# Biotechnology and Bioprocessing Laboratory for Chemical Engineering and Bioengineering

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## Introduction

With the revolutions in cell and molecular biology of the last three decades and the impending transformations that genomics and proteomics will bring, there has been increasing interest in incorporating biology and particularly biotechnology into the engineering curriculum. Bioengineering has often been considered only biomedical engineering; however, as described by Beth Panitz in ASEE Prism [1], it can include a variety of disciplines including biotechnology and bioprocessing, agricultural engineering, and food engineering.

This paper describes a biotechnology and bioprocessing course that was developed as a required senior laboratory for bioengineering students at the University of Toledo. The course is structured as an integrated series of laboratory experiments that follow a "biotechnology product" from conception to completion. The students guide their "product" through the research and development phases, into production and purification, and finally into analysis and "packaging" of the final product. This course differs from many traditional biochemical engineering laboratory courses [2-5] in that it incorporates a broad range of topics from an industrial processing perspective. The incorporation of techniques of modern molecular biology is also unique. While this course was designed in the context of a bioengineering curriculum, it could also be incorporated as a senior elective in a chemical engineering curriculum. It was expected that the students taking this course have had basic courses in the life sciences including laboratories. In addition, most of the engineering coursework in the bioengineering curriculum has a biological orientation. If it is taught to students without any prior courses in the life sciences, additional material should be provided in the lecture component.

This course has several educational objectives. First, the students gain an overview of the biotechnology industry and learn to appreciate the integration of the processes used in the industry. Second, the students would learn basic microbiology, molecular biology, and biochemistry laboratory techniques within the context of the use of these techniques in industrial and laboratory settings. Finally, the students see the application of these processes from reaction to separation and purification. In addition to these specific objectives, there are several other goals of this course in the context of the ABET 2000 criteria [6].

- Students will learn laboratory techniques, to design and conduct experiments and to analyze and interpret data.
- Students will apply concepts learned in previous courses to the design and analysis of experimental problems.
- Students will prepare written and oral reports on laboratory results and findings.
- Students will work in groups in the laboratory.
- Students will gain an overview of the biotechnology industry, its role in society, and the role of bioengineers in the biotechnology industry.

This paper will discuss the laboratory experiments in detail, the written and oral presentations by the students and the outcomes of the laboratory. This laboratory course was funded, in part, by a grant from the National Science Foundation Directorate for Undergraduate Education Instrumentation and Laboratory Equipment Program. A list of equipment purchased for the laboratory with suppliers and costs and estimated supplies costs are provided in Tables II and III at the end of the document.

## Laboratory Experiments

This Biotechnology and Bioprocessing Laboratory is a fifteen-week course with one and a half hours of lecture and three hours of laboratory per week. This course is structured as an integrated series of laboratory experiments that follow a "biotechnology product" from conception to completion. The students guide their "product" through the research and development phases, into production and purification, and finally into analysis and "packaging" of the final product. The list of experiments is shown in Table I. A detailed laboratory and teaching assistant manual is available at http://www.eng.utoledo.edu/~ssharfst/bioe4500/LabHomePage.htm

**Table I: Laboratory Schedule**

| Week | Lecture | Laboratory | Report |
|---|---|---|---|
| 1 | Introduction, sterile technique, microplate reader spectrophotometer software demo | Pouring/streaking plates<br>Cell mass determination | |
| 2 | Bacterial and mammalian cell morphology | Microscopy<br>Wet and dry mounts<br>Trypan blue exclusion | |
| 3 | Plasmids, restriction enzymes, gel electrophoresis | Plasmid purification<br>Restriction digest<br>Agarose gel | Experiments 1 and 2 |
| 4 | Bacterial transformation | Electroporation<br>Calcium heat shock | |
| 5 | Polymerase Chain Reaction | Polymerase Chain Reaction | |
| 6 | Growth kinetics<br>Nutrient uptake | Batch growth<br>Nutrient uptake<br>Induction experiments and activity | Experiments 3, 4 and 5 |
| 7 | Fermentor | Fermentor run<br>Sampling, plasmid stability w/o antibiotics | |
| 8 | Protein purification | Ammonium sulfate precipitation, fraction assay, protein assay | Experiments 6 and 7 |
| 9 | Protein purification II | Column chromatography | |
| 10 | Analytical techniques | Electrophoresis | |
| 11 | Enzyme kinetics | Kinetics | Experiments 8,9 and 10 |
| 12 | Immobilization | Immobilization | |
| 13 | Immobilized Enzyme Kinetics | Immobilized enzyme kinetics | |
| 14 | Field Trip | | Experiments 11,12, and 13 |
| 15 | Oral Reports | Oral Reports | |

The "product" that was chosen for this course is β-galactosidase. β-Galactosidase is a microbial enzyme that is responsible for the cleavage of lactose into its constituent monosacharides, glucose and galactose. We chose β-galactosidase as our product for two reasons. First, it is a well-characterized enzyme with readily available substrates that yield colored reaction products. Second, it is frequently used as a reporter enzyme in cell and molecular biology studies, making the DNA sequence available in a wide variety of cloning vectors. Other proteins could certainly be used. Bio-Rad Laboratories (www.bio-rad.com) has developed several educational kits based upon the use of green fluorescent protein. One of the authors (Susan Sharfstein) is currently developing a scaled down version of the laboratory for a chemical engineering unit operations lab using a recombinant subtilisin. The primary criteria for selecting a product are that the DNA sequence be readily obtainable and that a straightforward assay for detecting the protein be available. The host cell line chosen for these experiments is *Escherichia coli. E. coli* is the most commonly used microbial organism for recombinant protein work. Its genetics are well

characterized (the entire genome has been sequenced); it is easy to grow, not pathogenic, and a vast number of plasmids are available for genetic manipulation. With minor alterations, the lab could be restructured to use bacillus, yeast, or mammalian cells as the host organism.

The students were placed into lab groups of two or three and worked together on most experiments although some of them (e.g. plasmid purification) were performed individually. The first two weeks of the course are devoted to basic microbiology, microscopy, and spectrophotometry techniques. Students become familiar with culture techniques and learn to distinguish different types of organisms under the microscope to determine if a culture is contaminated with foreign species. One of the favorite samples for the students and the instructor is to look at the mold that grows when a cup of coffee is left sitting around for several weeks. Rather than purchasing several standard spectrophotometers for the course, we selected to buy a microplate reader spectrophotometer (Molecular Dynamics). The microplate reader spectrophotometer can read samples in both cuvettes and 96-well plates. Unlike traditional microplate readers that typically can measure absorbance at a few selected wavelengths, this instrument covers the entire spectral range down into the UV. It can perform spectral scans on samples in multi-well plates as well as kinetic assays. Using this instrument has several advantages. First, the students can perform a large number of assays simultaneously. Second, it exposes the students to microplate readers and high-throughput technology that will be a mainstay of the genomics and proteomics assays in the biotechnology industry.

The next phase of the laboratory emphasizes molecular biology techniques. The students purify plasmids from *E. coli* and analyze them using agarose gel electrophoresis and restriction enzyme analysis. In a subsequent laboratory, the students transform these plasmids containing the genes for β-galactosidase and antibiotic resistance back into plasmid-free *E. coli* and select colonies based upon antibiotic resistance. The students evaluate the transformation efficiency of both chemical transformation and electroporation. Through these experiments the students learn how microorganisms are genetically manipulated for the production of recombinant products. The final molecular biology experiment uses polymerase chain reaction (PCR) as an alternative method for obtaining a gene. The students use primers directed at the sequence of β-galactosidase to amplify the gene for β-galactosidase and observe the results using agarose gel electrophoresis. These experiments familiarize the students with both the preparative aspects of molecular biology as well as the analytical techniques.

The next section of the course is the cell growth or production phase. Initially, the students use shake flasks to monitor cell growth, nutrient uptake and β-galactosidase production in batch culture. This allows them to become familiar with the experimental techniques and biochemical assays. The following week, the process is scaled-up to the fermentor. The fermentor can be used in either batch or continuous mode. In the laboratory handbook developed for this course, the fermentor is run in fed-batch mode, as that is the most common mode used in the biotechnology industry today.

In the purification phase of the laboratory, the students are exposed to two preparative techniques, ammonium sulfate precipitation and gel filtration chromatography, and an analytical

technique, sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). The students start with a cell lysate and perform the two preparative techniques sequentially, collecting samples from each step. The samples are subjected to protein and activity assays to determine which fractions contain the highest specific activity of β-galactosidase. Samples of the crude lysate and purified enzyme fractions are then analyzed by SDS-PAGE to visualize the protein and the successive purifications.

The final phase of the laboratory consists of characterization of the enzyme, immobilization on a chromatography resin, and characterization of the immobilized enzyme. The students use a Michaelis-Menten model of enzyme kinetics to calculate the $V_{max}$ and $K_m$ of the enzyme. The enzyme is then immobilized on beads, and the students calculate the $V_{max}$ and $K_m$ for the immobilized enzyme. The immobilized enzyme kinetics are analyzed at different flow rates through a column to separate the mass transfer effects from the intrinsic enzyme kinetics.

In the final week of the course, we took the students on a field trip to see biotechnology and bioprocessing in an industrial setting. Since the biotechnology industry in Northwest Ohio is limited, we selected a local microbrewery where the students could view large-scale sterilization and cleaning, fermentation, purification, and packaging. The students then were able to sample some of the finished product.

Written and Oral Reports

In keeping with the overall model of an industrial process, the students were asked to submit brief memoranda on each phase of the laboratory rather than traditional lab reports. They were instructed to structure the memoranda to a supervisor and to keep them in the context of the overall course objectives. A sample memo given to the students as a model is shown below. The final report was a more formal document, detailing the entire project and its results to help maintain the overall context of the laboratory. In addition, the students prepared an oral report similar to the type of presentation that would be given in an industrial setting. As part of our ABET accreditation process, we videotaped the student presentations.

## Memo

To: M. Boss
From: A. Worker
Date: 12/30/00
Re: Experimental Progress January 11-January 22, 1999

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Objectives: The objective of my experimental work during the past two weeks was to develop the basic microbiological techniques necessary to carry out the remainder of the project. Specifically, I wished to develop proper aseptic technique to carry out all future microbial manipulations, to obtain a calibration curve that will allow us to determine cell mass using optical density measurements, and to perform microscopic studies to identify and characterize different organisms. In the area of aseptic technique, I had three specific objectives, to aseptically pour solid media plates for microbial growth, to develop a streak method to obtain isolated colonies on solid media plates, and to use those streaked plates to identify colonies of different organisms (in this case yeast and bacteria.)

Methods and Materials:

*Aseptic technique:* Solid media plates were prepared using either Luria-Bertani (LB) broth or yeast-tryptone-dextrose (YTD). LB favors the growth of bacteria, while YTD with its higher concentration of dextrose is a superior substrate for yeast. I obtained pure and mixed cultures of Escherichia coli--W3110 (bacteria) and Saccaromyces cerevisiae (yeast). Using either the quadrant streak or the continuous streak method [1], I applied pure bacterial culture and the mixed yeast and bacterial culture to the LB plates and the pure yeast and mixed culture to the YTD plates. LB plates were incubated at 37° C, and YTD plates were incubated at 30° C since yeast growth is optimal at the lower temperature.

*Cell mass determination:* A culture of E. coli with an optical density of ~2 was serially diluted (1:1). 200 µl samples of the diluted culture were added to a 96 well microplate. The optical density at 600 nm was measured and a calibration curve was obtained to determine the linear range of the assay.

*Microscopy:* Live (wet mount) samples of E. coli, S. cerevisiae, coffee mold, and hybridoma cells were prepared by placing a drop of culture on a microscope slide and covering with a coverslip. Slides were observed on an Olympus inverted microscope under brightfield and phase contrast illumination. Cultures of adenocarcinoma cells were observed directly in the culture dish using phase contrast illumination. Dry mounts of stained streptococcus were also observed.

Results:

*Aseptic technique:* The E. coli formed off-white colonies, while the yeast formed white, somewhat smaller colonies. A distinct "yeasty" smell was present in the plates containing yeast. As shown in the attached figures (1-3), the quadrant streak method was superior in isolating colonies. In the case of the mixed cultures, the yeast did not grow on the LB plates at 37°C; however, bacterial growth was seen on the YTD plates incubated at 30°C. The yeast and bacterial colonies on the YTD plates could be distinguished on the basis of color. Unfortunately, the plates grown at 37°C in general did not yield good results since they were partially dried from incubating in the shaker rather than the incubator. I strongly recommend that an additional incubator be purchased.

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*Cell mass determination:* As can be seen from the attached Figure 4, the linear range for use of optical density to measure cell mass is between $A_{600} = 0$ and $A_{600} = 0.6$. This range gives an $R^2$ value of 0.996. Extending the range beyond 0.6 significantly decreases the linearity of the curve as seen in Figure 5.

*Microscopy*

A summary of the organisms observed is given in the table below. Sketches of the organisms are shown in the appendix.

| Organism | Objective | BF/PC* | Description |
|---|---|---|---|
| E. Coli | 20X | PC | E. Coli are motile rods approximately 3 µm long and 1µm in diameter. |
| S. Cerevisiae | | | |
| | | | |
| | | | |

*Brightfield/Phase Contrast

In general, it was very difficult to see unstained cells using brightfield microscopy. The bacteria were easily distinguished from the other organisms by their size and in the case of E. coli, motility. It was difficult to distinguish the effects of bleach on the trypan blue stained cells since the hybridoma cells were at very low density.

Future work: The next step on the project is to isolate the plasmid DNA that we will use to clone our gene. After we isolate the plasmid DNA, we will insert a linear sequence that codes for β-galactosidase into the plasmid and transform our new plasmid into E. coli DH5α. We will investigate two different transformation techniques, heat shock of calcium competent bacteria and electroporation.

[1] Becker, J.M. et al., Biotechnology: A Laboratory Course, Academic Press, 1996.

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## Outcome

The laboratory course was first taught in spring 1999 to a small group of students as a trial run and to prepare for ABET accreditation. Based upon that experience, our equipment needs were reevaluated and with funding provided by the Ohio Board of Regents, additional equipment was purchased. It also became readily apparent that a technician was critically needed to prepare reagents, order supplies, and maintain equipment for the laboratory.

On the whole, the course was well received, and the students felt they learned a lot. There were several areas that frustrated and concerned them. As this was a first run, some of the labs did not work as expected, particularly the fermentation and enzyme immobilization. The students were also unhappy that some of the laboratory exercises required more than the three hours allotted and that in several cases, the students had to return either later or the next day to view the results. As a result of these concerns and as a part of continuous improvement in the course, we made several modifications to the original experiments. The students are now informed at the beginning of the semester which experiments require additional time or a return visit to the lab to view results so that they are able to plan it into their schedules. To alleviate frustration with experimental difficulties, several minor modifications have been made to the laboratory protocols. For PCR amplification of the gene, the number of thermocycles was reduced to allow completion within the laboratory period. A new plasmid was chosen that results in increased expression of β-galactosidase in the cultures. To decrease the time required for purification, the

columns for gel filtration chromatography were replaced with ones of smaller volume. Finally, the resin used for enzyme immobilization was changed improve the efficiency and retention of the β-galactosidase. Some of those modifications were implemented in spring 2000; the remainder will be implemented this spring (2001).

In spring 2000, the laboratory was taught to a full class (~20 students). Here we found some modifications were necessary to optimize use of the microplate spectrophotometer with a large number of students. We had considered several options for the microscopy lab. Initially, we proposed to buy a class set of inexpensive microscopes. We then reconsidered and decided to use microscopes available in the biology department since we would only be using them once during the semester. Ultimately, we found that the lab worked best by bringing the students in a few at a time and using a teaching microscope (with dual viewing) to insure that the students actually identified the organisms and structures correctly under the microscope. Our plan is to buy a second teaching microscope so that the instructor and TA or technician can each work with a small group of students to expedite the process.

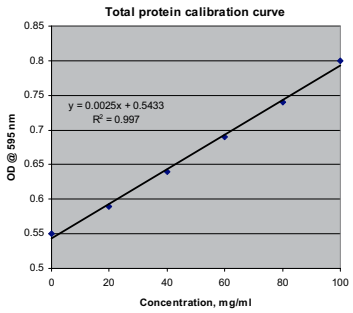
From an instructor's perspective, we found several things in the students' written and oral presentations that concerned us. Some students consistently submitted work with spelling and grammatical errors, despite the availability of spelling and grammar correction software. The students often had difficulty applying the material covered in the lecture to the laboratory. They also had difficulty with data analysis, leading us to question whether or not they were adequately prepared in the earlier courses in the curriculum. To help reinforce the students understanding of the material and aid in data analysis, we instituted quizzes between the laboratory period and the report due date to make sure they understood the concepts. A sample quiz is shown below. We noticed in the oral presentations, that even very good students made presentation errors such as using fonts that were too small to be seen on the screen and presenting slides that they did not understand. On the whole, however, the oral presentation quality was quite good, with the students demonstrating effective mastery of PowerPoint.

BIOE 4500: Bioengineering Laboratory Name_____
April 11, 2000
Quiz

Using the data given in the table and the graph below, please answer the following questions:

1. Fill in the empty columns in the table.
2. Using the sample with the highest β-galactosidase activity, what volume of that sample contains 20 mg total protein?

| Fraction | OD @ 595nm | Slope @ 420nm | Total protein | Specific β-gal activity |
|---|---|---|---|---|
| 1 | 0.72 | 221 | | |
| 2 | 0.81 | 249 | | |
| 3 | 0.67 | 162 | | |
| 4 | 0.62 | 100 | | |
| 5 | 0.59 | 20 | | |
| 6 | 0.58 | 5 | | |




## Appendix—Lists of Supplies and Equipment Purchased for the Laboratory

The list of equipment assumes that the department has basic equipment for biological work, including, an autoclave, water purification system, and a high speed centrifuge as well as other basic lab equipment such as balances, stir plates, refrigerators and freezers, and fume hoods. A biological safety cabinet or laminar flow hood and access to storage space in a –80 °C freezer are also useful. The cost of a fermentor is also not included since this was previously available in our research laboratories. A new fermentor costs approximately $30,000 although there are many other ways to conduct the fermentation experiment.

The supply lists are calculated for 20 students in the course. The list assumes basic biochemical supplies, such as salts, Tris etc. are available.

## Table II: List of Laboratory Equipment [a]

| Item | Supplier | Number | Unit cost | Total Cost |
|---|---|---|---|---|
| Micropipets (pipetmen) 10 µl, 20 µl, 200 µl, 1000 µl | Marsh Biomedical [b] | 80[c] | $123.50 | $9,880.00 |
| Multichannel pipetors | Marsh Biomedical | 3 | $390.00 | $1,170.00 |
| Microcentrifuge | Marsh Biomedical | 3 | $1,195.00 | $3,585.00 |
| Clinical Centrifuge (with rotors) | Fisher | 1 | $900.00 | $900.00 |
| Dual viewing compound microscope | Olympus | 1[d] | $9,792.64 | $9,792.64 |
| Vortex Mixers | Fisher | 2 | $201.00 | $402.00 |
| Airbath shaker | Fisher | 2 | $4,500.00 | $9,000.00 |
| Incubator | Fisher | 2 | $4,500.00 | $9,000.00 |
| Electrophoresis Equipment | Bio-Rad [e] | | | |
| Power Supplies (junior) | | 2 | $99.00 | $198.00 |
| Mini-protean 3 Module | | 2 | $300.00 | $600.00 |
| Wide mini subcell | | 1 | $200.00 | $200.00 |
| Gel Air Drying System [f] | | 1 | $556.00 | $556.00 |
| Microplate Reader [g] | Molecular Dynamics | 1 | $22,000.00 | $22,000.00 |
| Ultraviolet Transilluminator | Fisher | 1 | $1,200.00 | $1,200.00 |
| Gel Documentation System | Life Technologies | 1 | $2,500.00 | $2,500.00 |
| Rugged Rotator | Fisher | 1 | $424.00 | $424.00 |
| Electroporation System | Gentronics | 1 | $1,600.00 | $1,600.00 |
| Pumps | Cole Parmer | | | |
| Variable Speed Drive | | 10 | $283.50 | $2,835.00 |
| Pump-head | | 10 | $117.00 | $1,170.00 |
| Bunsen Burners | Fisher | 10 | $20.00 | $200.00 |
| Pipet Aids | Fisher | 10 | $50.00 | $500.00 |
| **Total** | | | | **$77,712.64** |

[a] In general these prices reflect educational or large purchase discounts
[b] Marsh Biomedical Systems gave us specific discounts on these items, but similar discounts can be negotiated with other vendors
[c] 20 of each size
[d] As mentioned in the text, we are planning on purchasing a second microscope when funds become available
[e] Bio-Rad has a special program with educational pricing on equipment for instructional use
[f] Not essential, but nice to have
[g] Traditional spectrophotometers can be used instead. Multichannel pipetors are unnecessary with traditional spectrophotometers.

**Table III: Supplies costs for one semester laboratory with 20 students**

| Item | quantity (per student or group ) | purchasing unit | unit cost | units needed | total cost |
|---|---|---|---|---|---|
| disposable inoculating loops | 1 pack of 10 | 1 case of 250 loops | $45.51 | 1 | $45.51 |
| Luria Bertani broth | to make 8 plates | 2 kg | $113.95 | 1 | $113.95 |
| YPD broth | to make 3 plates | 500 g | $42.70 | 1 | $42.70 |
| petri dishes | 11 | case of 500 | $92.25 | 1 | $92.25 |
| agar | to make 11 plates | 500 g | $83.20 | 2 | $166.40 |
| disposable test tubes | 5 | case of 1000 | $49.92 | 1 | $49.92 |
| microplates | 1 | case of 100 | $41.00 | 1 | $41.00 |
| pipet tips | 1 box each size | 10 racks of 100 | $25.95 | 3 | $77.85 |
| microscope slides | 5 | pack of 144 | $32.00 | 1 | $32.00 |
| cover slips | 5 | 1 oz. | $13.20 | 1 | $13.20 |
| pasteur pipettes | 5 | 1 box | $5.32 | 5 | $26.60 |
| Qiagen column | 1 | pack of 50 | $55.00 | 1 | $55.00 |
| microcentrifuge tubes 1.7 ml | 2 | bag of 500 | $12.85 | 1 | $12.85 |
| microcentrifuge tubes 2.0 ml | 2 | bag of 1000 | $23.75 | 1 | $23.75 |
| Electroporation cuvettes | 1 | pkg of 50 | $140.00 | 1 | $140.00 |
| sterile culture tubes | 2 | 8 bags of 125 | $132.75 | 1 | $132.75 |
| 50 ml sterile tubes | 1 | case of 500 | $75.00 | 1 | $75.00 |
| sterile pipets | several | | | | |
| 1 ml | | box of 1000 | $104.00 | 1 | $104.00 |
| 5 ml | | box of 200 | $34.50 | 1 | $34.50 |
| 10 ml | | box of 200 | $35.50 | 1 | $35.50 |
| 25 ml | | box of 200 | $84.00 | 1 | $84.00 |
| 0.5 ml thin wall tubes | 1 | box of 1000 | $31.95 | 1 | $31.95 |
| PCR reagent kit | 1/class | each | $95.00 | 1 | $95.00 |
| IPTG | 10 g/class | 10 g | $112.00 | 1 | $112.00 |
| ONPG | 5g/class | 5 g | $48.85 | 1 | $48.85 |
| glucose assay reagent | 1 kit/class | 1 kit (400 assays) | $105.00 | 1 | $105.00 |
| X-gal | 250 mg/class | 250 mg | $36.00 | 1 | $36.00 |
| Ammonium sulfate | | 1 kg | $12.32 | 1 | $12.32 |
| HiTrap desalting column | 1 | 5/pk | $102.00 | 4 | $408.00 |
| precast polyacrylamide gels | 1 per 3 students | each | $8.50 | 7 | $59.50 |
| chromatography package | | 1 kit for 16 students | $169.48 | 2 | $338.96 |
| β-galactosidase | 5000 units/class | | $85.85 | 1 | $85.85 |
| Oxirane activated beads | 1 ml | 10 g | $64.80 | 2 | $129.60 |
| econopac columns | 1 | pack of 50 | $90.00 | 1 | $90.00 |
| gloves | 1 case of each size | 1 case | $60.00 | 3 | $180.00 |
| other chemicals, shipping, etc. | | | | | $500.00 |
| **Total** | | | | | **$3,631.76** |

While the supplies costs are significant, they would not scale linearly with a larger student population, and they are not significantly higher than other chemical engineering laboratories. For example, the unit operations laboratory at UC Berkeley costs approximately $8900 a semester for 60 students, and a five-week laboratory in polymer science costs approximately $2400 for 65 students[7].

Acknowledgements

Funds for the purchase of laboratory equipment were provided by the National Science Foundation (DUE-9750627), the Ohio Board of Regents, and the University of Toledo. Susan Sharfstein received a summer faculty fellowship from the Center for Teaching Excellence at the University of Toledo to develop experiments and laboratory manuals for this course. We would like to thank Karthikeyan Jayavelu and Tammy Phares for technical assistance in course and laboratory development and Jonathan Schisler, John Fisher, Rui Zhou, and Jackie Chu for serving as teaching assistants for this course.

Bibliography

1. Panitz, B., *Bioengineering: a growing new discipline.* ASEE Prism, 1996. **6**: p. 22-8.
2. Lee, W.E., *A Course in Immobilized Enzyme and Cell Technology.* Chemical Engineering Education, 1991. **25**: p. 82-86.
3. Hooker, B.S., *A Project-Oriented Approach to an Undergraduate Biochemical Engineering Laboratory.* Chemical Engineering Education, 1994. **28**: p. 98-102.
4. Ng, T.K.-L., J.F. Gonzalez, and W.-S. Hu, *A course in Biochemical Engineering.* Chemical Engineering Education, 1988. **22**: p. 202-207.
5. Robinson-Piergiovanni, P.S., L.J. Crane, and D. Nau, R., *Solid Phase Extraction Columns: A tool for Teaching Biochromatography.* Chemical Engineering Education, 1993. **27**: p. 34-37.
6. *http://www.abet.org/eac/EAC_99-00_Criteria.htm,*.
7. Department of Chemical Engineering, UC Berkeley, personal communication

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