Introduction to molecular biophysics and general biology

Wednesdays, 11 a.m. - 1 p.m. (two lecture hours with a break), room B

The course starts on 6th March, 2019

This lecture course is thought as a concise introduction into the interdisciplinary field for newcomers as well as for those who study(ied) biophysics and need some clarification, ordering and extension of their knowledge.

The full course encompasses two semesters, *ca.* 30 hours of lectures (2 ECTS) each. Written exams in the form of open descriptive questions are planned at the end of each semester.

The lecturers come from the Laboratory of Biological Physics (their initials are given in the last column of the table below):

prof. dr hab. Marek Cieplak (MC)
dr hab. Anna Niedźwiecka, prof. IF PAN (AN) Coordinator, e-mail: annan@ifpan.edu.pl
dr hab. Bartosz Różycki (BR)
dr Remigiusz Worch (RW)

No.	Date	Summary	Who
		I semester	
		Fundamentals	
1	6.03.19	Physical bases of biological interactions: - atoms, molecules, biomolecules - types of interactions - temperature rages, energy scales, fundamental processes in the word of biomolecules - the role of water in biophysical processes	RW
2	13.03.19	Biomolecules, part 1: peptides and proteins, nucleic acids; structures and functions	RW
3	20.03.19	Biomolecules, part 2: - carbohydrates and lipids - biological membranes and other self-organizing structures	RW
		Principles, Phenomena, Processes	
4	27.03.19	**part 1**: Probability; Multiplicity; Combinatorics; Probability distributions; Mean value, variance, etc.; Probability density; Binomial distributon; Multinomial distribution; Useful distribution finctions: Poisson distribution, flat distributon, Lorentzian, Exponential distribution, Gaussian distribution; Example: random walk in one dimension. **part 2**: Extremum principles predict equilibria; Example: Extrema of potential energy predict mechanical equilibria; Maximizing multiplicity predicts the highest probability outcomes; Examples: Why do gases exert pressure? Why do materials mix and diffuse? Why is rubber elastic?	BR

5	03.04	**part 1**: Maximum entropy principle; Entropy - connection between microscopic and macroscopic worlds; Isolated system and the fundamental equation for entropy; Temperature describes the tendency for energy exchange; Pressure is a force for changing volume; Chemical potential is a tendency for particle exchange; Definitions of the thermodynamic driving forces; Internal energy: statistical view; Internal energy: thermodynamic view; Quasi-static processes; Again: temperature, pressure and chemical potential; Note: intensive and extensive variables. **part 2**: Systems at constant temperature; From maximum entropy to minimum free energy; Example 1: Modelof polymer collapse; Example 2: Model of dimerization; Fundamental equation for the Helmholtz free energy; Heat capacity; Example: the equilibrium temperature of objects in thermal contact; Enthalpy; Systems at constant temperature and pressure; Fundamental equation for enthalpy; Fundamental equation for the Gibbs free energy; Measuring expansion and compression; Summary of thermodynamic potentials; Connection between microscopic and macroscopic worlds: isolated system; Boltzmann distribution; Example 1: model for tetramer folding; Example 2: barometric pressure; Example 3: Maxwell-Boltzmann distribution.	BR
6	10.04	**part 1**: Probability perspective of entropy. Maximum entropy predicts flat distributions when there are no constraints. Maximum entropy predicts exponential distributions when there are constraints. The partition function determines the Helmholtz free energy. Program of statistical mechanics. Density of states. Partition function for distinguishable and indistinguishable particles. **part 2**: Ideal gas. Model for translational motion: quantum particle in a potential well. Model for vibrational motion: quantum harmonic oscillator. Model for rotational motion: rigid rotor. Ideal gas properties are predicted by Quantum Mechanics. Equation of state, heat capacity and chemical potential for ideal gases. Multi-component systems. Mixtures of ideal gases. Chemical potential for a mixture of ideal gases.	BR
7	17.04	**part 1 -** Chemical potential, chemical equilibria, chemical reactions. Chemical potential; Again: chemical potentials for a mixture of ideal gases; Conditions for chemical equilibria; Law of mass action; Example: receptors bind their ligands; Example: acid-base equilibria; Delta G; Example: ATP hydrolysis; Remark 1: Enzymes catalyze biochemical reactions; Remark 2: A thermodynamically unfavorable (Delta G > 0) reaction can be driven in the forward direction by coupling it to a spontaneous reaction (Delta G < 0) through a common intermediate. **part 2 -** Electrochemical potential, electrochemical equilibria - from batteries to ion channels. Electrostatic interactions can affect chemical equilibria; Electrochemical potential; Conditions for electrochemical equilibria; Example: potassium potential in skeletal muscle; Nerst equation; Making a battery out of salt solutions; Nerst equation: acid-base equilibria are shifted by electrostatic fields; Voltage-gated ion channels.	BR
8	24.04	**part 1** - Physical kinetics. Diffusion, permeation and flow. Random walk in one dimension; Diffusion; Defining the flux; Linear laws relate forces to flows; Diffusion equation; Example 1: diffusion from a point source; Example 2: diffusion through a membrane slab; Example 3: diffusion of particles toward a sphere; Example 4: diffusion coupled to a chemical reaction; Diffusing particles can be subject to additional forces; Einstein-Smoluchowski equation; Diffusion coefficient; (Fluctuation-dissipation theorem).	BR

		part 2 - Chemical kinetics. Reaction rates, detailed balance, catalysis, active transport. Note on active transport - chemical energy converted to work; Brownian ratchets; Kinetics of the decay process; Kinetics of a forward-backword process; At equilibrium rates obey detailed balance; Example: Carrier proteins transport solutes across cellular membranes; Kinetic law of mass action; Reaction rate coefficients depend on temperature; Catalysts speed up reactions; Pauling's principle.	
9	08.05	**part 1** – Catalysis. Michaelis-Menten model of enzyme kinetics, multiple substrates, inhibitors. Kinetics of uncatalyzed reactions; Kinetics of catalyzed reactions; Michaelis-Menten model; More intermediate states; Multiple substrates; Inhibitors; Competitive inhibition; Non-competitive inhibition; Uncompetitive inhibition, Allosteric inhibition; Allosteric activation; reaction speed can be modulated by pH. **part 2** - Cooperative effects. Multi-site and cooperative ligand binding; Positive cooperativity; Negative cooperativity; Hill coefficient; Example: two binding sites for titratable protons on a glycine; Aggregation and micelle formation; Hill plot for cooperative binding; Oxygen binding to hemoglobin; MWC model - allosteric effect; Helix-coil transition; Zimm-Bragg model.	BR
		Methods - Theoretical approaches	
10	22.05	**part 1**: Computer simulations in biophysics - general remarks and methodology. All-atom vs. coarse-grained models (*eg.* Go, CABS). **part 2**: Monte Carlo simulations - importance sampling, detailed balance, Metropolis algorithm. **part 3**: Molecular dynamics simulations - force fields, numerical integration of equations of motion, boundary conditions, thermostats and barostats, limitations of standard MD methods; enhanced sampling methods; replica exchange methods. **part 4**: Stochastic dynamics - Langevin dynamics, Brownian dynamics, dissipative particle dynamics.	BR
		Methods - Review of experimental methods and their applications	
11	29.05	Thermodynamics from the experimental point of view: microcalorimetry (DCS, ITC), van't Hoff equation. Complementarity and adequacy of biophysical methods. Typical energies and time-scales; resolution. UV/VIS Spectroscopy (absorption, CD, fluorescence, FRET, interference).	AN
12	05.06	Fluorescence anisotropy vs. hydrodynamics. Analytical ultracentrifugation with optical detection. Thermophoresis. Electrophoresis.	AN
13	12.06	Optical microscopy. Confocal miroscopy, fluorescent proteins, small molecules and quantum dots as probes, immunolabeling, colocalization, 3D imaging, FLIM, FRET, FRAP, FLIP, FLAP, PA/PC. Total internal reflection fluorecsence (TIRF) microscopy. Confocal microscopy vs. hydrodynamics (FCS, FCCS).	AN
	19.06	Exam after I semester (in written, open descriptive questions)	
II semester			
14	02.10	Scattering. Dynamic and static light scattering (DLS, MALS), Zimm equation, Debye plot, second virial coefficient vs. crystallization. Small-angle X-ray scattering (SAXS). Wide-angle X-ray scattering and diffraction.	AN
15	09.10	Surface plasmon resonance (SPR). Infrared spectroscopy, FTIR, attenuated total reflection (ATR), microvawes: electron paramagnetic/spin resonance (EPR/ESR) spectroscopy.	AN
16	16.10	Nuclear magnetic resonance (NMR) spectroscopy. Chemical shift, relaxation,	AN

		Overhauser effect, multidimensional spectra. Structure determination of small molecules and macromolecules. MRI, fMRI.	
17	23.10	X-ray diffraction crystalography. Protein crystallization. In-house diffractometers, synchrotrons, XFELs. Structure determination of macromolecules.	AN
18	30.10	Electron microscopy: scanning EM, transmission EM. Negative staining and cryo-microscopy. 3D reconstruction of macromolecules. Cryo-electron tomography of cells.	AN
19	06.11	Single-molecule methods vs. ensemble methods. Optical tweezers. Atomic force microscopy (AFM), force spectroscopy, imaging, real-time kinetics.	AN
20	13.11	Mass spectrometry, isotopic envelope, proteomics, hydrogen-deuterium exchange, cross-linking, protein conformational dynamics.	AN
		Large biomolecular complexes, their structures and mechanisms of interaction resolved by application of complementary methodological approaches	
21	20.11	Conformations of multi-domain proteins and protein complexes.	BR
22	27.11	Nuclear Pore Complex. Membrane G protein-coupled receptors (GPCR) and signal transduction, conformational equilibria vs. drug design.	AN
23	04.12	Spliceosome and alternative splicing. Ribosome and translation.	AN
24	11.12	Photosynthesis: photosystem II, photosystem I.	RW
25	18.12.19	Folding and stretching of proteins. Entanglements in proteins.	MC
		Big picture of life	
26	08.01.20	Big picture of life 1 - TBD	MC
27	15.01.20	Big picture of life 2 - TBD	MC
28	22.01.20	Big picture of life 3 - TBD	MC
	29.01.20	Consultations	
	05.02.20	Exam (in written, open descriptive questions)	