BSE 5614 Advances in Protein Production and Engineering

Course syllabus

Spring 2016 (CRN 19808)

Instructor: Mike Zhang, 210 Seitz Hall, 231-7601, cmzhang@vt.edu
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Location: Seitz 108, Tue, Thu, 9:30 – 10:45 a.m.

Office Hours:

Mike Zhang: Tuesday and Thursday, 10:45 a.m.-12:15 p.m, 210 Seitz Hall
Percival Zhang, Mon (1:30 -3:00 PM), Wed (9:00-10:30 AM), 304 Seitz Hall

Textbook and special teaching aids:

A. Required Teaching Aids:

Teaching aids: selected readings, handouts from instructor. Here are some examples:

- A. Cabanne, A.M. Noubhani, et al. Purification and on-column refolding of EGFP overexpressed as inclusion bodies in *Escherichia coli* with expanded bed anion exchange chromatography. J. Chromatography B. 818 (2005) 23-27.
- K.A. Kimberly, C.H. Schmelzer, S.A. Pizarro. Industrial case study: Evaluation of a mixed-mode resin for selective capture of a human growth factor recombinantly expressed in *E. coli*. J. Chromatography A. 1217 (2010) 235-242.
- A. Schmid, J.S. Dordick, A. Kiener, M. Wubbolts, B. Withold, Industrial biocatalysis today and tomorrow, Nature, 409 (2000) 258-268.
- U.T. Bornscheuer, G.W. Huisman, R.J. Kazlauskas, S. Lutz, J.C. Moore, K. Robins, Engineering the third wave of biocatalysis, Nature, 485 (2012) 185-194.
- Y.-H.P. Zhang, Production of biofuels and biochemicals by in vitro synthetic biosystems: Opportunities and challenges, Biotechnol. Adv., 33 (2015) 1467–1483.

Description

Concepts, principles and applications of various expression systems for protein and enzyme production, and the principles and applications of the most current unit operations used in bioseparations. Principles and applications of various methods for protein molecular modification to facilitate its downstream processing. Protein engineering by directed evolution and rational design. Mutant selection and identifications, and establishment of mutant library for protein engineering. In vitro synthetic enzymatic biosystems for biomanufacturing.

Learning Objectives

Upon successful completion of this course, students shall be able to:

- Compare different expression systems for recombinant protein/enzyme production;
- Evaluate different protein/enzyme separation techniques;
- Analyze the advantages and disadvantages of various molecular modification techniques for recombinant protein/enzyme purification;
- Distinguish the theory of directed evolution and rational design for enzyme engineering;
- Evaluate a number of in vitro DNA mutation technologies and differentiate selection and screening for directed enzyme evolution;

- Analyze in vitro synthetic enzymatic biosystems for biomanufacturing, and be able to compare in vitro biosystem-based biotransformation with microbial fermentation.

Syllabus:

	Percent of Course
Protein expression systems	15%
Protein purification techniques	20%
Protein molecular modifications for purification	15%
Introduction to protein engineering	10%
Directed evolution	20%
In vitro synthetic enzymatic biosystem	20%
	100%

Tentative course outline:

- Weeks 1 – 3: Various expression systems for recombinant protein production;
- Weeks 4 – 6: Newly developed protein purification techniques;
- Week 7: Molecular modification of proteins for enhanced purification;
- Week 8: Spring break (March 5-13)
- Weeks 9-10: Introduction of enzyme engineering;
- Weeks 10-12: Directed evolution;
- Weeks 13-16: in vitro synthetic enzymatic biosystems.

Paper reports:

- For the first half of the semester (in the first 7 weeks), you will submit 3 journal paper reports (timelines are to be announced later). You will need to search a relevant publication pertaining to the following topics, protein expression systems, a particular purification technique, and protein modification for enhanced purification, and write a 1-2 page summary. The template will be provided in the course scholar site.
- For the second half of the semester, you will submit weekly journal paper report. First one is due by the end of Week 10 (3/25), last one by the end of Week 15 (04/29). The total report number is six. You need to search a research paper pertaining to in vitro synthetic enzymatic biosystems (or in vitro metabolic engineering or cell free systems) and write one-page summary by using your language. The template of this report is available in the course scholar site.

Grading:

Paper reports (3)	12%
Mid-term take-home exam	38%
Weekly paper report (six)	12%
Final-term take-home exam	38%
Total	100%

Justification

Protein production and protein engineering are increasingly important in biopharmaceutical and biocommodity industries. This course offers the graduate students the opportunity to learn the current development in protein expression and purification and state-of-art methods for protein

engineering and their applications. The students will learn the various expression systems used for current protein therapeutic production, the cutting edge technologies for protein recovery and purification, the molecular considerations to enhance protein recovery and purification, various methods for protein engineering, and the cutting-edge in vitro synthetic enzymatic systems for next generation biomanufacturing.

The main change of the content is the addition of enzyme engineering (learning objectives #4-6). Most natural enzymes are not suitable for industrial biocatalysis. Protein engineering enables to improve enzyme performances (such as thermostability, optimal pH, solvent tolerance, enhanced catalytic efficiency, etc.). Inclusion of the related topics will give the students a broader view on protein engineering and a new area – cascade biocatalysis for implementing complicated biotransformation suitable for next generation biomanufacturing.

This class requires the students to have in-depth prior knowledge on protein biochemistry and extensive background on various unit operations used in bioprocess engineering. Students will develop the ability to select appropriate production host/system, synthesize a suitable process to purify proteins expressed in exogenous hosts, design methods for protein engineering, and evaluate biocatalysts suitable for industrial production.

Honor Code: The Honor Code will be STRICTLY enforced in this course. All assignments submitted shall be considered "graded work". All aspects of your coursework are covered by the honor system. All projects and homework assignments are to be completed individually unless otherwise specified. For more information, please check http://www.honorsystem.vt.edu/.

Students with disabilities: If you need adaptations or accommodations because of a disability (learning disability, attention deficit disorder psychological, physical, etc.); if you have emergency medical information to share with me; or if you need special arrangements in case the building must be evacuated please make an appointment with me as soon as possible.