Universitat Autònoma de Barcelona

2018/2019

Protein Chemistry and Engineering

Code: 100762
ECTS Credits: 6

Degree	Type	Year	Semester
2500250 Biology	OT	4	0

Contact

Name: Josep Vendrell Roca
Email: Josep.Vendrell@uab.cat

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 may be given in English

Prerequisites

There are no official prerequisites as this is an optional subject in the fourth year, but it is assumed that the student has previously acquired enough solid knowledge on Structure and Function of Biomolecules, Chemistry, Cell Biology, Metabolism and Bioinformatics during the first three courses of the degree.

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

Proteins are effector molecules of many biological processes, and knowledge of their structure and function is fundamental for the consolidation of concepts acquired in a number of subjects of the Biology degree. In Protein Chemistry and Engineering we will study the structural and functional characteristics of amino acids, peptides and proteins both from basic and applied points of view, the methodologies used in their analysis and modification and their applications to biomedicine and biotechnology. The specific objectives of the course 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 knowledgein the interpretation of the results of scientific experiments using the appropriate scientific terminology.

Skills

- Analyse and interpret the origin, evolution, diversity and behaviour of living beings.
- Apply statistical and computer resources to the interpretation of data.
- Be able to analyse and synthesise
- Be able to organise and plan.
- Develop critical thinking and reasoning and communicate ideas effectively, both in the mother tongue and in other languages.
- Develop independent learning strategies.
- Isolate, identify and analyse material of biological origin.
- Understand and interpret the physicochemical bases of the basic processes of living beings
- Understand the processes that determine the functioning of living beings in each of their levels of organisation.

Learning outcomes

1. Apply statistical and computer resources to the interpretation of data.
2. Be able to analyse and synthesise.
3. Be able to organise and plan.
4. Describe correctly the molecular bases of protein folding, transport, modification and replacement.
5. Design a basic protocol for obtaining mutants of a recombinant protein, expressing them and purifying them.
6. Develop critical thinking and reasoning and communicate ideas effectively, both in the mother tongue and in other languages.
7. Develop independent learning strategies.
8. Identify evolutionary relationships between proteins through sequential data analysis and use software for manipulating three-dimensional structures extracted from databases.
9. Identify the capacities of the different structural analysis techniques and decide how to apply them to specific experimental situations.
10. Interpret experimental data on protein stability and folding.
11. Interpret findings from structural studies of proteins and nucleic acids.
12. Use these techniques from protein chemistry and recombinant DNA to identify, clone and express target genes and proteins that can be used to design and obtain enzymes.

Content

T H E O R Y

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 r e l a t i o n s h i p s .

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. C onformation and function of fibrous proteins. IDPs- intrinsically disordered proteins.

V. 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. P*ost-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 e*volution 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 modeling. 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. Denovo protein design - computer algorithms.

Out of the programme scope. XIV. *Protein engineering: heterologous production*

Goals of the protein engineering and production cycle. General strategies for the heterologous expression of recombinant proteins. Heterologous expression in different organisms; choice of expression systems. Purification methodologies for the analysis of recombinant proteins.

This issue is not part of the program because its contents has already been treated in Recombinant DNA Technology or similar courses.

P R O B L E M S

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 selectedseminars 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

Activities

Title	Hours	ECTS	Learning outcomes
Type: Directed			
Problem/practical cases solving	7	0.28	1, 7, 9, 10, 11, 2, 12
Theory sessions	38	1.52	4, 5, 9, 8, 10, 11
Type: Supervised			
Homework delivery	4	0.16	1, 7, 9, 8, 10, 11, 2, 3
Seminar preparation	4	0.16	1, 7, 2, 3
Tutorials/seminar preparation	3	0.12	7, 6, 11, 3
Type: Autonomous			
Group or individual work to prepare problems/cases or seminars	20	0.8	1, 7, 9, 10, 11, 3
Group or individual work to prepare problems/cases or seminars	65	2.6	4, 7, 5, 9, 8, 10, 11, 2, 3, 12

Evaluation

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 that will consist 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 seen 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 grade for the section of written exams equal to the average of the three partial grades. A minimum grade of the third partial is not required to calculate this average.

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

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 grade is calculated as the average of the grades of all deliveries (three maximum).

Homework deliveries through the Virtual Campus

The exercices 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 willbe announced with sufficient advance.
The weight of this section in the total grade 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 retake the partial or partial exams on the day of the third exam. It is also possible to improve the grades of the first two partial exams, in which case the students who adhere to this option are supposed to renounce to the previous grades obtained. It should be noted that the third partial exam is not recoverable, nor are 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 retake process, students must have been previously evaluated in a set of activities whose weight equals a minimum of two thirds of the total grade of the subject, access to the retake assessment programmed together with the third partial of this subject will be only possible under the condition that the student must have obtained a grade 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 grade required to pass the subject is 3.5/10 in the average grade 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 teachingstaff 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.

Evaluation activities

Title	Weighting	Hours	ECTS	Learning outcomes
Answer to online questionaires during theory sessions	5%	1	0.04	4, 7, 6, 9, 8, 10, 11, 12
Homework delivery using CV	10%	1	0.04	1, 8, 10, 11, 2
In-class delivery of problems/cases	5%	1	0.04	5, 9, 10, 11, 2
Seminars	5%	1	0.04	1, 7, 6, 10, 11, 2, 3
Theory partial tests	75%	5	0.2	4, 6, 9, 8, 10, 11, 2, 12

Bibliography

Basic

(from oldest to newest)

- Brandën 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
- Kessel, A. & Ben-Tal, N., Introduction to Proteins: Structure, Function and Motion (2010) CRC Press
- Williamson, M., How Proteins Work (2012) Garland Science
- Kuriyan, J., Konforti, B. & Wemmer, D. The Molecules of Life (2013) Garland Science
- 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

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, Brandën & Tooze) but every reading will be onjoyable

Complementary

- Buckel, P. (ed), Recombinant Protein Drugs (2001), Birkhäuser Verlag

- Bujnicki, J.M. (ed.) Prediction of protein structure, functions and interactions (2008) Wiley

- Buxbaum, E., Fundamentals of Protein Structure and Function (2007), Springer

- 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 ProteinAnalysis (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

- Walsh, G. Proteins: Biochemistry and Biotechnology (2001) Wiley

Internet sites

NCBI PubMed search

Biblioteques de la UAB

Medline

Servers/Databases/Visualization

Many of these links are real relics nowadays, as addresses of webpages continuously change. They may drive you to substitution sites, though.

3Dee database

BLAST a NCBI

CATH

Comparative Sequence Analysis

DALI

EMBL

Human Genome

European Bioinformatics Institute

EXPASY (Swiss Inst. of Bioinformatics)

Molecular visualization resources

Molscript

National Center for Biotechnology Information

PIR

Pfam home page

Predict protein

Protein Engineering (2102) Edited by Pravin Kaumaya

Protein Engineering, Design and Selection

Protein Explorer

Protein sequence Analysis

ProteinDataBank

ProteinDataBank - Europe

PyMol home page

RasMol

SCOP

Structural protein domain classification

Swiss-PDBViewer/DeepView

SWISS-PROT

WHAT IF sotware

World index of molecular visualization resources

General sites for structural Biology

Molecular Models for Biochemistry

P. Reisberg's Biochemistry pages

BioMolecules in the Classroom

Curs de proteïnes amb temaris, auto-tests, etc

Principles of Protein Structure Using the Internet

Bioquímica - Devlin

Proteinexplorer

Medical Biochemistry

BioROM