CHEM 8520: Computational Chemistry

Spring Minimester II, 2020 (3 Semester Credit Hours)

Instructor: Xinqiu Yao, 523 Science Annex, (Email: xyao4@gsu.edu)

Lecture Time and Location: March 03 – April 23
Tuesday & Thursday, 2:30 PM – 5:00 PM, PSC 311

Office Hours: By appointment

Course Prerequisite: Physical Chemistry I and II

Suggested Reading:

Andrew R. Leach --- Molecular Modelling: Principles and Applications (Pearson, 2001)
Frenkel and Smit --- Understanding Molecular Simulation: From Algorithms to Applications (Academic Press, 2001)
Allen and Tildesley --- Computer Simulation of Liquids (Oxford, 2017)
McCammon and Harvey --- Dynamics of Proteins and Nucleic Acids (Cambridge, 1988)
Tamar Schlick --- Molecular Modeling and Simulation: An Interdisciplinary Guide (Springer, 2010)
Branden and Tooze --- Introduction to Protein Structure (Garland Science, 1999)

Software Used: R (Bio3D), VMD, AMBER, Autodock, PyMol

Course Description: Computational Chemistry is a 3-credit minimester course that covers the introduction to structural bioinformatics, molecular modeling and dynamics simulation, docking and drug discovery, and principles of computational methodologies and their applications. Students will develop fundamental knowledge of computational chemistry and gain hands-on excises of using software and programming to solve chemical and biophysical problems. The broader goal is to help students establish the attitude of appreciating biomolecular motions and their relevance to function.

Grading: Final grading will be based on homework assignments (30%), in-class assignments (50%), and final exam (paper presentation; 20%).

Tentative Course Outline and Schedule:

Week 1: **(3/3, Tuesday) Welcome to Computational Chemistry**
What is computational chemistry, course description, introduction to Linux
Lab: Practice Linux and complete worksheet
Homework: Complete the *Introduction to Shell* course on DataCamp (due 3/10)

(3/5, Thursday) Basic Probability Theory and Introduction to R
Random variables, probability, probability (density) distribution, Gaussian distribution, mean and variance, what is R, basic R commands, vector and matrix, plotting and simple statistics with R, further reading and where to find helps
Lab: Practice R and complete worksheet
Homework: Solve problem set (due 3/12)
(Optional) *Foundations of Probability* DataCamp course

Week 2: **(3/10, Tuesday) Structural Bioinformatics (Part 1)**
What is structural bioinformatics, dynamics is the key to link structure and function, fundamentals of biomolecular structure, Protein Data Bank (PDB), visualization (introduction to VMD), structural data manipulation with R (introduction to Bio3D)
Lab: Explore PDB, practice VMD and Bio3D

(3/12, Thursday) Structural Bioinformatics (Part 2)
Protein evolution, multiple sequence alignment, search for similar sequences, sequence analysis, writing R functions
Lab: Explore the DHFR family
Homework: *Introduction to R* DataCamp course (due 3/26)
(Optional) *Intermediate R* DataCamp course

Week 3: **Spring Break**

Week 4: **(3/24, Tuesday) Introduction to Machine Learning**
Clustering, heatmap representation, principal component analysis (PCA)
Lab: Case studies with R
Homework: Solve problem set (due 3/31)
(Optional) *Unsupervised Learning in R* DataCamp course

(3/26, Thursday) Structural Bioinformatics (Part 3)
Superimposition, structural comparison, PCA of biomolecular structures, introduction to Bio3D modules for multiple-structure analysis
Lab: PCA of DHFR structures
Homework: Summarize results in the lab session and write a report (due 4/2)
(Optional) Complete more selected courses on DataCamp

Week 5: **(3/31, Tuesday) Introduction to Statistical Mechanics**
Energy levels and distribution, ensembles, partition function, thermodynamic properties, classical limits
Homework: Solve problem set (due 4/7)

(4/2, Thursday) Classical Molecular Mechanics
Energy function, parameterization, force fields, water models, potential energy surface, energy minimization
(Introduction to the final exam: paper presentation)
Lab: Introduction to AMBER; practice leap and sander on DHFR (PDB: 1RA2)
Homework: Read selected papers and pick up one for the final exam (due 4/9)

Week 6: **(4/7, Tuesday) Molecular Dynamics Simulation (Part 1)**
A brief history, equation of motion, temperature coupling, diffusion, radial distribution
Lab: Setup and simulate a box of liquid water; use cpptraj to analyze trajectory

(4/9, Thursday) Molecular Dynamics Simulation (Part 2)
Periodic boundary condition, pressure coupling, best practices, trajectory analysis
(Paper for the final exam assigned)
Lab: Setup and simulate DHFR; use Bio3D to analyze the trajectory
Homework: Summarize results in the lab session and write a report (due 4/16)

Week 7: **(4/14, Tuesday) Limitations of Classical Molecular Mechanics and Advanced Simulation Methods**
Umbrella sampling, thermodynamic integration, pKa shift (a case study), accelerated MD, QM/MM
Lab: Estimate the free energy landscape of alanine dipeptide (collaborative)
Homework: Prepare for the final exam

(4/16, Thursday) Molecular Docking
Lab: Introduction to Autodock suite of programs and the PyMol plugin
Homework: Prepare for the final exam

Week 8: **(4/21, Tuesday) Virtual Screening and Computer Aided Drug Discovery**
Lab: Practice virtual screening using a subset of the Zinc database
Homework: Prepare for the final exam

(4/23, Thursday) Final Exam (Paper Presentation)