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BIOL 952: Introduction to Molecular Modeling

Instructor: Krzysztof Kuczera, 5090 Malott, 864-5060, kkuczera@ku.edu
Semester: Spring 2011
Time & place: TR 8: 30–9: 20, Room 2025 Haworth
Line #: 69214/69215 **Credit hours** : 3

The course consists of three parts: lecture, computer laboratory and student presentations. The lectures will be held in class, and will cover theory background ("theoretical" lectures) and technical background ("laboratory" lectures). The two-part computer laboratory will be performed in small groups on UNIX computers in the MGM Laboratory. The first part of the lab is a set of introductory exercises to be taken by all students. The second part contains specialized projects in three "tracks", designed for students with biological, chemical and chemical engineering interests. The instructor and/or other qualified personnel will be available for consultation during laboratory hours and at other times as needed. Finally, the lecture meetings at the end of the semester will be employed for 10-15 minute student presentations of selected research articles from the general field of modeling.

The goal of the course is to introduce students to computing and molecular modeling techniques so that they will be able to perform standard computational tasks as part of their research. There is no official textbook; the book by A. R. Leach is recommended. Some useful references are given below. There will be no separate exams in the class. The evaluation of performance will be based on laboratory reports, consisting of descriptions of methods, goals and results from the computer laboratory exercises and the literature presentation.

The whole class is organized around a central Web site, at

http: //oolung.chem.ku.edu/~kuczera/Public/web/html/molmod.html

This site will contain all course materials: theoretical and laboratory lecture notes, tutorials for major software, manuals for computer laboratory exercises, modeling case studies as well as a mini-manual for UNIX.

THEORETICAL LECTURE (outline)

1. **Introduction.** Modeling with potentials (2 sessions).
2. **Molecular mechanics.** Describing molecules; Force fields: intra– and intermolecular terms; Algorithms : energy evaluation & minimization, conformational search, docking, constraints, molecular vibrations. (5-6 sessions).
3. **Molecular dynamics and Monte Carlo methods.** Basic algorithms; Trajectory analysis; Applications; Special algorithms – boundaries, constraints, constant P,T, statistical mechanics. (5-6 sessions)
4. **Molecular modeling.** Using bioinformatics databases; Basic macromolecular structure analysis; Sequence alignment; Homology modeling and threading; Docking; (5-6 sessions)
5. **Quantum chemistry.** (2-3 sessions)
6. **Student presentations and special topics**. (4-6 sessions, may include finals period)

LABORATORY LECTURE (tentative topics)

1. Introduction to UNIX, computer workstations, networking and the WWW
2. BIOLAB: Introduction to modeling software
3. QUANTA/CHARMM : describing molecules
4. The Brookhaven Protein Data Bank
5. Cambridge Structural Database
6. QUANTA/CHARMM : structural and energetic dictionaries
7. QUANTA/CHARMM : calculating energy
8. QUANTA/CHARMM : energy minimization
9. QUANTA/CHARMM : molecular vibrations
10. QUANTA/CHARMM : manipulating molecules
11. QUANTA/CHARMM: Conformational search
12. AutoDock, DOCK, FTDOCK: Docking
13. LIGPLOT, NACCESS, HBPLUS: structure analysis
14. MODELLER: sequence alignment and homology modeling
15. CHARMM : molecular dynamics
16. CHARMM : solvation
17. GROMACS : flexible tool for molecular dynamics simulation and analysis
18. Gaussian: energy, optimization, vibrations
19. Gaussian: binding energies and transition states
20. MCCCS: advanced statistical mechanics

COMPUTER LABORATORY

GENERAL INTRODUCTION

0 Setting up computer accounts, lab groups and workstations (Week 1)
1 Introduction to UNIX and SYBYL program (Week 2)
2 Exploring the Protein Data Bank (Week 3)
3 RasMol and MolScript (Week 4)
4 Molecular graphics for screen, paper and Web (Week 5)
5 Molecular energy surfaces with QUANTA/CHARMM (Week 6)
6 Molecular dynamics with GROMACS (Week 7)
7 Introduction to GAUSSIAN (Week 8)

COMPUTATIONAL BIOCHEMISTRY TRACK: A

8A Normal mode analysis : water (Week 9)
9A Conformational search : energy minimization (Week 10)
10A Conformational search : molecular dynamics (Week 11)
11A CHARMM: MD simulation of a small protein : BPTI in vacuum (Week 12)
12A CHARMM: MD simulation of solvated peptide (Weeks 13-14)
13A Individual student-generated projects (Weeks 15–).

MOLECULAR MODELING TRACK: B

8B Bioinformatics: using the Web and the Cambridge Structural Database (Week 9)
9B LIGPLOT, NACCESS, HBPLUS : analyzing macromolecular structures (Week 10)
10B AutoDock and DOCK: docking (Week 11)
11B MODELLER: sequence alignment (Week 12)
12B MODELLER: homology modeling (Week 13-14)
13B Individual student-generated projects (Weeks 15–).

CHEMICAL ENGINEERING TRACK: C

8C Thermodynamics: vapor-liquid equilibria (Week 9)
9C Thermodynamics: alkane adsorbtion on zeolites (Week 10)
10C Kinetics: transport coefficients in solution (Week 11)
11C Quantum chemistry: electronic structure calculations - part 2 (Week 12)
12C Quantum chemistry: ligand binding to catalyst (Week 13-14)
13C Individual student-generated projects (Weeks 15–).

LITERATURE (in order of usefulness)

1. A. R. Leach, *Molecular Modeling. Principles and Applications*, Pearson Education Ltd., 2nd Ed., 2001.
2. A. K. Rappe and C. J. Casewit, *Molecular Mechanics Across Chemistry*, University Science Books, 1997.
3. M. Karplus, G.A. Petsko, *Molecular dynamics simulations in biology*, Nature,347,631–639 (1990).
4. W.F. van Gunsteren and H.J.C. Berendsen, *Computer Simulations of Molecular Dynamics: Methodology, Applications and Perspectives in Chemistry*, Angew. Chem. Int. Ed. Engl., 29, 992–1023, 1990.
5. C.L. Brooks III, M. Karplus, B.M. Pettitt, *Proteins: A Theoretical Perspective of Dynamics, Structure, and Thermodynamics*, John Wiley and Sons, New York, 1988.
6. J.A. McCammon and S.C. Harvey, *Dynamics of Proteins and Nucleic Acids*, Cambridge University Press, 1988.
7. G. Todino, J. Strang and J. Peek, *Learning the UNIX operating system*, 3rd Ed, O'Reilly & Associates, 1993.
8. J. M. Haile, *Molecular Dynamics Simulation. Elementary Methods*, John Wiley and Sons, New York, 1992.
9. Allen & Tildesley, *Computer Simulations of Liquids*, Clarendon, Oxford, 1987.
10. Frenkel & Smit, *Understanding Molecular Simulation*, Academic Press, San Diego, 1996.