Importance of Course:
Metabolic Engineering describes the field of study concerned with applying genetic engineering tools to alter flux through native or newly introduced metabolic pathways in biological systems. Synthetic Biology includes similar objectives but is more broadly focused on applications enabled more generally by advances in DNA synthesis and sequencing technologies. Together these fields are of central importance to efforts to produce chemicals, fuels, and materials via bioprocessing as well as a much broader range of emerging commercial applications; such as biosensing, consumer biotechnology, the microbiome, novel pharmaceuticals, etc.

Objectives:
- *With your help***,** make this the class you find most interesting and useful for your future career.
- See Course Learning Goals at the end of this syllabus for specifics.

Expectations:
- I expect you to attend all classes and be on time.
- I expect you to be responsible for your learning in this class. However, I also expect you to come to me with difficult to answer questions.
- The major responsibility for learning must be by doing the assigned readings and being actively engaged in class discussions, workshops, and interactive presentations.

Course Information
Instructor: Dr. Anushree Chatterjee, Assistant Professor, Chemical and Biological Engineering, chatterjee@colorado.edu
- **Class Meetings:** MWF, 11:30 AM-12:20 PM**,** BIOT A104

Textbook: None specific, though we will be following some parts of Metabolic Engineering: Principles and Methodologies by Gregory N. Stephanopoulus, Aristos A. Aristidou, and Jens Nielsen.
Readings: Will be posted on D2L Course webpage or provided as handouts in class.
Literature: Expected to read scientific papers
Homework: These will be bi-weekly (due on Friday), can use class notes, handouts and will involve using computational tools and reading scientific papers. Home works will be in the form of Q/A format as well as in some cases short reports.

Course Structure
Grades: total grades for this course are based on the following assessments.

       Midterm: 1x 20 pts
       Clickers: 5 pts
       Homework: 20 pts (~7)
       Group Project (report and presentation): 25 pts

Final Exam: 30 pts
Total: 100 pts
Letter Grades: Will be <u>guided</u> by the following distribution

>90: A
88-89: A-
86-87: B+
80-85: B
78-79: B-
75-77: C+
64-74: C
62-64: C-
<62: TBD

Assessments
<u>Midterms and final exam</u>: Tests will primarily utilize short answer type questions and will be based upon lecture materials and reading assignments. The final exam will be focused on the materials covered in entire course; it will be open book/notes. The final is scheduled for **Wednesday Dec 14 7:30-10:00 pm (nice!).**

<u>Group Project</u>: The last third of the class will involve student-group presentations of metabolic engineering case studies. Each group will be comprised of 3 students (with possibly one group of four). Each group will present on a particular research topic and will at least present 3 papers (at least 4 papers for the group of 4). Presentations must follow the specific format specified in the case study project description (to be posted on the course webpage). Presentations will be graded using the grading metric provided in the case study project description.

Prerequisites
Introduces basic concepts in metabolic engineering and explores modern approaches in metabolic and strain engineering. Application areas that will be discussed will include the use of metabolic engineering approaches in biofuels and biorefining as well as biopharmaceutical production. Prereq., CHEM 4611 or 4711 and 4731, and APPM 2360. CHEN 4803 and 5803 are the same course. Students who do not have the required pre-requisites and who do not have an approved variance (signed by the Chemical Engineering variance committee) will be automatically disenrolled from this class. Students can obtain a petition for variance from the chemical engineering departmental office. It is highly recommended that any students in question request and submit a completed petition for variance ASAP so as not to run up against the deadline. Generally, students not having a C- or better in a pre-requisite course will not have the variance approved. However, it is possible, for students with higher GPAs to have variances approved if they can show that they have received a C- or better in equivalent types of courses for preparation. Each petition is considered separately.

Accommodation for Disabilities
If you qualify for accommodations because of a disability, please submit to your professor a letter from Disability Services in a timely manner (for exam accommodations provide your letter at least one week prior to the exam) so that your needs can be addressed. Disability Services determines accommodations based on documented disabilities. Contact Disability Services at 303-492-8671 or by e-mail at <u>dsinfo@colorado.edu</u>. If you have a temporary medical condition or injury, see <u>Temporary Injuries</u> guidelines under the Quick Links at the <u>Disability Services website</u> and discuss your needs with your professor.

Religious Holidays
Campus policy regarding religious observances requires that faculty make every effort to deal reasonably and fairly with all students who, because of religious obligations, have conflicts with scheduled exams, assignments or required attendance. In this class, (*insert your procedures here*).

See the campus policy regarding religious observances for full details.

Classroom Behavior
Students and faculty each have responsibility for maintaining an appropriate learning environment. Those who fail to adhere to such behavioral standards may be subject to discipline. Professional courtesy and sensitivity are especially important with respect to individuals and topics dealing with differences of race, color, culture, religion, creed, politics, veteran's status, sexual orientation, gender, gender identity and gender expression, age, disability, and nationalities. Class rosters are provided to the instructor with the student's legal name. I will gladly honor your request to address you by an alternate name or gender pronoun. Please advise me of this preference early in the semester so that I may make appropriate changes to my records. For more information, see the policies on classroom behavior and the student code.

Sexual Misconduct, Discrimination, Harassment and/or Related Retaliation
The University of Colorado Boulder (CU Boulder) is committed to maintaining a positive learning, working, and living environment. CU Boulder will not tolerate acts of sexual misconduct, discrimination, harassment or related retaliation against or by any employee or student. CU's Sexual Misconduct Policy prohibits sexual assault, sexual exploitation, sexual harassment, intimate partner abuse (dating or domestic violence), stalking or related retaliation. CU Boulder's Discrimination and Harassment Policy prohibits discrimination, harassment or related retaliation based on race, color, national origin, sex, pregnancy, age, disability, creed, religion, sexual orientation, gender identity, gender expression, veteran status, political affiliation or political philosophy. Individuals who believe they have been subject to misconduct under either policy should contact the Office of Institutional Equity and Compliance (OIEC) at 303-492-2127. Information about the OIEC, the above referenced policies, and the campus resources available to assist individuals regarding sexual misconduct, discrimination, harassment or related retaliation can be found at the OIEC website.

Honor Code
All students enrolled in a University of Colorado Boulder course are responsible for knowing and adhering to the academic integrity policy of the institution. Violations of the policy may include: plagiarism, cheating, fabrication, lying, bribery, threat, unauthorized access, clicker fraud, resubmission, and aiding academic dishonesty. All incidents of academic misconduct will be reported to the Honor Code Council (honor@colorado.edu; 303-735-2273). Students who are found responsible for violating the academic integrity policy will be subject to nonacademic sanctions from the Honor Code Council as well as academic sanctions from the faculty member. Additional information regarding the academic integrity policy can be found at honorcode.colorado.edu.

Academic Dishonesty, Ethics, and Discipline
Any discovered incidents of academic dishonesty will be reported to the departmental disciplinary committee and the student(s) will be subject to a hearing. Sanctions can range from an F for the particular assignment to an F for the course. All confirmed incidents will be reported to the University Honor Council where further disciplinary action can be taken. Group activities (group homework) in which a student asks another student in their work group for a helpful suggestion such as group homework assignments will not constitute such an incident. However, using someone else's work, or allowing another student to use your work during individual examinations will be considered a dishonest act. The following list includes some of the examples of dishonest acts (not all of them) for which a hearing will result:
(1)   Talking to each other during a class individual exam
(2)   Plagiarizing solutions to homework such as using solutions from an Official Solutions Manual or pages from an Official Solutions Manual. This includes the Solutions Manual itself or solutions from previous class takers. Plagiarism is defined as the act of representing as one's own production the written work of another.

(4)   Any alteration, forgery, or falsification of official records (such as modification of graded homework problems or exams for which you are seeking additional credit)
(5)   Allowing another person to take an exam for you (false identification)
(6)   Knowingly providing material of your own or of others to a fellow student
(7)   Possession of or observation of examinations or solutions to examinations prior to the date and time of the exam (such as having in your possession or having access to Official Solution Manuals for homework problems - take home exam or a mid-term or final exam before it is actually given).

Tentative Schedule

CHEN 4803 COURSE SCHEDULE AND PLAN			
WEEK	**MODAY**	**WEDNESDAY**	**FRIDAY**
1	AUG 22: Introduction to Metabolic Engineering	AUG 24: Metabolic Engineering-1	AUG 26: Metabolic Engineering-
2	AUG 29: Metabolic Engineering-3	AUG 31: Enzyme Kinetics and growth kinetics	SEP 2: Enzyme Kinetics and growth kinetics **[HOME WORK 1 DUE]**
3	SEP 5: No class	SEP 7: Modeling kinetics	SEP 9: Kinetic modeling exercise (groups)-- COMPUTER ROOM/LAPTOPS
4	SEP 12: Modeling Genome scale	SEP 14: Flux Balance Analysis	SEP 16: FBA modeling exercise (groups) - COMPUTER ROOM/LAPTOPS **[HOME WORK 2 DUE]**
5	SEP 19: Reading DNA	SEP 21: Writing DNA-1	SEP 23: Writing DNA-2
6	SEP 26: Assembling DNA	SEP 28: Sequencing DNA	SEP 30: Design parameters overview **[HOME WORK 3 DUE]**
7	OCT 3: Design-Transcription	OCT 5: Design translation/post translation	OCT 7: Design pathways
8	OCT 10: Design software	OCT 12: Genome Engineering tools-1	OCT 14: Genome Engineering tools-2 **[HOME WORK 4 DUE]**
9	OCT 17: Review session	OCT 19: Genome Engineering tools-3	OCT 21: Synthetic Biology
(TENTATIVE) OCT 19, WED: MIDTERM EXAM, 6-8 PM			
10	OCT 24: Synthetic Biology	OCT 26: Synthetic Biology	OCT 28: Synthetic Biology **[HOME WORK 5 DUE]**
11	OCT 31: Synthetic Biology	NOV 2: Metabolic Engineering Case study	NOV 4: Metabolic Engineering Case study
12	NOV 7: Metabolic Engineering Case study	NOV 9: Project presentation	NOV 11: Project presentation **[HOME WORK 6 DUE]**
13	NOV 14: Project presentation	NOV 16: Project presentation	NOV 18: Project presentation
14	NOV 21: No class	NOV 23: No class	NOV 25: No class
15	NOV 28: Project presentation	NOV 30: Project presentation	DEC 2: Project presentation **[HOME WORK 7 DUE]**
16	DEC 5: Project	DEC 7: Review session	DEC 9: Review session

presentation/Review session		

Learning Goals
CHEN 4803 - - Metabolic Engineering (and Synthetic Biology)
Fall 2016

The following is a list of the specific instructional objectives for the course. These are the things you should be able to do by the time you complete the course. These objectives should serve as a useful study guide. I will design all exams to test these objectives. I reserve the right to add or delete objectives at the end of this list depending on how much time remains to cover special topics near the end of the course. However, I will make all amendments known in class well advance of any exams.

By the end of the course, the student should be able to:
1. Be able to define metabolism and describe the major metabolic pathways in microbes.
2. Describe the interrelationships between biokinetics and evolution. In particular, be able to discuss rationale for complex reaction networks in metabolism and role of regulation.
3. Explain what is an enzyme and how enzymes manage to increase rate of biological reactions.
4. Hypothesize the type of reaction catalyzed by an enzyme based on the name of the enzyme.
5. Develop kinetic equations for enzyme catalyzed reactions based on quasi-steady state and rapid equilibrium assumptions for the following scenarios
    a. No inhibitors
    b. Competitive inhibition
    c. Non-competitive inhibition
    d. Un-competitive inhibition
6. Determine kinetic parameters for different kinetic models, including both the strategy for performing experiments as well as the analytical methods for parameter estimation.
7. Postulate how changes in enzyme sequence and/or reaction media conditions might effect reaction kinetics and suggest strategies for testing.
8. Develop stoichiometric models based on yield coefficients and rates for metabolic pathways.
9. Use stoichiometric models to evaluate metabolic pathways (i.e. redox balanced?) and suggest genetic engineering strategies.
10. Develop "black-box" mass balance models for various bioprocesses.
11. Develop elemental mass balances models for various bioprocesses.
12. Use black-box and elemental balances to evaluate bioprocesses and suggest strain engineering and/or process engineering strategies.
13. Explain and model the different stages of cellular growth curves.
14. Explain the rationale behind the different equations for modeling cell growth based on substrate concentrate.
15. Develop kinetic models describing flow through metabolic pathways
16. Apply kinetic models to develop pathway designs that alter pathway flux in a specified manner.
17. Understand how to apply genome-scale stoichiometric models to improve understanding of metabolism
18. Apply genome-scale models to develop metabolic designs that improve flux to targeted metabolites.
19. Explain the core approaches to DNA sequencing.
20. Explain the main technologies for DNA synthesis, including current capabilities and key limitations.
21. Describe current strategies for assembling short-pieces of DNA into larger fragments, including advantages/disadvantages of each.

22. Explain the different features that go into a biological "design", what each feature contributes to the design, and what the various options are for each feature.
23. Detail a variety of biological design software packages and how they are used to improve biological engineering efforts.
24. Detail a variety of genetic and metabolic strategies used in commercial metabolic and strain engineering efforts to improve strain performance.
25. Describe the affect of different genetic and metabolic engineering strategies on overall strain performance based on case studies presented in class or in the assigned readings.
26. Assess the economic potential of a target molecule given a specific organism, production pathway, and substrate.
27. Describe several real-world examples of metabolic engineering that have had medical/commercial impact.