UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

COURSE SYLLABUS

Computational Tools for Bioinformatics

2425-1-F0802Q045

Aims

The goal of the course is to enable master students to get deep knowledge of the most popular computational methodologies employed in the context of structural bioinformatics. More specifically, both static properties and dynamic behavior of biological macromolecules will be addressed and characterized in detail. The course also aims to give a comprehensive survey of the implementation of such methodologies in the most popular software and computational platforms.

Knowledge and understanding. At the end of the course, the student will:

- know the computational strategies generally used to discern structure-function relationships in biological macromolecules.
- comprehend the algorithms on which such computational strategies rely.
- understand the differences among computational methods and tools, both from theoretical and practical standpoints, and their role in the study of moelcular systems with biological/industrial relevance.
- choose and use autonomously software and web-server for conformational search and molecular recognition simulations (protein-ligand, protein-peptide, protein-protein)

Applying knowledge and understanding.
At the end of this training activity, the student will be able to apply the gained knowledge, using it to recognize (theoretically and practically) potentialities and (eventual) limits of the bioinformatic strategies seen during the course.

Making judgments.
At the end of the course, the student will be able to choose the most suitable computational method to address a specific biological-chemical issue. He will be also able to critically analyze results obtained from computational calculations and to interpret them properly.

Abilità comunicative.
This training activity will allow the student to express himself adequately, and with scientific language, in the

explanation of the various addressed topics.

Learning skills.
At the end of the course the student will dispose of all the tools that are necessary to apply his knowledge to address issues others than those presented during the course. He will be able to plan bioinformatic calculations on the basis of his gained knowledge, together with skills of literature reading and understanding.

Contents

- The computational modelling of protein structure.
- Relationship between molecular structure and energy in molecular mechanics (MM).
- Hints of relationship between molecular structure and energy in quantum mechanics (QM) and Hybrid techniques (QM/MM).
- Global and local search algorithms, in theory and practice
- Molecular Docking (protein-ligand, protein-protein, covalent docking, protein-peptide), in theory and practice
- Simulation techniques.
- Computational protein design

Detailed program

- Introduction to structural bioinformatics: development, foundations and its applicability; hints of computer science and the concept of computability; computational modeling of the structure of biological macromolecules; the evaluation of the goodness of a molecular structure and its preparation for modeling.
- Relationship between molecular structure and energy: degrees of freedom, Z-matrix and symmetry; topological / mathematical analysis of the PES (definition of minimum point and transition state).
- Energy in molecular mechanics: determination of the terms of a force field (FF); comparison between different FFs and their applications; optimization of the FF parameters.
- Energy in quantum mechanics (outline) and overview of hybrid techniques (QM / MM, ONIOM) for the study of the reactivity of biological systems (with applications in catalysis and drug design). Practical QM / MM tutorial.
- Local optimizers: zero, first and second order algorithms (simplex, grid search, univariate search, steepest descent, conjugate gradients, Newton-Raphson (NR) and quasi-NR); transition state search algorithms for estimating the rate constants of chemical-biological processes. Practical exercise: use of different algorithms to search for a local minimum, in order to rationalize its performance on the basis of the theory.
- Global optimizers: deterministic and stochastic algorithms compared (multi-start, Floudas, Monte Carlo Metropolis, Simulated Annealing, evolutionary algorithms). Practical exercise: stochastic algorithms for the search for a global minimum and for the folding of a small peptide.
- Molecular Docking Algorithms: the computing architecture; search algorithms (stochastic and systematic); the scoring functions implemented in the most popular software; the potential energy grid; covalent docking; macromolecule-macromolecule docking and its applications; survey on the most popular software and web servers; practical information on using the programs. Practical exercises: docking with different FFs in order to understand the limits and potential of the technique; covalent docking with different applications (drug design / industrial); protein-protein docking and in silico mutagenesis using web-servers.
- Molecular Dynamics Theory: basics of statistical thermodynamics, thermodynamic ensembles; the integration of Verlet and other integration algorithms; thermostats and barostats; trajectory analysis and simulation interpretation; hints of coarse-grained. Tutorial / exercise: different dynamics protocols compared; how to use dynamics to obtain biological information and to calculate thermodynamic quantities.
- Protein Design: basic approaches for de novo design of proteins; machine learning-guided protein design (examples); useful webserver; applications.

Prerequisites

Background.
Specific knowledge of other topics is not required. All the theory necessary to deal with the various topics will be taken from scratch. It is preferable being motivated toward in silico investigations of molecular basis of chemical-biological processes.

Prerequisites. None

Teaching form

-14 two-hour lectures, in person, Delivered Didactics
-7 two-hour practical classes, in person, Interactive Teaching

Textbook and teaching resource

Slides. Available at the e-learning platform of the course.
Handouts. Available at the e-learning platform of the course.
Bibliography. Selected scientific papers and reviews.

Suggested textbooks

“Bioinformatica” , Stefano Pascarella, Alessandro Paiardini;

"Molecular Modelling", Andrew Leach.

"Introduction to Computational Chemistry", Frank Jensen (chapter 2).

Semester

Second semester

Assessment method

The exam consists in the preparation of a written report on some of the exercises / practical demonstrations carried out in class. This report will then be discussed orally.

Office hours

Contact: on demand by email to the lecturer.

Sustainable Development Goals