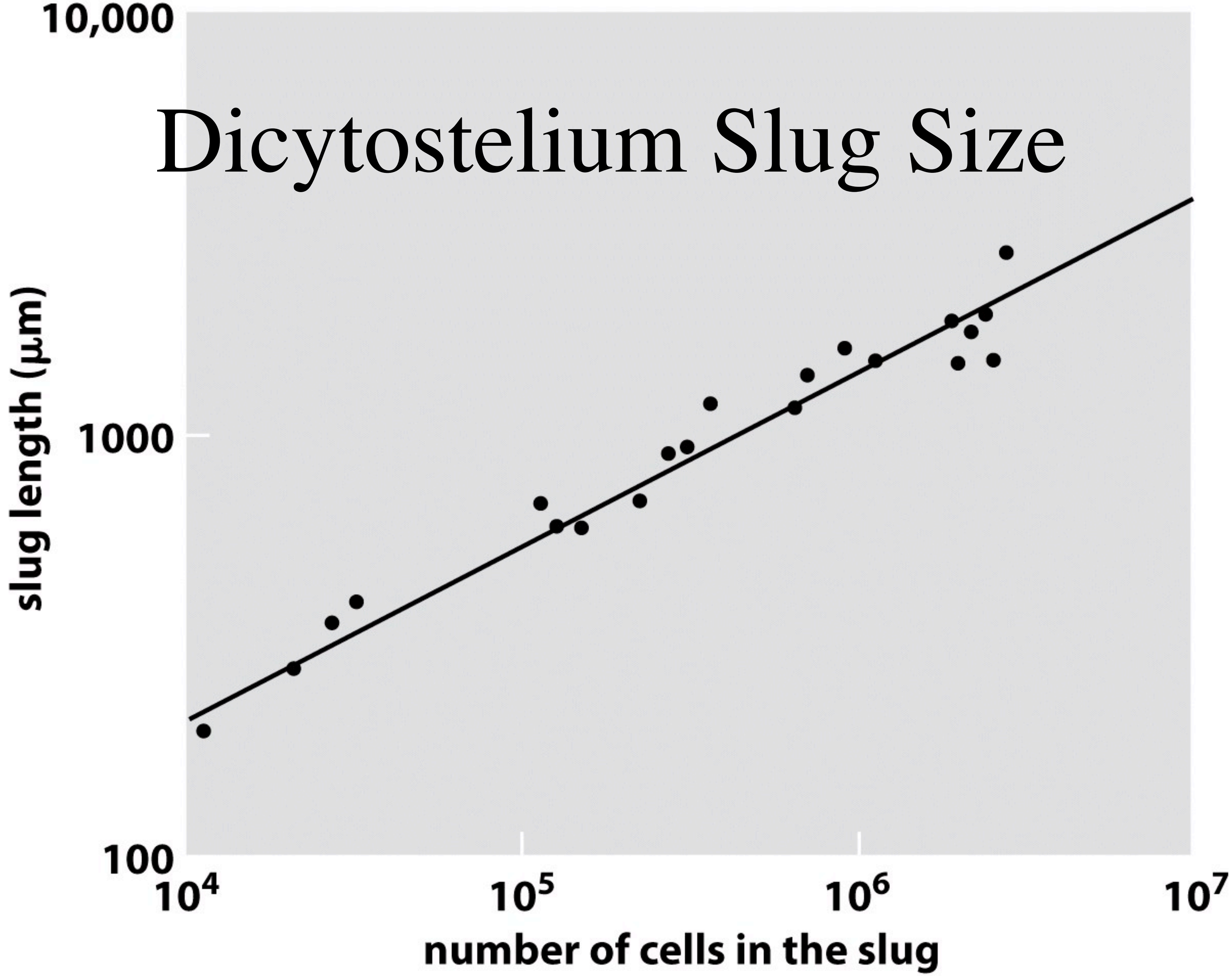


Figure 2.28 Physical Biology of the Cell (© Garland Science 2009)

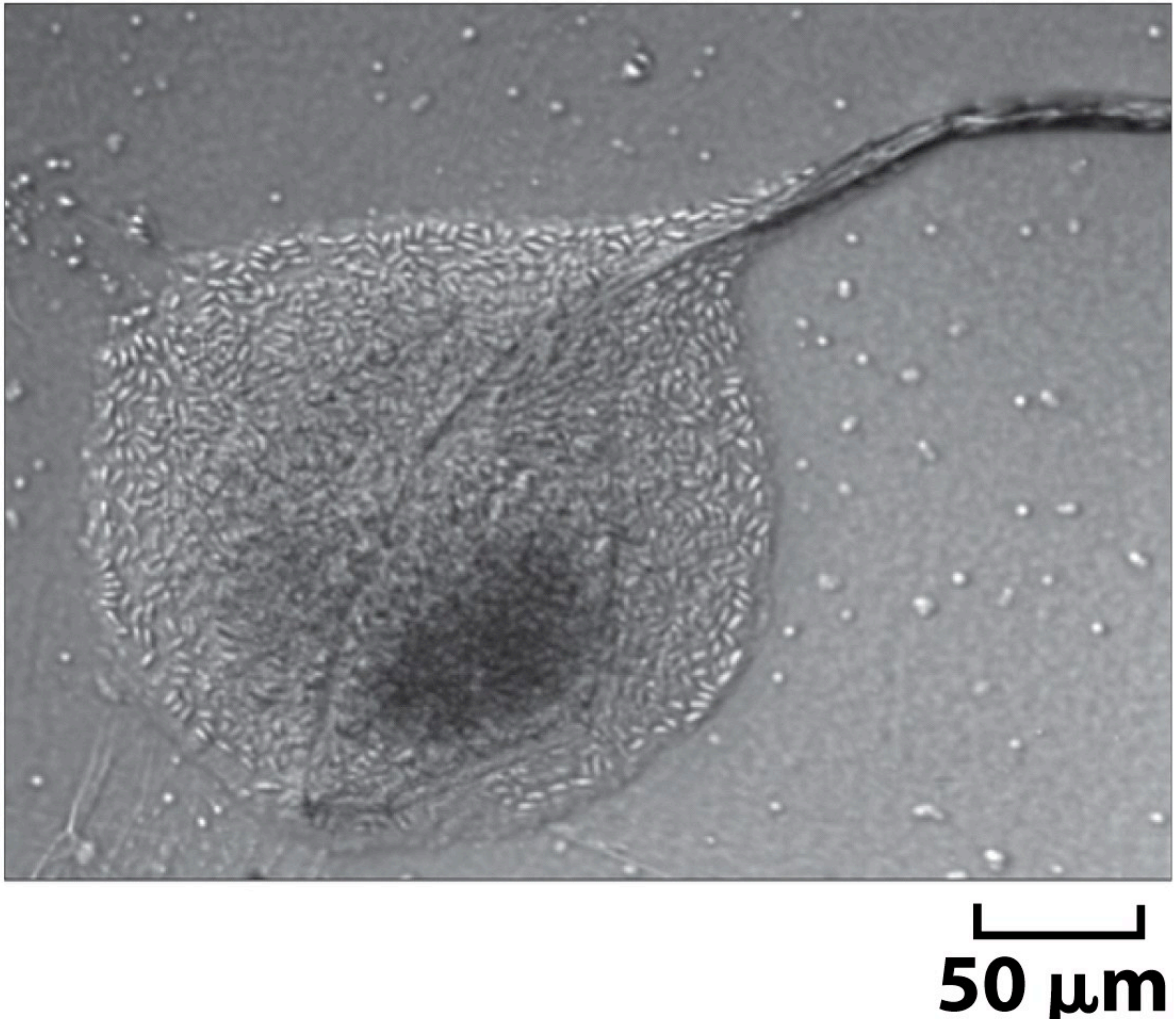


Figure 2.29 Physical Biology of the Cell (© Garland Science 2009)

Epithelial Sheets

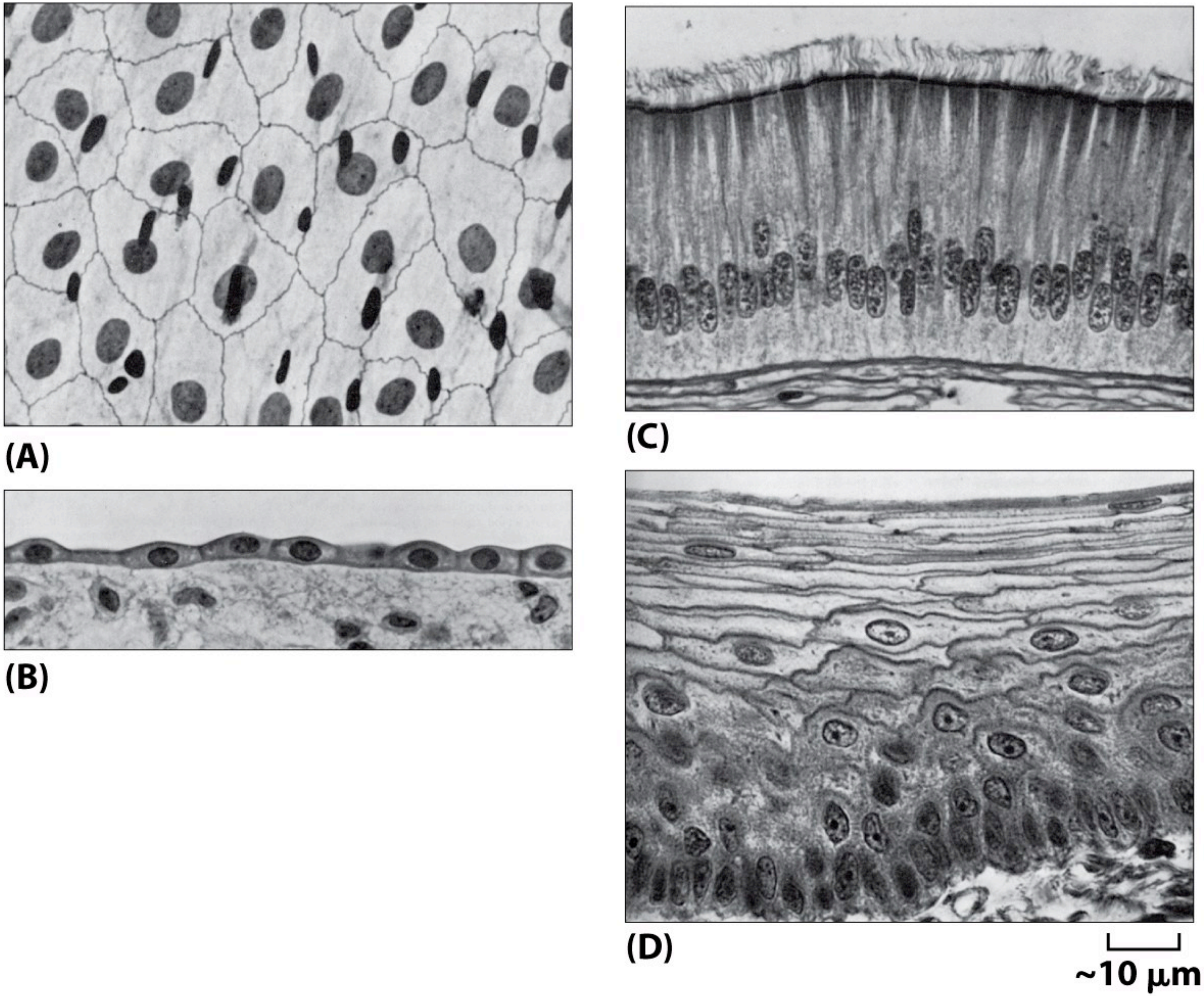


Figure 2.30 Physical Biology of the Cell (© Garland Science 2009)

Tissue Organization

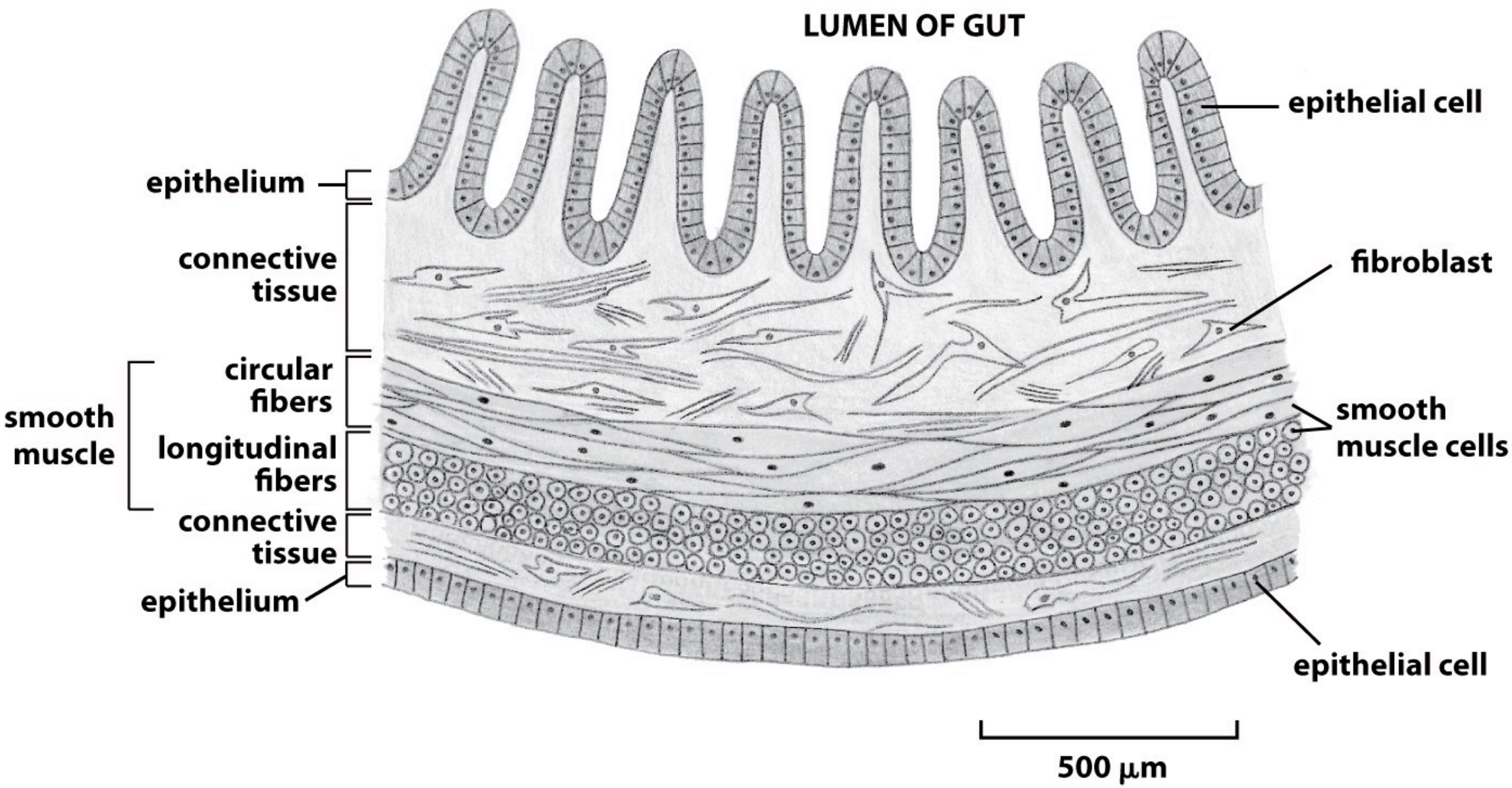


Figure 2.31 Physical Biology of the Cell (© Garland Science 2009)

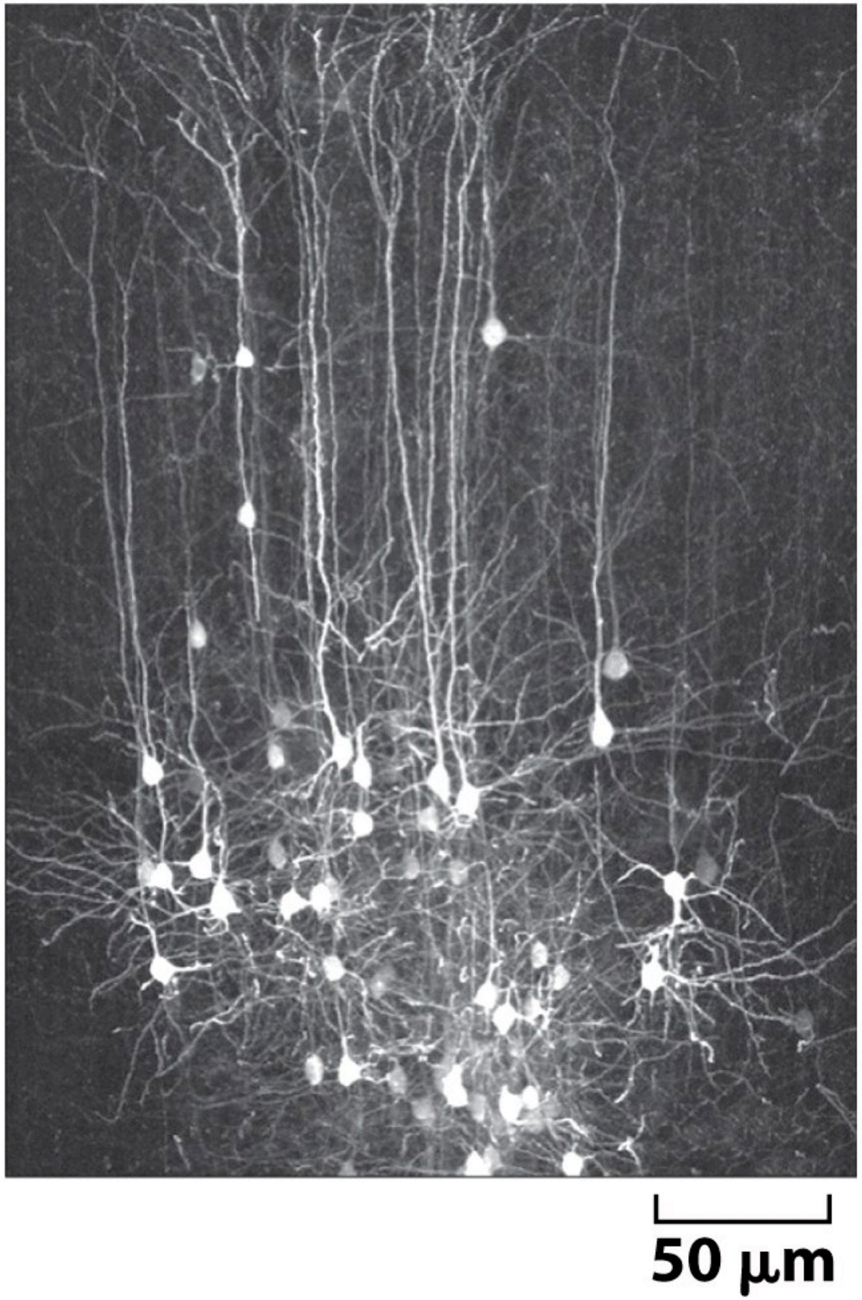


Figure 2.32 Physical Biology of the Cell (© Garland Science 2009)

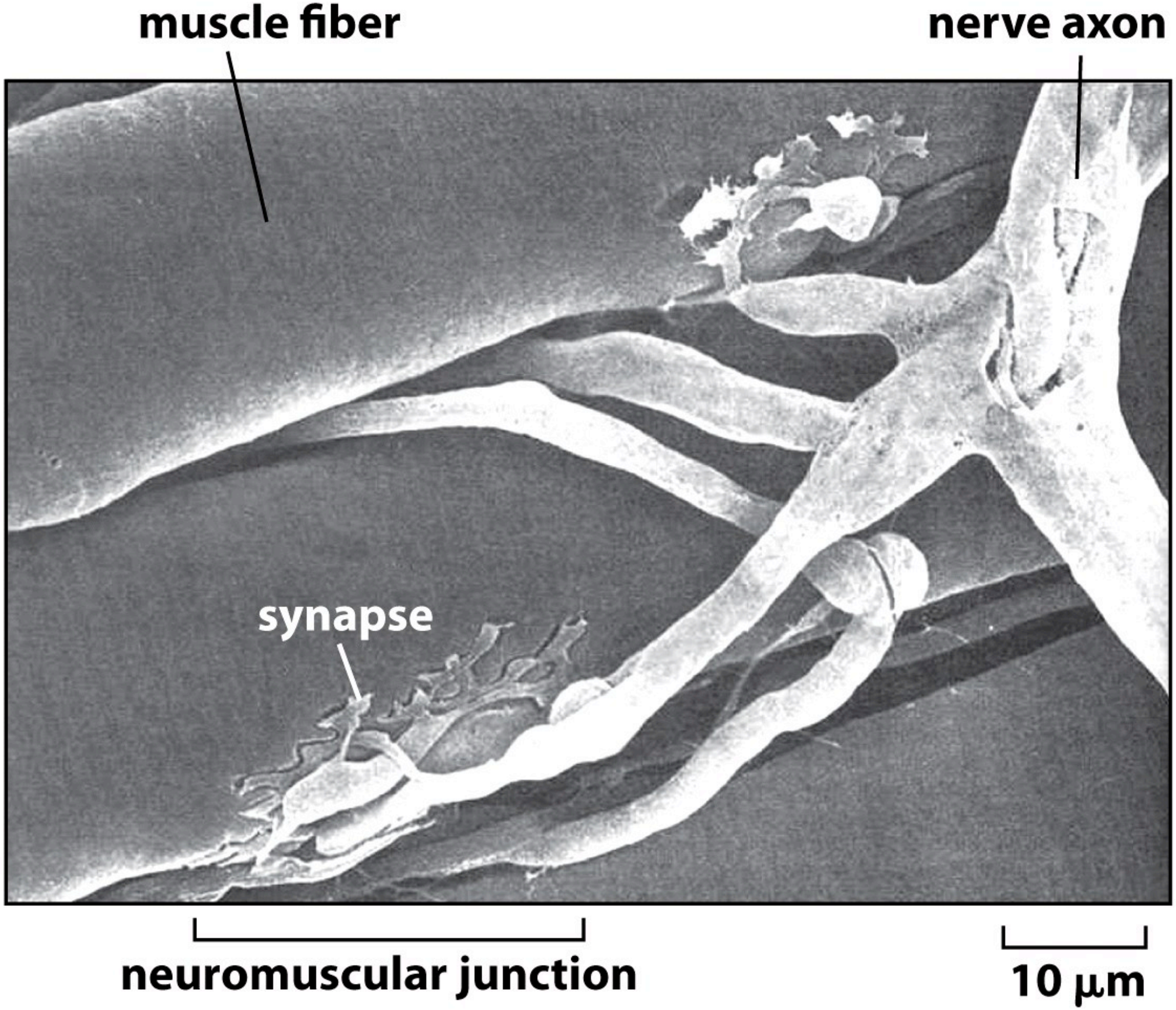


Figure 2.33 Physical Biology of the Cell (© Garland Science 2009)

Drosophila

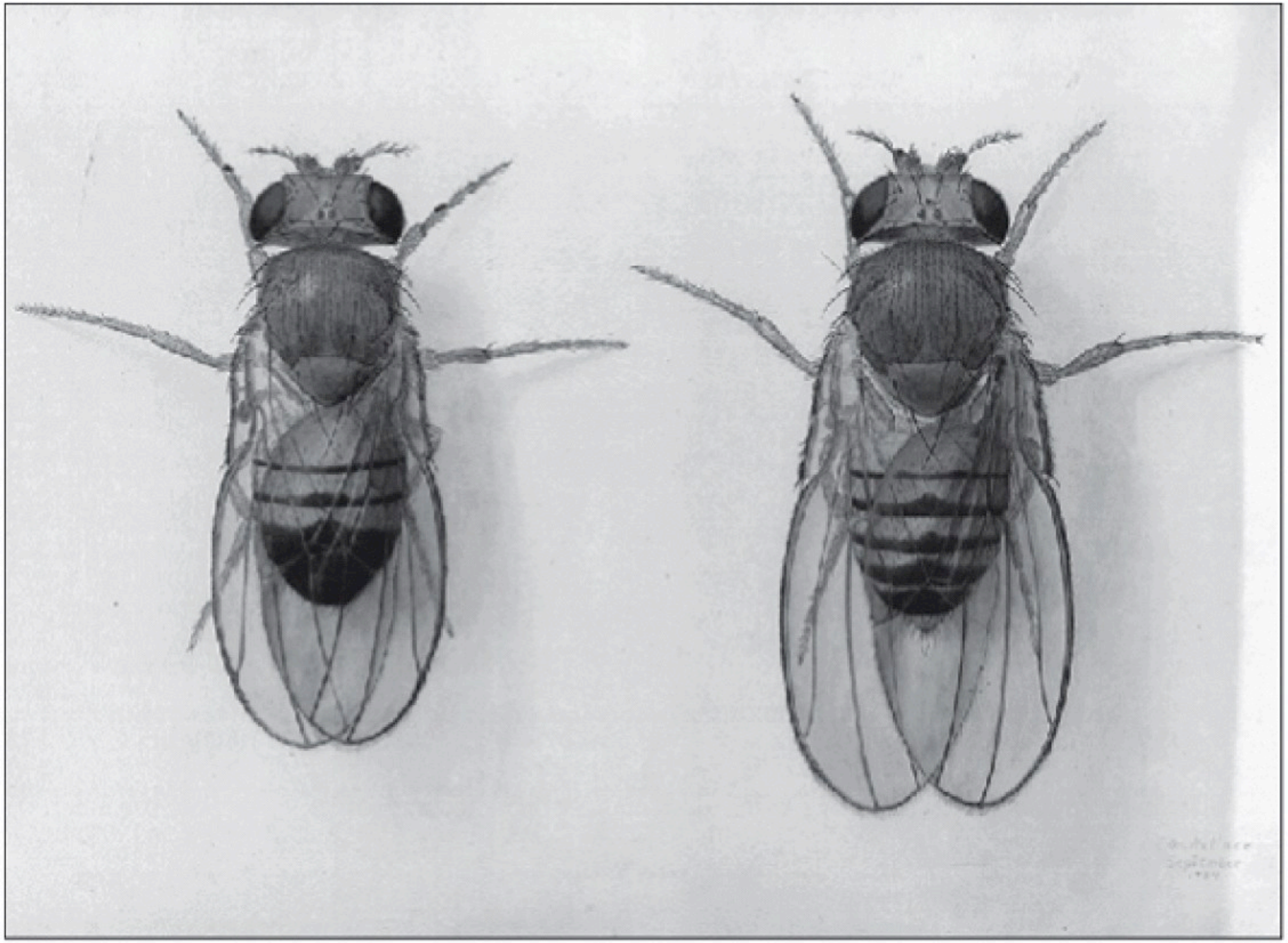
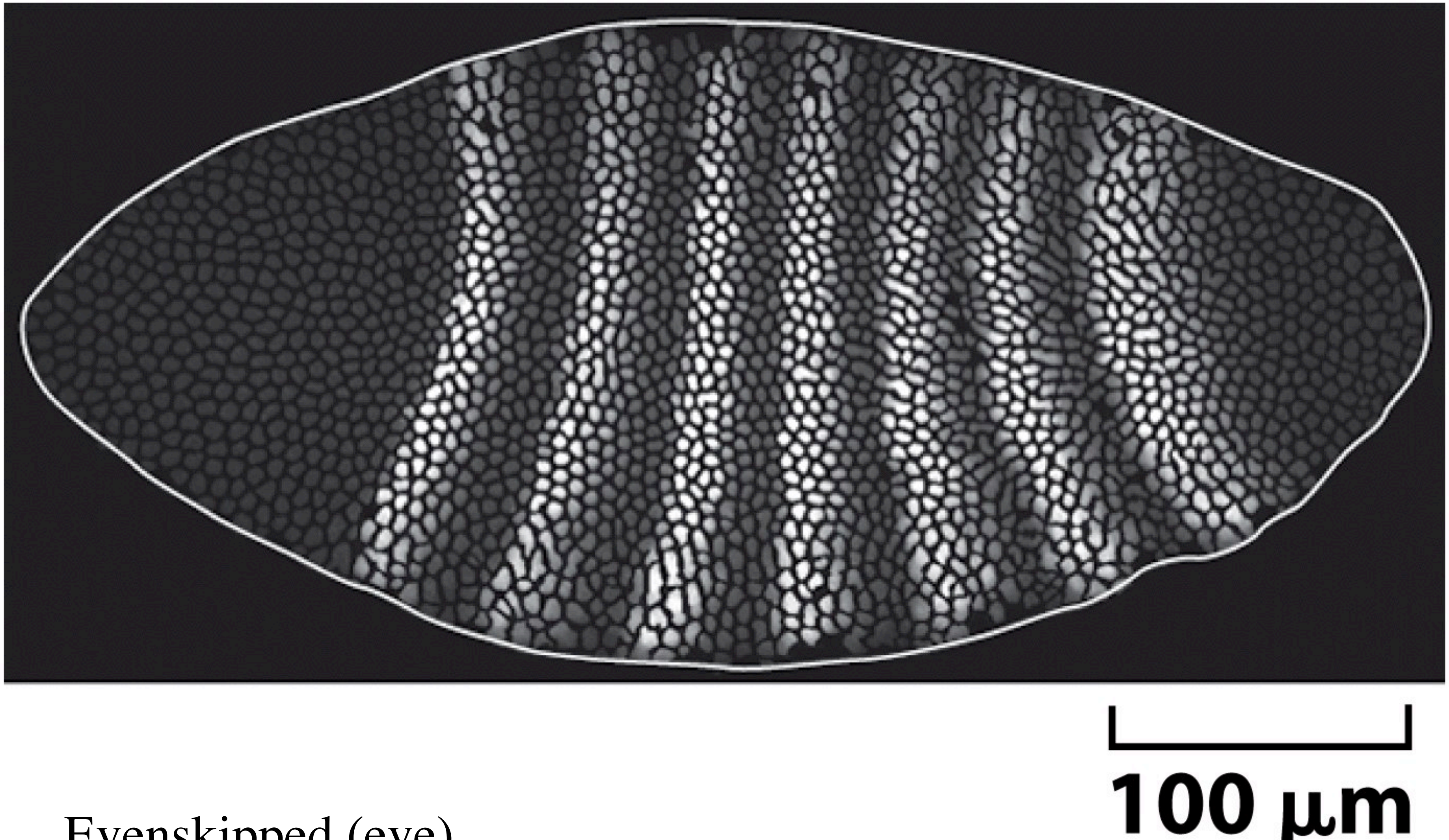


Figure 2.34 Physical Biology of the Cell (© Garland Science 2009)

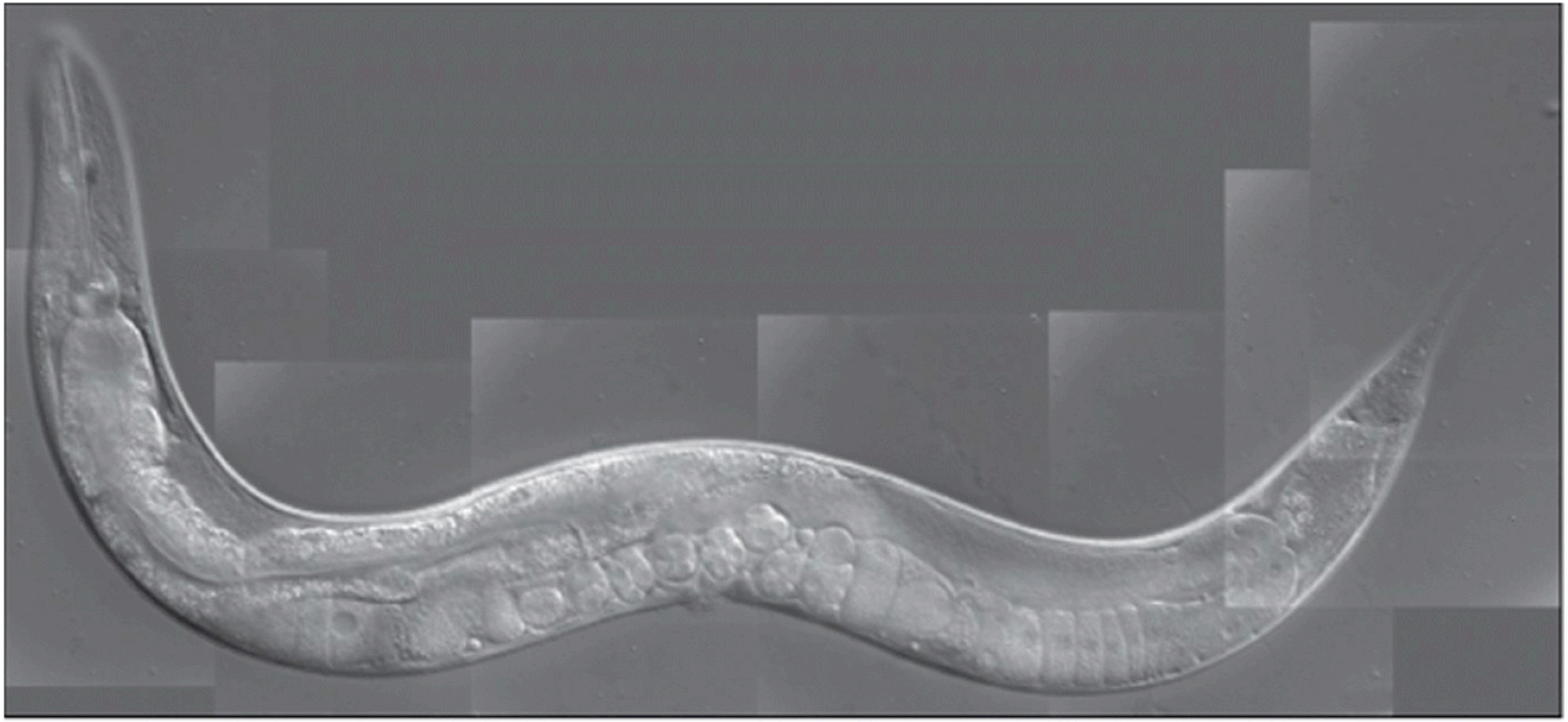
Gene Expression Patterns in Drosophila Development



Evenskipped (eve)

Figure 2.35 Physical Biology of the Cell (© Garland Science 2009)

C. elegans



959 cells

100 μm

Figure 2.36 Physical Biology of the Cell (© Garland Science 2009)

Cell Lineage of C. elegans

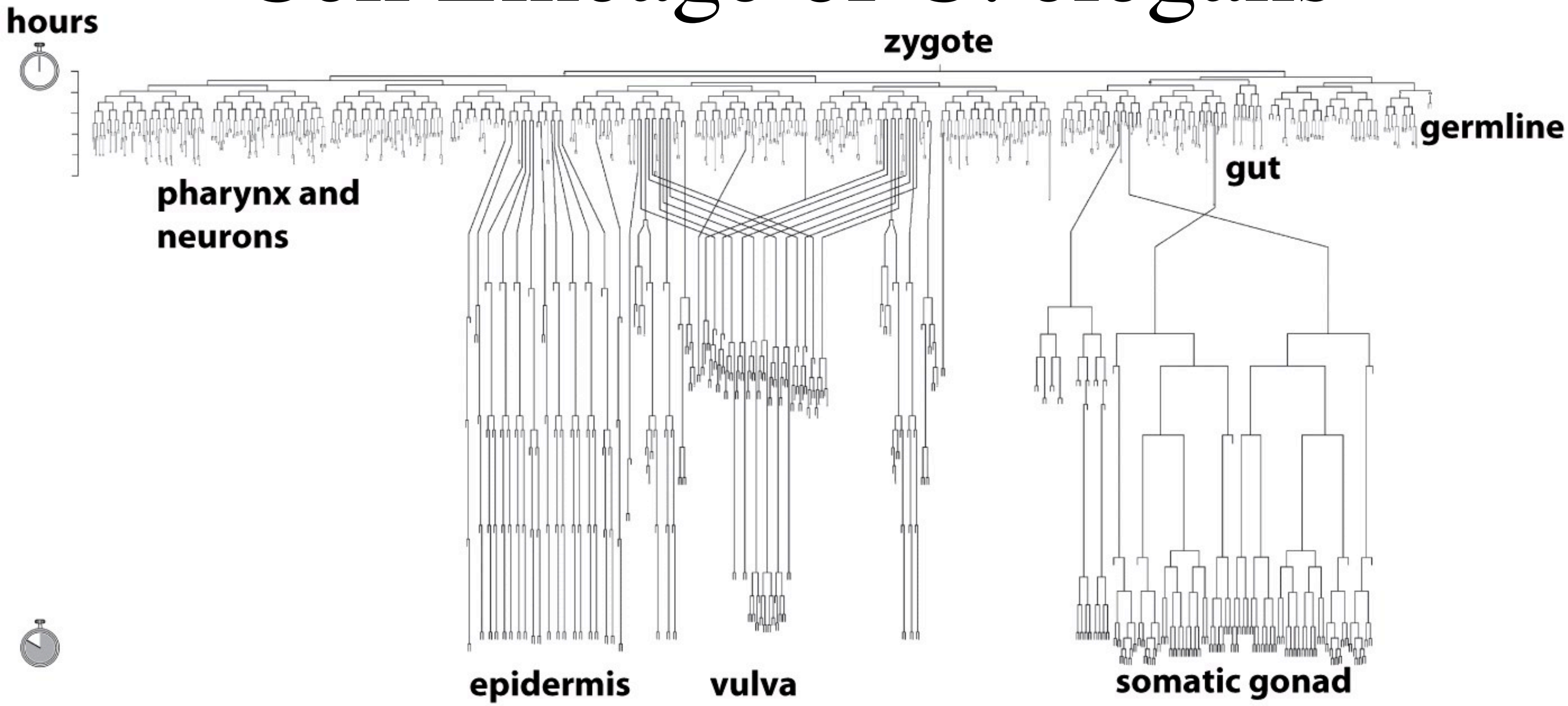


Figure 2.37 Physical Biology of the Cell (© Garland Science 2009)

Next

- Nucleic acids, peptides and proteins
- Biological reactions and interactions –
- function aspects of various bio-molecules
- ATPsynthases and motor proteins,
- Dynamics of molecular motors (2)
- engineering and design of biomolecules.