Teaching guide

IDENTIFICATION DETAILS

Degree:	Biotechnology
Field of Knowledge:	Science
Faculty/School:	Experimental Science
Course:	BIOREACTORS
Type:	Compulsory
ECTS credits:	6
Year:	3
Code:	2035
Teaching period:	Fifth semester
Area:	Biotechnological Process Engineering
Module:	Biotechnological Tools
Teaching type:	Classroom-based
Language:	English
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 course is teaching the basic guidelines for obtaining and maintaining 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 course are:

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

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

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

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

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

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: THE BASICS OF CELL CULTURE

Lesson 1.- *Introduction to cell culture*

1.1 Historical background
1.2 Applications
1.3 Biology of animal cells in culture
1.4 Types of animal cell culture

Lesson 2.- *Growth pattern of cultured cells and culture conditions*

2.1 Growth media, culture vessels and surfaces
2.2 Propagation and subculturing
2.3 Quantification of cell culture growth. Population doubling level (PDL) and population doubling time (PDT)
2.3 Aseptic techniques and contamination types
2.4 Cryopreservation
2.5 Biosecurity and basic equipment in animal cell culture
Practical session.- *Subculture of adherent cells*

Lesson 3.- *Isolation and maintenance of mammalian primary cultures and cell lines*

3.1 Basic guidelines for cell culture set up
3.2 Cell morphology
3.3 Cloning methods
3.4 Characterisation and authentication of cell lines

SECTION II: ANIMAL CELL CULTURE ANALYSES

Lesson 4.- *Generation of genetically modified cell cultures*

4.1 Methods of cell transfection
4.2 Methods of cell transduction
4.3 Methods of selection

Lesson 5.- *Specific techniques for cell culture analyses*

5.1 Viability, cytotoxicity and surveillance.
5.2 Cell transformation
5.3 Cell migration and invasion
5.4 Apoptosis and necrosis

SECTION III: BIOREACTORS DESING PRINCIPLES

Lesson 6.- *Introduction to bioprocess engineering*

Lesson 7.- *Bioprocess kinetics*

7.1 Enzyme kinetics
7.2 Metabolic stoichiometry
7.3 Whole-cells kinetic model
Practical session.- *Workshop on kinetic modelling of bioprocess*

Lesson 8.- *Bioreactor design principles*

8.1 Ideal mixed-tank bioreactor
8.2 Ideal plug flow bioreactor
8.3 Energy balance
8.4 Deviations from the ideal behaviour
Practical session.- *Steady state simulation of continuous stirred tank bioreactor*
Practical session.- *Study of residence time distribution in bioreactors*

Lesson 9.- *Phenomenology in bioprocesses*

9.1 Mass transfer phenomena
9.2 Fluid dynamic within the bioreactor
9.3 The role of aeration and agitation in bioreactors
Practical session.- *Determination of the volumetric mass transfer coefficient*
Practical session.- *Study of the influence of stirring rate on cell growth*

Lesson 10.- *Bioreactor configurations*

10.1 Mechanical mixing: stirred-tank
10.2 Pneumatic mixing: Bubble column and airlift bioreactor
10.3 Hydraulic mixing: packed and fluidized bed
10.4 Bioreactor configurations for eukaryotic cells

Lesson 11.- *Towards industrial bioprocesses*

11.1 Scale-up and scale-down methodologies
11.2 Bioreactor instrumentation and control
11.3 Upstream and downstream operations in bioprocesses

EDUCATION ACTIVITIES

- **Participative lectures:** The course syllabus will be presented by the lecturer, aided by IT methods to promote the student participation.
- **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 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
Participative lectures Workshops and seminars Practical sessions: practical work carried out in the laboratory, resolution of practical cases	Virtual work Theoretical study, and preparation of out-of-classroom activities

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 be able to plan time effectively.

To foster a concern for knowledge as a key tool in the personal and professional growth process of a student.

To value sciences as a cultural fact.

To recognise the mutual influence existing between science, society and technological development in order to strive for a sustainable future.

To develop capacity for and a commitment to learning and personal development.

To develop an ability to search for, take in, analyse, sum up and relate information.

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.

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

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

REGULAR ASSESSMENT SYSTEM

Final mark of **Section I and II** will be calculated considering the following parts:

- ***Resolution of a practical case proposed by the lecturer* (8%)**. It is not requiered a minimum score in this task to pass the course. It is not considered repeat attempt for this task´s submission.
- ***Written examination* (25%)**. Comprehension, reasoning, assimilation of the given content, and the ability of linking up different course concepts (theoretical and practical) will be assessed. 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.

Final mark of **Section III** will be calculated considering the following parts:

- **Reports of practical sessions (27%).** Each report must be graded with a mark equal or higher than of 4 points out of 10 to consider the work for the global average. In order to pass this section, average mark of reports must be equal or higher than 5 points out of 10. Students who do not reach this minimum must submit again the failed repots before extraordinary summons exam.
- ***Written examination* (40%)**. Comprehension, reasoning, assimilation of the given content, and the ability of linking up different course concepts (theoretical and practical) will be assessed. 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.

*** Non-attendance to any of the lab sessions without the corresponding justification will result in failing the course.**
**** The activities passed in the ordinary call will be saved for the extraordinary call during the same academic year but not for the following.**
ALTERNATIVE ASSESSMENT SYSTEM
For the students in second or following summoning, an alternative system calculated under the following percentages will be applied:

- ***Written examination: sections I and II* (33%) *and section III* (47%).** Comprehension, reasoning, assimilation of the given content, and the ability of linking up different course concepts (theoretical and practical) will be assessed. 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.
- ***Reports of workshops proposed by the lecturer* (20%)**. The mark corresponding to this module successfully evaluated will be kept until the following academic year. 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.

The decision should be communicated to the lecturer in charge within the first five days of the course. If the lecturer is not advised, the alternative assessment system will be applied.
Assignments with uncertain authorship will not be assessed. This considers content copied from other colleagues, websites... wrong bibliographic references or breaking copyright. Plagiarism behaviors or any illegitimate mean will be sanctioned according to the University Regulations.

BIBLIOGRAPHY AND OTHER RESOURCES

Basic

Luis Montuenga Badía, Francisco J. Esteban Ruiz y Alfonso Calvo González. Técnicas en histología y biología celular / Barcelona :Elsevier,2009.

Pablo E. Gil-Loyzaga. Cultivo de células animales y humanas: aplicaciones en medicina regenerativa / Madrid :Visión Libros,2011.

edited by Victor A. Vinci and Sarad R. Parekh. Handbook of industrial cell culture: mammalian, microbial and plant cells / New Jersey :Humana Press,2003.

A. Barba Juan, C. Clausell Terol. Problemas resueltos de reactores químicos y bioquímicos / Castelló de la Plana :Universitat Jaume I. Servei de Comunicació i Publicacions,[2015]

B. Atkinson. Reactores bioquímicos / Barcelona :Reverté,2002.

Pauline M. Doran. Bioprocess Engineering Principles / 2nd. ed. London :Academic Press,2012.

John Villadsen, Jens Nielsen, Gunnar Lidén. Bioreaction Engineering Principles / 3rd ed. New York :Springer,2011.

Levenspiel, Octave Ingeniería de las reacciones químicas Limusa Wiley

Shuler, Michael L. Bioprocess engineering: basic concepts Prentice Hall

Juan A. Asenjo, José C. Merchuk Bioreactor system design Marcel Dekker

Additional

Vicenta Muñoz Andrés, Ángel Maroto Valiente. Operaciones unitarias y reactores químicos / Madrid :Universidad Nacional de Educación a Distancia,[2013]