MSc in Bioinformatics for Health Sciences

CAD. Computer-Assisted Drug Discovery

Syllabus Information

Academic Course: 2018/19

Academic Center: 804 - Official Postgraduate Programme in Biomedicine

Study: 8045 – Bioinformatics for Health Sciences - MSc

Subject: 30179 – CAD. Computer-Assisted Drug Discovery

Credits: 5.0

Course: 1st

Teaching languages: English

Teachers: Manuel Pastor, Jordi Mestres, Jana Selent and Ismael Zamora

Teaching Period: 3rd term

Presentation

In modern drug discovery and development, computational methods play a central role. They are applied in the search of novel targets as well as at different stages of hit and lead finding and optimization.

In this course we aim to provide the student with an overview of the most important computational techniques and to put them in a general context.

Associated skills

General Competences:

- Understand how computational methods are applied in pharmaceutical research.

Specific competences:

- Understand the field of application of most common computational methods within the drug-discovery pipeline.
- Ability of see a drug from diverse points of view (chemical, computational, pharmacological, toxicological, physico-chemical).
- Understand the language of other professional (medicinal chemist, pharmacologist) working in the drug discovery and development field.
- Use common tools for:
    - store, manage, visualize and convert (small) molecular structures.
    - manage drug information and knowledge.
    - carry out SBDD.
    - carry out QSAR and 3D QSAR.
    - carry out Virtual Screening.

Learning outcomes

Student successfully completing this course:

- Have a general understanding of the drug discovery and development process.
- Know and understands the rationale and applicability of different computational techniques in the drug discovery and development process.
- Have a clear understanding of the advantages, disadvantages and limitations of diverse computational techniques.
- Have critical abilities needed to choose the most suitable computational technique for addressing a certain practical problem.
- Communicate efficiently with other professionals involved in the field of drug discovery and development.

Contents

The course contents are divided in five Units, starting with an introduction to the subject, providing essential background information required to understand the course, and following with blocks covering the most common methodologies.

Unit 1: Introduction to drug discovery and development

1.1. Overview of the drug discovery and development process and the role of computational methods. Objectives of the course.

1.2. Elements of medicinal chemistry.

- Role of chemistry in drug design.
- Inspiration for new products: natural products, natural ligands and pre-existing drugs.
- Paradigm changes in drug discovery.
- Combinatorial chemistry and HTS.
- Drug likeness.

1.3. Elements of molecular pharmacology.

- Concept of receptor and target.
- Receptor binding and activation.
- Ligand-receptor interaction, non-covalent bonds.
- Ligand into the binding site.
- Formats for small molecule representation.

1.4. Elements of Pharmacology.

- Role of Pharmacology in modern drug discovery and development.
- Affinity. Saturation and competition studies.
- Effect: functional studies. Pharmacological screening. Screening against multiple targets. In vivo screening.
- Automatization of screening processes (HTS and HCS).

1.5. Elements of Pharmacokinetics.

- The ADMET process.
- Main physiological process involved in ADMET.
- Strategies for characterizing the ADMET properties of a drug candidate.
- Interspecies ADMET transferability.

Unit 2: Knowledge management

2.1. Information systems in drug discovery.

- Computational resources for storing, searching and retrieving information in the field of drug discovery.
- Public databases containing information for drug discovery and development.

Unit 3: Structure-Based Drug Design.

3.1. Structure-based Drug Design (SBDD).

- 3D molecular structures. Conformational analysis.
- Docking.
- De-novo ligand design.
- Scaffold hopping.
- The analysis of protein-ligand interactions.

Unit 4: QSAR and related methodologies

4.1. QSAR and 3D-QSAR

- The QSAR approach.
- Classical and 3D-QSAR methods.
- Molecular descriptors and machine learning methods (MLR, PLS).
- Interpreting a 3D-QSAR model.

4. 2. In silico ADME.

- In silico prediction of ADME properties.
- Prediction of metabolism.

Unit 5: Virtual screening

5.1. From virtual chemical screening to virtual pharmacological profiling.

- Compound acquisition.
- Chemical libraries.
- Virtual chemical screening.
- Virtual biological profiling.

Teaching methods

Approach and general organization of the subject

Drug discovery is a multi-disciplinary subject with a clear practical orientation. The subject is introduced with an overview of the drug discovery and development process followed by an introduction to several disciplines, the understanding of which is essential for the rest of the course: elements of Medicinal Chemistry, Molecular Pharmacology, Pharmacokinetics. The rest of the course contents are organized in four blocks: Knowledge Management, Structure-Based Drug Design, QSAR and related methodologies and Virtual Screening, each one representing a family of computational methods commonly used in drug design and development.

Training activities

Teaching activities use one of the following formats:

- Theoretical lessons. Explanation of the topics by an expert with the support of Power Point presentations. All the material used in theoretical lessons is uploaded beforehand into the course intranet.
- Hands-on. Guided practical work on diverse computational methods. The work is individual, guided by an step-by-step protocol, and is carried out at the classroom with the individualized support of a teacher. The results of the hands-on sessions are reported in a document that is used for evaluation.
- Seminars. Students work in small groups to prepare a presentation on selected topics, using the material provided or any other that they obtain on their own. The topic is presented orally in front of all the class, under the supervision of a teacher that acts as moderator, and discussed in deep. The quality of the seminars (presentation and general discussion) is evaluated for grading the class.

Attendance to all teaching activities is compulsory. Attendance to hands-on sessions and seminars is controlled using a signature form.

Evaluation

Assessment system

The students are evaluated using two instruments

A. Evaluation of their participation in seminars and hands-on sessions.
B. A written exercise, including short questions focused on the most important contents of the course, simple practical problems (choosing methods, interpret results, solve a practical problem) or critical analysis of a given situation.

No second round of the written exercise or any other instrument is applied to the students not reaching the overall pass grade.

Grading system

The relative weight of these two above instruments in the final mark is 30% for A (the seminars and hands-on) and 70% for B (the written exercise).

Final marks will range from 0.0 to 10.0. A minimum grade of 5.0 is required to pass the course.

The evaluation will be divided in two parts, with percentages of the total grade indicated in parenthesis:

Bibliography and Information Resources

- Las Bases farmacológicas de la terapéutica / Goodman & Gilman ; editor: Laurence L. Brunton ; editores asociados: Bruce A. Chabner, Björn C. Knollmann
- Burger's medicinal chemistry and drug discovery / Alfred Burger
- Drug design course : a one-day course / Hugo Kubinyi
- Handbook of essential pharmacokinetics, pharmacodynamics and drug metabolism for industrial scientists [Recurs electrònic] / Younggil Kwon
- Introducción a la química farmacéutica / coordinación: Maria del Carmen Avendaño López
- An introduction to medicinal chemistry / Graham L Patrick
- Medicinal chemistry : principles and practice / edited by Frank D. King
- Medicinal chemistry : the role of organic chemistry in drug research / edited by C.R. Ganellin and S.M. Roberts
- Pharmacokinetics : development of an exquisitely practical Science / edited by P. du Souich and D. Lalka
- Virtual screening [Recurs electrònic] : an alternative or complement to high throughput screening / edited by Gerhard Klebe