Article

Highly Effective Active Learning in a One-Year Biochemistry Series with Limited Resources[S]

Norbert Reich †*
Yuedong Wang‡

From the †Department of Chemistry and Biochemistry, University of California, Santa Barbara, California, 93106, ‡Department of Statistics and Applied Probability, University of California, Santa Barbara, California, 93106

Abstract

We investigate the effectiveness of an active learning curriculum designed for an upper division Biochemistry series at a large, public research university. The goal was to determine how effective this format was when compared to a parallel conventional course, and to see if the active learning series can be run with limited resources (one instructor, one teaching assistant). The study involved 160 students in the first quarter and 92 students in the second quarter. The active learning curriculum consists of learning goals for each chapter, online quizzes, in-class questions targeting the problematic areas, small group (3–4 students) discussions during class in which students presented their assumptions and arguments in support of their responses to online and in-class questions, and two-stage exams involving the ability to "re-answer" as a group following a discussion). The in-class questions involved the use of a student response system (i > clicker) (multiple choice) and short answer formats. Students in the active learning course and a control, conventional lecture course, took identical midterms and finals for the first, and second quarters. We found that students enrolled in the active learning curriculum had consistently better performance, with statistically significant higher scores on all tests for both quarters. The effect sizes of the improvements are medium to large and are independent of prior GPA and grades in prerequisites. This model curriculum redesign offers promise for improved student learning with less monetary investment than a flipped course model relying on, for example, an extensive collection of instructor-produced videos. © 2018 International Union of Biochemistry and Molecular Biology, 47(1):7–15, 2019.

Keywords: *Active learning; curriculum development; assessment development*

Introduction

The incorporation of active learning concepts to teach university science courses (e.g., physics) has been going on for nearly 30 years [1,2]. The effectiveness of such approaches seems compelling [3–6], yet the extent to which these approaches are taken up by faculty at major universities seems surprisingly slow and limited [2,4]. Thus, other than the focus of this study, we know of no other University of California campus in which biochemistry is taught with an active learning emphasis. The highly diverse subject matter now covered in a 1-year biochemistry course for majors typically covers physical chemistry, genetics, physiology, molecular biology, and enzymology. Constructing an active learning environment with such a large number of topics and disciplines may be a barrier for research active faculty at major universities.

A related barrier is the lack of locally available resources to implement an active learning course, including online resources, in-class resources, and other faculty who are familiar with an active learning approach. Our premise is that a single, research active instructor and a graduate teaching assistant could use key active learning approaches to convert a challenging course, which was previously taught entirely in a conventional lecture format. In addition, our motivations were to address several long-term problems with the course and to determine if student scores improved when compared to a control course taught using a

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**To whom correspondence should be addressed. Tel.: 805 893 8368; Fax: 805 893 4120. E-mail: reich@chem.ucsb.edu.*
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TABLE I *Statistical analysis of student GPA in AL and CL for 142A*

	N	*Major GPA*	p-*value*	*Overall GPA*	p-*value*
Active (AL)	63	3.08	0.4598	3.17	0.4545
Conventional (CL)	97	3.02		3.12	

No statistically significant difference, with respect to GPA (either major or overall GPA) prior to enrolmment, between students the AL and CL classes (142A).

conventional lecture format. The long term problems we are trying to address include unacceptable attrition rates, poor attendance, student dissatisfaction with the amount of material covered, and a general lack of understanding of the scientific and experimental design thinking that led to the information in their texts. In this study we address the poor attendance and improved student understanding.

The Biochemistry series (142A, B, and C) is the core course for the Biochemistry major in the Department of Chemistry and Biochemistry at UCSB. At the start of the Fall quarter (2015) (Biochemistry 142A) the students were contacted by email and informed that there would be two sections of the course for the first quarter (142A), and how the two sections were organized. The students were free to enroll in either class, and a review of their scores in Organic chemistry and their GPAs showed no significant difference between students enrolled in these two classes (Tables I and II). The conventional lecture (CL) format course was taught by a senior biochemist very familiar with this first quarter (142A) of the biochemistry series (142A–C); 97 students selected this class. The active learning course (AL) was taught by a senior biochemist (N. Reich) who had not recently taught the first quarter of this course; this was the first quarter in which active learning activities were implemented for this quarter; 63 students enrolled in this class.

The curriculum for the active learning lecture (AL) was based on several concepts [3–8] (see supplemental information). On the first day of the class, the students were informed about how the course was organized, and the published studies showing the effectiveness of the various innovations used in the course [4,9]. Students were informed about the extensive online interactive resources (available through the course management system, "GauchoSpace," a Moodle platform) to view online quizzes, submit their answers and receive feedback, and to access additional course material. Five to ten learning goals (LG) and associated study guides for each chapter were used to focus students, in both the AL and CL classes, on the important concepts (Fig. 1) [8]. The LGs communicate the key ideas and level of understanding that are expected from the students regardless of being enrolled in AL or CL class (see Fig. 1 for sample LGs and Study Guidelines). Five to ten multiple choice online questions covering 10–20 pages of text material were posted online 2–3 days prior to each class meeting (Fig. 2). Students submitted their answers online, prior to the class meeting, and received credit for answering these questions correctly. Student performance on

TABLE II *Statistical analysis of student performance in prerequisite classes for 142A*

	109A		*109B*		*109C*		*6AL (lab)*		*6BL (lab)*	
Grades	*CL*	AL	*CL*	AL	*CL*	AL	*CL*	AL	*CL*	AL
A	25	15	25	14	20	14	20	14	25	14
B	38	23	38	26	34	18	54	28	43	34
C	21	14	21	12	31	20	10	10	15	4
D	0	0	2	0	2	0	0	0	0	0
p-value	0.9695		0.7006		0.6662		0.3738		0.1859	

No statistically significant differences in grades for organic chemistry class (109A–C), or organic chemistry lab (6AL and 6BL) between students in two groups. Students receiving a D or an F are combined as D. Pearson's chi-squared test was used where p-*values were computed by Monte Carlo simulation.*

Chapter 3 (Lehninger, Principles of Biochemistry 6th Edition)

Learning Goals: After completing Chapter 3 you should be able to:

1. Distinguish between the genome and the proteome, and define both terms.
2. Know the structures and side-chain chemistries of all 20 protein-forming amino acids.
3. Draw a peptide bond and describe in detail its chemistry and conformation space.
4. Define primary structure.
5. Describe how a quantitative enzyme assay is used to calculate the specific activity during protein purification.
6. List the properties of proteins that can be used to accomplish their separation and purification, and correlate them with the appropriate methods: gel-filtration chromatography, dialysis, salting out, ion-exchange chromatography, affinity chromatography, and high-performance liquid chromatography. Describe the basic principles of each of these methods.
7. Explain the determination of protein mass by SDS-PAGE: sodium dodecyl sulfate polyacrylamide gel electrophoresis.
8. Define the isoelectric point (pI) of a protein and describe isoelectric focusing as a separation method.
9. Outline the application of mass spectrometry to the analysis of proteins and compare merits of the various methods of determining the molecular weights of proteins.
10. Explain how peptides can be sequenced using mass spectrometry.
11. Give examples of the important information that amino acid sequences reveal. For example, comparison of sequences can reveal relationships in function, or evolutionary relationships.
12. List the most important uses of synthetic peptides.
13. Outline the steps of the solid-phase method for the synthesis of peptides.

Guidelines

The proteome is the constellation of proteins which determine a cell's function; the past and current methods used to identify and characterize these proteins forms an essential part of a biochemists toolkit. There isn't much in this chapter you should NOT know. Most of this should be second nature to you after finishing the chapter, certainly by the end of the quarter. You should know all the amino acids, their side chain functional groups (e.g., pKa, nucleophilicity, stereochemistry, etc.), their three and one letter codes, standard features of proteins (e.g., sizes), basics of their purification (SDS PAGE, chromatography) and of course, structure (primary, secondary, etc.). Their methods of characterization (e.g., MS, Edman sequencing) and finally, how their sequences vary and how this can be studied/used.

FIG 1 ***Example learning goals from the first quarter of Biochemistry (142A).*** *To facilitate the active learning environment a list of key concepts from each chapter was generated. These lists, like the above, were for the purpose of focusing the students' independent study of material to prepare for group class discussions during lecture. The SL class also had access to this list.*

these online questions formed the basis of the questions and discussions that occurred at the next class meeting. If 70% or more of the students answered a question correctly in the AL, little time was devoted to that topic or LG during the class meeting.

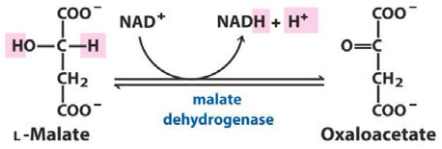
The topics identified as needing more attention were the focus of the subsequent class meeting. The problematic questions were reviewed with a summary of the class performance and students discussed their responses within their small (3–4 student) groups. The instructor ensured that each group was composed of students who had performed well in prior classes (e.g., organic chemistry) and students who had not performed well in the same classes. The groups were assigned to particular physical locations within the classroom to facilitate discussion; groups were moved around periodically during the term. This approach allowed the instructor and Teaching Assistant (TA) access to all groups, since in-class discussions often formed the basis of additional questions posed by the instructor, to address with misconceptions, or alternatively, appropriate insights made by particular groups. During these class-wide discussions, students in several groups were asked to present their reasoning, and

Which of the following experimental observations provide evidence for the formation of an acyl-enzyme intermediate during the chymotrypsin reaction?

(a) A biphasic release of *p*-nitrophenol occurs during the hydrolysis of the *p*-nitrophenyl ester of *N*-acetyl-phenylalanine.
(b) The active serine can be specifically labeled with organic fluorophosphates.
(c) The pH dependence of the catalytic rate is bell shaped, with a maximum at pH 8.
(d) A deep pocket on the enzyme can accommodate a large hydrophobic side chain of the recognized substrate.

FIG 2 ***Example online question (first quarter, Biochemistry 142A).*** *This question asks the student to determine which of the results are true and provide relevant evidence. While a, c, and d are all correct, only b is both correct and relevant. This type of question is not readily answered by searching the internet.*

A)



Short answer:
Describe two factors that make this thermodynamically disfavored reaction go forward.

Use the following data to explain why tight binding of the substrate by an enzyme (low Km) does not contribute to high rates of product formation. kcat/Km = 10^6 $M^{-1}s^{-1}$; [S] 10^{-3} M

K_m (M)	k_{cat} (s^{-1})	rate (s^{-1})
10^{-6}	1	1
10^{-4}	10^2	90
10^{-2}	10^4	909
1	10^6	999

FIG 3

Two short answer questions for first quarter (142A). *The top question requires that the student understand some of the most fundamental concepts of intermediate metabolism, including coupled equilibria, and importance of actual concentrations of the components of a reaction, as written. The bottom question requires that the student has a solid grasp of what drives efficient catalysis by enzymes; namely, that the highest rates of product formation are achieved through weak binding and high catalytic turnover. Thus, this question tests the students' ability to read tabular data, make a conclusion, and explain what a somewhat counter intuitive concept. [Color figure can be viewed at wileyonlinelibrary.com]*

supporting evidence to the entire class [10]. Other groups and students were asked to comment on the validity of the statements; this was often concluded with the instructor commenting on the correctness of the response and the reasoning, with occasional reference to material from the text (notes on the board, a prepared slide). This discussion of the online questions would end with an additional question or questions (using multiple choice questions answered with i > clickers, UCSB's student response system), or short answer questions, Figs. 3 and 4) on the same topic. For the i > clicker (multiple choice) questions, the scoring was immediately available, and if still below 70% correct, would warrant an additional cycle of i > clicker questions followed by class discussion from individual groups. The short answer questions were crafted with the style of free response questions on exams; several groups would be selected to present their answer and reasoning, which formed the basis of an additional discussion. A small number (10% or so) of these questions incorporated concepts focused on experimental design in addition to content (Fig. 5). The follow up questions used the multiple choice or short response format. Both the multiple-choice and short answer questions were graded for completion, however only 40% of the short answer questions were graded for correctness, to motivate the students to give the best possible answer they can. The rest simply contributed to an attendance score.

To calculate the turnover number of an enzyme, you need to know:

A) the enzyme concentration.
B) the initial velocity of the catalyzed reaction at [S] >> Km.
C) the initial velocity of the catalyzed reaction at low [S].
D) the Km for the substrate.
E) both A and B.

FIG 4

Multiple choice iClicker questions for the second quarter of biochemistry (142B). *This question requires the student to truly understand Michaelis Menten kinetics, beyond simply stating the relevant equation. The correct answer, "E" indicates that knowing only the maximal velocity (B) is insufficient since the turnover constant has units of reciprocal time, not velocity.*

Methods

Generation of LG

Prior to the beginning of the quarter both instructors decided on the content to be covered during the quarter for both 142A and B.

Generation of the Online Quizzes for AL Lecture

Following the learning goals provided in the syllabus, 10 questions were generated for quiz A and an additional 10 questions were generated for an optional, follow-up quiz B (that could replace a low score on quiz A) for 142A. These questions were crafted specifically for the class to prevent the students from using solutions found online. The five possible answers for each question were designed so that there was a clear rationale that could be used to exclude the incorrect choices while not giving the correct answer away. The quizzes were structured so that if a student performed poorly on quiz A they could choose to take quiz B to replace the score. The questions in each quiz tested the same concepts. The CL did not have access to these quiz questions or the AL course

You collected kinetic data for human succinate dehydrogenase (see below, monitoring the production of $FADH_2$ using absorbance), but are concerned with the production of product at time = zero. You are trying to determine the cause of this; which of the following is the **least useful experiment** to address this?

a. Repeat, without any enzyme.
b. Repeat, without succinate.
c. Repeat, without any FAD
d. Repeat using more enzyme.
e. Check the absorbance of the buffer

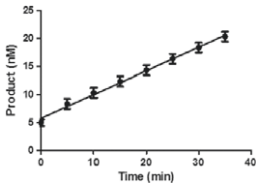


FIG 5 ***In class experimental design question (iClicker).*** *This question goes well beyond what is typically asked of biochemistry students, since it requires them to see why a non-zero product formation at time = zero is problematic, and then to identify which experiments are useful or not, to address this. The issue here is the background, which may not have been considered in the experimental design. Withholding each component (a, b, c, e) is designed to determine if these are contributing to this background; clearly, no time-dependent product with these controls is expected. In contrast, adding more enzyme, while similar to "a" may be less informative.*

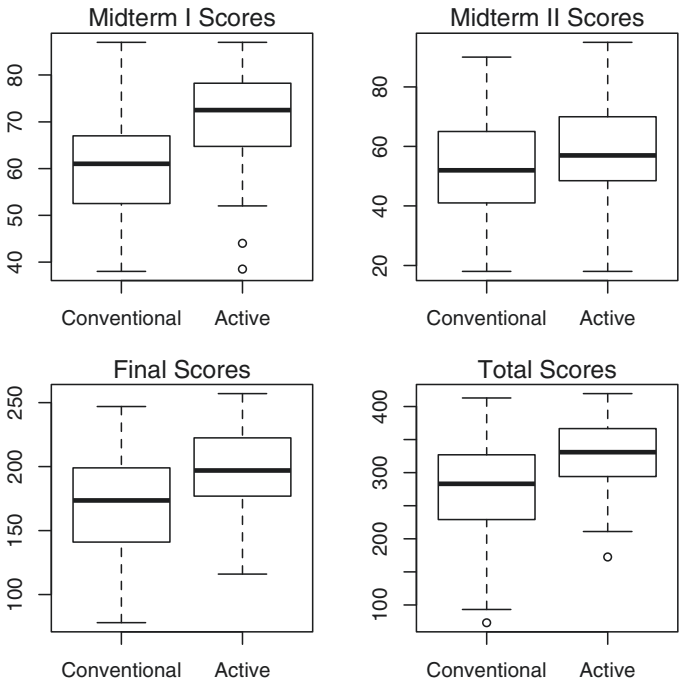


FIG 6 ***Boxplots comparing differences of the AL and CL 142A classes:*** *Comparing differences in midterm I, midterm II, final, and total scores in 142A between AL and CL. These plots clearly show that the students in AL have higher scores. Two students in the CL class missed the Midterm I and three students in the CL class missed the Final. No students in the active learning class missed any exams. Statistical analysis is present in Tables III–V.*

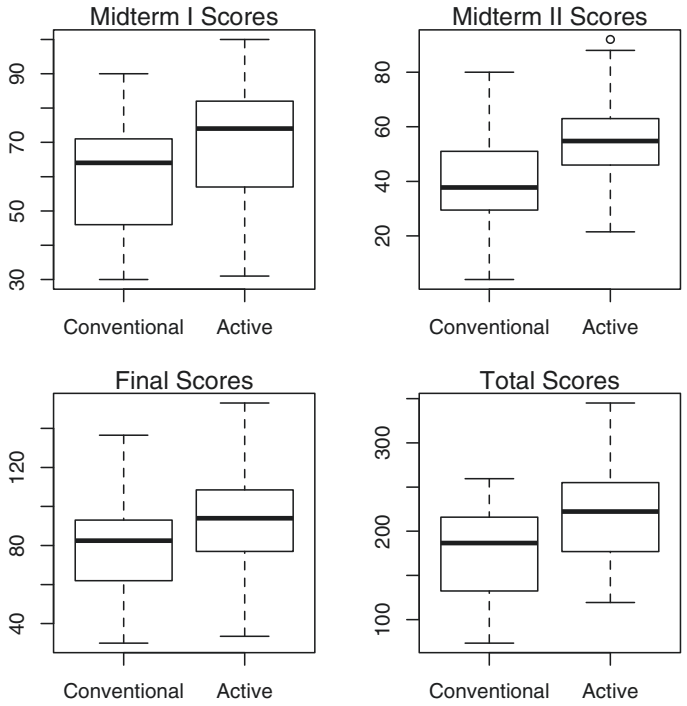


FIG 7 ***Boxplots comparing differences of the AL and CL 142B classes:*** *Comparing differences in midterm I, midterm II, final, and total scores in 142B between conventional and active lectures. These plots clearly show that the students in active learning class have higher scores. Statistical analysis is present in Table VIII.*

TABLE III ***Statistical analysis of student performance in 142A:*** **p-*values are based on* t-*test for differences between AL and CL differences between AL and CL of all scores are significant.***

		Mean Score	*Standard Deviation*	p-*value*	*Cohen's d*
Midterm I	*Conventional*	*60.55*	*10.94*	*<0.0001*	*0.95*
	Active	*70.78*	*10.52*		
Midterm II	Conventional	53.54	16.76	0.0465	0.33
	Active	58.91	16.01		
Final	*Conventional*	*169.87*	*40.45*	*<0.0001*	*0.68*
	Active	*195.56*	*33.86*		
Total Score	Conventional	283.97	59.98	<0.0001	0.72
	Active	325.24	53.48		

website. However, they did have access to a noncompulsory online homework. For the second quarter in the Biochemistry series, 142B, the number of questions for the online quizzes was reduced (in response to student feedback) from ten to five questions for quiz A and the optional quiz B, the CL still had access to noncompulsory online homework.

Generation of Midterms and Finals for both AL and CL Classes

The tests generated by the instructors had multiple choice and free response sections with close to a 50/50 distribution of points available per question type. The instructors collaborated to generate a question bank for the test from which they each chose questions for the joint midterm and final. The resultant test combined suggested questions from both instructors. The questions to be graded by the TAs from the AL and CL classes were selected so that a particular question was graded by a single TA for all students in both AL and CL classes to reduce potential grading bias.

TABLE IV ***Statistical analysis of 142A, AL, and CL, adjusting for Covariates.***

	Difference	*Standard error*	p-*value*
Midterm I	11.80	1.53	<0.0001
Midterm II	4.94	2.63	0.0633
Final	26.75	5.69	<0.0001
Total Score	43.49	7.70	<0.0001

Differences represent differences in scores between two groups after adjusting for GPAs and grades in the prerequisite courses where a positive difference means the active learning group has a higher score. All differences are significant except for midterm II which is borderline significant.

Data Collected

To investigate differences between students who enrolled in the AL and CL sections, we collected Major GPA, overall GPA, and the grades in the prerequisite Organic Chemistry Lecture and Organic Chemistry Labs for each student (Tables I and II for 142A, and Tables VI and VII for 142B). Scores from midterms (100 points each), Final (200 points), and Total score (400 points) for both 142A and B were used for comparison of performances.

Statistical Analysis

To compare students who enrolled in AL and CL, we used t-test to compare the major GPAs and overall GPAs prior to enrollment, and chi-square test to compare grades in Organic Chemistry courses (109A–C, 6AL and 6BL). To compare performances of AL and CL, we first conducted a Hotelling's T^2 test for differences between the means of all scores (Midterm I, Midterm II, Final), and then conducted *t*-tests for each score and the overall score. We estimated the effect sizes using Cohen's d. We used multiple regression models to investigate differences between AL and CL adjusting for possible covariates including Major GPA, and grades from 109A, 109B, 109C, 6AL, and 6BL.

Results

Our goal was to improve student learning and improve attendance. Both were achieved, in a core biochemistry, 1-year series, relying on the efforts of a single instructor and a TA. See Figs. 6 and 7 and Tables I–VIII. The attendance for the AL courses averaged 90% whereas the CL courses averaged 30–40%.

TABLE V ***Statistical Analysis of Student GPA in AL and CL for 142B.***

	N	*Major GPA*	p-*value*	*Overall GPA*	p-*value*
Active (AL)	54	3.03	0.5131	3.11	0.7437
Conventional (CL)	38	2.96		3.08	

No statistically significant difference, with respect to GPA (either major or overall GPA), between students in the start of AL and CL classes (142B). Two-sample Student t*-test with unequal variance was used to compute the* p*-values. This table compares the major GPAs, overall GPAs and finds no significant difference between the starting sample in the two classes.*

Demographics

There was no statistically significant difference between students who enrolled in the two sections of 142A in terms of GPAs (Table I) and grades earned in the prerequisite courses as well (Organic Chemistry 109 A–C, 6AL, and 6BL) (Table II). This was also true for 142B (Tables V and VI).

Student Learning

Figs. 6 and 7 show that the students in the active learning class attained higher scores in the midterms and final for 142A and 142B, respectively. For both 142A and 142B, the two-sample Hotelling's T^2 tests for differences between the means of all three test scores (Midterm I score, Midterm II score, Final score) are significant with p-values <0.0001. Further t-tests indicate that the active learning group consistently outperformed the conventional group on both midterm exams and on the final exam where all p-values < 0.05 (Tables III and VII). The effect size (Cohen's d in Tables III and VII) ranges from 0.3 to 1.0, indicating the differences are medium to large [11]. To control for possible confounding variables, for each score we fit a linear model with the score as the response variable, learning method (i.e., AL or Cl) as the predictor, and Major GPA, 109A, 109B, 109C, 6AL, and 6BL grades as covariates. Tables IV and VIII list the estimated differences for 142A and 142B, respectively after adjusting for covariates. These adjusted differences are similar to those in Table III and Table VII respectively, and all remain significant except for the Midterm II for 142A which is significant at level 0.1.

Discussion

A yearlong upper division biochemistry series is challenging to run in an active learning format because the topic is extremely diverse (physical chemistry, genetics, physiology, medical implications, enzymology, etc.), highly prone to information overload (memorization) which makes it challenging to convey core concepts. Further, the students in this study were not previously exposed to an active learning format at the university level.

Broadly acknowledged problems with contemporary university level science education have been identified by multiple groups [2,12] and have various unacceptable consequences, including attrition from classes and from STEM majors, poor performance in science courses, poor understanding of an ever increasing amount of course content [2,12], and the lack of student understanding of how science is actually done [13]. A number of well-researched approaches to these problems have been described, which provide strong evidence as to their effectiveness. While the number of large university courses which embrace such practices appears to be increasing [4], no course with an active learning approach is being taught by ladder science faculty at UCSB, and no equivalent active learning Biochemistry course is being taught at any of the University of California campuses. We sought to determine if a single instructor with limited resources could effectively

TABLE VI ***Statistical analysis of student performance in prerequisite classes for 142B.***

	109A/H		*109B/H*		*109C/H*		*6AL*		*6BL*	
	CL	AL	CL	AL	CL	AL	CL	AL	CL	AL
A	15	17	7	17	7	16	7	14	10	15
B	11	22	17	18	17	15	24	27	20	26
C	6	7	10	12	10	16	1	5	2	6
p-value	0.4918		0.3203		0.2269		0.2594		0.6042	

No statistically significant differences in grades for organic chemistry class (109A–C), or organic chemistry lab (6AL and 6BL) between students in two groups (CL, conventional lecture; AL, active learning) (For 142B). Pearson's chi-squared test was used where p*-values were computed by Monte Carlo simulation.*

TABLE VII ***Statistical Analysis of Student performance in 142B: Differences between AL and CL of all scores are significant.***

		Mean Score	*Standard Deviation*	p-*value*	*Cohen's d*
Midterm I	*Conventional*	*60.24*	*16.80*	*0.0101*	*0.57*
	Active	*69.64*	*16.40*		
Midterm II	Conventional	39.19	15.61	<0.0001	1.00
	Active	54.71	15.46		
Final	*Conventional*	*80.08*	*24.86*	*<0.0001*	*0.55*
	Active	*94.36*	*26.88*		
Total	Conventional	179.51	49.40	0.0005	0.77
	Active	218.71	52.37		

implement a conversion from a CL format to an active learning format to address the problems mentioned above.

Our results with a three quarter upper division biochemistry course are highly encouraging, since the overall 10% increase in student test performance in each of the two quarters which were analyzed, is clearly above the average increase (6%) observed in a comparison of >225 studies making use of similar approaches [4]. Furthermore, attendance improved from the 35–65% range for the CL course to over 90% in the AL series. Fewer students received failing grades in the AL series when compared to students in the CL course, as a direct result of their improved test scores.

Future Directions

The essential features of the approach used here include online resources and in-class problem solving and discussion; in other words, how students engage with course topics, each other, and the instructor/TA. The online resources were delivered through the local course management system (CMS, Moodle), which enabled the posting of self-grading quizzes. It is noteworthy that this CMS provides many additional resources that were not used, but are likely to improve students' learning and satisfaction in the course (e.g., feedback surveys to gauge students' satisfaction, podcasts of tutorial videos, and self-adapting lessons). The in-class resources primarily made use of the Student Response System (i > clicker) and short answer questions. The preparation of questions for the online quizzes, in class SRS and short answer problems, as well as the assembly of the computer graphics images could all be improved with additional time and effort. A promising area for future study is to determine if additional student gains can be achieved with additional and/or improved online quiz questions, in class SRS and short answer questions. This may be a significant impediment to the broader use of this approach to university science teaching.

Perhaps as important is that teaching in an active learning environment requires that the instructor be able to work with a less structured approach than the CL format. The ability to keep the class discussion "on topic," to allow students the time to express their arguments even when flawed, and to quickly locate and present relevant information to the discussion at hand, are all somewhat removed from the standard lecture format. The development of teaching aides for instructors may be of value. Finally, the reliance on technologies that may be new to instructors (e.g., SRS, interactive graphics, group video conferencing [-e.g., Zoom]) presents its own challenges. Additional training for instructors on their use could conceivably make the use of this teaching approach more accessible. All resources used in this Biochemistry series related to the active learning effort are freely available by contacting the corresponding author (reich@chem.ucsb.edu).

TABLE VIII ***Statistical Analysis of 142B, AL, and CL, adjusting for Covariates.***

	Difference	*Standard error*	p-*value*
Midterm I	5.80	3.51	0.1039
Midterm II	11.55	3.33	0.0010
Final	13.65	5.88	0.0241
Total	37.04	11.15	0.0016

Differences represent differences in scores between two groups after adjusting for GPAs and grades in the prerequisite courses where a positive difference means the active learning group has a higher score. All differences are significant.

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