Physical Biology of the Living Cell

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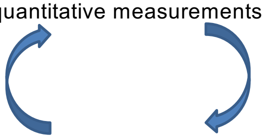
Topics – Semester I (http://biofiz.semmelweis.hu/)

Qualitative and quantitative modelling in biology (Dr. Szabolcs Osváth)	Feb. 11.
Structural hierarchy of proteins (Dr. László Smeller)	Feb. 18.
Stability of biological structures (Dr. László Smeller)	Feb. 25.
Formation of biological structures (Dr. Szabolcs Osváth)	Mar. 3.
Experimental methods to study biological structures - I (Dr. László Smeller)	Mar.10.
Experimental methods to study biological structures - II (Dr. Miklós Kellermayer)	Mar.17.
Microscopy studies of intracellular structures (Dr. Miklós Kellermayer)	Mar.24.
Super-resolution microscopy (Dr. Szabolcs Osváth)	Mar. 31.
Dynamic intracellular protein structures (Dr. Miklós Kellermayer)	Apr. 21.
Single molecule biological activity (Dr. Miklós Kellermayer)	Apr. 28.
Visit to the research laboratories of the Dept. of Biophysics and Radiation biology of the Semmelweis University (Dr. Szabolcs Osváth)	May 5.
Problem solving and consultation (Dr. Szabolcs Osváth)	May 12.

Science

science is humanity's endeavor to know and understand the world



the seven hundred-year-old linden from Szőkedencs

Mathematics

„ ... "Mathematics is the language with which God has written the universe."

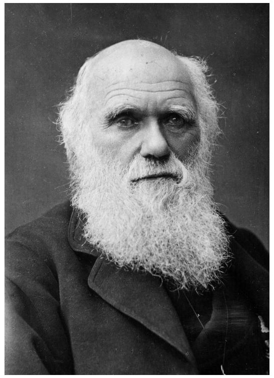
Advantages of applying math:

- accurate predictions (comparison with more sophisticated measurements)
- strict derivations
- abstract thinking

Galileo Galilei (1564 – 1642)

The role of mathematics

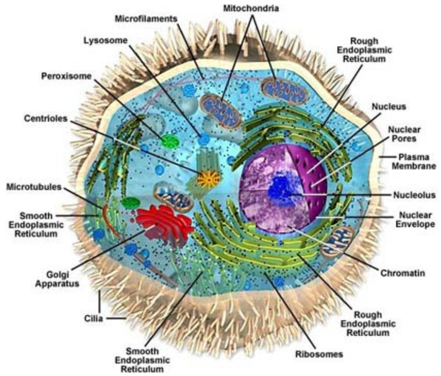
„… in after years I have deeply regretted that I did not proceed far enough at least to understand something of the great leading principles of mathematics, for men thus endowed seem to have an extra sense."



Charles Darwin (1809 –1882)

The role of mathematics

cell biology achieved great success without the use of mathematics



The role of mathematics

accumulated large amounts of observations of stars and planets

Tycho Brahe (1546 – 1601)

The role of mathematics

He recognized the laws of planetary motion - he created a mathematical model.

Johannes Kepler (1571 – 1630)

Premises of model building

Is the problem interesting or important?

Certainty level of “facts”
- Facts observable by anyone
  (e.g., the cell contains proteins)
- Facts accepted after extensive experimental testing
  (e.g., proteins are synthesized on the ribosome)
- Speculative statements
  (e.g., mitochondria are descendants of bacteria)

A fundamental idea: Biological entities must not violate the laws of physics and chemistry.

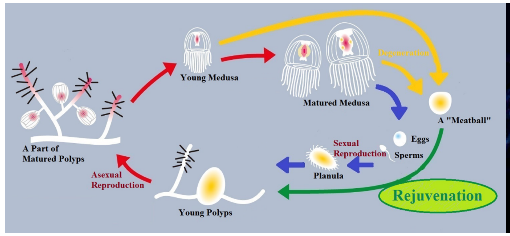
Why is life alive?

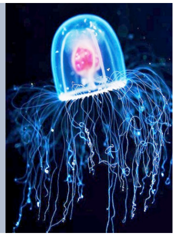
Central properties
- growth, energy utilization, reproduction, death

The living cell is built of surprisingly few elements

The cell contains structurally and functionally specialized macromolecules
- proteins, nucleic acids, carbohydrates, lipids
- macromolecules - combinatorial assembly of units

Turritopsis dohrnii





The oldest living creatures

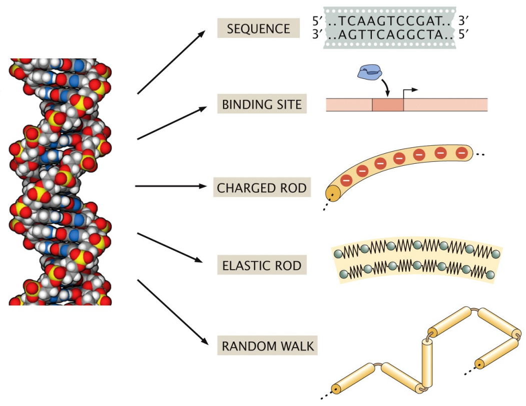
“Methuselah”, 4,851-year-old
Bristlecone Pine
(Pinus longaeva)

Pando 80,000-year-old
Populus tremuloides
(quaking aspen) forest

Biological model building

- Abstraction
- Simplification
- We cannot attain a complete atomic description of the macromolecules
- Projections are made, which reflect a certain property of the macromolecule
- Idealization

Idealization of the DNA molecule



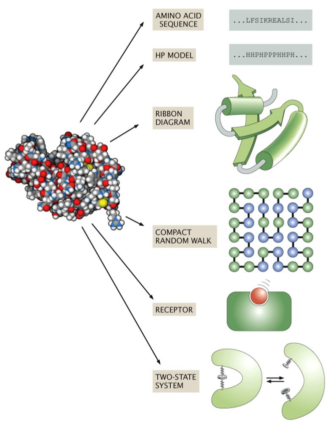
4 different bases

Ligand affinity varies along DNA

Axial and bending elasticity (rigidity)

Entropic elasticity, shape fluctuations

Idealization of a protein molecule



20 different AA

H=hydrophobic
P=polar

-α-helix
-β-chain
-random chain segment
-etc.

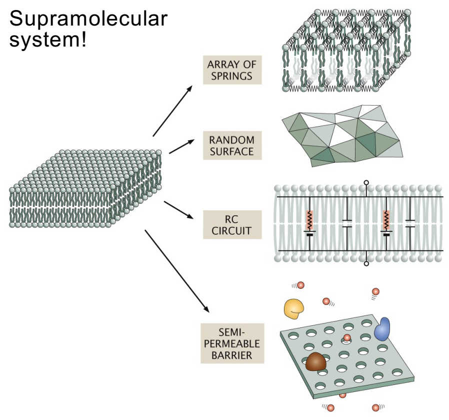
amino acids in the different lattice coordinates

Binding site - ligand

aktive-inactive
bound-dissociated
unfolded-folded
etc.

Idealization of lipids and membranes

Supramolecular system!



Elasticity

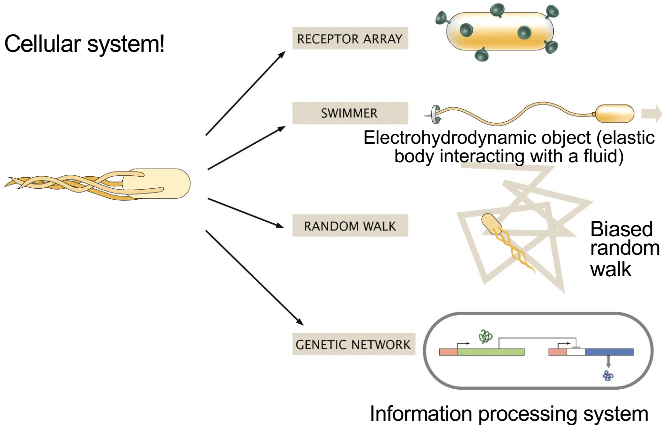
Fluidity

Electrical properties

Diffusion, osmosis, barrier functions

Idealization of an Escherichia coli cell

Cellular system!

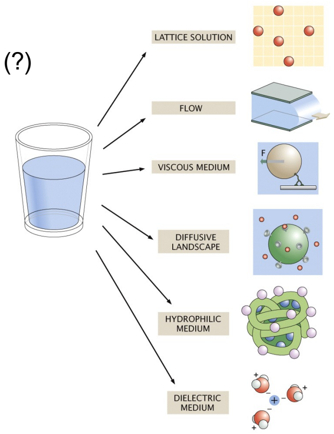


Idealization of a solution

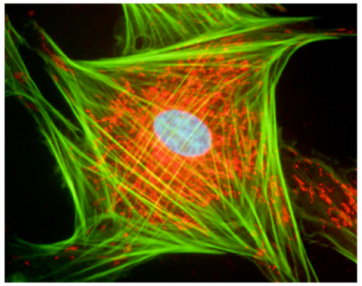
Living cells as an ideal solutions (?)

Homogenous

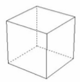
Isotropic



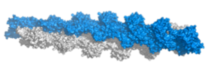
Length scale of the living cell



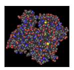
Simplified cell model: cube



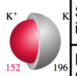
	Cell: cube with 20 μm edge	**Lecture hall:** cube with 20 m edge
Size of actin molecule	5 nm	5 mm
Number of actin molecules	~500 thousand	~500 thousand
Average distance between actins	~250 nm	~25 cm
Size of potassium ion	0.15 nm	0.15 mm
Number of potassium ions	~10^9	~10^9
Average distance between K^+ ions	~20 nm	~2 cm



Actin filament

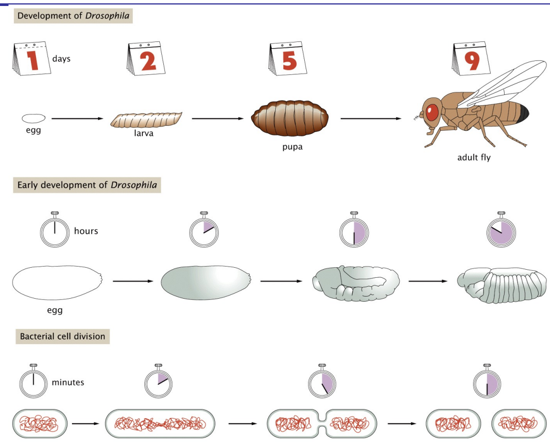


G-actin

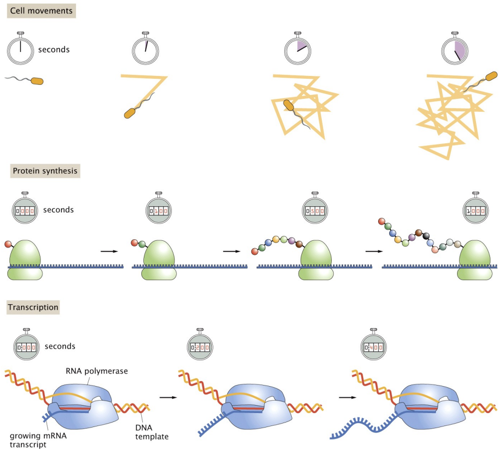


K^+ ion

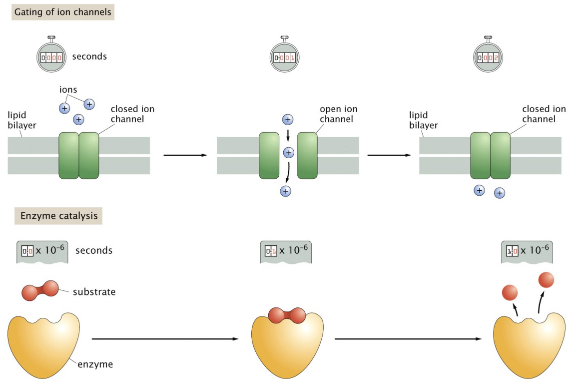
Time scales in biology I



Time scales in biology II

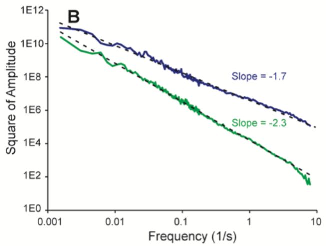


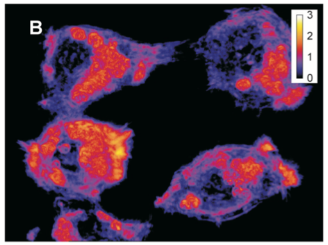
Time scales in biology III



Furthermore, light absorption 10^{-15} s!

Time scales of intracellular movements





Intracellular movements occur on all time scales

Some rules of thumb in quantitative biology

1 dalton (Da) = 1g/mol ≈ 1.6×10^{-24} g

1 nM ≈ 1 molecule/bacterium ≈10^{3}-10^{4} molecule/eukaryotic cell

1 M ≈ 1/nm^3

Cellular protein concentration ≈ 2-4 million/μm^3

1 mg of 1 kb DNA fragment ≈ 1 pmol ≈ 10^{12} molecules

Mean distance between molecules at 1 M concentration ≈ 1 nm

Molecular mass of a typical amino acid ≈ 100 Da

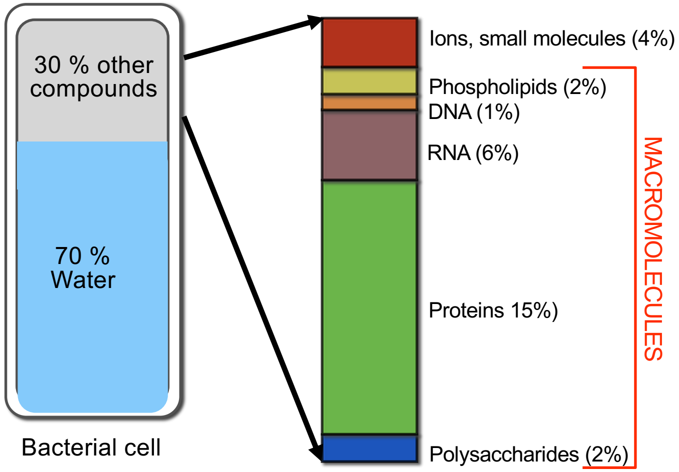
Water concentration/density ≈ 55 M ≈ 1000 kg/m^3

Volume of a water molecule ≈ 0.03 nm^3

Length of a base pair (along DNA) ≈ 0.3 nm

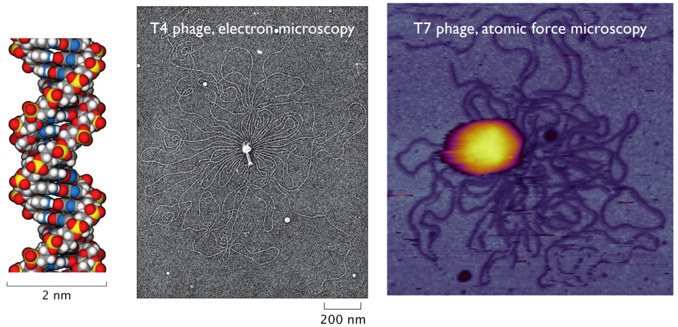
Volume of a base pair ≈ 1 nm^3

Proportion of macromolecules in the cell by mass is large



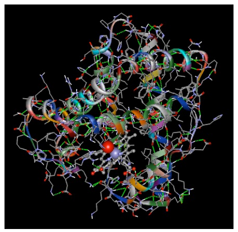
Bacterial cell

Biological macromolecules are giant molecules

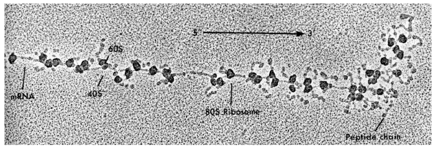


DNA released from bacteriophage head

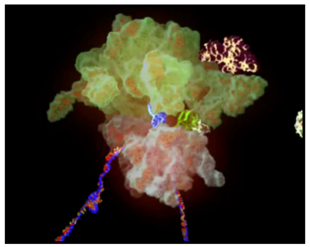
Biological macromolecules are exciting molecules



Structure of a hemoglobin subunit



Newly synthesized protein (silk fibroin)



Synthesis and folding of a nascent protein (on the ribosome)

Experiments can be done at single molecule level