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Article

Incorporating a Collaborative Web-Based Virtual Laboratory in an Undergraduate Bioinformatics Course

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Face-to-face bioinformatics courses commonly include a weekly, in-person computer lab to facilitate active learning, reinforce conceptual material, and teach practical skills. Similarly, fully-online bioinformatics courses employ hands-on exercises to achieve these outcomes, although students typically perform this work offsite. Combining a face-to-face lecture course with a web-based virtual laboratory presents new opportunities for collaborative learning of the conceptual material, and for fostering peer support of technical bioinformatics questions. To explore this combination, an in-person lecture-only undergraduate bioinformatics course was augmented with a remote web-based laboratory, and tested with a large class. This study hypothesized that the collaborative virtual lab would foster active learning and peer support, and tested this hypothesis by conducting a student survey near the end of the semester. Respondents broadly reported strong benefits from the online laboratory, and strong benefits from peer-provided technical support. In comparison with traditional in-person teaching labs, students preferred the virtual lab by a factor of two. Key aspects of the course architecture and design are described to encourage further experimentation in teaching collaborative online bioinformatics laboratories.

Keywords: Collaborative learning, bioinformatics, molecular evolution, online education, virtual laboratory, student peer review, web-enhanced, NCBI.

As bioinformatics has become a standard tool of scientific inquiry, application-oriented bioinformatics courses have become routine offerings at the undergraduate level [1–4]. These classes typically integrate a face-to-face lecture with a weekly teaching laboratory, following the traditional paradigm used in courses such as cell biology, genetics, and biochemistry. As with wet-lab training, the bioinformatics laboratory reinforces the conceptual course content and provides a broadly-applicable practical skill set. Commonly in training labs, the class divides into small groups that perform an exercise, implicitly creating an informal collaborative learning environment.

In distance education bioinformatics courses, the laboratory paradigm has been moved to an online setting [5–7], taking advantage of web-based learning tools. When thoughtfully applied, these technologies can foster a rich educational experience and encourage collaborative learning. However, despite the web-centric nature of bioinformatics itself, and despite the wide availability of web-based learning environments, face-to-face bioinformatics courses have retained the traditional on-site teaching laboratory. Combining the strengths of an in-person lecture with a remote web-based laboratory presents a new opportunity to improve bioinformatics education.

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An upper-level undergraduate, face-to-face, lecture-only bioinformatics course has been taught at the University of Massachusetts Boston since 2003. As part of a comprehensive course redesign, we hypothesized that students would benefit from the addition of a web-enhanced, collaborative, virtual laboratory. To study this hypothesis, the course was augmented with a substantive and required online component, and student opinion data was collected near the end of the semester. The experiment had several subcomponents: to test whether collaborative learning was practical in an online bioinformatics lab, to test whether student groups could provide peer support for routine questions regarding bioinformatics tools, and to compare the virtual lab with previous experiences in physical labs. This article describes the architecture of the course, reports quantitative and qualitative student data, and provides suggestions for teaching a virtual laboratory in similar bioinformatics classes.

COURSE OVERVIEW, CONTENT, AND METHODOLOGY

The bioinformatics course is offered through the UMass Boston Department of Biology and is targeted primarily to upper-level biology undergraduates. The prerequisites are a two-semester introductory biology sequence, a one-semester genetics course, general chemistry, and college-level algebra. The experimental course ran during Spring 2009 with one instructor and no teaching assistants. Of the 50 students initially enrolled, 48 remained after the add/drop date, and of those, five withdrew. The 43 students who completed

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the course had majors of BS-Biology ($n = 37$), BS-Biochemistry (1), MS-Biology (1), BA-Anthropology (1), BA-Psychology (1), and unknown (2). The class breakdown was eight juniors, 34 seniors, and one first-year graduate student.

Three strong unifying themes provide a coherent and central framework of the course, and these themes echo and interplay constantly throughout the semester. First, students learn about mechanisms of molecular evolution, and how selection frequently conserves sequence, structure, and function. At this point in their education, students have briefly encountered these ideas in their introductory biology and genetics classes, but most have not internalized that molecular-level evolution is a pillar of modern biology. In this regard, the course is effectively a primer in the theory and practical consequences of molecular evolution. The second recurring theme describes the exponentially-growing volume of biological sequence data, including its curation, storage, and retrieval. The course stresses the enormity and value of this resource, and how sequence data provides a direct window into molecular evolution. The final theme is the richness and practical value of cross-linked data, for example, how human diseases and drug targets are found in research literature, how research literature links with gene sequences, how gene sequences link with homologues and protein domains, and how protein domains link with structural data. Using this conceptual framework, the course covers standard introductory bioinformatics topics including PubMed, Online Mendelian Inheritance in Man (OMIM), GenBank, sequence curation and RefSeq, local alignment and sequence database searching, multiple sequence alignment, substitution matrices, phylogeny, gene feature prediction, protein domain architecture, protein modeling and visualization, and systems biology. Mathematics and computer science are not emphasized, although the lecture introduces rudiments of probability, statistical inference, and distance measure in high-dimensional space, as well as the notions of computational intractability and heuristic algorithms.

The virtual laboratory was conducted over Blackboard Vista (http://www.blackboard.com/). At the beginning of the semester, the class of 50 divided into 10 lab groups of five students each. A group size of five was chosen to create a critical mass that fosters meaningful collaboration, while avoiding the diffuse impersonality of a much larger group. As is common in wet-lab courses, students chose their own groups and retained their group membership over the semester. Because web-enhanced collaborative learning was new to most students, the instructor conveyed strong expectations of active participation throughout the semester. Both in the syllabus and in lecture, students were informed that 25% of the final course grade represented the quality and quantity of online collaboration, and a detailed grading rubric was also provided. Collaborations occurred within Blackboard Vista threaded group discussions; journal and blog software was not employed.

Students could read and post messages within their specific online group but could not access discussions in other groups. In addition to their private groups, everyone was also enrolled in a single class-wide group that was frequently used for clarifying lecture concepts and helping with bioinformatics tools. Instead of privately e-mailing the instructor, students were strongly encouraged to use the class-wide group for all topics of general interest. Because multiple students often have nearly identical questions, this tactic likely reduced the volume of redundant instructor e-mails and redundant office hour tutoring sessions. A tight feedback loop occurred as the instructor monitored discussion groups for gaps in comprehension, and addressed these gaps in the next lecture.

Two major course components were conducted within the virtual laboratory: weekly laboratory assignments, and several cycles of peer review of the final project. As in a traditional class, the weekly laboratory assignments were closely coupled to the lecture topics. Lab cycles ran Friday-to-Friday and had the following steps:

1. Each student ran a bioinformatics experiment. Depending on the particular assignment, experiments were identical for all students, or were varied by the instructor in specific ways, or were varied based on students' final project topics.
2. Each student posted initial findings and interpreted their results. Students were required to post by midweek to facilitate substantive collaboration during the remainder of the week.
3. The group discussed the findings and interpreted the results.
4. Each student was graded for the experimental approach and results, as well as for collaboration in the online discussion.

The lab exercises were similar to those used for conventional bioinformatics homework, although enhanced to facilitate group discussions. For example, everyone ran a BLAST for a single assigned gene, but each student chose an altered set of query parameters. Options included searching by mRNA or amino-acid sequence, changing the substitution matrix, altering gap penalties, specifying a database, and choosing a search algorithm. Students posted their results, and collectively interpreted the relationships between algorithm parameters and BLAST outputs. Students observed how various BLAST approaches were appropriate for specific biological investigations.

The virtual laboratory experiments were performed using standard web-based bioinformatics tools and databases. The bulk of the work was performed at NCBI, and students were also encouraged to find and explore other tools. Purchase of bioinformatics software or services was not required. To introduce practical use of the tools, in-class demonstrations provided a general overview of the experiment workflow; however, detailed, cookbook-style instructions were intentionally not provided. Instead, students were taught to become self-sufficient in locating and reading bioinformatic tool documentation. In addition, students were strongly encouraged to ask their online peers for help when encountering mechanical problems. This peer-support practice was designed to increase active learning, foster collaboration, and reduce the technical support burden of the laboratory instructor.

For the final project, students produced a substantive written report that described bioinformatic analyses of a gene. Students performed research and wrote their reports individually, and each was also required to provide constructive feedback to the peers in their group. The project began early in the semester, giving students an opportunity to experience a broad-themed bioinformatic study that closely related to

the lectures and labs. As a first step, after learning about PubMed, review papers, OMIM, NCBI Bookshelf, and GenBank, each student found an interesting gene to study. Many chose genes related to human diseases, often from an interest in a medical career or from firsthand knowledge of affected individuals. Several weekly lab assignments directly supported the final project by requiring specific analyses of the student's chosen gene. Overall, the final project was designed to maximize student engagement and learning throughout the semester, to connect the major themes and units of the course, to develop critical thinking and scientific writing skills, and to assess individual performance.

Milestones were required at specific dates, and are shown as weeks from the beginning of the semester:

- Week 4: Gene and topic choice, GenBank or Refseq accession numbers for gene and protein, and brief review of literature with citations
- Week 11: Paper outline
- Week 13: Paper draft
- Week 14: Near-final version
- Week 15: Final version to be graded

Following each checkpoint, students were required to read and provide constructive feedback on their peers' postings. This peer review process had several goals: to expose students to a collaborative review practice common in academia and industry; to raise the group's overall performance level; to prevent last minute surprises over project scope and expectations; and to cross-pollinate ideas within the group.

RESULTS

Survey Results

To quantitatively test the hypothesis that the virtual laboratory was beneficial to learning bioinformatics, students were polled two weeks before the end of the semester. Figure 1 describes the resulting data. The first group of questions evaluates the benefit of collaborative learning in the virtual laboratory. Questions A and B measure benefits of asking and answering online questions, respectively, and Question C measures the benefits from passive observation. On these points, the data broadly support the hypothesis that collaboration in the virtual lab was beneficial. Question D examined whether students found their peers to be helpful in a technical support role; the large majority of students found benefit from this service.

Question E asked whether students preferred a traditional lab experience to the online lab. Based on the course prerequisites, students had previously completed at least four traditional wet-lab courses. With that background, approximately two-thirds preferred the virtual lab, and of those, the large majority strongly preferred the virtual lab. The response to Question F supports the hypothesis that homework conducted within the virtual lab contributed towards learning the course conceptual material.

As bioinformatics is an interdisciplinary field and can be taught from multiple perspectives, and given that this course intentionally emphasized a biological perspective, Question G tests whether that emphasis successfully integrated bioinformatics with core biological principles. To examine whether this emphasis corresponded with students' interests, Question H asked whether more mathematics and computer science should be taught. Responses to these queries indicate that the course achieved its goals of presenting bioinformatics within a biological framework, and that this particular emphasis meshed with student interests.

Examples of Student Collaboration

To illustrate representative examples of collaborative learning in the virtual laboratory, Table I provides excerpts from several discussions.

DISCUSSION

The quantitative data in Fig. 1*A*–1*C* show that a large majority of students found the online collaborative lab environment benefited their learning. Similarly, Question D found that peer-support was valuable in resolving problems with bioinformatics tools. As this study does not include a control group measuring the results of an in-person lab, Question E asks students to compare the virtual lab to their previous experiences in physical labs. The strongly positive response suggests that students were enthusiastic about the virtual lab, and suggests that they found it more beneficial than a traditional lab. Further supporting this hypothesis, end-of-semester student evaluation forms reported that the virtual lab was highly educational (data not shown). Other factors, however, may have contributed to the students' preference, for example, having greater flexibility with their weekly schedules.

Several themes emerge from the discussions excerpted in Table I. First, students successfully provided their own technical support over routine mechanical issues such as input format problems and navigating GenBank. These postings are consistent with the survey data in Fig. 1*D*, as well as the rather low volume of technical questions directly addressed to the instructor (data not shown). Second, student collaboration explored the challenging conceptual material of the course, in this example, the K_a/K_s selective pressure ratio, as well as variable evolution rates within a gene. These discussions frequently integrated core biological concepts with practical bioinformatics, which was a key learning goal of the course. Third, the examples show that students put genuine effort into helping their peers and cross-pollinating ideas, which likely raised the overall quality of work. From these passages, it is clear that students offered ideas from their own projects, thereby demonstrating that they could apply acquired knowledge in new contexts.

Finally, from the last example in Table I, having a friendly peer support network was invaluable for students who were stuck. In a traditional setting, panicked students can consult with the instructor, although reticence due to embarrassment can cause unnecessarily poor grades or course failures. In contrast, in the virtual lab setting, students routinely approached their peers for help.

Collaborative learning within an online laboratory was new to most students in the class. All had previously collaborated, albeit informally, in their traditional lab courses, and many had worked on group projects in other classes. Still, online collaborative learning was unfamiliar territory and needed instructor coaching, as well as concrete requirements specified in the syllabus. Over the semester, activity

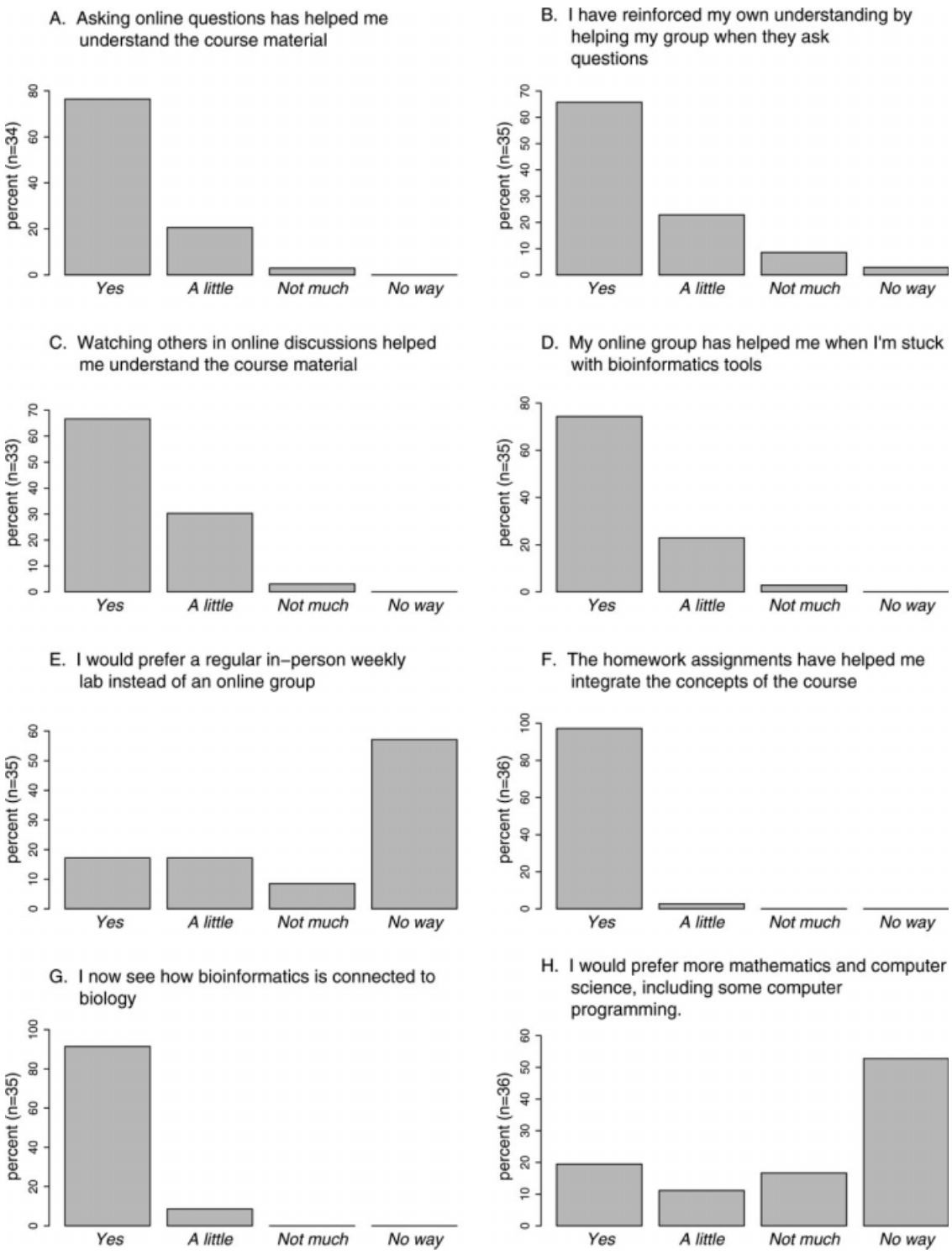

FIG. 1. **Results of student survey data taken two weeks before the final class**. The term *homework* refers to the virtual lab.

became more automatic as students developed working relationships and experienced the benefits of learning with their peers. The most substantive and beneficial online discussions occurred towards the end of the semester, when students provided feedback on the final projects. This upturn may have been partly due to increased stress of looming deadlines, the flexible nature of the research project, and the relative inexperience in writing substantive scientific reports. Throughout the semester, online behavior was consistently altruistic and positive, and appeared to elevate the group performance level.

Minimizing the instructor burden of providing remote technical support impacted several structural aspects of this course. Students own a highly heterogeneous mix of computers, which necessitated the use of web-based tools for all assignments, and ruled out the practicality of installing and running software locally. As an informal experiment, students were requested to install the molecular visualization

TABLE I
Excerpts from collaboration in the online virtual lab

- Sorry about your TCOFFEE problems. . . are you using all the same type of sequence data. . .i.e. all protein sequences or all nucleotide sequences? I ran into a couple problems when I had mixed formats.
- It looks like you have the right amino acid sequence for Question #7. The protein accession number (NP_000185) indicates that you are in RefSeq–two letter, underscore, numbers. I found the protein accession number by first searching the nucleotide db for "Lesch-Nyhan" and chose the entry Homo sapiens which contained the DNA accession number (NC_000023, again RefSeq format), clicked on this, chose GENBANK which led to the protein accession number–look for /protein-id=. Hope this helps.
- That's amazing that so many different mutations have been associated with the disease ? I'm not sure what to think about that, many mutations are allowed, but many are also pathogenic . . . It might not make sense if point mutations are a very rarely associated with Tay-Sachs, but it might be interesting to calculate the Ka/Ks ratio for your gene. I downloaded a program called KaKs calculator (http://evolution.genomics.org.cn/software.htm) - neat thing about it is it computes KaKs using several different models at once, counts the number of synomous and non-synonmous mutation sites and the number of synomous,non-synomous mutations but the bad thing is that I wasn't able to find any instructions on how to use the thing and its pretty picky about the format of the sequences it takes. There are also some KaKs tools online (http://services.cbu.uib.no/tools/kaks), but I haven't really tried them out. Is the gene under positive, neutral, negative selection? Are the point mutations associated with changes in the amino acid sequence? Do the pathogenic mutations tend to at specific places? For example my protein has a repeated segment at the N-terminus which binds with copper ion mutations (both point mutations and insertion/deletions) near this location are associated with the disease.
- Also you could use some of the other queries to identify regions of the protein which are particularly mutable or . . .? What protein domains are located in this gene? Are the mutations localized in a particular domain? Is there a domain which is generally associated with breaking down lipids or asked another way is there a class of proteins which is associated with breaking down lipids? Is there a particular domain/or set of domains common to them? Interesting that the HEXB is similar identity/structure(?) to HEXA, are mutations within HEXB also associated with Tay-Sachs?
- one thing I noticed that you did not mentioned about the structure of your gene. . . you can use tool like CND3 or Rasmol to see the structure and what kind of protein product your gene have. you can also include some of the catagories like mechanism and pathway of the gene in your paper. i think, using this kind of things will help to creat better research paper. let me know if I can help with anything
- so truth be told, i had absolutely no clue how to even start this paper. that was until i read all of your papers and saw what you guys did, what worked, what didnt. What was the same in your strategies and where you differed. ANd from here, i can actually finally start this daunting task, and put all my data together instead of just having scambles of random files on my computer. my full 1st draft should be done by tuesday and from there on i figure i can just post it to another discussion and have you guys just help me out some more from there.

Note: Comments were not edited for spelling or grammar.

tool Cn3D; and, even with such a widely-deployed program, several reported problems. Along similar lines, Holtzclaw *et al*. [8] remark, not surprisingly, that installing, maintaining, and troubleshooting bioinformatics software on multiple computers places a substantive burden on instructors.

To further minimize the technical support burden and maximize self-sufficiency, students performed most assignments at NCBI. Because documentation of NCBI resources is widely and freely available, and because NCBI pages commonly have 'help' icons, students were empowered to investigate details of tool use. Additionally, because NCBI web services are generally mature, students typically receive meaningful diagnostic messages rather than cryptic software errors; and, because the tools have been heavily exercised by the biology community, students are relatively unlikely to encounter server crashes or browser dependencies. At the same time, the individual NCBI tools such as PubMed, BLAST, GenBank, and CDD reflect their independent evolutionary development, rather than being components of a highly unified user-interface. As a consequence of this inconsistency, students must learn multiple usage paradigms. In contrast, environments such as the Next Generation Biology Workbench [9] present an integrated suite of tools, and adopting such an environment would presumably reduce the level of student problems. However, field usage of integrated environments is not particularly widespread, and, therefore, students are relatively unlikely to encounter these suites elsewhere. There is distinct value in knowing how to use ubiquitous tools, even if learning those tools requires some effort and support.

In addition, the strategic choice to avoid cookbook-style assignments likely increased student demand for support. Multiple compelling arguments drove this choice. Most importantly, students who become highly dependent on detailed instructions are likely to have difficulties approaching new tools, have problems when tools undergo user interface changes, and have little practice diagnosing routine errors. Locating and understanding documentation are essential bioinformatics skills, and an introductory course should provide ample opportunities to develop those skills. Such an approach is broadly consistent with learning through guided inquiry, and has been considered by other bioinformatics instructors [2, 3, 10, 11]. A second argument against producing detailed cookbooks is that the constant evolution of bioinformatic software makes these documents quickly obsolete, thereby requiring a large and open-ended maintenance effort by the instructor. Finally, a rigid set of instructions often becomes invalid when working with new data that causes the tools to respond differently. This brittleness would create new support problems, particularly as the students investigate unique genes for their final projects.

Having students choose the gene for their final project brought several benefits. First, it required that students search and explore research literature, a fundamental bioinformatic skill that is ideally developed in an upper-level biology course such as this. Many had never substantively explored PubMed before, and many were unaware of the existence or value of review papers. A second benefit of choosing their own gene was that students became quite engaged, curious, and motivated about their projects. Others have recommended that assignments follow the research interests of the professor as a means of optimizing instructor time [12]. While enticing, this idea was not adopted here, as fostering student engagement was of paramount importance. A final benefit of student choice came from the diversity of topics. Some chose heavily-researched genes, for example, p53, while others found barely-studied subjects such as the wheat protein alpha-gliadin involved in human

celiac disease. Both endpoints of that spectrum provide rich opportunities for exploration, yet require different bioinformatic approaches. This diversity was a good lesson that reflects real-world bioinformatics research.

A review of the literature found no reports of a face-to-face bioinformatics course with a web-enhanced collaborative virtual laboratory. However, distance education bioinformatics courses have employed online discussion forums and can be compared with the present work. Lim *et al*. [5] describe the graduate-level S*STAR project, which delivered lectures by video with synchronized slides, and constructed discussion forums. That study surveyed students on the effectiveness of the discussion forums and reported a wide, approximately Gaussian distribution of scores, with the average level between ineffective and very effective. This S*STAR survey data appears to contrast with the results here (Fig. 1*A*–1*E*), in which the large majority of students report strong benefits from the online laboratory. Lim *et al*. speculate that the wide distribution may have been caused by differences in learning styles and differences in comfort with online forums. The contrast between those results and the data reported here suggest other possible causes, for example, that preexisting relationships between group members, as were common in this course, improve the outcome of online collaboration. Another possible difference is that this course frequently encouraged and formally required collaboration, thereby fostering a beneficial atmosphere.

Tolvanen and Vihinen [7] describe a fully online bioinformatics course that made a tutor available for online discussions, but did not create a larger collaboration group. Their survey data reported high satisfaction with the virtual nature of the course but did not specifically assay the online tutor collaboration. The authors discuss the workload for this course; in addition to the online teaching, each tutor has an average of 15 contacts per student over a semester. In planning the course described here, it was clear that with 50 students, one instructor, and no teaching assistants, a large amount of peer support would be absolutely necessary as well as beneficial for the students. That realization was a key motivation for establishing online collaborative behavior as a foundation of this course.

Honts has reported success in introducing elementary computer programming in lab-based bioinformatics courses [3]; however, despite its potential value to bench scientists, that activity was considered impractical here. Students encountering programming for the first time typically require a high level of tutoring and support that is well beyond the volume a single instructor can provide to a large class. This problem becomes more acute when the class works remotely on heterogeneous hardware and operating system platforms. Additionally, as this bioinformatics course intentionally emphasizes biology over computer science, a substantive programming component would entail an opportunity cost of reducing the biological content. Finally, most students were broadly uninterested in programming (Fig. 1*H*), and while student opinion can not govern a curriculum, the negative effects of disinterest would be exacerbated by the lack of adequate support and tutoring.

Taken together, the quantitative and qualitative data reported in this study support the hypothesis that a virtual laboratory is beneficial to undergraduate bioinformatics students. Importantly, the data also support that web-enhanced collaborative learning is both practical and beneficial in a face-to-face bioinformatics course. To study the hypothesis further, it would be appropriate to perform a controlled experiment, randomly placing students in an in-person lab or a virtual lab, and assessing learning outcomes. The initial data are certainly encouraging, and it is hoped that this report stimulates further discussion and experiments in this area.

Supplementary Materials – Additional materials describing this course are available from the author.

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