

### **IDENTIFICATION DETAILS**

Degree:	Biotechnology			
Field of Knowledge:	Science			
Faculty/School:				
	Experimental Science			
Course				
Course.				
Type:	Compulsory		ECTS credits:	3
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Year:	3		Code:	2049
Teaching period	Sixth semester			
Area:	Applied Biotechnology			
Module:	Biotechnological Processes and Products			
Teaching type:	Classroom-based			
Language:	English			
Total number of student study hours:	75			

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## SUBJECT DESCRIPTION

La Microbiología Industrial es una disciplina cuyo objetivo es la obtención de productos de origen microbiano útiles para la sociedad, es por tanto una rama de la ciencia aplicada. La asignatura Microbiología Industrial I se inicia con un recorrido histórico de lo que ha sido la utilización y domesticación de los microorganismos por el hombre, para pasar a continuación a estudiar a fondo aquellos grupos de microorganismos mas interesantes desde el punto de vista industrial y biotecnológico. Se analiza el potencial de algunos microorganismos para la obtención de productos de interés y se explican las técnicas que existen para modificarlos e incrementar la productividad industrial. También se estudia a fondo lo que implica una fermentación microbiana a gran escala y se analizan en detalle algunos de los procesos industriales que proporcionan productos de consumo habitual en la sociedad.

Industrial Microbiology focuses on obtaining microbial products for societal benefits, aligning it with applied sciences. The Industrial Microbiology course starts with a historical perspective on the utilization and domestication of microorganisms, emphasizing those significant to the biotechnology industry. It examines the potential applications of specific microorganisms and the methods to enhance industrial productivity. The course covers all facets from small-scale to large-scale microbial fermentation and explores industrial processes that produce everyday consumer goods. This field uses microorganisms grown on a large scale to produce commercially valuable products and perform significant chemical transformations. Louis Pasteur's discovery of fermentation was a major milestone, leading to the exploration of both fermentative and non-fermentative processes that generate industrially important products, laying the groundwork for Industrial Biotechnology. Initially, fermentation processes for beer and wine production were developed, followed by processes for pharmaceuticals (antibiotics), food additives (amino acids), enzymes, and chemicals like butanol and citric acid. Previously, microbiologists used classical genetic methods to modify microorganisms for better process efficiency and higher product yields. The advent of recombinant DNA technologies introduced new genetic manipulation techniques, allowing to produce novel microbial products not naturally synthesized by microorganisms. In Industrial Microbiology course we will focuses on microorganisms of industrial interest, their characteristics, and methods to enhance their productivity. The course includes both traditional and modern genetic improvement techniques for creating genetically modified microorganisms. It also covers how to manage and adjust the parameters of microbial fermentations to ensure optimal system performance. Detailed studies of contemporary industrial fermentation processes are included and emphasizes with multiscale and integrative approaches used in strain optimization to enhance microbial metabolic pathways for increased production. The primary aim is to equip students with the skills to be able to analyse results and to propose an optimisation approach based on experimental data for the best possible outcomes. Additionally, the course addresses the intellectual properties protection alternative for the protection new microbial variants. Indeed, the course delves into the protection of intellectual property related to the creation of new microbial variants and emphasizes the importance of strains and process patent protection. It also focuses on the methods for managing and fine-tuning microbial fermentation parameters to ensure optimal system performance. The curriculum includes in-depth studies of microorganism strains optimization and production processes. The primary goal is to equip students with the ability to analyse experimental data and optimize industrial processes to achieve the best possible results.

### GOAL

The main objective of this course is for students to gain the necessary knowledge regarding the design, optimization, and control of industrial processes that utilize microorganisms. Specifically, the course will cover which microorganisms are of industrial significance, their characteristics, and the methods to boost their productivity. It also includes learning how to manage and adjust the parameters of microbial fermentations to ensure the system optimally performance, and how to enhance microbial productivity through multiscale and integrative approaches. The course's specific goal is to equip students with the skills to analyse results and propose optimization strategies based on experimental data to achieve the best possible outcomes.

The specific aims of the subject are:

- Identify and learn about the main microorganisms of interest for the biotechnological industry and its application Understand the structure and functioning of the biotechnological industry

- The course's specific goal is to equip students with the skills to analyse results and propose optimization strategies based on experimental data to achieve the best possible outcomes.

Prior knowledge on Microbiology I, Microbiology II, Biochemical Engineering, Molecular Genetics and Regulation of Gene Expression, Bioreactors, Biocatalysis is essential to be able to course this subject

## **COURSE SYLLABUS**

**SECTION I. From Microbiology to Industrial Microbiology** Chapter 1. Introduction and course Syllabus Chapter 2. From Industrial Microbiology to Microbial Biotechnology: the Flowchart used in Industrial Microbiology **SECTION II. Microorganisms and Products** Chapter 3. Micro-organisms of Industrial Interest Chapter 4. Substrates For Microbes and Microbial Products, Culture media & substrate, Media preparation Chapter 5. Microbial Products: Primary and secondary metabolites. Chapter 6. Recombinant Microorganism Strain Design and Selection Chapter 7. Microorganism Strains Optimization 7.1. In Procaryotic strain 7.2. In Eukaryotic strain **SECTION III. Industrial Process** Chapter 8. Industrial Fermentation and Type of Fermenters Classical and single use fermenters Chapter 9: Approaches in Microbial Biotechnology Development 9.1. Multi-scale Approach from small-scale to large-scale 9.2. Integrated Approach in Microbial Biotechnology Genetic Engineering, Synthetic Biology, Systems Biology, Omics Technologies, Metabolic Engineering and Directed Evolution Section IV. Patent in Industrial Microbiology Chapter 10: Securing intellectual property rights in the microbial and biotech sectors involves patenting innovative advancements. This legal process ensures exclusive ownership of novel microbial strains, genetic modifications, bioprocesses, and bio-based products. By obtaining patents, companies establish a competitive edge, attract investment, and drive the commercialization of innovative biotechnological discoveries. SECTION V. Applications Of Microbial Biotechnology Chapter 11. Pharmaceutical Industries 11.1. Production Of Human Interferon Alpha 11.2. Production Of Recombinant Insulin Chapter 12. Applications Of Microbial Biotechnology To Chemical And Energy

Chapter 13. Applications of Microbial Biotechnology to Food industry

# **EDUCATION ACTIVITIES**

-Participative Lecture sessions. Will be held by the corresponding teacher employing IT support. Besides, some sessions might be held by other teachers or professionals from other institutions according to their expertise in certain topics included in the subject's syllabus. To maximize the utilization of the assets of the lecture sessions, prior study of the unit (or at least a first read) is highly recommended. Students will study autonomously employing the recommended bibliography and all related material which will be available at the Aula Virtual of the course. During lecture sessions questions about what has been explained will be formulated and doubts will be solved too. -Development of Team projects work: Students will carry out a Project Based Learning (PBL) projects in groups of 3 students. The Project Based Learning is a teaching method in which students gain knowledge and skills by working for an extended period of time to investigate and respond to an authentic and complex question, problem, or challenge. Students work on a project over an extended period of time during the semester: This work will engage them in solving a problem and answering a complex question. They have to demonstrate their knowledge and skills by creating a public presentation for a real audience. As a Result, students will develop deep content knowledge as well as critical thinking, collaboration, creativity, and communication skills. Students will work with English-written bibliography illustrating any biotechnological process or product of industrial interest, which involve microbes. Therefore, students should acquire full understanding of the research described in the scientific articles or Patent document and checked bibliography in order to be able to propose an innovative approach. Indeed, inclusion of innovative proposal based on prior art will increase the quality of the final project.

- Seminars and Tutorials. Tutorials sessions will be arranged with the teacher who will advise and mentor each student in the topics demanded and aspects needed the most. These tutorials will seek the obtention of the greatest possible performance of the student and ensure the acquisition of the skills related to the subject. At least one tutorial will be considered compulsory concerning the teamwork project. performance, once the group has chosen the topic and defined the objective of their project. The tutor will give his/her conformity and advise an adequate schedule for its execution. A second tutorial will be offered near the end of the development of the proposal for a

final advice. Also, activities such as seminars given by researchers from different institutions dealing with one of the topics of interest, will be advanced.

-Complementary training activities. Depending on the logistic mean and the student semestrial schedule an activity about visiting an industry from diverse biotechnological areas (food, pharmaceutical and environmental fields) could take place. The main aim of these activities is providing the students a real view of an actual large-scale production system based on using microorganisms.

## DISTRIBUTION OF WORK TIME

CLASSROOM-BASED ACTIVITY	INDEPENDENT STUDY/OUT-OF-CLASSROOM ACTIVITY		
30 hours	45 hours		

### 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 be familiar with the applications of biotechnology in the healthcare, food, agrobiotechnological, environmental and chemical fields.

Capacity for teamwork and group management.

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

To identify the influence and contributions of new technologies on molecular and cellular biology in the pharmaceutical sector.

To be able to approach a subject by means of rigorous, profound and comprehensive thought.

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

To develop criteria for problem-solving and decision-making both professionally and personally.

To nurture an attitude of intellectual curiosity and a quest for truth in all areas of life.

## LEARNING RESULTS

Students should demonstrate comprehensive knowledge and understanding of advanced concepts in their field, integrating cutting-edge research, and applying critical thinking to practical applications based on advanced textbook information.

Students can apply their academic knowledge professionally, showcasing their ability to develop, defend arguments, and solve problems within their field of study.

Students will be able to collect and interpret relevant data within their field of study to make informed judgments, including reflections on significant social, scientific, or ethical issues.

Students will develop the ability to effectively communicate information, ideas, problems, and solutions to both specialist and non-specialist audiences.

At the completion of this course/module, students will have acquired the learning skills essential for pursuing further studies independently, demonstrating a high level of autonomy in their academic endeavors.

### LEARNING APPRAISAL SYSTEM

Learning assessment of the contents of this subject will take into account the work done by the student during the semester in the different activities. Ordinary evaluation system:

- **Theory Exam :** Will take place during the exams period. The score on this test will account for 65% of the final grade. It is compulsory to achieve at least a 50% in this test to pass the course and to take into account the rest of the grades.

- **Project Based Learning** is a teaching method in which students gain knowledge and skills by working for an extended period of time to investigate and respond to an authentic, engaging, and complex question, problem, or challenge. the Students work within a team work on a project during the semester. This activity will engage them in solving a problem or answering a complex question. They have to demonstrate their knowledge and skills by creating a public presentation for a real audience. As a Result, students develop deep content knowledge as well as critical thinking, collaboration, creativity, and communication skills. The search of literature, development and defence of the project, together with the design of the audiovisual support and/or its written report, will be graded on the basis of dedication, innovation, study and accuracy among the components of the team group. Therefore, an oral presentation of the project and/or a written brief summary/brochure of the scientific proposal should be submitted to the teacher and these documents should include proved evidence of the design, development and performance of the project in addition to the critical proposals generated. Topics, patents and scientific paper for analysis, will be proposed and the teacher will guide the progress of the projects through tutorials. The marks obtained will account for 25% of the final grade.

- **Active participation** theoretical lectures, in tutorials and preparation of programmed tutorials such as scientific paper analysis, Participation in scheduled supplementary activities related to the course, practical

exercises or tests drawn up in class and contributions or relevant questions directed to boost the activities and lecture's session progress will be evaluated here. Efficient attendance to the programmed tutorials is graded too. This item will mean 10% of the final grade. - The final grade of the course is obtained by applying the percentages previously indicated to the marks obtained in the different modules under evaluation.

- The final grade of the course is obtained by applying the percentages previously indicated to the marks obtained in the different modules under evaluation. To get a positive mark and pass the course, at least 50% of the points assigned to the theory exam must be obtained. \* No minimum grade is required unless it is otherwise specified (theory exam block). However, if after applying all the percentages the course results as failed, these sections can be retaken by delivering a written report and/or an offered activity, conveyed with the teacher. \*\*Each of the passed sections (team work, participation) will be maintained until the extraordinary call of the same academic course, but not for the following ones. Repeating the course in other academic years implies retaking all the activities to be evaluated again.

- Alternative Evaluation System for Repeating Students Eligibility: Students on their second attempt or further, or those with academic exemptions. They have 2 Options: 1- Follow the standard system, including class attendance. 2- Choose the alternative system with these percentages: - Final theory exam: 80% - Written project delivery: 20% Procedure: Notify the teacher via email within the first 2 weeks of the semester to apply for the alternative system. Without notification, the alternative system will be assumed. Plagiarism: Plagiarism and use of illegitimate materials during evaluations will be punished as per UFV University regulations.

# **BIBLIOGRAPHY AND OTHER RESOURCES**

### Basic

Michael J. Waites, Neil L. Morgan, John S. Rockey, Gary Higton I Industrial Microbiology: An Introduction Wiley-Blackwell

SBN: 978-1-118-68739-0 November 2013

https://www.wiley.com/en-us/Industrial+Microbiology%3A+An+Introduction-p-9781118687390

Richard H. Baltz, Julian E. Davies, Arnold L. Demain Manual Of Industrial Microbiology and Biotechnology ASM press. 2010

editors, Alan T. Bull ... [et al.]. 3rd edition. ASM press. 2010 https://onlinelibrary.wiley.com/doi/book/10.1128/9781555816827

Prof. Wim Soetaert, Prof. Erick J. Vandamme Industrial Biotechnology: Sustainable Growth and Economic Success/Chapter 1: History of Industrial Biotechnology 2010 WileyVCH Verlag GmbH & Co. KGaA *Chapter 1: History of Industrial Biotechnology : Pr. Arnold L. Demain* 21 April 2010 Print ISBN:9783527314423 | Online ISBN:9783527630233 |DOI:10.1002/9783527630233 https://www.google.es/books/edition/Industrial\_Biotechnology/9qDe3GZG96cC?hl=en&gbpv=1&printsec=frontcover

#### Additional

Maren Wehrs , Deepti Tanjore , Thomas Eng , Jeff Lievense, Todd R Pray, Aindrila Mukhopadhyay . Engineering Robust Production Microbes For Large-Scale Cultivation Trends Microbiol. 2019 doi: 10.1016/j.tim.2019.01.006 Trends Microbiol. 2019 Jun;27(6):524-537 Microbiol Biotechnol. 2013 DOI: 10.1007/s00253-013-4768-2 Appl Microbiol Biotechnol. 2013. May;97(9):3747-62

Sang Yup Lee & Hyun Uk Kim Systems Strategies For Developing Industrial Microbial Strains Nature Biotechnology.2015 DOI: 10.1038/nbt.3365 Nature Biotechnology volume 33, pages 1061–1072 (2015)

Angela Faustino Jozala et al., Biopharmaceuticals from microorganisms: from production to purification Braz J Microbiol. 2016 doi: 10.1016/j.bjm.2016.10.007 Braz J Microbiol. 2016 Dec;47 Suppl 1(Suppl 1):51-63

Glick, B.R., Pasternak, J.J., Patten, CL. Molecular Biotechnology. Principles and applications of recombinant DNA. ASM Press. 2010. 4th edition. ASM Press. 2010.

E.M.T. El-Mansi , C.F.A. Bryce , B. Dahhou S. Sanchez •, A.L. Demain , A.R. Allman Fermentation Microbiology and Biotechnology CRC Press. 2012 3rd Edition. CRC Press. 2012- Taylor & Francis Group

Régis Sodoyer Expression systems for the production of recombinant pharmaceuticals BioDrugs . 2004 DOI: 10.2165/00063030-200418010-00005 BioDrugs . 2004;18(1):51-62.

Jae Sung Cho, Gi Bae Kim, Hyunmin Eun, Cheon Woo Moon, and Sang Yup Lee\*, Hyunmin Eun, Cheon Woo Moon, and Sang Yup Lee Designing Microbial Cell Factories for the Production of Chemicals JACS. 2022, JACS. 2022, 2, 17811799

Divya Kapoor, Pankaj Sharma, Mayur Mukut Murlidhar Sharma, Anju Kumari & Rakesh Kumar Microbial Diversity, Interventions and Scope /Chapter: Microbes in Pharmaceutical Industry Springer Nature-2020 <u>https://link.springer.com/chapter/10.1007/978-981-15-4099-8\_16</u> First Online: 26 June 2020 Springer Nature Singapore Pte Ltd. 2020

Natalja Kulagina, Sébastien Besseau, Charlotte Godon, Gustavo H. Goldman, Nicolas Papon and Vincent Courdavault Yeasts as Biopharmaceutical Production Platforms Front. Fungal Biol. 2021 Front. Fungal Biol. Sec. Fungal Biotechnology Volume 2 - 2021 <u>https://doi.org/10.3389/ffunb.2021.733492</u>

Graumann, K. and Premstaller, A. Manufacturing Of Recombinant Therapeutic Proteins In Microbil Systems Biotechnol. J. 2006 https://doi.org/10.1002/biot.200500051

Hans Peter Sørensen and Kim Kusk Mortensen Soluble expression of recombinant proteins in the cytoplasm of Escherichia coli Microbial Cell Factories. 2005 DOI: 10.1186/1475-2859-4-1 Microbial Cell Factories volume 4, Article number: 1 (2005)

Malgorzata Kesik-Brodacka Progress in biopharmaceutical development Biotechnology and Applied Biochemistry. 2017

DOI: 10.1002/bab.1617

Rachel Daly, Milton T W Hearn Expression of heterologous proteins in Pichia pastoris : a useful experimental tool in protein engineering and production J. Mol. Recognit. 2005 DOI: 10.1002/jmr.687 J. Mol. Recognit. 2005; 18(2):119-38.

F R Schmidt Recombinant Expression Systems In The Pharmaceutical Industry Microbiol Biotechnol. 2004 DOI: 10.1007/s00253-004-1656-9 Microbiol Biotechnol. 2004 Sep;65(4):363-72.

Nagesh K. Tripathi and Ambuj ShrivastavaRecent Developments in Bioprocessing of Recombinant Proteins:Expression Hosts and Process Development Frontiers in Bioengineering and Biotechnology – 2019doi: 10.3389/fbioe.2019.00420Frontiers in Bioengineering and Biotechnology – 2019. December 2019 | Volume 7 | Article 420