Syllabus for the online course BINF641 "Biomolecular Modeling"

Name of Course: Biomolecular Modeling
Meeting place: Blackboard
Instructor Name: Dmitri Klimov
Course number: 201810.13732 BINF-641-DL1 (Spring 2018)
Credits: 3
Office location: Colgan Hall, Rm 328B, Science and Technology Campus (PWC)
Office hours: By appointment (email me to set up an in-person appointment or to speak over the telephone or to meet through Blackboard Collaborate)
Email address: dklimov@gmu.edu
Telephone number: 703-993-8395

Course Description

This graduate course is designed for the students with the background in biology, chemistry, physics, or computer science and who are interested in learning biomolecular modeling. The goal of the course is to introduce the principles of biomolecular modeling and to develop practical skills for using existing modeling software.

The course presents the foundations of molecular modeling and teaches practical modeling skills. As a result, it consists of two parts. The first starts with the introduction of fundamental concepts of physical chemistry, which are commonly used in the description of biological systems. Molecular interactions, from covalent bonding to electrostatic and van-der-Waals interactions, are discussed. The course shows how these interactions are combined to produce a complex array of biomolecular structures found in DNA, RNA, proteins, and lipid cellular membranes. The molecular mechanisms of protein folding are discussed in detail. The unfolding of proteins implicated in a variety of biological functions is also introduced. The consequences of protein aggregation are explored and linked to a new class of diseases. Cellular defensive mechanisms against protein misfolding and aggregation, including chaperone systems, are presented.

The second part of the course describes the basic concepts in biomolecular modeling, such as molecular mechanics. Practical implementation of biomolecular modeling, including the application of relevant simulation and visualization software, is emphasized. Several case studies illustrating the use of biomolecular modeling are discussed, including ligand binding and protein interactions with cellular membranes. As a final exam, students complete the course project on biomolecular modeling.

Course Prerequisites: Students are expected to be familiar with the basic concepts of physics, calculus, and biology on undergraduate level. Access to PC for course project is required.

Required Reading

1. Rodney Cotterill "Biophysics: An introduction", John Wiley & Sons, 2002.
2. Online lecture notes and slides (available on Blackboard)

Course Logistics

The course uses a distance learning format and the main meeting space will be on Blackboard. This course will be primarily asynchronous, except for weekly online meetings on Mondays from 2:30 to 3:30 pm using Blackboard Collaborate. Email, telephone, and Blackboard Collaborate will be used for communication. In a typical week, students will cover one topic by

- reading textbook chapters and lecture notes
- completing the assignments
- participating in weekly online discussion, which concludes a week

Note that the course contains introductory week "Week 0" describing course logistics, which is concluded with the online discussion session on Monday, Jan 22. The first week "Week 1" opens on Monday, Jan 22 after "Week 0" online discussion and ends next Monday, Jan 29 with "Week 1" online discussion. Subsequently, each week will begin on Monday and end the next Monday.

To Access Blackboard

1. Go to http://mymason.gmu.edu.
2. Login using your NETID and password.
3. Click on the 'Courses" tab.
4. Click on 201810.13732 BINF-641-DL1 (Spring 2018) under the "Course List" heading.

Instructor-Student Communication: The preferred way of communication is through email, to which I will respond promptly within 48 hours.

Email requirements:

1. Mason requires that Mason email be used for all courses. I will be sending messages to your Mason email and you are responsible for the access to these messages.
2. You may forward your Mason email to other accounts but always use your Mason e-mail when communicating with me to allow verification of your identity.
3. You are required to check your Mason email account regularly and to keep your mailbox maintained so that messages are not rejected for being over quota.
4. When you email me, you can expect a response within 48 hours. If I am going to be away from email for more than two days, I will send an announcement to the class.

5. When you email me, be sure to include **BINF641** at the beginning of the subject heading

Netiquette For Online Discussions [1]: Our discussion should be collaborative, not combative; you are creating a learning environment, sharing information and learning from one another. Respectful communication is important to your success in this course and as a professional. Please re-read your responses carefully before you post them so others will not to take them out of context or as personal attacks. Be positive to others and diplomatic with your words and I will try my best to do the same. Be careful when using sarcasm and humor. Without face-to-face communications your joke may be viewed as criticism. Experience shows that even an innocent remark in the online environment can be easily misconstrued.

[1] Netiquette prepared by Charlene Douglas, Associate Professor, College of Health & Human Services, GMU.

Technology Requirements for the Course

Hardware: You will need access to a Windows or Macintosh computer with at least 2 GB of RAM and to a fast and reliable broadband internet connection (e.g., cable, DSL). A larger screen is recommended for better visibility of course material. You will need speakers or headphones to hear recorded content and a headset with a microphone is highly recommended for the best experience. For the amount of Hard Disk Space required to take a distance education course consider and allow for:

1. the storage amount needed to install any additional software and
2. space to store work that you will do for the course.

Software: This course will use Blackboard as the learning management system. You will need a browser and operating system that are listed compatible or certified with the Blackboard version available on the myMason Portal. See supported browsers and operating systems. Log in to myMason to access BINF641. You will need Acrobat Reader, Flash, Java (Windows), and Windows Media Player, QuickTime and/or Real Media Player. Your computer should be capable of running current versions of those applications. Also, make sure your computer is protected from viruses by downloading the latest version of Symantec Endpoint Protection/Anti-Virus software for free at http://antivirus.gmu.edu.

Students owning Macs or Linux should be aware that some courses may use software that only runs on Windows. You can set up a Mac computer with Boot Camp or virtualization software so Windows will also run on it. Computers running Linux can also be configured with virtualization software or configured to dual boot with Windows.

Note: If you are using an employer-provided computer or corporate office for class attendance, please verify with your systems administrators that you will be able to install the necessary applications and that system or corporate firewalls do not block access to any sites or media types.

Course-specific Hardware/Software: Molecular dynamics program NAMD and molecular viewer VMD are required for completing course project and to access some course materials. Both programs are available for free download at http://www.ks.uiuc.edu/Research/namd/ and http://www.ks.uiuc.edu/Research/vmd/, respectively. It is recommended to download precompiled binaries of these programs for specific operating system (Windows, Mac, or Linux).

Technical Help: If you have difficulty with accessing Blackboard, please contact the ITU Support Center at 703.993.8870 or support@gmu.edu. If you have trouble with using the features in Blackboard, email courses@gmu.edu.

Student Responsibilities

MasonLive/Email: Students are responsible for the content of university communications sent to their George Mason University email account and are required to activate their account and check it regularly. All communication from the university, college, school, and program will be sent to students solely through their Mason email account.

Patriot Pass: Once you sign up for your Patriot Pass, your passwords will be synchronized, and you will use your Patriot Pass username and password to log in to the following systems: Blackboard, University Libraries, MasonLive, myMason, Patriot Web, Virtual Computing Lab, and WEMS. [See https://password.gmu.edu/index.jsp].

Students with Disabilities: Students with disabilities who seek accommodations in a course must be registered with the George Mason University Disability Services and inform their instructor, in writing, at the beginning of the semester [See Disability Services website: http://ds.gmu.edu/].

Academic Integrity: Students must be responsible for their own work, and students and faculty must take on the responsibility of dealing explicitly with violations. The tenet must be a foundation of our university culture. [See Academic Integrity website: http://masononline.gmu.edu/student-resources/academicintegrity/].

Honor Code and Virtual Classroom Conduct: Students must adhere to the guidelines of the George Mason University Honor Code (See Honor Code website: http://oai.gmu.edu/mason-honor-code/full-honor-code-document/).

Academic Honesty Policy of the course: Students are expected to follow the Honor Code. Academic dishonesty will not be tolerated in this class. Exams, projects, and homework must reflect individual work. If you have difficulty with the assignments, discuss it with the instructor.

University Policies: Students must follow the university policies. [See University Policies website: http://universitypolicy.gmu.edu].

Responsible Use of Computing: Students must follow the university policy for Responsible Use of Computing. [See University Policies website: http://universitypolicy.gmu.edu/policies/responsible-use-of-computing].

University Calendar: Students should consult the current Academic Calendar [See University Calendar website: http://calendar.gmu.edu].

University Catalog: Students should use the current university catalog [See University Catalog website: http://catalog.gmu.edu].

Student Services

Writing Center: The George Mason University Writing Center staff provides a variety of resources and services (e.g., tutoring, workshops, writing guides, handbooks) intended to support students as they work to construct and share knowledge through writing. (See Writing Center website: http://writingcenter.gmu.edu). ESL Help: The program was designed specifically for students whose first language is not English who feel they might benefit from additional, targeted support over the course of an entire semester.

University Libraries: University Libraries provide resources for distance students. [See Library website: http://library.gmu.edu/distance].

Counseling and Psychological Services: The George Mason University Counseling and Psychological Services (CAPS) staff consists of professional counseling and clinical psychologists, social workers, and counselors who offer a wide range of services (e.g., individual and group counseling, workshops and outreach programs) to enhance students' personal experience and academic performance [See Counseling and Psychological Services website: https://caps.gmu.edu].

Family Educational Rights and Privacy Act (FERPA): The Family Educational Rights and Privacy Act of 1974 (FERPA), also known as the "Buckley Amendment," is a federal law that gives protection to student educational records and provides students with certain rights. [See Registrar's Office website: https://registrar.gmu.edu/privacy].

Course Policies

Late assignments: Late assignments and project will not be accepted.

Grading basis: Students will be graded on the basis of homework (30%), class participation (30%), and final project (40%). Homework will include problems and practical assignments for molecular modeling. For each problem or assignment a student will earn up to one point. Homeworks are weighted equally. Class participation consists of attendance of discussions and submission of questions (together, up to one point per week). Final projects will include molecular modeling studies of particular system and presentation of the findings in a report. For a project a student will receive up to one point.

Grading Scale (points): A (90-100), B (80-89), C (≤79)

Other Considerations: If there are any issues related to religious holidays, please inform the instructor the first week of class.

Learning Outcomes

By the end of this course, students will be able to

1. apply the fundamental physicochemical principles and concepts, which underline molecular modeling
2. appraise recent applications of molecular modeling, which successfully addressed important biological questions
3. evaluate the scope of applicability of molecular modeling, including its advantages and limitations
4. develop practical skills necessary to perform molecular modeling studies
5. perform their own molecular dynamics study and analyze its results

Course Schedule*

*see Course Logistics for the definition of course week

Week	Topic	Readings and Videos	Activities	Assignments
0	Course Introduction	— Read syllabus — Watch "Welcome Video" and "How to Take This Course Video"	Class discussion 1/22	Read syllabus and watch videos before class discussion
1-1/22 Learning Outcome #1	Elements of thermodynamics and statistical mechanics	— Reading lecture notes — Reading Chapter 4.1-4.3 — Studying mini-lectures 1. Functions of state, laws of thermodynamics, and variational principle. 2. Ensembles in statistical mechanics: Microcanonical and canonical (Boltzmann) distributions. 3. Maxwell-Boltzmann distribution. 4. Energy barrier crossing.	Class discussion 1/29 Work on the assignments	problems 4.2, C.1, C.2, and a question for discussion
2 – 1/29 Learning outcomes #1-3	Biomolecular interactions and bonds. Molecular mechanics.	— Reading Chapters 2 and 3 — Studying mini-lectures: 1. Covalent and ionic bonds. Hydrogen bonds. Van-der-Waals interactions. 2. Describing interatomic interactions using empiric functions. Construction of molecular energy function.	Class discussion 2/5 Work on the assignments	Problems 3.2, 3.4, and a question for discussion
3 – 2/5 Learning outcomes #1 and 3	Biomolecular structure: DNA, RNA, polypeptides. Hydration	— Reading Chapter 7.1-7.4 — Reading lecture notes — Studying mini-lectures: 1. General properties of biomolecular structure. Existence of unique native state. 2. DNA and RNA. 3. Proteins. 4. Hydration: Water structure, hydrophobic effect, and screening of electrostatic interactions in water.	Class discussion 2/12 Work on the assignments	A question for discussion
4 – 2/12 Learning outcomes #1-3	Protein folding	— Reading lecture notes — Studying mini-lectures: 1. Physicochemical properties of proteins. 2. Protein folding problem: Levinthal paradox. Folding via intermediates vs two-state folding. Mechanisms of folding. 3. Illustration of two-state folding using lattice model. 4. Impacts of sequence and external conditions on folding. Timescales. 5. Simulation of protein folding.	Class discussion 2/19 Work on the assignments	Problems assigned in the lecture notes and a question for discussion

5 – 2/19 Learning outcomes #1-3	Protein aggregation	— Reading lecture notes — Studying mini-lectures: 1. Amyloids are the structures alternative to native states. 2. Structures of amyloid fibrils. 3. Mechanism of amyloid assembly. 4. Factors favoring or preventing amyloid assembly. 5. Simulations of protein aggregation.	Class discussion 2/26 Work on the assignments	Problems assigned in the lecture notes and a question for discussion
6 – 2/26 Learning outcomes #1-3	Mechanical unfolding of proteins	— Reading lecture notes — Studying mini-lectures: 1. Mechanically active proteins. 2. Experimental studies of mechanical unfolding. 3. Physics of mechanical unfolding. 4. Lattice model simulations of mechanical unfolding. 5. Native topology determines mechanical unfolding.	Class discussion 3/5 Work on the assignments	Problems assigned in the lecture notes and a question for discussion
7– 3/5 Learning outcomes #1-3	Monte-Carlo method	— Reading lecture notes — Studying mini-lectures: 1. Metropolis algorithm. 2. Choosing Monte-Carlo moves. 3. Practical implementation of Monte-Carlo method. 4. Measuring convergence in simulations.	Class discussion 3/19 Work on the assignments	Problems assigned in the lecture notes and a question for discussion
8– 3/19 Learning outcomes #3,4	Principles of biomolecular modeling	— Reading lecture notes — Studying mini-lectures: 1. Molecular mechanics: Applicability and principles. 2. CHARMM force field. 3. Energy function in CHARMM force field. 4. Computation of energy function. Periodic boundary conditions. 5. Molecular dynamics: Numerical solution of Newton equations of motion. 6. Ensembles in molecular dynamics. Computation of averages.	Class discussion 3/26 Work on the assignments	Question for discussion
9– 3/26 Learning outcomes #4	Biomolecular modeling in practice	— Reading lecture notes — Studying mini-lectures: 1. Introducing NAMD molecular dynamics program. 2. Minimization. 3. Heating. 4. Equilibration. 5. Production. 6. Running NAMD for polyvaline peptide. 7. Using VMD program.	Class discussion 4/2 Work on the assignments	Assignments given in the lecture notes and a question for discussion

10– 4/2 Learning outcomes #4,5	Course projects on biomolecular modeling	— Reading lecture notes — Studying mini-lectures: 1. Description of course projects - Temperature induced unfolding. 2. Description of course projects - Ibuprofen binding to Alzheimer's Abeta peptide.	Class discussion 4/9 Work on the course project and assignments	First course project assignment; a question for discussion
11– 4/9 Learning outcomes #4,5	Course projects on biomolecular modeling	— Reading lecture notes — Studying mini-lectures: 1. Temperature induced unfolding – production simulations and analysis 2. Ibuprofen binding - production simulations and analysis	Class discussion 4/16 Work on the course project and assignments	Question for discussion
12– 4/16 Learning outcomes #4,5	Course projects on biomolecular modeling .	— Reading lecture note "Continuing/restarting production simulations"	Class discussion 4/23 Work on the course project and assignments	Question for discussion
13– 4/23 Learning outcomes #2	Biomolecular modeling as a research tool: (i) Ligand binding to proteins, (ii) Protein interactions with cellular membranes	— Reading research papers 1. Applying replica exchange molecular dynamics (REMD) to study the impact of ibuprofen binding on the structure of Abeta peptide (published in J. Phys. Chem. B 116, 12922 (2012)). 2. Applying REMD to study interactions of Abeta peptide with lipid bilayers (published in J. Phys. Chem. B 118, 2638.	Class discussion 4/30 Work on the course project and assignments	Question for discussion
14– 4/30 Learning outcomes #4,5	Course projects on biomolecular modeling	-- Reading lecture note "Preparing project reports"	Work on the course project	Course project