Chemistry 430: Simulation in Chemistry & Biochemistry  Spring 2019

Class Meetings:  Monday and Wednesday, Lecture, 11:00am-Noon, 201 Lab Science  
Friday, Laboratory Sessions, 11:00am-2:00pm, 457 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 others. Many of the lab exercises target proteins, nucleic acids and other 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, useful introduction. Other useful books are listed below, and readings from these 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 targeted at advanced undergraduates, but is also suitable for 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. Basic familiarity with computers (text editing, writing small scripts or programs) is useful, but not required.

**Module 1:** Molecular Mechanics & Simulation Techniques

Jan 14  Overview of Molecular Modeling  
Jan 16  Introduction to Molecular Mechanics I  
Jan 18  Lab 1: Unix Tutorial: Using Chimera, VMD, FFE & Spartan  
Jan 21  Martin Luther King Day – No Class  
Jan 23  Introduction to Molecular Mechanics II  
Jan 25  Lab 2: Conformational Analysis of Alanine Dipeptide  
Jan 28  Potential Energy Surfaces & Optimization Methods  
Jan 30  Basics of Molecular Dynamics Simulation I  
Feb 1   Lab 3: Liquid Properties via Molecular Dynamics Simulation  
Feb 4   Basics of Molecular Dynamics Simulation II  
Feb 6   Using Molecular Dynamics to Compute Properties  
Feb 8   Lab 4: Global Optimization of Lennard-Jonesium & PolyAlanine  
Feb 11  Introduction to Monte Carlo Methods I  
Feb 13  Introduction to Monte Carlo Methods II  
Feb 15  Lab 5: Relative Hydration Free Energy of Monovalent Ions  
Feb 18  Methods for Free Energy Calculations  
Feb 20  Electrostatics & Solvation in Biomolecular Systems I  
Feb 22  Lab 6: APBS Poisson-Boltzmann Calculations on Lysozyme  
Feb 25  Electrostatics & Solvation in Biomolecular Systems II  
Feb 27  Proteins I: Amino Acids & Secondary Structure  
Mar 1   Lab 7: Homology Modeling of a Lactate Dehydrogenase  
Mar 4   Proteins II: Tertiary Structure, Motifs & Fold Classes  
Mar 6   Proteins III: Mechanism of Protein Folding  
Mar 8   Lab 8: Folding Simulation of the TrpCage Miniprotein, Part I  
Mar 11-15  Spring Break – No Class

**Module 2:** ab Initio & Semi-Empirical Quantum Mechanics

Mar 18  Basics of ab Initio Molecular Orbital Theory I  
Mar 20  Basics of ab Initio Molecular Orbital Theory II  
Mar 22  Lab 8: Folding Simulation of the TrpCage Miniprotein, Part II  
Mar 25  Methods for Treating Electron Correlation  
Mar 27  Semi-Empirical Molecular Orbital Methods  
Mar 29  Lab 9: Computing the Rotational Barrier in Hydrazine
Apr 1   Density Functional Theory (DFT)
Apr 3   Quantum Mechanics/Molecular Mechanics (QM/MM)
Apr 5   Lab 10: Frontier Orbital Analysis of Regioselectivity

Module 3: Electrostatics, Coarse Graining & Biomolecular Structure Prediction

Apr 8   Protein Structure Prediction, Engineering & Design
Apr 10  Small Molecule & Protein Docking I
Apr 12  Lab 11: Docking Indinavir to HIV Protease Using Autodock

Apr 15  Small Molecule & Protein Docking II
Apr 17  Computing Binding Rate Constants via Brownian Dynamics
Apr 19  Lab 12: Diffusional Association of the Barnase-Barstar Complex

Apr 22  Coarse Grained Molecular Modeling
Apr 24  Machine Learning in Computational Chemistry
Apr 26  Lab 13: Independent Project or Finish Previous Labs

May 8   Lab Reports & Take-Home Final Examination Due