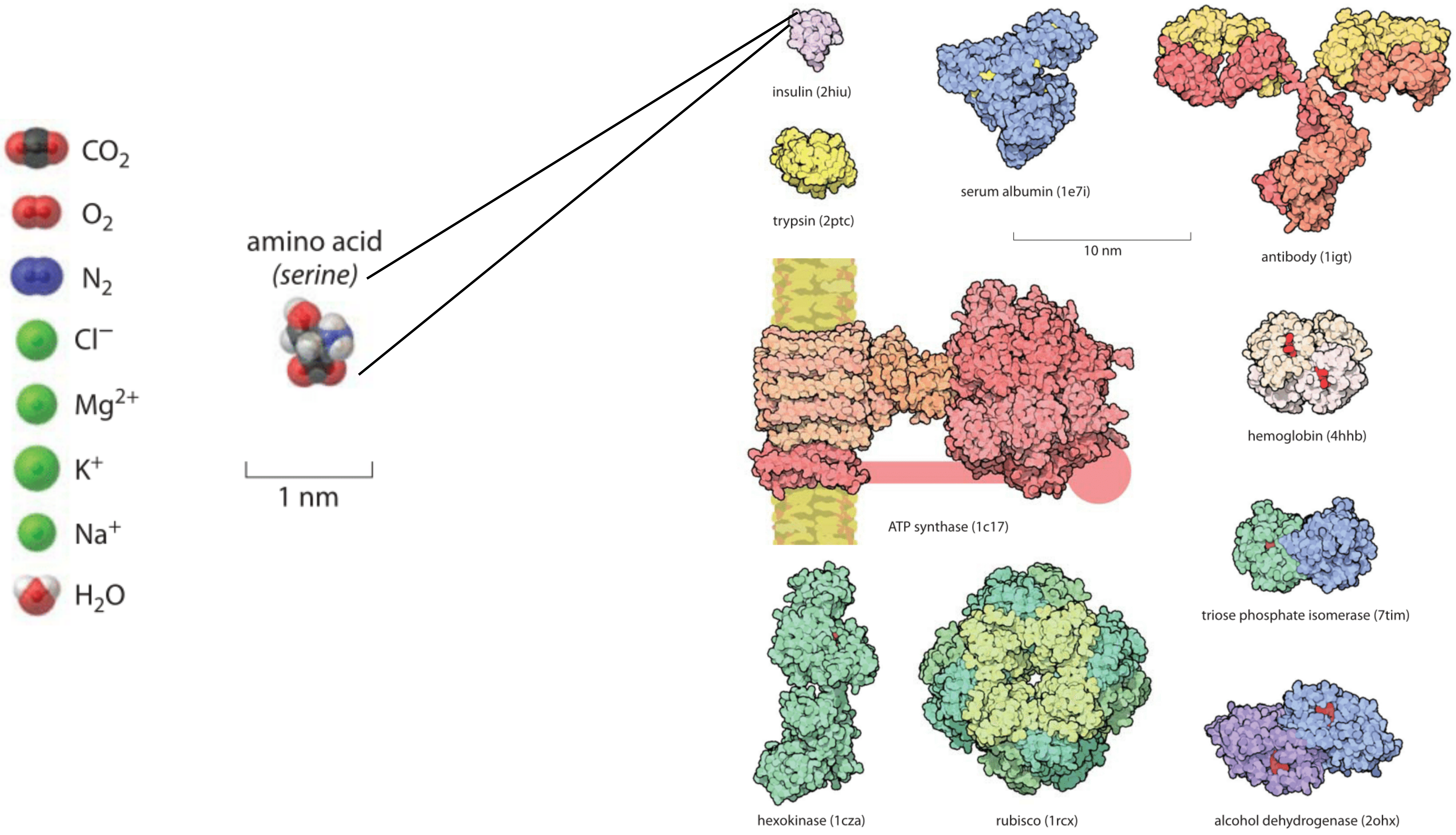
Crash course in cell and molecular biology + cell mechanics

ME-480 Lecture 1

Molecules of life

Proteins drive biological function

proteins are polymers of amino acids



DNA and RNA encode biological function

DNA and RNA are polymers of nucleic acids

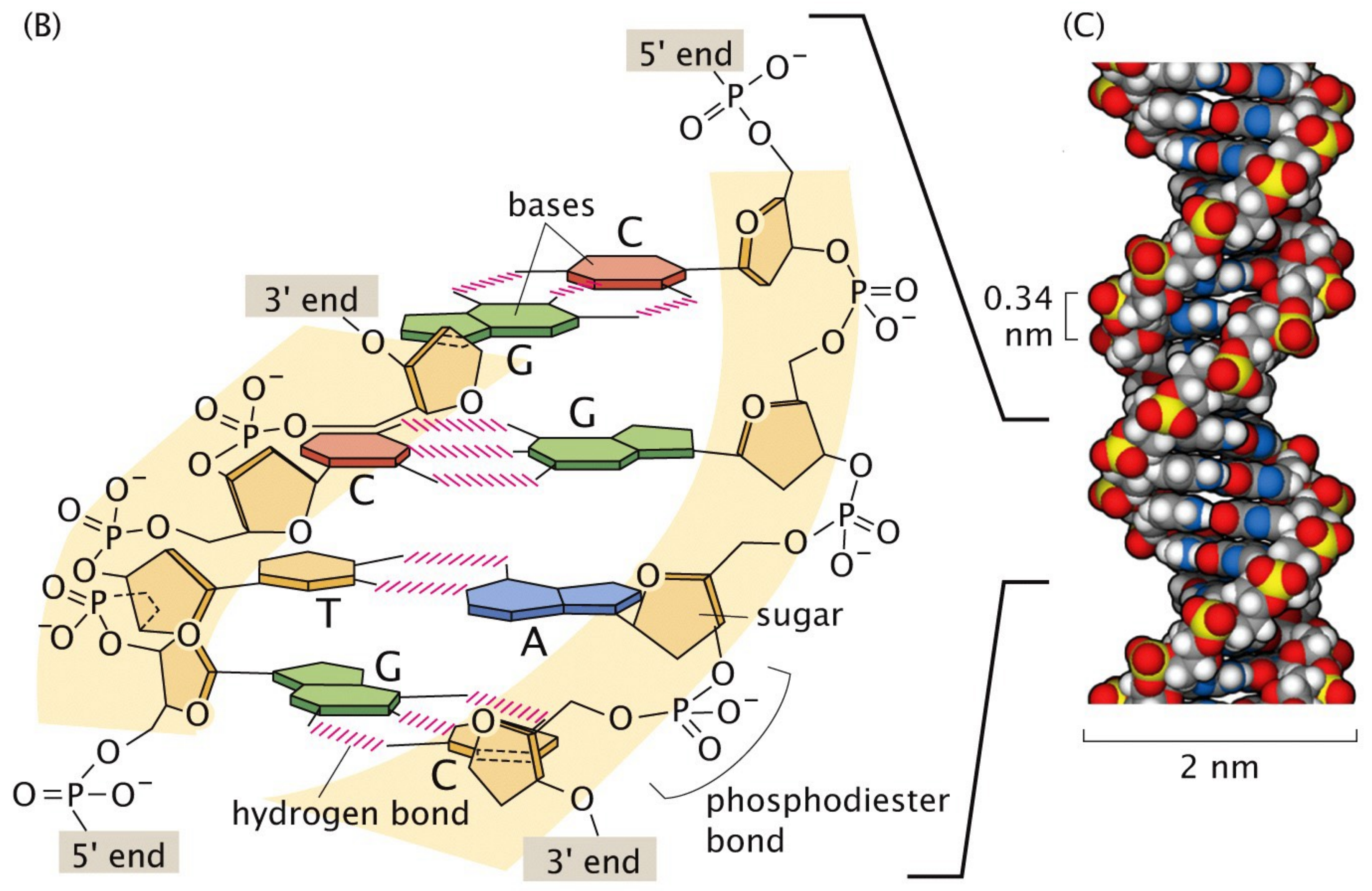
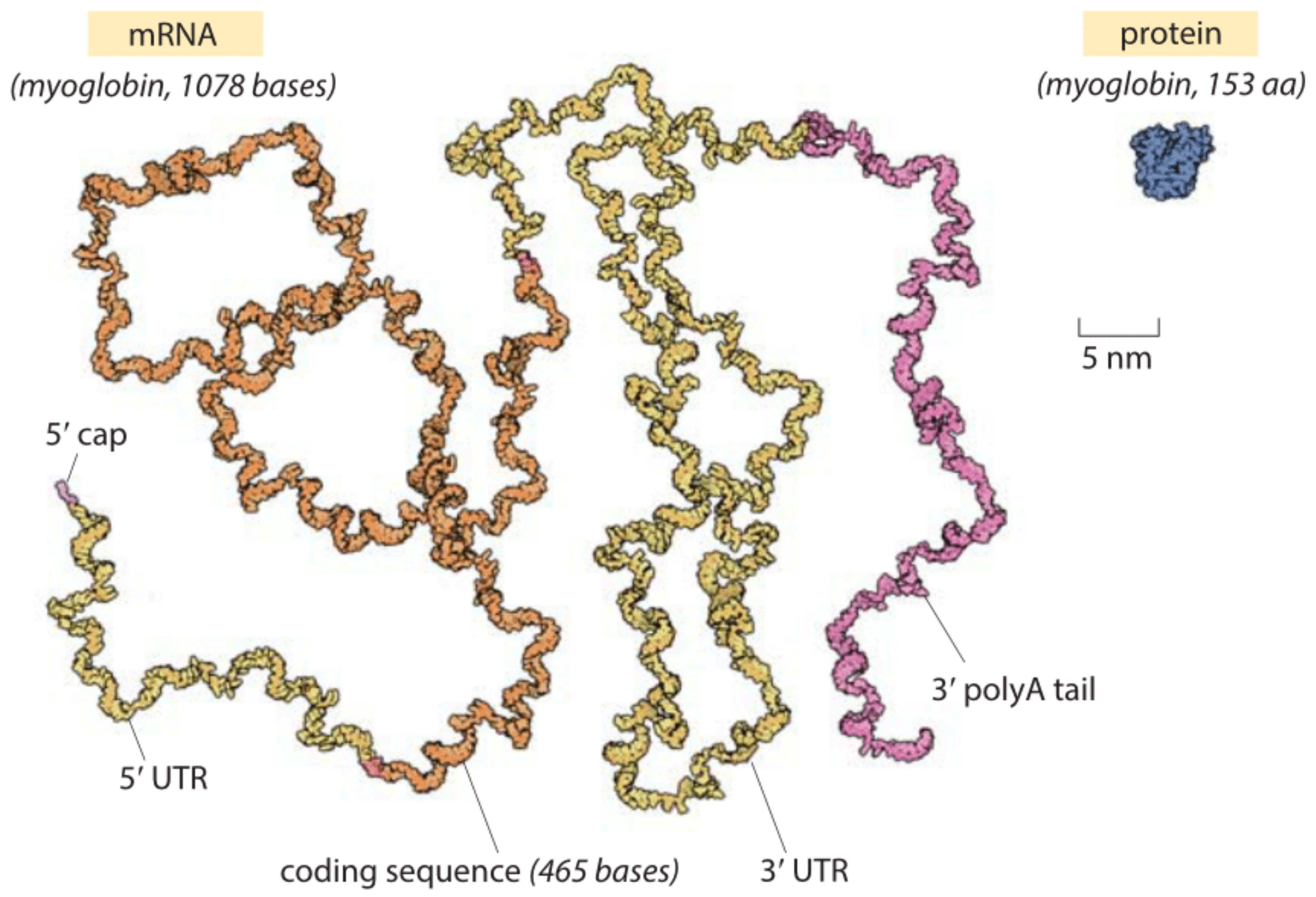
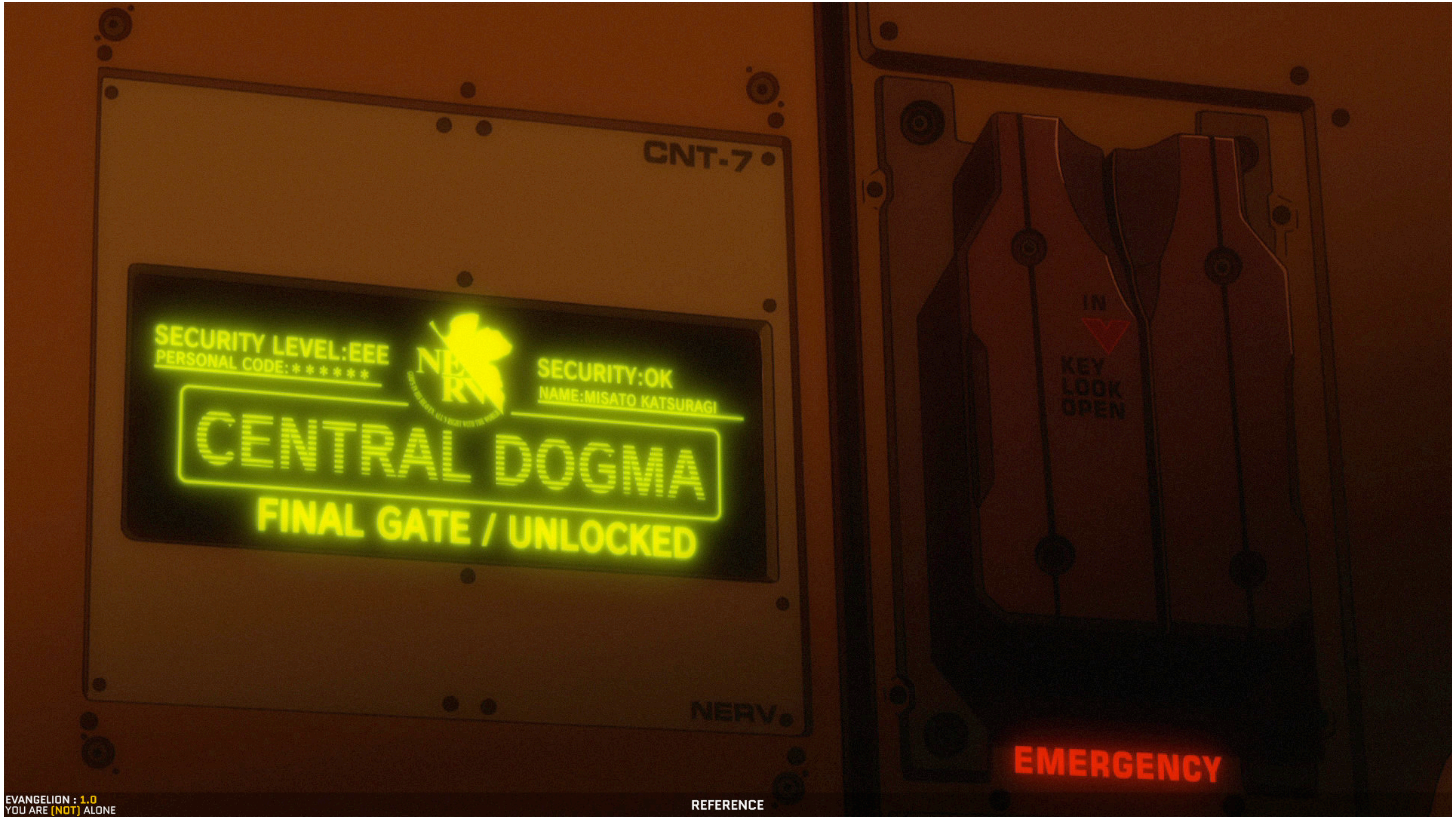


Figure 1.3b Physical Biology of the Cell, 2ed. (© Garland Science 2013)

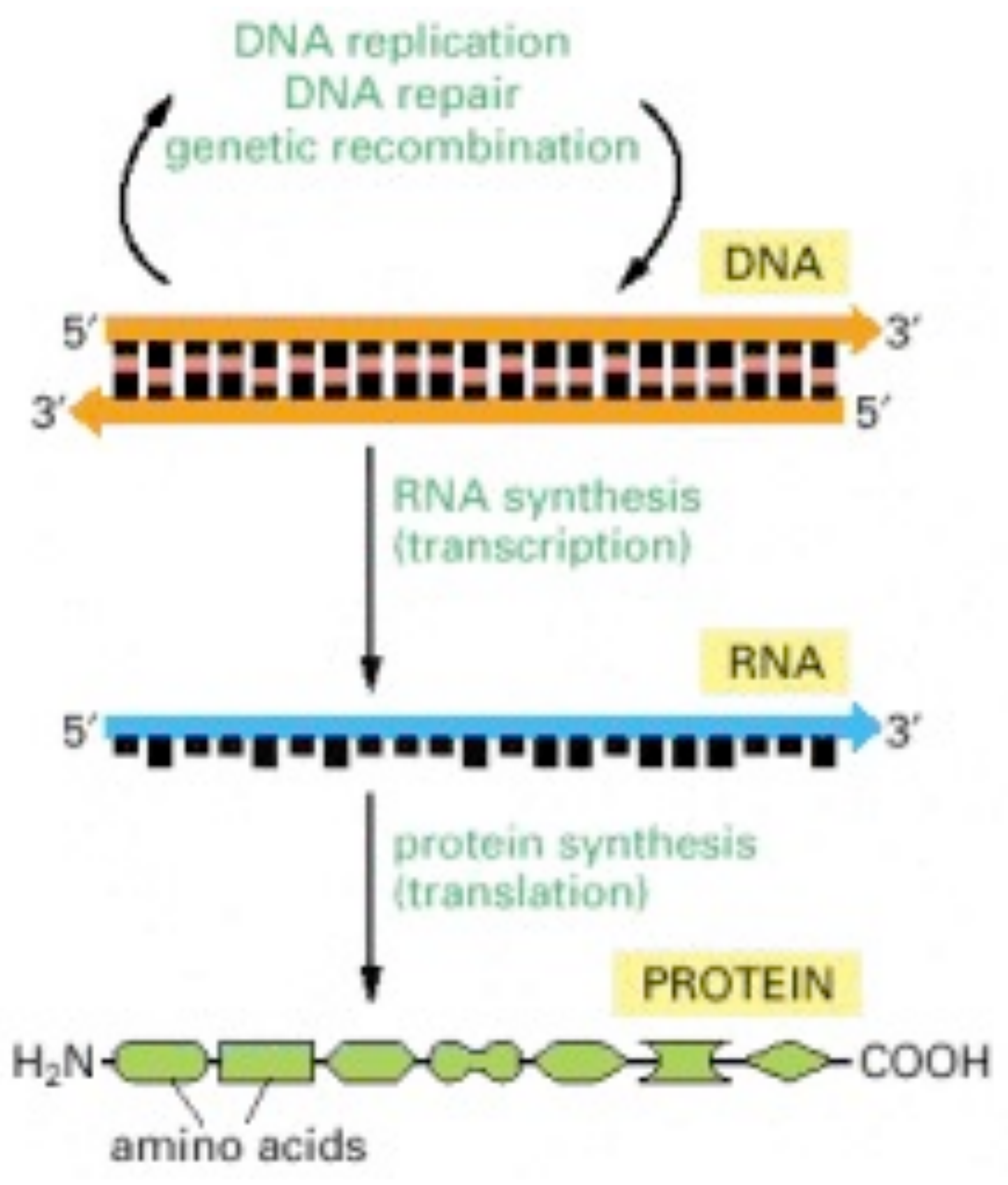


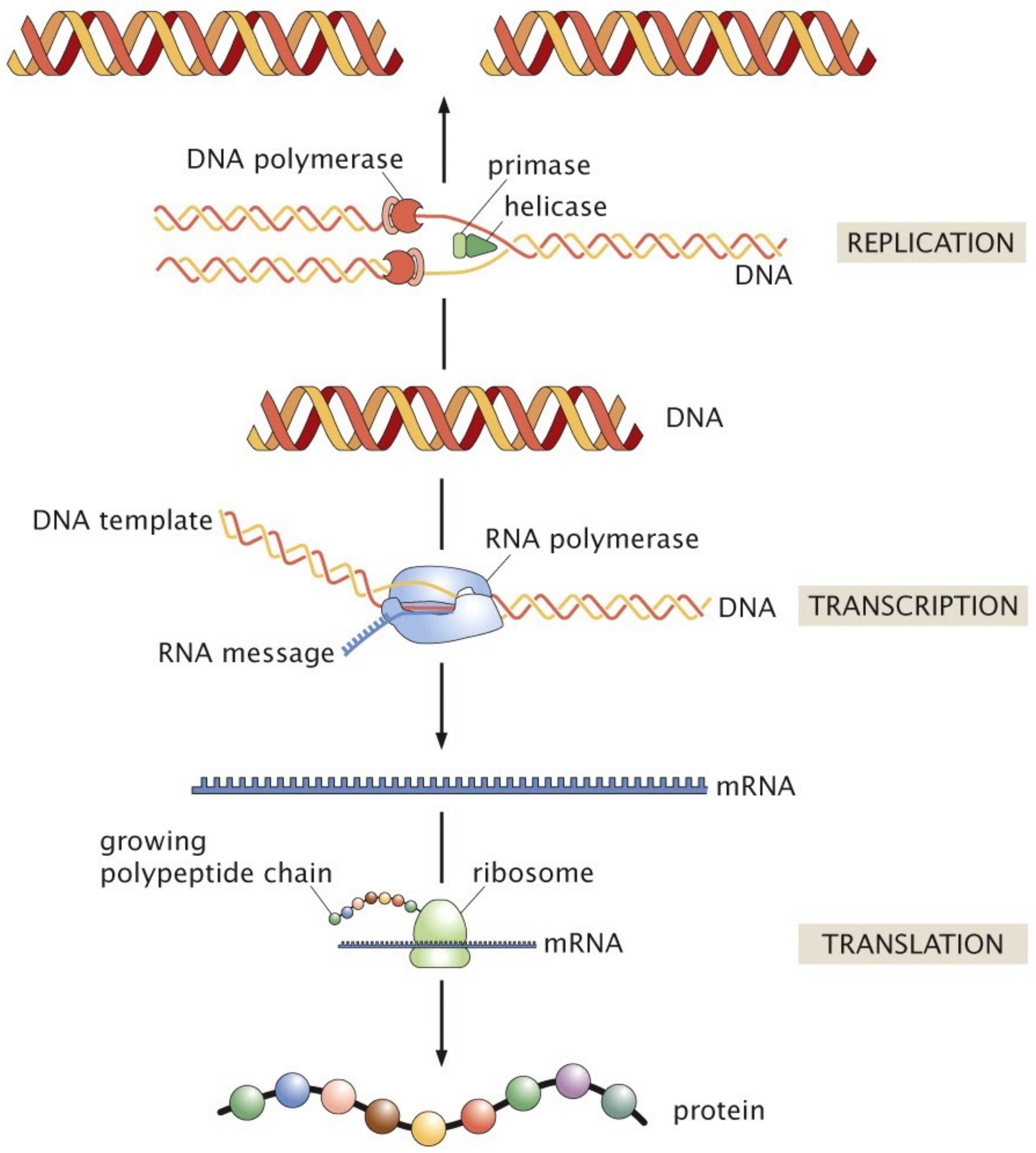
The central dogma



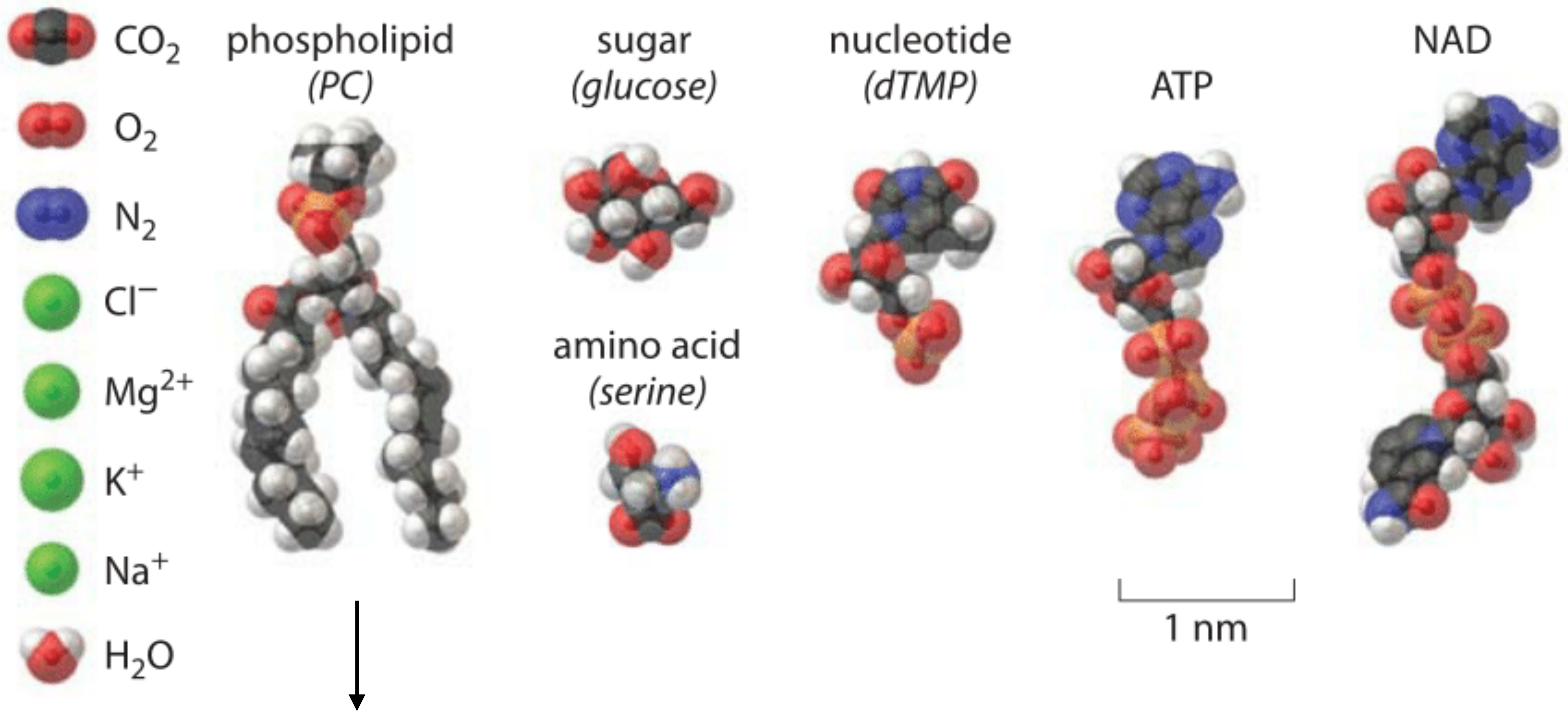
Neon Genesis Evangelion

The central dogma
from genotype to phenotype



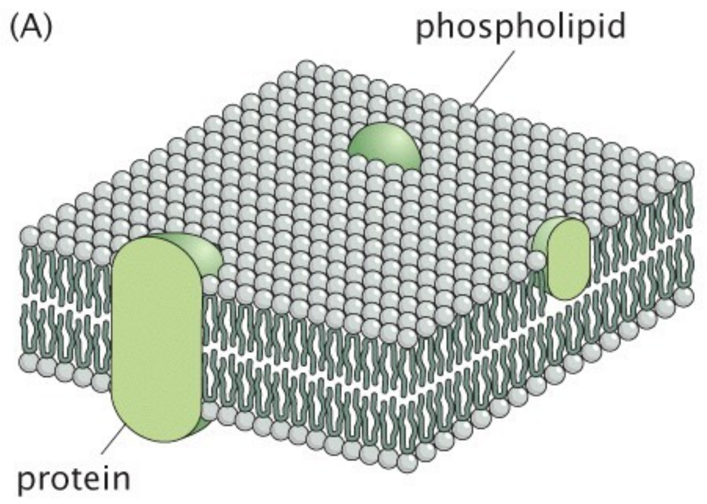


Other important molecules



metabolic

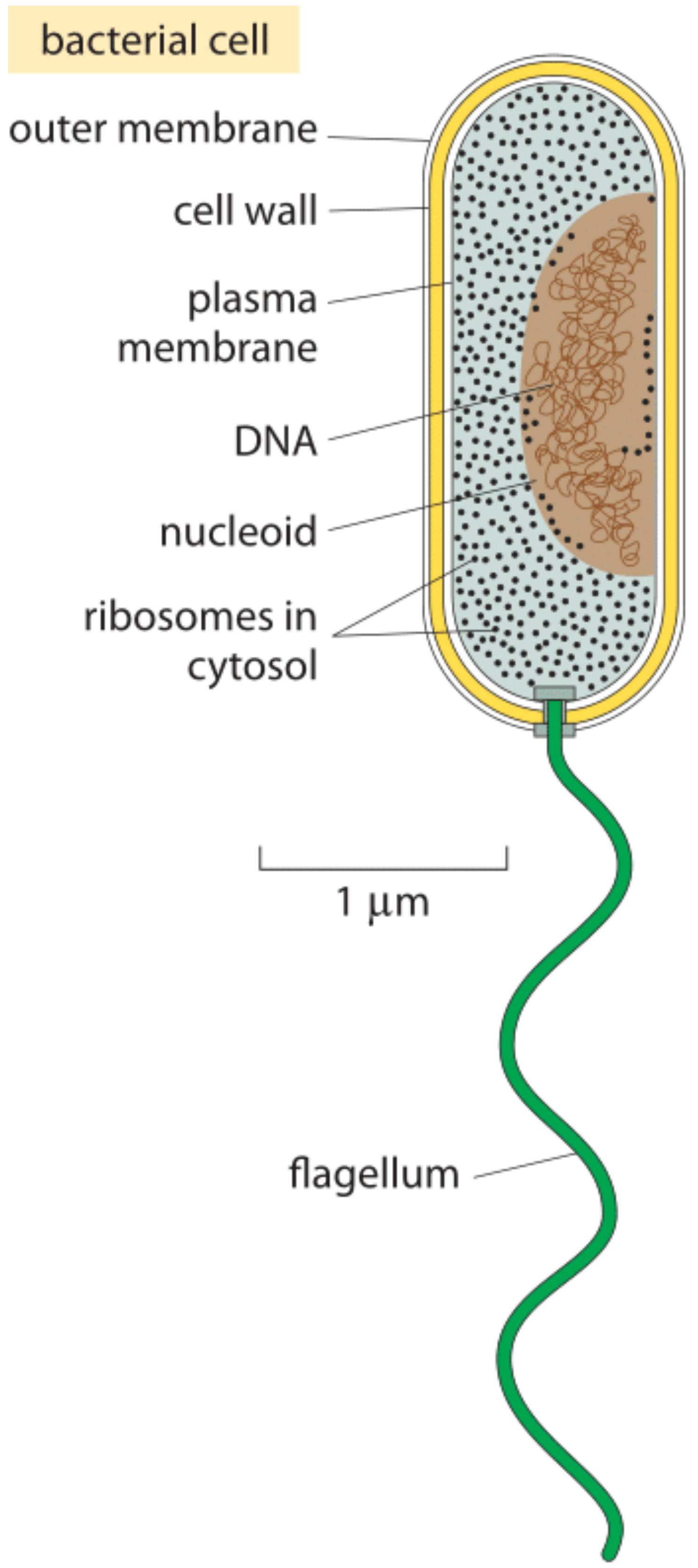
structural (membrane)

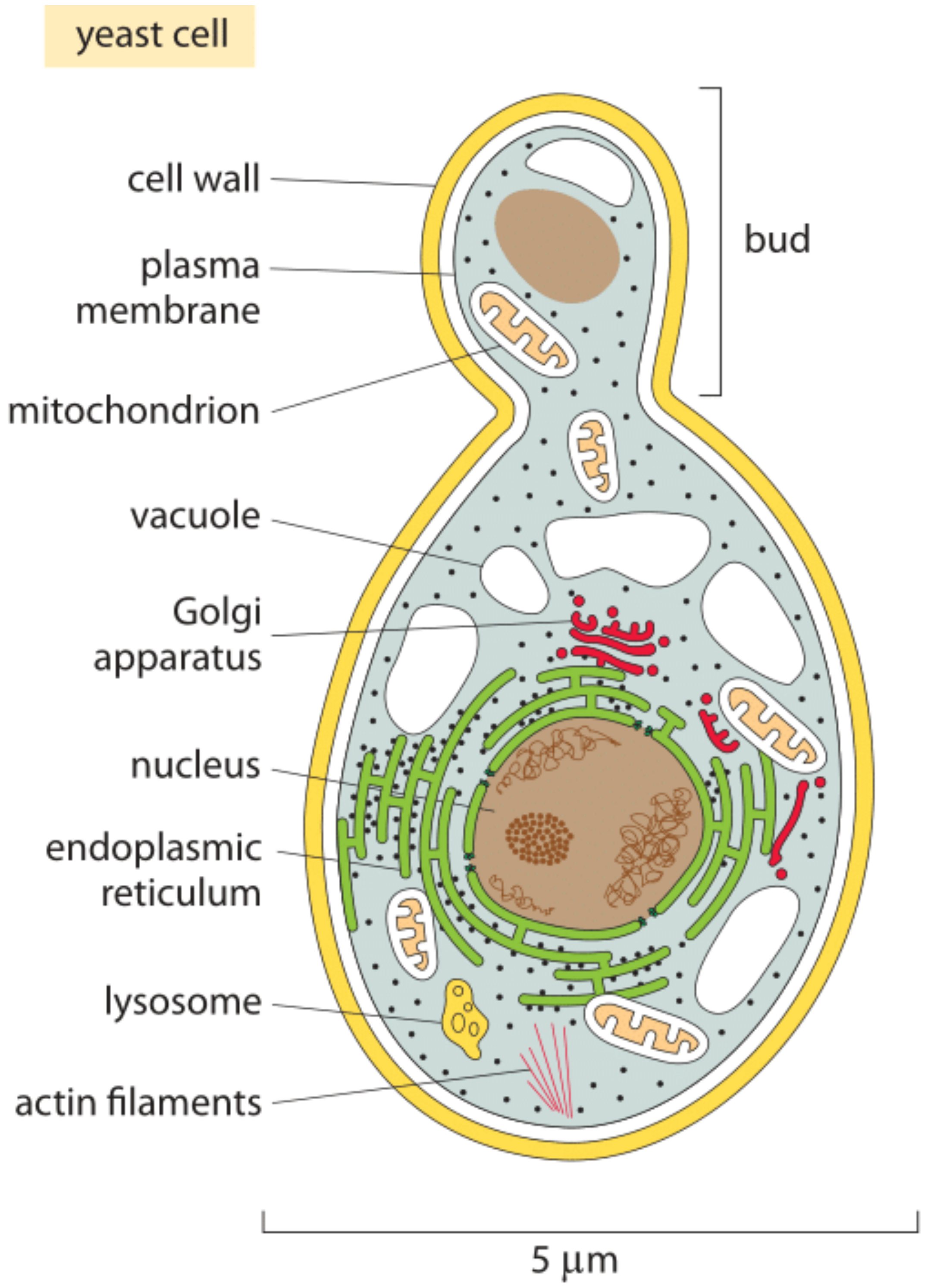


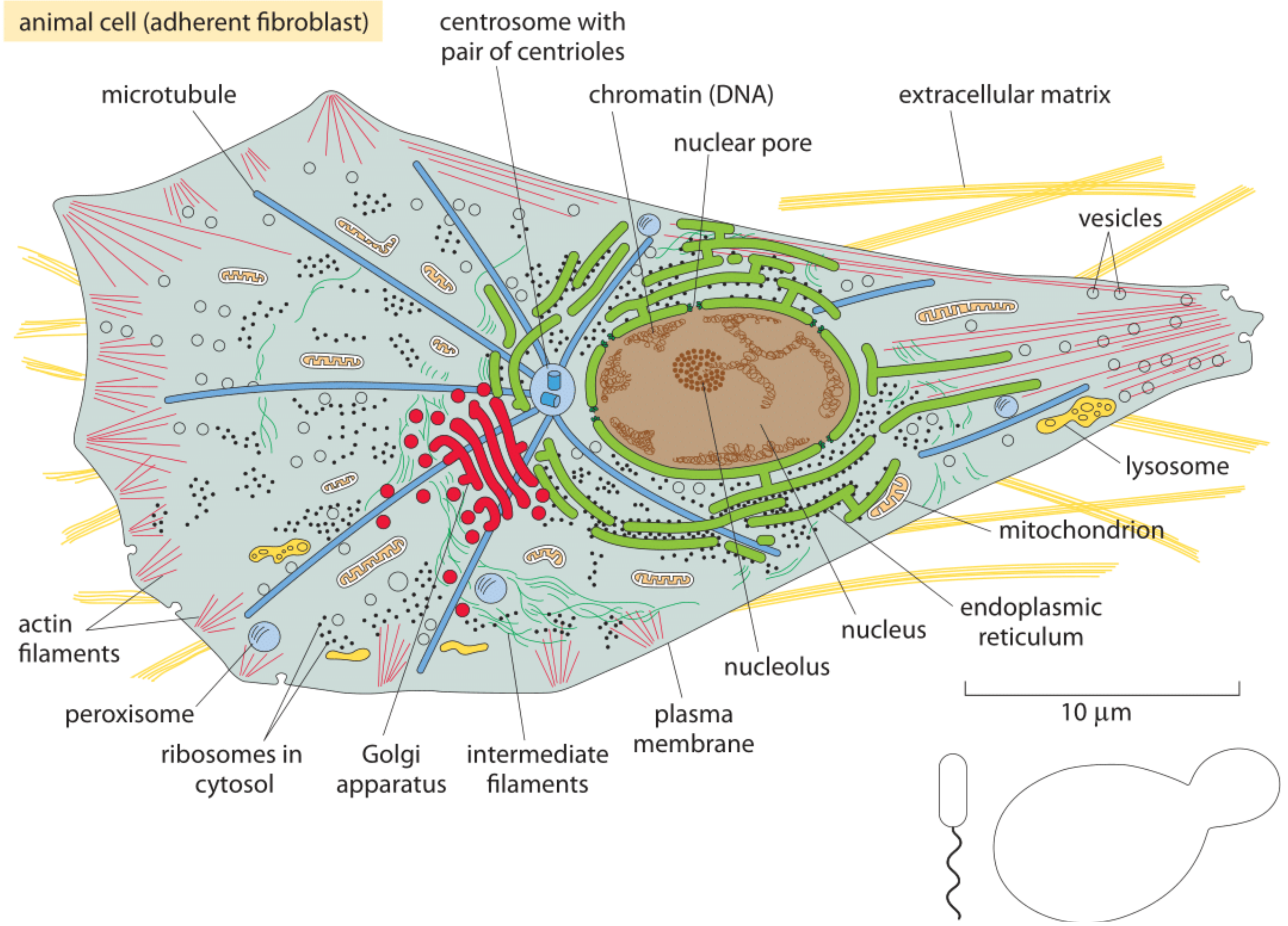
Cells

Prokaryotes and eukaryotes

Similar molecular components, different architectures

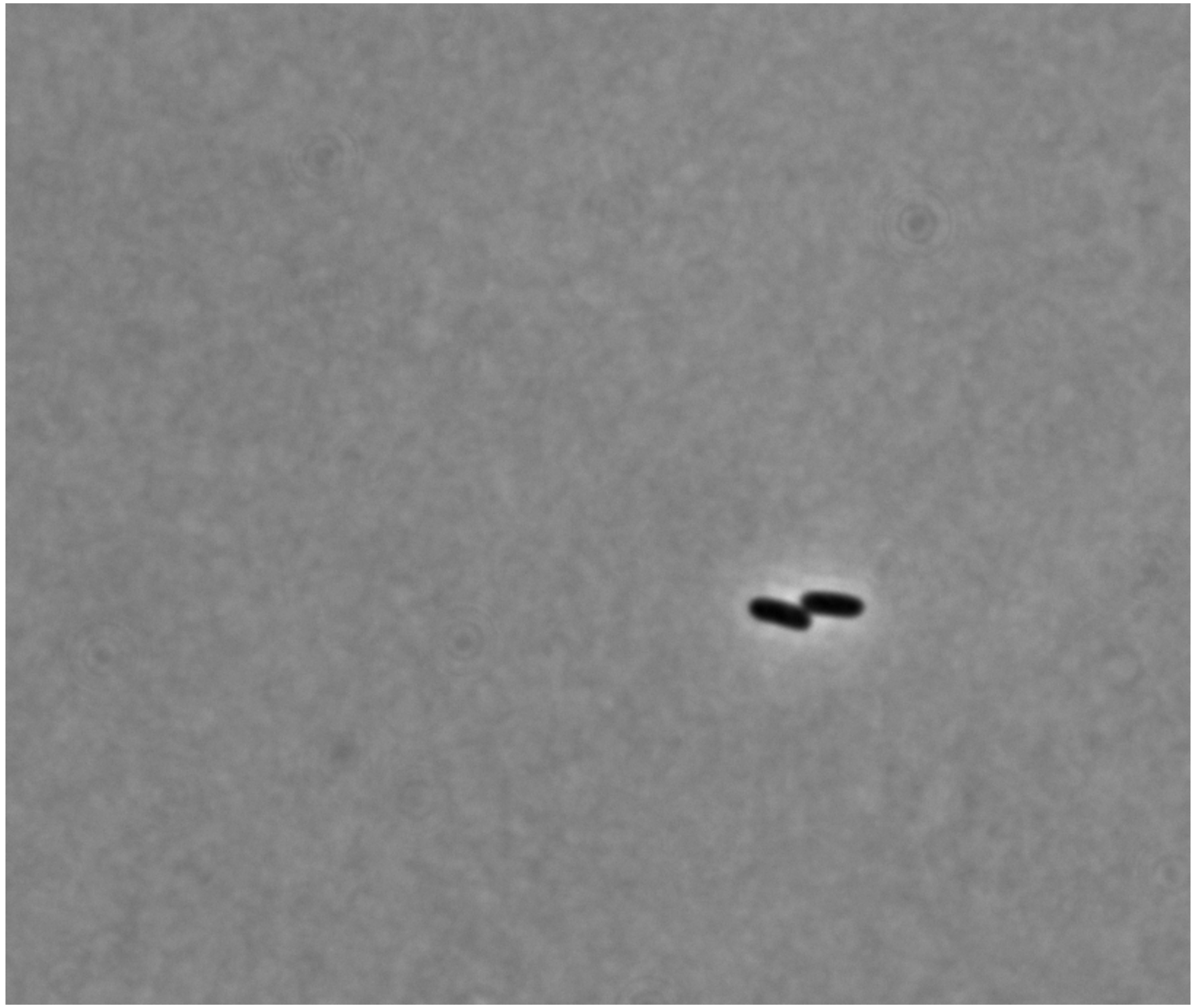






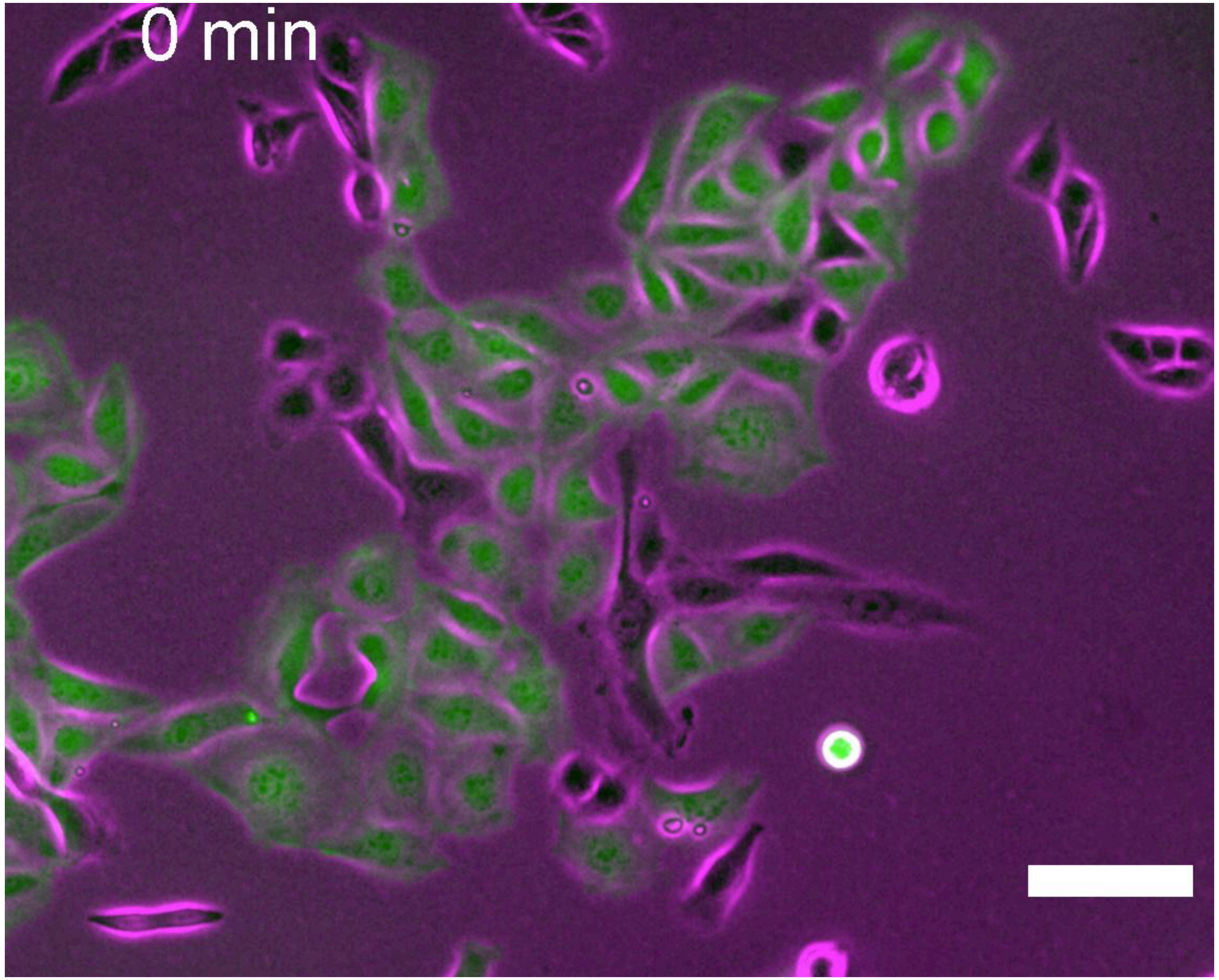
Unicellular organisms

bacteria, archaea…



E. coli

Tissues - cellular assemblies



Balasubramaniam et al, Nat Mat 2021

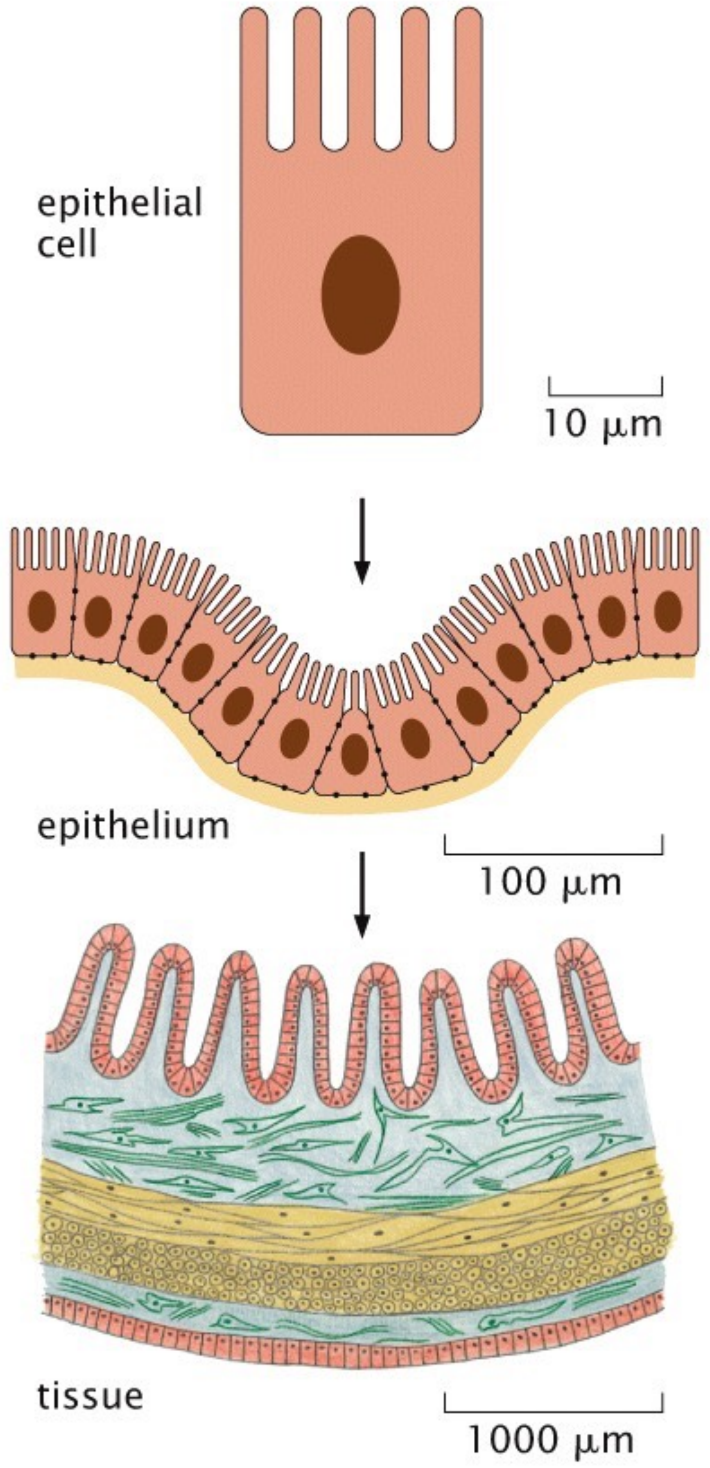
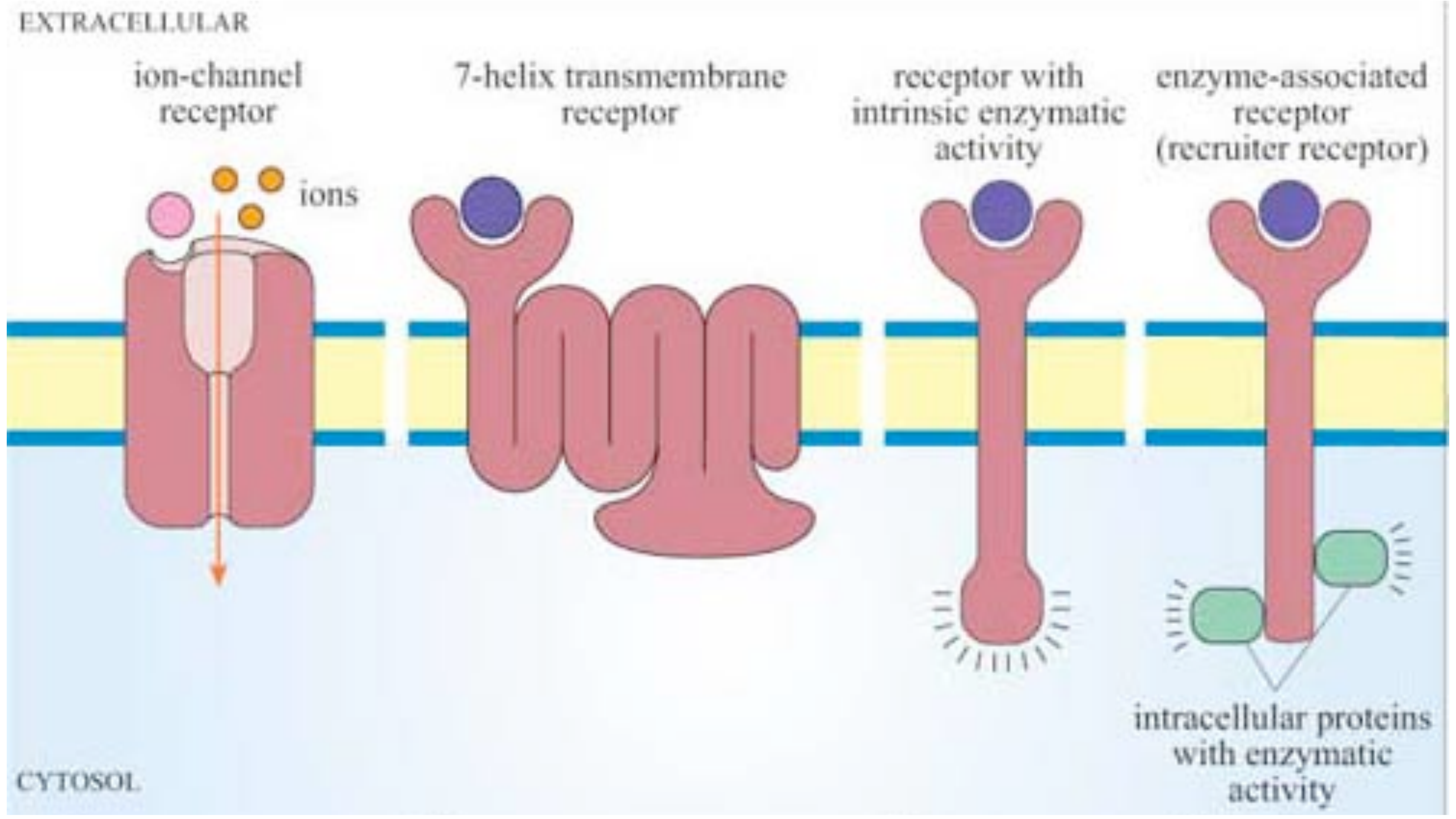


Figure 2.15 (part 2 of 2) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

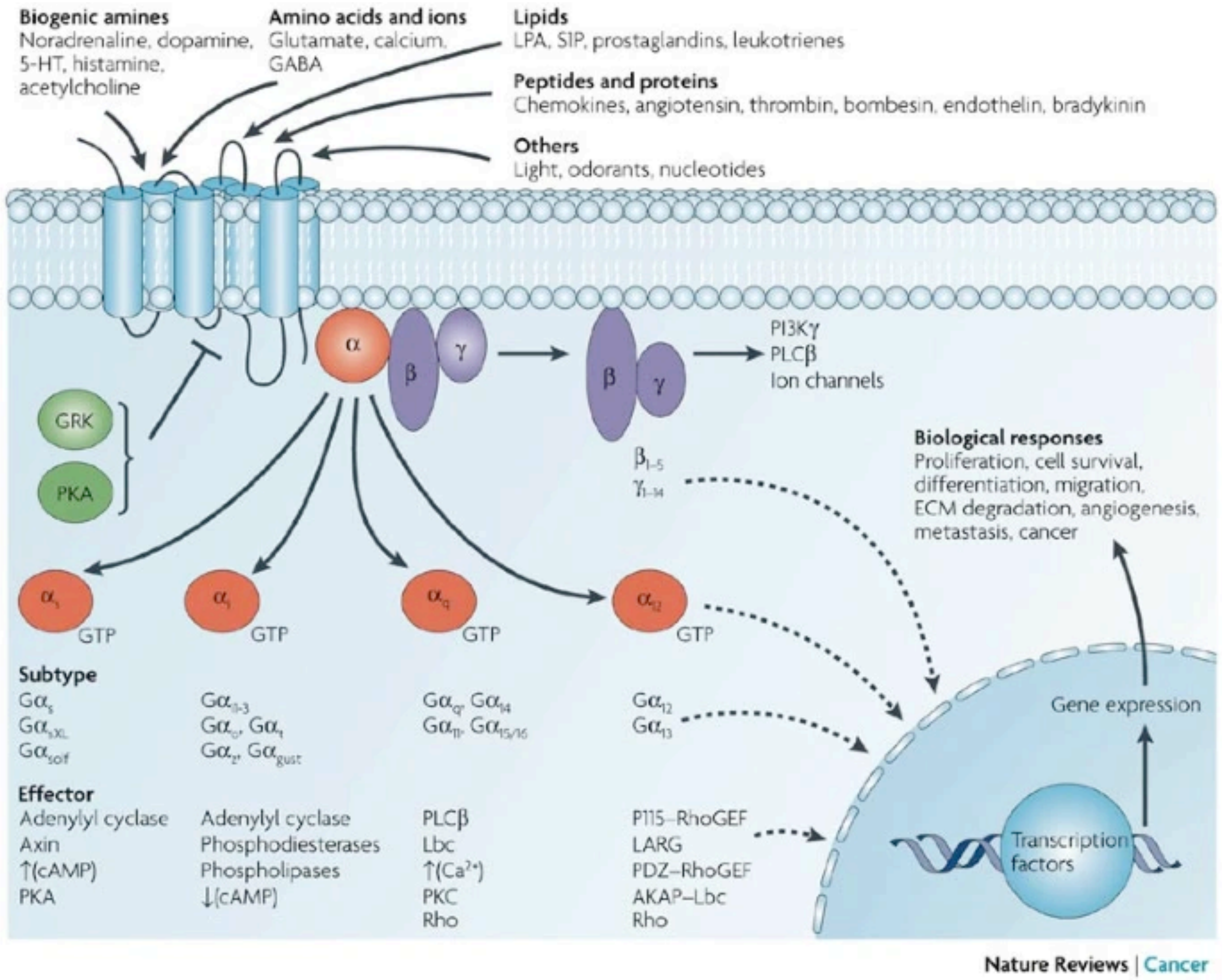
Taking information from the environment
proteins function as sensors



Membrane-bound receptors transmit external information to the cell:

- chemical (ligand)
- physical (temperature)
- mechanical (compression, shear)

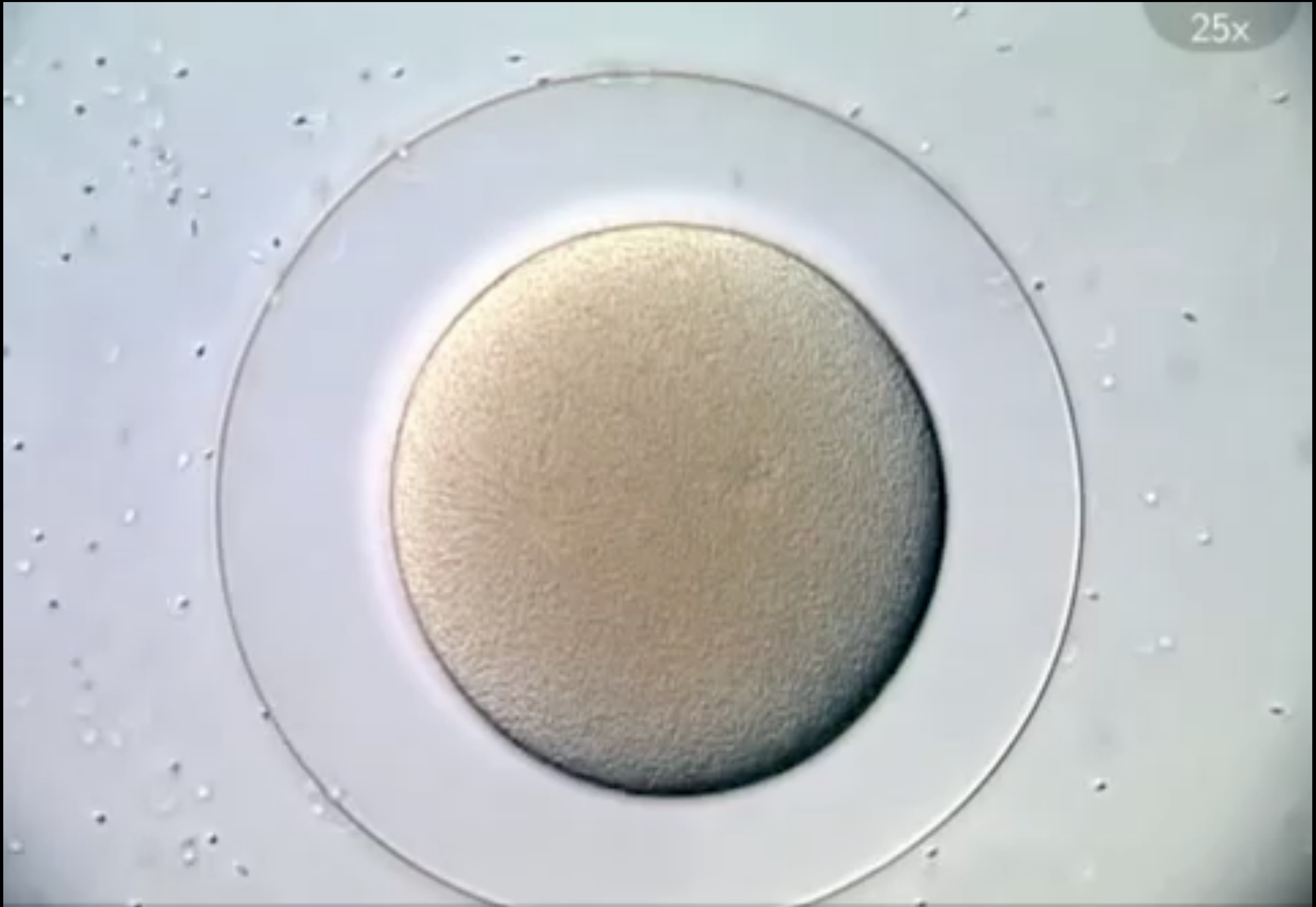
From input to output: biological signaling



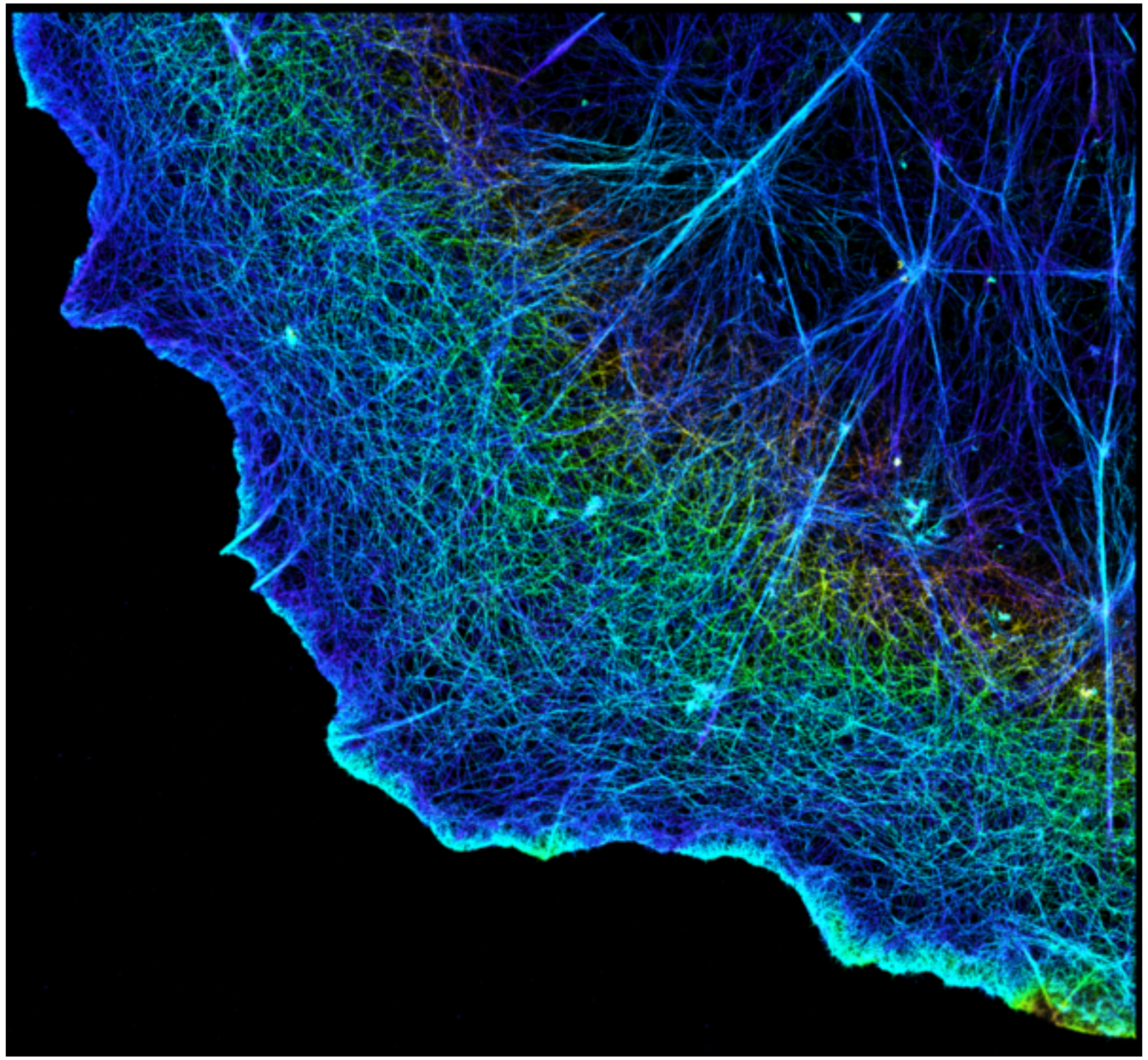
GPCRs

More or less complex signaling pathway link external input to phenotypic response

Mechanics at the cellular and molecular levels

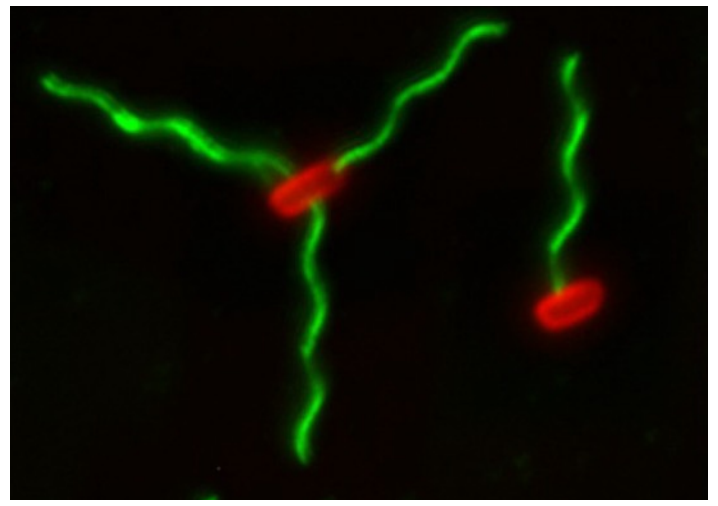

25x

Protein beams: actin

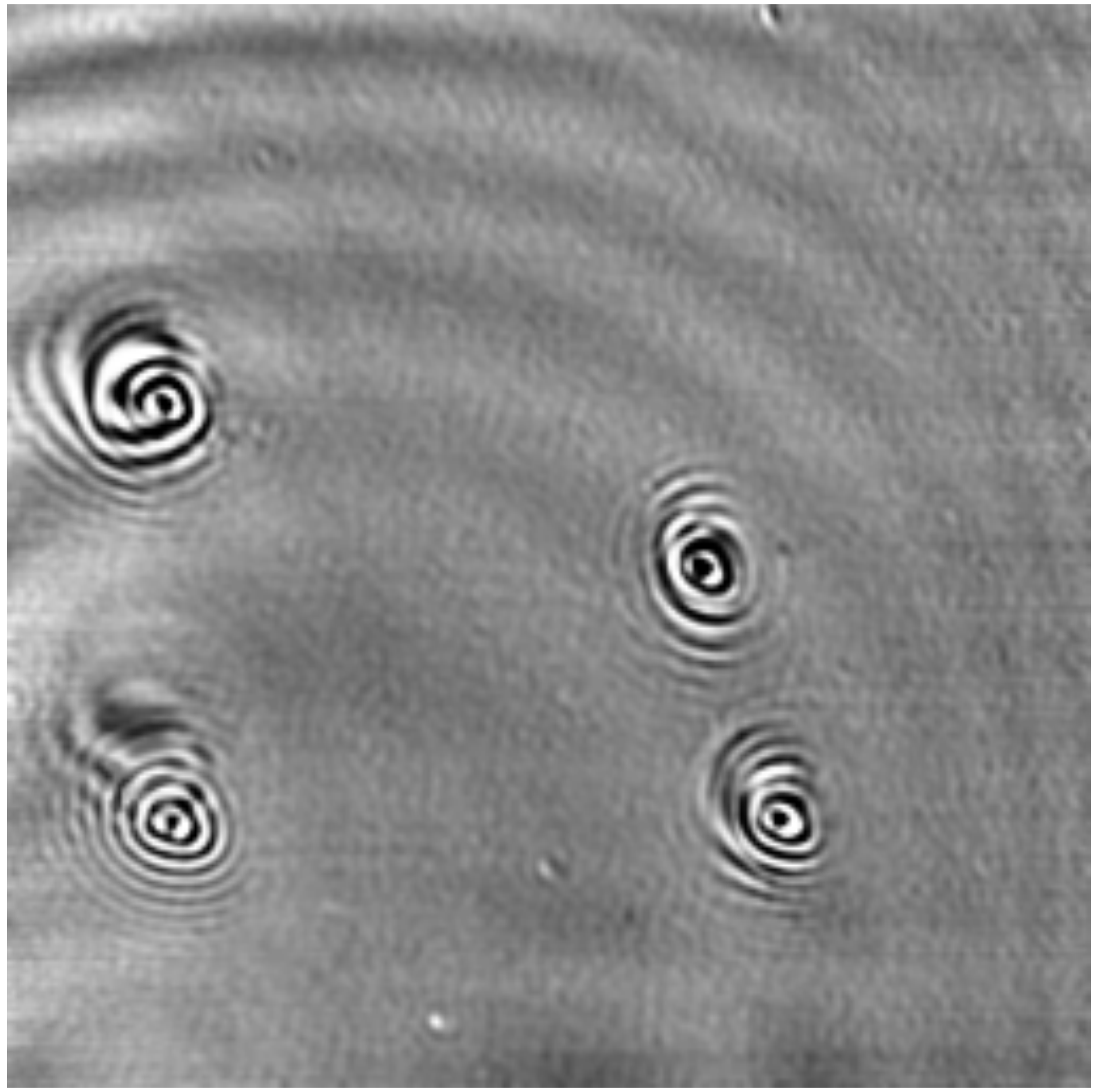


superresolution image of the actin cytoskeleton
X. Zhuang, Harvard

Protein beams:
bacterial flagellum and pili



Fuorescent flagella
Renaud, eLife 2017



Type IV pili
Lorenzo Tala, Nature Microbiology 2019

Solid mechanics: beam deformations

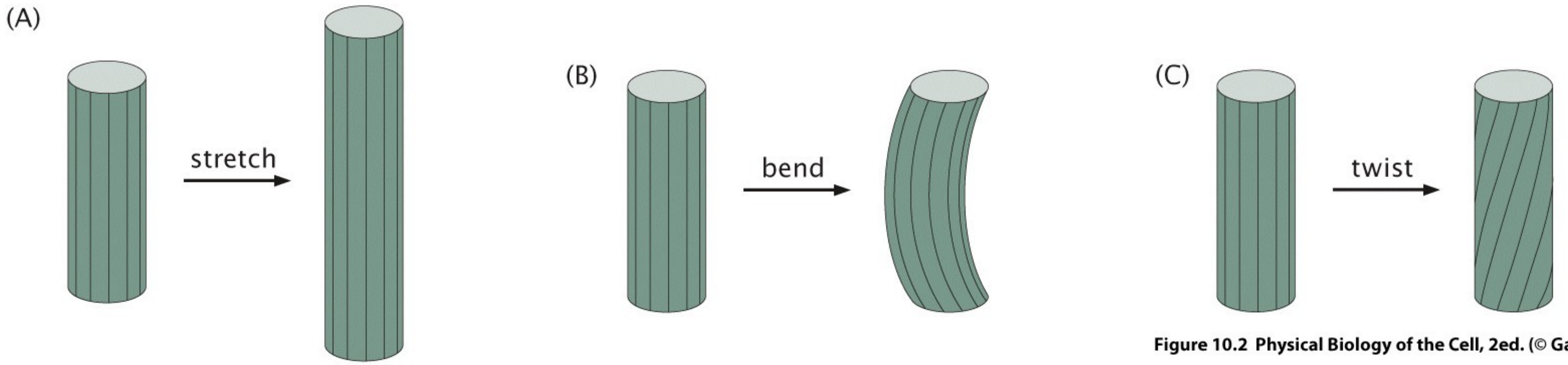
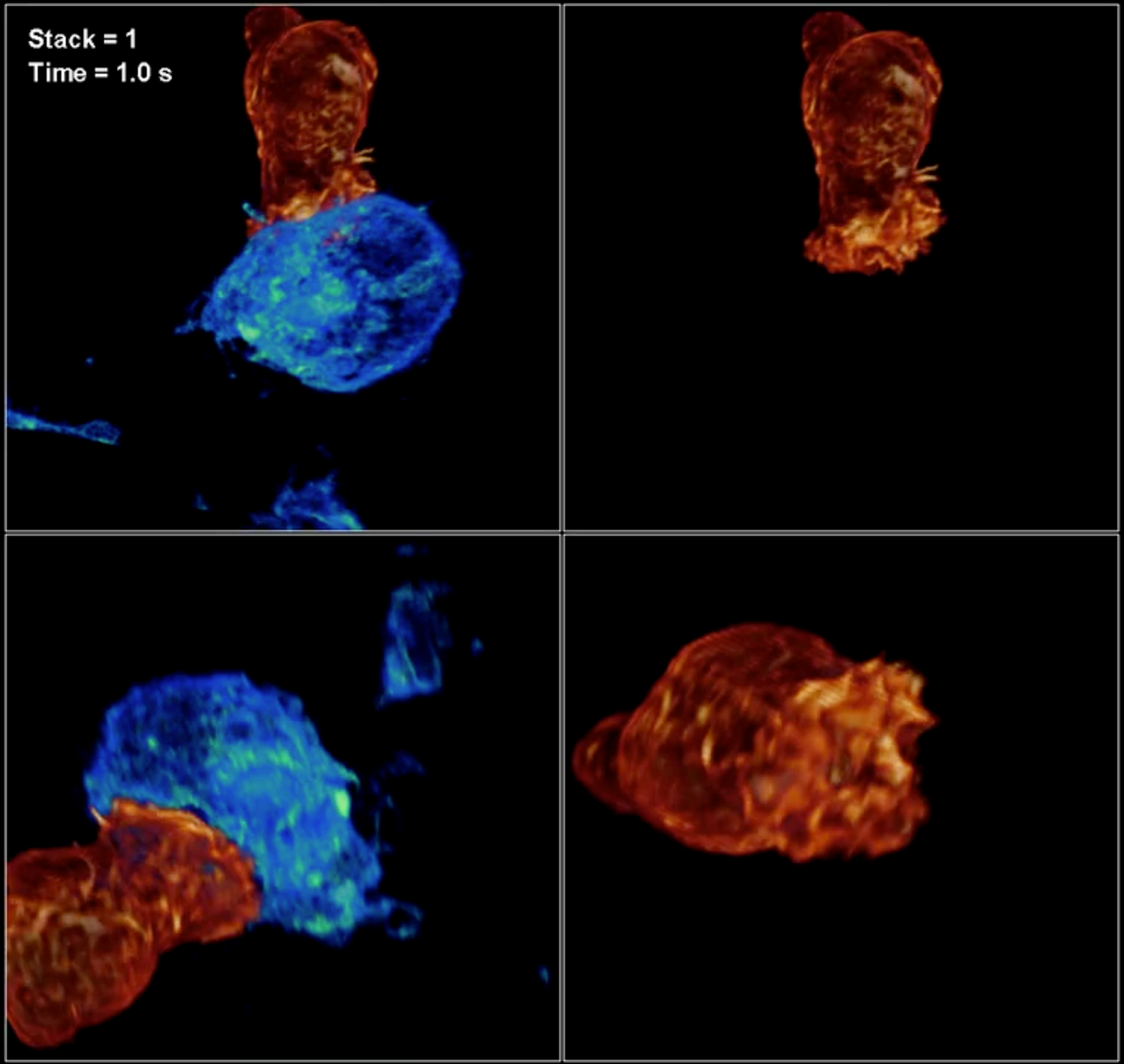


Figure 10.2 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

The elastic theory helps us link forces on a material to its deformations


Stack = 1
Time = 1.0 s

Physical requirements for membranes

- protection from extracellular environment
- plasticity to acquire specific morphologies and enable growth
- permeability to many molecules
- permeability to information

Membrane architecture

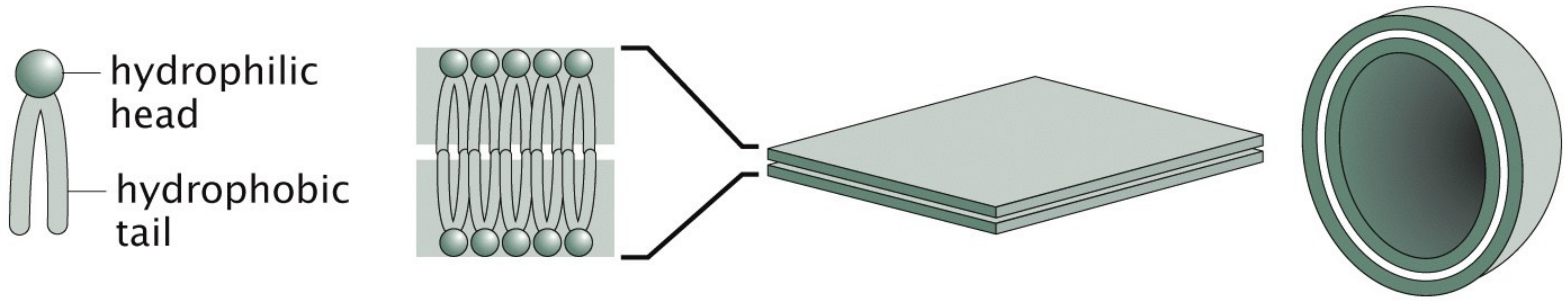


Figure 11.1a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Lipid bilayers behave like:
- a fluid in their 2D plane
- a solid in the normal direction

Describing a surface shape

1D (beams) | **2D (surfaces)** | **height function**

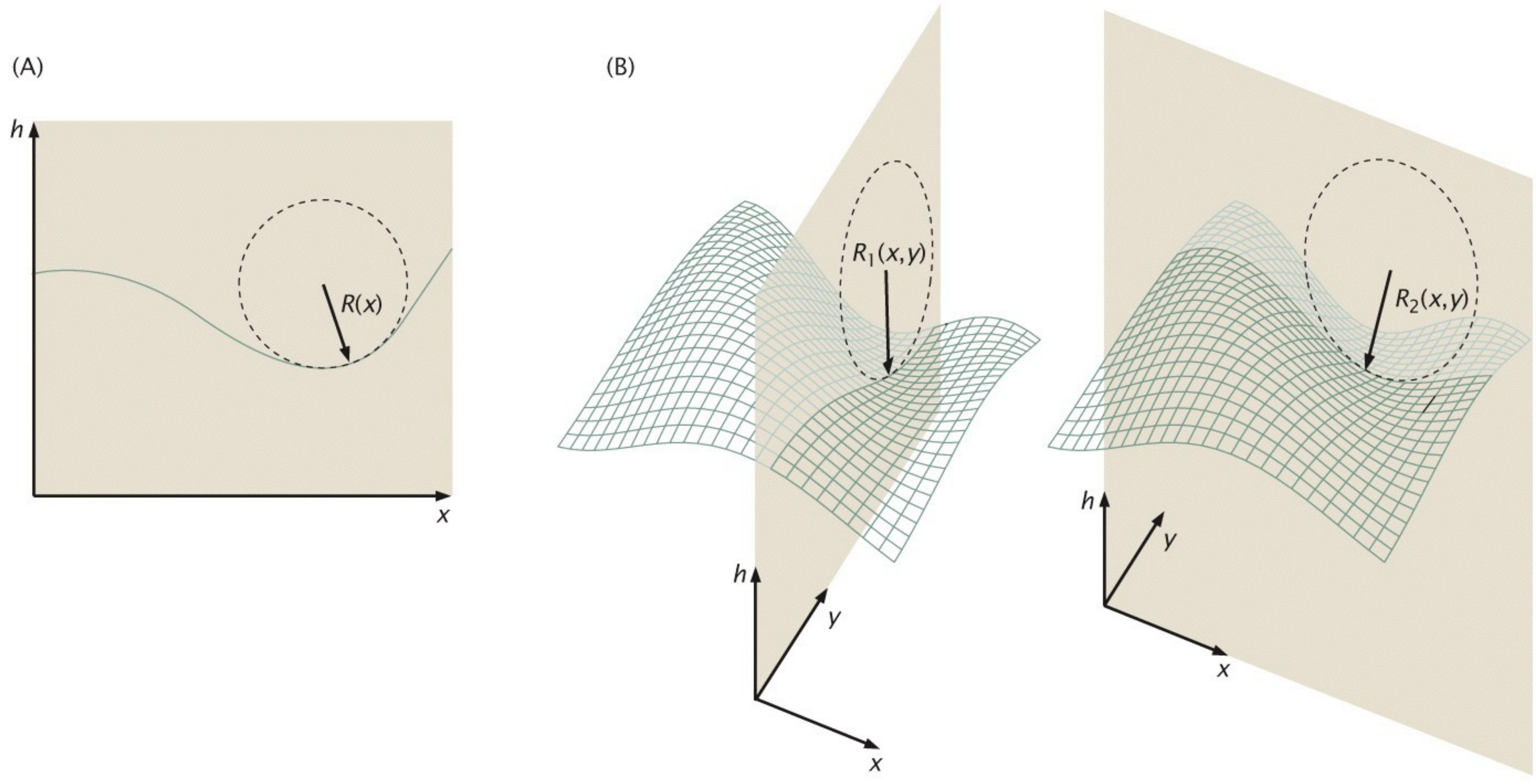


Figure 11.15 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

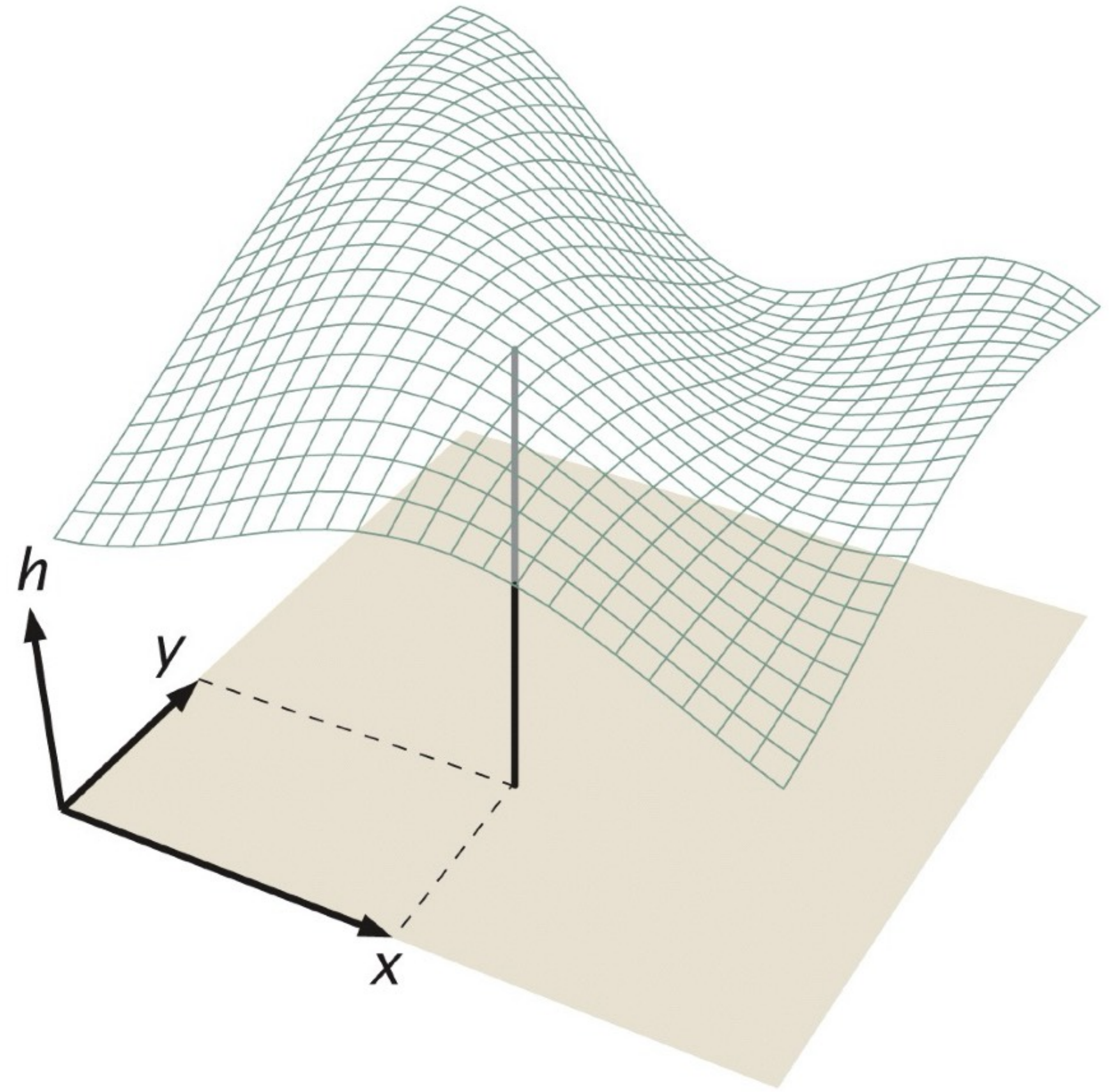


Figure 11.14 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Describing a surface deformation

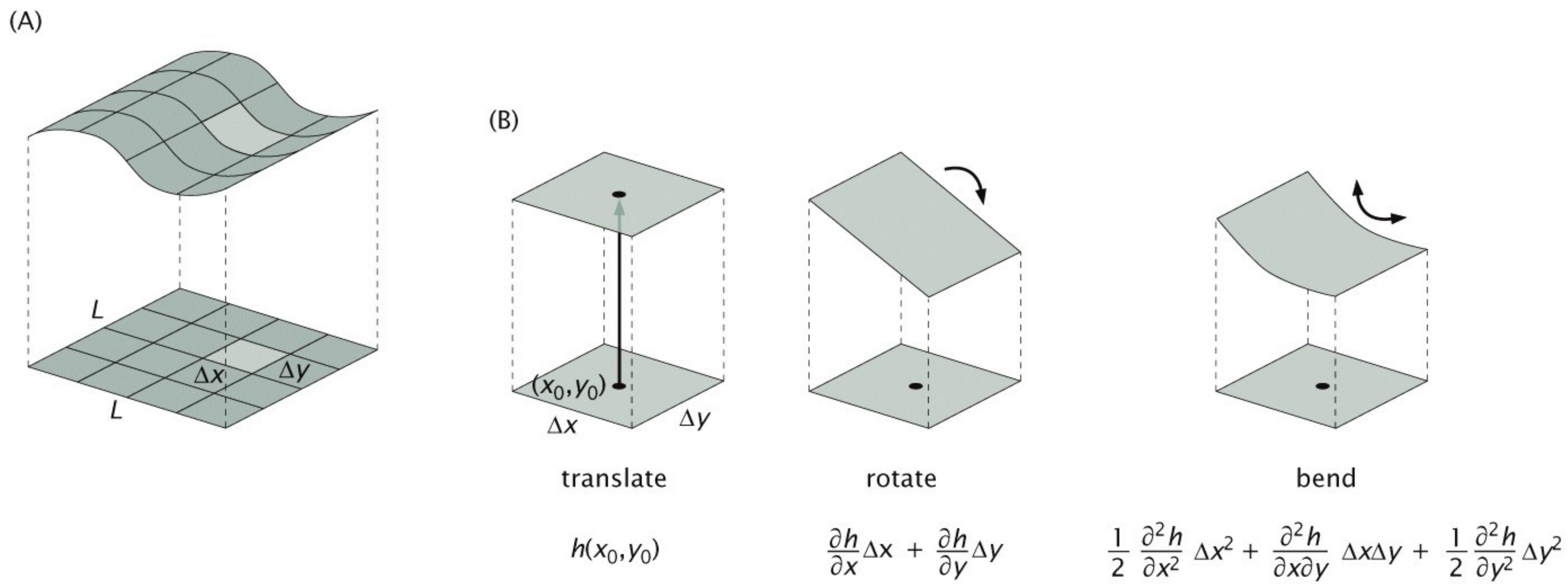


Figure 11.17 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

membrane stretching

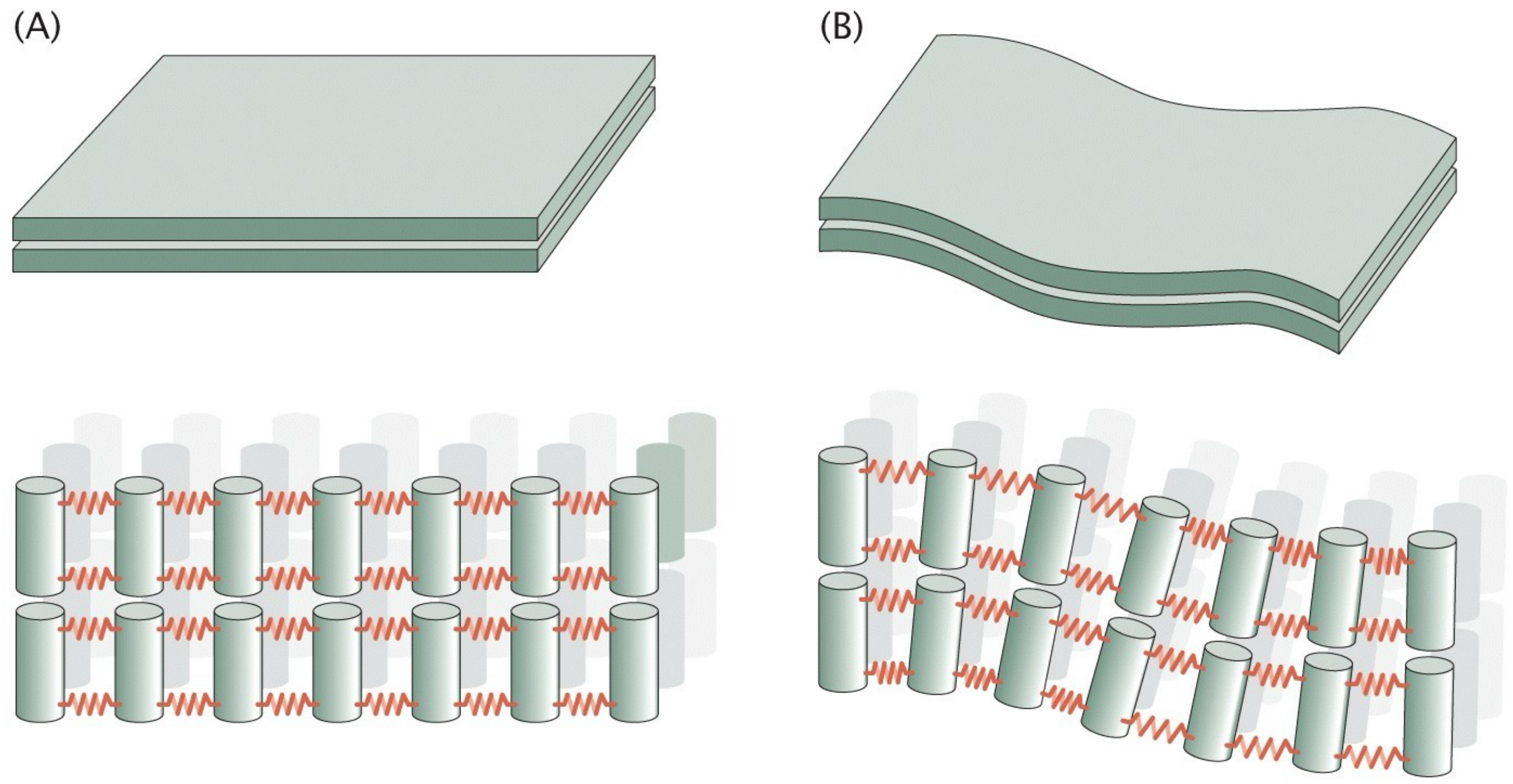


Figure 11.20 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

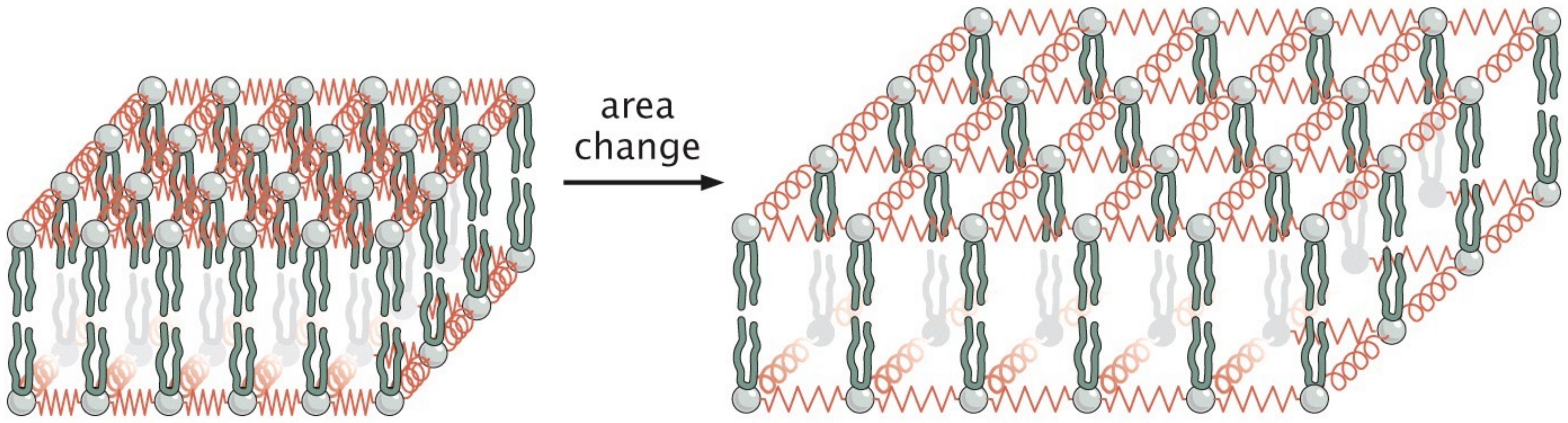


Figure 11.19 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

measuring membrane tension

the pipette aspiration experiment

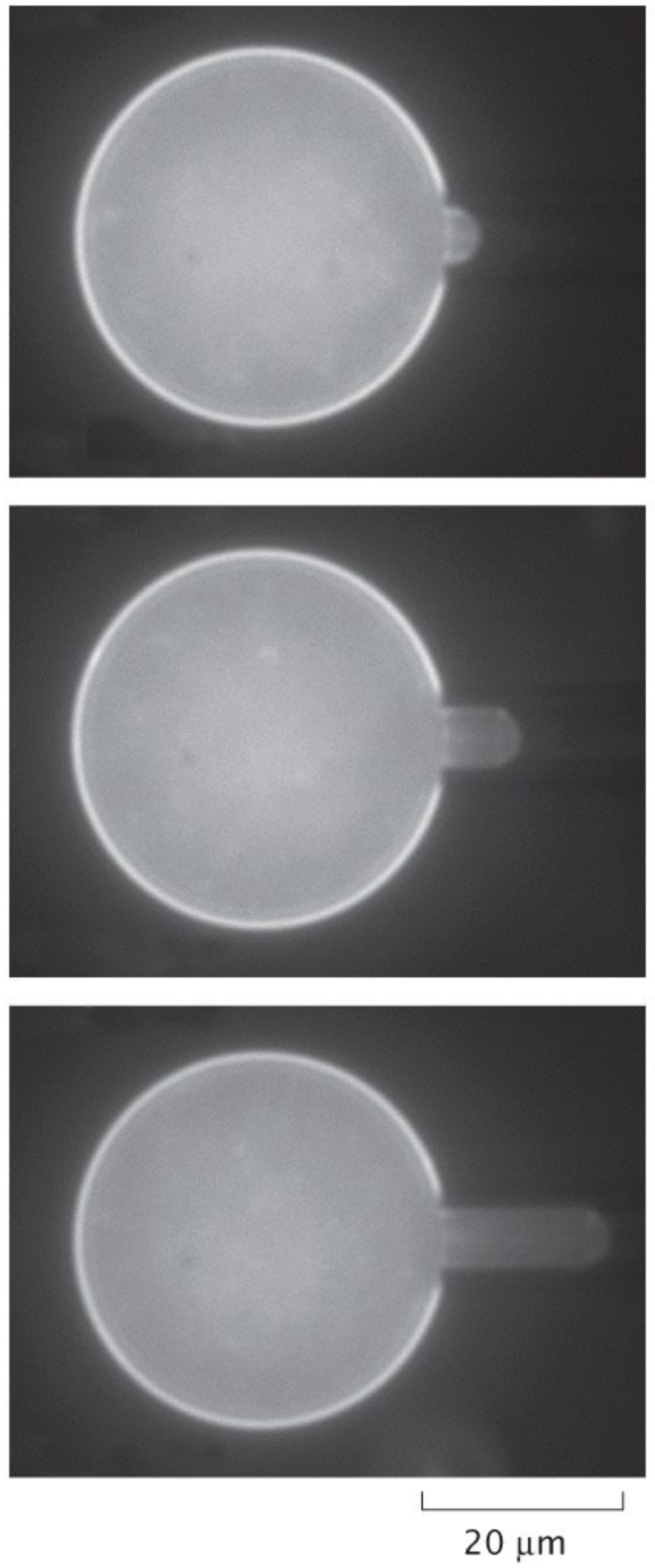
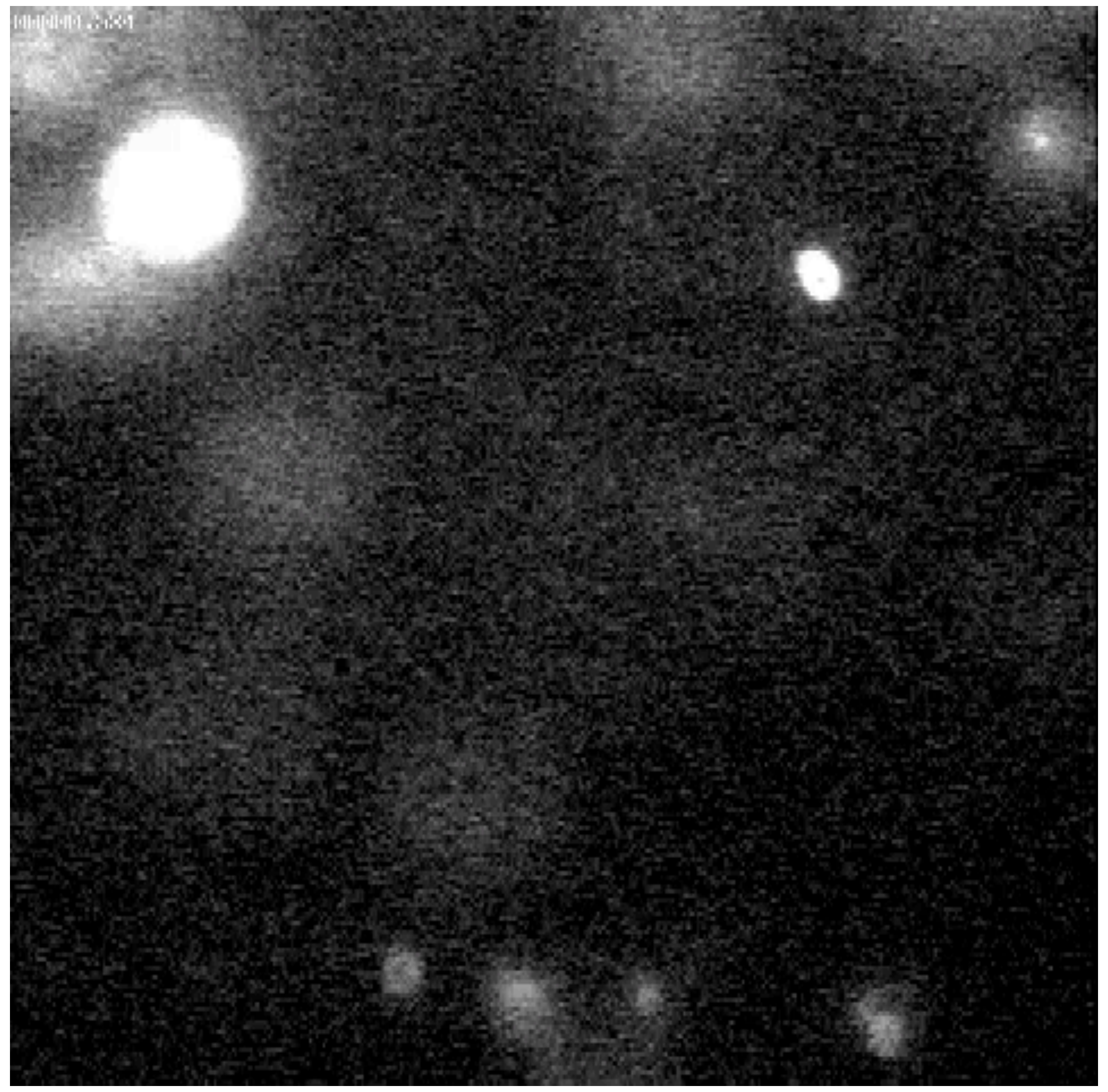


Figure 11.23 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

How to convert chemical energy into mechanical work



Two different scales but an identical goal

Type of molecular motors

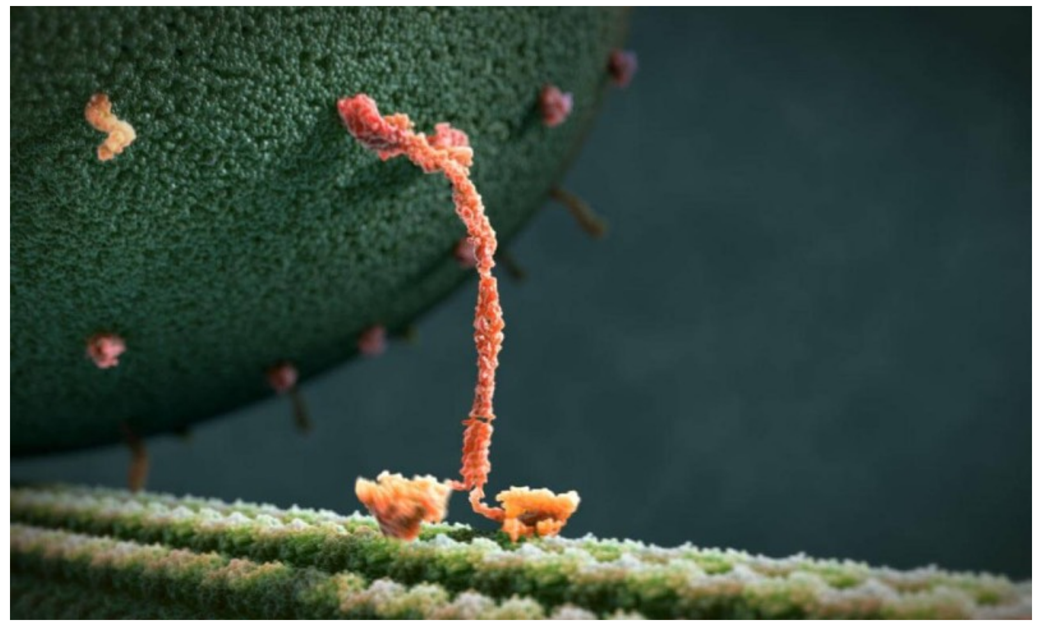
- **translational motors**
  steps on linear track: myosin, helicase

- **rotary motors**
  generate torque by rotation: flagellar motor

- **polymerization motors**
  polymerization generates force: actin

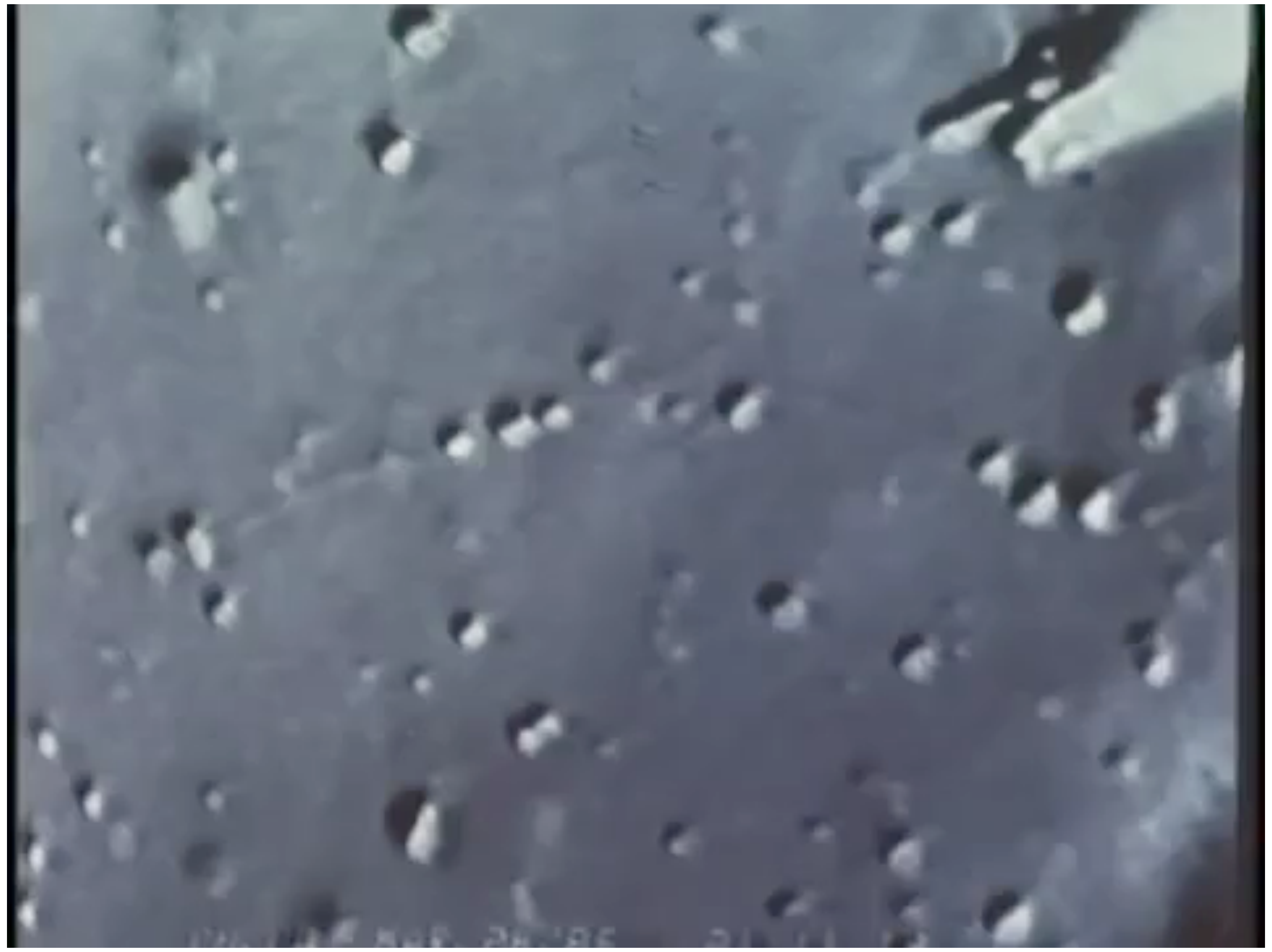
- **translocation motors**
  threading through a hole across membrane

Biological
vs man made motors



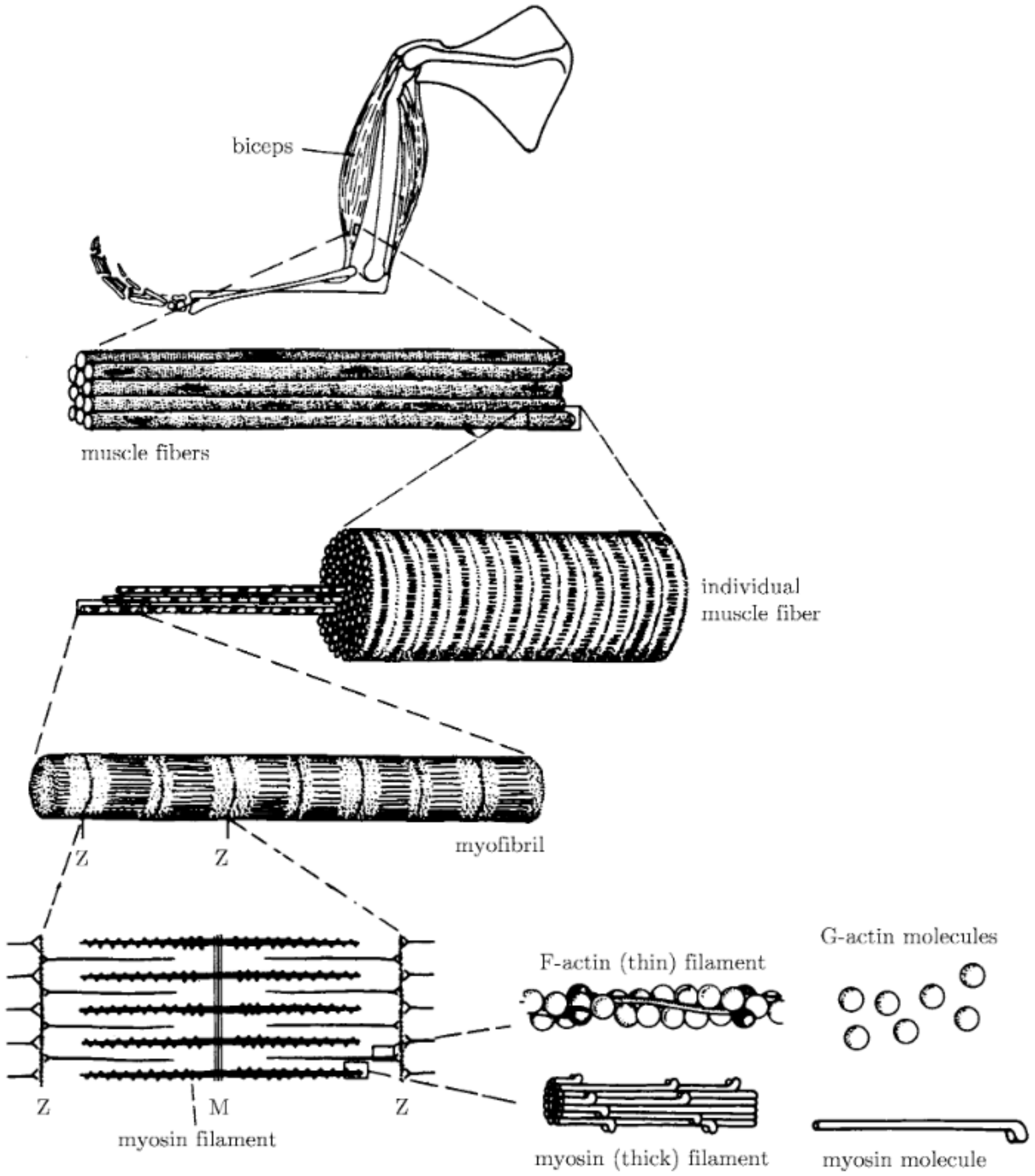
Size	10^{-8} m	1 m
Fuel	ATP	hydrocarbons
Speed	$4x10^{-3}$ m/h $4x10^{5}$ length/h	10^{5} m/h 10^{5} length/h
Efficiency	~60%	~10%

Translational motors move along tracks



beads attached to kinesin move long microtubules (Vale lab)

from muscle movement to molecular motors



Sliding motion of sarcomere is driven by myosin

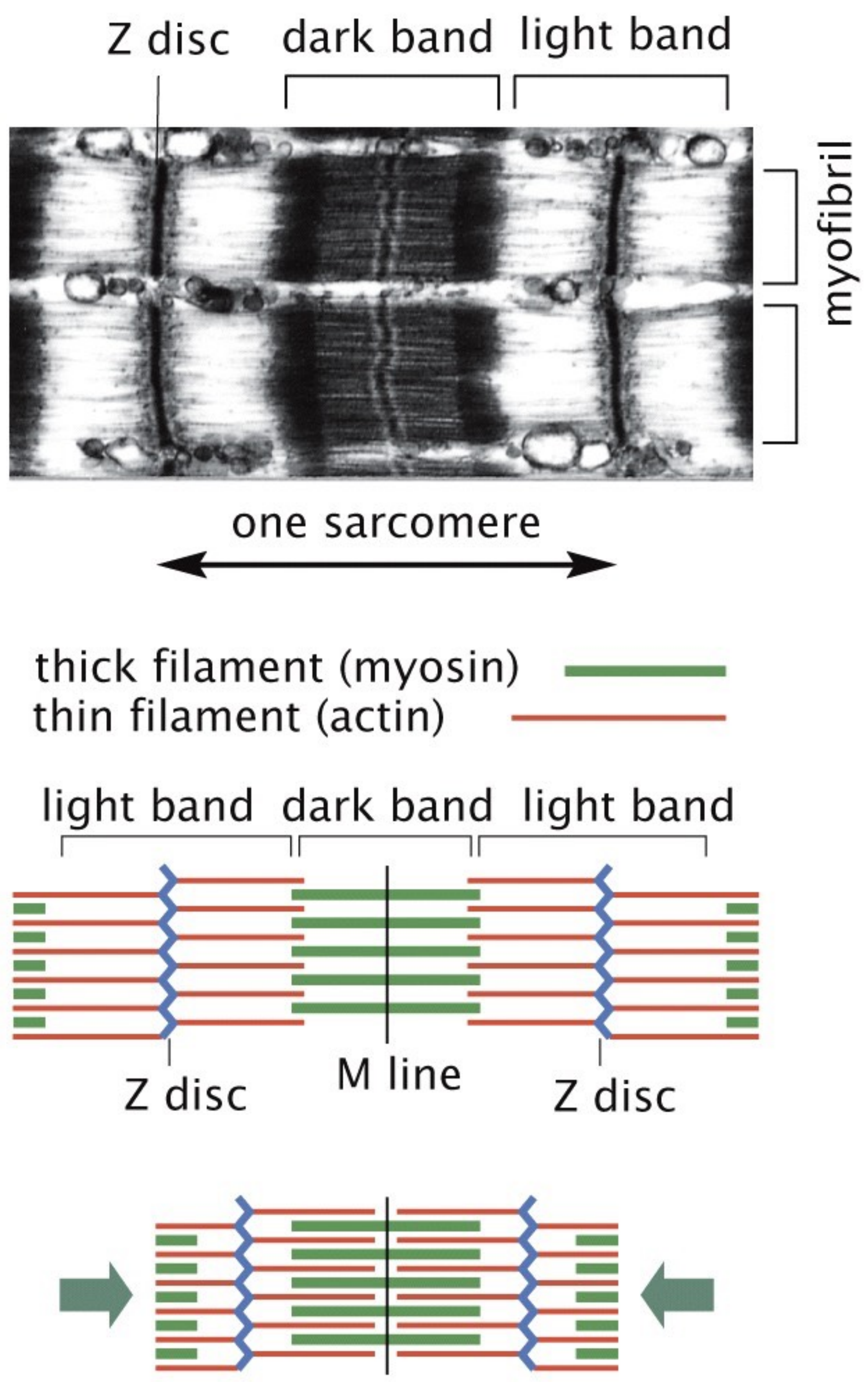
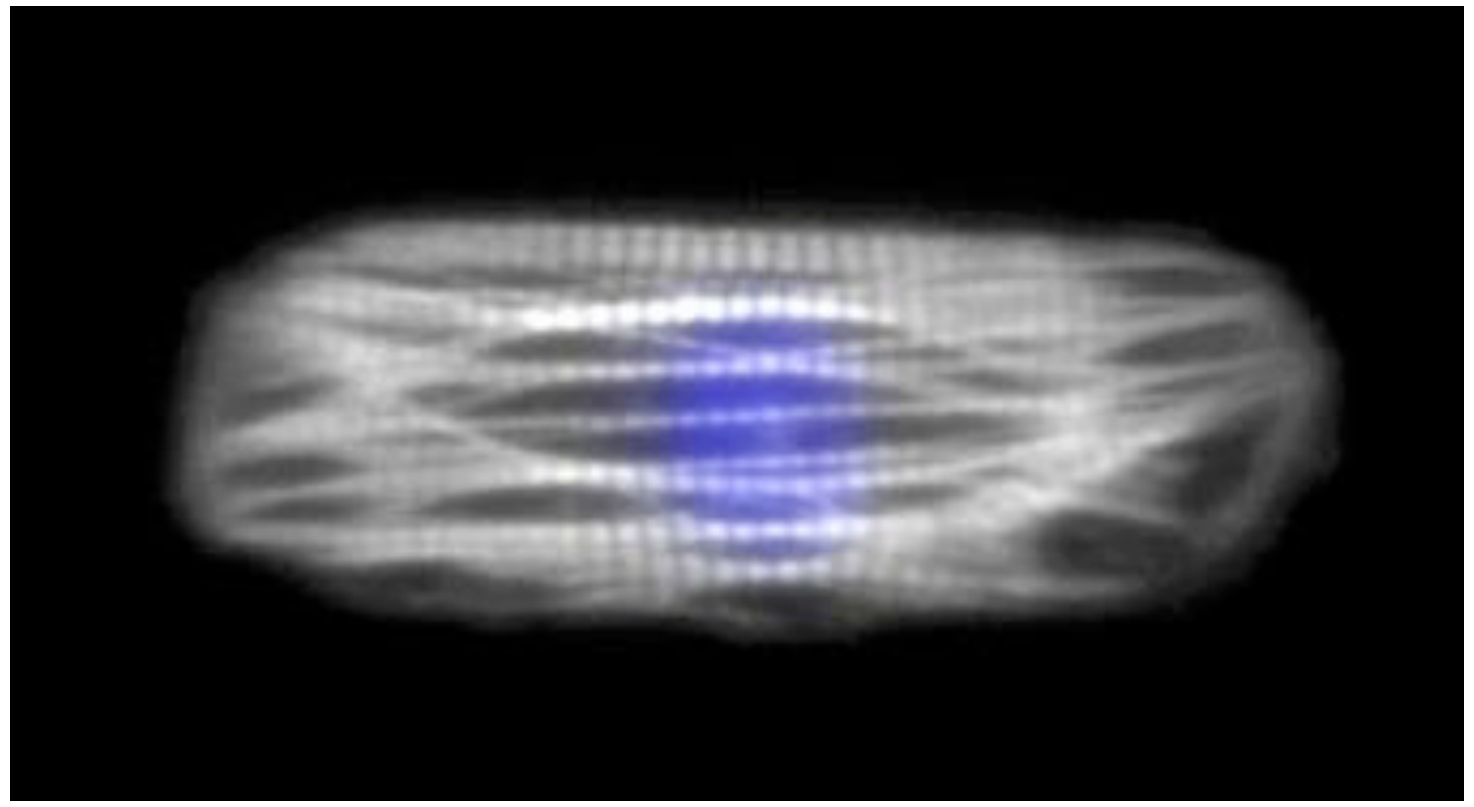
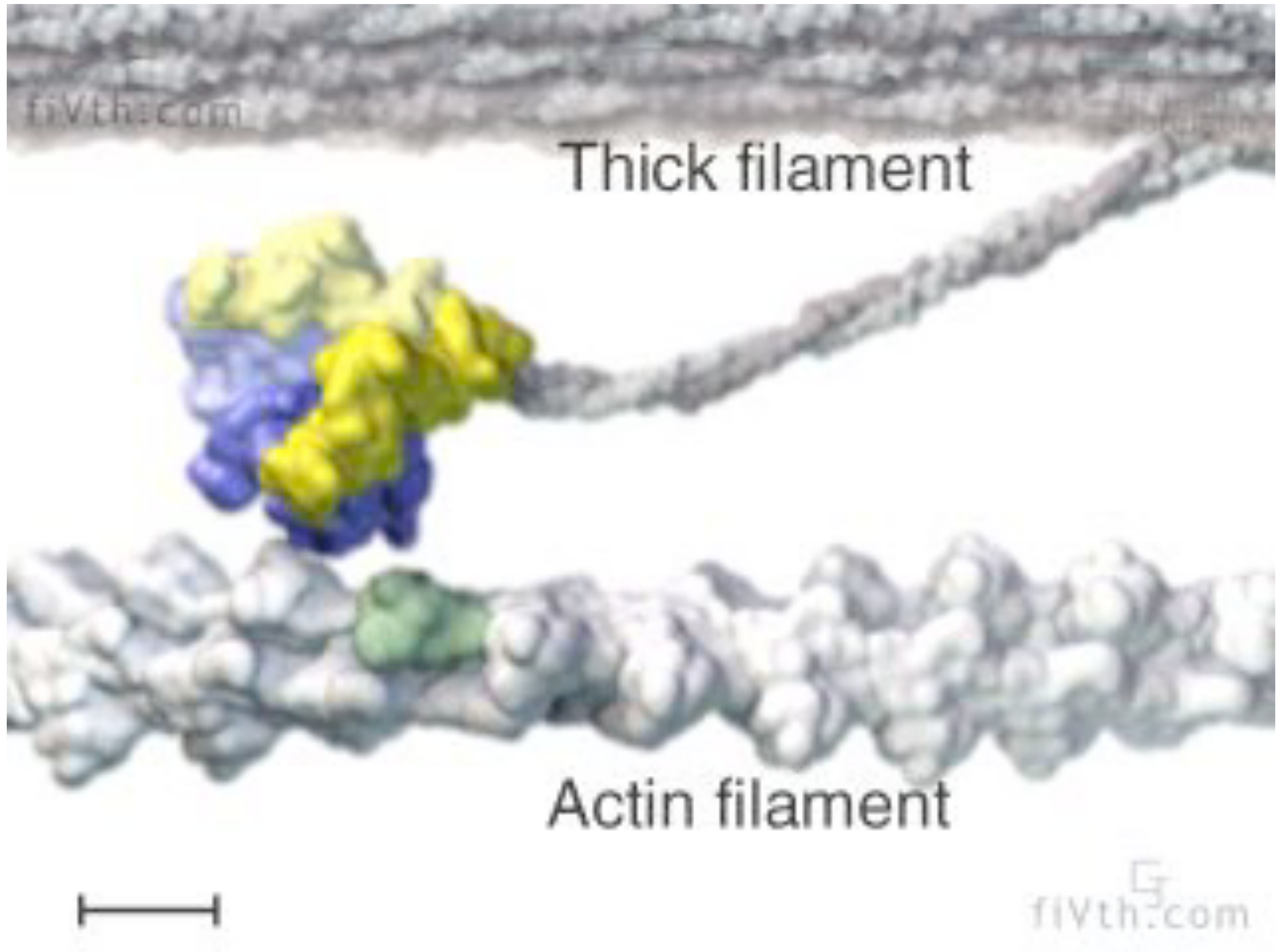


Figure 16.7a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

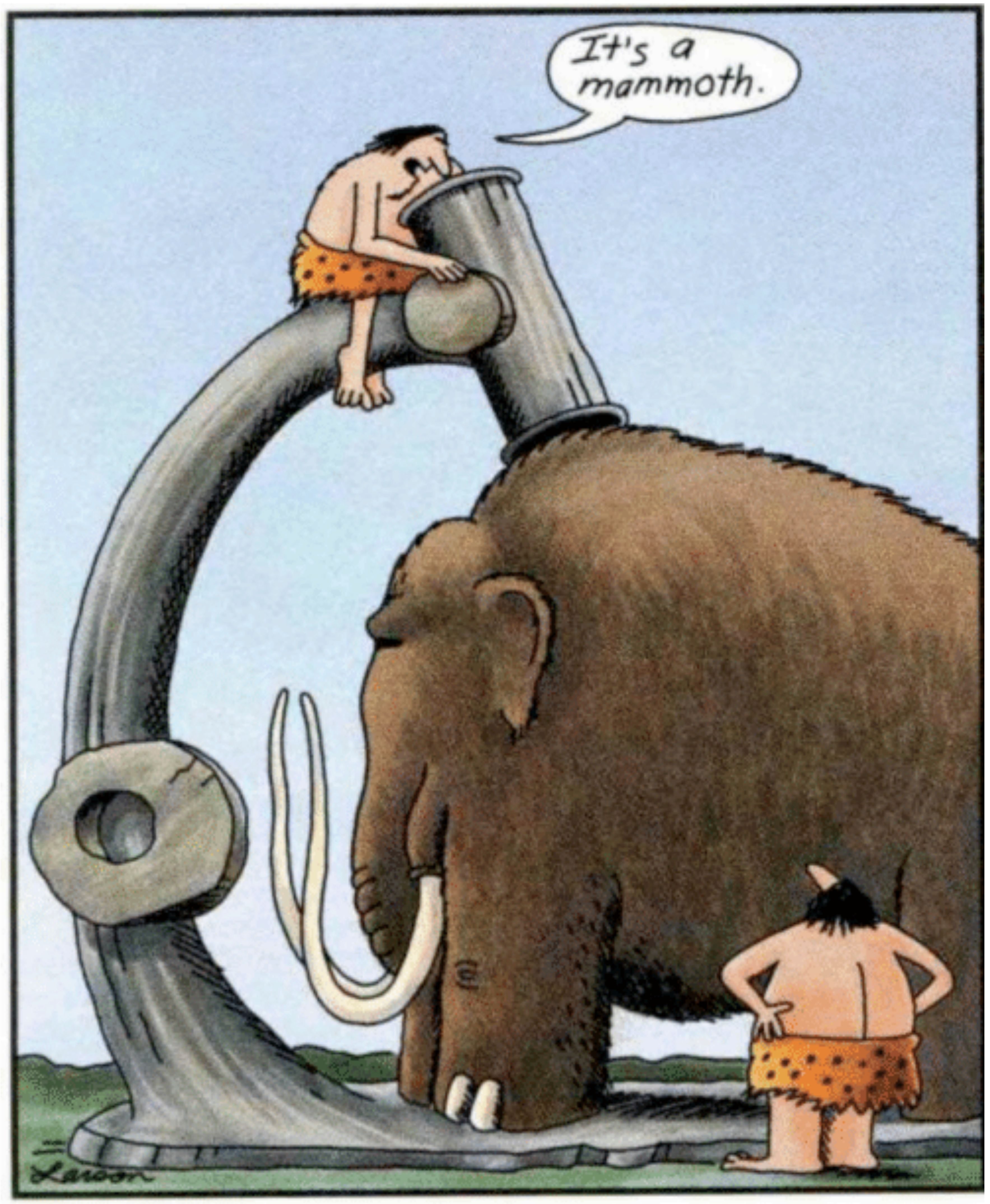


Cardiomyocite contraction
(white = actin)
Ribeiro and Pruitt, PNAS 2015



Thick filament
Actin filament
fIVth.com

Methods in biology



Early microscope

Analyzing biomolecules, cells and tissues

- identification of biomolecules: sequencing, mass spectrometry.
- resolve the structure of biomolecules: crystallography, cryoEM, computation
- identification of organisms: DNA sequencing
- measurement of physiological state: RNA sequencing

Current challenge:
linking structure to function

In other words: we can identify the biological parts, but we struggle to understand their function and how they work together.

Probing living systems mechanically

Apply force, measure response

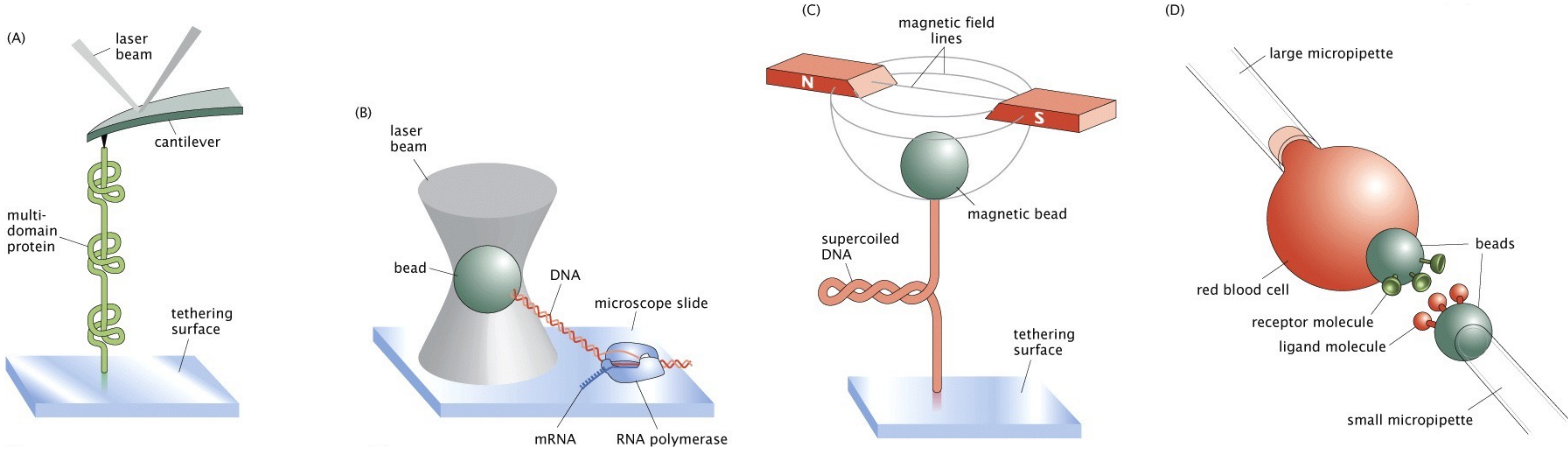


Figure 8.21 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

These methods allow us to probe mechanical functions of living systems