Syllabus for BINF641 "Biomolecular Modeling"

Course title: Biomolecular Modeling
Course number: BINF641
Instructor name: Dmitri Klimov
Semester and year: Spring 2025
Course credits: 3
Class meeting day/time/modality: asynchronous with weekly Zoom discussions on Mondays at 3pm.
Class website: 202510.18961 BINF-641-DL1 (Spring 2025)
Class zoom invitation: Provided via email
Instructor email address: dklimov@gmu.edu (preferred way of communication)
Instructor telephone number: 703-993-8395
Instructor office location: Colgan Hall, Rm 328B, Science and Technology Campus
Instructor office hours: By appointment (email to arrange zoom meeting or to speak over the telephone)

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 mechanisms of protein folding learned from molecular modeling are discussed.

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 a 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 as well as be reasonably proficient with programming. Access to PC for course project is required.

Required Reading

1. Rodney Cotterill “Biophysics: An introduction”.
2. Online lecture notes and slides (available via Blackboard).

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 address 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.
5. Perform their own molecular dynamics study and analyze its results.

Course Logistics

The course uses distance learning format and is primarily asynchronous with the exception for weekly online meetings on Mondays from 3:00 to 4:00 pm. These meetings will be conducted via Zoom. Email, telephone, and Zoom will be used for communication. In a typical week, students will cover one topic by

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

The course starts with Introduction folder, which describes course logistics. The first week “Week 1” opens on Tuesday, Jan 21 and ends next Monday, Jan 27, with online discussion. Subsequently, each week will begin on Tuesday and end the next Monday.

To Access Blackboard
1. Go to http:// mymasonportal.gmu.edu.
2. Login using your NETID and password.
3. Click on the ‘Courses” tab.
4. Click on 202510.18961 BINF-641-DL1 (Spring 2025) under the “Course List” heading.

Instructor-Student Communication: The preferred means 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 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 communication 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.

Course Policies

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 independent of the number of problems in the homework. Class participation consists of attendance of weekly discussions (synchronously or asynchronously) and submission of questions (together, up to one point per week). Final projects will include molecular modeling studies of a particular system and presentation of the findings in a report. For a project student will receive up to one point.

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

Campus Closure: If the campus closes or class is canceled due to weather or other concern, students should check Blackboard and/or contact instructor for updates on how to continue learning and information about any changes to events or assignments.

Participation and make-up work: In case of illness or quarantine, please contact the instructor to set up a plan for make-up work. Late assignments will not be accepted unless due to emergency, illness, quarantine, work-related, or other documented reasons.

Course Recordings: All synchronous meetings in this class will be recorded to provide necessary information for students in this class. Recordings will be stored on Zoom and will only be accessible to students taking this course during this semester.

Other considerations: If there are any schedule issues related to religious holidays, please inform the instructor during the first week of class. Completion of regular weekly homework is expected to take several hours.

Technology Requirements for the Course

Software and Hardware: This course uses Blackboard as a learning management system available at https://mymason.gmu.edu. Students are required to have regular, reliable access to a computer with an updated operating system (recommended: Windows 10 or 11 or Mac OSX 10.13 or higher) and a stable broadband Internet connection (cable modem, DSL, satellite broadband, etc., with a consistent 1.5 Mbps [megabits per second] download speed or higher). Activities in this course will regularly use Zoom web-conferencing software. In addition to the requirements above, students are required to have a device with a functional camera and microphone. A larger screen is recommended for better visibility of course material. In an emergency, students can connect through a telephone call, but video connection is the expected norm.

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 analysis viewer VMD are required for completing course project and to access some course materials. Both programs are available for free download at https://www.ks.uiuc.edu/Research/namd/ and https://www.ks.uiuc.edu/Research/vmd/, respectively. It is recommended to download precompiled binaries of these programs for specific operating systems (Windows, Mac, or Linux).

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

Common Polices Addendum

The course follows Common Policies Addendum available at https://stearnscenter.gmu.edu/home/gmu-common-course-policies/. Further information on policies is provided below.

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.

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: https://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 Standards website: https://academicstandards.gmu.edu/].

Academic Standards Code and Virtual Classroom Conduct: Students must adhere to the guidelines of the George Mason University Academic Standards Code [See Academic Standards Code website: https://academicstandards.gmu.edu/academic-standards-code/].

Academic Honesty Policy of the course: Students are expected to follow the Academic Standards 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: https://universitypolicy.gmu.edu].

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

University calendar: Students should consult the current Academic Calendar [See University Calendar website: https://www2.gmu.edu/academics/academic-calendar].

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: https://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 learning students [See Library website: http://library.gmu.edu/for/online].

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/ferpa/].

Course Materials and Student Privacy

Video recordings of class meetings that are shared only with the instructors and students officially enrolled in a class do not violate FERPA or any other privacy expectation. Video recordings that only include the instructor (no student names, images, voices, or identifiable texts) may be shared without violating FERPA (but see University Policies: Privacy, for some qualifications and recommendations). All course materials posted to Blackboard or other course site are private to this class; by federal law, any materials that identify specific students (via their name, voice, or image) must not be shared with anyone not enrolled in this class.

Video conferencing or recordings: Video recordings - whether made by instructors or students - of class meetings that include audio, visual, or textual information from other students are private and must not be shared outside the class. Live video conference meetings that include audio, textual, or visual information from other students must be viewed privately and not shared with others in your household or recorded and shared outside the class.

Course Schedule*

*see Course Logistics for the definition of course week

Week	Topic	Readings and Videos	Activities	Assignments
	Course Introduction	— Read syllabus — Watch "Welcome Video" and "How to Take This Course Video"		Read syllabus and watch videos
1-1/21 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 1/27 Work on the assignments	problems 4.2, C.1, C.2, and a question for discussion
2 – 1/28 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 2/3 Work on the assignments	Problems 3.2, 3.4, and a question for discussion
3 – 2/4 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 2/10 Work on the assignments	A question for discussion
4 – 2/11 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 2/17 Work on the assignments	Problems assigned in the lecture notes and a question for discussion
5– 2/18 Learning	Monte-Carlo method	— Reading lecture notes — Studying mini-lectures:	Class discussion	Problems assigned in

outcomes #1-3		1. Metropolis algorithm. 2. Choosing Monte-Carlo moves. 3. Practical implementation of Monte-Carlo method. 4. Measuring convergence in simulations.	2/24 Work on the assignments	the lecture notes and a question for discussion
6– 2/25 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 3/3 Work on the assignments	Question for discussion
7– 3/4 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 3/17 Work on the assignments	Assignments given in the lecture notes and a question for discussion

8– 3/18 Learning outcomes #4,5	Course projects on biomolecular modeling	— Reading lecture notes — Studying mini-lectures: A course project - Ibuprofen binding to Alzheimer's Abeta peptide.	Class discussion 3/24 Selecting the course project and work on assignments	Course project; a question for discussion
9– 3/25 Learning outcomes #4,5	Course projects on biomolecular modeling	— Reading lecture notes — Studying mini-lectures: 1. Ibuprofen binding - production simulations and analysis. 2. Impact of force field - production simulations and analysis.	Class discussion 3/31 Work on the course project and assignments	Course project; a question for discussion
10– 4/1 Learning outcomes #4,5	Course projects on biomolecular modeling	— Reading lecture note "Continuing/restarting production simulations"	Class discussion 4/7 Work on the course project and assignments	Course project; a question for discussion
11– 4/8 Learning outcomes #4,5	Course projects on biomolecular modeling		Class discussion 4/14 Work on the course project and assignments	Course project; a question for discussion
12– 4/15 Learning outcomes #4,5	Course projects on biomolecular modeling		Class discussion 4/21 Work on the course project and assignments	Course project; a question for discussion
13– 4/22 Learning outcomes #2	Biomolecular modeling as a research tool: (i) Ligand binding to proteins, (ii) Protein interactions with cellular membranes	— Reading research papers	Class discussion 4/28 Work on the course project and assignments	Course project; a question for discussion
14– 4/29 Learning outcomes #4,5	Course projects on biomolecular modeling	-- Reading lecture note "Preparing project reports"	Class discussion 5/5 Work on the course project	Course project