Metabolic Engineering, Synthetic Biology, and Natural Products- BIEN 4803-5803

Chemical and Biological Engineering

Spring 2026

Course Description:

What if cells could be programmed like code, allowing microbes to serve as living factories for producing fuels, pharmaceuticals, flavors, and advanced materials? This course explores the rapidly advancing fields of metabolic engineering, synthetic biology, and natural products, situated at the nexus of biology, design, computation, and chemistry. Students will gain a comprehensive understanding of the molecular logic of metabolism and the strategies used to engineer biological systems to produce valuable natural products and novel biomolecules. By integrating theoretical foundations with case studies and design-based projects, the course addresses topics such as pathway optimization, genome editing, enzyme kinetics and engineering, biosynthetic pathway discovery, natural products, and computational modeling of cellular systems.

Expectations:

- You are expected to attend all classes and arrive punctually.
- You are expected to take responsibility for your own learning and are encouraged to ask questions to support your understanding.
- I expect you to be respectful and courteous to everyone in the classroom.

Course Information:

Instructor: Dr. Antonio Del Rio Flores, Assistant Professor, Chemical and Biological Engineering, antonio.delrioflores@colorado.edu, 303-492-1271, JSCBB C226

Class Meetings: MWF, 4:00 PM-4:50 PM, JSCBB A108

Instructor Office Hours: M/W: 11:00 AM-12:00 PM, JSCBB C226. Other times are available by appointment. After class generally works for quick questions/discussions.

Available by email (antonio.delrioflores@colorado.edu) and if needed Zoom.

Teaching Assistant: Hatem Abdelrahman, Graduate Student, Biomedical Engineering, Hatem.Abdelrahman@colorado.edu

TA Office hours: T 3-4 PM at JSCBB A312 and F 5-6 PM at JSCBB B322. Other times are available by appointment. After class is generally fine for quick questions/discussions.

Available by email (Hatem.Abdelrahman@colorado.edu) and if needed Zoom

Textbook: None specifically, though we will be following some parts of Metabolic Engineering: Principles and Methodologies by Gregory N. Stephanopoulus, Aristos A. Aristidou, and Jens Nielsen and Bioprocess Engineering: Basic Concepts by Michael L. Shuler and Fikret Kargi.

Readings: Will be posted on our Canvas Course webpage or provided as handouts in class.

Literature: Expected to read, analyze, critically analyze scientific papers.

Homework and Group Mini Projects: These assignments will be given approximately every two weeks and will be due on Fridays via Canvas unless otherwise noted (11:59 PM MST). You may use class notes and handouts, and the assignments will involve reading scientific papers. Homework and Group Mini Projects will consist of Q/A tasks and, in some cases, short written reports. **No form of AI may be used to complete these assignments! All submitted work must be completed independently and reflect your own efforts.**

Course Structure:

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

Midterm: 25%

Homework and Mini Group Projects: 15% (~8 assignments)

Group Project (report and presentation): 30%

Final Exam: 30%

Assessments:

Midterms and final exam: Tests will primarily consist of short-answer and free-response questions and will be based on lecture content, homework, and assigned readings. The final exam will be cumulative, covering material from the entire course. It is scheduled for **Wednesday, April 29, 4:30-7:00 p.m at JSCBB A108.**

Group Project: The last third of the class will involve student-group presentations of metabolic engineering/natural product case studies. Each group will be comprised of 3-4 students that will present a particular research topic. 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: BCHM 4611. Students who do not have the required pre-requisites and who do not have an approved variance will be automatically disenrolled from this class. Students can obtain a petition for variance from the chemical and biological 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 prerequisite 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.

Policies and Procedures:

Disability statement: 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 dsinfo@colorado.edu. If you have a temporary medical condition or injury, see Temporary Medical Conditions: Injuries, Surgeries, and Illnesses guidelines under Quick Links at Disability Services website and discuss your needs with your professor.

Honor Code and Academic Dishonesty: All students of the University of Colorado at Boulder are responsible for knowing and adhering to the academic integrity policy of this institution. Violations of this policy may include: cheating, plagiarism, aid of academic dishonesty, fabrication, lying, bribery, and threatening behavior. All incidents of academic misconduct shall be reported to the Honor Code Council (honor@colorado.edu; 303-735-2273). Students who are found to be in violation of the academic integrity policy will be subject to both academic sanctions from the faculty member and non-academic sanctions (including but not limited to university probation, suspension, or expulsion). Other information on the Honor Code can at http://www.colorado.edu/policies/honor.html and at http://honorcode.colorado.edu. Additionally, be found the course instructor will report the incident to the Academic Ethics Committee of the Department of Chemical and Biological Engineering. This Committee will recommend to the instructor whether a sanction should be applied to the student. Typical sanctions may range from a zero on an assignment in question to an F in the course. Whether or not the student has admitted the act, in light of the preponderance of the evidence, may factor into the recommendation of the Committee.

Disabilities: If you qualify for accommodations because of a disability, please submit to me a letter from Disability Services in a timely manner so that your needs may be addressed. Disability Services determines

accommodations based on documented disabilities. Contact: 303-492-8671, Willard 322, and http://www.Colorado.EDU/disabilityservices.

Religious Observances: 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, the student must notify the professor at the beginning of the semester of any conflicts with regard to the examination times. For homework assignments, the student must notify the professor least 2 weeks in advance to make special arrangements. See full details at http://www.colorado.edu/policies/fac_relig.html.

Behavioral standards: 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. See policies at http://www.colorado.edu/policies/classbehavior.html and at http://www.colorado.edu/studentaffairs/judicialaffairs/code.html#student_code.

Discrimination and Sexual Harassment: 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 discrimination or harassment based upon Protected Classes or related retaliation against or by any employee or student. For purposes of this CU-Boulder policy, "Protected Classes" refers to 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 discriminated against should contact the Office of Discrimination and Harassment (ODH) at 303-492-2127 or the Office of Student Conduct (OSC) at 303-492-5550. Information about the ODH, the above referenced policies, and the campus resources available to assist individuals regarding discrimination or harassment can be obtained at http://hr.colorado.edu/dh/

CEAS Values Statement:

Preamble: The College of Engineering and Applied Science at the University of Colorado Boulder—like other higher education institutions in the United States—is in the midst of a mental health crisis with respect to its more recent entering student cohorts. These students are part of Generation Z and this generation is significantly more likely to arrive at college having had treatment for mental health challenges. Approximately 27% of Gen Z members characterize their mental health as fair to poor, a higher reported number than any cohort in American history (APA.org, 2018). These trends are felt here at CU; indeed Student Affairs reports an increased incidence rate of mental health concerns within the Gen Z cohort at CU. These statistics were made real for CEAS during the 2018-2019 academic year and subsequent summer when we experienced the loss of eight CEAS majors to suicide. Given this significant spike in the suicide rate, the Dean as well as multiple faculty and staff felt that the college must focus its efforts on the health and wellness of our students, faculty, and staff. To that end, a committee was formed at the end of the Spring 2019 semester to work over the summer to make recommendations on what the college should do. One recommendation was to generate an aspirational values statement for the college; a statement that identifies the characteristics we want to see in our community and the values we want to hold to help all members of our community balance work and life in a healthy and positive way and in a way that promotes mental health and wellness. Indeed, this effort supports and complements the 4th pillar of our CEAS Strategic Vision to "enrich our professional environment". We now seek endorsement of this statement of values from a wide range of faculty and staff so that we can use this statement to drive the creation of new policy, practices, and programs that prioritize mental health and health-seeking practices, and provide our students with the support they need to be able to tackle the challenges of higher education and engineering in manageable ways that allow them to be successful in achieving their academic and personal goals. We here at the College of Engineering and Applied Science (CEAS) value one another as human beings first and embrace practices to support the health, wellness, and success of all CEAS community members. We prioritize the well-being of all members of our community -- students, faculty, and

staff. Community wellness begins with respect, empathy and inclusion, and we strive to develop well balanced healthy individuals. We promote supportive conversations around mental health and health seeking practices. Engineering is a demanding curriculum where trial and error, taking risk, making mistakes, revising, correcting, and persisting is essential to learning. We help our community members find healthy and connected ways to learn from challenges and to productively integrate challenging experiences into their lives. Recognizing that all students come from diverse backgrounds and follow different paths to get to CU, we strive to adopt academic policies and best practices for flexibility at both the course and program levels to support student well-being. We expect students to follow their own path at CU by taking ownership of their education, believing that personal responsibility is key to healthy living. As faculty and staff, we strive to model the characteristics that we want to see in our students by being ethical, resilient, and creative educators and technologists, and prioritizing both our own health and well-being and the health and well-being of those around us. We share strategies with our students to grow intellectually, professionally, collaboratively, and personally. We Hear You, We Value You, We C U! We are Here for You.

Tentative Schedule for BIEN 4803/5803 for Spring 2026

Week	M	W	F
1			**Jan 9th** Syllabus/Intro to Course
2	**Jan 12th** Molecular and Cell Biology	**Jan 14th** Gene Expression	**Jan 16th** Gene Regulation and Energetics (Homework 1 Due)
3	**Jan 19th** MLK Holiday- NO CLASS	**Jan 21st** Energetics and Metabolism	**Jan 23rd** Energetics and Metabolism
4	**Jan 26th** Energetics and Metabolism	**Jan 28th** Enzyme Kinetics	**Jan 30th** Enzyme Kinetics
5	**Feb 2nd** Enzyme Kinetics	**Feb 4th** Metabolic Flux Analysis	**Feb 6th** Metabolic Flux Analysis
6	**Feb 9th** Cell Growth Kinetics (Homework 2 Due)	**Feb 11th** Cell Growth Kinetics	**Feb 13th** Molecular Cloning
7	**Feb 16th** Molecular Cloning	**Feb 18th** Protein Expression and Purification in *E. coli*	**Feb 20th** Fast Protein Liquid Chromatography and Enzymatic Assays (Mini Project 1 Due)
8	**Feb 23rd** Heterologous Expression and Recombination Knockouts	**Feb 25th** De Novo Pathway Design (Homework 3 Due)	**Feb 27th** Review Session
9	**Mar 2nd** **Midterm- 6-8 PM A108 JSCBB**	**Mar 4th** Genome Engineering	**Mar 6th** Genome Engineering
10	**Mar 9th** Genome Engineering	**Mar 11th** Genome Engineering	**Mar 13th** Synthetic Biology (Homework 4 Due)
11 (Mar 16th-20th)	Spring Break- NO CLASS		
12	**Mar 23rd** Synthetic Biology	**Mar 25th** Synthetic Biology	**Mar 27th** Synthetic Biology
13	**Mar 30th** Methods for Natural Product Biosynthesis and Engineering	**Apr 1st** Fatty Acid Biosynthesis (Homework 5 Due)	**Apr 3rd** Polyketide Biosynthesis (Mini Project 2 Due)
14	**Apr 6th** Polyketide Biosynthesis	**Apr 8th** Non-Ribosomal Peptides	**Apr 10th** Non-Ribosomal Peptides
15	**Apr 13th** Terpenoids and Alkaloids	**Apr 15th** Metalloenzymes	**Apr 17th** Biosynthesis/Biocatalysis (Homework 6 Due)
16	**Apr 20th** Presentation Day 1 **Project Due at 1 PM MST**	**Apr 22nd** Presentation Day 2	**Apr 24th** Presentation Day 3

Final Exam	**April 29th, 2026, at 4:30-7:00 PM JSCBB A108**

LEARNING GOALS:

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 bio kinetics and evolution. Be able to discuss rationale for complex reaction networks in metabolism and role of regulation.

3. Explain what an enzyme is and how enzymes manage to increase the 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 effect 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 natural products and metabolic engineering that have had a medical/commercial impact.

28. Propose a biosynthetic pathway for any given natural product based on knowledge of the biosynthetic gene cluster.

29. Understanding the role of regulation in natural product biosynthesis.

30. Apply knowledge of organic chemistry to propose basic enzymatic mechanisms for major enzyme classes.

ABET Student Outcomes:

(1) an ability to identify, formulate, and solve complex engineering problems by applying principles of engineering, science, and mathematics. (2) an ability to apply engineering design to produce solutions that meet specified needs with consideration of public health, safety, and welfare, as well as global, cultural, social, environmental, and economic factors (3) an ability to communicate effectively with a range of audiences (4) an ability to recognize ethical and professional responsibilities in engineering situations and make informed judgments, which must consider the impact of engineering solutions in global, economic, environmental, and societal contexts (5) an ability to function effectively on a team whose members together provide leadership, create a collaborative and inclusive environment, establish goals, plan tasks, and meet objectives (6) an ability to develop and conduct appropriate experimentation, analyze and interpret data, and use engineering judgment to draw conclusions (7) an ability to acquire and apply new knowledge as needed, using appropriate learning strategies "Biological" Program Criteria 1: a working knowledge of advanced biological sciences consistent with the program educational objectives. "Biological" Program Criteria 2: prepare graduates to apply engineering to biological systems.