IMPLEMENTATION OF PROJECT-BASED LEARNING IN SECOND-YEAR CELLULAR BIOPHYSICS COURSE AND STUDENTS’ PERCEPTION OF THE VALUE OF THE PRACTICE

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Abstract – This paper summarizes the perceptions and attitudes of sophomores in the School of Biomedical Engineering at the University of British Columbia (UBC) about the implementation of project-based learning (PjBL) in the instruction of cellular physiology and biophysics. The course is a core component of the undergraduate curriculum, and PjBL was deployed during the tutorial sessions. Students were assigned a research-oriented project to assess drug leads in-silico, and were trained in the use of an assortment of bioinformatics and computational tools. The tutorial also included some wet laboratory demonstrations of experiments that are typically performed to validate the in-silico results. The project comprised 20\% of the students’ grades and introduced them to a highly pertinent problem in the pharmaceutical industry, namely the development of a therapeutic for Parkinson’s disease. Effectiveness of the instruction was assessed through the use of online questionnaires, as well as an analysis of report quality and student performance in a final exam question on the topic. The use of PjBL was determined to be highly effective and student retention of the concepts contrasted markedly with that of concepts introduced in other modules of the course. Student satisfaction was also high, and student self-assessment of their knowledge revealed a high level of confidence in their proficiency with the software. In summary, PjBL promotes student learning, equips them with critical thinking skills and prepares them more effectively for the job force.

Keywords: Project-based learning, computational drug design, engineering education, student-centered learning, experiential learning.

1. INTRODUCTION

Project-based learning (PjBL) is an active learning paradigm that achieves its objectives by giving students a practical, open-ended problem to solve rather than providing them established facts or evaluating their grasp of the subject using typical modes of questioning [1]. PjBL seeks to foster an integrated understanding of concepts, tools and skills, and has been shown to not only enhance students understanding of basic concepts and principles, but also incubate skills that are essential for research [2]. A well-designed project encourages students to use a hands-on approach and can help learners understand concepts and develop critical thinking skills by subsequently applying the concepts to other cases. Many distinguished educators have implemented problem- and inquiry-based learning in the science, technology, engineering and mathematics (STEM) fields and have reported numerous advantages of such experiential learning. In general, the goal of is to hone and enhance creative and critical thinking skills of the students, and if it is implemented earlier in the undergraduate program, it could help students develop their problem solving and troubleshooting abilities [3,4].

In this study, sophomores in the School of Biomedical Engineering at the University of British Columbia (UBC) were presented with a real-word problem of the unavailability of a drug to treat Parkinson’s disease and were asked to computationally assess several promising drug leads that could act as an agonist for dopamine, the proposed therapeutic strategy. To this end, students were trained in the use of state-of-the-art bioinformatics and computational chemistry software packages, and were expected to apply their training for computational drug discovery. Demonstrations were also included to expose students to wet laboratory experiments used in the pharmaceutical industry to validate the computational predictions. At the end of the term, students completed a survey asking them to evaluate their comfort with the course material, their perception of their course-relevant abilities compared to those of their peers, and their impression of their performance on the exam. They were then given a description of the project and its goals and were asked about their experience in the computational project and whether they would like to participate in such kind of activities again. Overall trends in student responses are discussed in this paper, along with comments about the
overall class performance on the project. Relationships between students’ perception of their own abilities and their perception of the value of practical project are also explored. Student comments on future implementations of PjBL are also reported.

2. METHODOLOGY

2.1. Course Structure and Tutorials

Students received eight hours of lectures during the course’s tutorial hours on drug discovery and development and computational drug design. The list of topics covered during these lectures is summarized in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Topics covered during tutorial sessions</th>
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</thead>
<tbody>
<tr>
<td><strong>Title of the session</strong></td>
</tr>
<tr>
<td>1 Overview of the workflow for drug discovery and development, description of the therapeutic strategy</td>
</tr>
<tr>
<td>2 Protein data bases, an introduction to Marvin for viewing and manipulating chemical structures</td>
</tr>
<tr>
<td>3 Protein databank files, RCSB and UNIPROT repositories, finding protein structures, working with protein sequences, BLAST</td>
</tr>
<tr>
<td>4 Introduction to PyMol and Maestro for visualizing and manipulating structures</td>
</tr>
<tr>
<td>5 Protein modeling, homology modeling, using iTASSER or SWISS MODEL, differences between threading and force-based protein models</td>
</tr>
<tr>
<td>6 Introduction to Chimera, molecular docking, use of AUTODOCK, thermodynamic considerations</td>
</tr>
<tr>
<td>7 Overview of the methodologies involved in validating computational predictions in the laboratory</td>
</tr>
<tr>
<td>8 The next steps for drug design/development, lead optimization, clinical testing</td>
</tr>
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</table>

2.2. Project Description

Following the conclusion of the lectures listed in Table 1, the students were assigned a project that asked them to evaluate a library of drug leads to assess their ability to bind to the target protein, dopamine receptor D1 (DRD1). Inadequate agonism of this protein has been implicated in Parkinson’s Disease, a neurodegenerative disease which does not have any cure as of today. Specifically, a neurotransmitter called dopamine is not produced in required amounts, which disrupts downstream signaling pathways. This produces symptoms such as tremors, slowness of movement, stiffness, and loss of balance. There are no crystal structures available for DRD1, which has stymied drug discovery efforts. The students had to use the methodologies discussed in the lectures and also bridge their results with insights that they had acquired in courses that they had taken previously in the program, including thermodynamics and organic chemistry. The students were instructed to submit a short technical memo that summarized their calculations, included a short discussion on thermodynamics of ligand-protein binding, speculate on medicinal chemistry for lead optimization and provide a brief outline of downstream experiments that they would do to validate their in-silico predictions. The project provided a hands-on introduction to key steps in the initial phase of drug discovery and development, and the tools that the students use in this module are identical to those used in the pharmaceutical industry. It is hoped this broad introduction will provide students a foundation to pursue co-op opportunities in the field.

2.3. Software Tools

The students were introduced to several software packages including Marvin, PyMol, Chimera and Maestro which are widely used for computational drug discovery. Marvin Suite is a chemically intelligent desktop toolkit that allows drawing, editing, publishing, rendering, importing and exporting chemical structures and enables converting between various chemical and graphical file formats [5]. PyMol, on the other hand, is a molecular visualization system marketed by Schrödinger, Inc. and is widely used for structural biology. It allows for producing high-quality 3D images of small molecules and biological macromolecules [6]. UCSF Chimera is a highly extensible program developed by the Resource for Biocomputing, Visualization, and Informatics (RBVI), supported in part by the National Institutes of Health; and is widely used for interactive visualization and analysis of molecular structures and related data, including density maps, supramolecular assemblies, sequence alignments, docking results, trajectories, and conformational ensembles. Chimera allows for generating high-quality images and animations [7]. Maestro is another all-purpose molecular modeling environment developed by Schrödinger, widely used in pharmaceutical, biotechnology, and materials science research [8].

2.4. Survey Results

To evaluate students’ perception of the PjBL and their assessment of their own learning, a short voluntary survey was administered upon the completion of the proposed lectures. Students were encouraged to participate in the survey and provide feedback on what sorts of resources/support they would need for their project. In the survey, students were prompted to assess their own abilities and comfort level with the tutorial material, identify the steps involved in drug design by indicating their agreement with a list of statements using a 5-point Likert scale (1 = strongly disagree; 2 = disagree; 3 = neither agree nor disagree; 4 = agree; 5 = strongly agree) and answering three open-ended text-response questions. The
full list of questions is shown in Table 2, along with the short-hand tags used in the figures in the remainder of the
document). Question 7 in Table 2 was included as a quality
assurance check, to allow for the screening out of
unreliable responses. This was used as an indication of
students randomly selecting options in MCQs. Responses
from participants with the wrong answer to this question
were not taken into consideration for the analysis.

Survey results were analyzed, and trends in responses
warranting further investigation were identified. To gather
more information on the survey observations, a question on
final exam was devoted to assess students’ learning from
the project and if they can identify the steps associated with
computational drug design.

3. RESULTS AND DISCUSSION

3.1. Self-assessment: Technical-related questions

The tabulated responses to the self-assessment Likert-
scale questions are presented in Figure 1. Although the
weighted average of responses to these multiple-choice
questions were in almost all cases above 2.5/5 (except for
question 11), interesting trends are observed based on their
responses. For example, more than 50% of students
indicated that they would know the individual steps
involved in the process e.g. finding protein sequence,
sequence alignment, drawing and manipulating chemical
structures as well as visualizing the protein structures
(questions 2, 4, 5 and 6). However, when it comes to
implementing these learnings in the context and connecting
the dots between the steps, they seem to have a lower
confidence on what they need to do. For example, only
14% of students indicated that they would be able to
perform the protein-protein interaction and 30% indicated
they understand the mathematics behind the process. We
believe the this could be because the survey was
administered half-way through the term, just after they
have been introduced to the concepts. The higher levels of
learning outcomes, such as application, and analysis are
achieved with more practice and are best to be evaluated at
the end of the project. Therefore, the actual performance of
students on the report and the project-related question on
the final exam (discussed in the following section) is
considered as a mean to evaluate their ability to apply the
learning s from the lecture to the actual design.

Table 2. Survey questions used in this study.

<table>
<thead>
<tr>
<th>Technical-related questions</th>
<th>5-Point Likert Scale Questions</th>
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</thead>
<tbody>
<tr>
<td>1. I know how to get the sequence of a protein once I know its name/identity</td>
<td></td>
</tr>
<tr>
<td>2. I know how to find other sequences that are similar to the sequence of my target protein</td>
<td></td>
</tr>
<tr>
<td>3. I know how to access crystal structures of proteins</td>
<td></td>
</tr>
<tr>
<td>4. I know how to view and manipulate the crystal structures on my computer</td>
<td></td>
</tr>
<tr>
<td>5. I know how to draw and edit chemical structures</td>
<td></td>
</tr>
<tr>
<td>6. I know how to perform a sequence alignment of DNA or proteins</td>
<td></td>
</tr>
<tr>
<td>7. I know how to read with care. (Please answer somewhat disagree to this questions)</td>
<td></td>
</tr>
<tr>
<td>8. I know how to create structures of my target protein from its sequence</td>
<td></td>
</tr>
<tr>
<td>9. I know how to generate publication-quality, high resolution images of my protein structure</td>
<td></td>
</tr>
<tr>
<td>10. I know what ribbons, sticks, lines, cartoons and spheres are</td>
<td></td>
</tr>
<tr>
<td>11. I know how to prepare my target structure for analyzing its interaction with a drug or other ligand</td>
<td></td>
</tr>
<tr>
<td>12. I understand the mathematics of developing a good drug</td>
<td></td>
</tr>
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</table>

Open-ended Text Questions

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>1A. What is the name of the resource that you would use for getting the protein sequence?</td>
</tr>
<tr>
<td>3A. What is the name of resource that you would use to get crystal structure of proteins?</td>
</tr>
<tr>
<td>8A. How to create structures of the target protein from its sequence?</td>
</tr>
<tr>
<td>1P. The material covered in the lab is relevant to my professional needs</td>
</tr>
<tr>
<td>2P. I am confident going for an internship in pharmaceutical industry after doing this project</td>
</tr>
<tr>
<td>3P. The material covered in the lab is interesting</td>
</tr>
<tr>
<td>4P. The material covered in the lab could be improved</td>
</tr>
<tr>
<td>5P. How could we improve this project?</td>
</tr>
</tbody>
</table>

involved in the process e.g. finding protein sequence,
sequence alignment, drawing and manipulating chemical
structures as well as visualizing the protein structures
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students on the report and the project-related question on
the final exam (discussed in the following section) is
considered as a mean to evaluate their ability to apply the
learning s from the lecture to the actual design.
structures. Despite these observations, the actual performance of students in the final project was satisfactory and more than 70% of the students scored 85% and higher. Besides, one of the questions in the final exam was devoted to test students’ knowledge of the in-silico drug development. The average score on this question was 80% which shows that with the term-long hands-on project the students were indeed able to identify the step, understand the mathematics of molecular design and apply the thermodynamic and structural biology concepts to suggest a drug antagonist for dopamine receptor. An example of student analysis in their end term report is shown in Figure 4.

3.3. Project-related Questions

Three additional questions were also designed to assess the applicability of the project for students’ future career and their confident in using their learnings in the industrial context. More than 85% of students found the project interesting and applicable and 60% found it relevant to their professional career as a biomedical engineer. That being said, the biomedical engineering field focuses on a wide range of topics and concepts from biomechanics and prostheses, signal processing and medical device design, to biomaterials and tissue engineering. The lower percentage of project applicability for these sophomore students does not necessarily indicate much about the project itself, but rather is an indicative of students being in their early phase of engineering education and open explore different concepts in the field. Question 2P, has received an average 2.5 score among the participants. Higher percentage of students have indicated they are confident to perform similar tasks in the pharmaceutical industry context. Considering the survey was only administered half way through the term, and students’ just introduced to the project; this lower confidence can be explained. By the midterm, students have just finished the tutorials on the available toolkits for the computational protein design. The second half of the semester was dedicated to helping students apply the learning into the disease. We believe that applying the theory in the context as well as having hands-on the actual modeling steps to perform the project, would boost students’ confidence with these sorts of content, and indeed based on students’ reports, and performance in the final exam, it was clear that by the end of the term students’ had much better understanding of the project and higher confidence with implementing the knowledge and skills. The authors have instructed this same topic (computational drug discovery) in another second-year course in a different engineering department using conventional slide-based instruction. Student retention of the concepts was much lower in that instance, and students did not perform well on the examination question related to computational drug discovery (data not shown).
4. CONCLUSION

This paper describes the implementation of a dry (computational) lab project in a second-year biophysics course for biomedical engineering students, and students’ perception of this approach. The course entitled ‘Cellular Physiology and Biophysics’ being offered for the first time in the School of Biomedical Engineering (SBME) at UBC. The BME program at UBC aims to take the engineering principles and integrate them to medicine and biology for health care purposes. To this end, students are introduced to different streams of the BME (biomechanics & biomaterials, bioinformatics, cellular bioengineering, and biomedical systems and signals) in their second year and they will decide on their focus area in the third year. The course is multidisciplinary in scope and is composed of lectures, lab sessions tutorials. Topics covered in the course include cellular structures and mechanisms, mathematical models of biological phenomena, enzyme kinetics, gene circuits, signal transduction, diffusion, membrane biology and the hierarchical organization in tissues.

Conventionally courses like this are offered with a separate lab course designed to teach the students laboratory techniques such as microscopy, molecular biology techniques (cloning, DNA purification and gel electrophoresis), and protein production and purification. However, concepts like visualization and analysis of the molecular structures, bioinformatics, supramolecular assemblies and conformational ensembles are usually underrepresented in such courses, particularly their practical applications [9-10].

PjBL provides students with a learning environment that allows them to acquire knowledge, skills and interpersonal abilities. They will gain essential engineering skills such as critical thinking, problem solving, information retrieval, identifying relationships between components and engineering thinking. More importantly, by working on a clinically relevant, multi-concept topic, students are able to apply their learnings in not only biophysics, but also related courses on thermodynamics, organic chemistry and biochemistry to solve the problem effectively and make an appropriate recommendation for lead optimization. Incidentally, a number of students highlighted their proficiency in the use of the computational packages introduced in the tutorials and their familiarity with drug discovery in their resumes.

Acknowledgements

The authors would like to acknowledge the School of Biomedical Engineering and Department of Chemical & Biological Engineering at UBC for logistical support. The authors would also like to thank Tabea Stephan for her assistance with grading the reports and instructional support.

References


