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Teaching of Engineering Biotechnology

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Abstract

The goal of this project is to develop a pedagogically novel approach to teaching of modern discoveries of biotechnology at a level most students of engineering can comprehend and apply. Topics in molecular biology, biopharmaceutical manufacturing, drug delivery, and FDA regulations are combined cohesively in modular form. The primary focus is to broaden the development of an engineering student of Junior or Senior standing. One might even term our motive as developing a 'liberal engineering studies' emphasis. The pedagogical focus is on breadth rather than depth, and on cross-curricular education.

The talk will summarize our experience in teaching this course over the past eight years as a full 3-credit course and as a module in a multi-unit course over a three week period. Assessment includes student surveys and comparison of their assessment of this course with other traditional disciplinary courses.

Introduction

With the advent of significant fundamental advances in biosciences, increasing number of products, particularly therapeutic biologics are manufactured using biological agents such as cells and bacteria. New applications of genetic engineering in many industrial segments are reported at an increasing rate due to applications of DNA microarray technology. Consequently, a larger number of engineers of tomorrow would need to be familiar with the fundamental precepts of biosciences and genetic engineering applications.

The central idea in the Engineering Biotechnology course aimed at junior and senior students of engineering is to treat within a single course all significant scientific and engineering issues that encompass converting genes, the starting material, to a final product that is manufactured for the market place. In our view, it is important to tell the whole story in a single course with sufficient depth so that the relevancy and significance of the emerging area of biotechnology can be communicated effectively.

Traditionally the concepts covered in Engineering Biotechnology course would be developed over many courses, biochemistry, cell biology or cell physiology, genetic engineering, biotransport phenomena, bioprocess engineering and unit operations. Although the current course

does not cover the same material to the depth possible in the traditional courses, it does provide an engineering student with an important overview, and equip him with tools to pursue further study in biotechnology. The course builds upon the biological and engineering principles introduced in the freshman course called, Chemical and Biological Foundations of Engineering. Because the material is organized on a topic relevancy basis and the style of instruction is 'lateral' rather than 'pyramidal,' the biological principles and engineering science cane commingled to provide a more complete picture.

Rationale

To make a cohesive course illustrating the topic areas of genetic engineering, manufacturing and drug administration, we chose a thematic approach. Such an approach offers the advantage of integrating fairly diverse, yet connected, topic areas. We were determined from the start that the integrated course should avoid a survey-course flavor in its content. Among the various themes explored, we decided on the product theme, insulin. This theme has several advantages; including student familiarity and that it requires a biological manufacturing system. Other products considered were penicillin, granulocyte stimulating factor, interferon and others. Insulin is the first product of genetic engineering that was commercialized on a large scale and a fair amount of open literature is available on its manufacture. Although cloning strategies used for insulin is non-trivial, the processing steps that follow the biological step offered a good engineering balance.

The course was organized into four segments: insulin and genetic engineering, manufacture of insulin in bioreactors, delivery of insulin in the human body and biosensors. The course was team-taught by four instructors whose teaching and research background corresponds to the four topic areas. In the first edition of the course, the three non-lecturing instructors attended all the classes so that transition from topic to topic would be smoother. Additionally, availability of all four instructors in each class meeting enabled answering of certain student questions complete. The attending instructors provided important feedback with comments and suggestions to improve learning in the classroom.

Gateway Coalition

The Gateway Coalition (1), funded by the National Science Foundation, is intended to open new avenues for learning by altering engineering education from a focus on course content to the development of human resources and the broader experience in which individual curriculum components are connected and integrated. The scope of the program includes four major parts: curriculum structure; human potential development; instructional technology and methodology; quality assurance and evaluation measures. The current course in Engineering Biotechnology is being developed through Gateway Coalition.

The Gateway Engineering Education Coalition includes seven institutions, namely, Columbia University, Cooper Union, Drexel University, New Jersey Institute of Technology, Ohio State University, Polytechnic University and University of South Carolina.

Engineering Biotechnology and Drexel Curriculum

Over the past thirteen years, Drexel University had focused on major curriculum reform in undergraduate engineering education through the effort of E4 and Gateway programs (1-3). Initially, attention was directed to the freshman and sophomore years via the E4 program (1,2). This was not a simple repackaging of courses, but a major reconstruction with faculties from the

College of Engineering and the College of Arts and Sciences working together to develop an integrated lower division curriculum for all engineering students. In the upper division curriculum, all engineering students have the option of electing one or more from a choice of four interdisciplinary courses which address such areas as materials, biotechnology, environment, energy and communications. The Engineering Biotechnology course described in this paper is an integral part of the new Drexel Curricula broadening technical elective open to all engineering students.

First Offering of Engineering Biotechnology

The course was offered for the first time in a lecture format during winter quarter of 1993-94. This was team taught by four instructors belonging to three different departments - Raj Mutharasan (Chemical), Wayne Magee (Biosciences), Margaret Wheatley (Biomedical) and Young Lee (Chemical). Twenty-three students, most of who were seniors in chemical engineering, took the course for credit. Six other students, mostly graduate students, also attended the lectures. A second, slightly revised version was offered again during the spring quarter of 1994-95.A complete set of duplicates of material presented on overhead slides was provided to each student and quite extensive reference materials also were provided. In addition, standard reference works were placed on reserve in the library for student use.

The biological material in particular was quite new to most of the students and seemed to present the most difficulty. Homework problems and class discussion of how to go about gene manipulations were used to help overcome these problems. A short text on genetic engineering was used during the second offering of the course to provide students with an immediately available reference source. Instructors made use of assigned problem sets to give the students experience in the practical issues that arise in planning gene cloning, scale-up of fermentations, drug distribution in the body and biosensor operation. Thus, students were able to make the connection between such things as rate equations used in biological systems and those encountered previously in their engineering courses. Another useful approach was to briefly summarize previous class materials at the beginning of each session.

Problem sets were due weekly, and solutions were discussed in class so that each student could be helped to understand the concepts. The midterm exams and final were constructed in a similar way with discussion questions and numerical calculations. The students wrote weekly in a journal format about their likes, dislikes and any problems they were having with the material. The presence of all four instructors at most of the lectures helped catalyze discussions, and weekly faculty meetings helped in an analysis of how students understood each topic.

Course Content - 1993-94

The course was open to all senior engineering students as a three quarter-credit technical elective. A slightly enlarged version of this course was offered at junior level in 1996/97 when students of the new Drexel Curriculum needed cross-disciplinary electives. Until then, Engineering Biotechnology was offered as a senior elective because of the curricular constraints. A brief course outline is given in Table1.

The course was organized into four main sections: principles of genetic engineering, bioprocess engineering, drug delivery, and biosensor. A single instructor taught each section. The genetic engineering section introduced insulin physiology, cloning methods, as well as gene transfer,

expression, and regulation. Topics presented in the bioprocess engineering section were fundamental stoichiometry and thermodynamics of growth, design of high cell density reactors, separation and purification of insulin, manufacturing methods and GMP/FDA regulations. The drug delivery segment covered relevant protein properties, pharmacokinetics and dynamics, and insulin and other drug delivery methods. The biosensor module introduced fundamentals of sensor technology, the role of biomolecules, sensor design methods, and glucose sensing in medicine and bioprocesses.

Evaluation

The purpose of evaluation was to provide useful feedback on the course as well as to determine the impact the course was having on the students. We employed six strategies for evaluation: Each student was required to complete a short weekly journal, the teaching faculty and the teaching assistant met weekly to discuss the journal entries and general strategy, all faculty and the teaching assistant attended all lectures, lectures were videotaped, an end of term evaluation sheet was distributed to the students, and an external evaluator was employed.

Table 1 Course Content – 1993/94

- **Week 1:** Introduction, Insulin Physiology & Introduction to Cloning
- **Week 2:** Cloning, Identifying insulin gene & DNA amplification
- **Week 3:** Gene transfer, expression and regulation, Stoichiometry and thermodynamics of growth.
- **Week 4:** Design of High cell density reactors, Cell separation & disruption. Insulin Recovery
- **Week 5:** Good Manufacturing Practice & FDA Regulations
- **Week 6:** Protein properties relevant to drug delivery, Pharmacokinetics and dynamics: Insulin & others
- **Week 7:** Insulin delivery requirements - strategies, Controlled release mechanisms & methodology
- **Week 8:** Glucose sensing: application in insulin delivery, Detection methodology for *in vitro* applications.
- **Week 9:** Use of biomolecules for sensing.
- **Week 10:** Design of biosensors for *in vivo* applications, Review & Evaluation, Interview with Evaluator

Comments from weekly journals indicated that initially the students were somewhat uncomfortable with biological principles and the lack of a textbook. The students felt more comfortable with engineering problems. Many were complementary of the faculty effort, despite any difficulties with the course. Some, who expressed concern with the biology segment, later appreciated the value of fundamental science and its relevance to the topic. Many appreciated that the engineering principles that they have learned to date can be used in such "far-out fields" as biotechnology. Almost all said that the course contained more than they could digest. The end of the course review obtained similar results.

The external evaluator conducted post-course interviews with faculty and students as well as reviewed journals, the video and course materials and submitted a report analyzing various

factors of evaluation. From the student perspective she came to conclusions similar to ours, namely: biological terms were new and confusing, a sense of unease with the lack of a textbook, increased comfort level as course progressed, a supportive Teaching Assistant and outside tutoring were of great help. Student suggestions for improvements included: Use of a textbook, addition of a laboratory, reviews to tie topics together, learning through more problem solving, and most importantly reduction in the number of modules.

Course Content - 2001-03

During the late 90's, we saw the emergence of DNA microarrays as a discovery and molecular analytical tool for obtaining temporal gene expression profiles. This technology, central in both research and product development, was included as a topic within the course. Additionally, student feedback suggested increasing the biological content of the course. Hence, the genetic engineering section was expanded to 50% of the course, and a problem set that enabled application of concept was developed. Since manufacture and drug delivery were considered important areas that lie interface of biology and engineering, they were streamlined and re-oriented toward course goals. Given below is an approximate time allocated to each topic.

Table 2 Course Content – 2001/02

- **Week 1-4 :** Principles of Genetic Engineering – gene transfer, expression and regulation, cloning
- **Week 5-6:** Manufacture of Biologicals- Stoichiometry and thermodynamics of growth, bioreactors, GMP
- **Week 7-8:** Pharmacokinetics and drug Delivery- Controlled release mechanisms & methodology
- **Week 9-10:** DNA Microarray, Gene expression, drug discovery

As can be seen above, the fundamentals of genetic engineering have taken a greater prominence, and new topic of DNA microarray and the resulting application are included. Two classical papers from Science are discussed in class to illustrate the new applications. These are:

> *Exploring the Metabolic and Genetic Control of Gene Expression on a Genomic Scale.* Joseph L. DeRisi, Vishwanath R. Iyer, Patrick O. Brown, SCIENCE, 278, 680-686 (1997).
>
> *Molecular Classification of Cancer: Class Discovery and Class Prediction by Gene Expression Monitoring*. T. R. Golub, D. K. Slonim, P. Tamayo, C. Huard, M. Gaasenbeek, J. P. Mesirov, H. Coller, M. L. Loh, J. R. Downing, M. A. Caligiuri, C. D. Bloomfield, E. S. Lander, SCIENCE, 286, 531-537 (1999).

In the first article, DNA microarrays containing virtually every gene of *Saccharomyces cerevisiae* were used to investigate the temporal gene expression accompanying the metabolic shift from fermentation to respiration. The expression profiles, observed for genes with known metabolic functions, pointed to features of the metabolic reprogramming that occur during the diauxic shift, and the expression patterns of many previously uncharacterized genes provided clues to their possible functions. The article describes the measurement strategy clearly in an easily understandable form. It includes detailed gene expression profiles for discussion of the

relevant metabolic pathways. The content of the article was presented briefly in class, and the class was asked to read further and answer several descriptive questions for class discussion. The example illustrates the power of DNA microarrays and their potential in deciphering pathophysiology. Class discussion also includes manufacture of the microarrays, and level of engineering involved. Although details are left out, the students come away with the view that engineers have an important role to play in application of biotechnology.

The second paper deals with classification of cancer classes based on gene expression monitoring by DNA microarrays. Specific example treated is human acute leukemias where distinction between acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) is made without previous knowledge of these classes. The article illustrates the feasibility of cancer diagnosis and classification based on gene expression monitoring, and suggests a general strategy for discovering and predicting cancer classes for other types of cancer, independent of previous biological knowledge. Again, after a brief discussion in class, the students were asked to submit answers to several descriptive questions.

Introduction of these two scientific cases into the course has significantly broadened the scope of the course from its original version. In the context of Drexel, the purpose of course of the interdisciplinary courses is to develop a broad technical background. End-of-the-term surveys showed that 95% of the students polled rated this course to achieve the stated goal of broadening their background. In addition, there were several complementary comments stating that the course addressed current issues, offered an opportunity to be exposed to an area that they were not aware of. One shrewd student commented that this is an area in which he had not contemplated looking for a job, and the course opened him to a new opportunity.

Future Directions

Current effort is to keep the core area of genetic engineering principles, and expand application areas to new case studies similar to the two cases currently under study. That is newer version of the course will have five weeks of genetic engineering, and five weeks of genetic engineering applications.

References

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About the Author

RAJ MUTHARASAN, Frank A. Fletcher Professor of Chemical Engineering at Drexel University, is active both in education research and conventional engineering research. He has been an active member of the Gateway Coalition team since 1993, and has served as co-director of curriculum development team (upper curricula) and late as Governing Board member of Drexel Univesity. He is a fellow of American Institute of Chemical Engineers, and his area of research is biochemical engineering.