SYLLABUS
"COMPUTER MODELING OF BIOPHYSICAL
AND BIOCHEMICAL PROCESSES"

National Academy of Sciences of Ukraine

Institute for Condensed Matter Physics

Speciality: 104 Physics and astronomy

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Course Description

The course is a general introduction to computational approaches to problems in biophysics and biochemistry. The emphasis is on models and methods currently used to study proteins, nucleic acids and other biological molecules. The course will consists of an "Introduction" and three subsequent blocs, each addressing a specific topic. Each topic will be covered in classroom lectures and at least one problem-solving session. The latter will be conducted on computational clusters managed by the Institute. Familiarity with Unix-like computing environment is not required but would be beneficial. Same applies to prior programming experience, especially in Fortran77.

All teaching materials are posted at: **http://ph.icmp.lviv.ua/~andrij/biosim2019**

Course Goals

The general goal is for the students to learn about models and methods that are currently employed in computational studies of various biological molecules such as proteins and nucleic acids. This will be achieved through a combination of class-room teaching and problem solving sessions. To reinforce the acquired skills and abilities theoretical concepts will be explained in practical applications. At the end of the class students are expected to gain:

- Basic understanding of what biological molecules are at the physical and chemical level, their function and structure.

- Familiarity with computational models of proteins and nucleic acids. Modeling with varying degree of resolution. Coarse-grained models and atomistic force-fields. Strengths and limitations of various representations of proteins and nucleic acids.
- Awareness of challenges facing simulations of proteins and nucleic acids. Accelerated dynamics in non-Boltzmann ensembles.
- A good handle on methods to evaluate free energy. Solvation models.

Structure of the course

Components of the course	Total hours
Number of credits/hours	3/90
Hours of classes, including:	48
• lectures, hrs.	16
• seminars, hrs.	16
• calculus, hrs.	-
• laboratory simulations, hrs.	16
Hours of self-work, including:	42
• control tests, hrs.	-
• calculus, hrs.	-
• individual scientific study, hrs.	18
• preparation to lectures, laboratory simulations and control tests, hrs.	24
Exam	1
Modules	-

Part of class work in percents – 53.3%

Topics to be covered

Lectures

№	**Topic**	Hours
1	**Introduction to proteins and nucleic acids**	4

	Architecture of proteins and nucleic acids. Different levels of representation of proteins. Lattice models. Minimalistic continuous models. Atomic models. Atomic force-fields for proteins.	
2	**Electrostatic interactions and solvation models** Method of reaction field and simple truncation of potential. Method of lattice sums. Implicit solvation. Hybrid explicit/implicit models. Poisson-Boltzman equation. Generalized Born model.	4
3.	**Methods for evaluating free energy** Direct calculation. Thermodynamic integration. Artificial integration. Gibbs ensemble. Probability ratio. Free energy as potential of mean force. Umbrella sampling.	4
4.	**Methods of accelerated dynamics** Extended ensemble approach. Multicanonical ensemble. Method of parallel tempering. Simulated tempering. Multiple histogram analysis. Statistical reweighting	4
Total hours		16

In-class practice sessions

№	**Topic**	Hours
1	Learning the basics of GROMACS. Creating input files. Choosing a force field. Choosing cell size and shape. Understanding PDB format.	4
2	Solvation of protein molecules. Adding ions. Minimization of initial structures. Simulations in different ensembles.	4
3	Method of simulated tempering. Choosing critical parameters of the simulations: number of replicas, exchange frequency, upper and lower temperature, acceptance ratio.	4
4	Umbrella sampling method. Criteria for choosing the reaction coordinate. Conditions for the required number of “windows”. Test: the potential of mean force for hydrophobic particles.	
Total hours		16

Seminars

№	**Topic**	Hours
1	Atomistic force fields: status quo, progress and challenges	4
2	Effect of the ensemble on simulated observables	4
3	The effectiveness of the simulated tempering method	4
4	Comparative analysis of various methods for calculating free energy.	4
Total hours		16

Out-of-class self-study

№	**Topic**	Hours
1.	Investigation of the first solvation shell of the protein lysozyme. The	6

	behavior of water and solvating ions near charged amino acids.	
	The mechanism of folding of mini protein TRP Cage studied by replica-exchange simulations in implicit solvent.	6
	Calculation of the potential of mean force for a pair of Lys-Glu amino acids in water.	6
2.	Preparation for the final-exam presentation.	24
Total hours		42

Grading system

Maximum grade in points						
During the semester				**Final exam**		**In total**
Lab	**In-class problem-solving sessions**	**Out-of-class self-study sessions**	**Total points**	**Written component**	**Oral component**	
-	30	30	60	40	0	100

Sample Grade Cutoffs

88% A
80% B
70% C

Textbooks

1) M. Lesk, ***Introduction to Protein Architecture***, Oxford University Press, 2001.
2) R. Leach, ***Molecular Modeling: Principles and applications***, Pearson, 2001.
3) Fersht, ***Structure and Mechanism in Protein Science***, W H Freeman and Company, 1999.
4) T. E. Creighton, ***Proteins***, W H Freeman and Company, 2002
5) D.Frenkel, B.Smit. ***Understanding Molecular Simulation.*** Academic Press. SanDiego,1996
6) M.Allen, D.Tildesley. ***Computer simulation of liquids.*** Oxford Press, London, 1988.