ChE-437

Bioprocesses and downstream processing

Crelier Simon, Eyer Kurt, Zinn Manfred

Cursus	Sem.	Type
Biotechnology minor	E	Opt.
Ing.-chim.	MA2, MA4	Opt.

Language of teaching	English
Credits	4
Session	Summer
Semester	Spring
Exam	Oral
Workload	120h
Weeks	14
Hours	**4 weekly**
Lecture	4 weekly
Number of positions	

Summary

This course aims at a more advanced coverage of the basic aspects discussed in module ChE-311. It is however of a stand-alone nature, and even students who have little knowledge on - but a keen interest in - (bio)process engineering shall benefit as well from this module.

Content

Manfred Zinn

- Upstream processing: introduction and basics in cultivation
- Bioprocess design for batch, fed-batch and chemostat cultures
- Special bioprocesses and applications
- Paper studies including short presentations by students

Kurt Eyer

- Bioreactors & Fermenters: Basics
- Characterization of biological reactor systems
- Scale-up procedure: science or art?
- Applied examples and economic aspects of industrial bioprocesses

Simon Crelier

In the section on downstream processing (DSP), the main accent will be placed on the purification of (monoclonal) antibodies, which are emblematic product of today's biopharmaceutical industry. The following topics will be addressed:

- Context and relevance of DSP
- Solid-liquid separation techniques
- Membrane separations
- Chromatography
- Viral clearance

Keywords

Bioprocess engineering: Basic function of a bioreactor, different types of bioreactors, agitation and oxygen transfer, upstream processing, sterilization techniques, bioprocess automation, PAT, Liebig's law, mass and energy balances, oxygen requirements, yield coefficients, growth kinetics, Monod kinetics, microbial growth on defined and complex media, substrate inhibition, feed strategies, product formation, high cell-density fed-batches, chemostat, nutrient limitation, wash-out, optimal productivity, scale-up.
Process scale-up and bioreactor characterization: Overview of biochemical processes currently used on an industrial scale. Introduction to biochemical process design strategies for high value/low volume and low value/high volume

products. Aspects of mass transfer of importance in aerobic fermentations. Bioreactor design and selection for ideal batch, fed batch and ideal chemostat operations. Here we will discuss engineering aspects of bioreactor / fermenter systems (design, operation, scale-up) developed or adapted for cultivation of mammalian cells / microorganisms, such as bioreactors for suspension culture (stirred-tank reactors, bubble columns, and air-lift reactors), fixed bed and fluidized bed reactors, hollow fiber, and membrane reactors, and, finally, disposable bioreactors. Practical aspects of bioreactor operation and monitoring: sterilization, asepsis, inoculation, rheology, aeration, agitation, instrumentation, and sampling. **Downstream processing:** significance of DSP; chemical and biotechnological DSP; purity; yield; (bio)activity retention; physical and thermal separations; equilibrium; kinetics, sedimentation; centrifugation; Sigma factor; filtration; cake and filter resistance; cross-flow; membranes; transmembrane pressure; osmotic pressure; retention factor; molecular weight cut-off; adsorption isotherm; Langmuir; Freundlich; adsorption kinetics; breakthrough curve; ion exchange; hydrophobic interaction; affinity chromatography; SEC; van Deemter equation; resolution; peak symmetry; number of theoretical plate; scale-up;

Learning Prerequisites

Required courses

Since this lecture is open to students from various backgrounds, no particular course is required as a mandatory prerequisite. However, and although not mandatory - some basic knowledge of (cell) biology, process engineering and unit operations would be very helpful for a proper understanding of the course material.

Recommended courses

Although in no way absolute prerequisites, the topics covered in the courses below are certainly relevant to the material of this module.
ChE 201 - Introduction to chemical engineering
ChE 204 - Introduction to transport phenomena
CH 210 - Biochimie
ChE 310 - Fundamentals of separation processes
ChE 320 - Bioreactor modeling and simulation
CH 334 - Opérations unitaires et technologies des procédés
Basic knowledge in microbiology, biochemistry and process engineering would constitute a helpful background (although not mandatory) for a better understanding and mastering of the material to be presented in this lecture (a short list of recommended readings can be made available if desired).

Important concepts to start the course

This course heavily relies on the basic concepts of process engineering, mass and heat transfer, equilibrium and kinetics applied to living systems (microbial or mammalian cell cultures).

Learning Outcomes

By the end of the course, the student must be able to:

- Integrate Concepts and knowledge from various domains (biology, process engineering, (bio)chemistry)
- Discuss the merits, disadvantages and characteristics of the different types of bioreactors as well as their mode of operation
- Dimension unit operations
- Interpret data or observations from case studies
- Choose an appropriate fermentation or purification strategy
- Predict the outcome or the performance of a unit operation or specific equipment
- Justify his/her choices and assumptions
- Solve calculation problems

Transversal skills

- Use a work methodology appropriate to the task.

- Assess one's own level of skill acquisition, and plan their on-going learning goals.
- Manage priorities.
- Use both general and domain specific IT resources and tools

Teaching methods

The course will be held under the form of lectures also featuring the treatment of examples, the discussion of case studies and some exercises.

Expected student activities

Regularly attending the course is the best way to achieve the learning goals with a minimal amount of personal work at home. The proposed exercises and case studies are integrated to the lectures. They illustrate and complete the theoretical aspects presented during the course, and playing an active part in their resolution will make the learning process more efficient and rewarding.

Assessment methods

A written examination will take place at the end of the semester if 10 candidates or more have signed up. Under 10 candidates, the examination will be oral.

Supervision

Office hours	No
Assistants	No
Forum	No
Others	Since the three lecturers are not on the EPFL campus, there are no office hours. However, they shall remain reachable anytime via E-mail, phone or videoconference for enquiries or questions.

Resources

Bibliography

- M. L. Shuler, F. Kargi, M. DeLisa. Bioprocess engineering - basic concepts. 3rd edition, Prentice Hall, 2017
- P. M. Doran. Bioprocess engineering principles. 2md edition, Academic Press Ltd., 2013
- H. Chmiel, R. Takors & D. Weuster-Botz. Bioprozesstechnik. 4. Auflage, Springer, 2018

Ressources en bibliothèque

- Bioprocess Engineering Principles / Doran
- Bioprocess engineering basic concepts / Kargi
- Bioprozesstechnik / Chmiel

Notes/Handbook

There is no manuscript for the course. However, all the material that is presented (copies of transparencies, articles, case studies, additonal material, exercises and correction thereof) is available and can be downloaded from the Moodle platform.

Websites

- http://scgc.epfl.ch/telechargement_cours_chimie

Moodle Link

- https://go.epfl.ch/ChE-437