
AC 2011-2286: A STEP TOWARDS THE DEVELOPMENT OF A WET CELLULAR BIOENGINEERING LABORATORY

Josue Orellana, Washington State University

Josue Orellana is currently in his Junior year of his B.S. in Electrical Engineering with emphasis in Bio-engineering and Microelectronics at WSU. He has been involved in undergraduate research for two years. His research interests also include Bioelectronics and Sensing Technologies. josue.orellana@email.wsu.edu

Fabiola Quiroa, Washington State University

Fabiola Quiroa obtained an Associates of Science Degree from North Seattle Community College in 2009. She is currently in her Junior year in Chemical Engineering at WSU and is expected to graduate in 2012. She is a member of the Aerospace Club at WSU and has worked as an undergraduate research assistant at Dr. Abu-Lail's laboratory for one year. fabiola.quiroa@email.wsu.edu

Ala' Ibrahim Abu-Lail

Ala ' Abu-Lail is a Junior Biomedical Engineering Student at Jordan University of Science and Technology, Irbid , Jordan . She joined WSU past summer for an internship and worked on this project along with other students. 011-962-799-567596, alo2a13789@hotmail.com

Nehal I. Abu-lail, Washington State University

Nehal Abu-Lail is an assistant professor of Chemical Engineering and Bioengineering at Washington State University . She did her M.S. at Jordan University of Science and Technology, Irbid Jordan , her Ph.D. at Worcester Polytechnic Institute, Worcester MA . She also worked as a post doctoral researcher at Duke University, Durham NC. She has been at WSU since 2006. Her research is focused mainly on cellular interactions with surfaces. She has always been interested in integrating her research expertise in the classroom as described in this manuscript. nehal@wsu.edu (509) 335-4961

**A Step towards the Development of a Wet Cellular
Bioengineering Laboratory**

Introduction

Since the past decade, the awareness of utilizing engineering tools and principles to address problems in cellular biology has been continuously increasing¹. Motivated by such demands, a cellular engineering sub-discipline has been incorporated in the curricula of many biomedical engineering departments nation-wide¹. According to recommendations of the engineering education summit sponsored by the Whitaker foundation in 2005, competent cellular engineers should have a strong foundational knowledge in mathematics, possess appropriate engineering skills, be well trained in cell biology and chemistry and have been exposed to many interdisciplinary topics. With such skills and backgrounds, cellular engineers are expected to contribute largely to solving many real life problems that range from medical ones such as designing better therapeutics and improving the field of tissue engineering to sustainable problems such as harnessing clean energy and bioremediation of contaminated sites¹.

Despite the need to equip cellular engineers with the appropriate hands-on training to solve practical problems² and the fact that the accreditation board for engineering and technology (ABET) states that biomedical engineering students should be able to “make measurements on and interpret data from living systems, addressing the problems associated with the interactions between living and non-living materials and systems”³, cellular engineering courses are still largely theoretical⁴⁻⁶. Even in curricula where labs are offered, the approach used is generally a traditional one where students perform prescribed experiments with little or no critical reasoning of what they are performing⁷. Therefore, students should be provided with integrative lab experiences that promote inquiry relevance using hands on experiences and team oriented approaches. Such labs satisfy the vision of the National Science Foundation to improve engineering education⁸.

Although very important to biomedical engineers, implementing a cellular engineering laboratory in the biomedical curriculum is challenging for the following three main reasons. First, handling cells require students’ prior training on issues associated with safety, sterilization and contamination⁵. Second, experimental protocols dependent on using cells generally require longer periods of time compared to the commonly used three-hours time periods for traditional labs⁹. Third, the cost of the equipment needed to run the experiments is generally an impediment to have duplicates or triplicates that would allow for multiple experiments to be carried out by the students at the same time in a teaching laboratory.

Current examples on cellular engineering laboratories are largely found in the chemical engineering curricula where educators in that field have paid special attention to prepare their students to take leading roles in the biotech and bioprocessing industries¹⁰⁻¹². However, most of these labs are biochemical in nature and consists only of several modules⁵. Examples includes modules focused on fermentation technologies¹⁰, design of sterilizers¹⁰ and experimental investigation of a hydrolytic enzyme¹².

In an attempt to offer interdisciplinary, comprehensive and problem-based cellular engineering laboratories that target bioengineering students; four hands-on, learners-centered modules that cross the borders of chemical, biological and physical disciplines were incorporated in the “Introduction to Cellular Engineering” class within the bioengineering

curriculum at Washington State University (WSU). The four implemented modules were: (1) an experiment that introduces students to changes in the kinetics of bacterial growth in response to chemical, physical or biological stresses; (2) an experiment that allows students to observe and quantify transport of solutes and water across cellular membranes; (3) an experiment that allows students to measure and model the transport of bacteria in saturated porous media; and (4) finally an experiment that allows students to quantify enzyme kinetics of glucose oxidation.

Implementation of the hands-on modules in the “Introduction to Cellular Engineering” course

Considering the budget constrains most US universities had to deal with over the past few years, we have chosen to implement the four hands-on modules within the structure of the Introduction to Cellular Bioengineering (BE 350) course and not as a stand-alone laboratory course. The BE350 course is a three-credit hours’ core bioengineering graduate and an undergraduate course that meets three times a week and follows a lecture-based standard format. Each lecture extends for an hour. The course is offered as well as an elective to other engineering disciplines including chemical, mechanical and electrical engineering. This course is unique because of the breadth of the topics covered in the context of a single dynamic system, the cell, making the course highly interdisciplinary. Once the subject of a module was covered in the lectures, the module designed to reinforce that particular subject and its concepts gets carried out by the students in the lab. Because, our current curriculum does not have a wet-cellular engineering undergraduate laboratory, the experimental modules were carried out in the instructor’s research laboratory. This was possible due to the small class size which consisted of 11 undergraduate students and 2 graduate ones. Students were responsible for partial design of the modules, running the modules and analyzing and interpreting the data collected during the experiment.

To perform each module of interest, the students were divided into groups. The size of each group was limited to three students at the most to ensure that each student in the group participated in carrying out the module. Students also rotated between teams. This way, each student was able to work with most of his/her classmates during the semester. The two graduate students were assigned to different groups. Having both graduate and undergraduate students in the same course can be beneficial. Graduate students were able to assist undergraduates in dealing with sophisticated protocols or in teaching them how to use some of the typical lab equipment. Because the modules were carried out in a research laboratory that does not have duplicates of certain needed equipment, each group carried the experimental module at an allocated time during the week. The time spent performing each module varied from group to group based on the current knowledge and research experiences of the students in the team. When all teams finished running a certain module, the teams were required to share the data and the experimental results with other teams. Students were required to analyze, model and discuss results collected by all teams. While running the module, a teaching assistant (TA) was always present in the lab. The role of the TA was to oversee the experiment, prepare necessary bacterial cultures to reduce procedural time, sterilize glass and answer questions with regards to safety. The TA was specifically instructed not to answer questions with respect to experimental design. The instructor was also available to guide the students as needed.

Modules were generally run after the students were exposed to the necessary background needed to understand the module and to play with its design in the course lectures. Students were

given a short manual describing the experimental setup as well as basic equipment operational instructions. As will be detailed later, the students were allowed to choose the input variables to test in the module and after collecting and sharing the data with other groups, they were required to represent and discuss their findings using comprehensive mathematical, visual and statistical tools.

Design of the hands-on active-learning modules

The four hands-on modules were designed to be student-centered as well as to take advantage of active and visual learning styles¹³. Applying these modules in the course is an effective way to establish high-quality learning environments that promote students' engagement and satisfy Chickering and Gamson's seven principles of good practice in educating students and other teaching strategies known to promote learning¹⁴⁻¹⁶. It is also well known in the learning theory that people learn better by doing, not just by watching and listening⁷. Therefore, engineering laboratory modules should follow a problem-based learning (PBL) approach. PBL approach is expected to provide students with life-long learning and team skills¹². In addition, lab modular experiences should promote collaborative and team work where students learn from each other as well as teach each other¹⁷.

Therefore, the above four modules were designed to be flexible¹⁸. For example, in the module on measuring and modeling bacterial transport through saturated porous media, students were allowed to vary the type and size of the porous media, salinity and flow rate of the bacterial solution, and they can run the column in upward or downward modes of flow. The flexibility of the modules allows students to: 1) think critically about how to investigate the effect of a specific parameter on a specified cell behavior, 2) troubleshoot problems as they arise during the experiments using an inquiry-based approach, 3) use a cooperative-learning (team-based) approach to communicate findings verbally and in written formats and 4) elevate analytical, critical thinking and problem solving skills through mathematical modeling and discussion of real experimental data collected by all groups.

The four modules were designed to: 1) reinforce and illustrate basic principles in the minds of students with regards to cellular functions and operations through hands-on experiences; 2) provide students with necessary skills needed to work with cells safely, 3) familiarize students with available equipment in cellular engineering laboratories as well as familiarize them with common measuring and calibration techniques¹⁹, improve students' troubleshooting skills; 4) elevate students design skills; 5) train students in technical report writing; 6) improve students' critical thinking skills *via* analysis of the design and assumptions of the experimental module, theoretical modeling of their results and statistical investigations of the significance of their results; 7) expose students to how engineering models can be used to address real-world problems; 8) prepare students for careers that cross disciplinary boundaries; 9) help students in developing teamwork abilities; and 10) promote students interests in science and engineering³.

Individual experimental active-learning hands-on modules

All four modules were composed of two parts. The first part was experimental and the second part was theoretical focused mainly on mathematical modeling of experimental data collected in part 1 of the module. A brief description of these four modules is given below.

Module 1: Diffusion across cellular membrane

This module aimed at introducing students to the concept of passive transport across a cellular membrane. Raw and hard-boiled eggs were used to represent cells with different membrane characteristics. This module was performed after students were exposed in class to Fick's law of diffusion, tonicity of the solutions inside and outside the cell, the concept of osmolarity and selectivity and transport mechanisms across cell membranes²⁰. Each group of students was asked to quantify the diffusion of different solutions across the membranes of six raw and boiled eggs. Students were allowed to choose their solutions based on parameters such as ionic strength. Prior to running the module, the students were asked to devise ways to: 1) remove egg outer shell; 2) observe osmosis in action; 3) test whether the diffusion process is reversible across the cell membrane; 4) test whether larger molecules can cross the cell membrane and 5) test if equilibrium can be achieved across the cell membrane. The diffusion of the solutions across the cell membrane was followed using a gravimetric analysis by measuring the difference in the weight of the eggs within a time interval specified by the students.

Students were given an assignment asking them to generate hypotheses that predict the direction of transport of the used solutions through the eggs' membranes. Students were also asked to provide reasoning behind their hypotheses and to use experimental data to validate or reject their hypotheses. In the assignment as well, higher-level questions that elevate the critical thinking skills of the students were given. For example,

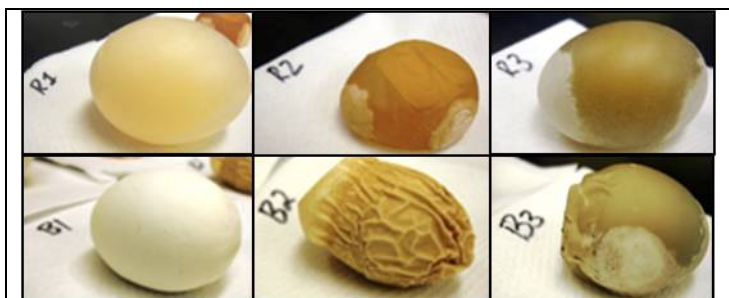


Figure 1: Raw (R) and hardboiled (B) eggs after 24 hours of incubation in water (1), syrup (2) and energy drink (3).

students were asked to explain why boiled and raw eggs behaved differently in transporting solutions (Figure 1)? Answers should have reflected on the concepts of permeability and protein denaturation at elevated temperatures. In their assignment too, students were asked to quantify the diffusion across the cellular membrane as well as the ionic strength concentration of the inner environment of the egg using Fick's law. Based on their computational results, students were asked to classify the solutions used as hypo-, hyper- or iso- tonic solutions. Finally, the data collected by all student teams were shared and statistically compared. Statistical analysis included quantifying mean, standard deviation, standard error of mean, and percentage error of triplicate or more measurements of diffusion of certain solvents and solutes across an egg membrane. Students were asked to discuss potential error sources in their measurements. In summary, although this module was a very simple experiment to conduct, it allowed students to quantify and model the transport across a cellular membrane and enhanced their understanding of the process of passive diffusion.

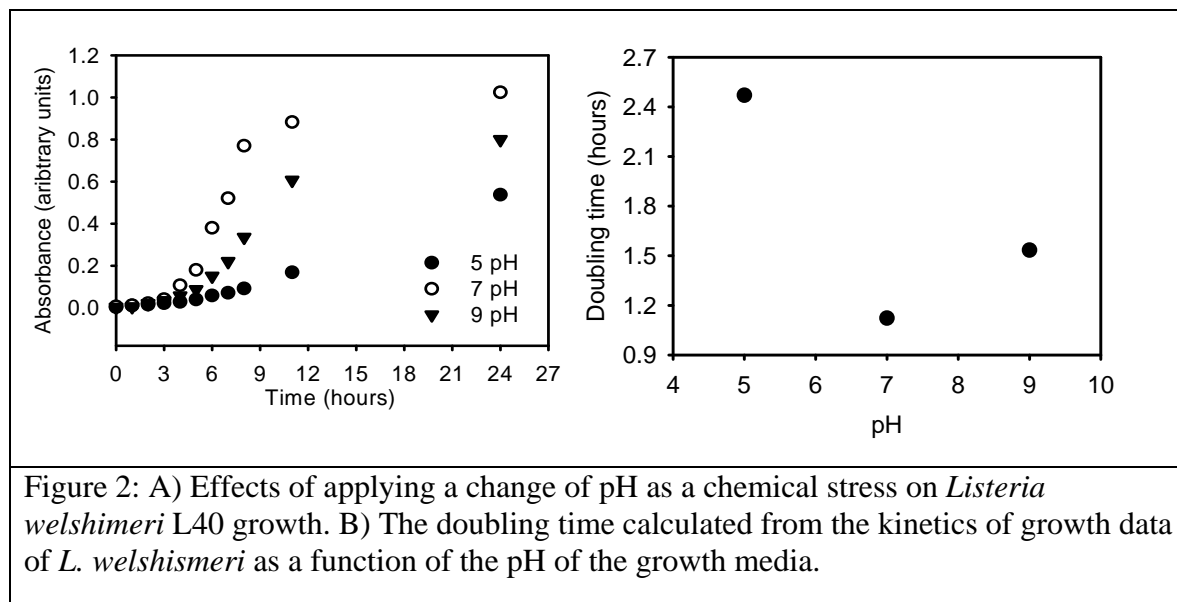
Module 2: Bacterial growth in batch bioreactors-adaptation to chemical, physical and biological stresses

This module was designed to: (1) train students on handling cells safely and appropriately, (2) allow students to quantify the kinetics of bacterial growth as a function of chemical and physical stresses, (3) expose students to the different phases of bacterial growth, and (4) allow students to apply theoretical models to the measured kinetics of bacterial growth. Prior to running the module, students in class were exposed to the phases of bacterial growth and to models used in predicting the kinetics of bacterial growth²¹. In addition to the material covered in class, students were given a manual with more detailed information about the classification of the bacteria used and protocols on how to prepare and grow bacteria in batch bioreactors. Students had no prior training in how to handle bacteria safely. The TA in the class demonstrated for the students how bacteria can be handled carefully. He also helped them in sterilizing glass and in preparing sterilized brain heart infusion broth (BHIB), the substrate used to grow the bacteria. The bacteria used in this experiment were *Listeria welshimeri* L40 which is a non-pathogenic Gram-positive, facultative anaerobic bacterium that is ubiquitous in nature. A biosafety level 1 bacterium was chosen for the safety of students.

Students were divided into six groups composed of two students in each for this particular module. Each group selected a stress factor to investigate its role on bacterial growth kinetics and adaptation strategies. The stresses applied were chemical, physical and biological. A chemical stress was introduced to the bacterial cells by changing the pH of the BHIB growth media. A physical stress was introduced to the bacterial cells by changing the ionic strength of the BHIB growth media and finally a biological stress was applied to the bacterial cells by means of induced starvation. Each group of students investigated three different levels of stress. For example, the pH of the growth media was changed between pH values of 5, 7 and 9 to bracket the normal conditions of bacterial growth. The ionic strength was changed by adding NaCl and the bacteria were starved by diluting the BHIB growth media using deionized water. Each stress factor was investigated by two groups. Each group also ran a control culture at the known standard conditions for this bacterium. The kinetics of growth for each reactor was followed every hour by reading the absorbance of the bacterial solution using a UV/Vis. spectrophotometer at 600 nm wavelength.

At the end of the experiment, data were shared among all groups. Students were asked to generate a growth curve for each stress condition applied by graphing the measured light absorbance versus time (Figure 2A). Students were given an assignment that asked them to highlight the different regimes of the growth phases of bacteria and to compare their periods for different stresses applied. Students were as well required to model their data to quantify the doubling time of the bacterial cells (Figure 2B). Students also were asked to run a statistical analysis to compare the findings of different groups with respect to an individual stress. Students were asked to interpret their results and discuss potential strategies employed by bacteria to adapt to stress. Students were asked to survey the literature to find relevant real-world applications that can be studied using the simple module they ran in the laboratory. Finally, students were asked to design future experiments based on their module to help solve potential real-world bacterial-related problems.

After running this module, the students were able to grow bacteria in batch cultures and to follow and quantify bacterial growth kinetics using spectrophotometric measurements. They also learned how to identify the growth phases of the bacteria. They were able to discuss how bacteria adapt to different type of stresses as well as to explore ways to apply their module to solve relevant real-world problems.



Module 3: Transport in saturated porous media

This project aimed at allowing students to: (1) quantify the effects of different factors on the transport of bacteria in saturated porous media and (2) quantify the strength of attachment between bacteria and glass beads or sand under flow conditions. Prior to running the module, students were exposed to the principles of one-dimensional colloidal transport in class. In the lecture, the article titled “Clarification of Clean-Bed Filtration Models by Logan, B. E. et. al”²² was discussed. To run the module, students were divided into groups of three students each. Each group was given time to get acquainted with the experimental setup. Students used that time to learn how to automate the fractionator as well as to learn how to connect the tubes and how to calibrate the pump. Students experienced troubleshooting skills quite a bit while running this module.

Students were allowed to design their module to investigate the effect of two variables on the transport of bacteria in saturated packed columns. The variables to investigate included the flow rate of bacterial solution fed to the column, the salinity of the bacterial solution, the concentration of the bacterial solution fed to the column, the diameter of the column, the height of the porous material packed in the column, the diameter of the glass beads (collectors), the type of the collector (sand versus glass) and whether the column should be run in upward or downward modes of flow. Once the group had decided on the parameters to investigate, they collected a break-through curve that quantifies the concentration of bacteria leaving the column (C) to that fed to the column (C_0) as a function of time (Figure 3). Bacterial solutions of the non-pathogenic *Listeria monocytogenes* ATCC 15313 were prepared in advance by the TA to all

groups to reduce experimental time. Bacterial concentrations were quantified using a UV/Vis. spectrophotometer at 600 nm wavelength at variable time intervals decided by the students. At the end of the experiment, students were required to clean the columns and detach the experimental setup to let other groups design their own experiments.

The assignment given to students asked them to devise a way to estimate the porosity in the column, to justify their choice of all variables used to run the module and to define sources of error in their measurements. Students were as well required to represent their results in clear figures. Students then were required to refer to the article discussed in class²² to quantify the collision efficiency of bacteria as well as the collectors' efficiency. Students were required to analyze data collected by all groups and to compare results statistically. Students were required to interpret the results obtained and discuss their implications on real-world applications such as transfer of pathogens in the subsurface. By the end of this experiment, students were able to model the transport of bacteria through saturated porous media as well as to investigate the role of important factors such as flow rates and collector types on the bacterial transport process.

Module 4: Enzyme kinetics of glucose oxidation

This module was focused on introducing students to enzyme kinetics of glucose oxidation. The experiment was performed after the subject of enzyme kinetics was introduced during class lectures. A readily available kit from Sigma-Aldrich Inc. (St. Louis, MO) was used for this experiment. However, students had a choice on the range of glucose (substrate) concentrations to investigate as well as on the concentrations of chemical reagents (other reactants and enzymes) to use.

Students were divided into groups of three. A student was responsible for mixing the reactants, another for measuring the products concentrations and the third one for recording the measurements. The reactions kinetics for different glucose substrate concentrations were monitored by following the concentration of one of the reaction products using a spectrophotometer at a wavelength of 340 nm (Figure 4).

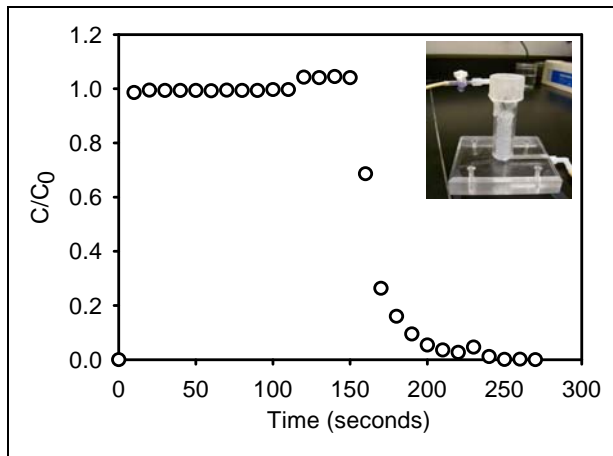


Figure 3: An example of a break-through curve collected for the transport of *L. monocytogenes* in a column packed with 3 mm glass beads (inset) running in downwards flow mode. A measurement was collected every 10 seconds.

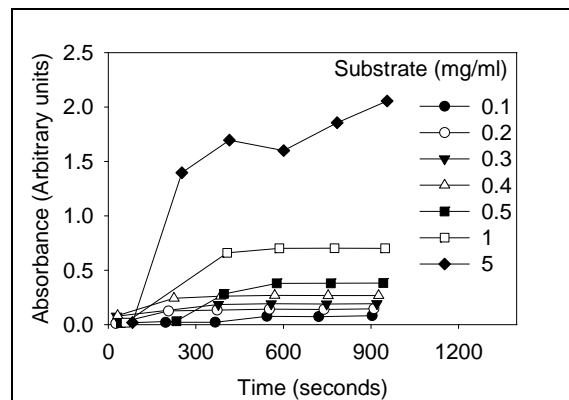


Figure 4: Reaction kinetics obtained using 7 different initial substrate concentrations and using the standard reagent concentrations defined for the reaction by the kit obtained from Sigma Aldrich, Inc. St. Louis, MO.

Students had a choice of the time intervals of measurements and for how long to follow the reaction.

At the end of the experiment, students shared the data obtained by all groups. Students were required to use all the data obtained to calculate the reaction rates of glucose oxidation. Students were required to use four different linearization schemes to quantify the Michaelis-Menten kinetics' parameters. These four methods were the line Weaver-Burk plot, Hanes-Woolf plot, Eadie-Hofstee plot and a graphical method from the commonly-known Michaelis-Menten type plot²¹. Students were required to judge the abilities of the different linearization schemes to predict the Michaelis-Menten kinetics' parameters using linear regressions and to discuss which model was best to fit the experimental data. Students were also required to discuss the assumptions of their modeling techniques such as the rapid equilibrium and the pertinent quasi steady-state assumptions. This module aimed largely at improving students abilities in mathematical modeling²³. This module allowed students to practice the quantification of enzyme kinetics *via* a hands-on real experiment. The data analysis of this module is expected to enrich the students' skills in statistics, mathematical modeling and sophisticated representation of experimental data. This experimental module is one of the most interdisciplinary modules as it makes practical use of principles from biology, chemical engineering, chemistry and mathematics.

Assessment and students feedback

The success of implementing the described four experimental modules in class was assessed based on the experiences of thirteen students. The students' population consisted of 2 graduate students and 11 undergraduate students divided as 7 seniors and 4 juniors. Three assessment measures were considered. Those were the overall assessment of the course, the grades of the technical reports written by students for the four modules and a voluntary in-class survey conducted after all modules were performed.

The overall student impression of the course was extremely favorable. The end of the semester survey that is usually ran by the college of engineering yielded a 4.67/5.0 rating for the course. 64% of the students completed the end of semester course survey. Students enjoyed the flexibility of the hands-on modules and commented that the modules were very helpful in reinforcing specific concepts in their minds. The grading of the technical reports was performed according to a rubric. This rubric was shared with the students prior to report submission. Clear expectations on what the report should include were as well given to the students. The reports were graded for technical accuracy as well as for presentation quality⁷. For example, students were graded based on how accurately they performed the necessary calculations and statistics as well as to how they discussed their findings. Students were graded also based on the quality and clarity of the Figures, the quality of the writing and the appearance of the whole report. Although the submitted technical reports following the modules were group efforts, assignments were given to students in class to test how well they understood a certain concept. These conceptual assignments were graded individually. Such grading system was designed to assure both positive interdependence and individual accountability for the team performance⁷.

Feedback was also requested from students in the Fall 2010 course, in the form of a voluntary in-class survey conducted after all modules were performed. 12 out of the 13 students enrolled in class answered the survey. The survey given to students and its results are attached in appendix A. In general, students agreed that the lab was beneficial in reinforcing some of the concepts discussed in the lecture. Most students as well agreed that working in teams helped them in running the experiment better, helped them to learn from each other and to have better communication skills. Criticism of the modules was mainly due to time constraints. The modules were implemented in a course that is only three credit hours. Finding time to run the modules, which sometimes lasted for more than a single day was an issue to most students. When asked if an extra credit hour should be added to the course to develop a stands-alone lab where such modules can be performed, all students answered yes with the exception of one who was uncertain. The majority of students indicated that they liked rotating in different teams throughout the semester. Finally, few students commented that they prefer modules that can be finished in a regular lab format and not last for several days.

Challenges associated with modules implementation

Several issues were associated with implementing the four hands-on modules in the cellular engineering course during the semester. First, the hands-on modules were implemented within a three credit-hour course that has no pre-allocated time to perform laboratory work. This meant an extra time commitment from participating students in the course as well as from the TA and instructor. Finding a common time between the team members was an issue sometimes. Having two of the modules ran for more than a single day was another issue. To rectify the time issues associated with implementing the modules in class, we have two possible solutions. First, to offer the modules as an open ended project associated with the course. Students would have to work on one particular hands-on module of their choice for the whole semester. The student would then design the module so they can test the effects of different input variables on a desired output variable. The project would count for 25% of the course grade. Students would be given access to work on the project during flexible times. The second option is to add a fourth credit to the course to perform the modules. If this option was granted, two additional modules will be added to the current four existing modules. The first one would be an indentation-force experiment to determine the elastic module of a material of interest and the second one would be to investigate bacterial biofilms using optical and fluorescence microscopes. Another issue that we have faced was the lack of prior training of students on how to handle cells safely. We minimized the effects of this issue by having the two graduate students who have previous expertise in working with cells be on two different teams. Two undergraduates also had prior research expertise on working with cells. These two students were assigned to other two teams too. The TA was responsible for overseeing the safety of the students while they were performing the experiments. In addition, the microbes chosen for the modules were biosafety level one. The last issue we faced was the lack of resources and the lack of a laboratory space to run these experiments. However, the small class size allowed us to be able to accommodate the students in the instructor's research laboratory. Each group also was allowed to run the module at a different time from the other groups. This way each group had a full access to the resources and equipment in the lab.

Conclusions

We have developed four hands-on cellular engineering modular lab experiences in the areas of enzyme kinetics, transport across cell membrane, transport in saturated porous media, and bacterial stress adaptations. The modules implemented were proven successful to reinforce specific cellular engineering concepts in the mind of students, improve students' abilities to work in teams, enhance students' skills in communication, critical thinking, mathematical modeling, statistical analysis of data, clear representation of results and troubleshooting. The modules implemented were also successful in exposing students to engineering thinking towards finding solutions to real world problems. We hope that our experience will stimulate the interests of other instructors to introduce such active-learning hands-on modules in their classrooms for both graduate and undergraduate students.

Future Plans

Our future plans include implementing these modules in the classroom again next year. One of the main concerns addressed by the students is the time commitment to such hands-on modules within a 3 credit-hours lecture course. Currently, the BE faculty are addressing the need to add a cellular bioengineering laboratory to the curriculum. If approved, these hands-on modules will be implemented in a three hours lab period that will be added to the 3 credit-hours lecture course. The course will be assigned 4 credit hours. If a lab was added to the curriculum, two additional hands-on modules will also be incorporated as discussed above. Finally, we plan to submit a NSF proposal to the "transforming undergraduate education in science, technology, engineering and mathematics (TUES)" program formally known as course, curriculum, and laboratory improvement (CCLI) program. The proposal will request money to develop the two additional modules described above as well as to purchase few in-expensive equipment needed to develop a wet Cellular Bioengineering laboratory at WSU.

Acknowledgements

We would like to thank the cellular bioengineering students for participating in this lab experience. Implementing the modules in the class was time demanding for a lecture-based course. We would like to thank the Ashley Ater-Kranov from the center of innovation and assessment at WSU who helped in designing and reviewing the in-class survey. We would like to thank Dr. James Petersen, the chair of the Gene and Linda Voiland School of Chemical Engineering and Bioengineering at WSU for providing the money needed to purchase supplies for the hands-on modules. We would like to thank Mr. Bong-Jae Park for helping in setting up the experiments and in the design of the modules. We would like to Thank Dr. Nurdan Beyenal for her help in developing the kinetics of glucose oxidation module. Finally, we would like to thank the National Science Foundation grant EEC-0823901 for partial support of Ala ' Abu-Lail and Josue Orellana.

Appendix A: In-class survey and its results

The survey that was given to students in class after all modules were carried out is given below. Each question in the survey and the answers received from the twelve students who participated are also included. Every number indicates a student response. In this way for example, number 5 below each question indicates the response received from a particular student designated as number 5.

Survey and responses

Dear Cellular Engineers

Thanks a lot for taking the time to answer this survey. We value your input. We will use your feedback to improve the course and the student experience next time we teach it.

Please answer the following using short statements

Have the hands-on experiences implemented in this class helped you understand new concepts introduced in class? If so, how/in what ways? If not, why not?

1. Yes. Hands on experiences definitely help me understand topics discussed in class. For example, diffusion was performed in lab using eggs to illustrate the diffusivity of various fluids
2. I feel that they were rather helpful. I was hoping that we could have done some genetic engineering. In my cell biology class, we used plasmids to make E. coli produce GFP. I thought that would be interesting
3. They have helped with some concepts such as membrane transfer, but other concepts were no clearer due to explanation of the concept being unclear
4. The labs felt rushed. The hands on experiments were fun and interesting but it felt like we did not really have the time to get a deep understanding of the core concepts. Finding blocks of time when the whole lab group could meet was difficult
5. Yes. It lets us learn by doing which sticks with me better
6. Yes. The hands on experiments helped. The labs are good ways to let us visualize the lectures
7. The hands on lab did help understand some new concepts. It mostly gave us something to visualize with the concept instead of just learning it from a paper
8. Yes. The labs helped reinforce the practical real-life techniques and approaches that incorporate the theory taught in class
9. Yes. Doing the experiment and seeing the results really helped solidify some of the concepts we learned in class. Especially the enzyme kinetics section
10. Yes. They help give a physical context for the material learned in class
11. Some of them did. The egg experiment was a little elementary but going through the calculations and explanations was helpful to reiterate the concepts
12. Yes. Seeing how concentrations are measured also manipulating data

Give one specific example of a concept that you learned in class that was reinforced or clarified using the hands-on experiments implemented?

1. Diffusion experiment using eggs as media

2. Sodium ion channels was one concept that was further reinforced
3. The transfer of ions across membrane due to permeability and concentrations
4. One concept I remember most was the packed fluid bed. It was very interesting to see the effect of the glass beads on the exiting concentrations of bacteria
5. Spectroscopy to measure various values
6. The enzyme lab allowed us to visualize the fast growing rate of the bacteria
7. The egg diffusion lab seemed to me to have the most visual learning to reinforce the concepts. It was a simple lab, but allowed us to actually see the diffusion take place. Other labs we just got data and used it
8. The enzyme lab helped reinforce the different techniques used to analyze kinetics such as the Michaelis-Menten. Analyzing real data helped reinforce these techniques
9. The enzyme kinetics lab. The analysis we had to do helped me to understand the calculations we have learned in class
10. Osmosis was well demonstrated with the "egg" experiment
11. Batch reactors and sticking coefficient lab
12. Bacterial attachment

How did working in groups influence your hands-on experience?

1. Working in groups made things easier in lab
2. I felt like it was easier to perform more complex tasks with a group
3. It allowed for labs that, although complex, permit a better understanding of the concept and partners are able to help in the comprehension of an unclear concept
4. Working in groups really helped during the experiments. It helped the experiment to go smoother and by writing the lab reports together. It was easier to understand the concepts of the experiments
5. It helps to work together and discuss
6. It is nice to have a second person looking over your work and discuss about the concepts
7. Working in groups seemed beneficial because if one person understood the concept more than the others then they could help the rest of the group with it
8. Working in groups presented the opportunity to practice teamwork and communication skills that are important and practical to other academic and life experiences
9. It was a good way to be able to share the work that needed to be accomplished
10. Working in groups helped when solving problems and generating ideas
11. It distributed the workload so it was less stressful to have a lab in a 3 credit class and it was much better to have two minds while doing the calculations and post lab questions
12. Better communication skills and delegation of tasks

Give one specific example of something you learned from the group that you probably would not have learned working alone.

1. As a group, I learned some new things on excel that I did not know before
2. No answer
3. How to apply the different growth models properly
4. I did not really learn any thing specific from the group itself. Working as a group just made the labs go more smoothly and helped solidify the concepts by talking about them

5. No answer
6. In terms of learning, I do not think there would be much difference. But I tend to make mistakes during the labs. My group members can point the mistakes out quickly
7. The first lab my partner was X (name was deleted for privacy). She knew how to work the spectrophotometer and I did not. She taught me the basic concepts. I would not have understood without her help or without a TA. Also, she helped in how to plot that lab.
8. On many instances, I learned how to adjust my ideas and approaches to writing a report that I would have done alone to a way that was suitable for a cooperative group effort
9. Learned that was going on with the transport mechanisms in the egg lab. For example, if water was moving in or out of the egg
10. I learned to take different approaches to the problems than I would have taken on my own
11. No specific example in mind but it was helpful to have multiple brains thinking/explaining our ideas to each other
12. How to better communicate with people

Suggest one change that should be done to improve these hands-on modules.

1. Make it an actual class
2. Something that would involve a microscope would be nice. Some of us are better visual learners
3. Keep the labs short enough that they can occur within pre-allotted time, either a single lab time or spaced properly to cover weeks but still only in class time
4. Having a set of lab time each week. Finding a time when the whole group could meet to do the lab was difficult
5. Make it a 4 credit class and do similar or more experiments
6. Teaching the classes in the laboratory would help. The students can really visualize the instruments and the procedures as they learn from the lecture
7. A big change would be to make the class 4 credits. With lecture and homework it seemed like a time overload for lab for a 3 credit course. People will be more excited and motivated for the lab if they are getting credit for it and it would give them heads up when signing up for the class
8. The labs that required multiple trips through out the week were difficult to manage at times
9. Either credit needs to be given or the actual lab work needs to be less and be more in class work and not all out of class work
10. They need to have all of the “bugs” worked out before the students start them
11. Schedule a lab time when we register for the class that is 4 hours and have two groups work in the first two hours and other two groups in the last two hours of the four hours block so there is not the entire class working in small lab at the same time
12. More time to develop lab approach

Answer the following by indicating True or False

1. The hands-on modules improved my learning of specific concepts introduced in class. T, T, T, A little, T, T, T, T, T, T, Neutral, T
2. Working in teams helped me run the experiment better. T, T, T, T, T, T, T, T, T, T, T, F
3. Working in teams helped me understand the data collected better. T, T, T, T, T, T, T, F, T, T, T, F

4. Working in different teams through out the semester was something I liked. T, T, T, T, T, T, F every time we changed groups we had to learn how everyone worked together as well as everyone's strengths and weakness in lab reports. This was time consuming and got annoying, T, T, F, T, T
5. Introducing an extra one credit hour lab for this course would be beneficial. T, very T, T, T, T for sure, T, T, T, T, may be depends on the length of the labs and quality of each lab and time required, very true, T

Bibliographic Information

1. Hammer, D.A. and R.E. Waugh, *Teaching Cellular Engineering*. Annals of Biomedical Engineering, 2006. **34**(2): p. 253-256.
2. Giuffrida, J.P. *Bridging biomedical basics with practical applications in BME laboratory education in The 26th Annual International Conference of the IEEE EMBS 2004*. San Francisco, CA.
3. Clase, K.L., P.W. Hein, and N.J. Pelaez, *Demand for interdisciplinary laboratories for physiology research by undergraduate students in biosciences and biomedical engineering*. Adv Physiol Educ 2008. **32**: p. 256-260.
4. Moraes, C., K. Wyss, E. Brisson, B. Keith, Y. Sun, and C.A. Simmons, *An undergraduate lab (on-a-chip): Probing single cell mechanics on a microfluidic platform*. Cellular and Molecular Bioengineering, 2010. **3**(3): p. 319-330.
5. Carson, S., J.R. Chisnell, and R.M. Kelly, *Integrating modern biology into the ChE biomolecular engineering concentration through a campus wide core laboratory education program* Chemical Engineering Education, 2009. **43**(4): p. 257-264.
6. Dymond, J.S., L.Z. Scheifele, S. Richardson, P. Lee, S. Chandrasegaran, J.S. Bader, and J.D. Boeke, *Teaching Synthetic Biology, Bioinformatics and Engineering to Undergraduates: The Interdisciplinary Build-a-Genome Course*. Genetics, 2009. **181**: p. 13-21.
7. Felder, R.M. and S.W. Peretti, *A learning theory-based approach to the undergraduate laboratory* Proceedings of the annual ASEE conference 1998. **Session 2413**
8. Meyers, C. and E. Ernst, *Restructuring Engineering Education: A Focus On Change*, in *Report on NSF workshop on engineering education*. 1995, Division of Engineering Education, Directorate for Education and Human Resources, National Science Foundation Wilmington, VA.
9. Hooker, B., *A project-oriented approach to an undergraduate biochemical engineering laboratory* Chemical Engineering Education, 1994. **28**(2): p. 98-102.
10. Ng, T.K.-L., J.F. Gonzalez, and W.-S. Hu, *A course in Biomedical Engineering*. Chemical Engineering Education, 1988. **22**(4): p. 202-207.
11. Komives, C., S. Rech, and M. McNeil, *Lab experiment on gene subcloning for chemical engineering students* Chemical Engineering Education, 2004. **38**(3): p. 212-221.
12. Glatz, C.E., R. Gonzalez, M.E. Huba, S.K. Mallapragada, B. Narasimhan, P.J. Reilly, K.P. Saunders, and J.V. Shanks, *Problem-based learning biotechnology courses in chemical engineering*. Biotechnol. Prog. , 2006. **22**: p. 173-178.
13. Bransford, J.D., A.L. Brown, and R.R. Cocking, *How people learn: brain, mind, experience, and school*. 2000, Washington, D.C: National Academic Press.
14. Chickering, A.W. and Z.F. Gamson, *Seven Principles for Good Practice*. AAHE Bulletin, 1987. **39**: p. 3-7.
15. *How people learn: brain, mind, experience, and school*, ed. J.D. Bransford, A.L. Brown, and R. Cocking. 2003, Washington, DC: National Academy Press.
16. Svinicki, M., *Learning and Motivation in the Postsecondary Classroom*. 2004, Bolton, MA: Anker Publishing Company, Inc. .
17. Biernacki, J.J. and J.B. Ayers, *Teaching cellular automation concepts through interdisciplinary collaborative learning* Chemical Engineering Education, 2000. **34**(4): p. 304-310.

18. Middleberg, A.P.J., *Laboratory projects: should students do them or design them?* Chemical Engineering Education, 1995: p. 34-39.
19. Caprette, D.R., S. Armstrong, and K.B. Beason, *Modular laboratory courses: An alternative to a traditional laboratory program* Biochemistry and Molecular Biology Education 2005. **33**(5): p. 351-355.
20. Truskey, G.A., F. Yuan, and D.F. Katz, *Transport phenomena in biological systems* Second ed. 2009, New Jersey: Pearson Prentice Hall Bioengineering 859.
21. Fogler, H.S., *Elements of Chemical Reaction Engineering* Second ed. 1999, New Delhi: prentice Hall of India 838.
22. Logan, B.E., D.G. Jewett, R.G. Arnold, E.J. Bouwer, and C.R. Omelia, *Clarification of Clean-Bed Filtration Models*. Journal of Environmental Engineering-ASCE, 1995. **121**(12): p. 869-873.
23. Abu-Khalaf, A.M., *Getting the most out of a laboratory experience* Chemical Engineering Education, 1998: p. 184-189.