

AC 2009-437: BIOPROCESS ENGINEERING CURRICULUM DEVELOPMENT AND ASSESSMENT

Stacy Klein, Vanderbilt University

Stacy Klein is the Associate Dean for Outreach and an Associate Professor of the Practice of Biomedical Engineering in the Vanderbilt University School of Engineering.

Rick Williams, East Carolina University

Rick Williams is an Assistant Professor in the Department of Engineering at East Carolina University.

Stephanie Sullivan, East Carolina University

Stephanie Sullivan is a Teaching Instructor in the Department of Engineering at East Carolina University.

Loren Limberis, East Carolina University

Loren Limberis is an Assistant Professor in the Department of Engineering at East Carolina University.

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Abstract

East Carolina University's new general engineering program is built around the goal of excellence in undergraduate education. The faculty of the program are encouraged to pursue novel approaches to engineering education in order to achieve this goal. The newly created concentration in bioprocess engineering provides an excellent opportunity to develop and implement a novel curriculum based upon proven pedagogical approaches designed to engage the students and improve their mastery of concepts. The objectives of this NSF sponsored CCLI grant (DUE #0737198) include the utilization of proven techniques to develop nine instructional modules for three bioprocess engineering courses (three modules per course) and to assess the effectiveness of the instructional modules. One module in the bioprocesses separation engineering course challenges students to determine a process to produce ethanol from locally grown feedstock. The unit ends with students developing a laboratory manual that allows for the evaluation of process efficiency of ethanol production of a locally grown feedstock. One module in the bioprocess validation and quality engineering course challenges students to understand the process validation required for bioproduct production. Ultimately, students must create a process validation for laboratory scale ethanol production based on the previous module's ethanol laboratory manual. Pre- and post-tests have been created for both of these modules that include three types of questions: terminology, problems and skills from the unit, and a near-transfer question. Results of ethanol module's pre- and post-tests indicate a statistically significant growth in knowledge.

Project Introduction and Objectives

East Carolina University (ECU) is a large regional university that serves eastern rural North Carolina and the southeast region of the United States. The industries and businesses located among the small towns of eastern North Carolina have a need for a broadly skilled general engineer. The rationale for a general engineering program at ECU is made by Kauffmann et al.¹ "Instead of the traditional engineering disciplines, these operations require engineering generalists with a strong theoretical background, broad knowledge in a range of areas, and specific skills in problem solving to give them a sound but flexible base for managing and implementing technology change and operations." In 2004, East Carolina University initiated a bachelor's degree program in general engineering (BSE) to fulfill this requirement. The BSE curriculum is implemented "through a concept and program identified as the Integrated Collaborative Engineering Educational Environment (ICEE). The ICEE program... emphasizes a broad but highly integrated foundation of engineering fundamentals and engineering sciences necessary for a general engineer."¹

The ECU engineering program features a common core that develops the fundamental engineering skills and four concentrations that build specialized knowledge: systems engineering, engineering management, biomedical engineering, and bioprocess engineering. The engineering graduates that specialize in the bioprocessing concentration will work in one of the fastest growing segments of the eastern North Carolina's economy; bioprocessing and pharmaceutical manufacturing. These engineers will require the skills to support, operate, and

improve these biomanufacturing processes. The current bioprocessing curriculum has six additional courses beyond the engineering core curriculum: Microbiology, Organic Chemistry, Introduction to Bioprocess Engineering (BIOE 3000), Bioprocess Validation, Quality and Design of Experiments (BIOE 4000), Bioprocess Separation Engineering (BIOE 4010), Bioprocess Plant Design, and Simulation and Analysis (BIOE 4020). The bioprocess engineering concentration courses are in addition to the two semester capstone design sequence that will also have some bioprocess related component.

The faculty of ECU's engineering program are encouraged to pursue novel approaches to engineering education. The newly created concentration in bioprocess engineering provides an excellent opportunity to develop and implement a novel curriculum based upon proven pedagogical approaches designed to engage the students and improve their mastery of concepts. This paper highlights two curriculum modules developed for a bioprocess engineering program as part of a larger curriculum improvement program.

Project Background

In 1999, the National Research Council published *How People Learn: Mind, Brain, Experience, and School*² as the summary of what we know from research about the first three words of this title. This document proposed four “centerednesses” that, taken together, optimize learning: *knowledge-centeredness, student-centeredness, assessment-centeredness, and community-centeredness*. When these four are in place, studies show that students increase both their content knowledge and their ability to apply that knowledge in new situations – i.e., their *adaptive expertise*.³⁻⁸ First, the learning environment must be *knowledge-centered*; that is, appropriate information should be presented in an appropriately sequenced and organized way. Second, the environment must be *student-centered*. Lessons should seek out students' prior conceptions and misconceptions, help students make connections with prior knowledge, and be relevant to students' own lives. Third, the learning environment must be *assessment-centered*; it should include opportunities for formative feedback for both students and instructors. Students benefit from opportunities to check their own understanding and instructors benefit from opportunities to assess the effectiveness of their teaching. Finally, a learning environment must be *community-centered*, one in which students are provided opportunities to learn collaboratively.

There are many efforts underway within STEM education to move away from traditional lecture methods of delivery towards more novel methods designed to engage the students in the learning process.⁹⁻¹² In many cases, these methods are taking the How People Learn concepts from theory to practice. The highlights of two specific programs, Project Galileo¹¹ and VaNTH¹² follow.

Project Galileo has developed two novel pedagogical approaches: Peer Instruction and Just-in-Time Teaching. These approaches are designed to provide students “with greater opportunity for synthesizing concepts while instructors get timely feedback that can help focus instruction on the points that are most difficult to learn.”¹³ The strategies also maximize the efficacy of the

classroom session, where human instructors are present, structure the out-of-class time for maximum learning benefit, and create and sustain team spirit.¹⁴

In their study of ten years of peer instruction, Crouch and Mazur¹¹ report: “Peer Instruction engages students during class through activities that require each student to apply core concepts being presented and then explain these concepts to fellow students. Unlike the traditional method of asking informal questions during lecture, which often only engages a few highly motivated students, Peer Instruction is more structured and designed to engage every student in the classroom.” Peer Instruction consists of (1) preclass reading, (2) mini-lectures, (3) concept tests, and (4) discussion, and can be combined with both traditional lecture and other interactive techniques.¹³

Novak¹⁴ describes Just-in-Time Teaching (JiTT for short) as “a teaching and learning strategy based on the interaction between web-based study assignments and an active learner classroom. Students respond electronically to carefully constructed web-based assignments which are due shortly before class. The instructor reads the student submissions ‘just-in-time’ to adjust the classroom lesson to suit the students' needs. Thus, the heart of JiTT is the ‘feedback loop’ formed by the students' outside-of-class preparation that fundamentally affects what happens during the subsequent in-class time together.” JiTT can be viewed as a technology that facilitates the preclass reading and, to some extent, the concept tests in the Peer Learning environment. JiTT makes use of the web; however, it should not be confused with distance learning or computer-aided instruction since nearly all the instruction still occurs face-to-face in the classroom. JiTT content is typically classified into three categories: student assignments such as warm-ups and puzzles in preparation for classroom activity; enrichment pages such as short essay or URL links highlighting practical, everyday applications of the subject matter or other interesting related material; and stand-alone instructional material such as simulations or spreadsheet programs.

The approach taken by VaNTH has focused more directly on HPL theory in developing an approach to improve the efficacy of teaching STEM material. According to HPL theory, students learn best when (1) presented with organized information that (2) relates in some way to their own experiences, and they are given the opportunity to (3) test themselves on their own understanding and to (4) work to develop their understanding with other students. The STAR.Legacy Cycle (Figure 1 – note that the terms “Legacy Cycle” and “STAR.Legacy Cycle” are used interchangeably) was created as a means of implementing the HPL ideas in the classroom.^{15,16} The Legacy cycle incorporates these four influences on learning by providing a rich, contextually-based problem, relevant in some way to students' lives, and allowing students to engage deeply with that problem in ways that include opportunities for collaboration with other students and for self-assessment.

The Legacy cycle consists of six phases as illustrated in Fig. 1¹⁵. In the *Challenge* phase, students are presented a problem that they are to solve. From the problem statement, the students are encouraged to generate ideas in a brainstorming session. During this *Generate Ideas* phase, the instructor accepts all ideas without criticism or comment. Following the *Generate Ideas* phase, the students are steered towards the desired path by receiving multiple perspectives on the subject. These could be opinion such as pre-recorded opinions of known experts, excerpts from

journal articles, or a quick visit to a website. In any case, the *Multiple Perspectives* phase is intended to be short and immediate, and requires pre-planning from the instructor (it is not a literature review done by the students). After the students obtain the additional insight and intended steering of the multiple perspectives, they move into the *Research and Revise* phase. This is the phase in which most of the learning and teaching occurs. This phase could consist of student-driven research and experimentation, passive lectures, homework assignments, or any other combination of concept delivery. During the *Research and Revise* phase, the students will occasionally test their mettle. In the *Test Your Mettle* phase, the instructor will implement formative assessment to evaluate the students' understanding of various concepts. Finally, the students answer the challenge through the *Go Public* phase. The *Go Public* phase is intended to provide summative assessment of the students' performance of the challenge.

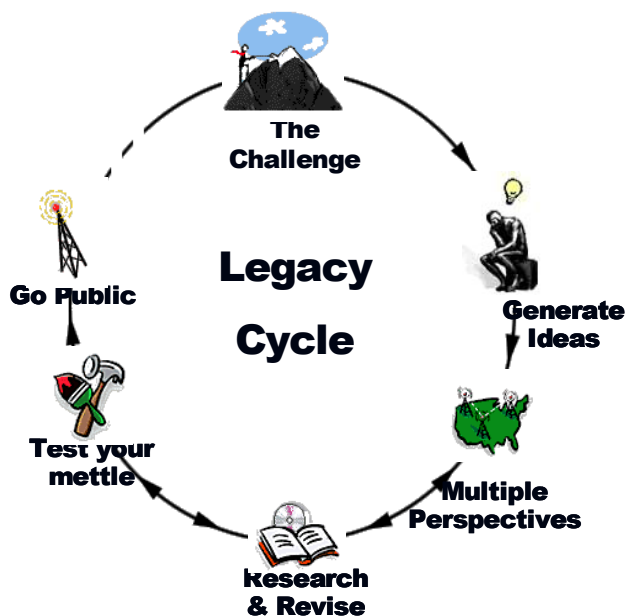


Figure 1: STAR Legacy Cycle Diagram¹⁵

Case-based learning has been used in other fields such as medicine and law with success in learning for some time now.¹⁷ These cases are similar to the Legacy Cycle in the use of an initial “challenge” or problem that must be solved. However, Legacy Cycle lesson design adds more specific structure to the traditional problem-based learning format, as after the stated Challenge and following the Generate Ideas activity, students examine selected thoughts from experts that relate to the problem and direct their thoughts in the desired direction(s) before engaging in “Research and Revise” activities. These steps are supported by additional research that has demonstrated improved learning when students first generate their own ideas and then hear experts’ ideas prior to consulting resources or learning new material.¹⁸ Formative assessment or feedback is useful to students and instructors as well in generating actual learning¹⁹ and is incorporated in the Legacy Cycle at the Test Your Mettle stage. Lastly, students are motivated by creating a product or answering an authentic question^{20,21} as is done in the “Go Public” stage of the Legacy Cycle.

Engineering curricula utilizing the STAR.Legacy Cycle design have been developed and implemented with great success in the college engineering classroom.^{16,22} Roselli²³ and Pandey²⁴ have demonstrated the efficacy of the Legacy Cycle in biomechanics education. Measures in Roselli's biomechanics class show an increase in both student ratings of the course and instructor on evaluations as well as an increase in the understanding of difficult concepts. In other engineering courses, concepts such as Fourier analysis and signal processing have been taught effectively.^{25,26} Measures in Greenberg's²⁶ physiology course show a statistically significant improvement in Fourier spectral analysis skills. These examples, along with studies at the high school level all illustrate a mastery of science concepts beyond that of control classrooms for concepts taught using the Legacy Cycle design.^{7-8,27-29}

The techniques of the Peer Instruction and Just-in-Time Teaching dovetail well with Legacy Cycle approach. The Research and Revise and Test Your Mettle phases of the Legacy Cycle contain activities such as lectures, readings, and student to student teaching that can be enhanced by using the Peer Instruction and Just-in-Time techniques.

Project Scope and Benefits

The bioprocess engineering concentration consists of six courses beyond the general engineering core curriculum. Two of the courses, organic chemistry and microbiology, are valuable prerequisites for the bioprocess engineering courses that follow. Of the four remaining courses, we are creating novel content for three of the courses: Introduction to Bioprocess Engineering (BIOE 3000), Bioprocess Validation, Quality and Design of Experiments (BIOE 4000), and Bioprocess Separation Engineering (BIOE 4010). The first course, BIOE 3000 is a sixth semester course, while the other two courses are normally taken in the student's seventh semester. Specifically, three modules per course (nine modules total) utilizing the Legacy Cycle approach for engaging students are being developed. Each module will nominally represent two to three weeks of content such that about 50% of each course will be initially delivered utilizing the Legacy Cycle. In addition to the Legacy Cycle, both Peer Instruction and Just-in-Time Teaching will be incorporated into the modules to increase the learning effectiveness of these courses.

Consistent with ECU's adaptation of vertically integrated engineering modules³⁰, six of the developed Legacy Cycles contain some aspect of integration. In general, this integration will be through the use of a common theme. Thematically linking the modules across courses will help the students make connections between seemingly unrelated materials and reinforce selected concepts, thus enhancing their learning. The proposed plan for integrated modules is shown in Fig. 2. One of the Legacy Cycles from BIOE 3000 will serve as a stepping stone for a Legacy cycle utilized in BIOE 4000. A second Legacy Cycle from BIOE 3000 will serve as a stepping stone for a Legacy cycle utilized in BIOE 4010. Finally, a Legacy Cycle from BIOE 4000 will be integrated into a Legacy cycle utilized in BIOE 4010.

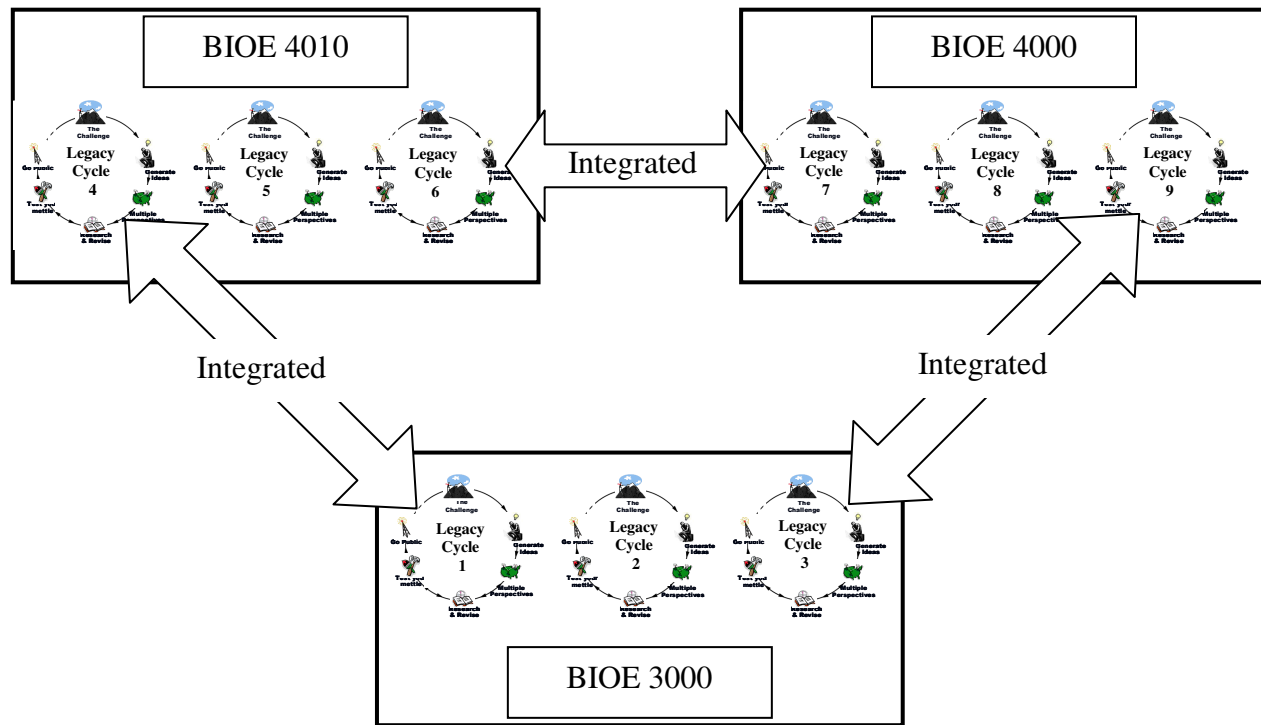


Figure 2: Proposed Legacy Cycle module implementation showing the integration between selected modules

The unique benefit of developing integrated Legacy Cycles is that it allows students to build upon the knowledge gained from the previous cycle, improving the efficiency of delivery of the second cycle, thus allowing more depth and breadth of coverage of the second cycle. The challenge of this approach is ensuring the ability to run the second cycle independent of the first cycle. We strongly believe that integrated modules must have some ability to stand alone to ensure portability to other programs and to allow for the case in which a student was not exposed to the earlier module within a series (perhaps due to receiving transfer credit for the earlier course). To affect this end, the modules must be loosely integrated so they can stand alone with only minor modifications.

The direct benefits of providing challenging integrated bioprocess engineering modules are the critical thinking skills the students will develop for use throughout their careers. Successful graduates of a general engineering program, with concentrated studies on bioprocess engineering, will need to extend themselves and apply the fundamental concepts of engineering and mathematics they learn to a variety of conditions and situations. They will most likely be the cohesive component in a project requiring a multifaceted approach for successful completion. The more the students are engaged, as occurs with this proposed approach, the better the subject matter will be retained and applied. Utilizing the skills gained through completing Legacy Cycles, the graduates will be able to apply their experiences to tackle challenges, generate ideas, use their resources, and test hypotheses and ideas culminating in a successful approach to managing and solving problems.

A Sample Module – Growing Ethanol from Locally Grown Feedstock

The ethanol module is part of the Bioprocess Separation Engineering course. The unit begins with by posing the following challenge question to the students: “As a newly minted bioprocess engineer, you have been asked to develop a process to produce ethanol using locally grown feedstock. How will you go about selecting and testing to determine the best feedstock?” Students are immediately asked to generate their own ideas about how to solve this challenge question and are given the following prompts:

- (1) What are your initial ideas about how ethanol is produced?
- (2) What are the desirable characteristics of a good feedstock for ethanol production?
- (3) What are the undesirable characteristics of a good feedstock for ethanol production?
- (4) How can you quantify a “good feedstock” for ethanol production?

The instructor then guides the students to share their individual ideas with the class, and these initial ideas are recorded. Next an expert interview that will guide the students to an appropriate feedstock (sweet potatoes) is shown to the class. The instructor then leads a guided discussion using the student and expert ideas to guide the students to see the need for a clear understanding of (1) the conversion of starches to sugars and sugars to ethanol, (2) the processes required to separate the ethanol from the fermentation broth, and (3) the need to perform assays of the processes in order to measure the effectiveness of each step.

Student instruction begins with how starches are converted to sugars and sugars to ethanol using a mixture of teaching methods. Students are taught that plant matter is made up of starches and sugars and how the conversion of starches into sugars takes place on a microbiological level. The need for enzymatic activity to accelerate the process of starch to sugar conversion is established. Students are taught how the fermentation process occurs on a microbiological level. The instructor discusses the importance of controlling parameters such as temperature and oxygen content of the fermentor. The methods used to measure the fermentation rate are taught.

Student instruction continues with how the liquid and solids of the fermentation broth can be separated. The instructor discusses the options of sedimentation, centrifugation, and filtration. Students are taught the concept of flocculation and how it improves the separation processes.

Student instruction is completed with how the ethanol can be separated from the other liquids of the fermentation broth. The instructor discusses Raoult’s law and Vapor Liquid Equilibrium curves for ideal mixture along with non-ideal mixtures and the concept of an azeotrope. Students are taught about fractional distillation and the concept stages or trays. Students discuss and analyze the water-ethanol phase diagram and finally are taught techniques to measure the efficiency of the distillation process.

In addition to PRS assessment for understanding concepts, formative assessment in the Test Your Mettle phase of the module primarily includes work in the lab. Students are first given the assignment of outlining their procedure for making ethanol. They are reminded that they will perform the lab in three steps; starch conversion, sugar fermentation, and ethanol purification. At the next class, students present their procedures and revise them as necessary so that they will

work. Students actually perform their procedures for this step and then repeat the process for the next two steps.

For the Go Public summative assessment stage, students are asked to develop a laboratory manual that allows for the evaluation of process efficiency (kg ethanol/kg feedstock) of ethanol production of a feedstock.

The administering of the material in the ethanol module takes place over five 50-minute lectures and four 3-hour laboratory sessions. Tables 1 and 2 provide a summary of the material covered and assignments in each of the lecture and laboratory sessions.

Table 1: Ethanol module lectures summarizing the material covered and assignments by lecture day

LECTURE DAY ONE
<ul style="list-style-type: none"> • Introduce the Challenge Question.
<ul style="list-style-type: none"> • Students independently work in their journals to answer the Generate Ideas questions.
<ul style="list-style-type: none"> • As a class, review all journal entries for the Challenge Question.
<ul style="list-style-type: none"> • On the board, record the needed knowledge areas that students identified. Also record any specific ideas that were generated
<ul style="list-style-type: none"> • Guide students to see that they must understand (1) the conversion of starches to sugars and sugars to ethanol, (2) the processes required to separate the ethanol from the fermentation broth, and (3) the need to perform assays of the processes in order to measure the effectiveness of each step.
<ul style="list-style-type: none"> • Review the expert interview that guides the students towards the appropriate feedstock.
<ul style="list-style-type: none"> • Assignment: Visit the following websites and write a one-page summary of the ethanol conversion process. http://www.ethanolrfa.org http://running_on_alcohol.tripod.com/id20.html http://journeytoforever.org/biofuel_library/ethanol_motherearth/meCh1.html
LECTURE DAY TWO
<ul style="list-style-type: none"> • Use the Personal Response System (PRS) for formative assessment of the following terms: saccharification, fermentation, distillation, starch
<ul style="list-style-type: none"> • Discuss the conversion of starch to sugar. Establish the need for enzymatic activity for liquefaction and saccharification. Establish the need to control process parameters such as water dilution, temperature, and pH.
<ul style="list-style-type: none"> • Perform the enzyme demonstration.
<ul style="list-style-type: none"> • Discuss the conversion of sugar to ethanol. Discuss cell respiration vs. cell fermentation. Establish the need to control process parameters such as water dilution, temperature, pH, and oxygen content.
<ul style="list-style-type: none"> • Assignment: Research assays for determining starch to sugar conversion and fermentation

progress.
LECTURE DAY THREE
<ul style="list-style-type: none"> • Pair or team up the students and have them report their assay recommendations. • Discuss the content of the fermentation broth and the need to separate the liquid and solids. • Discuss solid-liquid separation processes of sedimentation, centrifugation, and flocculation. • Derive the equation for Stokes settling velocity. • Perform the flocculation demonstration. • Assignment: Complete the solid-liquid separation HW assignment.
LECTURE DAY FOUR
<ul style="list-style-type: none"> • Use the PRS for formative assessment of the following terms: Stokes Radius, Reynolds Number, and inertial acceleration • Use Peer Instruction techniques to clarify any misconceptions of the terminology. • Discuss Raoult's Law. • Discuss Vapor Liquid Equilibrium curves for ideal mixtures. • Discuss batch and fractional distillation of ideal mixtures. • Assignment: Review the following websites on distillation. http://www.chemguide.co.uk/physical/phaseeqiamenu.html#top http://lorien.ncl.ac.uk/ming/distil/distildes.htm
LECTURE DAY FIVE
<ul style="list-style-type: none"> • Administer the distillation quiz. • Discuss Vapor Liquid Equilibrium curves for non-ideal binary mixtures. Discuss the concept of an azeotrope. • Discuss Vapor Liquid Equilibrium curves for water-ethanol mixtures. • Discuss fractional distillation of water-ethanol. • Discuss other techniques of separating azeotropic mixtures (optional). • Assignment: Develop a fractional distillation calculator using Excel.

Table 2: Ethanol module laboratories summarizing the material covered and assignments by laboratory day

LAB DAY ONE (After LECTURE DAY ONE)
<ul style="list-style-type: none"> • Introduce the students to the available lab equipment. • Discuss good laboratory procedures such as cleanliness and proper documentation. • Assign the Go Public Lab Manual

<ul style="list-style-type: none"> • Have the students individually outline their procedure for making ethanol. Remind them that they will perform the lab in three steps; starch conversion, sugar fermentation, and ethanol purification.
<ul style="list-style-type: none"> • Pair or team up the students and have them present their procedure to the class.
<ul style="list-style-type: none"> • Allow the students to perform any preparation for the conversion step. Ensure that the students document the steps in their lab notebooks.
<ul style="list-style-type: none"> • Assignment: Prepare their team's lab procedure for the starch conversion phase.
<p>LAB DAY TWO (After LECTURE DAY TWO)</p>
<ul style="list-style-type: none"> • Students will present their procedures as pairs/teams. As a class, discuss each team's procedure. Does each team include an assay to check for conversion? Allow each team to revise their procedure as necessary. This also allows the lab instructor to monitor the procedures for safety.
<ul style="list-style-type: none"> • Allow each team to complete their starch conversion. Note that the converted mash will be refrigerated until the next lab period.
<ul style="list-style-type: none"> • Assignment: Prepare their team's lab procedure for the fermentation phase.
<p>LAB DAY THREE (After LECTURE DAY FOUR)</p>
<ul style="list-style-type: none"> • Students will present their procedures as pairs/teams. As a class, discuss each team's procedure. Does each team include an assay to check for fermentation completion? Allow each team to revise their procedure as necessary. This also allows the lab instructor to monitor the procedures for safety.
<ul style="list-style-type: none"> • Allow each team to complete their fermentation. Note that the fermentation may require greater than a lab period to complete and the students may need lab access to complete the process. Also note that the broth will be refrigerated until the next lab period.
<ul style="list-style-type: none"> • Assignment: Prepare their team's lab procedure for the purification phase including an assay for ethanol purity.
<p>LAB DAY FOUR (After LECTURE DAY FIVE)</p>
<ul style="list-style-type: none"> • Students will present their procedures as pairs/teams. As a class, discuss each team's procedure. Does each team include an assay to check for ethanol purity? Allow each team to revise their procedure as necessary. This also allows the lab instructor to monitor the procedures for safety.
<ul style="list-style-type: none"> • Allow each team to complete their purification. Note that the purification may require greater than a lab period to complete and the students may need lab access to complete the process.
<ul style="list-style-type: none"> • Assignment: Calculate the conversion efficiency.

A Sample Module – Bioproduct Process Validation

The bioproduct process validation module is part of the Bioprocess Validation and Quality Engineering course. The unit begins with by posing the following challenge question to the

students: “Miss Wormwood fell and broke her hip and has to have surgery. Due to her age, cigarette smoking habit, being overweight, and having been bed-ridden since the fall that caused the break, she is at risk for a pulmonary embolism. Although Calvin may present the attitude that he does not care about the course material, he now sees a legitimate reason why what he has learned in his class is so important. The hospital plans to give Miss Wormwood a recombinant therapeutic protein to prevent a pulmonary embolism. Calvin wants to do his best to understand how the company that produces the protein (that also retained his father as a patent attorney) insures that the protein is not only effective but safe for her to take.” Students are immediately asked to generate their own ideas about how to solve this challenge question and are given the following prompts:

- (1) What are your initial ideas about how recombinant therapeutic proteins are produced?
- (2) What are the critical process parameters in each process step? If you don’t know, how would you determine what they are?
- (3) For each process step, how many and what types of measurements would you make to ensure that the process design is consistent?
- (4) How would you document this?
- (5) Who would need to approve your methods and why?

The instructor then guides the students to share their individual ideas with the class, and these initial ideas are recorded. Next, an expert interview that will guide the students to seeing a need for a process validation program is shown to the class. The instructor then leads a guided discussion using the student and expert ideas to guide the students to see the need for a clear understanding of (1) the protein production process, (2) the critical process parameters associated with each step of the process, and (3) the need to measure, validate and document each process step to insure reproducibility, safety and efficacy.

Students begin the Research and Revise stage of the module by reviewing and learning about the protein production process as necessary by reading a Scientific American article and playing a recombinant protein process game. Students then Review FDA CDER/CBER Q9 Quality Risk Management guidance for industry on the world wide web and give brief presentations on assigned Q9 sections to the class. The class then reviews the Pharmaceutical Inspection Co-operation Scheme (PICScheme) recommendation on Quality System Requirements and must engage in a Blackboard discussion group with their peers responding to the prompt, “What are the three most important points you learned in reading this portion of PICScheme and why?”

The instructor gives lectures on topics including regulatory basis for process validation, prospective process validation, and validation of biotechnology processes. Students take a quiz on biotechnology process validation. Students then review the Process Validation procedure VAL -106 template provided by Jesse Gillikin, President and CEO of cGMP Validation, LLC. During the overview of the template, the instructor discusses statistical evaluation that may be included in process validation activities to assess process data.

The instructor then proceeds with lectures on statistics covering topics such as prediction, tolerance and confidence intervals and ANOVA using process validation examples such as uniformity and dissolution testing. Students complete a related homework assignment. After

completing reading assignments on advanced statistical techniques for biotechnology, students submit outlines and descriptions of techniques discussed in the articles and their importance. As another formative assessment and a Test Your Mettle activity, the students are given the following assignment; "You lead Marketing Designers in the marketing department of a large biotechnology company. You have been asked to research, develop and design a poster about the production, quality and safety of a bioproduct. This poster will be used to market a planned new product at health fairs around the country, and thus should be something that Miss Wormwood would understand, but uses and defines terms from this course."

Finally, as the Go Public assessment, the students develop a Process Validation Protocol for the BIOE 4010 Ethanol laboratory (for which a laboratory procedure is prepared), using the process validation procedure VAL -106 as a guide.

The administering of the material in the Bioproduct Process Validation module takes place over fourteen 50-minute class periods. Table 3 provides a summary of the material covered and assignments in each of the lecture and laboratory sessions.

Table 3: Bioproduct Process Validation module class periods summarizing the material covered and assignments by day.

DAY ONE
<ul style="list-style-type: none"> • Introduce the challenge.
<ul style="list-style-type: none"> • Have the students independently work in their journals to answer the Generate Ideas questions. If possible, have journal responses submitted electronically so that all entries can easily be pulled into one document.
<ul style="list-style-type: none"> • As a class, review all journal entries.
<ul style="list-style-type: none"> • On the board, record the needed knowledge areas that students identified. Also record any specific ideas that were generated.
<ul style="list-style-type: none"> • Read multiple perspective provided as a class.
<ul style="list-style-type: none"> • Assignment to read articles on recombinant proteins.
DAY TWO
<ul style="list-style-type: none"> • Recombinant therapeutic protein process game
<ul style="list-style-type: none"> • Assignment to read FDA CDER/CBER Q9 Quality Risk Management guidance for industry and develop power point presentations on assigned section.
DAY THREE
<ul style="list-style-type: none"> • Students present five minute power point presentations on assigned Q9 sections. (Number of days required to accomplish this will vary dependent on class size. We allot one day in this schedule assuming a class size of ten or less)
<ul style="list-style-type: none"> • Assignment to read Pharmaceutical Inspection Co-operation Scheme recommendation on Quality System Requirements – documentation, change control and records. Students to

<p>discuss in Blackboard discussion board and respond to at least two of their classmates “What are the three most important points you learned in reading this portion of PICScheme and why?”</p>
<p>DAY FOUR</p>
<ul style="list-style-type: none"> • Lecture on the regulatory basis for process validation.
<ul style="list-style-type: none"> • Introduce “test your mettle” poster assignment. Provide the requirements of and guidelines for the poster. Assignment to be accomplished by teams of 2-3 students.
<p>DAY FIVE</p>
<ul style="list-style-type: none"> • Lecture on prospective process validation.
<ul style="list-style-type: none"> • Assignment to read article on process validation. Students to discuss in Blackboard discussion board and respond to at least two of their classmates “At what point in the development of a new biotechnology product should validation be considered and why?”
<p>DAY SIX</p>
<ul style="list-style-type: none"> • Lecture on validation of biotechnology processes.
<p>DAY SEVEN</p>
<ul style="list-style-type: none"> • Introduce “go public” assignment, providing ethanol production process lab manual (or if Module 4 is used, students are to utilize what they developed for the “go public” lab manual assignment). Review Process Validation procedure VAL -106 template provided by Jesse Gillikin, President and CEO of cGMP Validation, LLC: http://www.cgmpvalidation.com/index.php and data analysis that should be included in the procedure including any statistical evaluation.
<ul style="list-style-type: none"> • Quiz on biotechnology process validation (given in Blackboard).
<p>DAY EIGHT</p>
<ul style="list-style-type: none"> • Bioproduct health fair expo. Students present and review posters (10 minute presentations). Class votes on the product they would most likely want to use based on the poster and presentation.
<p>DAY NINE</p>
<ul style="list-style-type: none"> • Lecture on tolerance, prediction and confidence intervals.
<p>DAY TEN</p>
<ul style="list-style-type: none"> • Lecture on tolerance, prediction and confidence intervals.
<ul style="list-style-type: none"> • Homework assignment (statistical problem set) on tolerance, prediction and confidence intervals.

DAY ELEVEN
<ul style="list-style-type: none"> Lecture on ANOVA. Discuss the Analysis-of-Variance approach to understanding the variation of the dependent variable by observing its meaningful components. Overview of the strategy of experimental design and using ANOVA in that strategy.
DAY TWELVE
<ul style="list-style-type: none"> Lecture on use of ANOVA in MS Excel, understanding ANOVA output and what it means, including working in-class problems. Provide first reading assignment on advanced statistical techniques for biotechnology. Students to submit outline and description of techniques discussed in the article and their importance in MS Word document.
DAY THIRTEEN
<ul style="list-style-type: none"> Lecture on Statistical Methods for Uniformity & Dissolution Testing (that utilizes tolerance, prediction & confidence intervals as well as ANOVA) Provide second reading assignment on advanced statistical techniques for biotechnology. Students to submit outline and description of techniques discussed in the article and their importance in MS Word document.
DAY FOURTEEN
<ul style="list-style-type: none"> Lecture on Statistical Methods for Uniformity & Dissolution Testing (continued). Submit “go public”, discuss student work, and how Calvin may now better understand and be comfortable knowing that Miss Wormwood’s medicine

Module Integration

The Bioproduct Process Validation module in the Bioprocess Validation and Quality Engineering course is integrated with the Ethanol Production module in the Bioprocess Separation Engineering course. Students in the validation course are required to create a validation protocol of the ethanol production process they created in the Bioprocess Separations Engineering Course. However, although the integration is important to in providing the students context and motivation, the Bioproduct Process Validation module could be administered in a non-integrated mode by simply providing the students the ethanol production protocol.

Project Assessment Instruments

The effectiveness of the proposed modules will be assessed using three methods: *Concept Map Analysis, Individual Course Content Master Analysis, and a HPL Survey*. Data from the concept map and HPL Survey analyses are not ready at this time and will be presented in a separate publication at a later date.

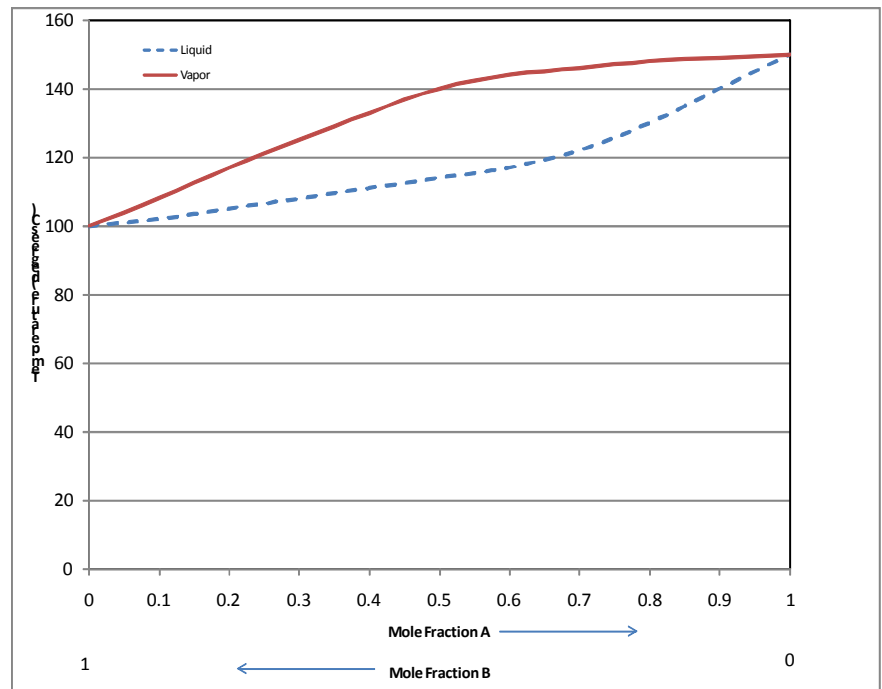
Individual Course Content Mastery Analysis

For each module that is created, a module-specific pre-test and post-test has been written. Each test includes questions that focus on basic terminology, problems and skills from the unit, and a near-transfer question. The near-transfer question is intended to measure how well students are able to take the concepts learned in the curriculum unit and apply them in a new setting. Pre-test and post-test scores are being compared using a paired t-test.

The Ethanol Production Module content mastery test includes the following problem, which is typically of the types of problems a student should be able to solve after this unit whether they have learned about the topic through a Legacy Cycle based unit or not:

4. An ideal mixture contains 20% of component A by mole fraction. The mixture's liquid-vapor phase diagram is shown to the right. What is the mole fraction of component A after one distillation stage?

5. For the mixture described above, what is the minimum number of distillation stages would be required to obtain greater than 90% purity of component A?



The near-transfer question for the ethanol production module is:

11. Dry particles of sugar tend to easily flow or pour, while dry particles of baking flour tend to clump and not easily flow or pour. How can you account for this difference in behavior?

The Bioproduct Process Validation module content mastery test includes the following question, which is typically of the types of facts a student should know after this unit whether they have learned about the topic through a Legacy Cycle based unit or not:

6. Quality Assurance review is required for which of the following documents? Circle all that apply.

- a. Validated cleanout batch sheets
- b. Non-Validated cleanout batch sheets undergoing a validation attempt
- c. Batch sheets for validated steps
- d. Ancillary batch sheets
- e. Relabeling and subdivision batch sheets for validated steps

Project Assessment Results

Tables 4 and 5 show the results of the pre- and post-test for the Ethanol Production and Bioproduct Process Validation modules.

Table 4. Ethanol Production Module Course Content Mastery Results. n=5; paired t-test

Pre-test Mean (max)	Post-test Mean (max)	P-value	Transfer Mean (max)
5.9(18)	12.7(18)	<0.01	1.8(4)

Table 5. Bioproduct Process Validation Module Course Content Mastery Results. NS = not significant; n=3; paired t-test

Pre-test Mean (max)	Post-test Mean (max)	P-value	Transfer Mean (max)
13.7(25)	14(25)	NS	NS

Project Assessment Analysis

The results of the ethanol production content mastery test indicate a significant improvement in student understanding of the basic concepts of ethanol production as well as how to solve basic problems in this area. The results of the near-transfer question indicate that students are able to take their new knowledge from this module and apply to a related, but still new, area. Though on average students did not fully master the concepts tested in the quizzes, it should be noted that the high demands of this study's rubrics for evaluating student performance artificially lower the reported achievement. Open ended questions had multiple aspects to a complete correct answer that often included small details most students either did not remember or think were necessary for their response. Although the challenging rubric would likely not be appropriate for use by an instructor as a standard for student mastery of the overall concepts of ethanol production, it was helpful in evaluating the effectiveness of the curriculum unit. Additionally, the percent mastery reported here on the pre-test, post-test, and near-transfer scores mirror those of other experimental groups using Legacy Cycle based curriculum units.^{8,23,24,26} Though a control classroom was not used in this instance, the literature has shown the students using these Legacy Cycle based modules out-perform their control classroom pairs significantly in both mastery of basic content and their ability to become adaptive experts, transferring their knowledge to new situations.

Unfortunately, the results of the Bioproduct Process Validation module during their first implementation do not accurately reflect the growth in knowledge of the students from pre- to

post-test. The faculty member responsible for this course has significant industrial experience, but is new to the academic setting and assessment development. The majority of the test questions were True-False format, too easily guessed at and solved correctly using basic logic, rather than accurately measuring knowledge gained in this module. These tests will be re-written before the next implementation of this course. Additionally, no near transfer question was given in the first implementation and this will be changed for the second implementation of this course.

Conclusions

Nine learning modules for a bioprocess engineering curriculum have been developed using the Legacy Cycle approach. Six of these modules have been successfully implemented into the classroom during the fall of 2008, while the remaining three modules are being implemented during the spring of 2009. Assessment of the six implemented modules is ongoing through the use of module pre- and post-test, concept maps, and a How People Learn student survey. Results of two modules' content mastery tests are reported here with the ethanol module's tests proving to be effective means of assessment with student results showing a significant improvement in content knowledge after completing the Ethanol Product Module. While the Bioproduct Process Validation module appears to be effective in the classroom, current content mastery tests do not indicate this and will require a revision to deter students from guessing based on logic.

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