

# Teaching guide

## IDENTIFICATION DETAILS

Degree:	Biotechnology
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Field of Knowledge:	Science
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Faculty/School:	Experimental Science
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Course:	BIOREACTORS
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Type:	Compulsory
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ECTS credits:	6
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Year:	3
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Code:	2035
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Teaching period:	Fifth semester
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Area:	Biotechnological Process Engineering
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Module:	Biotechnological Tools
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Teaching type:	Classroom-based
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Language:	English
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Total number of student study hours:	150
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## SUBJECT DESCRIPTION

Bioreactors are adequately conditioned vessels in order to carry out transformations by means of biological systems. They constitute one of the most important tools of Biotechnological Process Engineering and Industrial Biotechnology to obtain knowledge, goods and services.

The aim of this course is providing basic tools so that the student can manage within this discipline. This considers acquiring skills dealing with biological reactor description and design, and realising the importance of bioreactor diversity and versatility regarding biotechnological applications. This course also looks for providing the student

with the necessary knowledge to obtain and manage cell cultures and their possible applications in areas such as agrobiotechnological and biomedical research and the design of advanced therapies such as cell regeneration and tissue engineering.

This course, as the other disciplines within this degree, aims at equipping our students with knowledge and skills that help them to participate in the generation of new processes and biotechnological products that contribute to the common good and the development of society from the respect for life and the environment in which it develops. Likewise, and as reflected in the proposed thinking, the student is encouraged to be able to integrate the anthropological, ethical and philosophical aspects that do not limit the explanation of reality to a single source of knowledge.

## GOAL

The main aim of the subject is teaching the basic guidelines for obtaining and maintaining of cell cultures, looking for a broad and updated knowledge on the applicable techniques, and the acquisition of skills dealing with description and design of biological reactors, as well as presenting the diversity and versatility of the bioreactors for biotechnological applications.

The specific aims of the subject are:

(F1) Indicating and tagging the influence and contributions of the new technologies in Molecular and Cellular Biology on the pharmaceutical sector.

(F2) Learning about the requirements of microorganisms and established cell lines in large-scale cultivation and fermentation.

(F3) Understanding how the basic knowledge generated in the laboratory using different models are turned into biotechnological applications for the benefit of society.

(F4) Working properly in a laboratory involving biological material (bacteria, fungi, viruses, animal and plant cells.) including safety and handling biological waste.

(F5) Being able to properly design and execute an experimental protocol based on the theoretical knowledge from different courses.

(F6) Identifying and define laboratory instruments and materials.

## PRIOR KNOWLEDGE

In order to obtain the best academic progress, proper basis on the first year subjects, such as Mathematics, Physics, Cell Biology, General Chemistry and Biochemistry, are advised. Sufficient knowledge on Physiology, Metabolic Biochemistry, Microbiology and Biochemical Engineering from the second year are also recommended.

## COURSE SYLLABUS

### SECTION I: CELL CULTURE AND TISSUE ENGINEERING

#### Lesson 1

Introduction to cell culture. Historical background. Applications. Biology of animal cells in culture. Types of animal cell culture.

#### Lesson 2

Basic techniques in animal cell culture. Culture conditions, growth media, culture vessels and surfaces. Propagation and subculturing. Aseptic techniques. Cryopreservation. Basic equipment and facilities in animal cell culture.

#### Lesson 3

Guidelines for isolation and maintenance of mammalian primary cultures and cell lines. Cell morphology, viability and growth. Cloning methods and cellular characterisation.

#### Lesson 4

Animal cell culture analyses. Cell differentiation and transformation. Cell migration. Angiogenesis. Viability cytotoxicity and surveillance. Apoptosis and necrosis.

#### Lesson 5

Specific techniques in cell culture. Cell transfection, production of recombinant proteins, cellular fusion and antibody production.

#### Lesson 6

Stem cells. Culture and in vitro characterisation. Dedifferentiation, reprogramming and pluripotency.

#### Lesson 7

Three-dimensional cell culture. Preparation and maintenance of organotypic cultures. Introduction to tissue engineering. Applications for regenerative medicine.

### SECTION II: KINETICS AND BIOREACTOR DESIGN

#### Lesson 8

Introduction to Bioprocesses, Biocatalysts and Bioreactors. Kinds of bioreactors according to shape, phenomenology, operation way and state of biocatalyst.

#### Lesson 9

Enzymatic kinetics, microbial kinetics and metabolic stoichiometry - Brief review on enzymatic reaction kinetics. Kinetics on processes carried out by living cells. Microbial kinetics. Structured models and segregated models. Stoichiometry of cell growth and product formation. Yield.

#### Lesson 10

Bioreactor design – Ideal mixture hypothesis. Discontinuous, semi-continuous and continuous reactors. Systems with recycle. Deviations from ideality: dead zones and short circuits. Plug flow hypothesis. Fixed-bed bioreactors, fluidized bed bioreactors, bubble columns and air-lift. Bioreactors with immobilized biocatalysts.

#### Lesson 11

Special bioreactors - Fermentations in solid state. Pulsed bioreactors. Photobioreactors. Membrane bioreactors. Microbial fuel cells.

### SECTION III: PHENOMENOLOGY AND BIOPROCESS RUNNING

#### Lesson 12

Transport phenomena in bioprocesses - Phenomenology of bioprocesses. Heat transfer. Transfer of matter. Fluid dynamics. Aeration and agitation.

#### Lesson 13

Upstream and downstream processes - Separation and purification. Thermal processing .

#### Lesson 14

Scaling-up and scaling-down methodologies.

#### Lesson 15

Services, instrumentation and control - Auxiliary services. Control systems. Types of control. Control variables.

### SECTION IV: LABORATORY WORK

Lab Unit 1.- Introduction to cell culture

Lab Unit 2.- Kinetic modelling and simulation of biotechnological processes

Lab Unit 3.- Monitoring of biotechnological processes

Lab Unit 4.- Validation of kinetic models. Bioreactor design

## EDUCATION ACTIVITIES

#### Lectures:

The course syllabus will be presented by the lecturer, aided by IT methods.

#### Assignments:

At the end of each section the lecturer will set out different assignments or activities related to each section.

#### Practical classes:

Case studies and laboratory work will be set out by the lecturer.

#### Tutorials:

Tutorial sessions can be organized by the lecturer when required by the student following the scheduled hours.

During these sessions the student can raise questions or discussions related to the course. The tutorials will guide the students throughout the learning process and help them to gain a deep understanding of the subject.

(\*) The number and type of proposed activities will be explained at the beginning of the course.

(\*\*) The virtual classroom platform will be the communication tool used between participants and teachers.

Activities, their nature, evaluation criteria, modalities of participation and delivery will be informed by means of this platform.

## DISTRIBUTION OF WORK TIME

CLASSROOM-BASED ACTIVITY	INDEPENDENT STUDY/OUT-OF-CLASSROOM ACTIVITY
60 hours	90 hours
Lectures 36h Laboratory work 16h Tutorials 2h Assessment 6h	Personal study 48h Study and preparation of exercises and activities 30h Individual and team work 10h Preparation of tutorials 2h

## SKILLS

### Basic Skills

Students must have demonstrated knowledge and understanding in an area of study that is founded on general secondary education. Moreover, the area of study is typically at a level that includes certain aspects implying knowledge at the forefront of its field of study, albeit supported by advanced textbooks

Students must be able to apply their knowledge to their work or vocation in a professional manner and possess skills that can typically be demonstrated by coming up with and sustaining arguments and solving problems within their field of study

Students must have the ability to gather and interpret relevant data (usually within their field of study) in order to make judgments that include reflections on pertinent social, scientific or ethical issues

Students must be able to convey information, ideas, problems and solutions to both an expert and non-expert audience

Students must have developed the learning skills needed to undertake further study with a high degree of independence

### General Skills

To acquire firm theoretical, practical, technological and humanistic training needed to develop professional activity.

To have acquired the ability for analytical, synthetic, reflective, critical, theoretical and practical thought.

Capacity for problem-solving and decision-making.

To understand the fundamental laws and principles of physics, mathematics, chemistry and biology as the foundation for the mental structure of a biotechnician.

To acquire the skills needed for experimental work: design, preparation, the compilation of results and the obtainment of conclusions, understanding the limitations of an experimental approach.

### Specific skills

To be able to design and optimise a bioreactor and a biotechnological plant based on firm knowledge of engineering.

To calculate and accurately interpret the relevant parameters in the phenomena of transport and different balances of material and energy in bio industrial processes.

To be familiar with the various techniques and types of cell culture applicable to research and biotechnological industry.

To acquire the technological and engineering knowledge needed in process design.

To organise and suitably plan work in the laboratory.

To identify and define laboratory instruments and materials.

To be able to describe, quantify, analyse and critically assess the results of experiments performed in the laboratory.

To be able to apply the theoretical knowledge acquired for solving problems and practical cases linked to the various subjects.

To be able to work in a team in an efficient and coordinated manner.

To analyse and sum up key ideas and content regarding all manner of texts; to discover the theses incorporated within them and the issues raised; and to make critical judgments about their form and content.

## LEARNING RESULTS

Working with eukaryotic cell cultures under the appropriate conditions according to aseptic method carried out in laminar flow hood.

Identifying basic elements (equipment, supports, culture media, ...) and the physicochemical conditions involved in the cultivation of animal cells.

Defining the right method for obtaining, culture and necessary characterization for each different cell type.

Applying cell cultures to study the effect that different drugs or physical conditions can have on cells.

Developing skills on understanding and discussing scientific works.

Designing experiments and interpreting results.

Defining a bioprocess from the kinetic and stoichiometric points of view.

Describing techniques for enzyme, microorganisms and higher cells immobilization.

Distinguishing different types of bioreactors and their different modes of operation with reactors.

Describing transport phenomena involved in a bioprocess, including: upstream and downstream stages, the different methodologies that allow scaling up, auxiliary services, instrumentation and control needs of a bioreactor.

Correctly applying design equations studied for different modes of operation.

Interpreting experimental results obtained from a bioprocess carried out in the laboratory.

## LEARNING APPRAISAL SYSTEM

The final marks will be calculated considering the following parts:

Final written examination (70%)

Comprehension, reasoning, assimilation of the given content, and the ability of linking up different course concepts will be assessed. The written exam will contain practical exercises, short-answer questions and multiple-choice questions. In order to pass this section it is required to obtain a mark equal or higher than 5 points out of 10. Students who do not reach this minimum, should take an exam in the extraordinary summons according to the academic calendar.

#### Assignment and other activities (10%)

The ability of the student to apply the learned concepts to specific research works set out by the lecturer will be assessed.

#### Practical work in the laboratory (20%)

It will be individually assessed through reports or files submitted through the Virtual Classroom Platform. In order to pass this section of the course it is required to obtain a grade equal or higher than 5 points out of 10. Students who do not reach this minimum must take an exam in the extraordinary summons, according to the academic calendar, considering contents dealing with laboratory work. Non-attendance to any of the lab sessions without the corresponding justification will result in failing the course.

(\*) Unless otherwise indicated, a minimum final mark is not required to pass certain parts. However, if the calculated final mark is failed, each failed module can be optionally reassessed through extra questions in the extraordinary summons according to the academic calendar.

(\*\*) The marks corresponding to the modules successfully evaluated will be kept in the extraordinary summons within the same academic year, but not in the following ones.

(\*\*\*) Assignments with uncertain authorship will not be assessed. This considers content copied from other colleagues, websites, ..., wrong bibliographic references or breaking copyright.

(\*\*\*\*) Only in the students in second or following summoning, or with special needs may voluntarily join the proposed assessment system (fulfilling all the requirements, including class attendance), or an alternative system calculated under the following percentages:

- Final written examination (70%)
- Practical work examination (20%)
- Successfully resolve questions about the assignments developed during the course (10%)

The decision should be communicated to the lecturer in charge during the first two weeks of the course. If the lecturer is not advised, the alternative assessment system will be applied.

## BIBLIOGRAPHY AND OTHER RESOURCES

### Basic

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Gil-Loyzaga, P.E. (2011), "Cultivo de Células Animales y Humanas. Aplicaciones en Medicina Regenerativa", Vision Libros

Montuenga, L. y col. (2009), "Técnicas en Histología y Biología Celular", Elsevier Masson.

Schuler M.L. y Kargi F. (2014), "Bioprocess Engineering. Basic Concepts", Prentice Hall, Upper Saddle River, New Jersey.

Viladsen, J., Nielsen, J. y Gunnar, L., (2011), "Bioreaction Engineering Principles", Springer, Berlín.

Vinci, V.A. y Parekh, S.R. (2003), "Handbook of industrial cell culture", Human Press

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### Additional

Asenjo, J.A. y Merchuck, J.C. (1994), "Bioreactor System Design". Marcel Dekker, Nueva York.

Blanch H.W. y Clark D.S. (1997), "Biochemical Engineering", Prentice Hall, Upper Saddle River, New Jersey.

Casas Alvero, C. y col. (1998), "Ingeniería Bioquímica", Editorial Síntesis, S.A., Madrid.

Gòdia, F. y López Santin J. (2010), "Ingeniería Bioquímica, Volumen 30 de Ciencias químicas. Tecnología bioquímica y de los alimentos", Editorial Síntesis, S.A., Madrid.

Marangoni, A. G. (2003), "Enzyme Kinetics. A Modern Approach", John Wiley & Sons, Nueva York.

Price N.C. y Stevens L. (2000) "Fundamentals of Enzymology". 3ª Ed. Oxford: Oxford University Press.

Santamaría, J. y col. (2002), "Ingeniería de Reactores", Ed. Síntesis, Madrid.