Medical Biophysics

Introduction
Miklós Kellermayer

Medical biophysics

- Introduction: what is medical biophysics?
- Length scale of biology
- Atomic theory

Foundation of scientific truth

„the test of any idea is the **experiment**"

Scientific method:	Scientific attitude:
Observation	Wondering
Consideration	Critical thinking
Experiment	Asking and doubting

Medical biophysics

Biological processes are
Simplified,
Quantified

Objective: **Physical description of biomedical phenomena**

Physical description of biological phenomenon

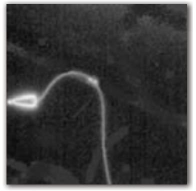
Question:

1. How much force (F) is necessary for a spermatocyte to travel with a given velocity (v)?
2. How does it happen (what is the exact mechanism)? Building a predictive model.

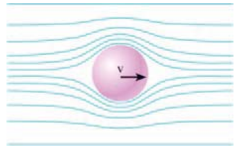
Drag coefficient of the spermatocyte

How much force (F) is necessary for a spermatocyte to travel with a given velocity (v)?

Simplified spermatocyte model: object with circular cross-section



Stokes' Law:



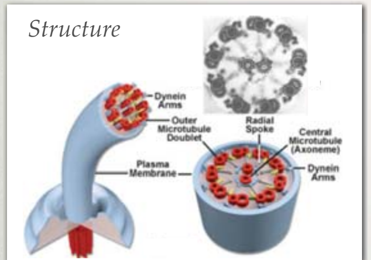
$$F = \gamma v = 6 r \pi \eta v$$

$$\gamma = 6 r \pi \eta = 6 \cdot 1.6 \times 10^{-6} (m) \cdot \pi \cdot 10^{-3} (Pas) = 3 \times 10^{-8} Ns/m$$

$$F = \gamma v = 3 \times 10^{-8} Ns/m \cdot 5 \times 10^{-5} m/s = 1.5 \times 10^{-12} N = 1.5\, pN$$

Mechanisms behind spermatocyte motility?

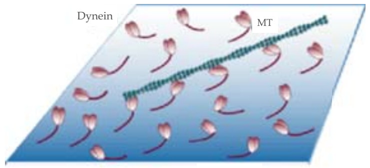
How does it happen (what is the exact mechanism)? Building a predictive model.



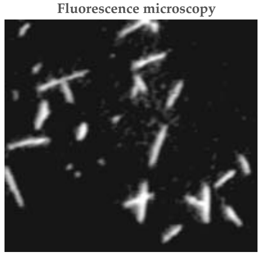
Step size: 8 nm (distance between every other tubulin subunit)

*Note: Figure shows kinesin, and not dynein!

Functional test: "In vitro motility assay"



Fluorescence microscopy



*Note: Figure shows kinesin-dependent motility!

Lecture topics

Semester I.

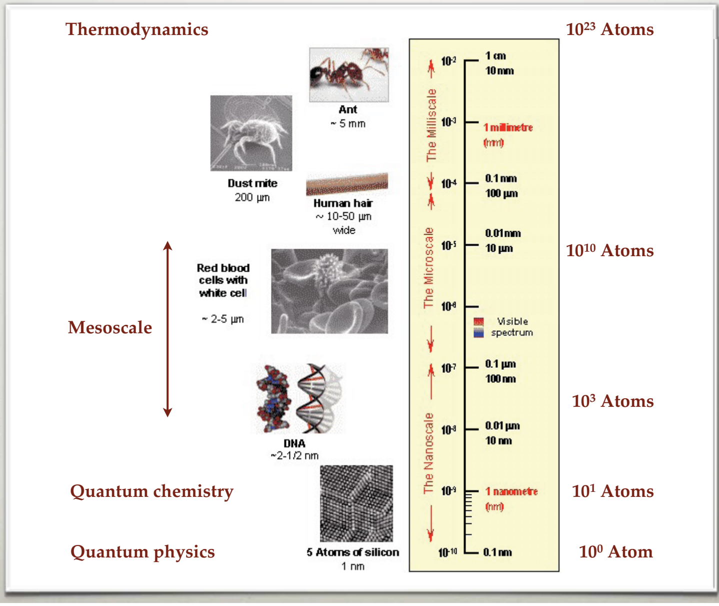
1. Length scale of biology. Atomic physics
2. Electromagnetic radiation. Dual nature of light. Matter waves
3. The atomic nucleus. Radioactivity. Nuclear radiation
4. Interaction of electromagnetic radiation with matter
5. Radioactivity in the medical practice. Dosimetry, nuclear medicine
6. Luminescence
7. Laser and its medical applications
8. X-ray
9. Multi-atom systems. The Boltzmann distribution
10. Molecular biophysics. Water, macromolecules, biopolymers
11. Nucleic acids and proteins. Folding of RNA and proteins
12. Atomic and molecular interactions. Scanning probe microscopies
13. Biomolecular structure. Diffraction, X-ray crystallography, light- and electron microscopy. Mass spectrometry, CD
14. Biomolecular structural dynamics. Fluorescence, ESR, NMR. Basics of MRI

Semester II.

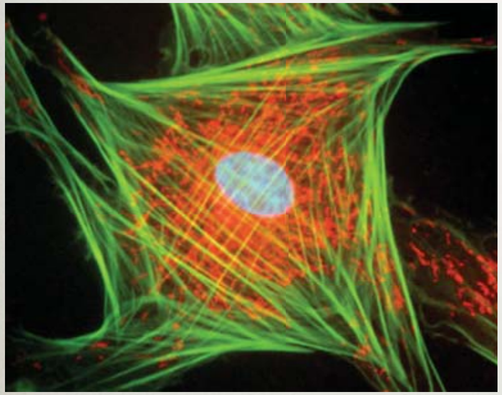
1. Gas laws. Pulmonary biophysics
2. Thermodynamics. Thermodynamic system, laws
3. Equilibrium and change. Kinetics. Entropy an its microscopic interpretation
4. Irreversible thermodynamics. Transport processes. Diffusion, Brownian motion
5. Cytoskeletal system. Motor proteins. Mechanisms of biological motion
6. Biomechanics. Biomolecular and tissue elasticity
7. Fluid dynamics. Circulatory biophysics
8. Muscle biophysics. Striated muscle, smooth muscle
9. Cardiac biophysics. Work of the heart. The cardiac cycle
10. Bioelectric phenomena. Resting potential
11. Action potential. Biophysics of electrically active tissues. EKG, EMG, EEG. Principles of sensory function
12. Sound, ultrasound. Auditory biophysics
13. Optics of the eye, biophysics of vision
14. Collective processes in ensembles. Complex systems, networks

Complexity

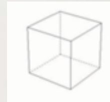
Dimensions of Living Systems



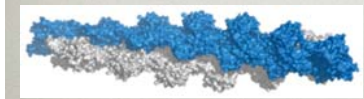
Length scale of the living cell



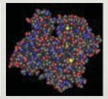
Simplified cell model: cube



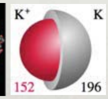
	Cell: cube with 20 μm edge	Analogue - **Lecture hall:** cube with 20 m edge
Size of actin molecule	5 nm	5 mm
Number of actin molecules	~500 thousand	~500 thousand
Average distance between actins	~250 nm	~25 cm
Size of potassium ion	0.15 nm	0.15 mm
Number of potassium ions	~10^{9}	~10^{9}
Average distance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



Actin filament (d=7 nm)



G-actin (d=5 nm, cc~100 μM)



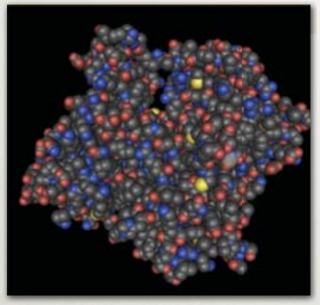
Potassium ion (d=0.15 nm, cc~150 mM)

Deficiencies of the model:

- concentrations vary locally
- dynamics: constant motion and collisions
- interactions, many types due to dynamics

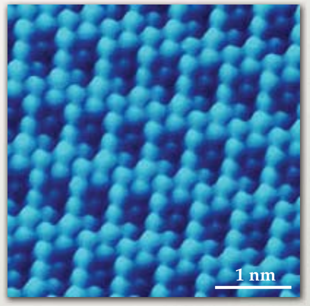
Can we explore the smallest parts of a biomolecular system?

Model



Structural model of globular actin
gray - C; red - O; blue - N; yellow - S

"Reality" (measurement)



Oxygen atoms on the surface of a rhodium single crystal
(scanning probe microscopic image)

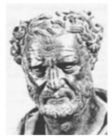
Richard P. Feynman (Nobel prize, 1965):

If, due to a disaster, the knowledge of humankind were destroyed, and only one sentence could be passed on to future generations, what would be the statement that best summarizes our knowledge?
Atomic theory: The entire natural world is made up of particles that constantly move and attract or repel each other. The characteristics and processes of nature can be described through the atomic particles.

Atomic theory

- Early atomic models
- Famous experiments
- Quantum mechanics
- Quantum numbers
- Biomedical significance

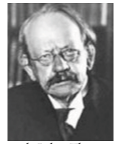
Early atomic models



Democritus (460-370 BC)
Matter composed undivisible particles (atomos).

John Dalton (1766-1844)
A given element composed of identical, undivisible atoms.

Dalton's atom

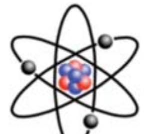


Joseph John Thomson
(1856-1940)
Discovery of the electron.

Cathode ray (electron beam) in vacuum tube.

"Plum pudding" atomic model

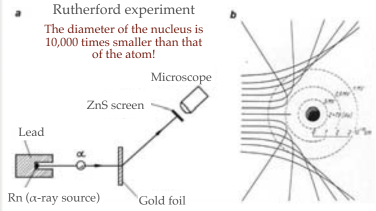
Ernest Rutherford
(1871-1937)



Rutherford's atomic model: miniature planetary system

Rutherford experiment

The diameter of the nucleus is 10,000 times smaller than that of the atom!



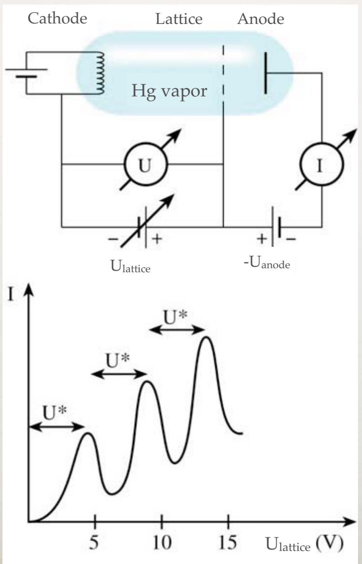
Problem:
-unstable atom
-electrons: centripetal acceleration - light emission
-energy loss - falling into the nucleus

Energy of the atom changes in discrete steps

Franck-Hertz experiment (1914)

James Franck
(1882-1964)

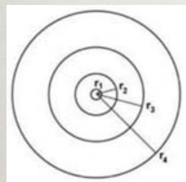
Gustav Ludwig Hertz
(1887-1875)



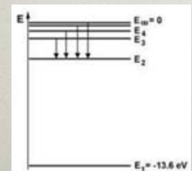
The electrons accelerated by the lattice voltage ($U_{lattice}$), upon inelastic collision with the Hg atoms, loose their energy in discrete packages ("quantum" - *sing.*, "quanta" - *pl.*).

Bohr model of the atom

Niels Bohr (1885-1962)



Bohr model of the hydrogen atom



Energy levels in the hydrogen atom.

Bohr's postulates*

1. Quantum condition:

- The electrons of an atom are on given orbits.
- On the given orbit the elctron does not emit, its energy is constant.
- The angular momentum (L) of the orbital electron is an integer multiple of h/2π:

$$L = mvr = n\frac{h}{2\pi}$$

n= principal quantum number. The radii of the orbits can be calculated.. The radius of the first orbit is $r_1 = 5,3\ 10^{-11}$ m ("Bohr-radius"). The radii of the further orbits are:

$$r_n = n^2 r_1$$

2. Frequency condition:

- The atom radiates (i.e., emits light) only if the elctron "jumps" from one orbit to the other.
- Energy of the radiation is the difference between the orbit energies:

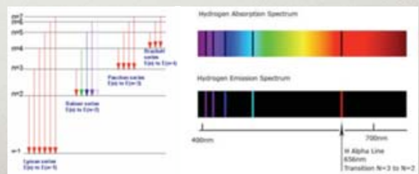
$$E_{foton} = h\nu = E_2 - E_1$$

The orbit energies can be calculated. Energy of the first orbit is E_1=-13.6 eV. Further orbit energies are:

$$E_n = \frac{E_1}{n^2}$$

Significance

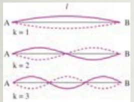
- The model explained the spectra of the hydrogen atom. But only that of the hydrogen atom.



*N.B.: postulate: fundamental requirement, condition

The electron as a wave

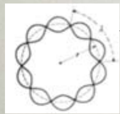
Quantized behavior in the stationary waves of a stretched string



The electron as a wave

Louis V. de Broglie (1892-1978)

$$\lambda = \frac{h}{p} = \frac{h}{m_e v}$$



Atomic electron as a standing wave

Quantum condition:

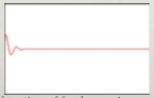
$$2\pi r = n\lambda = n\frac{h}{mv}$$

Propagation law of electron waves

Erwin Schrödinger (1887-1961)

Ψ (psi) wavefunction:

- $[\Psi(x,t)]$: gives the amplitude of the electron wave as a function of position (x) and time (t).
- Ψ^2: gives the probability of finding the electron.
- Ψ^2: integrated across the entire space = 1 (i.e., the electron can be found somewhere).
- Ψ: with the help of Schrödinger's equation, allows calculation of electron energies.
- For a free electron Ψ is a sine wave: momentum is precisely known ($p=h/\lambda$), but position (x) entirely unknown (uncertainty principle!)

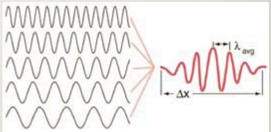


Wavefunction of freely moving particle (potential energy = 0)

Uncertainty principle

Werner Heisenberg (1901-1976)

To localize the wave, we need to superimpose waves of different wavelength (λ) (interference):



Upon spreading λ ($\Delta\lambda$), localization will be more certain (Δx decreases), but it also spreads the momentum values (Δp increases), thereby increasing the uncertainty of determining momentum:

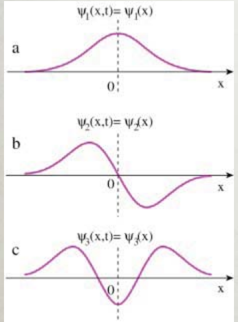
$$\Delta x \cdot \Delta p \geq \frac{h}{2\pi}$$

Quantum mechanical atomic model

Within the atom every electron has a given state, and the probability of finding it around the nucleus has a specific shape.

Quantum mechanics:

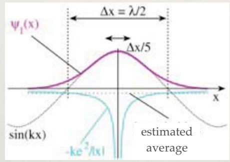
1. describes the states of the electron (one state → one wavefunction, Ψ)



2. calculates the electron's most probable location (orbital, r) and energy (E)

$$E = E_{kin} + E_{pot} = \frac{mv^2}{2} - \frac{e^2}{r}$$

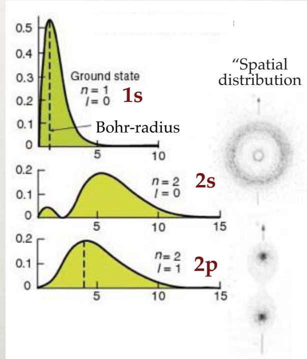
In the atom, Coulombic attraction determines the potential energy:



Simplified Schrödinger's equation:

$$\left(\frac{mv^2}{2} - \frac{e^2}{r}\right)\Psi = E\Psi$$

Probability of finding the electron in the atom:



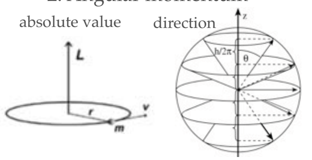
Quantum numbers

The quantum numbers refer to ***physical quantities*** that describe the state of the electron:

1. Energy

Energy of the electron in a given quantum state

2. Angular momentum



3. Spin

Intrinsic angular momentum and magnetic momentum

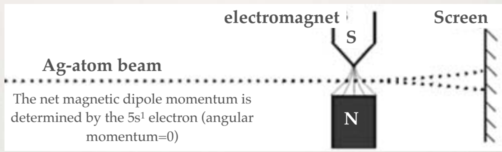
name	symbol	orbital meaning	range of values	value example
principal quantum number	n	shell	$1 \leq n$	$n = 1, 2, 3...$
azimuthal quantum number (angular momentum)	ℓ	subshell	$(0 \leq \ell \leq n-1)$	for $n = 3$: $\ell = 0, 1, 2\ (s, p, d)$
magnetic quantum number, (projection of angular momentum)	m_ℓ	energy shift	$-\ell \leq m_\ell \leq \ell$	for $\ell = 2$: $m_\ell = -2, -1, 0, 1, 2$
spin projection quantum number	m_s	spin	$-\frac{1}{2}, \frac{1}{2}$	for an electron, either: $-\frac{1}{2}, \frac{1}{2}$

The spin quantum number

Stern-Gerlach experiment (1922)

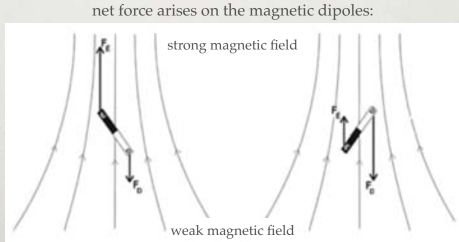
Otto Stern (1888-1969)

Walther Gerlach (1889-1979)



Silver beam splits in two

In an inhomogenous magnetic field, in addition to torque, net force arises on the magnetic dipoles:



The spin magnetic moment may take on two values (+1/2, -1/2)

Effect of external electric field on the bound electron

Weak external electric field ($-E_1xe$):

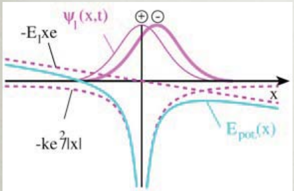
- Ψ is deformed
- Atom becomes polarized

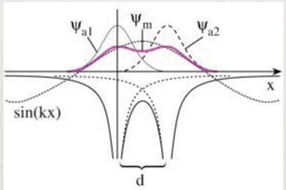
Upon the approach of another proton (nucleus):

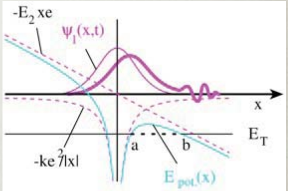
- Intermediate Ψ is formed
- The electron belongs to both atoms
- formation of covalent bond

Strong external electric field ($-E_2xe$):

- Ψ is deformed
- The electron may escape the atom without excitation
- Tunneling effect







Building the periodic table of elements

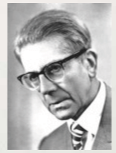
Characterization of bound atomic electronic states: with n, l, m_l, m_s quantum numbers

$n \rightarrow$ electron shell
$n, l \rightarrow$ electron subshell
$n, l, m_l \rightarrow$ electron orbital

Wolfgang Pauli
(1900-1958)

Pauli's exclusion principle:

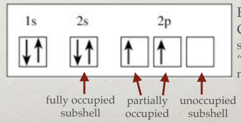
- Each quantum state can be occupied by a single electron.
- Within an atom there cannot be two electrons for which all four quantum numbers are identical.



Friedrich Hermann Hund
(1896-1997)

Hund principle:

- Order of filling up the quantum states.
- For a given electron configuration, the state with maximum total spin has the lowest energy.

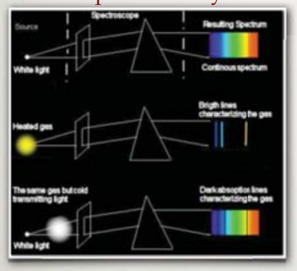


Electron configuration of the C atom
s: "sharp", p: "principal", d: "deformed" (spectroscopic nomenclature)

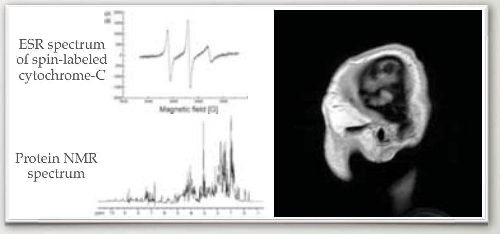
Biomedical significance

Chemistry, biochemistry!

Spectrometry

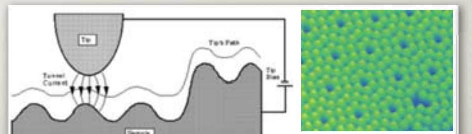


Electron Spin Resonance (ESR), Nuclear Magnetic Resonance (NMR), MRI



Laser

Scanning Tunneling Microscopy, STM



Si atoms