UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

# SYLLABUS DEL CORSO

# Biochimica delle Proteine

**2526-1-F0602Q060**

## Aims

This course aims to deepen concepts related to the relationships between the structure and function of proteins within a pathway that, starting from physiological and evolutionary aspects, considers pathological implications and biotechnological applications of proteins. Some biophysical and biochemical techniques suitable for studying the structure, function and modification of individual proteins or biochemical circuits will be described. By emphasising the need for a multidisciplinary approach, the course aims to offer not only cognitive but also methodological tools useful for the study, control and biotechnological exploitation of complex biological phenomena involving proteins. The general objectives are as follows:

**Knowledge and understanding**
By the end of the course, students will have acquired knowledge about the mechanisms of protein folding, the relevance of structural flexibility and functional promiscuity, conformational and functional transitions, natural evolution and *directed-evolution* of proteins, conformational transitions often associated with the establishment of protein-protein interactions, under both physiological and pathological conditions. Students will acquire knowledge of some techniques for structural and functional studies of some classes of proteins.

**Ability to apply knowledge and understanding**
The examples illustrated during the lectures bring out the main mechanisms of (mal)functioning of proteins, associated with their structural peculiarities and interaction with the environment. It is expected that they can be recognised in contexts other than those exemplified and are potentially applied, for example, to design new 'synthetic' proteins. It is expected that students learn to recognise the various contexts in which the techniques outlined in the course are profitably applicable.

**Autonomy of judgment**
Students will be stimulated to recognise the relationships between protein structure and function and to predict the effects of certain environmental contexts on both these aspects.
Students will be encouraged to personally identify the wealth of connections between the main topics of this course. The identification of complex biological problems and the development of original solutions increasingly requires the use of knowledge from different and complementary disciplinary fields - from cell biology to chemistry

to physics. Grasping relationships between different phenomena (e.g. molecular and biophysical) and exploiting the complementarity of different investigative techniques creates the prerequisites for proposing new visions, developing a critical sense and offering new solutions.
Students will be able to predict the effects of various environmental contexts on proteins, developing a critical and original perspective in interpreting and solving complex biological problems.

**Communication skills**
By the end of the course, students will have acquired the appropriate vocabulary and linguistic skills to describe the biochemical and molecular phenomena covered in the course.

**Learning skills**
Students will be able to successfully tackle advanced courses in Protein Science and understand the scientific literature in these disciplinary areas.

## Contents

1. Protein structure and methods for their study.
2. *In vitro* and *in vivo* studies on protein folding.
3. Protein-protein interactions, biomolecule phase separation and transition.
4. Protein turnover mechanisms.
5. Principles of natural evolution and directed evolution of proteins

## Detailed program

**1. Protein structure and methods for their study**
Structural order and disorder. Structural elements and motifs.
Techniques for structural protein studies: X-ray Crystallography, Cryo-electron Microscopy, NMR Spectroscopy.
Mass Spectrometry (MS) for protein characterization and post-translational modification analysis.
Measuring protein similarity.
Convergence/divergence in protein structure analyzed through case studies.
Introduction to bioinformatic tools for structural prediction (e.g., AlphaFold) and molecular modeling.

**2. In vitro and in vivo studies on protein folding**
Thermodynamic and kinetic aspects of protein folding.
Theories of protein folding.
Protein folding in vivo and the role of chaperonins.
Importance of translational events on protein folding.
Biotechnological implications of controlling translation speed.
Protein misfolding and its implications in human pathologies.

**3. Protein-protein interactions, biomolecule phase separation and Ttransition**
Methods for studying protein-protein interactions: Microcalorimetry, Surface Plasmon Resonance, FRET, Pull-down & MS.
Physicochemical phenomena underlying biomolecule condensation.
Examples of biological relevance of biomolecule condensation.
From liquid condensates to solid aggregates: physiological and pathological aspects of phase transition.
Types of protein aggregates. Amyloid fibrils and prion proteins. Hallmarks of amyloid aggregation.
From propagation mechanisms to diagnostic devices for amyloid pathologies.

**4. Mechanisms of protein turnover**
Overview of cellular protein turnover mechanisms.
Introduction to autophagy as a cellular degradation and recycling mechanism.
Protein degradation via the ubiquitin-proteasome system (UPS).
Pharmacological potential of natural UPS mechanisms and "dual target degrader" drugs.
Case studies

**5. Principles of natural and nirected protein evolution**
General concepts of natural evolution and evolvability from the perspective of biotechnological protein design.
Protein evolution rate and protein fitness landscape.
Role of phenotypic variation and neutral drift in protein evolution.
Various protein engineering approaches and an overview of directed evolution techniques (e.g., random mutagenesis, DNA shuffling, site-directed mutagenesis).
Case studies of biotechnological applications of protein engineering and directed evolution (e.g., industrial enzymes, biopharmaceuticals).

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## Prerequisites

• Basic knowledge of Biochemistry and Cell Biology.
• No prerequisite courses are required.

## Teaching form

The course consists of 24 lessons (6 ECTS) delivered in a mixed mode, conventional and interactive. The conventional lecture-based format necessitates in-person attendance, whereas the interactive format encourages active student participation in the analysis and interpretation of recently published scientific papers.

A number of lessons (up to four) will be conducted with guest experts who will deliver seminars illustrating the application of specific techniques for the structural or functional study of proteins.

New study topics may be introduced based on student requests
Depending on the number and requests of attending students, group work aimed at analyzing scientific literature may be carried out.

## Textbook and teaching resource

• Recommended textbooks: Lehninger Principles of Biochemistry, Voet & Voet Biochemistry; Branden & Tooze Introduction to Protein Structure.
• Slides and video lessons: available on the course Moodle page (http://elearning.unimib.it/).
• Scientific articles cited/described during lectures.

## Semester

First semester

## Assessment method

An **oral examination** lasting 30-40 minutes, structured in **two parts**:
• **Presentation with PowerPoint slides** of a scientific article agreed upon with the lecturer (duration: 15 minutes), followed by questions related to the article (5-10 minutes).
• **Questions on the content of the frontal lectures** (from at least two of the five thematic blocks) (10-15 minutes).
The evaluation considers the degree of **understanding of the topics, the ability to identify connections** between disciplinary contents, the use of **appropriate language**, and **clarity** of exposition.
Students enrolled for the first examination session may present their scientific article in the form of a seminar to the class.

## Office hours

By appointment, contact via email at stefania.brocca@unimib.it

## Sustainable Development Goals

GOOD HEALTH AND WELL-BEING | QUALITY EDUCATION | INDUSTRY, INNOVATION AND INFRASTRUCTURE