

Protein Chemistry and Engineering

Code: 100935
ECTS Credits: 6

| Degree | Type | Year | Semester |
|-----------------------|------|------|----------|
| 2500253 Biotechnology | OB | 3 | 1 |

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Use of Languages

Principal working language: catalan (cat)
Some groups entirely in English: No
Some groups entirely in Catalan: Yes
Some groups entirely in Spanish: No

Other comments on languages

Based on an agreement with the students enrolled, part of the theory programme will be given in English

Prerequisites

There are no official prerequisites, but it is assumed that students have previously acquired enough solid knowledge on subjects like Fundamentals of Chemistry, Organic Chemistry, Biochemistry and Recombinant DNA Technology.

As in most subjects, much of the literature is in the English language, which is also used in the figures projected in theory classes and also for oral communication, when needed.

Objectives and Contextualisation

The course on Protein Chemistry and Engineering belongs to the main subject "Proteins and nucleic acids: structure, function and engineering" of which a part has been taught in the second year of the Biotechnology degree. This course examines the structural and functional characteristics of amino acids, peptides and proteins both from a basic and applied point of view, the methodologies used in their analysis and modification, and their biomedical and biotechnological applications.

Proteins are effector molecules of many biochemical and biological processes, most of which have been studied in the first two years. However, knowledge of their structure and function is crucial to a deep understanding of a number of subjects in the Biotechnology degree. The knowledge acquired in the course of Protein Chemistry and Engineering is complemented by a practical training in the Integrated Laboratory Course 5. The specific objectives are:

- To reach a deeper understanding of the physicochemical characteristics of amino acids and peptides
- To describe and apply methods for the analysis of protein sequences and peptide synthesis.
- To recognize the structural elements, the different complexity levels, the types of protein folding and their capacity to build higher order structures.
- To reach a knowledge on the use of information resources to establish structural classifications of proteins.
- To understand and explain the most common methods for the analysis of the conformation and stability of proteins, including three-dimensional analysis.

- To describe the molecular basis of protein folding, molecular dynamics, post-translational processing and intra- and extracellular protein traffic.
- To establish evolutionary relationships and learn the methods of structural analysis and structure prediction.
- To understand and apply the most common methods for the production and purification of recombinant proteins.
- To design strategies for modifying and optimizing the properties of proteins and to understand the basis for protein design and the methodologies used in these processes.
- To achieve an global vision about the structure-function relationships in proteins and about the application of these biomolecules in medicine, industry and research.
- To integrate the theoretical knowledge in the interpretation of the results of scientific experiments using the appropriate scientific terminology.

Competences

- Act with ethical responsibility and respect for fundamental rights and duties, diversity and democratic values.
- Describe the molecular, cellular and physiological bases of the organisation, functioning and integration of living organisms in the framework of their application to biotechnological processes.
- Interpret experimental results and identify consistent and inconsistent elements.
- Introduce changes in the methods and processes of the field of knowledge to provide innovative responses to the needs and demands of society.
- Make an oral, written and visual presentation of one's work to a professional or non-professional audience in English or in one's own language.
- Obtain information from databases and use the software necessary to establish correlations between the structure, function and evolution of macromolecules.
- Read specialised texts both in English and one's own language.
- Take account of social, economic and environmental impacts when operating within one's own area of knowledge.
- Take sex- or gender-based inequalities into consideration when operating within one's own area of knowledge.
- Use ICT for communication, information searching, data processing and calculations.

Learning Outcomes

1. Act with ethical responsibility and respect for fundamental rights and duties, diversity and democratic values.
2. Classify proteins in structural families based on data on sequence and secondary and tertiary structures.
3. Correctly analyse data on ligand-macromolecule affinity constants and binding points.
4. Deduce evolutionary relationships between macromolecules from the analysis of sequential data.
5. Describe correctly the molecular bases of protein folding, transport, modification and replacement
6. Evaluate the different techniques of structural analysis and decide on their application to specific experimental situations.
7. Extract information from genomic and proteomic databases.
8. Extract three-dimensional structures of macromolecules from databases and use the software needed to visualise and understand structure-function relationships.
9. Identify conserved protein motifs and domains.
10. Interpret experimental data on protein stability and folding.
11. Interpret experimental results and identify consistent and inconsistent elements.
12. Interpret findings from structural studies of proteins and nucleic acids
13. Introduce changes in the methods and processes of the field of knowledge to provide innovative responses to the needs and demands of society.
14. Make an oral, written and visual presentation of one's work to a professional or non-professional audience in English or in one's own language.
15. Read specialised texts both in English and one's own language.

16. Take account of social, economic and environmental impacts when operating within one's own area of knowledge.
17. Take sex- or gender-based inequalities into consideration when operating within one's own area of knowledge.
18. Use ICT for communication, information searching, data processing and calculations.

Content

THEORY

I. Fundamental properties of amino acids and proteins

Proteins, peptides and their functions in living beings. Structure and physicochemical properties of amino acids. Chemical reactivity. Differential contribution of amino acids to protein properties. Evolutionary relationships.

II. The peptide bond and the sequence polypeptide

Stereochemistry of the peptide bond. Types of natural peptides. Chemical reactivity of peptides. The polypeptide sequence. Strategies for determining the sequence of proteins. Chemical synthesis of peptides; combinatorial libraries.

III. Conformational determinants. Secondary structures

Structural hierarchy. Types of conformation-stabilizing forces. Cooperativity of weak interactions. Determinants of protein folding. Main types of secondary structures.

IV. Structural Classification of Proteins

Supersecondary structures and motifs. Structural domains. Tertiary structure. Domain classification. Conformation and function of fibrous proteins. IDPs- intrinsically disordered proteins.

Structure-function correlation . Examples

General functions of proteins. Enzymatic proteins: examples. Proteins that bind to nucleic acids: examples. Molecular motors: examples. Membrane proteins.

VI. Quaternary structure of proteins

Advantages of quaternary structures. Protomers and subunits. General principles: interfaces, geometries, symmetries. Examples of oligomeric proteins: structure-function and regulation of the activity

VII. Determining the three-dimensional structure of proteins

General methodologies for the structural characterization of proteins. Dissolution analysis: IR, DC, UV-Vis, fluorescence. Analysis in solid phase: X-ray crystallography and cryo-electron microscopy. NMR spectroscopy: 3D structure in solution.

VIII. Folding and conformational dynamics

Protein folding and unfolding: native state and unfolded state. Methods for the analysis of folding. Thermodynamics and mechanistics of the folding process; models that describe it. Folding and aggregation; conformational diseases. Protein folding *in vivo*: the molecular chaperones. Molecular dynamics of proteins.

IX. Post-translational modifications

Types of post-translational modifications and their functional implications. Transport and associated changes. Limited proteolysis: pre-proteins, zymogens. Examples of regulation by limited proteolysis: coagulation, digestive enzymes. Degradation and protein turnover *in vivo*.

X. Protein-ligand interaction

Forces involved in protein-ligand association. Methods of study of the interaction. Determination of kinetic and thermodynamic parameters. Designing drugs based on the structure.

XI. Biochemical evolution of proteins

Protein evolutionary relationships. Detection and analysis of homologies; sequential databases; phylogenetic trees. Convergent and divergent evolution; examples. Sequence structure and function. 3D structure prediction; conformational modelling. Evolution of genomes and protein evolution.

XII. Protein engineering: rational design

Rational design: directed mutagenesis as a tool for the analysis and modification of proteins. Examples and applications of protein engineering in the analysis, modification and improvement of the structure, stability, and functionality.

XIII. Protein engineering: directed evolution and de novo synthesis

Directed evolution: random mutagenesis and combinatorial protein engineering methods. Methods for the generation and selection of variants. Examples of redesigned proteins. *De novo* protein design - computer algorithms.

PROBLEMS

The content of this section will be given in the form of a dossier at the beginning of the semester via the Virtual Campus. It involves a certain amount of problems related to the topics developed in the theory class. The dossier will be updated periodically. The characteristics of the various parts of the theory syllabus make the subjects of the problems class to be concentrated in a limited number of aspects. Thus, the evaluation of problems may vary between partial examinations.

Methodology

The training activities of the subject are divided into theory classes, practical sessions for problem solving, and delivery of homework through the Virtual Campus and seminars/tutorials. These last sessions complement the official schedule and will be held during the last third of the course to discuss selected seminars.

Theory classes

The teaching staff will explain the content of the syllabus with the support of audio-visual material that will be available in advance to students in the Virtual Campus. These lecture sessions, 38 of which are planned, will be the most important part of presential teaching. It is recommended that the students have the material published in the CV available in printed or digital format in order to be able to follow the classes more comfortably and that they regularly consult the books recommended in the Bibliography section of this teaching guide.

The theory lectures will be mainly expositive. However, alternative methodologies such as flipped classes, questionnaire proposals on parts of the syllabus prepared by self-study or on-line mini-tests may be held during some of the theory sessions.

Practical sessions for problem solving

The class group will be divided into two subgroups (A and B). It is expected that 7 sessions will be devoted to the resolution of practical cases and experimental problems related to the contents of the theory program.

Groups of 3-4 students will work on the proposed problems before the actual class session. The presential sessions will be generally non-expository, in such a way that the resolution of problems or practical cases will be done jointly between students and professors. The collection of problems that must be resolved and

delivered at the beginning of a class and the proposal of new ones in randomly selected sessions will be announced when necessary.

Delivery of homework

Previously announced in the Virtual Campus, practical cases or exercises will be proposed for the students to solve them before a specific date, working within the same groups formed for problem solving sessions. A total of two or three deliveries are to be expected. Once solved, they will be sent in PDF format, through the Virtual Campus specific tool. This teaching activity is designed to complement the teaching of both theory and practical classes.

Seminars / tutorials

Being the contents of the subject quite extensive, it is advisable that students work autonomously to prepare some parts of the subject. The information on the list of subjects proposed and its schedule will be published at mid-term. Initiatives to prepare seminars not previously scheduled but clearly related to the subject will be welcome. The seminar activity is not strictly mandatory, but strongly recommended.

As mentioned at the beginning of this section on teaching methodology, three sessions of seminars will be scheduled outside the official calendar, with 2-3 selected seminars per session. This selection will not necessarily obey quality criteria but opportunity criteria regarding the complementation of presential sessions.

Material available on the Virtual Campus of the subject

Teaching guide

Presentations used in theory classes

Problem/practical cases dossier

Schematic calendar of teaching activities

And all that material that is generated throughout the semester

Annotation: Within the schedule set by the centre or degree programme, 15 minutes of one class will be reserved for students to evaluate their lecturers and their courses or modules through questionnaires.

Activities

| Title | Hours | ECTS | Learning Outcomes |
|---------------------------------|-------|------|-------------------------------|
| Type: Directed | | | |
| Problem/practical cases solving | 7 | 0.28 | 3, 4, 7, 10, 12, 11, 6 |
| Theory sessions | 38 | 1.52 | 3, 2, 5, 9, 10, 11, 15, 6 |
| Type: Supervised | | | |
| Homework delivery | 4 | 0.16 | 18, 4, 8, 7, 9, 10, 12 |
| Seminar preparation | 4 | 0.16 | 16, 18, 8, 14, 12, 11, 13, 15 |
| Seminar presentations | 3 | 0.12 | 1, 17, 18, 14, 12, 11 |

Type: Autonomous

| | | | |
|--|----|-----|--|
| Group or individual work to prepare problems/cases or seminars | 20 | 0.8 | 18, 4, 8, 7, 12, 11 |
| Study - autonomous work | 65 | 2.6 | 3, 2, 4, 5, 8, 7, 9, 10, 12, 11, 15, 6 |

Assessment

The evaluation of the subject will be individual and continuous; it will be subdivided into the following modules: partial exams - integrating theory and problems-, presential online resolution of mini-tests, resolution of problems, homework deliveries through the Virtual Campus and the preparation of a seminar.

Partial integrated exams

There will be three partial exams consisting of multiple-choice questions, short questions and exercises-problems. Both multiple choice questions and the short, written questions and exercises-problems will amount to a 50% of the total score of each exam. This procedure intends to obtain an integrated assessment of all the concepts presented in presential classes.

The minimum mark to pass a partial exam is 4.0; thus, those students who have obtained a mark equal or superior to 4.0 in the first two exams will obtain a mark for the section of written exams equal to the average of the three partial marks. A minimum mark of the third partial exam is not required to calculate this average.

Each of the partial tests will have a 25% weight on the global mark of the course; therefore, the total weight of this section in the final mark is 75%.

Classroom online mini-tests

Three - four short online tests will be proposed during the semester to be answered in the classroom. They will not be announced previously and will be answered in groups of two. The weight of this section is 5% of the global mark.

Problem solving

A problem/case dossier will be uploaded in the CV. As explained earlier, students will have to prepare the problems planned for each of the sessions beforehand. In some sessions, students will be asked to submit the proposed exercises, while in others new exercises will be proposed to be solved in class.

The total weight of this section is 5% of the total mark, calculated as the average of all deliveries (three maximum).

Homework deliveries through the Virtual Campus

The exercises will be discussed and prepared in groups, similarly to the problem solving procedure. The documents will be delivered through the corresponding tool of the CV before a specific date that will be announced with sufficient advance.

The weight of this section in the total mark is 10%.

Seminars

The evaluation of the seminars prepared in groups of 3-4 people will amount to a 5% of the final mark (except in the case of people who choose not to present a seminar, for whom a specific calculation of their final grades will be used). In the three sessions that will be scheduled outside of the official timetable some selected seminars will be presented, especially those that cover the parts of the syllabus not exhibited in class. The third partial exam will contain a limited number of questions about the seminars exposed. The answer to these questions will be considered as a small additional mark to the total grades obtained.

Global evaluation

The students who have not passed the score of 4.0 in any of the first two partial exams must take a resit examination at the day of the third exam. It is also possible to improve the marks of the first two partial exams, in which case the students who adhere to this option are supposed to renounce to the marks previously obtained. It should be noted that no resit examination will be offered for the third partial exam or for the presential activities based on problems, the mini-tests, homework deliveries and seminars.

Considering that, according to the UAB evaluation regulations, in order to be eligible for the resit exam, students must have been previously evaluated in a set of activities whose weight equals a minimum of two thirds of the total marksof the subject, access to this exam will be only possible under the condition that the student must have obtained a mark in at least one of the two previous partial exams and has participated in the activities of file delivery through the CV and in the problems exercises.

Students must participate and be evaluated in all the sections of the subject to be able to pass it. The minimum mark required to pass the subject is 3.5/10 in the average of the three partial exams. The subject will be considered passed when, after completing the aforementioned condition, the final sum of the various sections in which the note is subdivided reaches 5.0.

Other considerations

Students who cannot attend an individual assessment test for causes such as illness, death of a first-degree relative or accident and provide the corresponding official documentation to the Degree Coordination and the teaching staff will have the right to answer the test on another date.

The student will be graded as "No Avaluable" if the weighting of all conducted evaluation activities is less than 67% of the final score.

Assessment Activities

| Title | Weighting | Hours | ECTS | Learning Outcomes |
|--|-----------|-------|------|------------------------------------|
| Answer to online questionnaires during theory sessions | 5% | 1 | 0.04 | 3, 2, 5, 9, 10, 12, 11, 6 |
| Homework delivery using CV | 10% | 1 | 0.04 | 2, 4, 7, 14, 12, 13, 15 |
| In-class delivery of problems/cases | 5% | 1 | 0.04 | 3, 12, 11, 6 |
| Partial exams | 75% | 5 | 0.2 | 3, 2, 4, 5, 9, 10, 12, 11, 15, 6 |
| Seminars | 5% | 1 | 0.04 | 1, 17, 16, 18, 8, 7, 14, 9, 10, 15 |

Bibliography

Basic

(from oldest to newest)

- Brandèn C. & Tooze J., Introduction to Protein Structure (1999) Garland Science
- Gómez-Moreno C i Sancho J. (eds.) Estructura de Proteínas (2003) Ariel Ciencia
- Petsko, R. & Ringe, D., Protein Structure and Function (2003) Blackwell Publishing
- Whitford, D., Proteins: Structure and Function (2005) Wiley
- Buxbaum, E., Fundamentals of Protein Structure and Function (2015), Springer (2015, *Electronic document, UAB accessible*)
- Kessel, A. & Ben-Tal, N., Introduction to Proteins: Structure, Function and Motion (2010) CRC Press (2015, *Electronic document, UAB accessible*)

- Williamson, M., How Proteins Work (2012) Garland Science
- Kuriyan, J., Konforti, B. & Wemmer, D. The Molecules of Life (2013) Garland Science
- Walsh, G. Proteins: Biochemistry and Biotechnology (2014) Wiley (2019, *Electronic document, UAB accessible*)
- Lesk, A.M., Introduction to Protein Science 3rd ed. (2016) Oxford University Press
- Almeida, P., Proteins. Concepts in Biochemistry (2016) Garland Science
- Bahar I., Jernigan R.L. & Dill, K.A., Protein Actions (2017) Garland Science
- Backman, L. Protein Chemistry (2020) De Gruyter

Any of these books contains many interesting notions for the course. However, no one of them may be used as a lone-standing textbook. Some are more didactically-oriented (Petsko & Ringe, Williamson, Brandén & Tooze) but every reading will be enjoyable

Complementary

- Buckel, P. (ed), Recombinant Protein Drugs (2001), Birkhäuser Verlag
- Bujnicki, J.M. (ed.) Prediction of protein structure, functions and interactions (2008) Wiley
- Creighton T.E., Proteins. Structures and Molecular Properties. (1993) (2nd ed.) Freeman W.H. & Co.
- Fersht A. Structure and Mechanism in Protein Science (1999) W.H. Freeman & Co.
- Glick, B.R. & Pasternak, J.J. Molecular Biotechnology (1998) ASM Press
- Kamp, R.M., Calvete, J. J., Choli-Papadopoulou, T. Methods in Proteome and Protein Analysis (2004) Springer-Verlag
- Kraj, A. & Silberring, J. (eds) Introduction to Proteomics (2008) Wiley
- Kyte, J. Structurein Protein Chemistry 2nd ed. (2007) Garland Science
- Lutz, S., Bornscheuer, U.T. (eds.) Protein Engineering Handbook (2008) Wiley
- Nussinov, R. & Schreiber, G. Computational Protein-Protein Interactions (2017) CRC Press
- Oxender D.L. & Fox C.F., Protein Engineering (1987) Alan Liss Inc.
- Patthy, L. Protein Evolution (2007) (2nd ed.) Wiley
- Perutz M., Protein Structure. New Approaches to Disease and Therapy. (1992). Freeman W.H. & Co.
- Schultz, G.E. & Schirmer, R.H. Principles of Protein Structure (1979) Springer Verlag
- Park, S.J., Cochran, J.R. Protein Engineering and design (2009) CRC Press
- Sternberg M.J.E. Protein Structure Prediction. (1996) IRL- Oxford University Press
- Tompa, P. & Fersht, A. Structure and function of intrinsically disordered proteins (2009) CRC Press
- Twyman, R., Principles of Proteomics (2004) Taylor & Francis
- Veenstra, T.D. & Yates, J.R. Proteomics for Biological Discovery (2006) Wiley

Internet sites

Links to selected sites may be found at: https://catalegclassic.uab.cat/search*cat/r?SEARCH=100935

Software

PyMol: <https://pymol.org/2/>

JMol: <http://jmol.sourceforge.net/>