MSc in Bioinformatics for Health Sciences

IEO. Information Extraction from "omics" Technologies

Syllabus Information

Academic Course: 2018/19

Academic Center: 804 - Official Postgraduate Programme in Biomedicine

Study: 8045 – Bioinformatics for Health Sciences - MSc

Subject: 30170 – MSI. Molecular Simulations

Credits: 5.0

Course: 1st

Teaching languages: English

Teachers: Jana Selent

Teaching Period: 3rd term

Presentation

Molecular Simulations can bridge static representations of biomolecular structures (Structural Bioinformatics) to structure-guided drug discovery and design (Computer Assisted Drug Discovery). The MSI course shows the student how to use structural information, along with basic physical laws and statistical thermodynamics tools, to obtain the relevant free energy values that will be comparable with several types of experimental information. The focus of this course is to provide the tools, knowledge and practice to perform biochemical experiments on proteins and other molecules (drugs) in-silico using molecular dynamics simulations.

The subject is based on the understanding of key methodological concepts and tools and on the application of common software used in labs around the world. The course will be evaluated by means of an individual exam based on short questions/answers and some problems. Additionally, a substantial percentage of the final qualification will also be based on group projects continuously evaluated focusing on homework assignments and hands-on practical assignments.

Associated skills

General competences:

Instrumental:

1. Proficient reading/writing/listening scientific English.

2. Knowledge of office software to do quality scientific presentations and reports.

Interpersonal:

1. Group work

2. Ability to solve a given problem by yourself

Systemic:

1. Analysis and synthesis abilities
2. Ability to search for information

Specific competences:

1. Practical knowledge on performing molecular dynamics simulations
2. Practical knowledge on analyzing molecular dynamics simulations
3. Capacity to design and prepare a molecular simulation experiment
4. Practical knowledge of a molecular visualization software

Learning outcomes

To understand and apply algorithms and methods currently used in molecular simulations to perform computational experiments.

Prerequisites

Previous basic programming skills and basic understanding of structural biology

Contents

Class 1: Introduction to molecular dynamics (theory)

Notions of structural biology (Proteins, aminoacids, atoms, structure)

Concept of classical dynamics

Class 2: Visualization and basic analysis of simulations (hands-on)

VMD software: Load molecule and navigate it, representations, selections (resname, name, type, resid), within of, same residue as, loading trajectories

Example of Tcl scripting (atomselect, measure)

Class 3: GROMACS - Molecular simulation software package

Setting up a simulation system: generate topology, solvate, add ions, energy minimization, equilibration, run production

Class 4: Application of MD to a water solvated Protein-Ligand Complex (hands-on)

Setting up and analysing the T4 lysozyme L99A/M102Q in complex with a ligand

Class 5: Application of MD to a membrane proteins (hands-on)

Using the CHARMM-GUI membrane builder

Class 6: Comparative MD data analysis tools (hands-on)

Class 7: Digest on classical simulations (seminar)

Class 8: Beyond classical MD: enhanced sampling (theory)

Metadynamics, replica exchange, umbrella sampling

Class 9: Sampling problem: Metadynamics (hands-on)

Setting up and running a metadynamics calculation using PLUMED

Playing with collective variables

Estimating the error in free-energies using block-analysis

Class 10: Sampling problem: Umbrella sampling (hands-on)

Setting up simulations with restraints

Using multiple-restraint umbrella sampling simulations to enhance the transition across a free-energy barrier.

Calculating weighted averages and free-energy profiles

Class 11: Sampling problem: Replica exchange (hands-on)

Setting up and running a parallel tempering (PT) simulation using PLUMED

Calculating free energies from the simulation

Class 12: Digest on the enhanced sampling (seminar)

Class 13-14: Progress of final project

Class 15: Project defense

Teaching methods

Lectures during classes and hands-on sessions.

Evaluation

General assessment criteria:

The evaluation will consist of a final exam at the end of the course, worth ~50%, the evaluation of the exercises performed during the course (~20%) and the final project at the end of the course (~30%).

Grading system

Grades are between 0 and 10 and an overall 5 is needed to pass

Bibliography and Information Resources

The future of molecular dynamics simulations in drug discovery, David W. Borhani & David E. Shaw

VMD manual

GROMACS manual

PLUMED manual