ANX-PR/CL/001-01

LEARNING GUIDE

SUBJECT

203000030 - Computational Structural Biology For Lead Discovery

DEGREE PROGRAMME

20BC - Master Universitario En Biologia Computacional

ACADEMIC YEAR & SEMESTER

2021/22 - Semester 1

Index

Learning guide

1. Description

1.1. Subject details

Name of the subject	203000030 - Computational Structural Biology For Lead Discovery
No of credits	3 ECTS
Type	Optional
Academic year ot the programme	First year
Semester of tuition	Semester 1
Tuition period	September-January
Tuition languages	English
Degree programme	20BC - Master Universitario en Biologia Computacional
Centre	20 - E.T.S. De Ingenieria Agronomica, Alimentaria Y De Biosistemas
Academic year	2021-22

2. Faculty

2.1. Faculty members with subject teaching role

Name and surname	Office/Room	Email	Tutoring hours *
Maria Garrido Arandia (Subject coordinator)	06 (microb)	maria.garrido@upm.es	M - 08:00 - 13:00 Request an appointment with the teacher via e-mail.

* The tutoring schedule is indicative and subject to possible changes. Please check tutoring times with the faculty member in charge.

3. Prior knowledge recommended to take the subject

3.1. Recommended (passed) subjects

The subject - recommended (passed), are not defined.

3.2. Other recommended learning outcomes

- Knowledge about protein structure

4. Skills and learning outcomes *

4.1. Skills to be learned

CE02 - Utilizar sistemas operativos, programas y herramientas de uso común en biología computacional, así como, manejar plataformas de cómputo de altas prestaciones, lenguajes de programación y análisis bioinformáticos

CE03 - Analizar e interpretar bioinformáticamente los datos que se derivan de las tecnologías ómicas, y proponer soluciones bioinformáticas en relación a dichos datos.

CE05 - Utilizar herramientas de biología computacional para el análisis genómico, incluida la genómica comparativa y biología evolutiva.

CE10 - Conocimiento de las técnicas de representación del conocimiento reutilizables y modelos de razonamiento en entornos centralizados y distribuidos a utilizar en la resolución de problemas que impliquen conducta inteligente.

CG01 - Poseer los conocimientos que constituyen la base científica y tecnológica de la Biología computacional, lo que permitirá el desarrollo de ideas originales en este campo, en un contexto de investigación o desarrollo.

CG03 - Que los estudiantes sepan aplicar los conocimientos adquiridos y su capacidad de resolución de problemas en entornos nuevos o poco conocidos dentro de contextos más amplios (o multidisciplinares) relacionados con el area de la Biología Computacional.

CT02 - Capacidad para aplicar el método científico para la resolución de problemas de forma efectiva y creativa.

4.2. Learning outcomes

RA31 - Adquirir destreza en el manejo de software para el estudio de estructuras e interacciones en sistemas biomoleculares fármaco-diana

RA32 - Conocer los fundamentos y el manejo de los métodos de docking y de determinación in silico de sitios de unión y centros activos en proteínas

RA33 - Conocer los fundamentos y el manejo de los métodos computacionales para obtener in silico estructuras de biomoléculas, tanto proteínas como fármacos

* The Learning Guides should reflect the Skills and Learning Outcomes in the same way as indicated in the Degree Verification Memory. For this reason, they have not been translated into English and appear in Spanish.

5. Brief description of the subject and syllabus

5.1. Brief description of the subject

The course provides an updated view of the computational methodologies for the study of structures and interactions of complexes between receptor biomolecules (mainly proteins) and small molecules or drugs. The course is designed in an interactive way, so students will put into practice in the classroom the computational techniques necessary for the study of these complexes. The course begins with a brief historical review of the field, then the fundamental physicochemical concepts and the sources of information (databases) to be used are introduced. After that, the course will focus on the study of the different techniques used in the drug discovery process. Firstly, the methods used in ligand-based virtual screening are presented, describing the essential concepts of similarity and molecular descriptors at the three levels of analysis (1D, 2D and 3D) together with the methods to calculate the parameters of statistical significance (scoring).Then the course focus on the essential pharmacophore concept and on the techniques of structure-based virtual screening following two complementary approaches: protein-ligand docking and *de novo* design. At the end of the course, the students will have acquired the computational skills to perform a process to discover a lead compound (i.e., drug design)

5.2. Syllabus

1. Introduction to Computational Methods for Lead Discovery
    1.1. Basic concepts
        1.1.1. Overview of drug discovery
        1.1.2. Polypharmacology
        1.1.3. Pharmacodynamics
        1.1.4. Pharmacokinetics
    1.2. Databases
        1.2.1. Drug datasets
        1.2.2. Protein Data Bank
2. Ligand-based virtual screening
    2.1. Similarity
    2.2. Molecular descriptors
    2.3. Molecular Fingerprint
    2.4. Shape-based analysis
    2.5. QSAR methods
3. Pharmacophore
    3.1. Ligand-based pharmacophore modelling
    3.2. Structure-based pharmacophore modelling
        3.2.1. Identification of binding sites
4. Receptor-based virtual screening
    4.1. Protein Structure
    4.2. De novo design
    4.3. Protein-ligand Docking

6. Schedule

6.1. Subject schedule*

Week	Face-to-face classroom activities	Face-to-face laboratory activities	Distant / On-line	Assessment activities
1			**Tema 1** Duration: 02:00	
2			**Tema 1** Duration: 01:00 **Aplicaciones tema 1 (ordenador)** Duration: 01:00	
3			**Aplicaciones tema 1 (ordenador)** Duration: 02:00	
4			**Tema 2** Duration: 01:00 **Aplicaciones tema 2 (ordenador)** Duration: 01:00	
5			**Tema 2** Duration: 01:00 **Aplicaciones tema 2 (ordenador)** Duration: 01:00	
6			**Tema 2** Duration: 01:00 **Aplicaciones tema 2 (ordenador)** Duration: 01:00	
7			**Tema 3** Duration: 01:00 **Aplicaciones tema 3 (ordenador)** Duration: 01:00	**Assignment 1. Selection of the target and ligand based virtual screening** Continuous assessment Not Presential Duration: 02:00
8			**Tema 3** Duration: 02:00	

9			**Aplicaciones tema 3 (ordenador)** Duration: 02:00	
10			**Tema 4** Duration: 02:00	**Assignment 2:Pharmacophore design** Continuous assessment Not Presential Duration: 02:00
11			**Aplicaciones tema 4 (ordenador)** Duration: 02:00	
12			**Tema 4** Duration: 01:00 **Aplicaciones tema 4 (ordenador)** Duration: 01:00	
13			**Estudios de casos prácticos / trabajo computacional aplicado** Duration: 03:00	
14			**Estudios de casos prácticos / trabajo computacional aplicado** Duration: 03:00	
15				**Assignment 3. Structure-based visrtual screening and ADMET analysis** Continuous assessment Not Presential Duration: 02:00
16				**Exam** Final examination Presential Duration: 03:00
17				

Depending on the programme study plan, total values will be calculated according to the ECTS credit unit as 26/27 hours of student face-to-face contact and independent study time.

* The schedule is based on an a priori planning of the subject; it might be modified during the academic year, especially considering the COVID19 evolution.

7. Activities and assessment criteria

7.1. Assessment activities

7.1.1. Continuous assessment

Week	Description	Modality	Type	Duration	Weight	Minimum grade	Evaluated skills
7	Assignment 1. Selection of the target and ligand based virtual screening		No Presential	02:00	30%	5 / 10	CG01 CT02
10	Assignment 2:Pharmacophore design		No Presential	02:00	30%	5 / 10	
15	Assignment 3. Structure-based visrtual screening and ADMET analysis		No Presential	02:00	40%	5 / 10	CG01 CE05 CG03 CE10 CE03 CE02 CT02

7.1.2. Final examination

Week	Description	Modality	Type	Duration	Weight	Minimum grade	Evaluated skills
16	Exam		Face-to-face	03:00	100%	5 / 10	CG01 CE05 CG03 CE10 CE03 CE02 CT02

7.1.3. Referred (re-sit) examination

Description	Modality	Type	Duration	Weight	Minimum grade	Evaluated skills
Exam		Face-to-face	03:00	100%	5 / 10	CG03 CE10 CG01 CE05 CE03 CE02 CT02

7.2. Assessment criteria

In the **continuous assessmen**t system, the course will be passed upon delivering **three individual works**. The first work covers the topics discussed in parts 1 and 2 of the Syllabus, it has tol be delivered in the middle of the course and it will count **30%** of the final grade. The second work, included the design of a pharmacophore and it will count 30% of the final degree and the last assignment included the analysis of structure-based virtual screening and the analysis of ADMET properties and it will count the **40%** of the final grade. The teacher will evaluate in these three works the acquisition of the skills to be learned as well as the creativity and degree of initiative of the students.

In the system of **final examination** there will be a single final exam that represents **100%** of the grade in which, it will be composed by a practical exam that must be solved by means of the software used in the course.

8. Teaching resources

8.1. Teaching resources for the subject

Name	Type	Notes
Speck-Planche, A. (Ed.), Multi-scale Approaches in Drug Discovery, Elsevier, 2017	Bibliography	
Varnek, A. (Ed.) Tutorials in Chemoinformatics, Wiley, 2017	Bibliography	
Cavasotto, C.N. (Ed), In Silico Drug Discovery and Design, CRC Press, 2016	Bibliography	
Stromgaard K, Krogsgaard-Larsem P. and Madsen U. (Eds), Drug Design and Discovery, 5th edition, CRC Press, 2017	Bibliography	
ZINC Database	Web resource	http://zinc15.docking.org/
ChEMBL Database	Web resource	https://www.ebi.ac.uk/chembl/
Click2Drug	Web resource	http://www.click2drug.org/
SwissADME	Web resource	http://www.swissadme.ch/index.php
Swiss Similarity	Web resource	http://www.swisssimilarity.ch/
Swiss Target Prediction	Web resource	http://www.swisstargetprediction.ch/
Pocket Query	Web resource	http://pocketquery.csb.pitt.edu/pocket.html?JMOL=1
SmoothDock	Web resource	http://smoothdock.ccbb.pitt.edu/pharmer/
Chimera program	Others	Free software available at http://www.cgl.ucsf.edu/chimera/index.html
AutoDock VINA program	Others	Protein-ligand docking. Free software available at: http://vina.scripps.edu/

9. Other information

9.1. Other information about the subject

Due to the methodological approach of the course as explained in the "Course Description", the teaching activities are an indistinguishable mixture of "theory and practice". It is thus necessary that each student uses his/her laptop in classroom classes.The software needed to follow the course (Chimera, essentially, in addition to multiple web resources) will be presented on the first day of class and consists of programs freely available on the web for academic users, as indicated in the Teaching Resources section. In parallel, students will have to use their own computer tools for file editing, scientific graphics, programming environment (Python, preferably) and mathematical analysis.

UPM addresses Sustainable Development Goals (SDG) from an integrated perspective that includes, not only research and innovation initiatives, but also teaching and governance activities within the institution.

UPM's Biotechnology Degree in general, and the subject "Computational Structural Biology For Lead Discovery" in particular, aims to respond to those challenges that the ODS address through the potential applications of the knowledge aquired by the students along their academic formation.

The own scientific nature of the subject "Computational Structural Biology For Lead Discovery" is fully aligned with the following challenge included within UN's SDG initiative :
-SDG 3 - Health and Welfare: the acquisition of knowledge related to those computational tools useful for the design of new drugs allows the students to gain the ability to address the first development stages of new drugs in order to improve the quality of life of patients undergoing numerous pathological conditions.

10. Adendas

- "El cronograma que se muestra en el apartado 6 de esta guía sigue una planificación de la asignatura para su impartición en modo telemático debido a la situacion derivada por la COVID-19, pero puede sufrir modificaciones durante el curso primando siempre la docencia presencial si fuese posible"