Chemistry 430: Simulation in Chemistry & Biochemistry  Spring 2022

Class Meetings:  Monday and Wednesday, Lecture, 11:00-11:50, Cupples II L001  
Friday, Laboratory Sessions, One Hour Sessions, 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’s book is a well-written, basic introduction. Useful books are listed below, and 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)
Molecular Orbitals & Organic Chemical Reactions, Ian Fleming, 2010

*Simulation & Biochemical Applications:*

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 19  Overview of Molecular Modeling
Jan 21  Unix Tutorial & Using Chimera, VMD, FFE & Spartan
Jan 24  Introduction to Molecular Mechanics I
Jan 26  Introduction to Molecular Mechanics II
Jan 28  Lab 1: Conformational Analysis of Alanine Dipeptide
Jan 31  Potential Energy Surfaces & Optimization Methods
Feb  2  Basics of Molecular Dynamics Simulation I
Feb  4  Lab 2: Liquid Properties via Molecular Dynamics Simulation
Feb  7  Basics of Molecular Dynamics Simulation II
Feb  9  Using Molecular Dynamics to Compute Properties I
Feb 11  Lab 3: Global Optimization of Lennard-Jonesium & PolyAlanine
Feb 14  Using Molecular Dynamics to Compute Properties II
Feb 21  Introduction to Monte Carlo Methods I
Feb 23  Introduction to Monte Carlo Methods II
Feb 25  Lab 5: Monte Carlo Lab (To be Determined)
Feb 28  Electrostatics & Solvation in Biomolecular Systems I
Mar  2  Electrostatics & Solvation in Biomolecular Systems II
Mar  4  Lab 6: APBS Poisson-Boltzmann Calculations on Lysozyme
Mar  7  Proteins I: Amino Acids, Secondary & Tertiary Structure
Mar  9  Proteins II: Motifs, Folding & Homology Modelling
Mar 11  Lab 7: Folding Simulation of the TrpCage Miniprotein, Part I

Module 2: ab Initio & Semi-Empirical Quantum Mechanics

Mar 21  Basics of ab Initio Molecular Orbital Theory I
Mar 23  Basics of ab Initio Molecular Orbital Theory II
Mar 25  Lab 7: Folding Simulation of the TrpCage Miniprotein, Part II
Mar 28  Methods for Treating Electron Correlation
Mar 30  Semi-Empirical Molecular Orbital Methods
Apr  1  Lab 8: Computing the Rotational Barrier in Hydrazine
Apr  4  Density Functional Theory (DFT)
Apr  6  Quantum Mechanics/Molecular Mechanics (QM/MM)
Apr  8  Lab 9: Frontier Orbital Analysis of Regioselectivity
| Module 3: Biomolecular Modeling, Structure Prediction & Machine Learning |
|-----------------------------|---------------------------------|
| Apr 11 | Protein Structure Prediction, Engineering & Design |
| Apr 13 | Small Molecule & Protein Docking I |
| Apr 15 | Lab 10: Docking Indinavir to HIV Protease Using Autodock |
| Apr 18 | Small Molecule & Protein Docking II |
| Apr 20 | Computing Binding Rate Constants via Brownian Dynamics |
| Apr 22 | Lab 11: Diffusional Association of the Barnase-Barstar Complex |
| Apr 25 | Introduction to Convolutional Neural Networks |
| Apr 27 | Machine Learning in Computational Chemistry |
| Apr 29 | Lab 12: Protein Structure Prediction via DeepMind AlphaFold II |
| May 11 | Lab Reports & Take-Home Assignments Due |