BSE 4564/5984G: Metabolic Engineering

Syllabus and Course Outline
Spring 2016

Instructor: Xueyang Feng
Office: 301J HABB1
Office Phone: 540-231-2974
Email: xueyang@vt.edu
Office Hours: M 1-3pm, W 1-3pm

TA: Weihua Guo
Email: gweihua2@vt.edu
Office Hours: F 3-5 pm
Location: HABB1 302-6

Course (Catalog) Description:

4564: **Metabolic Engineering**
Engineering concepts for analyzing, designing, and modifying metabolic pathways to convert raw materials to food, pharmaceuticals, fuels and chemicals. Cell metabolism, pathway design, bioenergetics, regulatory mechanisms, metabolic modeling, and genetic tools.

Prerequisites and Co-requisites: BSE 3534. BSE 3534 Bioprocess Engineering is a prerequisite for this course. BSE 4564 builds on the concepts of metabolic pathway analysis, enzyme kinetics, and cell growth kinetics by designing and analyzing genetic manipulations that must be made to a metabolic network to enable new functions, such as the production of chemicals or remediation of toxins.

Textbook: No textbook is proposed for this course. Research and review articles identified by the instructor will serve as the reading material for this course and will be made available on the course website.

Recommended references:

1. Stephanopoulos, G.N., Aristidou, A.A., Nielsen, J. (1998) Metabolic engineering: Principles and methodologies. 1st ed. San Diego: Academic Press. 725 p.
2. Smolke, C.S. (2010) Metabolic pathway engineering handbook: Fundamentals. 1st ed. New York: CRC Press. 678 p.
3. Smolke, C.S. (2010) Metabolic pathway engineering handbook: Tools and applications. 1st ed. New York: CRC Press. 581 p.

Graduate and Undergraduate Students: Graduate students register for BSE 5984G, and undergraduate students register for BSE 4564. In addition to the homework, exams, and case studies assigned to BSE 4564, graduate students will be required to complete three writing assignments throughout the semester. Each writing assignment will consist of a "mini-review" of relevant (and recent) publications in the student's research area of interest. Each mini-review must be four typed pages in length.

Course Objectives: Metabolic engineering involves the redesign of metabolism to enable cells to produce new products, such as valuable chemicals and biofuels, and/or remediate toxins. This field is growing rapidly in both academia and the biotechnology industry and requires skilled engineers with knowledge of how to apply engineering principles to metabolic pathways in order to analyze, design, and alter cell functions. The introduction of basic concepts, current technologies, and challenges within the field will provide students with a valuable toolset to address metabolic engineering problems that are relevant to the emerging biotechnology industry. This course will include computational and experimental approaches to metabolic engineering so students learn how to design strategies through mathematical modeling. In addition, students will learn "rational" (design driven) approaches as well as "combinatorial" (randomized) approaches to metabolic engineering. Having successfully completed this course, students will be able to:

1. Identify the appropriate host and/or metabolic pathways to produce a desired product or remediate a toxin
2. Compare potential metabolic engineering strategies using quantitative metabolic modeling
3. Design ^{13}C-labeling strategies and perform metabolic flux analysis to determine metabolic pathway utilization
4. Construct genome-scale metabolic flux models using available tools and software and perform simulations
5. Devise effective strategies to implement genetic manipulations
6. Derive effective combinatorial metabolic engineering strategies

Evaluation and Grading

	BSE 4564	**BSE 5964G**
Homework	30%	20%
Exam 1	25%	20%
Exam 2	25%	20%
Participation	20%	20%
Writing assignment	N/A	20%
Total	100%	100%

Course Outline (Tentative): The following schedule is subject to change.

Date (2016)	Lecture
1/20	Introduction
1/22	Biological Basics: Metabolic Pathways
1/25	Biological Basics: Transcriptional Machinery **(HW1 release) (5984G: WA1 release)**
1/27	**Journal Club 1: What is Metabolic Engineering?**
1/29	Kinetic Models: Michaelis-Menten Kinetics
2/1	Kinetic Models: Monod Model
2/3	**Journal Club 2: How to Design Enzymes? (HW1 Due)**
2/5	Genetic Modification: Overview
2/8	Genetic Modification: Promoter Engineering **(5984G: WA1 Due)**
2/10	**Journal Club 3: How to Design a Yeast Promoter?** **(HW2 release) (5984G: WA2 release)**
2/12	Protein Engineering: Rational Design
2/15	Protein Engineering: Directed Evolution
2/17	**Journal Club 4: How to Enable the Impossibilities of a Protein?**
2/19	Genome Engineering: Overview
2/22	Genome Engineering: CRISPR
2/24	**Journal Club 5: How will CRISPR Change Life Sciences?** **(HW2 Due) (5984G: WA2 Due)**
2/26	Combinational Engineering: Random Mutagenesis **(Exam 1 release)**
2/29	Combinational Engineering: Genomic Libraries
3/2	**Journal Club 6: How to Improve Microbial Stress Responses?** **(Exam 1 Due)**
3/4	Canceled
3/7	**Spring break**
3/9	**Spring break**
3/11	**Spring break**
3/14	Canceled
3/16	Canceled
3/18	Combinational Engineering: Screening Technologies
3/21	Combinational Engineering: Applications
3/23	Synthetic Biology: Circuit Design
3/25	Synthetic Biology: Molecular Sensors
3/28	**Group presentation 1**
3/30	Flux Balance Analysis: Principles
4/1	Flux Balance Analysis: Applications
4/4	**Group presentation 2 (HW3 release) (5984G: WA3 release)**
4/6	^{13}C Metabolic Flux Analysis: Principles
4/8	^{13}C Metabolic Flux Analysis: Applications
4/11	**Group presentation 3 (HW3 Due)**
4/13	MATLAB: Synthetic Circuit Design
4/15	MATLAB: Metabolic Flux Analysis

4/18	**Group presentation 4 (5984G: WA3 Due)**
4/20	Omics: Principle and Analysis
4/22	Omics: Applications
4/25	**Group presentation 5**
4/27	Worked Example in Metabolic Engineering: Artemisinin
4/29	Worked Example in Metabolic Engineering: Butanol
5/2	**Help session**
5/7	**Final Exam (1:05-3:05 pm, SEITZ 108)**

Course Policies

Scholar: The course syllabus, lectures, schedule, and other relevant materials will be placed on the Scholar website developed for this course. Students unable to access this website should contact the instructor immediately. https://scholar.vt.edu/portal

Homework: Assignments will be posted on Scholar at least one week before the due date. Students are encouraged to work in teams and consult with classmates regarding homework problems. However, each student must submit his or her own homework assignments. Any assignment submitted with two or more names will not be graded. Even though teamwork is encouraged, all submitted homework assignments must be the student's own work. In other words, no two homework assignments should be identical. Homework assignments must be turned in at the beginning of class on the due date. Half of the points deduced from the original homework will be returned if 1) all the mistakes in the homework are corrected; and 2) the corrected homework is submitted as a pdf file to the instructor by the end of the day that the homework is gone over on the class.

Class Attendance: It is strongly recommended that students attend all class periods and participate in class discussions. This will be reflected in the student's grade through better performance on homework assignments and exams. Spontaneous class discussions may not appear in the pre-prepared lecture notes posted on the Scholar website; however, this material may appear in a homework or exam question. Class attendance is not formally considered in the student's final grade; however, class participation is formally considered.

Class Participation: Talking in class by asking questions or answering questions is considered class participation. The class participation grade will be assessed by the instructor and cannot be disputed. Students should contribute in class every at least once every week to receive a good class participation score.

Privacy: It is against Virginia Tech policy for the instructor to retain any document (or email) containing the student's identification number. Do not include this on any assignments or in any emails. The instructor is authorized to only discuss a student's grades or performance with the student him/herself.

Plagiarism: To avoid plagiarism, students are encouraged to never copy from another work. The use of vocabulary terms coined in other works (e.g., "systems biology") is widely accepted. However, the use of long phrases (not to mention sentences or paragraphs) from other works is technically considered plagiarism. This section is particularly relevant to BSE 5984G students in preparing the writing assignments.

Wireless Devices: Wireless communications on electronics (e.g., laptop) used during an exam must be disabled (e.g., airplane mode).

Virginia Tech Honor System: As a University requirement, all incidents of cheating and plagiarism must be reported by the course instructor to the VT Honor Code Panel. This includes the use of unapproved wireless devices during tests and multiple students submitting identical homework assignments. Any incidence of suspected plagiarism must be reported. For more information, please see: http://www.honorsystem.vt.edu/.

Late Assignments: Homework assignments are due at the beginning of class on the due date. Homework assignments received on the due date but after the start of class will receive at 10% penalty. Homework assignments received after the due date will receive at penalty of 10% per day. Late assignments must be turned into Dr. Feng directly (or placed under his office door in HABB1). Assignments must NOT be placed in Dr. Feng's mailbox in the mailroom. This is now a violation of student privacy guidelines at Virginia Tech.

Students with Disabilities: Any student who feels he or she may need accommodation because of a disability (e.g., learning disability, attention deficit disorder, psychological, physical, etc.), please make an appointment to see me during office hours.

Principles of Community: A learning environment will be created strictly adhering to the Virginia Tech Principles of Community. http://www.vt.edu/diversity/principlesofcommunity.html

Pledges of the Instructor

1. Mutual respect to all students.
2. To provide all lecture materials before they are discussed in class.
3. To return graded homework assignments and exams within 2 class periods. In most cases, graded work will be returned by the next class period.
4. Provide up-to-date and relevant "real world" examples for materials covered in class.
5. To enable every student to have a voice in the class.
6. To provide each student an honest assessment on how they can improve their performance in this class (office hours appointment required).
7. To provide adequate help with homework assignments and test preparation.
8. To routinely summarize important points and provide adequate reviews for exams.
9. To give challenging exams and homework assignments.