



**Office Hours:** By an appointment.

## **SYLLABUS**

### **Course Objectives:**

The course is an introduction to computational methods for molecular modeling of biological systems such as proteins and nucleic acids. Our goal is to provide a general overview of computational quantum chemistry, molecular mechanics, and combined QM/MM calculations as applied to molecules of biological interest. The objective of the course is to give a basic understanding of computational chemistry and molecular mechanics methodologies, and how to apply these computational techniques to study biologically relevant problems. Please visit the course home page for details:

[www.ccr.buffalo.edu/display/~mfrein/Computer+Modeling+of+Biological+Systems](http://www.ccr.buffalo.edu/display/~mfrein/Computer+Modeling+of+Biological+Systems)

### **Course Form:**

The course is in the form of a computational laboratory, based on Windows PC work-stations, Q-Chem/AMBER software for calculations and Spartan/Accelrys software for visualization, utilizing computing resources of UB's Center for Computational Research ([www.ccr.buffalo.edu](http://www.ccr.buffalo.edu)).

### **Course Outline:**

#### **I. Quantum Mechanical Theory.**

1. Schrodinger Equation.
2. Born-Oppenheimer Approximation.
3. Hartree-Fock Theory.
4. Basis Set and Molecular Orbitals.
5. Group Theory.
6. Electron Correlation.
7. Density Functional Theory.

#### **II. Quantum Mechanical Applications.**

1. Calculations of molecular properties of amino acids and DNA base pairs, including: optimal geometry, dipole moment, atomic charges, electrostatic potential, electronic density, molecular oscillations, infrared and raman spectra.

2. Calculations of hydrogen bond interactions in amino acids and DNA base pairs: hydrogen bond energy, hydrogen bond geometry, tautomers, conformational analysis, hydrogen bond oscillations, hydrogen bond network in proteins.
3. Calculations of NMR chemical shielding in atoms involving amino acids and DNA base pairs.
4. Calculations of chemical reactions involving amino acids and DNA base pairs: potential energy surface, zero-point energy, reaction coordinates, transition states.
5. Electronic transitions and electronic spectra of amino acids and DNA base pairs: electronic transition moments, excitation energies, UV spectra.

### III. Molecular Mechanical Theory.

1. Newton's Equations.
2. Potential Functions.
3. Parameters Evaluation.
4. Temperature Control.
5. Energy Minimization.
6. Molecular Dynamics with Stochastic Boundary Conditions.
7. Molecular Dynamics with Periodic Boundary Conditions.

### IV. Molecular Mechanical Applications.

1. Calculations of molecular mechanical parameters involving amino acids and DNA base pairs: distances, angles and dihedral angles between atoms, force constants, atomic charges, van der Waals constants.
2. Energy minimization of amino acids, DNA base pairs, simple proteins and nucleic acids, constrain minimization.
3. Molecular mechanical dynamics with stochastic boundary conditions of proteins in water solution, constrained dynamics.
4. Molecular mechanical dynamics with periodic boundary conditions of proteins and nucleic acids, temperature control.
5. Calculating properties from molecular mechanical trajectories.

### V. Combined QM/MM Theory.

1. Interaction between QM and MM particles.
2. Link atom approximation.
3. Lennard-Jones Potential.

### VI. Combined QM/MM Applications.

1. Calculations of parameters describing the interaction between QM and MM atoms in proteins and nucleic acids.
2. Geometry optimization of active-sites in proteins.
3. Calculations of molecular properties of active-sites in proteins: electronic density, electrostatic potential, molecular oscillations, electronic states.

4. Calculations of protein-ligand interactions: ligand docking, ligand-water interactions, ligand-protein electrostatic potential, chemical reactions between ligands and proteins.

**Final Exam:** Oral presentation of individual projects.

**Literature:**

- Ab Initio Molecular Orbital Theory, W.J. Hehre, L. Radom, P.v.R. Schleyer, J.A. Pople, Eds., John Wiley @ Sons Inc. 1986.
- Modern Quantum Chemistry: Introduction to Advanced Electronic Structure Theory, A. Szabo, N.S. Ostlund, Dover Publications Inc., 1996.
- Chemical Applications of Group Theory, F.A. Cotton, John Wiley @ Sons, Inc. 1990.
- Dynamics of Proteins and Nucleic Acids, J.A. McCammon, S.C. Harvey, Cambridge University Press, Cambridge, 1987.
- Proteins: A Theoretical Perspective of Dynamics, Structure, and Thermodynamics, C.L. Brooks III, M. Karplus, B.M. Pettitt, John Wiley @ Sons Inc. 1988.
- Molecular Modeling Principles and Applications, A.R. Leach, Prentice Hall, 2001.
- Quantum Chemistry, M. Freindorf, Electronic Textbook (Pdf), University at Buffalo, 2006.
- Molecular Mechanics, M. Freindorf, Electronic Textbook (Pdf), University at Buffalo, 2006.
- Combined QM/MM method, M. Freindorf, Electronic Textbook (Pdf), University at Buffalo, 2006.