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Article

Integrating Quantitative Thinking into an Introductory Biology Course Improves Students' Mathematical Reasoning in Biological Contexts

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Recent calls for improving undergraduate biology education have emphasized the importance of students learning to apply quantitative skills to biological problems. Motivated by students' apparent inability to transfer their existing quantitative skills to biological contexts, we designed and taught an introductory molecular and cell biology course in which we integrated application of prerequisite mathematical skills with biology content and reasoning throughout all aspects of the course. In this paper, we describe the principles of our course design and present illustrative examples of course materials integrating mathematics and biology. We also designed an outcome assessment made up of items testing students' understanding of biology concepts and their ability to apply mathematical skills in biological contexts and administered it as a pre/postcourse test to students in the experimental section and other sections of the same course. Precourse results confirmed students' inability to spontaneously transfer their prerequisite mathematics skills to biological problems. Pre/postcourse outcome assessment comparisons showed that, compared with students in other sections, students in the experimental section made greater gains on integrated math/biology items. They also made comparable gains on biology items, indicating that integrating quantitative skills into an introductory biology course does not have a deleterious effect on students' biology learning.

INTRODUCTION

Over the past several years, there has been a call to revolutionize undergraduate biology education to reflect the field of modern biology. A recurrent theme throughout the resulting recommendations and guidelines is that undergraduate biology students must develop quantitative skills and learn to apply them in biological contexts (National Research Council [NRC], 2003, 2009; Association of American Medical Colleges and Howard Hughes Medical Institute [AAMC/HHMI], 2009; Labov *et al.*, 2010; Woodin *et al.*, 2010). Among the conclusions reached in the National Research Council's *BIO2010* and *A New Biology for the 21st Century* reports was that greater integration of quantitative skills into introductory biology classes is vital to the ongoing success of graduates from biology programs, as well as to recruitment of quantitatively talented students into biological fields (NRC, 2003, 2009). At the same time, the medical community has been revising its list of qualifications for future physicians. The AAMC/HHMI 2009 report, *Scientific Foundations for Future Physicians*, identified the ability to "apply quantitative knowledge and reasoning" as a key competency for those entering medicine (AAMC/HHMI, 2009).

Traditionally, life sciences students rarely experience mathematics within the context of their own disciplines. Indeed, anecdotal evidence suggests that students who perceive themselves as math-weak gravitate toward biology,

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because they consider biology to be relatively math-free. These attitudes persist, despite mathematics course requirements for most life sciences students, because failure to integrate mathematics in meaningful ways for life sciences majors contributes to the perception that mathematics is irrelevant outside its discipline (Zan *et al.*, 2006). Thus, in the minds of many biology students, mathematics and biology remain in two distinct, separate compartments. Increasing the quantitative thinking that students encounter in their biology courses may be a more effective way to challenge this perception and encourage transfer of mathematics skills than increasing traditional mathematics requirements for biology students alone.

Among its recommendations, the *BIO2010* report encouraged exposing life sciences majors to quantitative thinking in their first year of study. Quantitative problem solving is a skill, and a difficult one to learn and master—if we want students to use quantitative problem solving in their advanced classes, we should lay the foundation for their success in introductory classes. The stakes are high when students first encounter math in biology in high-level classes in which both the biology concepts and mathematics skills are advanced. Introducing quantitative thinking earlier in the biology curriculum may increase the quantitative competency of students entering more advanced courses, paving the way for greater overall development of students' quantitative abilities by the time they complete their undergraduate course work. It may also give life sciences students a chance to reconsider their planned undergraduate training in math, an opportunity that will be lost to many students if their first exposure to math in a biological context occurs during their junior or senior year. Moreover, using quantitative thinking methods in introductory biology has the added benefit of exposing those students who will not continue in advanced biology courses to a better picture of modern biology as an integrated, analytical science (NRC, 2009).

Several efforts to bring mathematics into introductory biology classes have focused on the development of online or written modules targeting particular skills (e.g., Robeva *et al.*, 2010; Thompson *et al.*, 2010). Our own previous efforts to develop and implement similar modules had disappointing results; we found that stand-alone modules, done on the students' own time, perpetuated the perception that math was an "add-on" that was not representative of the core content in biology (K. Dixon, personal communication). In light of this, we chose to follow a more integrated approach in which students would encounter brief in-class exercises in quantitative application throughout the semester that would repeatedly call on the same set of quantitative skills in different biological contexts. This approach is similar to that taken by Matthews and colleagues (2010) in developing an introductory survey course for biology majors and by Speth and colleagues (2010) in developing an introductory course in genetics, evolution, and ecology. One way in which our approach differed, however, is that we primarily emphasized skills that the students were expected to have acquired previously in fulfilling the mathematical prerequisites for the course. Rather than introduce new quantitative skills, our goal was to encourage greater mastery and transfer of existing skills to biological contexts.

We designed an introductory molecular and cell biology course in which we targeted quantitative skills that we identified as supporting the biological concepts taught in the course and as being generally useful to students as they progress through their advanced biology courses. Throughout the course, we integrated quantitative and biological reasoning in course learning outcomes, in-class student activities, assignments, and exams.

In the process of initial course design, we defined a set of learning outcomes for introductory molecular and cell biology that encompassed both "traditional" concepts covered in such courses and the ability to apply a particular set of quantitative skills to biological problems. We designed a multiple-choice instrument intended to assess students according to a subset of those course learning outcomes. We administered the outcome assessment as a pre/postcourse test to measure the disparity between incoming students' grasp of biology concepts and their ability to apply quantitative skills along with those concepts, as well as to compare students in our experimental section of the course with their peers in other sections of the same course. Our precourse outcome assessment results confirm that students are unable to spontaneously transfer prerequisite mathematics skills to biological problems. Comparing pre/postcourse outcome assessment gains across sections showed students in the experimental section making greater gains in applying quantitative skills to biological problems than students in other sections, while making similar gains in biological concepts.

In the following, we describe the development of our outcome assessment instrument and our course, provide examples of course materials to illustrate our philosophy and methods, and present the results from administering our pre/postcourse outcome assessment.

MATERIALS AND METHODS

The courses described in this study were taught at the University of Arizona, a large state university (total student enrollment is ~39,000) located in Tucson. One of the authors (S.H.) instructed the experimental section of the course; another author (L.E.) instructed one of the large comparison sections using traditional (nonquantitative) learning outcomes.

Study design and data collection were approved by an internal review board through the University of Arizona Human Subjects Protection office.

MCB181R: Introduction to Molecular and Cellular Biology

MCB 181R: Introduction to Molecular and Cellular Biology is one of a pair of introductory biology lecture courses offered at the University of Arizona. In terms of student population and course content, MCB 181R is representative of introductory biology courses at state universities throughout the United States (Gregory *et al.*, 2011). The majority of the roughly 2000 students per year who take the course—life sciences majors and those preparing for entry into medical and medicine-related fields—are precisely the students identified as needing greater exposure to mathematics and application of mathematics in biological contexts. Despite this, the content of MCB 181R has traditionally been and remains almost entirely qualitative.

MCB 181R is taught by several instructors each year. Instructors choose a common textbook for the course and typically cover similar topics (e.g., macromolecules, central dogma, cell structures), but do not teach from a common set of materials. The associated lab section, MCB 181L, is also independent of the lecture sections; students may take the lab section before, concurrent with, or after the lecture section. Thus, conceptual emphasis, degree of detail covered in particular topics, ordering of and pacing through the topics, and pedagogical styles and strategies differ greatly across the different lecture sections and between the lab and lecture sections.

We Identified Biological and Quantitative Learning Outcomes for the Course

Identifying biological learning outcomes for the course was relatively straightforward. Using syllabi and learning outcomes from experienced MCB 181 instructors, we assembled a set of molecular and cell biology learning objectives. The biological learning outcomes that we identified emphasize such concepts as "structure affects function" and topics such as macromolecules, enzyme-catalyzed reactions, central dogma, and genetics, which are typical of such courses (Gregory *et al.*, 2011).

Establishing quantitative learning outcomes for the course required more consideration. To choose an appropriate set of skills to integrate into course materials, we began by considering skills that 1) students should have developed by fulfilling their mathematical prerequisites for the course and 2) integrated naturally into molecular and cell biology materials. Our motivation for these two criteria was that we wished to build quantitative learning outcomes that were accessible to the students and that supported the biological learning outcomes instead of being distracting and contrived. The skills that we identified were algebra and manipulating units; scale, exponents, and logarithms; reading and creating graphs and tables; and counting[1] and probability. Once we had identified these skills, we discussed them with other MCB 181 instructors, instructors of other classes for biology- and medical-track students, and mathematics faculty interested in the integration of mathematics and biology. In these conversations, we verified that these faculty members felt it was reasonable to expect students to apply the skills we had identified, but were often frustrated by their students' inability to do so in the contexts of their biology courses.

We Designed a Pre/Postcourse Outcome Assessment to Measure Student Gains in Course Learning Outcomes

Having established the biological and quantitative learning outcomes for the course, we designed an instrument to measure student gains for certain outcomes. We developed a 24-item outcome assessment targeting learning outcomes in four central topics of molecular and cell biology (meiosis, genetics, and inheritance; nucleic acid structure and function; enzymes, energy, and the reactions of life; and gene regulation and central dogma) and application of three quantitative skill areas (algebra and units, counting and probability, and analyzing graphs) in the context of these topics.[2] We modeled our instrument design after the Introductory Molecular and Cell Biology Assessment (IMCA; Shi *et al.*, 2010), and four of the items in our final outcome assessment are adapted from the IMCA. We found it necessary, however, to develop additional items to address target concepts and competencies not addressed by existing concept inventories. Our outcome assessment was developed over five semesters (Fall 2010 to Spring 2012) before its use in Fall 2012. Each semester, we sought and received feedback from molecular and cellular biology (MCB) faculty, MCB 181R and other introductory biology instructors, upper-division MCB undergraduates, and MCB graduate students by asking them to critically evaluate the items. We also administered versions of the outcome assessment to students in several sections of MCB 181R over four semesters (Spring 2011 to Spring 2012) before Fall 2012. Our outcome assessment instrument is included in the Supplemental Material.

Our outcome assessment consists of 13 items addressing biological concepts alone (referred to as "Bio" items throughout this text) and 11 items requiring quantitative application in the context of the same biological concepts (referred to as "BioMath" items throughout this text). In developing the Bio items, we focused in particular on learning outcomes shared by all participating sections of MCB 181R; when seeking feedback from instructors about these items, we asked that instructors discuss whether their postcourse students should be able to answer the items correctly given the items' content and wording. Concepts in each biological topic were addressed by at least three nonquantitative items and three of the four were addressed by three quantitative items (the fourth was addressed by two quantitative items). Each quantitative skill was applied in at least three items. Table 1 categorizes each item by the biological concept and quantitative skill (if any) addressed. Items adapted from the IMCA are indicated in Table 1.

We chose not to include math skill–only items on the outcome assessment, because we anticipated a decrease in student effort had they been asked to complete an overly long assessment for which they were receiving participation credit only.

We Integrated Quantitative and Biological Concepts in All Aspects of the Course

We developed course materials over four semesters (Spring 2011 to Fall 2012) in a small experimental section of ~35 students (in Fall 2012, 37 students were enrolled in the course). The section was not advertised as being experimental or as including quantitative content; it was listed alongside other sections with the same course number, and students were allowed to enroll based on their schedule preferences. The number of seats available per class is available to students, so we cannot rule out the possibility that some students chose the course based on its small size (the experimental section had an enrollment cap of 40, as opposed to the typical

[1]That is, finding the total number of possible sequences of a given length and number of possibilities for each place in the sequence.

[2]Due to a constraint on the number of items included in the assessment, we did not assess logarithms, exponents, and scale on the outcome assessment. These skills were, however, integrated into course materials.

Table 1. Pre/post assessment questions by biology concept and quantitative skill

Bio concept	Meiosis, genetics, and inheritance	Nucleic acid structure and function	Enzymes, energy, and the reactions of life	Gene regulation and central dogma
Math Skill				
None	9, 10, 19, 23[a]	3, 5, 7	1, 21,[a] 22[a]	13,[a] 17, 24
Algebra and units		4, 8	15	6
Counting and probability	11, 12, 18	2		
Analyzing graphs			14, 16	20

[a]Question adapted from the IMCA (Shi *et al.*, 2010).

enrollment cap of 300–350), but according to a postcourse survey, most students chose the experimental section based on schedule constraints over other factors in the Fall 2012 semester.

The guiding principle behind our course design was that the quantitative exercises should support and reinforce the biology curriculum, rather than distract students from it. Applications of quantitative skills and numeracy were treated as part of the material covered: just as the concept "structure affects function" is an idea that students are expected to revisit and apply in various contexts, calculating and making sense of simple probabilities or interpreting graphical representations of data are skills that students practiced many times throughout the course and applied in various situations. We anticipated that applying specific quantitative skills to biology would be foreign to students when first introduced but would be increasingly intuitively applied and understood as the semester progressed, much like more "traditional" biology concepts.

On the basis of initial observations in the pilot sections between Spring 2011 and Spring 2012, we designed new course materials, adapted existing ones, and piloted and refined materials and course design. By Fall 2012, the materials and course had evolved into the form described here. Table 2 indicates the intersection between traditional MCB 181 course topics and quantitative skills in the integrated exercises implemented in the Fall 2012 semester.

We Followed a Learner-Centered Approach in Course Design

For each topic covered in the course, we gave students a set of learning outcomes, assignments, and exercises. Before most class meetings, we posted learning outcomes online and assigned students a preclass assignment typically consisting of reading and either online or written questions intended to introduce students to the topic and its vocabulary. In class, lectures were punctuated every 5–20 min with think–pair–share questions (Lyman, 1981, 1987) or in-class written exercises that students completed in groups of three to four. These exercises provided students with guided practice and helped both students and the instructor to assess students' developing understanding. Students also completed four in-class case studies over the semester. At the end of each week, we assigned an online multiple-choice/multi-select quiz to provide students with additional practice and an opportunity to assess their understanding of the week's topic. Three quarterly exams (administered every 4 wk) and the cumulative final exam each consisted of multiple-choice and free-response sections and assessed students at the comprehension and application levels.

We integrated quantitative-skill application into course objectives, in-class exercises, quizzes and exams. Typically, we introduced the majority of quantitative-skill application during the in-class practice, although when we suspected many students did not have previous instruction (in particular, in probability and counting), we assigned tutorials accompanied by online instructional videos prior to using the skill in class (online videos are freely available from the Kahn Academy: www.khanacademy.org/video/basic-probability?topic=probability and www.khanacademy.org/video/compound-probability-of-independent-events?topic=probability).

While student groups worked on exercises in class, the instructor and three undergraduate "preceptors" (near-peer instructors selected based on excellent performance in a previous semester's MCB 181 course and concurrently trained in techniques such as active listening and Socratic questioning) circulated throughout the room facilitating student discussion and providing help where needed. We found that a brief refresher supplied by the instructor, the help of undergraduate preceptors, and/or group work in which students could guide one another in solving problems was sufficient to remind students of the quantitative skills they already possessed and to allow them to complete the problems. This approach was largely successful because students had applied the skills in other contexts previously—they were not grappling with learning entirely new quantitative skills at the same time they were struggling to apply them in novel contexts—and those students who did struggle with the skills themselves had immediate coaching available from other students in their groups, the circulating preceptors, and/or the instructor.

Because each skill was revisited many times throughout the course, students had ample opportunities for building skill proficiency. Also, knowing that they could not simply ride out a few isolated instances of math use during class seemed to encourage students to put more effort into mastering quantitative skills and application than they would have otherwise. It is reasonable to believe that students were less likely to "blow off" quantitative exercises—knowing as they did that the applied skills were going to "come around again" in future exercises and exam questions—than they would have been if quantitative exercises were less frequent, novel to the point of being excessively difficult, independent of explicit course learning outcomes, or not expected to appear on exams.

Table 2. Quantitative exercises by topic: Fall 2012

Math Skill / Course Topic	Intro to the Scientific Method	Evolution and Natural Selection	Bonding, Water Chemistry and pH	Thermodynamics	Macromolecules	Enzymes/Energy of Reactions	Diffusion and Osmosis	Membrane Transport	Cell Structure and Function	Cell-Cell Interactions	Cell Cycle and Mitosis	Mendelian Genetics	Meiosis	DNA Structure, Replication and Repair	Intro to Central Dogma	Transcription	Translation and the Genetic Code	Regulating Gene Expression	Cellular Respiration and Fermentation	Photosynthesis	Analyzing and Engineering Genes
Algebra				x	x		x							x	x	x	x	x	x		
Counting and probability					x							x	x		x						
Reading/creating graphs and tables	x	x	x	x	x	x	x	x			x	x		x					x	x	
Understanding and manipulating units				x	x		x				x			x				x	x		
Scale, exponents and logarithms		x	x			x	x		x		x			x				x	x		

Below, we present examples from the course topic "error correction during DNA replication" in order to illustrate our approach. During this unit, quantitative activities emphasized manipulating powers of 10.

Example of Quantitative Integration throughout Class Materials: Error Correction during DNA Replication

Learning Outcomes. At the beginning of each unit, the instructor posted a list of learning outcomes on the course website. The instructor encouraged the students to print out the learning outcomes, bring them to class, and identify which class activities corresponded with which outcomes. Many students used the lists of learning outcomes as study aids when reviewing for exams. By making desired quantitative learning outcomes explicit and placing them alongside qualitative ones, we emphasized the importance of quantitative skill application in the course and set the expectation that students be able to apply quantitative skills on exams. Such explicit expectations give students incentive to master the quantitative skills in addition to the qualitative material.

Learning Outcomes—Error Correction during DNA Replication

- Describe why it is important that cells correct errors that occur during DNA replication.
- Describe DNA polymerase proofreading.
- Explain why DNA is synthesized in the 5′ → 3′ direction in cells (i.e., what this has to do with proofreading).
- Describe mismatch repair, including how mismatch repair enzymes recognize old and new strands of DNA and why it is important that they do.
- Given error rates in DNA polymerization, DNA polymerase proofreading and mismatch repair, predict the final overall DNA replication error rate (and the number of errors per replication expected in a genome of a given size) a) normally and b) when proofreading or mismatch repair fails.

Preclass Assignment. Students were assigned a preclass assignment before the topic was introduced in class. The assignment included reading sections covering DNA replication error correction in a molecular biology text (*Biological Science*, 4th ed., vol. 1, Scott Freeman) and completing a series of Web activities and tutorials from a commercial online package (Mastering Biology, Pearson Education). The assignment familiarized students with the vocabulary, major enzymatic players, and processes of DNA polymerase proofreading and mismatch repair.

In-Class Activities. We opened class with a discussion of mutations—what mutations are and their potential effects on individual cells or organisms and on populations. Students discussed a short list of prompts, first in groups of three to four and then as an entire class. The instructor then delivered a review lecture on DNA polymerase, DNA polymerase proofreading, and mismatch repair. The lecture was punctuated with short discussion questions and the exercises shown in Box 1. Students worked on each exercise in groups of three to four while undergraduate preceptors and the instructor circulated through the classroom monitoring students' progress and offering help where needed. Giving students time to work through these types of exercises during class (for credit and under the eyes of preceptors and instructors) encouraged them to put forth the necessary effort to grapple with skills they found difficult and provided an opportunity for peer coaching among the students.

Box 1. In-class activity: error correction during DNA replication

In exercises (a)–(c), students calculated the number of mutations, on average, that a human cell would accumulate every time it divided (a) in the absence of error correction, (b) with DNA polymerase proofreading only, and (c) with both DNA polymerase and mismatch repair. Part (a) is shown as an example.

During the discussion introducing the exercises, the instructor led students in a discussion about when the two error correction mechanisms will come into play—that is, that proofreading will "get a shot at" correcting errors made by DNA polymerase and only the errors that are left over will be corrected by mismatch repair enzymes. They were also told that it is safe to assume for the sake of the exercise that there are not special errors that both correction mechanisms are likely to miss (i.e., it is safe to assume that the error rates for the two are independent).

(a) DNA polymerase III inserts an incorrect base an average of once in every 100,000 bases added. For a human cell with ~12 billion DNA bases (1 billion = 10^9) in its chromosomes, estimate how many mutations this would result in per cell replication in the absence of error correction. **Please show your work.**

(b) Using the information from (a)–(c), complete the following table:

Replication step	Error rate (chance of error)
5′ → 3′ DNA polymerization (DNA polymerase)	1 in 10^5
3′ → 5′ DNA polymerase proofreading	
Mismatch repair	
Final overall error rate	

(c) If a mutation in the gene coding for DNA polymerase increased its error rate to 1 in 10^3, what would the **final overall** error rate be for DNA replication? **Please show your work.**

(d) *Escherichia coli* cells have **an overall** mutation rate per cell division that is similar to the one that you found above. Yet populations of *E. coli* evolve much faster than human populations. Why is this?

Weekly Quiz Questions. Online weekly quizzes gave students a chance to apply the knowledge and skills from class on their own. Weekly quizzes served as periodic self-assessment opportunities for the students and provided practice with exam-style questions. They included questions both quantitative and nonquantitative in nature. An example of a quantitative weekly quiz question is shown in Box 2.

Box 2. Weekly quiz question: error correction during DNA replication

The three steps that give rise to high-fidelity DNA synthesis

Replication step	Error rate (chance of error per nucleotide added)
DNA polymerization	1 in 10^5
DNA polymerase proofreading	1 in 10^2
Mismatch repair	1 in 10^2
Final overall error rate	1 in 10^9

If a mutation in the gene coding for DNA polymerase knocked out the DNA polymerase proofreading function but otherwise left the protein functional, the mutant's **final overall** error rate during DNA synthesis . . .

(a) would increase to 1 in 10^{11}.
(b) would decrease to 1 in 10^{11}.
(c) would increase to 1 in 10^9.
(d) would decrease to 1 in 10^9.
(e) would increase to 1 in 10^7.
(f) would decrease to 1 in 10^7.
(g) would increase to 1 in 10^5.
(h) would decrease to 1 in 10^5.
(i) would increase to 1 in 10^2.
(j) would decrease to 1 in 10^2.

Box 3. Quarterly exam questions: error correction during DNA replication

Questions 5 and 6 refer to the table below.
The three steps that give rise to high-fidelity DNA synthesis

Replication step	Error rate (chance of error per nucleotide added)
DNA polymerization	1 in 10^5
DNA polymerase proofreading	1 in 10^2
Mismatch repair	1 in 10^2
Final overall error rate	1 in 10^9

5. The dog genome contains ~5 billion (5×10^9) nucleotides. If all DNA synthesis error correction enzymes are functioning, roughly____mutation(s) will be introduced into the DNA each time a dog cell divides.

(a) less than one
(b) 5
(c) 50
(d) 500
(e) 5000

6. If a mutation increases the error rate of DNA polymerization to 1 in 100, roughly____mutations will be introduced into the DNA each time a dog cell divides.

(a) 5
(b) 15
(c) 50
(d) 500
(e) 5000

Exam Questions. Similar to the weekly quiz questions, exam questions asked students to apply the (by now) familiar skills practiced in class in similar but (from the perspective of the students) somewhat different contexts. Examples of questions from the quarterly exam, including error correction during DNA replication, are shown in Box 3. Weekly quizzes and exams also included questions asking students to apply skills practiced in one set of contexts to a more novel context—an example of this type of question from the final exam is shown in Box 4. These types of questions, in addition to the reappearance of skills in in-class exercises over many different topics, encouraged generalization and transfer of those skills. For example, the final exam question in Box 4 requires that students apply the skill of interpreting the slope of a line from a scatter plot to a new context—the effect of a breakdown in error correction during DNA replication—and in conjunction with the often-practiced task of using information from a specific table. It is important to note here that, although the example given is of a final exam question, these types of questions were used in in-class activities, weekly quiz questions, quarterly exam questions, and, to a lesser extent, preclass assignments.

Data Collection and Analysis

In Fall 2012, we administered the outcome assessment as an online quiz through the Desire2Learn course-management system for each MCB 181R section. We administered the outcome assessment as a precourse test during the first week of classes and as a postcourse test during the last week of classes. Before we asked students to complete the pretest, a study representative visited each classroom and introduced the outcome assessment to students, explaining that the purpose of the study was to measure the students' growth throughout the semester in order to evaluate the effectiveness of the course and requesting that students answer the questions to the best of their ability without looking up any of the answers or seeking help answering the questions. The representative visited each classroom once again at the end of the semester, reminding students of the purpose of the outcome assessment, asking once again that students try their best without looking up answers or seeking help, and reassuring students that any compensation their instructors had offered for completion (in most cases, a small number of extra credit points) was contingent on full completion of the outcome assessment but not on answering the assessment questions correctly. Students were also reassured that the purpose of the postcourse outcome assessment was to evaluate the effectiveness of the course, not to judge them as students.

Pre- and posttest data were matched for all students who completed both tests and consented to the use of their data

Box 4. Final exam question: error correction during DNA replication

Questions 31 and 32 refer to the following table.
The three steps that give rise to high-fidelity DNA synthesis

Replication step	Error rate (chance of error per nucleotide added)
DNA polymerization	1 in 10^5
DNA polymerase proofreading	1 in 10^2
Mismatch repair	1 in 10^2
Final overall error rate	1 in 10^9

32. The data in which of the following graphs would provide evidence that the **mismatch repair enzymes** in a patient's cells were not properly functioning?

(a) I
(b) II
(c) III
(d) II and III
(e) None of them

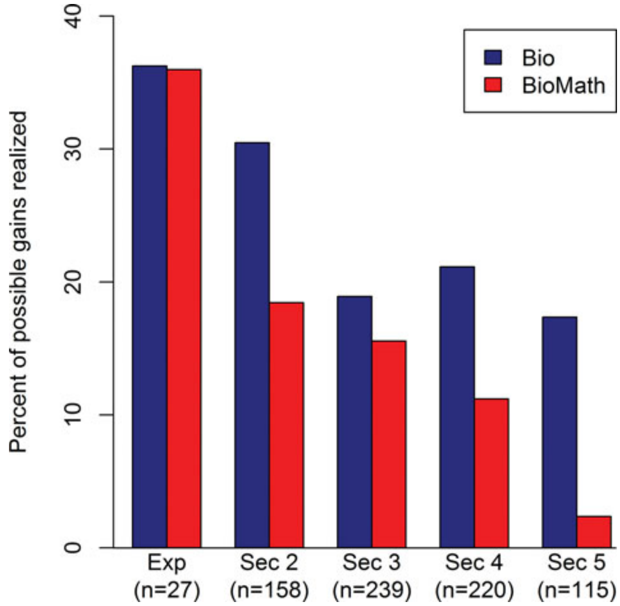

Figure 1. Student gains on Bio and BioMath assessment items. Student gains were measured as the percent of possible gain realized: gain = (post score − pre score)/(total possible − pre score). In the experimental section, students made similar gains on Bio and BioMath items (mean gains of 36.24% on Bio items and 35.97% on BioMath items; $p \approx 0.98$ for two-tailed t test comparing Bio and BioMath gains). In other sections, students made significantly lower gains on BioMath items than on Bio items (for all other sections combined, mean gains of 21.83% on Bio items and 12.80% on BioMath items; $p \ll 0.0001$ for two-tailed t test comparing Bio and BioMath gains).

in the study. Data from students who completed only the pre- or posttest were not included in our analysis. Data from 28 students from the experimental section and 732 students from other sections were included in our analysis. We measured gain as the percentage of possible gain realized: 100% × (post score − pre score)/(total possible score − pre score). In judging significance of multiple-group comparisons, we corrected for the increased possibility of a type I error using the Holm-Bonferroni method (Supplemental Table S1). Table S2 gives Bio, BioMath, and total gains, and SEM for each section.

RESULTS

Incoming Student Performance Supports an Inability to Transfer Skills from Prerequisite Mathematics Courses

Students enrolled in introductory biology at the University of Arizona must demonstrate a certain level of proficiency in pre–college algebra skills through an online math readiness test, Assessment and Learning in Knowledge Spaces (ALEKS; www.aleks.com). Topics assessed by the readiness test include functions, rates of change, linear functions, exponentials, logarithmic functions, and systems of equations. On the basis of our own experience and anecdotal evidence from other introductory biology instructors, however, we questioned whether students were truly proficient at applying the required set of skills. Students' performance on the precourse outcome assessment supported the belief that students entering MCB 181 were unable to apply quantitative skills from previous courses in the context of biology. Despite having completed mathematics prerequisites that covered the skills tested on the outcome assessment, incoming students scored lower on BioMath items than on Bio items (Table 3; $p < 0.001$ for two-tailed t test comparison between Bio and BioMath precourse scores for all sections combined). This finding is consistent with the literature—it is widely recognized that students have difficulty spontaneously transferring skills to novel contexts (NRC, 2000) and that students in other fields have difficulty transferring even relatively simple mathematical skills to new contexts (Britton, 2002). This result also confirms our earlier observations that students perform significantly lower on tasks requiring application of mathematical skills to biological problems than on context-free use of the same mathematical skills (Supplemental Text ST1 in the Supplemental Materials).

Students in the Experimental Section Had Higher Gains Than Students in Other Sections on BioMath Items

Figure 1 shows the gains on Bio and BioMath items by class section; Figure 2 shows these gains broken down by category. Students in the experimental section had significantly higher BioMath gains than students in each of the comparison sections: 35.97 ± 6.26% for the experimental section versus 18.55 ± 2.94%, 13.89 ± 2.06%, 11.20 ± 2.50%, and 2.36 ± 3.45% for sections 2, 3, 4 and 5, respectively (p = 0.020, 0.001, 0.001, and < 0.001, respectively, when compared

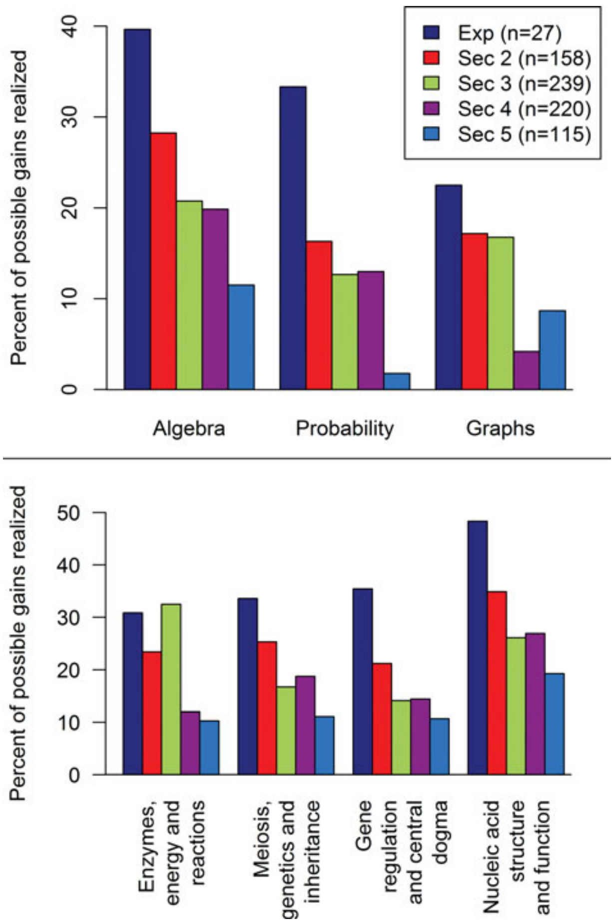

Figure 2. Student gains on pre/postassessment items by category. Student gains were measured as the percent of possible gain realized: gain = (post score − pre score)/(total possible − pre score).

with the experimental section). These differences are to be expected: many of the BioMath items on the outcome assessment were testing abilities that were explicit learning outcomes in the experimental section but were only addressed briefly, if at all, in the other sections. That students in the experimental section experienced higher BioMath gains supports the idea that students can improve their ability to apply quantitative skills in biological contexts within an introductory biology course if doing so is an explicit objective of the course.

Students in the Experimental Section Did Not Have Lower Gains Than Students in Other Sections on Bio Items

As seen in Figure 1, student Bio gains in the experimental section were not adversely affected by the inclusion of quantitative skills in the course. Bio gains were not significantly different between the experimental section and sections 2, 3, or 4; Bio gains in section 5 were significantly lower than for other sections (see Table S1). This supports the idea that, by integrating quantitative skill application alongside biology concepts, we can increase students' ability to use mathematics in biological contexts without harming their understanding of the biology concepts.

DISCUSSION

The mathematics skills on which we focused—algebra and manipulating units; scale, exponents, and logarithms; reading and creating graphs and tables; and basic counting and probability—are skills that many (particularly advanced) biology instructors assume their students have and can apply at some level to biological problems. These skills and their application "fly under the radar" when instructors think about what it means to apply mathematics to biological problems: they tend to think instead of more sophisticated skills, such as using differential equations or interpreting probability distributions. Expecting that students can apply these skills (or at least follow their application), instructors present graphical data in lecture to support their course content, ask students to calculate and understand probabilities for basic genetics problems, and otherwise rely on their students' assumed quantitative skill set. Yet, as seen in our precourse outcome assessment results, students can have a difficult time spontaneously transferring even relatively simple mathematics skills to novel contexts. The resulting mismatch between instructors' expectations of their students and the abilities that students actually bring into the classroom can be immensely frustrating for both instructors and their students. We have documented here that, with practice and feedback, students can learn to apply quantitative skills to biological contexts. By making quantitative reasoning an explicit objective of our course design, we improved students' ability to apply their existing mathematical skills to biological problems.

Integrating Quantitative Thinking Does Not Come at the Cost of Teaching the Biology

One criticism faced by those encouraging math-integration efforts in introductory biology classes is that spending time

Table 3. Pretest scores on Bio and BioMath assessment items

Section	Bio pretest score (mean % score ± SEM)	BioMath pretest score (mean % score ± SEM)	Difference between Bio and BioMath pretest score (mean % ± SEM)
Experimental ($n = 28$)	43.13 ± 3.52	38.96 ± 3.91	4.17 ± 3.09
2 ($n = 158$)	40.56 ± 1.27	37.17 ± 1.37	3.39 ± 1.37
3 ($n = 239$)	45.48 ±± 1.11	41.15 ± 1.12	4.32 ± 1.26
4 ($n = 220$)	40.28 ± 1.01	39.13 ± 1.09	1.15 ± 1.17
5 ($n = 115$)	41.94 ± 1.38	37.55 ± 1.65	4.39 ± 1.76
All sections combined ($n = 760$)	42.33 ± 0.58	39.11 ± 0.62	3.21 ± 0.66

on quantitative skills limits coverage of topical material. This concern has merit—on the face of it, time spent instructing students on reading graphs, algebra skills, and other quantitative concepts is time not spent presenting new biological content. Our results, however, do not support this complaint: students in the experimental section performed no worse than their peers in other sections of MCB 181 on the Bio items on the outcome assessment, while outperforming them on BioMath items. Moreover, our approach minimizes "lost" time by having students practice quantitative skills in the context of the biological material. These results defy the assumption that time spent "doing math" is time spent not doing biology by requiring students to apply quantitative skills *and* biological concepts in order to solve the problems. This approach is possible, in part, because we emphasize skills that are not entirely new to the students; we are guiding them in how to transfer skills from their required mathematics courses to tackling biological problems. Although problem solving in class does decrease the time available for an instructor to present material, this is time well spent: active learning during class time has been demonstrated to increase students' class attendance, course performance, and ability to apply concepts; and to decrease the achievement gap among higher- and lower-performing students (Smith *et al.*, 2005; Freeman *et al.*, 2007; Haak *et al.*, 2011). At the same time, many valuable tools—from online companion activities offered alongside textbooks to instructor-recorded lectures—have become available to increase and assess students' learning before their arrival in the classroom, making prolonged in-class presentation and explanation of the material less necessary.

Instructional Approach and Course Design Are Crucial When Integrating Mathematics into Biology

The approach described here is most successfully used with active-learning techniques. Students require a sense of relevance, extensive practice, and prompt feedback in order to develop confidence and proficiency applying quantitative skills in biological contexts. Our approach, however, did not require fundamental changes to the MCB 181 curriculum, and none of the pedagogical strategies we used are revolutionary. We integrated quantitative skill application into the existing curriculum and based our course design on recognized effective teaching practice centered on active learning and providing frequent formative assessment opportunities for the instructor and students. Notably, three of the MCB 181 sections used for comparison (sections 2, 3, and 4) make extensive use of learner-centered techniques: the instructors explicitly define learning outcomes for the students; assign online preclass assignments similar to those assigned in the experimental course; and frequently punctuate their lectures with think–pair–share and/or personal-response system (clicker) questions and written activities mediated by trained undergraduate preceptors. The development of the experimental course was highly informed by these instructors' methods and experience; one of the three was directly involved in the development of the experimental course and the other two were frequently consulted for advice, material sharing, and feedback on how best to design materials that would be portable into a large lecture-style class in the future. The active-learning environment in these three classes likely explains why Bio gains were not significantly different between any of these sections and the experimental section despite the smaller class size for the experimental course: these three instructors expertly implement techniques that minimize the deleterious effects of large class size on student learning (Smith *et al.*, 2005; Freeman *et al.*, 2007). Bio gains were significantly lower in section 5, a traditionally taught lecture course without an active-learning component, supporting this interpretation of the results.

It is important to note that all of the instructors involved in this study had access to and were involved in giving feedback on the outcome assessment items. Because we shared each section's pre/postcourse outcome assessment results with the instructors during the instrument's development, many of the instructors involved in the project gained insights into their students' strengths, weaknesses, and misconceptions. Instructors reported that they used these results to target specific conceptual areas for course improvement. For instance, instructors reported finding themselves devoting more class time to allowing students to practice interpreting graphs. However, instructors were directed to not use the outcome assessment items in their classes (e.g., as clicker or exam questions).

Sharing Materials

One of the greatest challenges of developing the course described was the relative dearth of available classroom materials integrating mathematical tools and molecular and cell biology concepts. We believe that some of the most useful products of this project are shareable class materials that do so. For this reason, we are eager to share any of the materials we have developed with interested instructors. If you are an instructor who would like access to our course materials, please email the corresponding author.

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