Chemistry 430: Simulation in Chemistry & Biochemistry Spring 2023

Class Meetings: Monday and Wednesday, Lecture, 11:00-11:50, Life Sciences 118
Friday, Laboratory Sessions, 11:00-12:00 and 12:00-1:00, 454 Louderman

Instructor: Jay Ponder (453 Louderman, 935-4275, ponder@dasher.wustl.edu)

Web Site: http://dasher.wustl.edu/chem430/

Objectives: Chemistry 430 explores a wide range of computational applications in molecular modeling, biochemistry and biophysics, including *ab initio* and semi-empirical electronic structure theory, molecular mechanics, molecular dynamics simulation, coarse-grained models, electrostatic methods, biomolecular structure prediction and machine learning in molecular modeling.

A major component of the course consists of weekly laboratory sessions using software programs including VMD, Avogadro, Spartan, Q-Chem, Psi4, Gaussian, VMD, Chimera, Tinker, FFE, APBS, Modeller, AutoDock, SDA7 and AlphaFold. Many of the lab exercises target proteins, nucleic acids and biological structures.

Books: The book that most closely follows the course outline is Molecular Modeling by Andrew Leach. While not required, Leach is a well-written, basic introduction. Useful books are listed below, and additional readings will be provided.

General Molecular Modeling:

Molecular Modeling – Principles and Applications, 2nd Ed., Andrew Leach, 2001
Molecular Modeling and Simulation, 2nd Ed., Tamar Schlick, 2010
Introduction to Computational Chemistry, 3rd Ed., Frank Jensen, 2017
Essentials of Computational Chemistry, 2nd Ed., Christopher Cramer, 2004
Computational Chemistry, 2nd Ed., Errol Lewers, 2010

Algorithms & Theory for Quantum Chemistry:

Modern Quantum Chemistry, Attila Szabo & Neil Ostland, 1982 (reprinted by Dover)
Quantum Chemistry, 3rd Ed., John Lowe and Kirk Petersen, 2006
Frontier Orbitals – A Practical Manual, Nguyen Trong Anh, 2007
Molecular Orbitals & Organic Chemical Reactions, Ian Fleming, 2010
The Theory of Intermolecular Forces, 2nd Ed., Anthony Stone, 2013

Simulation & Biochemical Applications:

Computer Simulation of Liquids, 2nd Ed., M. P. Allen & D. J. Tildesley, 2017
Understanding Molecular Simulation, 2nd Ed., Daan Frenkel & Berend Smit, 2002
Computational Biochemistry & Biophysics, Becker, *et al*., 2001
A Guide to Biomolecular Simulations, Becker & Karplus, 2006

Other Info: Chemistry 430 is intended for advanced undergraduates and early graduate students wanting to learn modern computational and modeling approaches to chemical, biochemical and biophysical problems. A course in physical chemistry is recommended as background, but not required. Familiarity with computers to the level of writing scripts or small programs is recommended, but not required.

Module 1:	**Molecular Mechanics & Simulation Techniques**
Jan 18	Overview of Molecular Modeling
Jan 20	Lab 1: Unix Tutorial & Using Chimera, VMD, FFE & Spartan
Jan 23	Introduction to Molecular Mechanics I
Jan 25	Introduction to Molecular Mechanics II
Jan 27	Lab 2: Conformational Analysis of Alanine Dipeptide
Jan 30	Potential Energy Surfaces & Optimization Methods
Feb 1	Basics of Molecular Dynamics Simulation I
Feb 3	Lab 3: Liquid Properties *via* Molecular Dynamics Simulation
Feb 6	Basics of Molecular Dynamics Simulation II
Feb 8	Using Molecular Dynamics to Compute Properties I
Feb 10	Lab 4: Global Optimization of Lennard-Jonesium & PolyAlanine
Feb 13	Using Molecular Dynamics to Compute Properties II
Feb 15	Methods for Free Energy Calculations
Feb 17	Lab 5: Relative Hydration Free Energy of Monovalent Ions
Feb 20	Proteins Structure: Structure Motifs & Fold Classes (conflict for Prof. Ponder)
Feb 22	Proteins Folding: Forces & Mechanisms of Folding (conflict for Prof. Ponder)
Feb 24	Make-up Day to Work on Labs 1-5
Feb 27	Electrostatics & Solvation in Biomolecular Systems I
Mar 1	Electrostatics & Solvation in Biomolecular Systems II
Mar 2	Lab 6: APBS Poisson-Boltzmann Calculations on Lysozyme
Mar 6	Introduction to Monte Carlo Methods I
Mar 8	Introduction to Monte Carlo Methods II
Mar 10	Lab 7: Folding Simulation of the TrpCage Miniprotein, Part I
Module 2:	***ab Initio* & Semi-Empirical Quantum Mechanics**
Mar 20	Basics of *ab Initio* Molecular Orbital Theory I
Mar 22	Basics of *ab Initio* Molecular Orbital Theory II
Mar 24	Lab 7: Folding Simulation of the TrpCage Miniprotein, Part II
Mar 27	Methods for Treating Electron Correlation
Mar 29	Semi-Empirical Molecular Orbital Methods
Mar 31	Lab 8: Computing the Rotational Barrier in Hydrazine
Apr 3	Density Functional Theory (DFT)
Apr 5	Quantum Mechanics/Molecular Mechanics (QM/MM)
Apr 7	Lab 9: Frontier Orbital Analysis of Regioselectivity

Module 3:	**Biomolecular Modeling, Structure Prediction & Machine Learning**
Apr 10	Protein Structure Prediction, Engineering & Design
Apr 12	Small Molecule & Protein Docking I
Apr 14	Lab 10: Docking Indinavir to HIV Protease Using Autodock
Apr 17	Small Molecule & Protein Docking II
Apr 19	Computing Binding Rate Constants *via* Brownian Dynamics
Apr 21	Lab 11: Diffusional Association of the Barnase-Barstar Complex
Apr 24	Introduction to Convolutional Neural Networks
Apr 26	Machine Learning in Computational Chemistry
Apr 28	Lab 12: Protein Structure Prediction via DeepMind AlphaFold
May 10	**Lab Reports & Take-Home Assignments Due**