Computational Biophysics and Structure Based Drug Discovery

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Class sessions on Wednesdays, 3:00 – 4:50 PM

Overview

The goal of this course is to enable students to gain an understanding of protein structure and dynamics, set up and run molecular dynamics simulations, and search for small molecule inhibitors using state-of-the-art methods in computer-aided drug discovery.

Course Description

This graduate-level seminar course will walk students through the basic techniques of biomolecular simulation and computer-aided drug design, including application of massively parallel molecular dynamics simulations and associated analysis techniques to enable new discoveries within the vast quantity of digital data, such as finding new potential drug leads through virtual screening and small molecule docking. Lectures on course concepts will be closely combined with hands-on tutorials that allow the practical application of computational methods and statistical data analysis in a project-based format. Students will be granted access to the national supercomputers centers as well as local high performance computing cluster resources to run their simulations and analyze the resulting data.

Course Outcomes and Objectives

At the conclusion of the course, students shall be able to:

1. Understand the basic principles and concepts of protein structure, molecular dynamics simulations, and computer-aided drug discovery
2. Set up and run their own protein / biomolecular system MD simulation on both personal computers as well as cluster architectures
3. Perform and understand the interpretation of basic (statistical) analysis techniques on the resulting MD trajectories
4. Perform and understand the results of a virtual screening experiment

Optional Textbooks

There are no required textbooks for this seminar course. However, a list of helpful reading materials will be presented during course lectures, and the broadest references are included here:

Introduction to Protein Structure: Second Edition, by Carl Branden and John Tooze
http://www.amazon.com/Introduction-Protein-Structure-Carl-Branden/dp/0815323050

Molecular Modelling: Principles and Applications, by Andrew Leach
http://www.amazon.com/Molecular-Modelling-Applications-Andrew-Leach/dp/0582239338

Molecular Modeling and Simulation, by Tamar Schlick
http://www.amazon.com/Molecular-Modeling-Simulation-Tamar-Schlick/dp/038795404X

Course Grading and Schedule
This is a project-based course with no formal exams. Attendance and class participation in the 10 class sessions constitute a substantial portion of the final grade.

Assessment	Contribution
Attendance	20%
Participation	20%
Project	60%

Week	Topic	Hands-on session
1	Introduction to protein structure and visualization	VMD tutorial
2	Introduction to molecular dynamics simulation methods, part 1	MD tutorial, part 1
3	Introduction to molecular dynamics simulation methods, part 2	MD tutorial, part 2
4	Introduction to molecular dynamics analysis methods	MD analysis tutorial
5	Force fields and parameterization	Parameterization module
6	Computer-aided drug design and docking methods	AutoDockTools tutorial
7	Ensemble-based methods, including the relaxed complex scheme	Relaxed complex tutorial
8	GPU computing	Molecular Movies tutorial
9	Project time and consultation	Project
10	Project time and consultation	Project
11	Project presentations	

Course Philosophy
The course will be structured around ability-based education. Students will integrate knowledge, attitudes, and skills in a variety of ways to accomplish key outcomes.

Ability-based education procedures include:
- Clearly define the ability outcome and objectives expected
- Give students multiple opportunities to achieve the course objectives
- Provide clear criteria so students can know how well they are performing
- Provide feedback from the faculty, peers, and self to determine how successfully students are meeting the criteria