Syllabus

BEC (CHE) 577

Advanced Biomanufacturing & Biocatalysis

Spring Semester, 2016
6:00 – 8:15 PM Tuesday

Location: Centennial Campus EB II 1230 (EOL Studio classroom)
(Also offered for distance students through Engineering On-Line)

Instructor: Professor Michael C. Flickinger (CBE, BTEC)
BTEC Associate Director for Academic Programs
Office: 196 BTEC
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Email: michael_flickinger@ncsu.edu

Teaching Assistant: Kisurb Choe (BIOM graduate student)
Email: kchoe@ncsu.edu

Course web site: Login for combined BEC (CHE) 577 Moodle course site (both sections 001 and 601) at: http://moodle.wolfware.ncsu.edu. There is no separate Moodle site for CHE 577.

All email correspondence from the instructor and course TA will be sent to your NCSU email account. All students must use their ncsu.edu account to receive course information and to email the instructor and TA.

On-campus office hours: Arranged by email

Prerequisites: Graduate standing in engineering or life science graduate program or consent of instructor. Previous coursework in microbiology, cell biology, microbial biochemistry or molecular biology will be helpful.

Course Structure: Two hour and 15 minute evening lectures with in-class learning activities, quizzes and examinations. See course Moodle site for current lecture schedule, course slides, study guide, resources, assignments and announcements. Several lectures will be given by guest lecturers depending upon their availability. The lecture topics and pace of the course may be adjusted depending on the mastery of the material by the class (determined by quizzes, exams), weather delays, and the availability of guest lecturers.

Note: Not all lecture materials will be covered in class (some lecture materials will be flipped) to enable class time to be devoted to emphasize comprehension (answer questions about the material), study/evaluation of poster design and problem solving (individual or in groups). Review all lecture materials on the Moodle site before coming to each class.
Course Content: This is an advanced graduate overview of selected topics in biomanufacturing using microorganisms (bacteria, yeast, fungi), eukaryotic cells (insect, CHO, plant cell cultures), plants, and recombinant enzymes engineered for specific applications. This course focuses on how microbes, cell lines, plants and enzymes are used to manufacture components of foods, pharmaceuticals, biopharmaceuticals, consumer products and biomaterials regulated by the U.S. FDA. Advanced protein engineering, gene expression and cellular pathway engineering techniques used to screen for and generate improved biocatalysts will be described. Industry case study examples will be presented on how microbial metabolism is altered or “engineered” to generate strains capable of producing: organic acids, amino acids, alcohols, chemical intermediates, lipids, polyketides, carbohydrate and peptide antibiotics, biopolymers (carbohydrate polymers, polyesters), antibodies (intact, fragments, chimeric, Ab fusion proteins) or to alter pathways to generate novel bio-active metabolites. This class will also present concepts and ‘strategy’ in designing screening strategies using engineered microbes, cell lines and the metagenome for new drug substance discovery. A major emphasis of the course is on how to choose microbial/cell line host & vector expression systems for the production of heterologous peptides, proteins, antibodies or glycoproteins and how this choice affects overall process strategy. An overview of cell growth kinetics and immobilized biocatalyst kinetics is included as well as discussion of intellectual property (IP), ethical and social/perception of risk implications of producing products from genetically modified organisms (GMOs). Selected examples from recent publications will be presented for most topics. Emphasis will be given on each student preparing an effective technical poster on a proposed process using engineered microbes or enzymes for industrial biomanufacturing along with a comprehensive Technology Brief final paper based on the same topic as the poster.

Course Learning Objectives: By the end of this class, students will be able to:

- Explain the methods used in industrial biomanufacturing to alter microbial, insect, plants or mammalian cells to optimize the production of a variety of products such as organic acids, amino acids, alcohols, antibiotics, enzymes, peptides or biotherapeutic proteins.
- Solve problems using metabolic pathway engineering approaches to engineer microbes, enzymes and cell lines for the over-production of metabolic intermediates and to generate novel bioactive compounds.
- Explain the advantages and disadvantages of production of small molecules, antibiotics, peptides, proteins, glycoproteins, and antibodies in native hosts, surrogate hosts, or alternate hosts such as Gram negative, Gram positive, yeast, Archaea, insect, plants and mammalian cell expression systems.
- Describe microbial growth and product formation in batch, fed-batch, continuous cultures and the reactivity of immobilized enzymes or cells in biomanufacturing processes. Explain the choice of each of these methods in industrial practice.
- Recite the importance of patents for commercial development of a microbial bioprocess; the impact of GMO versus non-GMO organisms in a process, and how
the steps of development of a human therapeutic or food component are regulated by the U.S. Food and Drug Administration (FDA).

- Explain how biosynthetic pathways leading to production of a variety of primary and secondary metabolites, biopolymers, peptide and polyketide antibiotics are being altered in order to generate new pathways or entirely new compounds as biotherapeutics, or as chemical, fuel or pharmaceutical intermediates.
- Recount how microbial enzymes and genetically engineered microbes are used as industrial biocatalysts for the production of sweeteners, vitamins, chemical or pharmaceutical intermediates, and generation of fuels from biomass.
- Design an effective poster in both U.S. and European A0 format on an advanced biomanufacturing process utilizing a recombinant enzyme, engineered microorganism or cell line.
- Write a concise Technology Brief on a topic in advanced biomanufacturing.

Course Materials: There is no textbook required for this course. All lecture slides, study guides and most resource reading materials will be available on the course Moodle site. For those students with only basic knowledge of biotechnology or industrial microbiology, a suggested text is *Basic Biotechnology*, 3rd edition, 2006, by Colin Ratledge and Bjørn Kristiansen, Cambridge University Press (ISBN-13 978-0-521-54958-5, soft cover), which can be obtained on Amazon™ new for ~$80 or used from $20 to $30. Additional useful monographs are listed below, however you are not required to purchase any book for this course.

Lecture Slides, Study Guide and Supplemental Resources: Lecture slides (Power Point) are numbered by topic as listed on the lecture schedule. A pdf Study Guide for each lecture topic will be uploaded each week to assist you in mastering the material presented in the lectures. The study guide includes example quiz and exam questions as well as a list of important terms for you to create a glossary. It will be helpful to learning this material by compiling a glossary starting with the first topic and add to this listing each week with each topic presented.

For additional background in preparing your Technology Brief paper and poster, reading sections from one of the encyclopedias or chapters from several books listed below as well as current review articles and recent journal articles are highly recommended. The instructors will provide guidance as to reading that may be most beneficial to you.

- *Upstream Industrial Biotechnology* (2 volumes), *Downstream Industrial Biotechnology*, 2013. Michael C. Flickinger Editor, John Wiley & Sons (available in the NC State Hunt Library)
When specific chapters or articles are listed as required reading, it is the responsibility of each student to obtain these articles.
Restrictions: Lecture slides and the Study Guide will be available on the NCSU course Moodle site and are the property of North Carolina State University. *Distribution of these course materials to students or individuals not registered for this NC State course is unlawful.* The use of cell phones or electronic devices during class other than for taking notes is strictly forbidden! All electronic devices are required to be deactivated during quizzes and examinations in this course.

Assignments: Class attendance is required and will be recorded each period. Some lectures may include interactive learning activities. Ask questions during class. Emails to the instructor and TA will be answered usually within one to two days – rarely on the weekends. All assignments are due on the stated due date. Late assignments will have 2 points deducted for each day late, including weekend days.

Point Values: The required course assignments and % of the total course points are:

<table>
<thead>
<tr>
<th>Class Assignments</th>
<th>Point Value (% of Total Points)</th>
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<tbody>
<tr>
<td>Class participation/activities*</td>
<td>15 6%</td>
</tr>
<tr>
<td>Quizzes or problem sets</td>
<td>30 12%</td>
</tr>
<tr>
<td>Examinations (2)</td>
<td>50 20%</td>
</tr>
<tr>
<td>Draft mini-poster (11 x 17 inch)</td>
<td>10 4%</td>
</tr>
<tr>
<td>Topical poster, presentation</td>
<td>60 24%</td>
</tr>
<tr>
<td>(printed poster + A0 poster file + oral poster presentation)</td>
<td></td>
</tr>
<tr>
<td>Technology Brief</td>
<td>35 14%</td>
</tr>
<tr>
<td>Final examination</td>
<td>50 20%</td>
</tr>
<tr>
<td>Total Points</td>
<td>250 100%</td>
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Quizzes and Examinations: Quizzes and tests will be short answer, multiple response or short essay (closed book/closed notes) and will be given in class on the dates indicated in the lecture schedule. *All course assignments must be done individually unless indicated as a group activity by the instructor.* Sample quiz questions are included in the course study guide. Quizzes and exams may contain Extra Credit questions. You cannot decrease your grade by answering extra credit questions - you can improve your score. Additional extra credit assignments may be announced by the instructor. Earning points on these extra credit assignments will increase your total score, but will not change the total points for the course (250 points). An answer Key for each quiz and examination (including answers to extra credit questions) will be posted on the course Moodle site after all students have completed the examination. Make up quizzes/examinations will be given only for valid circumstances such as illness, calamity, professional travel or a conflict with a documented job interview or employment responsibility. Arrangement for make-up
examinations should be made by contacting the TA by email preferably the week before the scheduled quiz or exam.

Mini-Poster (10 points): A 11 inch by 17 inch mini-poster draft of your final poster in U.S. format is due during week 8. The specific requirements for the mini-poster and guidance of how to create effective technical posters will be discussed in class. It is the responsibility of all students to submit a printed mini-poster in color and to submit an electronic version as a single Power Point file in the correct size (not Power Point slides).

Professional Posters and Oral Presentation (60 points): Each student (or pairs of students as determined by the instructor) will prepare both a 36 inch tall by 48 inch wide poster in U.S. format and a version of this same poster in European (A0 paper) format, 46.8 inch tall by 33.1 inch wide (~ 1 m², oriented vertically) as Power Point files (not Power Point slides). The U.S. format poster will be printed in color (at BTEC or at another poster printing facility). Students will be assisted by the TA to print their final posters full size at BTEC. You must also prepare a brief oral script, and present the printed poster to a jury of the Graduate Faculty in Biomanufacturing. Both the U.S. poster file and the European format poster file will be submitted to the Instructor before the date of the oral poster presentation. You will not print the European format poster on A0 paper.

This poster will be a concise Technology Brief describing a biomanufacturing technology (by your review of the published literature) and how you would use this technology to address a contemporary biomanufacturing problem by engineering a new microbial biocatalyst, cell line, enzyme(s) or process strategy. A detailed description of how the microbial host will be engineered to overexpress this product or how enzymes will be engineered, selected and stabilized is required. Suggested topics will be identified by the instructor beginning in week 3.

Technology Brief (35 points): A 15 page concise, objective final paper based on the same topic as the poster will be written by each student (or pair of poster authors). The format will include a stand-alone Executive Summary, Technology Description (based on your literature review), Applications addressing a contemporary biomanufacturing problem (including figures, tables) and References (complete and correctly formatted). Finding resources for preparation of the poster and paper will be the responsibility of each student and may include published patents, monographs and journal articles. References to vendor information that is not published in the scientific literature are not acceptable. Instructions for preparing a Technology Brief will be discussed in class.

Course grading: This course will be graded on the percentage of the maximum course points accumulated by each student by the end of the semester. The maximum points available for each quiz or assignment will be identified by the instructor. No curve will be
used to determine the student’s final grade. Your performance depends on your effort, not how everyone else in the class does. All students have an equal chance to receive a high score in this class and therefore studying for quizzes in groups and class participation in groups is encouraged. However, each student must complete assignments individually. Cheating on assignments and quizzes will not be tolerated (see Policies and Procedures).

In class quizzes and exams will be graded by the TA and handed back at the beginning of the next class period. Consult the Key to quizzes and exams which will be posted on the course Moodle site for the correct answers. If you believe that an error was made in grading your homework or calculating your total points, write a short justification of your claim and attach it to your original quiz and return it to the TA at the beginning of the next class period. The TA will re-grade your entire work, not just the portion in dispute. The “statute of limitations” for submitting re-grades or computational error claims is one week after the quiz or exam is returned.

**Grading scale:** The following grading scale will be used for this course calculated as the total points earned as a percentage of the maximum possible course points. This grading scale may be adjusted based on the performance of the class and the material presented.

<table>
<thead>
<tr>
<th>Score (%)</th>
<th>Grade</th>
</tr>
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<tbody>
<tr>
<td>&gt;97</td>
<td>A+</td>
</tr>
<tr>
<td>92-96.99</td>
<td>A</td>
</tr>
<tr>
<td>89-91.99</td>
<td>A-</td>
</tr>
<tr>
<td>86-88.99</td>
<td>B+</td>
</tr>
<tr>
<td>82-85.99</td>
<td>B</td>
</tr>
<tr>
<td>79-81.99</td>
<td>B-</td>
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<tr>
<td>76-78.99</td>
<td>C+</td>
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<tr>
<td>72-75.99</td>
<td>C</td>
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<tr>
<td>69-71.99</td>
<td>C-</td>
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<td>66-68.99</td>
<td>D+</td>
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<tr>
<td>62-65.99</td>
<td>D</td>
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<tr>
<td>59-61.99</td>
<td>D-</td>
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<td>&lt;59</td>
<td>F</td>
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**Complementary Laboratory Class BEC (CHE) 563.** Many students reinforce what they learn in this lecture course by enrolling in the 8-week laboratory class *Fermentation of Recombinant Microorganisms*, BEC (CHE) 563 at the NC State Biomanufacturing Training and Education Center (BTEC). This hands-on lab course is offered each semester (fall, spring, summer). There may be an evening laboratory section offered for working professionals. All students learn how to operate laboratory fermentors to produce, isolate and determine the activity of several recombinant proteins (a thermostable enzyme, and a single chain antibody fragment) expressed in *E. coli* or yeast expression platforms.
**Policies and Procedures:** Students are responsible for reviewing the NC State University PRR’s located at [http://oucc.ncsu.edu/course-rights-and-responsibilities](http://oucc.ncsu.edu/course-rights-and-responsibilities) which pertains to their course rights and responsibilities.

**Academic integrity:** It is expected that each student will complete his/her homework, quizzes, exams and problem sets individually with academic integrity. In class activities may be done in small groups based on the requirements of the instructor for that class period. Students shall follow the [NCSU Code of Student Conduct](http://policies.ncsu.edu/policy/pol-11-35-01). In addition, your signature on any quiz or assignment means that you are required to adhere to the University Honor Pledge: “I have neither given nor received unauthorized aid on this test or assignment.” Cheating on quizzes or examinations will not be tolerated. The first time a student is found to be cheating, he or she will receive a grade of zero for that quiz or exam. If the student is found to be cheating a second time during the course, he or she will be given an F for the course.

**Attendance:** Students are expected to attend each class period, participate in activities, and ask questions. Attendance will be taken. It is the student’s responsibility to obtain assignments and information for any missed classes. For NCSU attendance regulations please refer to: [http://policies.ncsu.edu/regulation/reg-02-20-03](http://policies.ncsu.edu/regulation/reg-02-20-03).

**Incomplete Grade:** The university policy on IN grades applies to this course. See [http://policies.ncsu.edu/regulation/reg-02-50-03](http://policies.ncsu.edu/regulation/reg-02-50-03). If an extended deadline is not authorized by the instructor, an unfinished incomplete grade will automatically change to an F after either (a) the end of the next regular semester in which the student is enrolled (not including summer sessions), or (b) the end of 12 months if the student is not enrolled, whichever is shorter. Incompletes that change to F will count as an attempted course on transcripts. The burden of fulfilling an incomplete grade is the responsibility of the student.

**Students with disabilities:** Reasonable accommodations will be made for students with verifiable disabilities. In order to take advantage of available accommodations, students must register with Disability Services for Students, 1900 Student Health Center, Campus Box 7509, (919) 515-7653 [http://www.ncsu.edu/dso/](http://www.ncsu.edu/dso/). Students with disabilities should contact the instructor on the first day of class for any additional assistance. NC State’s Academic Regulations for providing accommodations for students with disabilities can be found at: [http://policies.ncsu.edu/regulation/reg-02-20-01](http://policies.ncsu.edu/regulation/reg-02-20-01).

**Supporting fellow students in distress:** As members of the NC State Wolfpack community, we each share a personal responsibility to express concern for one another and to ensure that this classroom and the campus as a whole remains a safe environment for learning. Occasionally, you may come across a fellow classmate whose personal behavior concerns or worries you. When this is the case, I would encourage you to report this behavior to the NC State Students of Concern website: [http://studentsofconcern.ncsu.edu/](http://studentsofconcern.ncsu.edu/). Although you can report anonymously, it is preferred that you share your contact information so they
can follow-up with you personally.

**ClassEval:** Online class evaluations that are used by the instructors and TA to improve this course will be available for students to complete during the last two weeks of class. Students will receive an email message directing them to a website where they can login using their Unity ID, complete evaluations and add comments. All evaluations are confidential; instructors will never know how any one student responded to any question, and students will never know the ratings for any particular instructor. Evaluation website: classeval@ncsu.edu.

**Equal Opportunity:** NC State University provides equality of opportunity in education and employment for all students and employees. Accordingly, NC State affirms its commitment to maintain a work environment for all employees and an academic environment for all students that is free from all forms of discrimination. Discrimination based on race, color, religion, creed, sex, national origin, age, disability, veteran status, or sexual orientation is a violation of state and federal law and/or NC State University policy and will not be tolerated. Harassment of any person (either in the form of quid pro quo or creation of a hostile environment) based on race, color, religion, creed, sex, national origin, age, disability, veteran status, or sexual orientation also is a violation of state and federal law and/or NC State University policy and will not be tolerated. Retaliation against any person who complains about discrimination is also prohibited. NC State's policies and regulations covering discrimination, harassment, and retaliation may be accessed at http://policies.ncsu.edu/policy/pol-04-25-05 or http://www.ncsu.edu/equal_op/. Any person who feels that he or she has been the subject of prohibited discrimination, harassment, or retaliation should contact the Office for Equal Opportunity (OEO) at 919-515-3148.

Please copy, sign and return to the TA by the second week of class.

**BEC (CHE) 577**
**Advanced Biomanufacturing & Biocatalysis**
Spring Semester, 2016

I, (print your name) ……………………………………….  have read and understand the content, assignments and grading as described in the above syllabus and I will follow the specifications as outlined in this document.

Date…………………………………….. Signature…………………………………………………