# MASTER'S DEGREE IN BIOINFORMATICS (2025–2029)
# Research track: In Silico Drug Design – Bioactive Molecules

## SEMESTER 3 (30 ECTS)

## COURSE BLOCK: REFRESHER COURSES

### BQ8AE015: Introduction to Unix and R (English)

**Knowledge objectives:** Acquire basic knowledge of the Unix operating system and the R programming environment.

**Targeted skills:** Become familiar with Unix and R so as to work independently during practical sessions in computer science, bioinformatics and statistics courses.

**Syllabus:**
Fundamental concepts of the Unix operating system and the R programming environment.

### BQBCE035: Biostatistics and methodology, chemistry (English)

**Knowledge objectives:** Acquire fundamental knowledge of R programming and biostatistics, together with the chemical and biophysical concepts essential for drug design and the analysis of molecular interactions.

**Targeted skills:**
• Manipulate and analyze biological data using R.
• Select and apply statistical methods to address biological questions.
• Interpret statistical and biological results.
• Understand the main chemical tools used in drug design projects.

**Syllabus:**
• Introduction to R for data manipulation and statistical analysis.
• Review of probability theory and introduction to biostatistics.
• Statistical estimation and inference.
• Classical statistical tests (Student's t-test, chi-square test).
• Pearson correlation test and simple linear regression.
• Introduction to chemical and biophysical tools for drug design.
• Characterization of molecular interactions.

# COURSE BLOCK: STRUCTURAL & AI ANALYSIS FOR DRUG DESIGN (12 ECTS)

## BQ2CE045: Advanced dynamics analysis (English)

**Knowledge objectives:** Apply knowledge of protein dynamics to modelling a therapeutic target.

**Targeted skills:**
• Model a simple molecular system (a biomolecule in an aqueous environment).
• Apply molecular modelling concepts to biomolecules such as peptides and proteins.
• Select appropriate bioinformatics and molecular modelling tools for investigating protein flexibility.
• Analyze and interpret molecular dynamics simulation results.
• Critically read and evaluate scientific publications involving molecular modelling.
• Be prepared to undertake a laboratory internship involving molecular dynamics approaches.

**Syllabus:**
• Theoretical principles underlying molecular modelling techniques (force fields, energy minimization and molecular dynamics).
• Semi-empirical force fields and molecular mechanics: fundamental interactions (harmonic and torsional potentials, electrostatic and van der Waals interactions).
• Molecular geometry optimization (energy minimization).
• Molecular dynamics simulations and trajectory analysis (algorithms and computation of conformational properties).
• Study of protein flexibility.
• Analysis of molecular dynamics simulation results.
• Each topic is covered through theoretical lectures and practical tutorials/laboratory sessions, including modelling a biomolecule in aqueous solution with GROMACS.

## BQBCE055: Practical molecular dynamics & structure (English)

**Knowledge objectives:** Understand how to design and implement protocols combining protein structural and dynamic analyses using molecular dynamics simulations, including methods for estimating binding free energies.

**Targeted skills:**
• Understand and master bioinformatics tools used to study protein structure and dynamics.
• Generate and analyze protein structures extracted from molecular dynamics trajectories.
• Propose and implement protocols combining protein structural and dynamic analyses.
• Apply MM-PBSA methods to estimate binding free energies.

**Syllabus:**
• Generation and analysis of protein structures obtained from molecular dynamics trajectories of a protein of interest.
• Protein structural and dynamic analysis based on molecular dynamics simulations.
• Design and implementation of protocols combining structural and dynamic analyses.
• Estimation of binding free energies using the MM-PBSA method.

## BQ2CE065: Protein structural exploration (English)

**Knowledge objectives:** Acquire advanced knowledge of three-dimensional structural analysis of therapeutic targets in order to prepare and optimize protein structures for structure-based drug design.

**Targeted skills:**
• Perform advanced structural analyses of protein targets in the context of structure-based drug design.
• Build three-dimensional protein models using homology modelling and advanced sequence alignment.
• Optimize protein loop regions and refine target structures.
• Analyze global and local structural variability, including the effects of mutations.
• Identify and assess binding pockets and estimate their druggability.
• Use state-of-the-art co-folding approaches (AlphaFold).

**Syllabus:**
Structural analysis and preparation of therapeutic targets for 3D structure-based drug design.
Three-dimensional macromolecular analysis:
• Building 3D protein models using homology modelling and advanced sequence alignment (MODELLER, PyMOL); loop modelling and optimization.
• Investigation of mutations and structural variability at global and local scales.
• Identification and assessment of binding pockets and druggability estimation (PockDrug).
• Identification and prioritization of binding sites accounting for protein flexibility using structural ensembles (PockFlex).
• Application of co-folding approaches to predict protein–ligand complex structures (AlphaFold).

## BQ2CE085: Advanced artificial intelligence for drug design (English)

**Knowledge objectives:** Train students to combine and optimize supervised learning methods for analyzing drug design datasets in both target space (structure-based approaches) and molecular space (ligand-based approaches), addressing descriptor selection, optimization criteria, model comparison, and robustness assessment through cross-validation.

**Targeted skills:**
• Apply and combine advanced supervised learning methods to drug design datasets.
• Design and implement appropriate cross-validation protocols and optimization criteria.
• Select relevant molecular and target descriptors and suitable model selection criteria.
• Analyze drug design data in structure-based and ligand-based contexts.
• Train and assess linear models and partial least-squares (PLS) regression, Random Forest and Gradient Boosting models, support vector machines, and deep learning models using R/Python.
• Critically analyze and present scientific articles or book chapters on machine learning for drug design.

**Syllabus:**
Optimization and combination of supervised learning methods applied to drug design datasets:
• Cross-validation protocols and optimization criteria.
• Linear models and partial least-squares (PLS) regression.
• Random Forest and Gradient Boosting methods.
• Support vector machines (SVM).
• Overview of deep learning.
Practical applications and projects using different R/Python packages.

# COURSE BLOCK: STRUCTURE AND LIGAND-BASED HIGH-THROUGHPUT SCREENING (6 ECTS)

## BQ2CE095: Structure-based (English)

**Knowledge objectives:** Acquire advanced theoretical knowledge of the concepts, algorithms and software tools used in structure-based design of therapeutic molecules from the 3D structure of a target protein, including protein and ligand flexibility.

**Targeted skills:**
• Understand and master bioinformatics tools used in structure-based drug design.
• Account for protein and ligand flexibility in docking and virtual screening protocols.
• Evaluate the stability of protein–ligand interactions using molecular dynamics simulations.
• Use and compare different docking and virtual screening software packages.
• Use and compare conventional and AI-based scoring functions, including deep learning methods.
• Apply deep-learning-based co-folding and docking approaches to generate protein–ligand complex poses, particularly using diffusion models.
• Conduct a virtual screening campaign against a therapeutic target.

**Syllabus:**
• Advanced theoretical concepts, algorithms and software for structure-based drug design.
• Accounting for protein and ligand flexibility in docking approaches.
• Assessing the stability of protein–ligand interactions using molecular dynamics simulations.
• Presentation and practical use of docking and virtual screening software.
• Presentation and application of conventional and AI-based scoring functions for evaluating docking and virtual screening performance.
• Presentation and application of AlphaFold and DiffDock approaches.

## BQ2CE105: Ligand-based (English)

**Knowledge objectives:**
Acquire practical skills in preparing chemical libraries in silico for virtual screening based on reference ligands. This includes:
• Generating 3D molecular models of small molecules (1D/2D → 3D) and understanding conversions between representations.
• Calculating ligand descriptors.
• Assessing pharmacokinetic and toxicological properties (ADME/Tox) using specific physicochemical criteria.
• Applying ligand-based virtual screening approaches.

**Targeted skills:**
• Prepare and manipulate chemical libraries for virtual screening.
• Work with different molecular file formats (PDB, SMILES, SMARTS, mol2, MDL-SDF and 3D molecules) and understand their advantages, limitations and applications.
• Generate 3D molecular models from 1D/2D representations using KNIME, RDKit, Frog, Open Babel and MOE, accounting for isomerism, tautomers and stereochemistry.

• Calculate, visualize and interpret ligand descriptors.
• Apply pharmacophore models and basic ADME/Tox rules (Lipinski, Veber, Egan, etc.).
• Identify frequent hitters, aggregators and toxic fragments using tools such as FAF-Drugs.
• Perform ligand-based virtual screening, including the use of decoys.

**Syllabus:**
• Working with molecular file formats (PDB, SMILES, SMARTS, mol2, MDL-SDF and 3D molecules), including visualization with tools such as PyMOL.
• Generation of 3D small-molecule models from 1D/2D representations.
• Calculation and visualization of ligand descriptors.
• Pharmacophore modelling and ADME/Tox assessment (Lipinski, Veber, Egan, etc.).
• Identification of frequent hitters, aggregators and toxic fragments (FAF-Drugs).
• Ligand-based virtual screening, including designing and analyzing decoys.
• Investigation of molecular fragments comprising ligands.
• Practical sessions using KNIME, RDKit, Frog, Open Babel and MOE.

## BQ2CE115: Hits to lead (English)

**Knowledge objectives:** Understand the theoretical and practical principles underlying the progression from initial hits to lead compounds in drug discovery. Learn about experimental and in silico rational design approaches used to optimize interactions with therapeutic targets while considering pharmacokinetics, specificity and safety.

**Targeted skills:**
• Identify and apply experimental and computational hit-to-lead optimization strategies, including (i) X-ray diffraction, NMR, medicinal chemistry, structure–activity relationships (SAR) and QSAR; and (ii) molecular simulations, ligand- and fragment-based design, and rescoring methods.
• Analyze hit-to-lead optimization case studies in therapeutic fields including infectious diseases, cancer, cardiovascular diseases and reproductive health.
• Understand high-throughput screening (in vitro and in silico) and its role in identifying biologically active molecules.
• Assess additional drug candidate requirements, including specificity, bioavailability, pharmacokinetic properties and toxicity.
• Evaluate workflows from initial hit identification to selecting lead compounds for subsequent preclinical and clinical evaluation.

**Syllabus:**
Introduction to hit identification through high-throughput screening (HTS) and initial selection of biologically active molecules.
Hit-to-lead optimization strategies and methodologies:
• Experimental approaches: X-ray diffraction, NMR, medicinal chemistry, SAR and QSAR.
• Computational approaches: rescoring, molecular simulations, ligand- and fragment-based design.
• Lead optimization case studies across therapeutic fields (infectious diseases, cancer, cardiovascular diseases and the reproductive system).
• Critical drug candidate properties: specificity, bioavailability, pharmacokinetics and lack of toxicity.
• Integration of medicinal chemistry and drug design principles to guide the transition from hits to marketable therapeutic compounds.

# COURSE BLOCK: DRUG DESIGN APPLICATIONS (6 ECTS)

## BQBCE115: QSAR application & AI application (English)

**Knowledge objectives:** Apply supervised and unsupervised learning techniques to develop quantitative structure–activity relationship (QSAR) models that predict small-molecule activity against a given target. Understand how to use these models to design filters for chemical libraries and guide the discovery of new inhibitors.

**Targeted skills:**
- Implement a protocol to identify the best QSAR model for predicting molecular activity.
- Develop chemical library filters based on supervised learning methods for drug design projects.
- Design, optimize and execute R scripts to develop supervised predictive models.
- Apply QSAR models to prioritize compounds for experimental campaigns or virtual screening.

**Syllabus:**
- Application of the supervised and unsupervised learning methods covered in class.
- Development of QSAR models for small molecules targeting a specific protein.
- Construction and application of chemical library filters using supervised approaches.
- Practical implementation and optimization of predictive models using R statistical software.
- Project-based practical sessions to identify potential inhibitors of a molecular target.

## BQ8CE095: Dynamic and molecular modeling application (English)

**Knowledge objectives:** Understand the principles and applications of structural and dynamic modelling to the study of therapeutic molecules.

**Targeted skills:**
- Apply structural and dynamic modelling to assess ligand–protein interactions.
- Integrate these approaches into a workflow in a professional setting.

**Syllabus:**
- Structural and dynamic modelling to predict ligand–protein complexes.
- Analysis of results and selection of candidate molecules for optimization.

# BQ2CE165: Virtual screening application (English)

**Knowledge objectives:** Acquire the fundamental knowledge required to implement a structure-based virtual screening strategy for a target protein.

**Targeted skills:**
• Analyze and prepare the structure of a target protein.
• Prepare a chemical library tailored to the target and screening strategy.
• Select and configure appropriate virtual screening tools.
• Analyze results to identify and prioritize candidate inhibitory molecules.

**Syllabus:**
• Analysis and preparation of a target protein structure.
• Preparation and filtering of a chemical library.
• Selection and adaptation of a virtual screening protocol.
• Implementation of screening and analysis of results; identification and prioritization of candidate inhibitory molecules.

# COURSE BLOCK: CHALLENGES OF RESEARCH IN DRUG DESIGN (6 ECTS)

## BQ2CE125: Research protocol in In silico drug design (English)

**Knowledge objectives:** Develop an integrated understanding of in silico drug design by applying molecular modelling, chemical library optimization, and ligand- and structure-based virtual screening to the same target system. Understand how these approaches complement one another within a complete drug design workflow.

**Targeted skills:**
• Apply, analyze and combine the different stages of a drug design protocol.
• Understand and implement a complete drug design protocol to identify potential inhibitors of a target protein.
• Integrate results from several projects addressing the same target to understand the complementarity and purpose of each approach.
• Develop an optimized workflow combining diverse computational tools for drug design.

**Syllabus:**
Integrated project combining:
• Molecular modelling of a target to assess its flexibility.
• Selection of candidate compounds using statistical filters to build an optimized chemical library.
• Virtual screening of the target with the optimized chemical library (ligand-based and structure-based) to predict inhibitory molecules.
• Practical application and analysis of results from several modules to build a complete in silico drug design project.
• Development of an optimized protocol and workflow for identifying new inhibitors of a target protein.

## BQ2CE205: Medicinal chemistry (English)

**Knowledge objectives:** Acquire foundational concepts relating to structure–pharmacokinetic relationships, metabolism and associated chemical reactions, and hit optimization.

**Targeted skills:**
• Explain key concepts and terminology in medicinal chemistry, including lipophilicity, ionization, membrane permeation, metabolic intermediates, privileged structures and hit-to-lead optimization.
• Apply acquired knowledge to solve exercises and problems in medicinal chemistry and drug design.

**Syllabus:**
• Structure–pharmacokinetic relationships: lipophilicity (logP) and logP calculation methods; ionization of chemical compounds; passive and active membrane permeation; crossing the blood–brain barrier to reach the central nervous system (physicochemical properties that promote or limit permeation).
• Metabolism and toxicophores: phases I and II of metabolism (reaction types and catalysts); metabolic intermediates.
• Structural modification strategies for hit-to-lead optimization: privileged hit structures from the literature, optimization by substitution, molecular extension, bioisosteric replacement, incorporation of metabolically blocking groups, vinylogues and benzologues.

## BQ2CE135: Networking in drug design (English)

**Knowledge objectives:** Enable students to understand the structure and operation of drug design (ISDD) research networks in academia and industry (start-ups and major pharmaceutical companies). Provide knowledge about building a professional network and preparing for career opportunities after the Master's degree.

**Targeted skills:**
• Develop strategies for building and maintaining a professional network in drug design.
• Create and optimize a LinkedIn profile and CV to improve visibility in academia and industry.
• Participate in Master's student groups and professional scientific societies.
• Understand research career paths in France and internationally (doctoral schools and funding opportunities).
• Identify national, European and international doctoral funding schemes (e.g., ANR, regional DIM programs and European funding).

**Syllabus:**
Introduction to research networks in academia and industry (start-ups and large pharmaceutical companies).
Practical advice on professional networking: creating and optimizing a LinkedIn profile, ISDD Master's student groups, participation in relevant scientific societies.
Preparing for life after the Master's degree: overview of doctoral schools and research career paths in France and internationally, national and international funding opportunities for doctoral projects (DIM, ANR and European funding).

## BQ2CE215: Cheminformatics tools for biological therapeutics (English)

**Knowledge objectives:** Expose students to real-world challenges and current issues in drug design through interactions with academic and industry professionals, focusing on cheminformatics tools for designing and optimizing therapeutic molecules. Promote understanding of career paths, research environments and practical applications in computational drug design, structural bioinformatics and cheminformatics.

**Targeted skills:**
• Interact with professionals in academia and industry to discuss contemporary challenges in drug design.
• Gain practical experience applying cheminformatics and bioinformatics tools to design, analyze and optimize therapeutic molecules.
• Understand research workflows in laboratories, platforms (e.g. RPBS, Orphanet), start-ups and major pharmaceutical companies (e.g. Sanofi, Servier, Dassault Systèmes).
• Understand how cheminformatics tools support decision-making in target analysis, chemical library preparation, docking, virtual screening and QSAR modelling.
• Attend scientific conferences and seminars to develop communication, networking and critical assessment skills.

**Syllabus:**
• Seminars featuring leading national and international laboratories in drug design, structural bioinformatics and cheminformatics.
• Talks and career guidance sessions with ISDD Master's alumni, highlighting career paths, research projects and securing funding.
• Meetings with professionals from pharmaceutical companies, start-ups and software firms to understand real-world workflows and practical applications of cheminformatics in drug discovery.

• Participation in scientific conferences (e.g. SFCI and GGMM meetings) and company visits, depending on the year.

## COURSE BLOCK: COMPLEMENTARY CHEMISTRY OPTIONS

### BQBCE135: Quantum chemistry (English)

**Knowledge objectives:** Acquire foundational knowledge of quantum chemistry concepts and computational methods, including semi-empirical calculations (MOPAC, XTB), Hartree–Fock (HF) methods and density functional theory (DFT) applied to small molecules using WebMO.

**Targeted skills:**
• Understand fundamental quantum chemistry methods and their applications to small molecules.
• Perform semi-empirical, Hartree–Fock and DFT calculations using WebMO.
• Interpret computational results in terms of molecular properties and electronic structure.
• Gain practical experience with computational chemistry software workflows.

**Syllabus:**
• Lectures and tutorials introducing the principles of quantum chemistry and computational methods.
• Practical sessions using WebMO for semi-empirical calculations (MOPAC, XTB), Hartree–Fock (HF) calculations, and density functional theory (DFT) calculations.
• Analysis and interpretation of results obtained for small molecules.

### BQ8CE115: Chemical interaction: thermodynamics (English)

**Knowledge objectives:** Acquire an in-depth understanding of chemical interactions and thermodynamic principles governing biomolecular systems. Understand how energy, enthalpy, entropy and kinetics influence the stability of molecular complexes and the specificity of ligand–protein interactions.

**Targeted skills:**
• Understand and explain fundamental thermodynamic and chemical kinetic concepts applied to biomolecules: Gibbs free energy, enthalpy, entropy, equilibria and dissociation constants.
• Model and interpret non-covalent molecular interactions (hydrogen bonds, hydrophobic interactions, electrostatic forces and van der Waals interactions).
• Apply thermodynamic concepts to predict the stability and specificity of protein–ligand complexes.
• Use simple computational and analytical approaches to evaluate chemical interactions and their contributions to complex formation.
• Relate thermodynamic properties to biological phenomena such as ligand binding, enzyme inhibition and allosteric regulation.

**Syllabus:**
• Basic thermodynamics applied to biomolecules: free energy, enthalpy, entropy and Gibbs–Helmholtz relations.
• Chemical equilibria and dissociation constants in protein–ligand systems.
• Chemical kinetics and determination of reaction rates and association/dissociation rate constants.
• Non-covalent interactions: hydrogen bonding, hydrophobic and electrostatic interactions, van der Waals forces and π–π stacking.

• Applications to biological systems: ligand–protein binding, enzyme inhibition, allosteric regulation and complex stability.
• Introduction to computational approaches for estimating binding energy and the contributions of chemical interactions to complex stability.

## COURSE BLOCK: OBLIGATORY MODULE FOR THE ERASMUS MUNDUS JOINT MASTER'S PROGRAM

## BQ8CE135: Project in collaboration with industry (English)

**Exclusively for students of the Erasmus Mundus Joint Master's program of "ChEMoinformatics+"**

**Knowledge objectives:** Understand how cheminformatics approaches and computational methods can be applied to address real-world challenges in an industrial research and development context. Identify the scientific and technical requirements associated with an industry-proposed project. Understand the principles of collaborative project development, including task distribution, coordination and interaction with academic and industrial stakeholders. Recognize the importance of critically evaluating computational results and considering their practical relevance to industrial applications....

**Targeted skills:**
• Analyze a scientific or technical problem proposed by an industrial partner and identify appropriate cheminformatics approaches to address it.
• Apply relevant computational methods, tools and workflows to tackle a defined project.
• Collaborate effectively within a multidisciplinary team of 3–5 students and contribute to shared project objectives.
• Organize and coordinate group work, distribute tasks and monitor project progress.
• Communicate regularly with the academic supervisor to discuss project development, address challenges and interpret results.
• Critically analyze and interpret the results obtained, identify potential limitations and formulate relevant conclusions.
• Present and defend the project's objectives, methodology, results and conclusions during an oral presentation in front of academic and industrial stakeholders.

# SEMESTER 4 (30 ECTS)

## BQBDE025: Research internship (Single-Degree and Double-Degree programs)

## BQ8DE015: Erasmus Mundus M2 training period (Erasmus Mundus Joint Master's program of "ChEMoinformatics+")

**Knowledge objectives:** Introduce students to research in an academic or private-sector laboratory, enabling them to discover and apply scientific research methods and approaches within their career plans.

**Syllabus:**
• Completion of an internship in a research laboratory.
• Assessment of the internship report and oral defense before an examination committee.

During the second year of the program (Master 2), students are required to complete a compulsory research internship, subject to the assessment and validation rules established by the French partner institution.

The internship may be experimental or theoretical and may take place in a partner laboratory or another laboratory, either in Europe or internationally, provided that the internship project is approved by both the French and Italian coordinators, in the case of the double-degree program.

Within the framework of the double-degree program, students shall undertake a research internship organized as follows:

**French Master's Degree:** A research internship lasting five to six months, leading to the submission of an internship report and an oral defense, in accordance with the regulations and assessment procedures of the French institution.

**Italian Laurea Magistrale Degree:** Following the six-month internship, students shall complete an additional three-month period dedicated to the preparation of their Master's thesis (*tesi di laurea magistrale*). This additional period does not constitute an internship under the applicable internship regulations but is devoted to independent research and thesis writing, under the academic responsibility of the Italian university and the supervision of a thesis supervisor (*relatore*).
The purpose of this period is to further develop the scientific work carried out during the internship and to prepare the Master's thesis in accordance with Italian academic requirements, with a view to its defense during the final Laurea Magistrale examination (*discussione della tesi di laurea*).
The thesis supervisor shall be the head of the research group in which the internship is carried out, while the academic coordinators of the double-degree program shall act as tutors, ensuring that the internship is conducted in accordance with the conditions established in the double-degree agreement.
The Master's thesis/internship report shall be written in English.

# BQ2DE015 : Préparation de stage de recherche (Single-Degree and Double-Degree programs)

**Not included in the Erasmus Mundus Joint Master's program of "ChEMoinformatics+"**

**Knowledge objectives:** Acquire the knowledge and methods required to design and prepare a research project related to the subjects covered in the Master's program.

**Targeted skills:**
• Develop and define a research project based on a scientific question.
• Conduct a literature review and identify relevant potential collaborations.
• Mobilize and integrate the in silico knowledge and tools acquired throughout the Master's programme.
• Develop a work plan for a research project.
• Present and defend a scientific project.

**Syllabus:**
• Define the research internship project and consider its practical implementation.
• Conduct a literature review and identify potential collaborations.
• Integrate the knowledge and in silico tools acquired throughout the Master's programme into the project.
• Develop a work plan.
• Monitor project progress: prepare an interim report (2–3 pages) halfway through the internship, outlining the progress made and any necessary adjustments to the research project.