MASTER IN BIOINFORMATICS
In Silico Drug Design – Macromolecules MSc
Université Paris Cité
2024-2025

SEMESTER 1 (30 ECTS)

EU 0 UPGRADE
Coordinator: G. MOROY

EC 100 Unix and R:Base (Upgrade)
Coordinator: G. MOROY

Title: Unix and R:Base (Upgrade)
Teaching coordinator: Gautier Moroy

Knowledge objectives: Acquire the basics of using the Unix operating system and R software.

Targeted skills : To be familiar with Unix and R to be autonomous during the practical sessions of computer science, bioinformatics, and statistics.

Programme
Fundamentals of the Unix operating system and R software.

UE1 FUNDAMENTALS (7 ECTS)
Coordinator: C. ETCHEBEST

BQAAY240 Structure of biomolecules (2 ECTS)
Responsable: N. CAULET

Title: Structure of biomolecules
Teacher: N. Caulet

Knowledge objectives:
- Principles and spectroscopic methods for studying the 3D structure and dynamics of biological macromolecules

Targeted skills:
To master the specificities of the structures and interactions of biological macromolecules and their characterization by experimental techniques.

Program:
- Genomics and structural proteomics: 3D folding of macromolecules: DNA, RNA and proteins, biological membranes.
- Biophysical techniques: Circular dichroism, Fluorescence, Electrophoresis, Mass spectrometry, Electronic microscopy

BQAAY210 Enzymology (4 ECTS)
Coordinator : J. Dairou

Title: Biochemistry
Teaching coordinators: J. Dairou

Knowledge objectives:
- Principles of thermodynamics
- Concept of Enzymology and Chemical Kinetics

Targeted skills:
To master the specificities of the structures and interactions of biological macromolecules and The characterization by experimental techniques.

Programme:
- Genomics and structural proteomics: 3D folding of macromolecules: DNA, RNA and proteins, biological membranes.
- Biophysical techniques: Circular dichroism, Fluorescence, Electrophoresis, Mass spectrometry, Electronic microscopy
- Thermodynamic techniques for the study of interactions: microcalorimetry, equilibrium dialysis
- Advanced concepts of enzymology
- Interaction kinetics.

EC 103 Biostatistics and R programming (3 ECTS)
Coordinator: L. REGAD

Title: Biostatistics and R programming
Teaching coordinator: L. Regad

Knowledge objectives: The purpose of the education provided is to provide students with basic biostatistics training.

Targeted skills: Master the statistical bases of biological data exploration, and processing in R language.

Programme:
Reminders of probabilities, introduction to biostatistics

Estimation and statistical inference

Classical tests, Student test, Chi2 test, Pearson's correlation coefficient test

Analysis of variance and introduction to factorial designs

Non parametric tests

Introduction to learning techniques supervised by the methods of CART / or Factorial plan

or

EC 104 Tutored project in biostatistics and R (3 ECTS)
Coordinators: AC CAMPROUX & A. BADEL

Title: Tutored project in Biostatistics and R
Teaching coordinators: AC Camproux & A.Badel

Knowledge objectives: At the end of the training, students will be able to determine the statistical analysis that can answer the biological question asked, and implement this analysis.

Conclude on the statistical and biological results of their study

Targeted skills: Appropriately apply the concepts of biostatisitics and R programming to solve a biological problem. Analysis of biological files from FP in biology

Programme: Tutored project in biostatistics and R

EC 105: English communication (2 ECTS)
Coordinator: Teachers from EILA (Université Paris Cité)

Title: Communication in english

Teaching coordinator: ELAAE teacher

Program: Disciplinary English

Practice written and spoken English.

Targeted skills:

In-depth knowledge of English for science.

Program:

Online training in English specialty, scientific understanding and writing.

UE2 PROGRAMMING AND MATHEMATICAL TOOLS (9 ECTS)
Coordinators: JC GELLY & A. BADEL
3 ECUs according to the level

EC 201 Mathematics I (3 ECTS)
Coordinator: AC. CAMPROUX

Title: Mathematics I
Teaching coordinator: AC Camproux

Knowledge objectives:
The purpose of this module is to provide basic mathematical and algorithmic principles for drug design.

Targeted skills: Understand the mathematical principles of commonly used numerical methods. Ability to analyse a modelling problem, and correctly use the appropriate methods.

Programme:

- Study of functions: limits, derivatives, graphs.
- Linear algebra: vectors and matrices, operators in space (rotations, dilatations), inversion of matrices, eigenvalues and determinants, solutions to linear differential equations.
- Optimisation: multidimensional functions, Hessian matrices
- Introduction to energy functions (docking-scoring)

(Or EC202 if advanced level)

EC 202 Optimisation and biology learning (3 ECTS)
Coordinators: D. FLATTERS, F. GUYON

Title: Optimisation and biology learning
Teaching coordinators : D. Flatters, F. Guyon

Knowledge objectives:
Principles of optimisation and its applications to modelling in biology;
Applications and implementation of mathematics to the problems of computational biology (accessible to biologists)

Targeted skills: Understanding and development of algorithms used for modelling for data analysis and learning methods

Programme:
Analysis of the functions with several variables: gradient, Hessian and limited developments, optimality conditions;
Gradient algorithms, conjugate gradients, quasi-Newton methods
Classic applications from optimisation to data analysis;

EC 203 Python programming 1 (3 ECTS)
Coordinators: P. FUCHS & P. POULAIN

Title: Python programming 1
Teaching coordinators: P. Fuchs & P. Poulain

Knowledge objectives: Train biologists in Python programming. Python is the most used programming language today in bioinformatics, especially for data analysis.

Targeted skills: Know the main concepts related to Python programming.
Be able to write simple analysis scripts.
To evaluate the relevance of a result returned by a program.

Programme:

- Programming concept
- Introduction to the Python language
- Main data types (integers, real numbers, lists, character strings, dictionaries, tuples)
- Loops, comparisons, tests
- Modules
- Input/output management with files
- Functions

EC 204 Programming python 2 (3 ECTS)
Coordinators: P. FUCHS & P. POULAIN

Title: Python programming 2
Teaching coordinators: P. Fuchs & P. Poulain

Knowledge objectives: Train bioinformaticians in Python programming. Acquire autonomy in the development of a Python program. Python is the most used programming language today in bioinformatics, especially for data analysis. It is in great demand in laboratories, but also in private companies.

Targeted skills: Understand the main concepts related to Python programming.
Be able to write programs (i) for analysing large amounts of data, (ii) producing data (e.g. a system simulation).
Be able to develop/debug a program in Python.

Programme:
Main data types (integers, real numbers, lists, character strings, dictionaries, tuples)

- Loops, comparisons, tests
- Modules
- Input/output management with files
- Functions
- Regular expressions

Python classes

EC 205 Algorithmic I (3 ECTS)
Coordinators: C. DELPORTE & H. FAUCONNIER

Title: Algorithms 1
Teaching coordinators : C. Delporte, H. Fauconnier

The course will introduce the general methods of algorithm design (recursion, programming dynamics, greedy algorithms, etc.) about basic algorithms: the different elementary sorts, sorting, fast sorting, heap structure, search binary trees, hash functions, graph traversal.
This course will present the main algorithms used to solve in an approximate or exact way some of the problems arising from biology. The goal is to enable students to understand the principles underlying the methods implemented in software (e.g. BLAST) and to be able to evaluate critically the tools that can be made available to them during their professional career.

Targeted skills:
The concepts of complexity (NP-completeness and polynomial approximation) will be taught based on the problems addressed.

EC 206 ECUE in M1 BI-UE2 (3 ECTS)

UE3 PRACTICAL AND IN-DEPTH STUDY (8 ECTS)
Coordinator: V. GRUBER
3 ECUs of your choice

EC 304 Toxicology Database (3 ECTS)
Coordinator: A. BAEZA

Title: Toxicology database
Teaching coordinator: A. Baeza

Knowledge objectives:
Introduction to toxicology, the fate of xenobiotics and drugs.

Targeted skills:
To provide the basics of the fate of xenobiotics (drugs) and toxicology

Programme:
- Introduction to toxicology, cell, toxic targets (necrosis, apoptosis, adaptation)
- The fate of xenobiotics, chemical reactivity of oxidising species. Implication in toxicology. Oxidative stress and protective mechanisms.
- Signalling pathways and mechanisms of toxicity. Structure-toxicity relationships. ECOTOX
- Xenobiotics-inflammation and xenobiotics-reproduction
- Cell models in predictive toxicology. The omics. Toxicity assessment methods and regulatory records

EC 305 ADME/Chemistry (in English) (2 ECTS)
Coordinator: O. TABOUREAU

Title: ADME/chemometrics
Teaching coordinator: O. Taboureau

Knowledge objectives:
The objective of this module is to give an introduction to the ADMET properties and to propose tools that can predict in advance the possible problems of ADMET (Administration-Distribution-Metabolism-Excretion-Toxicity) associated with a small molecule.

Targeted skills:
Understanding and using ADMET tools to optimise the design of a molecule and to limit or avoid side effects or toxic associated with it. (KNIME)

Programme:
- Chemical descriptors and ligand-based pharmacophores
- Training and practical of KNIME
- Description of ADMET properties
- Use of tools to predict the sites of metabolism, groups of reactive and toxic atoms, protein targets associated with side effects.
- Evaluation of the potential risks associated with a molecule and how to optimise the design of this molecule.

EC 605 Chemistry RéSO (Reactivity and organic synthesis) (3 ECTS)
Coordinator: F. Chau

Title: Chemistry ROS (Reactivity and organic synthesis)
Teaching coordinator: F. Chau

Knowledge objectives:
To provide students with molecular chemistry tools to:
- understand chemical/biochemical/biological processes and the reactivity of natural/synthetic molecules.
- know how to master the main reaction mechanisms of organic chemistry, and apply them to the synthesis of target molecules.

Targeted skills:
- understand chemical/biochemical/biological processes and the reactivity of natural/synthetic molecules.
- know how to master the main reaction mechanisms of organic chemistry, and apply them to the synthesis of target molecules.

Programme
- Stereochemistry of organic compounds.
- Electronic and steric effects.
- Reactivity of chemical functional groups of biomolecules: hydroxyl, carbonyl, carboxyl, amine, thiol, and phosphate.
- Chemistry of large classes of organic molecules: description, reactivity, and applications.

UE4 THEMATIC ORIENTATION I (6 ECTS)
Coordinators: O. TABOUREAU, D. FLATTERS
2 ECUs of your choice

EC 401 Chemoinformatics (3 ECTS)
Coordinator: J. DIHARCE

Title: Chemoinformatics
Teaching coordinator: J. Diharce

Knowledge objectives:
The objective of this module is to introduce students to the field of chemoinformatics and its application in Drug Design.

Targeted skills:
Introduction to chemoinformatics. Chemical representation, chemical descriptors, visualisation. Introduction to analysis methods

Programme:

- Chemical representation (1D, 2D, 3D)
- Chemical database
- Chemical descriptors and pharmacophores.
- Visualisation of descriptors and molecules
- Similarity of molecules and cluster
- Introduction to Structure-Activity Methods (QSAR)
- Virtual screening

EC 402 Chemistry: chirality - non-covalent bonds (3 ECTS)
Coordinators: F. MAUREL, O. TABOUREAU

Title : Chemistry: chirality - non-covalent bonds
Teaching coordinators: F. Maurel, O. Taboureau

Knowledge objectives:
Presentation of the main non-covalent interactions that are established within biological systems or in biological ligand - macromolecule complexes. The focus is on the characteristics and distinctive features (nature and intensity) of these interactions. The aim is to show how these forces are distinguished by their nature and their intensity of covalent chemical bonds, which leads them to play an essential role in ensuring the three-dimensional structures of living molecules, or to guide the interaction of a small molecule in a biological receptor (protein or DNA). We will show how it is possible to translate the characteristics of each of these forces into suitable potentials. Finally, strategies for implementing these terms in molecular modelling calculations will be introduced. A practical part on computer will allow concrete cases to be addressed where each one of these forces plays a particular role.

Targeted skills:
Presentation of the main non-covalent interactions that are established within biological systems or in biological ligand - macromolecule complexes.

Programme:
- Introduction to chemistry
- Basics of chemistry such as atoms, chemical functions, and heterocycles useful for drug development. Preferred conformations, and reactive groups will also be introduced.

EC 403 Option for Drug Design (3 ECTS)
Coordinator: O. TABOUREAU

Title: Option in Drug Design / Chemoinformartics
Teaching coordinator: O. Taboureau
Teachers: invited professors, researchers…

Knowledge objectives:
Discovery of useful tools and technologies for drug design, QSAR, deep learning, structural bioinformatics, thermodynamic approach…

Targeted skills:
Learn about tools/softwares used in chemoinformatics and molecular modelling.

SEMESTER 2 (30 ECTS) Université Paris Cité

EU 5 ADVANCED FUNDAMENTALS (6 ECTS)
Coordinator: AC. CAMPROUX

EC 501 Big Data Analysis (3 ECTS)
Coordinators: AC Camproux, A. Badel

Title: Massive Data Analysis
Teaching coordinators: AC. Camproux, A. Badel

Knowledge objectives: The purpose of the course is to introduce students to unsupervised (classification, principal component analysis) and supervised learning methods (Cart, Random Forest linear regression and PLS, linear discriminant analysis and regression logistics) to enable them to analyse and process large multidimensional data sets in bioinformatics. The application of the different concepts will be made using the statistical software R. The performance evaluation of methods and selection of descriptors will be covered.

Targeted skills: Learn to apply and choose different learning methods on a data set

Programme
Protein space example
- Descriptive or exploratory methods:

Factorial methods (Principal Component Analysis), which essentially produce plane or three-dimensional graphical visualisations to describe a set of data. Classification methods (hierarchical or partitioning), which propose groupings into object classes following algorithmic calculations

- Explanatory and/or predictive methods:

Methods for explaining or predicting, according to decision rules, a variable of quantitative or qualitative interest using a set of explanatory variables. Linear model, PLS, Logistic regression, CART. Discriminant analysis. Cross-validation.

EC 502 Biophysical approaches for the study of interactions (3 ECTS)
Coordinators: V. Gruber & W. Majeran

Title: Biophysical approaches to the study of interactions
Teaching coordinators : V. Gruber & W. Majeran

Knowledge objectives: Learn biophysical, molecular and cellular methods for the study of interactions between macromolecules. Understand the concepts of systems biology and interactomes.

Targeted **skills:** Master the biophysical, molecular and cellular methods for the study of interactions between macromolecules. Master the concepts of systems biology and interactomes.

Programme
- Concept of interactome
- Biophysical principles and techniques of protein interactions-protein (double hybrid, co-immunoprecipitation, TAP-Tag, FRET, BRET, protein-fragment complementation assays, mass spectrometry)
- Biophysical principles and techniques of interactions between macromolecules
- Dynamic and structural studies of NMR interactions
- Concept of systems biology and applications

UE 6 THEMATIC ORIENTATION II (18 ECTS)
Coordinators: G. MOROY, O. TABOUREAU

EC 601 Protein-Protein Docking* in English (3 ECTS)
Coordinators: AC. Camproux, O. Taboureau

Title: Protein-Protein Docking* English course
Teaching coordinators: AC Camproux, O. Taboureau

Knowledge objectives: Prediction of protein interactions. Prediction of protein-protein interactions. Protein-protein docking

Targeted skills: Students will learn the state-of-the-art computational methods for prediction of protein interactions by docking simulations. They will be able to approach real docking protein issues and use the available methods and web servers for modelling the protein-protein complex structure from unrelated subunits. They will learn to integrate information from docking, mutation data, sequence conservation and link site prediction.

Programme
Prediction of protein interactions. Prediction of protein-protein interactions. Protein-protein docking. Calculation methods to define score and affinity functions. Modelling the flexibility of protein-protein association. Identification of hot-spot binding in the design of drugs. Multi-docking molecular approaches.

EC 602 Introduction to In Silico Drug Design (3 ECTS)
Coordinator: G. Moroy

Title: Introduction to In Silico Drug Design
Teaching coordinator: G. Moroy

Knowledge objectives: The objective of this course is to present the theoretical bases, the algorithms, and the programs used to carry out research in *drug design*. In particular, chemoinformatic approaches that concern the study of potentially therapeutic molecules and bioinformatic approaches based on the structure of the targeted protein.

Targeted skills:
- Representation and manipulation of chemical structures.
- Molecular descriptors for virtual screening, and structure-activity and structure-property relationships.
- Introduction to structure-based drug design by identifying the targeted protein (docking, virtual screening, receptor flexibility).
- Protein structures
- Online tools to aid drug designs.

Programme
Introduction to drug design: Structure-based approaches
Protein-ligand interaction, docking, virtual screening, flexibility, pharmacophore

EC 603 Structural bioinformatics 2: Dynamics* (3 ECTS)
Coordinators: D. Flatters, P. Fuchs

Title: Structural bioinformatics 2: Dynamics*
Teaching coordinators: D. Flatters, P. Fuchs

Knowledge objectives: The purpose of this course is to provide the essential basis for understanding the principles governing molecular modelling techniques. These techniques are used during the refinement stages of structures developed by conventional biophysical techniques (RX, NMR).

Targeted skills:
The aim of the course is to introduce students to different experimental methods for detecting and characterising molecular interactions. A molecular modelling project will be carried out by the students so that they acquire a practical experience of molecular modelling, whereby two levels of difficulty will be proposed for the project following their preliminary training in M1

Programme
This module will outline the approaches which allow the theoretical calculation of different physicochemical properties studied experimentally.
- Semi-empirical force field. Molecular Mechanics
- Description of the basic forces
- Harmonic potential (spring). Electrostatic interaction.
- Packing forces and van der Waals interaction
- Determination of force field parameters
- Energy minimisation and methods of exploration of conformational space
- Minimisation
- Introduction
- Molecular Dynamics Calculations of different properties Dynamic quantity measurements
- Error estimation

EC 604 Structural bioinformatics in Toxicology
Macromolecules + Systems pharmacology (3 ECTS)
Coordinator: D. Flatters & O. Taboureau

Title: Structural bioinformatics in Toxicology
Teaching coordinators: D. Flatters, G. Moroy, O. Taboureau

Macromolecules Systems pharmacology

Knowledge objectives: Introduction to the 3D structure of Macromolecules
3D structures of biological macromolecules and visualisation with Pymol. Construction of 3D models of proteins by homology modelling.
Pharmacology of systems.

Targeted skills:
3D structures of biological macromolecules and visualisation with Pymol. Construction of 3D models of proteins by homology modelling.
Understand the pharmacology of a drug, the action of a drug at different levels of a biological system.

Programme
Visualisation of macromolecules. Sequence alignment Comparison of structures.
Definition of systems pharmacology Description of the different sources of data useful for analysing the action of a molecule on a biological system. Presentation and application of a tool to visualise this type of data.

EC 303 Biological systems & ligands, database (3 ECTS)
Coordinators: O. TABOUREAU

Title : Biological systems & ligands, database
Teaching coordinators: O. Taboureau

Knowledge objectives:
2 technics will be learned during this course. One on de development of databases using MySQL. The second one will be on the manipulation of tools to develop and analyse biological networks using Cytoscape.

Targeted skills:
Understanding the association of molecules, proteins, phenotypes in the form of networks. Use of data from the biological systems. Initiation to the development of databases. Overview of databases in this field.

Programme:
- Association of chemical compounds-proteins-phenotypes (diseases, toxicity, etc.)
- Representation in the form of networks (hierarchical, circular, etc.)
- Measurements associated with network topology
- Tool to develop and analyse networks (Cytoscape)
- Development and use of databases using MySQL

1 ECUE to choose among the following 3

EC 606 *In silico* practices in 3D protein complexes (3 ECTS)
Coordinators: K. Moncoq, O. Taboureau

Title: *In silico* practices in 3D protein complexes (Protein-protein project + experimental approaches)
Teaching coordinators: K. Moncoq, O. Taboureau

Knowledge objectives:
Using protein-protein docking tools on a project.
Determine the 3D structure of a protein using crystallography and its analysis.

Targeted skills:
Perform a 3D analysis from a protein crystal

Programme
Crystallography: from diffraction to modelling. Visit of the synchrotron. Diffraction. Refinement of a structure. Validation of a structure.

- Crystallisation: what is a crystallisable protein?
- Crystallography: from diffraction to modelling.
- Refinement and validation of a 3D structure for the PDB

- Processing of diffraction data
- Phasing and molecular replacement
- Refinement of the structure (placement of a ligand, water molecules, etc.) and validation
- 3D structure analysis
- Molecular dynamics (analysis of a simulation trajectory by VMD)

EC 607 Advanced simulation methods (3 ECTS)
Coordinator: S. Murail

Title: Advanced simulation methods
Teaching coordinator: S. Murail

Knowledge objectives:
The exploration of the targets will focus on the conformational exploration of the target of a local level (conformation of the loops, side chains) at the level of collective movements intra or inter domains (normal modes, grosgrain simulation) + notion of thermodynamics

Targeted skills:
Understanding the impact of structural flexibility through normal modes and coarse-grained simulations

Programme
The exploration of the targets will focus on the conformational exploration of the target of a local level (conformation of the loops, side chains) at the level of collective movements intra or inter domains (normal modes, grosgrain simulation) + notion of thermodynamics

EC 608 Visiting professor or drug design option (3 ECTS)
Coordinator: O. Taboureau

Title: Visiting professor or drug design option
Teaching coordinator: O. Taboureau, A- C Camproux

Knowledge objectives:
Discovery of useful tools and technologies for drug design

Targeted skills:
Discovery of the platform in structural bioinformatics, chemoinformatics, and drug design

Programme
on-site visit, seminar and practical

Or ECUE WEB or Internship

UE 7 INTERNSHIP PROFESSIONALISATION I (6 ECTS)
Coordinators: G. MOROY, O. TABOUREAU, C. ETCHEBEST, V. GRUBER

EC 701 Internship 4 (6 ECTS)
Coordinators: G. Moroy / V. Gruber / O. Taboureau

Title: Internship 4
Teaching coordinators: G. Moroy, V. Gruber, O. Taboureau

Knowledge objectives:
Research training in a context of laboratories (R&D), or platforms in drug design, bioinformatics and chemoinformatics.

Targeted skills: Apply correctly the concepts of biology, chemistry, drug design and/or computer science in order to lead a research and development project in a laboratory or a platform. Adapt to a work environment Be proficient in communication tools.

Programme
- To conduct a research and development project within the professional environment
- To adapt to the professional environment
- To acquire tools for bibliographic research, communication and editorial methods

OR SEMESTER 2 ERASMUS University of Milan (30 ECTS)
(Semester 2 of the course ISDD Bioactive Molecules)