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Article

A Semester-Long Project-Oriented Biochemistry Laboratory Based on *Helicobacter pylori* Urease[S]

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Abstract

Here we present the development of a 13 week project-oriented biochemistry laboratory designed to introduce students to foundational biochemical techniques and then enable students to perform original research projects once they have mastered these techniques. In particular, we describe a semester-long laboratory that focuses on a biomedically relevant enzyme—*Helicobacter pylori* (*Hp*) urease—the activity of which is absolutely required for the gastric pathogen *Hp* to colonize the human stomach. Over the course of the semester, students undertake a biochemical purification of *Hp* urease, assess the success of their purification, and investigate the activity of their purified enzyme. In the final weeks of the semester, students design and implement their own experiments to study *Hp* urease. This laboratory provides students with an understanding of the importance of biochemistry in human health while empowering them to engage in an active area of research. © 2015 by The International Union of Biochemistry and Molecular Biology, 43(5):333–340, 2015.

Keywords: *Helicobacter pylori; urease; biochemistry laboratory; inquiry-based; upper-division undergraduate*

Background and Pedagogy

The 13-week laboratory sequence described here is part of an advanced undergraduate Biochemistry course in the Department of Chemistry & Biochemistry at Bowdoin College. The laboratory was implemented in Spring 2012 with two primary goals: (1) to help students integrate concepts introduced in the classroom in a hands-on setting to solidify their understanding, and (2) to better prepare students to undertake biochemistry research, both on and off campus. Given the rich pedagogy about the effectiveness of introducing students to scientific investigation through project-based experiments [1, 2], we sought to achieve these goals in the context of a semester-long project-based laboratory experience that closely reflects a "real" research experience and could provide students an opportunity to implement their own experiments. Finally, we felt it was important to include a biomedically-relevant theme in the design of the laboratory, as many of our biochemistry majors ultimately pursue careers in biomedical research and medicine. To realize this vision and meet these varied goals, we designed a semester-long laboratory that is related to *Helicobacter pylori* (*Hp*), a bacterial pathogen studied in the Dube laboratory.

Hp is a pathogenic bacterium that is found in the stomachs of roughly 50% of humans worldwide [3]. Approximately 15% of infected individuals develop duodenal ulcers, and 1% of infected individuals develop gastric cancer [4]. Current treatment to clear infection requires "triple therapy" [5], a combination of multiple antibiotics and a proton pump inhibitor that is often associated with negative side effects [6]. Because of poor patient compliance and the evolution of antibiotic resistance, existing antibiotics are no longer effective at eradicating *Hp* infection [6]. New treatment methods are needed to eliminate *Hp* from the human gastric tract. *Hp*'s enzyme urease [7] serves as a logical target of therapeutic intervention because this enzyme is directly linked to *Hp*'s ability to colonize the host's stomach [8]. Urease catalyzes the hydrolysis of urea to produce ammonia (Fig. 1), a base that serves to neutralize the acidic stomach and facilitate *Hp* infection [9]; *Hp* strains that lack this enzyme display colonization defects in murine and pig infection models [8, 10]. Therefore, *Hp* urease is a potential drug target.

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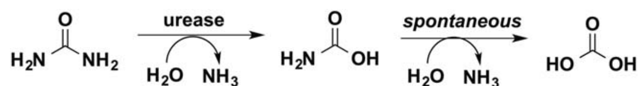

FIG 1 *Urease catalyzes the hydrolysis of urea to produce ammonia.*

Inspired by several integrated laboratory approaches that have been described in the literature [2, 11–16], we sought to create a semester-long project-oriented biochemistry laboratory course that would include "research-like" independence. Therefore, we implemented a biochemistry laboratory in which students purify *Hp* urease from the heterologous host *Escherichia coli*, study its enzymatic activity, then design and implement their own experiments to study *Hp* urease. Crucially, these studies serve to provide students with a semester-long laboratory that is research-inspired, focuses on a broad overarching goal, introduces and builds upon an experimental skillset, and fosters creativity and a sense of personal ownership. Thus, this biochemistry laboratory introduces students to the thought process involved in scientific investigation. As an added benefit, the student-designed studies performed in this laboratory have the potential to shed light on the biomedically important enzyme urease.

Implementation

The advanced undergraduate Biochemistry course that this laboratory was introduced into serves chemistry and biochemistry majors, and it meets for seven hours per week throughout our 13-week semester. Students spend 3 h/week in the classroom and 4 h/week in the laboratory. Our average course enrollment is 36 students, with students typically distributed into three laboratory sections containing 12 students/section. Each section is scheduled for a 4 h time block that meets once a week in a biochemistry teaching laboratory, and each weekly experiment is designed for students to complete in pairs during this 4 h period. Speed and efficiency depend upon how well prepared students are, how much equipment and instrumentation must be shared, and finally how constructively student pairs work together. One laboratory instructor is dedicated to this course full time during the semester. The laboratory instructor prepares the materials for and guides all of the laboratory sections. Further, the laboratory instructor serves as the primary student resource for questions related to the experiments and laboratory assignments and is responsible for grading students on the laboratory portion of the course.

Although students work in pairs throughout the semester, they are graded independently on all of their work. The laboratory grade is worth 25% of the course grade and is based on participation and preparedness, keeping a laboratory notebook, quizzes, final project presentation, and a final paper. To prepare for the laboratory each week, students are assigned background readings (e.g., chapters from Clive Dennison's "A Guide to Protein Isolation") and are expected to compose the purpose, introduction, and methods sections of their laboratory notebook for that week's experiment. To encourage students to effectively integrate concepts and engage with their data, they craft "Results" and "Conclusion" sections in their laboratory notebook after each week's experiments. In these sections, they present their data, interpret their results, and discuss their findings in light of concepts learned in laboratory, lecture, and in the assigned background readings. Laboratory notebooks are collected and graded two to three times during the semester to evaluate student comprehension. Finally, students write a formal, *Journal of Biological Chemistry*-style article throughout the semester. Students receive feedback on their papers at four discrete points in the semester, including on their (1) initial methods section, (2) results plus revised and edited methods, (3) introduction plus revised and edited methods and results, and finally (4) full paper, complete with a discussion section. The final paper reflects a culmination of the entire semester, and it is an excellent measure of each student's mastery of biochemistry laboratory concepts.

Hp Urease Is the Central Focus of the Biochemistry Lab

Hp urease is an attractive choice for the Biochemistry laboratory, as it can be heterologously expressed in *E. coli* [17], its crystal structure has been solved [18], and there are a variety of rapid assays that measure urease activity [19, 20]. We utilize *E. coli* strain SE5000, generated and donated by Hu and Mobley, that expresses catalytically active, recombinant *Hp* urease at wild type levels [17]. In essence, this strain contains plasmids encoding the entire *Hp* urease gene cluster (ureC, ureD, ureA, ureC, ureB, ureI, ureE, ureF, ureG, and ureH) as well as structural genes (ureA and ureB) and, when grown in the presence of $NiCl_2$, produces active, nickel-dependent *Hp* urease [17]. The active enzyme is composed of two different subunits, α and β, encoded by ureA and ureB; a crystal structure of *Hp* urease solved by Ha *et al.* reveals a dodecameric structure composed of four $(\alpha\beta)_3$ units [18]. *Hp* urease can be purified from cellular components via successive column chromatography steps (e.g., hydrophobic interaction chromatography, size-exclusion chromatography, ion exchange chromatography) [7, 21, 22]. The presence of active *Hp* urease in cell lysates and in purification fractions can be measured via spectrophotometric urease activity assays, such as the phenol red assay [20] or the indophenol assay [19]. On the basis of the ease of expressing, purifying, and assaying *Hp* urease, as well as its biomedical importance, we concluded that *Hp* urease is an excellent choice for this course.

Therefore, we designed a Biochemistry laboratory based on *Hp* urease. The laboratory schedule, specific

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techniques, and instrumentation for each part of the course are listed in Table 1. The laboratory is divided into three parts: purifying *Hp* urease (labs 1–6), characterizing the purified enzyme (labs 7–9), and exploring the biochemistry of *Hp* urease through an original project (labs 10–13). Each laboratory session includes a short introduction by the instructor and a brief discussion of laboratory goals and procedures. The goal of each laboratory period, a list of equipment, supplies, and reagents necessary, and detailed protocols are provided in Supporting Information, along with representative student data (Supplemental Figures 1–7).

Course Schedule

Week 1: Measuring the Absorptivity Coefficient of Indophenol

Prior to beginning the purification of *Hp* urease, students first learn how to pipette, perform dilutions, create a standard curve, and use a spectrophotometer. This skill set is developed in two contexts: (1) measuring protein concentration via A_{280} on a UV–vis spectrophotometer and (2) determining the absorptivity constant of indophenol at A_{637} based on known concentrations of ammonia. The first goal, the ability to measure protein concentration, is critical throughout the protein purification process. The second goal is crucial for the quantitative indophenol assay that students use throughout the semester to measure urease activity, which results in the formation of ammonia. Outside of class, students construct a standard curve of A_{637} vs. [ammonia] and, based on this curve, determine the absorptivity coefficient of indophenol.

Week 2: Primary Purification of *Hp* Urease from *E. coli*

In the second week of the laboratory, students are provided with *E. coli* strain SE5000 [17] cell pellets (from 800 mL cultures) as a source of raw material from which to isolate *Hp* urease. Students lyse cells to prepare a cell-free extract, clarify the lysate via high-speed centrifugation, and determine protein concentration and urease activity of the clarified lysate. Protein concentration is measured via A_{280}, and specific activity is determined by the indophenol assay [19] (Fig. 2). At this stage of purification and all subsequent ones, students prepare and store a sample for later SDS-polyacrylamide gel electrophoresis (SDS–PAGE) analysis. This laboratory builds upon the skillset developed during week 1 and utilizes the indophenol absorptivity coefficient to determine urease activity. Further, this set of experiments yields crude material for subsequent urease purification.

Week 3–6: Urease Purification via Column Chromatography

Two column chromatography steps are used to purify urease from clarified lysate. In week 3, gel filtration chromatography is performed using BioGel A 1.5 coarse beads (BioRad) via gravity filtration, and fractions are collected with a fraction collector. Students measure protein concentration via A_{280}, perform a colorimetric phenol red urease detection assay (PRUDA) [20] to identify column fractions that contain urease activity, and then pool active fractions. In the fourth week, students concentrate and buffer exchange the gel filtration purified material, then measure protein concentration and urease activity. In the fifth week, ion exchange chromatography with a strong anion exchanger (Mono Q) is performed. For this second chromatography step, students are given a single, journal-style methods paragraph to guide them and must convert the bare-bones guidelines into their own step-by-step protocol for the laboratory period. This exercise encourages students to explicitly think through and plan their experiment. Moreover, this task provides a model paragraph that primes students for their upcoming methods writing assignment. During the sixth laboratory period, students analyze column fractions to determine protein concentration (A_{280}) and urease activity (PRUDA), then pool and concentrate active fractions.

Week 7–8: Characterization of Partially Purified *Hp* Urease

To evaluate the success of their purification, students create a purification table that lists, for each step of the purification, the total volume of sample (mL), total amount of material (mg protein), total urease activity (units), and specific activity (units/mg) (see Table 2 for purification table with representative student data). This analysis enables students to quantitatively visualize the effectiveness of each purification step as well as calculate fold purification and percent yield (Table 2).

During weeks seven and eight, students analyze samples from various stages of the purification (whole cell lysate, clarified lysate, gel filtration chromatography sample, and ion exchange chromatography material) via SDS–PAGE and western blot analysis. The SDS–PAGE is conducted to visualize the effectiveness of each purification step, to enable estimation of purity, to corroborate data presented in the purification table, and to discern the molecular weight of *Hp* urease subunits (ureA and ureB) [7]. An immunoblot is performed with commercially available antibodies raised against *Hp* ureA and ureB (Santa Cruz Biotechnology). This experiment confirms that the protein bands enriched over the purification correspond to *Hp* urease subunits.

Week 9: Enzyme Kinetics of *Hp* Urease

Using their partially purified enzyme, students undertake enzyme kinetics experiments to measure K_m, V_{max}, and k_{cat} values for *Hp* urease. They also determine the nature of inhibition (e.g., competitive or noncompetitive) of the inhibitor acetohydroxamic acid (AHA) [23–25] on urease activity. Students conduct end-point assays using varied [urea] and [AHA], and measure urease activity via the quantitative

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TABLE 1 *Experiments, specific techniques, and instrumentation for each week of the biochemistry laboratory course*

Week	Experiment	Techniques	Instrumentation
1	Measuring the absorptivity coefficient of indophenol using known [ammonia]	Pipetting, dilutions, standard curve, spectrophotometry	UV–vis spectrophotometer
2	Primary purification of *Hp* urease from *E. coli*	Cell lysis, urease activity assay	UV–vis spectrophotometer, high-speed centrifuge
3	Purification by gel filtration chromatography	Gel filtration chromatography, multichannel pipetting	Fraction collector, microplate reader, spectrophotometer
4	Ultrafiltration of column samples and measuring specific activity	Ultrafiltration, buffer exchange	High-speed centrifuge
5	Purification by ion exchange chromatography	Ion exchange chromatography, develop detailed protocol	Fraction collector, microplate reader, spectrophotometer
6	Concentrate purified protein and measure specific activity	Ultrafiltration, indophenol assay	High-speed centrifuge
7	Gel electrophoresis of purification fractions	SDS–PAGE and western transfer	Protein gel electrophoresis apparatus
8	Immunoblotting of purification fractions	Western blot analysis	Orbital shaker
9	Enzyme kinetics of partially purified urease	Enzyme kinetics	UV–vis spectrophotometer
10	Laboratory project: project conception, literature searching, and experimental design	Literature searching, project proposal, experimental design	Student computers
11	Laboratory project: prepare solutions, begin experiments	Scientific independence, ownership, and exploration	Miscellaneous equipment used through the semester
12	Laboratory project: conduct and complete experiments	Scientific independence, ownership, and exploration	Miscellaneous equipment used through the semester
13	Laboratory project: presentation of results and discussion	Presentation of project and experimental results	Computer and projector, or poster printer

indophenol assay. Outside of the laboratory, students perform graphical analyses of their kinetic data using Michaelis-Menton, Lineweaver-Burk, and Eadie-Hofstee plots, and then determine kinetic parameters and the nature of AHA inhibition. Three different graphical analyses are performed to demonstrate that subjecting one's data to different algorithms yields more or less accurate kinetic parameters. For their laboratory reports, students are expected to compare their findings to what has been previously reported in the literature.

Weeks 10–13: Laboratory Project

In the final weeks of the semester, students are given the freedom to design and implement their own research project to study *Hp* urease. The project is described in very general terms, and students may focus on studying any biochemical aspect of urease that they are interested in. As a guideline to aid in project conception, students are given suggested goals, such as (1) screening for a urease inhibitor, (2) comparing the kinetics of *Hp* urease to jack bean urease (Sigma), (3) determining urease's protease susceptibility, (4) assessing urease's pH stability, (5) conducting protein folding experiments, and (6) evaluating another aspect of urease's biochemistry. Students then conduct a brainstorming exercise, in which they discuss potential ideas, search the literature to find relevant background information and experimental protocols, as well as search for commercially available materials that might aid in their

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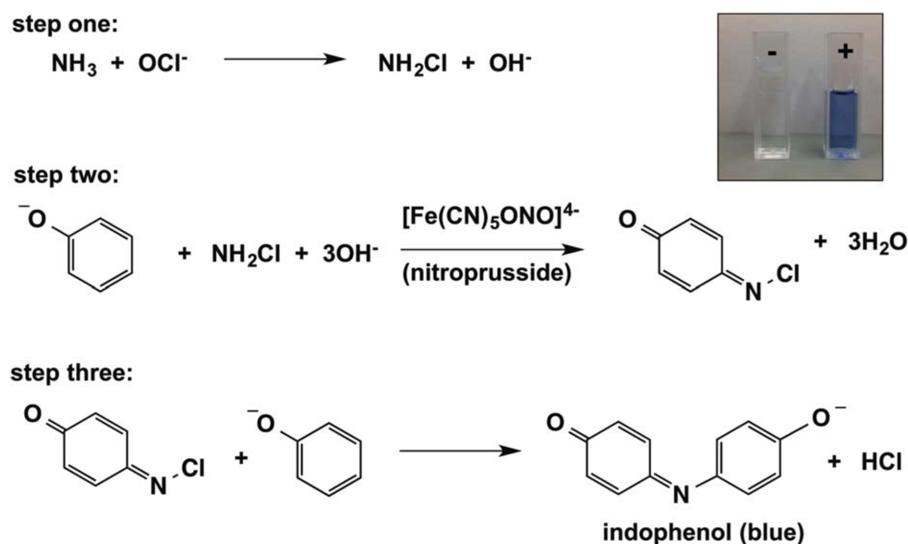

FIG 2 *Detection of ammonia using the indophenol assay. Phenol and hypochlorite react with ammonia to form indophenol, a blue compound. Inset: indophenol assay produces a blue compound in response to urease-catalyzed production of ammonia (+), wherease a urease-free control remains colorless (−). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]*

proposed studies. The biggest challenge during the brainstorming and planning session is guiding students to propose an experimental plan that is feasible given time, equipment, and material constraints. With some leading questions (e.g., How many assays will you be able to perform in one laboratory period? How will you control for background absorbance of green tea? How will you graph and analyze the data? What do you predict you will see?), students can develop thoughtful, well-controlled experiments that can be performed within the course constraints. By the end of the project planning laboratory, students provide the laboratory instructor with a list of materials, chemicals, and reagents that are absolutely critical to perform the work, as well as information about where the materials are (in the building vs. available commercially) and how much they cost, if purchasing is feasible within budgetary constraints. Students also map out how they will utilize the experimental project laboratory time—two laboratory periods—to achieve their goals.

In preparation for week 11, students are tasked with transforming their experimental methods from broad strokes to a detailed, step-by-step procedure. They perform calculations in advance of the laboratory and then utilize time in the laboratory to prepare materials (e.g., make buffers and stock solution, cast gels, concentrate/dilute enzyme samples, etc.) and conduct pilot studies (e.g., test whether reaction components are compatible with an indophenol reaction). If time allows, students begin experiments to test their hypothesis during week 11. During week 12, students conduct and complete their independent experiments. Finally, in week 13, students present their projects to their classmates. For the presentation, students assemble and present a poster that describes the background of their project, their hypothesis, the motivation for the work, their experimental design, their results, and finally their conclusions and suggestions for future directions. Finally, students include, analyze, and discuss the results of their laboratory project in their Journal-style final papers.

TABLE 2 ***Purification table containing representative student results, with activity of each fraction quantified using the indophenol assay***

Purification step	*Volume (mL)*	*Total protein (mg)*	*Total activity (U)*	*Specific activity (U/mg)*	*Fold purification*	*Yield (%)*
Primary	9.0	400	1801	4.5	1	100
Gel filtration	5.0	36	436	12	2.7	24
Ion exchange	0.640	0.65	229	352	78	13

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Using the above-described laboratory project format, students have designed and executed diverse projects, which have included, for example, 1) assessing the effectiveness of home remedies (e.g., vitamin C; garlic and ginger; cinnamon and nutmeg; capsaicin; green tea catechins) on urease inhibition, 2) determining the temperature or pH profile of urease activity, 3) exploring the role of metal cations on urease activity, 4) comparing the kinetics of jack bean urease to *Hp* urease, and 5) determining whether urease is glycosylated. Sample student data from two of these projects are showcased in the Supporting Information (Supplemental Figures 6 and 7).

Avenues for Modification and Potential Pitfalls

This project laboratory could be adopted as described, or it could be adapted to meet the needs of different institutions, course structures, and instructor styles. As described, the laboratory is designed to fit a 13 week semester schedule. To adapt this laboratory to shorter time frames, such as those found in the quarter system, the student-driven purification of urease could be implemented in a stand-alone course, as could the design and implementation of (potentially longer) independent projects to explore urease. To adapt this laboratory to a large university setting rather than a small undergraduate college, parallel laboratory sessions could be led by teaching assistants, with support staff in charge of preparing the materials for each weekly laboratory session. There are also opportunities to incorporate student input in experimental design earlier. For example, students could devise their own purification plan by choosing appropriate column media and buffers, ideally guided by the literature or by the theory of protein separation by column chromatography. Furthermore, there is ample opportunity to improve upon the urease enzyme kinetics experiments. In particular, the work described herein relies upon a fixed time point assay, due in part to instrument limitations. With a real-time spectrophotometric assay, a running time assay could be performed, ultimately facilitating the collection of more data points. Finally, a mutagenesis module could be developed [16] to enable students to create and study urease point mutants. In sum, this semester-long project laboratory could be modified to meet varied needs.

Although we were able to successfully implement this urease-based laboratory, using a research project based on enzyme activity to drive pedagogy has very real challenges. One challenge we encountered when implementing this laboratory was the high variability of urease activity in *E. coli* lysates. Some students would have lysates with very high urease activity, and others would start with lysates with little urease activity. To minimize this variability, we now pool and split *E. coli* pellets, therefore giving each student group identical "starting material" for their purifications. We also found that the student-designed project labs require variable levels of urease; some groups design experiments that use very little urease, and others conduct experiments that necessitate large amounts of urease. To address this challenge, we pool the partially purified urease samples and split them among the laboratory groups according to how much each laboratory group needs for their project laboratory.

While the above examples describe challenges we were able to address, some of the challenges associated with this laboratory are inherent. Urease loses activity over the course of the semester; improper student handling of samples at each stage of the purification can compound this loss of activity. The purification steps themselves contribute to loss of product. This loss of activity is exacerbated by the fact we conduct chromatography steps under suboptimal conditions (e.g., higher than optimal temperature or column flow rate) due to time and space constraints. Finally, the student-designed laboratory project is unpredictable, and students and the laboratory instructor must act in response to unexpected results. For example, certain compounds (e.g., thiols) interfere with the indophenol assay and lead to a high level of blue absorbance even in the absence of urease. In these instances, creative alternatives must be explored (e.g., assay relative urease activity with PRUDA). Despite these drawbacks, we have concluded that the challenges do not trump the many advantages associated with this laboratory, the biggest in having students conducting "real" biochemistry experiments and responding to real-time experimental challenges.

Connection Between Class Work and Laboratory Experiments

With the addition of this semester-long project laboratory to a biochemistry course, the laboratory provides a common theme that can be related back to in lectures. For each new topic presented in lecture, the implications and links to urease can be emphasized. Indeed, for Bowdoin College's biochemistry class, course content was revised to include urease-based examples throughout the semester. For instance, when the importance of pH in biological systems is introduced, students learn how *Hp* neutralizes the low pH of the stomach with urease [26]. When protein structures are described, some aspects of urease's structure that are crucial for function are highlighted [18]. When features of enzymes that enable them to catalyze reactions are covered, students are challenged to consider what features urease's active site must have to bind to urea and catalyze its hydrolysis [27]. Moreover, urease-relevant examples are included in class problems and exams. These changes have enhanced the course by creating a synergistic learning experience.

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TABLE 3 *Average responses from 72 students to questions on a laboratory exit survey, with 5 = strongly agree, 4 = agree, 3 = neutral, 2 = disagree, and 1 = strongly disagree*

Question	Average response (std dev)
1. I found that learning biochemical techniques in the context of an overarching research project made learning more interesting	4.4 (1.6)
2. Analyzing my data throughout the semester required me to use scientific reasoning and strengthened my command of biochemistry concepts	4.3 (0.7)
3. The project component of the laboratory helped me think about the factors that go into designing an experiment	4.3 (0.6)
4. The project component of the laboratory gave me a sense of ownership and the laboratory a broader sense of purpose	4.1 (0.8)
5. I enjoyed being given the freedom to design and implement an experiment to answer a question of my own choosing	4.3 (0.7)
6. I would have preferred to have had each laboratory technique introduced separately, rather than as part of an ongoing research project	1.9 (0.7)
7. I preferred labs that had a step-by-step procedure rather than those where I had to map out my own experiments	3.4 (1.0)
8. As a result of this laboratory, I have a better understanding of how biochemical research can have an impact on human health and medicine	4.1 (0.8)
9. Future biochemistry students should perform this urease-based semester long lab	4.1 (0.8)

Assessment

One way we assessed the success of this project laboratory was through exit surveys. On the basis of two years of laboratory exit surveys (total of 72 students), the vast majority of students strongly agreed that learning biochemical techniques in the context of an overarching research project is interesting, they enjoyed the freedom to design and implement an experiment, and they have a better understanding of how biochemical research can have an impact on human health and medicine as a result of this laboratory (Table 3). Some student comments include that "the semester long project idea was great and made me keep my perspective broad," the project laboratory was "awesome!" and a "great way to learn the techniques and contextualize the material" and compelled them "to think about why (they) were conducting each experiment." Therefore, we conclude that this *Hp* urease laboratory is an exciting venue for learning laboratory techniques, mastering experimental design, and connecting research to human health.

We also assessed the effectiveness of this project laboratory by evaluating the depth of knowledge students exhibited in assignments. Laboratory notebooks, final presentations, and Journal-style final papers revealed the extent to which students synthesized and applied biochemistry concepts to their laboratory projects. On the basis of the quality of these assignments, the majority of students (48 out of 72) demonstrated mastery of the material, exceptional critical skills, and a strong command of their project, while nearly all students (70 out of 72) demonstrated a thorough and above-average understanding of the material. Another relevant measure of educational effectiveness was the extent to which student confidence and independence developed over the course of the semester; many students started the laboratory without knowing how to pipette and were ultimately able to design and implement their own biochemistry experiments. Finally, anecdotal evidence suggests that the experience students gained in this laboratory with protein purification and experimental design helped some of our students secure biochemistry research jobs. On the basis of these measures, this laboratory experience effectively teaches students biochemistry laboratory skills, helps students integrate concepts, and better prepares students to undertake biochemistry research—all in the context of a biochemically important problem that excites students.

Summary

In summary, we report the design and implementation of a highly successful semester-long biochemistry project-based laboratory. This laboratory enables students to focus on a single research problem, the biochemistry of *Hp* urease, for a full semester, and it challenges students to apply their newly gained biochemistry skill set to devise and conduct independent projects in the final weeks of the semester. On the basis of instructor and student assessment, this course effectively provides an opportunity for students to learn biochemical concepts and experimental techniques, as well as hone their oral and scientific writing skills, ultimately enabling students to feel that they personally can perform biomedically-relevant research.

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E. coli SE5000. We thank Aimee Eldridge for her insight and help identifying purification steps that substantially increase the purity of *Hp* urease. Further, we thank students enrolled in Chemistry 232(0) in 2012, 2013, and 2014 for representative student data. Finally, this work was supported by Bowdoin College, by a Henry Dreyfus Teacher-Scholar Award, and by grants from the National Center for Research Resources (5P20RR016463-12) and the National Institute of General Medical Sciences (8 P20 GM103423-12) from the National Institutes of Health.

Supporting Information

Laboratory syllabus, weekly laboratory equipment, supplies, and protocols, project laboratory design handouts, sample student data, and a laboratory exit survey are available as supporting information.

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