Course PM Biocatalysis

BB2460 7.5 hp

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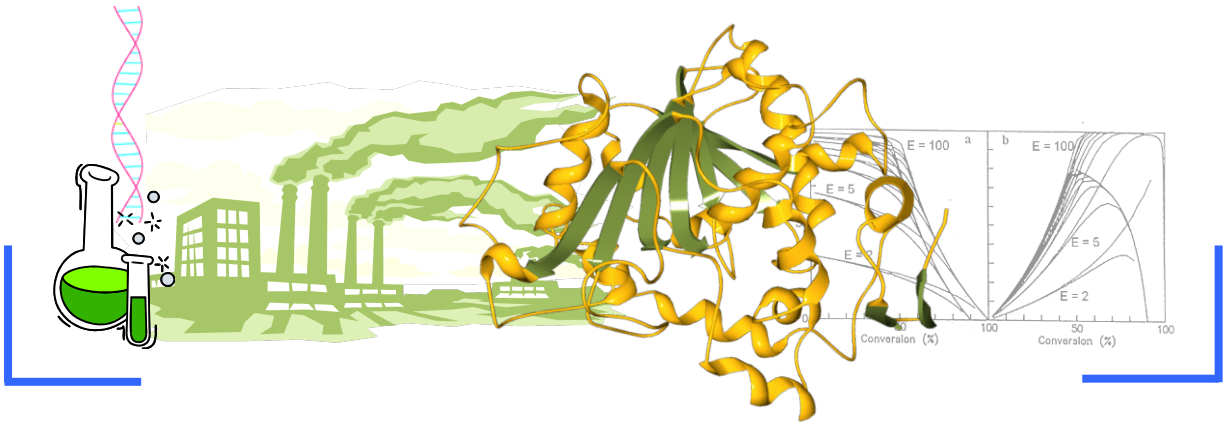


1. Detailed schedule and contact persons

Responsible: Per Berglund, perbe@kth.se, 08-790 7037
Assistants: Rebecka Karmakar, karmak@kth.se and Katarina Petrovic, kpetr@kth.se
Lecturers: Per Berglund (10 lectures), Yves Hsieh (1 lecture), Karim Engelmark Cassimjee from Enginzyme AB (1 lecture)

Detailed schedule with instructions: https://www.kth.se/social/course/BB2460/calendar/
Course material: Canvas

2. Course Objectives

The course is aimed to teach how enzymes are used in industrial processes for production of chemical products like fine chemicals, pharmaceuticals, and other refined products. It provides an overview of the different enzyme classes coupled to the catalyzed chemical reactions and it describes stereochemistry and methods to optimize the stereochemical outcome. Several industrial processes are described as examples.

After passing the course, the student should:

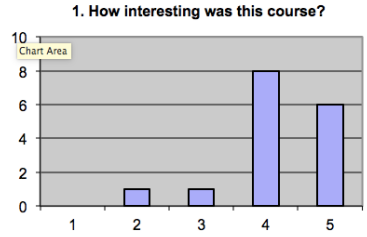
- Be able to exploit and apply knowledge from basic biotechnology and chemistry courses to design enzymatic processes for industrial production of chemical products.
- Be able to distinguish reaction mechanisms of enzymes from the different main classes and be able to decide which chemical reactions that enzymes from a certain class can exhibit.
- Be able to explain and exemplify different enzyme-catalyzed processes for stereoselective chemical production. For example, kinetic resolution, dynamic kinetic resolution, and stereoselective synthesis, and also be able to suggest strategies for optimization.
- Recognize advantages and disadvantages of different reaction media for enzymatic reactions and be able to decide suitable reaction conditions in individual cases.
- Be aware of the Swedish and foreign industry which uses enzymatic processes and be able to exemplify products and types of enzymes used.
- Be able to incorporate research literature and be familiar with the search tools for electronic databases which are available at KTH.

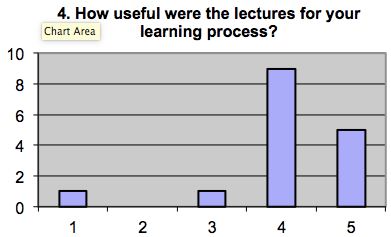
3. Course setup

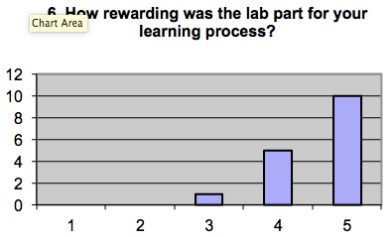
The course is compulsory for students at the advanced level within Industrial & Environmental Biotechnology. It is an elective course in a few other programs, but is also aimed for exchange students and others with pre-required knowledge. It consists of lectures, exercises and a research project, which includes searching for literature, labs and a seminar. The course's lab portion is designed, planned and documented by the students themselves and is a part of the research project. The entire research project is presented in a seminar at the end of the course.

4. What did previous students say?

From student evaluations 2017:







Some comments from students:

- Best course so far at KTH, the lab teachers were both very patient and helpful and all teachers showed great enthusiasm and everything was planned very well. - Awesome course, especially the lab! - It might seem a bit scary to plan the lab but the learning outcome will be great, and it will probably end up one of the best/most fun labs during the education! - We got a chance to use knowledge from many courses. - It would be beneficial to brush up on organic chemistry before.

Implemented changes 2017:
The lecture on fundamental enzymology was criticized to overlap with the molecular enzymology course and has been deleted (lecture slides are available on Canvas for interested students). A new lecture on cascade biocatalysis has been added.

Implemented changes 2018:
The guest lecture from industry has changed and is now included with a technology lecture on enzyme immobilization. All deadlines are modified and added in Canvas. The course PM document has been edited and shortened.

5. How should I study during this course?

The number of lectures is kept to a minimum but still cover the basics of Biocatalysis. They therefore contain quite a lot of material necessary to discuss. The review articles connected to each lecture have been chosen to give more information around some topics covered in the lectures but, still, these articles do not cover all information. The handouts/lecture notes and the literature are distributed through Canvas, which you access with your kth.se account after registering to the course. Lecture notes will be posted beforehand not later than the day before each lecture.

For each lecture, you have to prepare in advance by reading through the lecture notes/handouts that you can download and print. Go through them carefully before each lecture and prepare questions to ask at the lecture. It is a good idea to bring the paper printouts to the lecture and take notes directly on the lecture handouts.

A course of 7.5 credits corresponds to 200 working hours. About 60 hours are scheduled on the program as lectures, lab, tutorials and seminars and the rest is for you to distribute on the various tasks. This is a rough recommendation on how you could distribute your time:

• Scheduled on the program (lectures + lab + tutorials)	60 h
• Preparation before each of the 12 lectures	12 h
• Reading and repeating immediately after each lecture	24 h
• Studying the course literature	48 h
• Learning ChemBioDraw, PDB viewing software etc	8 h
• For deadline 1 (literature searching, reading and planning)	12 h
• For deadlines 2 & 3	8 h
• For deadline 4 (planning the lab investigation)	12 h
• Preparation of the final seminar	16 h
Total:	***200 h***

6. The course literature

All material connected to the lectures, for example the PowerPoint slides, and the material from the students produced for the seminars, are included as compulsory course literature. All compulsory material are distributed through Canvas.

Compulsory course literature
- Review articles connected to each lecture
- Handouts from the 12 lectures
- Handouts from the students' seminars

Recommended books
1. Peter Grunwald, *BIOCATALYSIS - Biochemical Fundamentals and Applications*, Imperial College Press 2009. ISBN 978-1-86094-771-1 (used as course text book 2012, reading list available in Canvas)
2. Kurt Faber. *Biotransformations in Organic Chemistry: A Textbook*, 6th Edition. Springer-Verlag: Heidelberg. 2011. e-ISBN 978-3-642-17393-6. **Available as e-book at KTH**
3. Andreas Liese, Karsten Seelbach, Christian Wandrey (Eds.). *Industrial Biotransformations*. 2nd ed. Wiley-VCH. 2006. ISBN: 3527310010. DOI: 10.1002/3527608184. **Available as e-book at KTH**
4. Bommarius & Riebel, *Biocatalysis - Fundamentals and Applications*, Wiley-VCH 2004. ISBN-10: 3-527-30344-8. **Available as e-book at KTH**
5. Silverman, R. B. *The Organic Chemistry of Enzyme-Catalyzed Reactions*, Academic Press. 2002

6. Adrie J. J. Straathof, Patrick Adlercreutz (Eds.) *Applied biocatalysis*. 2nd ed. Taylor & Francis 2000
7. Stanley M. Roberts, G. Casy, M.-B. Nielsen, S. Phythian, C. Todd, K. Wiggins. *Biocatalysts for Fine Chemicals Synthesis*. Wiley 1999. ISBN: 978-0-471-97901-2

7. The research project

This section contains important information about your research project such as details for the different assignments and deadlines, instructions about working in the lab and how to prepare for the seminars. You should read this section carefully.

Overview

The research project constitutes about 50% of the workload of the course. The main goal of the research project is that you will use your knowledge from previous courses and, according to your own interest and background, **design and plan your own research investigation** in the lab based on your literature studies. Four sessions (2 x 45 min each) are scheduled for tutorials related to the research project. You may have some training in literature searching to collect scientific information from previous courses, for instance, the bachelor-level courses Organic Chemistry and Microbiology. You will benefit from efficient database searching in this course. The tutorial sessions are taking place in a computer class room where you will work on your project in the presence of the course assistants. You should take the opportunity during these tutorials to ask questions to the assistants.

You are going to work on one research project throughout this course and you are proposing what to examine in the lab yourself related to the enzyme you have been assigned to (one of those listed below). This means that you have to search in the literature and read several research articles in order to plan your lab investigation in great detail. You will give an oral presentation at one of the seminars at the end of the course, which, apart from the lab results, also should contain details about the enzyme, its structure and the process from the biocatalysis perspective and according to your own interest. You should find relevant research articles from data bases such as SciFinder Scholar and others containing peer-reviewed scientific information which are available through the library KTHB. Searches on Google, Wikipedia or equivalent are not recommended since you cannot completely trust that information obtained from those sources is scientifically correct. Make sure you save the references for the articles you use – these will be needed for your oral presentations at the end of the course.

Project planning and exercises (deadlines 1-4)

Planning your research project (deadline 1)

Time is devoted to this at the first exercise session. In Canvas you can read more details about this task and when to upload your results to meet deadline 1.

Simulation exercise after lecture 3 (deadline 2)

Time is devoted to this at the second exercise session. In Canvas you can read more details about this task and when to upload your results to meet deadline 2.

Mechanism exercise after lecture 4 (deadline 3)

Time is devoted to this at the third exercise session. In Canvas you can read more details about this task and when to upload your results to meet deadline 3.

Handing in your lab plan (deadline 4)

Time is devoted to this at the fourth exercise session. In Canvas you can read more details about this task and when to upload your results to meet deadline 4.

In the laboratory (deadline 5)

The lab journal

Each group will get a lab journal which should be used to document the work in the lab. One of the aims of this lab project is that you will get an insight into what a normal day in a research lab can look like. Therefore, you are supposed to write everything in the lab journal as if you are working in a research project in industry or academia. You should note with an **ink pen**. Preliminary results and primary data should never be erased. The lab journal should be organized like a diary and contain a continuous description of the lab work and detailed experimental

procedures. This includes result data as well as detailed descriptions of how solutions and reactions were prepared. It is important to always note **everything** that happens during the lab work since you sometimes need to go back and look up what you did or how a reaction behaved. The lab journals will be handed in to the assistants for inspection after the seminars (deadline 5).

Working in the lab

Before entering the lab you should read the course lab safety document which can be found on Canvas. You should also review the safety assessment you wrote for deadline 4 and make sure you are aware of the hazards of the chemicals you will use. While working in the lab, it is highly recommended to use lab coats and gloves at all times. Also use lab goggles if necessary (for example when working with acids or bases).

In this course, we will supply the chemicals in their pure forms. Please note that many of these chemicals, primarily the liquid ones, are volatile and can be smelly and/or toxic if inhaled. When you open these chemical bottles, do it inside a fume hood. For example, you can make a stock solution of your chemical inside the fume hood, and when the chemical is diluted you can take it out and work at your bench (but keep the container closed when you are not using it). If your chemical is toxic by inhalation or if you are working with solvents, you should always work in a fume hood. If you are unsure, ask a lab assistant. Any work involving organic solvents, such as extractions or TLC, should always be performed in a fume hood. All pipette tips used for organic solvents or pure chemicals should be discarded inside the fume hood as well.

When you are finished in the lab, you will have to clean up after yourselves. This includes for example cleaning your bench and disposing off any stock solutions you might have left in the fume hood, fridge or freezer. Make sure to dispose off your waste properly. Non-toxic chemicals in dilute water solutions can be poured out in the sink, while organic solvents should be collected in the organic waste. **Never pour solvents or pure chemicals in the sink!** If you are unsure of how to handle your waste, ask a lab assistant. Not cleaning properly will affect your grade!

Important information about enzymes and solutions

Experiments don't always go as planned. Some of the most common problems encountered by students in this course are related to enzyme stability and the solubility of organic compounds. You should keep the following information in mind:

Enzyme stability: Enzymes are sensitive and you have to be careful with them. For example, do not freeze, shake, vortex or bubble air into enzyme solutions.

Solubility: Many chemicals are not very soluble in water. This is something to think about especially before making stock solutions of substrates with concentrations much higher than what you plan to have in the reaction. If a chemical is not properly solubilized, the concentration in the solution might be much lower than expected.

Seminars (deadlines 6-7)

You will not write a lab report in this course. Instead, you will present your research project in an oral presentation using PowerPoint or alike. This presentation should be 10-12 minutes long and should contain details about your research project and your lab results, but also some more general information about your enzyme. A detailed description of what to include on the presentation slides is found in Canvas.

You need to **discuss the presentation with your assistant before the seminars**. This discussion will take about 30 minutes, and you should contact your assistant before deadline 6 to schedule a meeting for this purpose. Note that this is the deadline for **scheduling** the meeting – the meeting itself can be later, as long as it takes place at least the day before the seminar on which you will present. At the meeting your presentation slides should be finished and you should either print them or bring a computer so that you can show the slides to your assistant. Please make sure you don't have too many slides – the presentation should only be 10-12 minutes. After the meeting you will most likely have to make some changes and adjustments.

You upload your slides in Canvas (deadline 7). The slides will be distributed to everyone in the course through Canvas and the slides will be compulsory course literature.

8. Deadlines

You will be given a grade A-F on the research project. This grade is based on your fulfilment according to the deadlines during the research project. More details about what to do to meet all the deadlines can be found in Canvas.

Deadline 1. Idea presentation.
After the first tutorial session, you need to present an idea to your course assistant about your investigation. Details on how you will perform the experiments are not needed but you need to explain the objectives of the study and equipment needed. Upload a summary on Canvas.

Deadline 2. Simulation of E.
After lecture 3, the exercises about simulation of enantioselectivity have to be solved and uploaded.

Deadline 3. Reaction mechanism exercise.
After lecture 4, the exercise about reactions and mechanisms has to be solved and uploaded.

Deadline 4. Lab plan.
The lab planning should be ready after the last tutorial and the plan should be described in detail including a list of all chemicals needed and the amount in weight or volume. You will also need to make a safety assessment, where you describe the main hazards of the chemicals you will use. A detailed description of what you are expected to hand in for this deadline is provided in Canvas. You should also make an appointment with your assistant for discussion and approval of the plan.

Deadline 5. The lab journal.
The lab journal should be handed in to your assistant for inspection. It should contain a detailed description of the laboratory experiments and results. See further details about your lab work and what to do at this deadline in Canvas.

Deadline 6. Make an appointment to meet your assistant.
You should make an appointment with your assistant **before this deadline** to schedule a 30 minutes meeting about your seminar. Note that you only need to **schedule** the meeting before this deadline – the meeting itself can be later, as long as it takes place at least the day before the seminar on which you will present. The slides should be ready, printed out and brought to the meeting.

Deadline 7. Upload your seminar slides.
You will be scheduled for your seminar at one of the occasions on the schedule. Upload the presentation slides to Canvas. It is recommended to attend all the seminars since the slides presented by the other groups are compulsory course material. You are required to use presentation software such as PowerPoint (or pdf) from a computer. A PC computer will be available at the seminar.

9. Examination and Grades

The assessment of the research project

You will be given an individual grade A-F on the research project. This grade will primarily be based on:

- Your ability to plan the research project. You should come up with your own ideas based on literature research and your final lab plan should include all the necessary details.
- Your work in the lab, and your ability to document the work in the lab journal.
- Your ability to interpret your results, draw conclusions and identify potential sources of error.
- Your ability to meet all the deadlines and hand in assignments on time.
- Your oral presentation.

Note that good results in the lab are not necessary to get a good grade. The important thing is how well you plan, perform, analyze and present your experiments.

The written examination

You will be given a grade on the written examination related to the number of points obtained, according to:
<46% F
46% Fx
50% E
61% D
71% C
81% B
92% A

Final grade on the course

The course comprises written examination (4.5 hp, grading A-F) and the research project (1.5 hp project, grading A-F, and 1.5 hp lab, grading pass/fail).

The final grade will be calculated from 75% based on the written examination and 25% based on the grade on the project. If the written examination gave an F then the final grade is F independently of the grade of the project. The grade on the research project can increase the final grade one step, not more. The grade on the research project will not give a final grade lower than the grade on the written examination.