West Virginia University - School of Pharmacy (Rev 08/21/2005)
Intro to Molecular Modeling - PHAR 780
Fall 2003 (4 cr hr)

Course Coordinator

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Other Faculty

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Class times: Lecture: T/Th 9:00-10:00a, 1128C HSN
Lab: W/F, 9:00a-12:00n, Rm 1128 HSN

Website: http://www.hsc.wvu.edu/sop/compchem/index.htm/

Restrictions: Graduate student status or permission of the instructor

Required Text

N/A

Suggested Textbooks

General

1) Leach, A.R., "Molecular Modeling: Principles and Applications", 2nd edition, Prentice Hall, Harlow, England, 2001.

2) "Computational Biochemistry and Biophysics", Becker, O.M., MacKerell, Jr., A.D., Roux, B., Watanabe, M, Eds., Marcel Dekker, New York, Basel, 2001.

3) Young, D., "Computational Chemistry: A practical Guide for Applying Techniques to Real World Problems", John Wiley and Sons, New York, Chichester, 2001.

Proteins

1) Proteins: Structures and Molecular Properties (2nd Edition) by Thomas E. Creighton, 1992.

<u>Nucleic Acids</u>

1) Principles of Nucleic Acid Structure by Wolfram Saenger, 1996

<u>Advanced Quantum Mechanical</u>

1) Modern Quantum Chemistry: Introduction to Advanced Electronic Structure Theory. by Attila Szabo, Neil S. Ostlund, 1996.

2) Cramer, C.J., "Essentials of Computational Chemistry: Theories and Models", John Wiley and Sons, Chichester, England, 2002.

Other Required Items

N/A

Catalog Description

Introduction to Molecular Modeling describes computational methods for chemical and biological problems and is designed to enable the student to use molecular modeling methods as a research tool in their current or future research activities.

Course Overview

This special topics course is offered during the Fall semester (odd numbered years only). It is open to all graduate students though enrollment will be limited. The objective of the course is to enable the student to use molecular modeling as a research tool for their current or future research activity. Students whose current research requires or would benefit from molecular modeling are encouraged to work on their research problems in this course. Students without a specific, research related problem will be provide with one.

The course will be taught as a mix of lecture/discussion and laboratory, with an emphasis on laboratory work. Initially, lecture will provide the student with necessary tools for using the molecular modeling workstations (Windows, Linux, and Unix workstations) and introduce some fundamental concepts needed to understand and apply molecular modeling methods to research problems. Later, the classroom work will provide students the opportunity to discuss the research problem they are working on, the problems they have encountered, and solutions to these problems.

The topics covered in the course begin with an introduction to Unix operating systems. Next, modeling methods for oligonucleotides and proteins are described and finally, methods appropriate for small molecules are covered. Selection of software for a particular problem (small molecules versus large, biological molecules) is also discussed.

Educational Outcomes

1) The Student will gain an understanding for the hardware and software typically used for molecular modeling and computation chemistry.
2) Describe the different approaches to molecular modeling and select an appropriate method for a given problem.
3) Apply molecular modeling methods appropriately to a research problem.
4) Evaluate methods used for a computational problem and the resulting structures obtained.

Ability-Based Outcomes

1) Operate computers running different operating systems including Windows, Linux, and Unix.
2) Describe how molecular modeling packages for biological molecules fundamentally work and those used for small molecules.
3) Generate and energy minimize structures of oligonucleotides and proteins using the appropriate molecular modeling software
4) Optimize the structure of small molecules using the appropriate computational chemistry software.

Examinations and Grading Policies

Evaluation

Exams	Three (3) exams	50 pts each	150 pts
Lababoratory Reports	Ten (10) Laboratory Reports	10 pts each	100 pts
Final Course Project	One Project	100 pts	100 pts
Total			350 pts

Course Grades:

Grades will be based on the total points earned on the examinations listed above as follows:

A	(90-100%)
B	(80-89.9%)
C	(70-79.9%)
D	(60-69.9%)
F	(< 60%)

Student Responsibilities and Attendance:

Regular attendance at lectures is expected although roll will not be taken. Attendance in the laboratory portion of the course is required and roll will be taken. Failure to attend lab, in lieu of a bonafide medical excuse or other legitimate reason beyond the control of the student will result in a 10%

reduction of the score received for the laboratory, which still must be conducted on the students own time. Students who miss lectures are responsible for getting the material and any announcements from a classmate. With respect to quizzes, students are responsible for all text book material assigned and for lecture material covered (handouts are considered material covered). Makeup quizzes will be given only if the student has a bonafide medical excuse or other legitimate reason beyond the student's control. Time and type of makeup quiz will be at the convenience of the instructor.

Social Justice Statement

West Virginia University is committee to social justice. We concur with that commitment and will foster a nurturing learning environment based upon open communication, mutual respect, and non-discrimination. Our University does not discriminate on the basis of race, sex, age, disability, veteran status, religion, sexual orientation, color or national origin. Any suggestions as to how to further such a positive and open environment in this class will be appreciated and given serious consideration. If you are a person with a disability and anticipate needing any type of accommodation in order to participate in this class, please advise us and make appropriate arrangements with Disability Services at 293-6700.

Course Outline (Draft) ***Week of***

I) Introduction (1)[1] 8/22 (Gannett)

II) Computer System Navigation (1) 8/22 (Gannett)

A) Basic Unix Commands
B) GUI Interface

Lab 1 - Introduction to Unix (CCMM_Lab1)[2]

III) Basic Molecular Modeling Concepts (2) 8/29 (Gannett)

A) Fundamental Equation
B) Qualitative Conformational Analysis
C) Force Fields

Lab 2 - Modeling Input Files - Amber Graphical Editor (CCMM_Lab2)

IV) Energy Minimization and Molecular Mechanics (2) 9/5 (Gannett)

A) Basic Parameters
B) Programs and Routines

Lab 3 - Building Small Molecules and Molecular Mechanics Energy Minimization (CCMM_Lab3)

VI) Molecular Dynamics (2) 9/12 (Szklarz)

A) Molecular Mechanics (MM) vs Molecular Dynamics (MD)
B) Approaches
C) Simulating flexibility

Lab 4 - Building DNAs and Molecular Mechanics Energy Minimization (Amber)

V) DNA -Molecular Mechanics Energy Minimization (2)
9/19 (Gannett)

A) Basic Parameters
B) *In vacuo* vs solvate DNAs
C) Interpretation of the results

Lab 5 -Building and Molecular Mechanics of DNAs Containing Base-Pair Mis-

Matches (CCMM_Lab7)

VII) Molecular Modeling of DNA - Molecular Dynamics I (2) 9/26 (Gannett)

A) Molecular Mechanics verses Molecular Dynamics for DNA
B) How to set up and run MD for DNAs
C) How to analyze the results.

Lab 5 - Molecular Dynamics Energy Minimization (Amber) I

VIII) Molecular Modeling of Modified DNA (2) 10/3 (Gannett)

A) Construction of Modified DNA bases/DNAs
B) Force-Field parameter generation.
C) Energy Minimization

Lab 6 - Molecular Dynamics Energy Minimization (Amber) II

IX) Molecular Modeling of Proteins - Structural Considerations (2) 10/10 (Szklarz)

A) Peptide bonds vs. protein conformation
B) Secondary structures
C) Dominant effects in protein folding

Lab 7 - InsightII: Viewing molecules, building small molecules and mimimizing their energy

X) Molecular Modeling of Proteins - Simulating Flexibility (2) 10/17 (Szklarz)

A) Protein motion and flexibility
B) Energy Minimization and Molecular Dynamics
C) Limitations of protein dynamics

Lab 8 - InsightII: Building and modifying peptides, minimization and molecular dynamics simulations

XI) Homology Modeling (2) 10/24 (Szklarz)

A) Construction of Model
B) Evaluation and utilization of protein models

Lab 9 - Homology Modeling and Docking

XII) Docking (2) 10/31 (Szklarz)

A) Docking programs
B) Limitations

Lab 9 - Homology Modeling and Docking (Continued)

XIII) Free Energy Calculations (4) 11/7-11/14 (Demchuk/Gannett)

A) Review of General Thermodynamics
B) Review of Statistical Mechanics
C) Free Energy Calculations

XIV) Quantum Chemistry (4) 11/28 and 12/5 (Stolzenberg)

A) *Ab initio* calculations - Introduction
B) Compromises and approximations
C) Basis sets and related topics

Lab 10 - Sybyl and CoMFA
Lab 11 - Autodock
Lab 12 - Sprout
Lab 13 - Molecular Modeling of Proteins with Amber

XIV) Student Presentations of Course Projects[3] (2) 12/12 (Student Presentations)

[1]Numbers in parenthesis refer to the approximate number of 50 minute lectures.
[2]Each laboratory requires two, three hour laboratory periods.
[3]Students and faculty can chose one of the three areas to work. Individual research projects can also be worked on (with or without Homology modeling, Docking, or QSAR).