

Computer-Aided Drug Discovery

Descriptive details concerning the subject:

• **Name of the subject:** Computer-Aided Drug Discovery

• **Code :** 30179

• **Type of subject:** presencial

• **Module:** 5

• **Credits:** 5

• **ECTS:** 5

• **Total hours:** 125.0

• **Scheduling:**

• **Curs:** 1st

• **Període:** 3rd term

• **Coordination:** Manuel Pastor

• **Department:** Experimental and Health Sciences

• **Edifici:** Mar 60.119

• **Horari:** 8:30-10:30 From April 10th to May 10th

Teaching staff:

• **Language:** English

• **Lecturer:** Manuel Pastor

• **Department:** Experimental and Health Sciences

• **Language:** English

• **Lecturer:** Ismael Zamora

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• **Lecturer:** Jana Selent

• **Department:** Experimental and Health Sciences

Subject presentation:

• Presentation:

In modern Drug Discovery, computational methods play a central role. They are applied in the search of novel targets, an 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.

Prerequisites in order to follow the itinerary:

• Prerequisites:

The students must have some basic knowledge of organic chemistry, physical-chemistry, biology, computation and pharmacology.

Competences to be attained in the subject

General competences:

Instrumentals:

1. Use common computational tools for carrying out typical actions (visualize, copy, etc.) on data commonly used in Drug Discovery

When confronted with practical problems in the areas of Drug Discovery:

- identify relevant techniques
- choose the more appropriate
- identify advantages, disadvantages and limitations

Find in Internet some common open source tools useful for drug discovery and install them in a computer

Interpersonal:

1.

Develop a "common language" to communicate with other professionals in

the field of Drug Discovery

Develop ability to teamwork

Systemic:

1. Gain awareness of the interdependence between the different steps and the diverse computational techniques used in Drug Discovery.

Specific:

1.

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, physico-chemical)

Understand the language of other professional (medicinal chemist, pharmacologist) working in the Drug Discovery field

Use common tools for:

- store, manage, visualize and convert (small) molecular structures
- manage drug information
- carry out SBDD
- carry out QSAR and 3D QSAR

- carry out Virtual Screening

Learning aims:

· Aims:

- Provide an overview of the Drug Discovery process and of the role of the computation methods in this process
- Present at an elementary level some important computational methods used in Drug Discovery
- Provide the student with criteria to select the most suitable computational method for solving a practical problem
- Improve the communication skills with researchers working in the Drug Discovery process
- Stress the importance of the interrelations between different aspects of the process. See the Drug Discovery as a whole with a practical goal: obtain a drug.

Avaluació

General assessment criteria:

The student would have completed successfully this course if he is able to:

- Have a general understanding of the Drug Discovery process
- Know and understand the rationale and applicability of different computational techniques in the Drug Discovery process

- Have a clear understanding of the advantages, disadvantages and limitations of diverse computational techniques
- Develop the critical abilities needed to choose the most suitable computational technique for addressing a certain practical problem
- Communicate with other professionals involved in the field of Drug Discovery

Avaluació de competències

Attainment indicator

Assessment procedure

Scheduling

Instrumentals:			
1. Use common computational tools for carrying out typical actions (visualize, copy, etc.) on data commonly used in Drug Discovery	The student is able to manipulate Drug Discovery relevant data without effort	Practical exercise, in which the student must use such tools in practical situations	
When confronted with practical problems in the areas of Drug Discovery:			
<ul style="list-style-type: none"> • identify relevant techniques • choose the more appropriate • identify advantages, disadvantages and limitations 	The student can make sensible choices when it needs to select a tool and its expectations about the results are realistic	Practical exercise, in which the student is asked to select the most suitable tool and is asked to evaluate it critically	These competence must be gained along the course, in no particular order
	The student is able to set-up a working environment on its own	The student must set up its computer during the course. The quality of this set-up will be evaluated	
Find in Internet some common open source tools useful for drug discovery and install them in a computer			

Interpersonal:

1. Develop a "common language" to communicate with other professionals in the field of Drug Discovery

Informs and supervised conversations indicate an efficient communication level
Teamwork is successful

Evaluation of the language used in informs and teacher-student communication
Evaluation of teamwork results

Gain good communication skill is difficult and improvements could be expected only at the end.
Working in groups is a

Develop ability to teamwork

transversal competence that must be improved continuously during the whole master.

<p>Systemic: 1. Gain awareness of the interdependence between the different steps and the diverse computational techniques used in Drug Discovery.</p>	<p>When involved in a certain Drug Discovery problem, the student is able to identify the relationships between separate aspects of the problem and understand the need of reaching compromises.</p>	<p>Confront the student with a problem that require the contemporaneous considerations of different aspects (for example pharmacokinetic + pharmacodinamic + synthetic accesibility) for being solved.</p>	<p>This competence could be gained only after the student is familiar with the different techniques and their relationships</p>
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<p>Specific: 1. Understand the field of application of most common computational methods within the drug-discovery pipeline</p>	<p>The student is familiar with the techniques and know when, where and who applies them</p>	<p>Practical and theoretical exercices requiring the student to make a sensible use of a certain tecnique</p>	<p>Competences should be gained progressively during the course.</p>
<p>Ability of see a drug from diverse points of view (chemical, computational, pharmacological, physico-chemical)</p>	<p>The student can swich from one point of view to another</p>	<p>Practical exercices requiring the user to analyse a drug from different points of view</p>	
<p>Understand the lenguaje of other professional (medicinal chemist, pharmacologist) working in the Drug Discovery field</p>	<p>The student can make use of sources of information used by other professionals working in the Drug Discovery field</p>	<p>Evaluation of reports requiring from the student the access to such source of information</p>	
<p>Use common tools for:</p>	<p>The student has the ability to use these tools and methologies, at least at a basic level</p>	<p>Practical exercices on the use of such tools</p>	
<ul style="list-style-type: none"> store, manage, visualize and convert (small) molecular structures 			

- manage drug information
- carry out SBDD
- carry out QSAR and 3D QSAR
- carry out Virtual Screening

Contents

Contingut

The course contents are divided in an introduction, a few blocks aiming to provide the student the context (chemical, biological, computational) required and some blocks introducing diverse computational techniques. These techniques have been divided in direct (receptor-based) approaches, and indirect (ligand-based) approaches. Hit finding computational methods (virtual screening) were described at the end, in a separate block.

Contents 1: Introduction

Conceptes	Procedures	Attitudes
1. Introduction Overview of the Drug Discovery process and the role of computational methods. Objectives of the course. Case study presentation	Presentation of contents	Receptive

Contents 2: Chemical aspects

Conceptes	Procedures	Attitudes
1. 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.	Presentation of contents Seminar Search for series of compounds in Medicinal Chemistry literature Discussion on chemical peculiarities of the compounds (enantiomers, tautomers, charge, counter-ions) Hands-on Molecules in the computer. 2D and 3D representation and manipulation.	Receptive
2. Elements of molecular	SMILES, SMARTS, SDFfiles	

pharmacology..
 Concept of receptor and target.
 Receptor binding and activation.
 Ligand-receptor interaction, non-covalent bonds. mol2, pdb file formats
 Ligand into the binding site. 2D to 3D conversion
 Concepts of pharmacophore, bioactive conformation and Active Analog Approach.
 Formats for small molecule representation.

Contents 3: Biological aspects

Conceptes	Procedures	Attitude s
1. Elements of pharmacology Role of pharmacology in modern drug discovery. Concept of screening. Screening against multiple targets. Affinity. Saturation and competition studies. Effect: functional studies. In vivo screening. Automatization of screening processes (HTS and HCS)	Presentation of contents Seminars Find in the literature pharmacological data about the case-study series. Discuss (pKD, IC50, selectivity, functional data) Find in the literature ADMET data about the case-study. Discuss (metabolism, oral absorption, toxicity, binding to plasmatic proteins)	Receptive
2. Pharmacokinetics The ADMET process Main physiological process involved in ADMET Strategies for characterizing the ADMET properties of a drug candidate Pharmacological screening In silico ADMET prediction Interspecies ADMET transferability		

Contents 4: Computational aspects

Conceptes	Procedures	Attitudes
1. Information systems in drug discovery Presentation of computational resources for	presentation of contents	Critical attitude

storing, searching and retrieving information
in the field of drug discovery

2. Classification schemes of knowledge
management. From data to knowledge
Principles of chemogenomics.

Hands-on
session
Demo of
Integrity

Contents 5: Molecular design (I). Direct approaches.

Conceptes	Procedures	Attitudes
1. Structure-based Drug Design (SBDD) 3D molecular structures. Conformational analysis. Docking. De-novo ligand design. Scaffold hopping. The analysis of protein-ligand interactions.	Presentation of contents Hand-on session	Critical attitude

Contents 6: Molecular design (II). Indirect approaches.

Conceptes	Procedures	Attitudes
1. QSAR and 3D-QSAR The QSAR approach. Classical and 3D-QSAR methods Molecular descriptors and statistical tools (MLR, PLS) Interpreting a 3D-QSAR model	Presentation of contents Seminar Find in the literature examples of 3D-QSAR models carried out on the case-study. Discuss SAR and 3D-QSAR results. Hands-on Demo of 3D QSAR analysis carried out on a series of the case-study.	Critical attitude

Contents 7: Virtual screening

Conceptes	Procedures	Attitudes
1. From virtual chemical screening to virtual pharmacological profiling	Presentation of contents	Critical

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

Hands-on session
case study on
chemogenomics

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