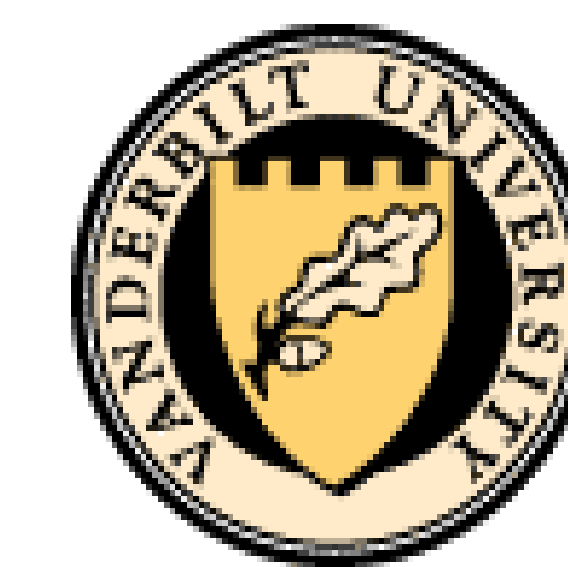




# Implementation of Educational Modules in a Biotechnology Course: A Challenge Based Education Approach



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## Motivation

Biotechnology is one of the active domains in the NSF funded Engineering Research Center VaNTH (Vanderbilt, Northwestern, University of Texas, and Harvard/MIT) where an educational mosaic is currently being developed. Aspects of this mosaic have been tested by students at Vanderbilt University and have proven to be useful. Based on the results from these studies, the challenges relating to bioreactors and mass/momentum transfer are currently being refined. At Northwestern, Birol and coworkers have developed challenge-based educational materials that focus on microbial kinetics and downstream processing. The combination of the work developed at Vanderbilt with the new challenge topics at Northwestern form the basis of the 'mosaic' for a course on biotechnology. The aim of this study was to design a new biotechnology course centered on challenge-based education and to implement the new educational tools. This paper focuses on the implementation of the mosaic at Northwestern in the new Bioprocess Technology Course (BME 395). We also focus on how the new biotechnology course at Northwestern builds on the work from Vanderbilt and discuss issues relating to the implementation of innovative course materials.

## Course Description: Bioprocess Technology

Quarter system:  
9 ½ to 10 ½ weeks  
Class meetings:  
Two times a week  
(80 minutes each)  
Grading policy:  
Two take-home exams  
(20% each)  
Homework (30%)  
Team project (20%)  
Class participation (10%)  
Communication:  
Office hours  
E-mail  
Blackboard system

The primary **learning goals** of the course were

- to provide students with basic principles in cellular and molecular biology of microbial and mammalian cells,
- give them a working knowledge of bioreactor operations and microbial kinetics and their industrial applications,
- to promote and help students develop lifelong skills such as adaptive expertise, presentation and communication skills in an active learning environment.

*A Summary of Priorities of Topics, Learning Objectives and Educational Modules Used in Bioprocess Technology Course, M1 and M2: Bioreactor Operation Module, M3: Microbial Kinetics Module*

Topics (Priority Levels, F: Familiar, I: Important, E: Essential)	Module	Learning Objective
1. Biology (I) • Cellular Biology (I) • Molecular Biology (F)		<ul style="list-style-type: none"> <li>Identify specific classifications of cells such as microbial, plant and animal,</li> <li>Notice (or recognize) the importance of cells in biotechnology, and be aware of cells' capabilities,</li> <li>Learn their physiology, morphology, reproduction characteristics,</li> <li>Define their growth environments and conditions</li> <li>Be aware of the benefits of the recombinant DNA technology and techniques and of gene manipulation</li> </ul>
2. Bioreactors (E) • Cell Cultivation (E) • Operation and Analysis (E) • Momentum and Mass Transfer Issues (I)	M1 and M2	<ul style="list-style-type: none"> <li>Classify bioreactor types,</li> <li>Explain the major differences among various bioreactor types, and recognize the constraints of bioreactors,</li> <li>Learn the different types of cultivations,</li> <li>Recognize the constraints for cultivation of different cell types</li> <li>Be able to choose the right bioreactor configuration for a given cell culture conditions,</li> <li>Learn the operation and analysis of bioreactors,</li> <li>Learn the mass transfer limitations in bioreactors,</li> <li>Explain the effects of manipulated variables (e.g. agitation rate, aeration rate etc) on cell growth and product formation,</li> </ul>
3. Microbial Kinetics (E) • Stoichiometry of Growth and Product Formation (E) • Biomass Formation (E) • Product Formation (E) • Substrate Utilization (E)	M3	<ul style="list-style-type: none"> <li>Know how to make use of stoichiometric information,</li> <li>Learn to perform elemental material balances, and estimate yield coefficients,</li> <li>Explain how and why cell, product and substrate concentrations change in batch cultures,</li> <li>Learn what the specific growth rate, specific product formation rate,</li> <li>Define rate expressions for cell growth, for product formation given the growth conditions,</li> <li>Explain the differences in rate expressions for cell growth and for product formation</li> <li>Recognize the limitations of growth and of product formation</li> <li>Demonstrate the ability to write down a rate expression for a given data set and solve it,</li> <li>Compute the specific growth rate, the specific product formation rate,</li> <li>Demonstrate the ability to combine cell growth and product formation data to find substrate utilization,</li> <li>Learn how to apply yield coefficient information to define substrate utilization,</li> </ul>
4. Product Recovery (F) • Separation of Insolubles (F) • Primary Purification (F) • Final Purification (F)		<ul style="list-style-type: none"> <li>Identify the major steps in product recovery for a given product,</li> <li>Recognize the different purification methods,</li> <li>Explain the differences between different levels of purification</li> </ul>

## Assessment

### Overall Plan

- Pre and post tests<sup>1</sup>
- Exam questions
- Presentations by students
  - student presentations were videotaped
  - notes taken regarding the discussion
  - student generated reports were archived
- Surveys
- Muddiest points<sup>1</sup>
- Concept mapping activities<sup>1</sup>
- Reflection activities

*Assessment Summary: Class Time Distribution and the Corresponding Methods of Assessment on the Topics Covered*

<b>Week 1-2: Biology</b>	<ul style="list-style-type: none"> <li>Pre Test</li> <li>Concept Mapping Activity</li> </ul>
<b>Week 3-7: Bioreactors and M1 and M2</b>	<ul style="list-style-type: none"> <li>Survey on each Module</li> <li>Muddiest Points</li> <li>Reflection Activity</li> <li>Post Test 1 (as part of Midterm Exam 1)</li> </ul>
<b>Week 8-10: Microbial Kinetics and M3</b>	<ul style="list-style-type: none"> <li>Survey on Module</li> <li>Muddiest Points</li> <li>Reflection Activity</li> <li>Post Test 2 (as part of Midterm Exam 2)</li> <li>Concept Mapping Activity</li> </ul>

### Pre and Post Test

- Part A: Open-Ended Challenge Question** attempted to capture general, "adaptable" problem solving skills such as:
  - ability to design a plan,
  - ability to identify necessary resources,
  - considers multiple solution paths,
  - identifies technical, business, ethical, safety, etc. issues.
- Part B: Bioreactor Question** assessed quantitative understanding of bioreactor design based on oxygen mass transfer and mixing momentum transfer consistent with the learning objectives of **M1 and M2**.
- Part C: Kinetic Model Question** assessed quantitative understanding of microbial kinetics consistent with the learning objectives of **M3**.

### Survey for M3

(1 - 5 scale)

- The challenge was interesting.
- Investigating the challenge helped me to learn about the assumptions and constraints in generating a kinetic model.
- The challenge related to the course content.
- Listening to the group presentations helped me to generate ideas about how to approach the problem.
- The challenge was difficult.
- Investigating the challenge helped me to learn about solving open-ended problems.
- The challenge assignment was a valuable learning activity.
- I found it difficult to make connections between the lecture material and the challenge assignments.
- Listening to the group presentations helped me to interpret the data.
- Adequate time was given to complete assignments.
- Listening to the group presentations helped me to think about how to generate a kinetic model of the system.
- It was difficult to use PenSim.
- Investigating the challenge did not help me to learn about penicillin production.

### Concept Mapping Activity

- At the beginning and at the end of the course:
  - "What is **Biotechnology**? And how does it relate to Biomedical Engineering?"
- Before and after M1 and M2:
  - "What are the **factors affecting a bioreactor's performance**? Relate them to transport (mass and momentum) phenomena, microbial kinetics when appropriate."
- Before and after M3:
  - "What are the factors affecting **cell growth rate**? What are the factors affecting **product formation rate**? How are they related?"

### Reflection Activity

Earlier in the previous challenge (M1 or M2) you responded to several thought questions. Take a moment to review your responses (distributed by your instructor) and expand on them by answering the questions listed below. Articulating what you currently know will help you identify potential ideas for how to refine your exploration of the challenge question in PreTest.

- What more could I teach someone about producing the ProteinPlus product?
- What did I record earlier that is not right and why?
- What more do I need to know to solve this challenge?
- Where could I find this additional information?



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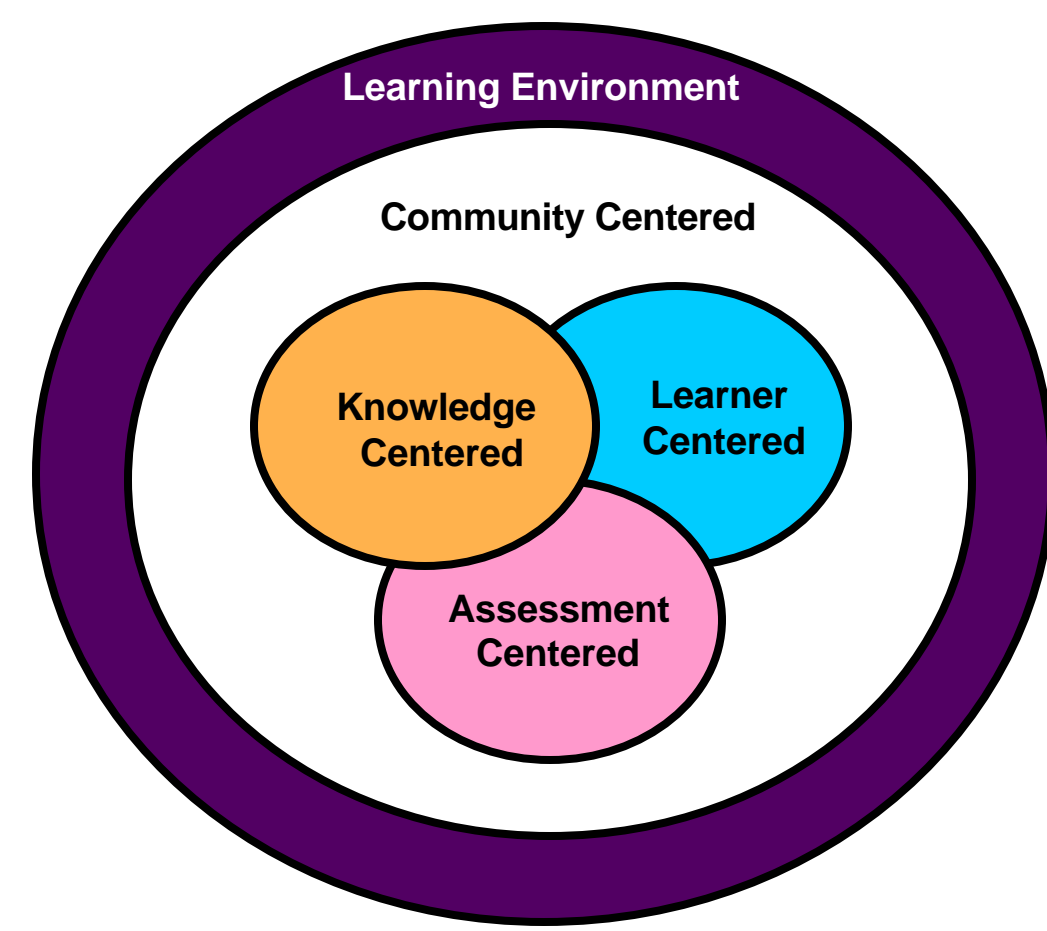
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## Educational Modules

The "How People Learn" Framework<sup>2</sup>



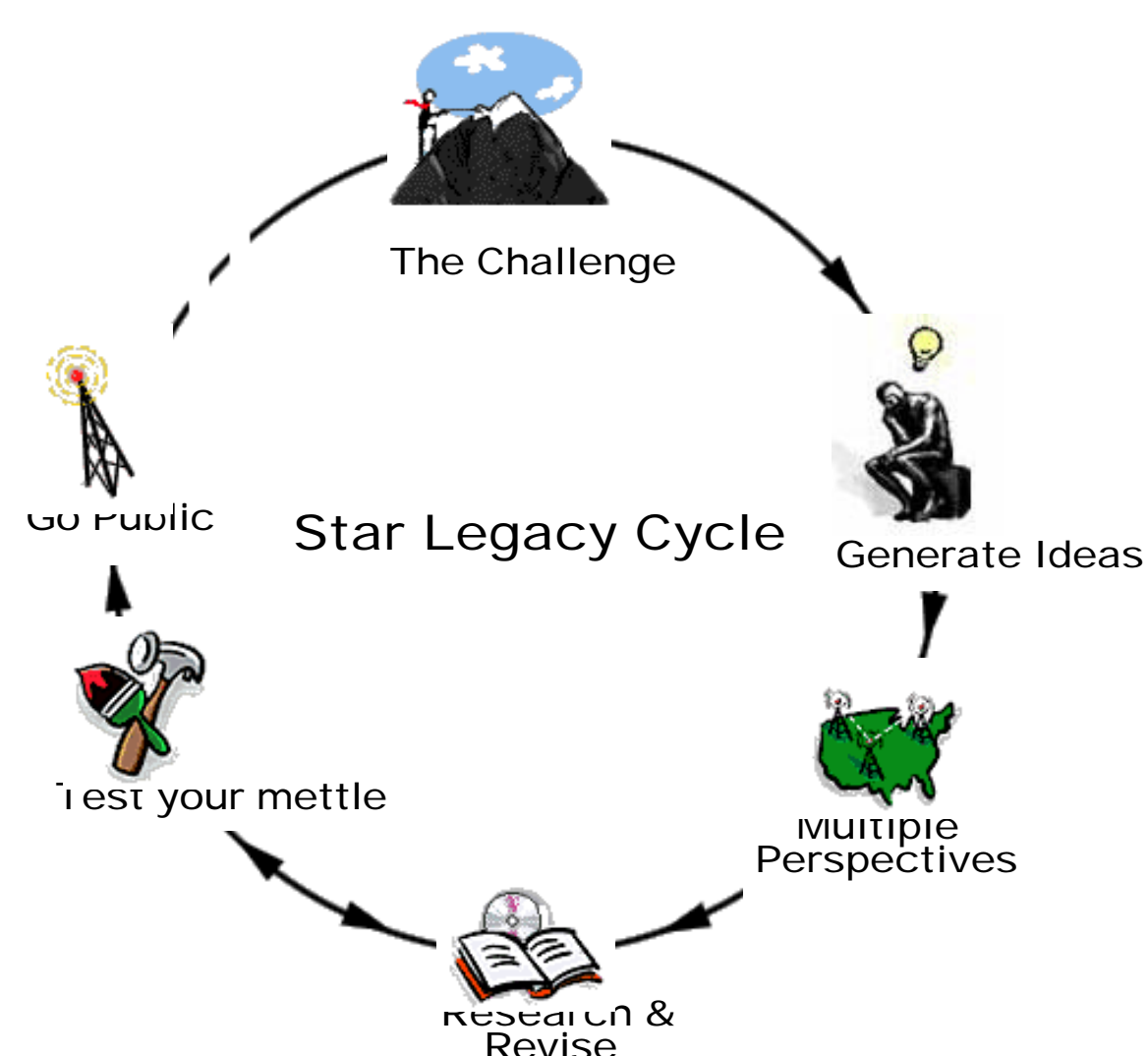
**Learner-centered:** i.e., the environment and class activities should take into account the knowledge, skills, preconceptions and learning styles of the learners,

**Knowledge-centered:** i.e., it helps students learn with understanding by thinking qualitatively, and organizing their knowledge around key concepts,

**Assessment-centered:** i.e., it provides frequent opportunities for students to make their thinking visible so that their understanding can be refined as needed,

**Community-centered:** i.e., it fosters norms that encourage students to learn from one another, plus encourages faculty to do likewise.

The Star Legacy Cycle



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Each module included a **Challenge**, methods to stimulate **Idea Generation**, presentations of **Multiple Perspectives**, questions and materials to support **Research and Revision**, opportunities to **Test Your Mettle** and methods to **Go Public**.

### Module 1 (M1): Exploring Bioreactor Designs<sup>3</sup>

The production of therapeutic proteins from mammalian cells requires consideration of multiple, connected issues. The optimal conditions for cell growth depend of the cell type, the desired rate of product synthesis, bioreactor design and operating conditions. Commercial production of therapeutic proteins presents a particular set of challenges resulting from the large scale required.

We will consider **two cell types** that could be used to support the production of rFVIII - '293 cells' and CHO (Chinese hamster ovary) cells.

We **need to decide which one of these cells** will be the best host for producing the product in terms of both efficient and correct synthesis. Our first challenge is to identify the conditions that will best sustain robust growth for each of these cell types.

Therefore, what is **the best bioreactor design** for growing the desired amount of each cell type?

### Module 3 (M3): Exploring Microbial Kinetics<sup>4</sup>

The Board of Directors of Microbaway Antibiotics, Inc. has just voted on allocating funds towards construction of a **new production facility** to be used for the production of penicillin, a highly profitable antibiotic. As members of the Microbaway Antibiotics, Inc. Product Development team, it is **your task to develop a mathematical model describing the microbial kinetics of penicillin production**. This model will be used to maximize penicillin production at the new plant prior to production.

You will need to review production data in order to generate your model. Anne T. Biotic, a fermentation expert from SporeTech Pharmaceuticals, will help you **run some experiments** at one of SporeTech's penicillin production facilities, PenSim. Anne will provide you with the initial operating conditions from the last several production runs as a starting point in your analysis (we are also planning to run our plant at these operating conditions). Microbaway's management has requested that a **preliminary report** defining and assessing the kinetics of penicillin production be presented at the manager's meeting next week. This report should include the proposed model of the **relationship between biomass, nutrients, penicillin and/or others as they are related, any assumptions, simplifications** etc. It is very important that you substantiate your proposed model via simulation results and support your findings.

After the development of this initial report, your team will need to **test your proposed model** based on a set of experimental data that will be provided to you by the fermentation expert. This will allow you to validate/invalidate your model. Your team will need to generate another report for **presentation** at the quarterly Director's meeting to take place in Maui, Hawaii, in November.

### Module 2 (M2): Exploring Bioreactor Mass Transfer and Mixing<sup>3</sup>

CHO cells grown on 200 micron diameter microcarriers have been selected for the large scale production of recombinant. Economic analysis suggests that the optimum production strategy requires recovery of 2,200 liters of raw cell culture product per day. The resulting bioreactor volume is 2,500 liters and three such bioreactors are required. For this production volume, and the specified use of microcarriers, the design must be a stirred bioreactor.

The goal of our challenge is to **design the bioreactor to optimize recombinant production**. Therefore, you need to consider at least two important questions:

1. What **physical and operating characteristics** must be considered?
2. What **additional data is required** before the optimum conditions can be predicted?

## Preliminary Results

1. Assessment **aligned** with learning goals
  - capture content understanding: biotechnology concepts
  - open-ended problem solving ability: aspects of adaptive expertise.
2. Assessment **matched** to curricula materials
  - assessment similar to what we ask students to do as part of the class
    - challenge-based
    - support goals of course
    - assessment-centered
3. Survey instruments included an opportunity for **free-form learner responses** providing opportunities for refinement.
4. Muddiest points provided **insight into learner interest, enthusiasm and discomfort** enhancing opportunities for further improvement.
5. There is **evidence of increased learner capabilities and interest** in HPL-based classes.
6. **Cross institution collaboration** has been promoted resulting in new opportunities for educational research.

## Summary

- A **new** Bioprocess Technology course was designed and successfully implemented.
- Three **educational modules** based on the how people learn framework were effectively integrated into class material facilitating the achievement of the learning objectives of the course.
  - Integration of educational modules helped the instructor cover more course material than would have covered in a classical lecture format.
- An **extensive assessment** plan was developed and implemented.
  - The assessment plan developed will be refined and used in other courses as well as in the refinement of the modules (M1 and M2) and in the design of the new module (M3).
- Student **involvement** was very high.

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