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# Specifications Grading Is an Effective Approach to Teaching Biochemistry

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**Specifications grading is a relatively recent approach to assessing student learning. In this approach, students make progress toward completion of a course by demonstrating mastery of specific skills or material. The assessment tools are short, frequent exercises that can be attempted multiple times until mastered. This contrasts with the traditional, exam-based assessment of student learning. There are multiple benefits to the specifications grading-based strategy, including reduced test anxiety, better knowledge retention, and increased flexibility. In this study, specifications grading was implemented into an upper-level biochemistry course at a private, liberal arts university. The student cohort consisted almost exclusively of junior and senior biochemistry, biology, and chemistry majors. Students earned points for demonstrating mastery on each of 12 short quizzes in addition to points earned from laboratory exercises and on the cumulative final exam. Student attitudes were assessed using three surveys that were administered at the beginning, middle, and end of the course. The survey results indicated that the students had overall favorable opinions of the specifications grading approach and its use in this course. A comparison of student performance on the quizzes to their performance on the final exam showed that the students learned and retained the course material. Combining the survey and performance data, we demonstrated that the students' perceptions of their learning correlated well with their performances on the specifications grading tools. Together, these results indicated that specifications grading is an effective approach to assessing student learning and to maintaining student enthusiasm in an upper-level biochemistry course.**

**KEYWORDS** specifications grading, biochemistry, mastery learning

## INTRODUCTION

Assessment of student learning in science, technology, engineering, and math (STEM) traditionally involves high-stakes examinations that cover a relatively large set of concepts. While this approach is efficient and is the type of assessment many students are used to, using traditional high-stakes exams as the primary means for assessing students' acquisition of knowledge and skills can lead to student practices that are ineffective for attaining concept mastery and retention (1, 2). Improving knowledge retention and critical thinking and reasoning for all students is a significant motivating factor in STEM education, and it has brought about the development and implementation of alternative mechanisms for assessing student learning, such as specifications grading (3).

Improving student learning in undergraduate STEM courses is positively impacted by increased course structures that include active learning and attention to student study practices in preparation for exams (4). Advances in information technology and sharing of information broadly on the Internet are valuable resources; however, these tools enable students to adopt a study strategy to easily locate online solutions to homework assignments, encouraging memorization of example problems rather than understanding of core concepts (5). Additionally, the spacing of study activities can lead to "cramming," which often leads students to guess at what the most likely problems will be on an exam rather than focusing on learning the fundamental concepts that would result in success in solving a problem they have not encountered before. These are recognized as common issues across STEM disciplines and have given rise to a variety of innovative approaches, such as mastery learning and specifications (specs) grading, that are effective in promoting deeper learning and retention compared to rote memorization (surface learning). Specs grading is an assessment tool whereby students earn points toward their final grade by successfully completing specific assignments. In the context of this course, points were earned by demonstrating content mastery on learning outcomes (LOs). Specs grading and mastery learning assessment systems are designed to circumvent the "cram-and-purge" strategy students often employ to manage the many demands associated with high-stakes exam assessment (6).

Alternative testing strategies can also reduce achievement gaps for underrepresented students and reduce test anxiety that can often negatively affect a student's performance on

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learning assessments (7, 8). Specs grading systems can minimize these negative impacts by reducing student anxiety as a result of their having the ability to reattempt LOs multiple times to demonstrate mastery. Further improvements in reducing anxiety can be achieved through clear communication of expectations for the levels of preparation, rigor, and instructional support (9).

The term "mastery" used in the context of this study refers to the in-depth knowledge of a particular subject (10). The broad concept of mastery can vary in the specific criteria for demonstrating knowledge or skill about a particular topic (11). In our biochemistry course, mastery includes demonstrating the ability, use, knowledge, and skills in applied problem solving that are assessed through a specs grading system. The key features of specifications grading approaches are frequent testing of concept knowledge, rapid feedback to students on their performance in meeting course objectives, and two or more opportunities to demonstrate mastery of concepts and consultation with instructors to correct misconceptions and errors in thinking. A greater number of low-stakes assignments enables students to focus on concepts with greater depth and greater retention (12, 13). This is particularly true when students have an opportunity to correct mistakes and misconceptions with little to no penalty for reattempting to master specific material. Implementation of specs grading in an introductory chemistry setting resulted in improved performance and retention of knowledge (14). Implementation of specs grading in engineering courses resulted in improved performance on course learning assessments with no gaps in overall performance across all demographic groups (15). Given the positive impacts specs grading has shown in numerous introductory and intermediate STEM courses, the hypothesis that it can also be successfully used in upper-level chemistry courses served as the motivation for the present study (6, 16, 17).

The goal of the current study was to determine if specs grading could be used in Biochemistry I (CHEM 440) to enhance student performance and maintain positive student attitudes toward the course. The Chemistry Department at the University of St. Thomas is solely an undergraduate program that serves a regional population of traditional and nontraditional students. The University of St. Thomas is an urban, private, liberal arts institution located in St. Paul, Minnesota. Our biochemistry course is a junior- and senior-level course taught using a chemical perspective to describe the structure and function of biomolecules and chemical processes in living things. We teach biochemistry as a two-course sequence, CHEM 440 and CHEM 442, to cover the entirety of the biochemical subdiscipline. The first-semester course, CHEM 440, is focused on protein structure and function and the primary metabolism of carbon. Two sections of CHEM440 were offered during the semester when this study was conducted, and we implemented the mastery grading system in both. The learning goals for the course sequentially build on structure-function relationships of biomolecules, with a focus on applying chemical concepts to gain a deeper understanding of primary metabolism. The nature of topics in biochemistry fit well with scaffolded course goals and use of the specs grading approach to student learning assessment.

There are multiple accounts in the literature of the successes of this approach when implemented in introductory and intermediate-level STEM courses; however, there are comparatively few accounts of successfully integrating the specs grading approach into an upper-level course. We found that this approach is an effective way to facilitate student learning and retention, while also generating student enthusiasm for the course.

## METHODS

### Implementation and grading structure

The course where the mastery learning approach was studied is the first semester of a two-semester undergraduate biochemistry course. This course, CHEM 440, was taught in two sections with each section being taught by one of the authors of this study. Of the 37 students who completed this course, a total of 36 students from across both sections participated in the research study. Three students failed to submit a midterm survey, so they were not included in the midterm data.

Students enrolled in each section of CHEM 440 were enrolled in this study, and the mastery learning approach was used by instructors in both sections. Therefore, all the students were considered together as one cohort in all analyses. While the underlying principle that students earn points for mastering material is common across courses that employ a mastery learning approach, there are features of the course structure that are unique to each individual course. In the case of CHEM 440, the following parameters were implemented. Students were offered a total of 12 LOs. The skills associated with each LO are listed in Table 1. Each LO included five questions. Students demonstrated mastery by correctly answering at least four questions entirely correctly (no partial credit was awarded). The questions on each LO were designed to address multiple levels of Bloom's taxonomy. The early questions focused on information recall, while subsequent questions built toward higher-level analytical considerations of the material. Figure S1 in the supplemental material contains one version of LO 2, which was representative of this approach to the LO design.

Each student was afforded up to three opportunities to demonstrate mastery of each LO, with the highest score being the one that counted toward the course grade. To discourage procrastination, the first attempt to complete each LO needed to occur within 2 weeks of the completion of that material's presentation in class. To maximize flexibility, the remaining two attempts at any given LO could occur at any time during the semester. Students used an online scheduling tool, built into the course Canvas site, to schedule LO attempts. If a student received any score on an LO other than a perfect score, students were encouraged to reengage the material and to meet with their instructor to discuss their performance. This was facilitated by barring the students from taking more than one LO in any 24-h period except for under special circumstances. The grades for LO attempts were posted to Canvas

TABLE 1
Skills and content assessed in each LO

| LO | Students should be able to: |
|---|---|
| 1 | Identify and characterize weak intermolecular forces between biomolecules |
| 2 | Perform basic solution chemistry calculations and articulate the molecular impacts of the calculated values |
| 3 | Draw polypeptides, describe basic biophysical properties of proteins, and use those properties to predict the behavior of proteins in routine assays (e.g., gel electrophoresis or column chromatography) |
| 4 | Use quantitative models to describe protein-ligand interactions, with particular emphasis on hemoglobin |
| 5 | Use the Michaelis-Menten kinetic model to quantitatively describe enzyme catalysis |
| 6 | Apply the basic principles of transition state theory to describe enzyme catalysis |
| 7 | Perform thermodynamic calculations to predict biochemical reactivity |
| 8 | Detail the processes involved in glucose metabolism and fermentation |
| 9 | Describe in detail the process and impacts of the TCA cycle on central metabolism |
| 10 | Describe in detail the molecular transformations associated with lipid metabolism |
| 11 | Perform calculations pertaining to membrane transport thermodynamics and articulate the impacts of those calculations |
| 12 | Apply the knowledge of transport thermodynamics to understand oxidative phosphorylation and photosynthesis |

within 24 h, so the students received their results as soon as was practical.

This course contained both classroom and laboratory components that contributed to the final grade. In total, students had the opportunity to earn up to 1,000 points. Laboratory exercises accounted for 200 points, while the final exam accounted for 100 points. Of the remaining 700 points, 100 points were awarded for completion of the online homework, and 600 points could be earned through content mastery as measured with the LO system detailed in this work.

### Ethics statement

The study design, data collection, and process for reporting data were reviewed and approved by our Institutional Review Board (project 1482047-3). Student participation was voluntary and only data from students who completed the course were included in the analysis and reporting.

### Data collection

Two types of data were collected for this study. The first was learning assessment data. These data included student performance on the LOs as well as on the cumulative final exam. The second type of data were student perceptions and attitudes. These were collected as surveys that were administered at the beginning, middle, and end of the course (weeks 1, 9, and 14, respectively). All data were analyzed and plotted using Microsoft Excel.

### Comparison between specs grading and traditional exam-based grading

Data representing the final exam performance were collected and analyzed from representative semesters when CHEM440 was offered over the past 10 years. During that time, the class size in each section ranged from 16 to 36 students. Aside from the specs grading implementation as described in this study, semesters where there was a significant structural change in the course delivery (e.g., online course delivery during the 2019 coronavirus disease pandemic) were omitted from the analysis. Many of the questions that appeared on the LOs were identical to questions that appeared on exams during the traditional offerings. The same final exam was used in all semesters included in this analysis, regardless of whether a specs grading or exam-based approach was used in a given semester. All sections were taught by one of the two instructors who coauthored this study.

## RESULTS

Student perception of mastery and their perception of learning are important components of success in a course. Student perceptions of knowledge on each of the 12 LO topics were measured on the first day of the course, at midterm, and on the last day of the course, using a five-point scale. A score of one indicated the perception of little to no knowledge of a given topic, while a score of five indicated perceived mastery of the topic. Perceived learning was measured as the difference in scores reported by the students at either the midterm or the end of the course and the score reported on the first day (Fig. 1). For the midterm survey, learning gains were only reported through LO 7, since that reflected the amount of material that was meaningfully covered in the course at that time. In all cases, the students reported an increase in their perceived mastery of the topics in the course. The largest reported learning gain was in LO 9 (the tricarboxylic acid [TCA] cycle), while the smallest gains were reported in LOs 1 and 2 (weak intermolecular forces and solution chemistry, respectively).

While the perception of mastery is a valuable component of the student experience in a course, perception of mastery can

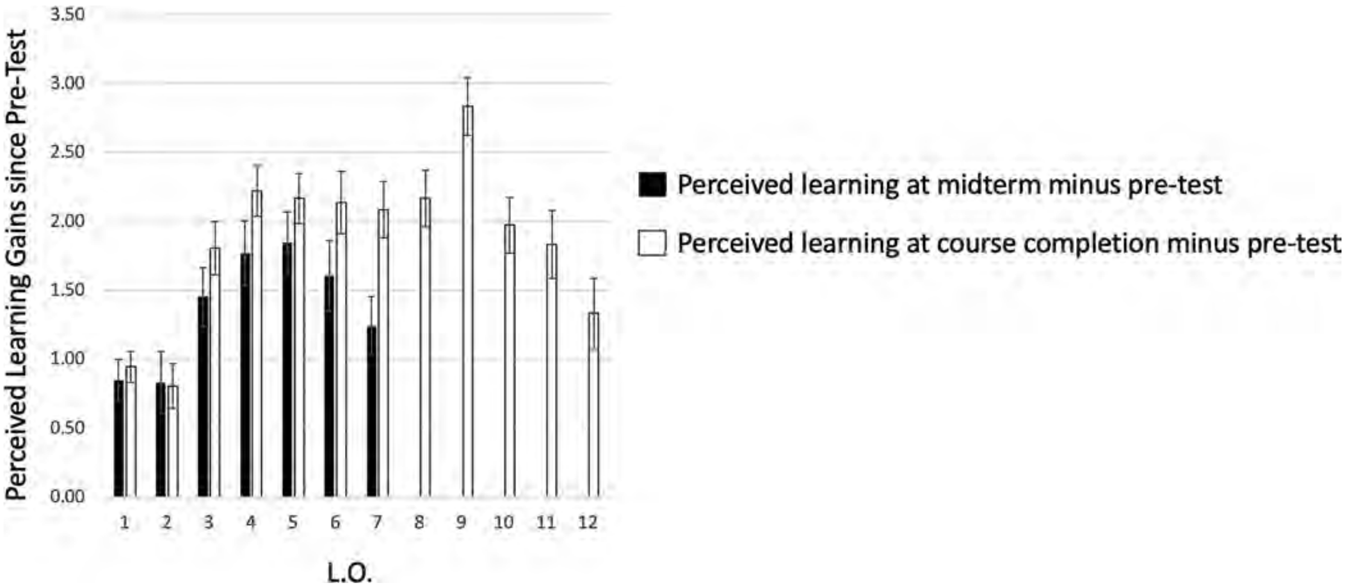


FIG 1. Perceived learning gains, shown as the difference in students' self-perception of their concept mastery pre- and post-LO completion, surveyed at midterm ($n = 33$) and at the end of the course ($n = 36$). Black bars indicate data recorded at midterm. Midterm data were only reported through LO 7, as material on the later LOs had not yet been introduced in class at that time. White bars indicate data recorded at the end of the course. Error bars indicate standard errors.

be inaccurate (18). Therefore, the perception of mastery on each LO topic was compared to mastery of the topic, as measured through the average performance on the corresponding LO (Fig. 2). Overall, there was good agreement between the perception of mastery and the measured mastery, as all but one LO topic showed a difference of less than 0.4. For 7 of the 12 LOs, the differences between perception and reality were less than 0.2. There were only three instances (LOs 3, 5, and 7) where the perception of mastery outweighed the students' performances on the corresponding LOs.

As with any new approach to evaluation, adopting a mastery approach can artificially impact student outcomes in the course. To compare the effectiveness of the mastery learning approach to a more traditional, exam-based approach, student performance on the LOs was compared to their performance on the final exam. The final exam was a cumulative exam that contained

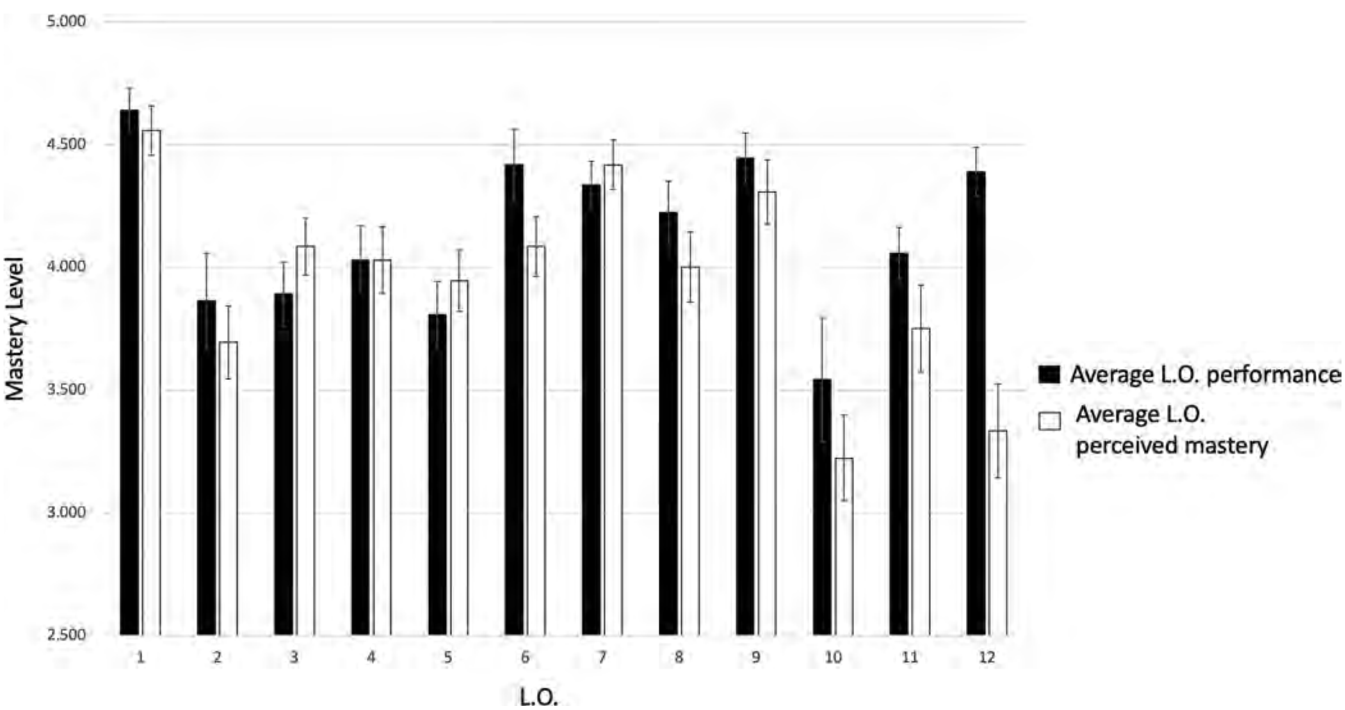


FIG 2. Actual learning gains compared to students' self-perceived learning gains for each LO. Values were calculated by averaging either student performance on each LO (black bars) or perceived mastery as reported on the final survey (white bars) across all students in the study ($n = 36$).

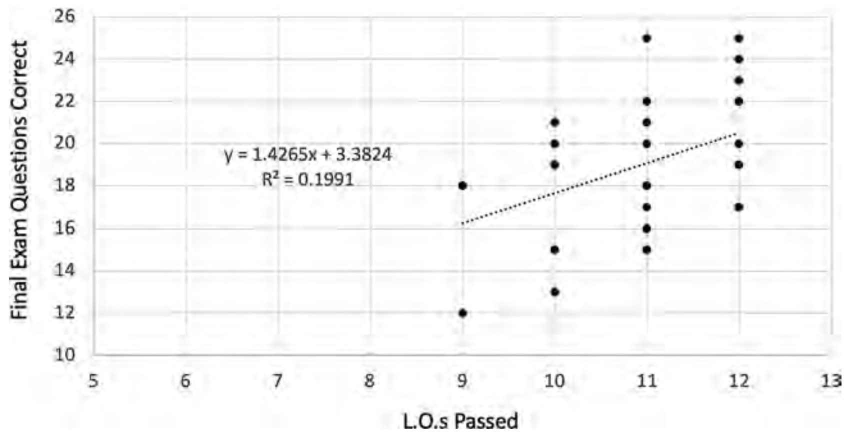


FIG 3. Scatterplot of individual student performance ($n = 31$) on the cumulative final exam as a function of total LOs passed. The final exam had a total of 30 questions. A correct answer was one that was entirely correct; questions on which students received partial credit were classified as incorrect for this analysis.

30 questions covering the material from LOs 1 to 10, and all questions were multiple choice. It was the only traditional exam that was administered in the course. That meant all students took the final exam at the same time, there was an opportunity to earn partial credit on some questions, and there was no opportunity to retake the exam to increase a student's score. Individual student performances on the LOs was compared to their performances on the final exam (Fig. 3). For students who successfully mastered at least nine of the topics in the course, there was a positive correlation between the number of LOs that were passed and the number of correct answers on the final exam. For this analysis, final exam answers that only earned partial credit were counted as incorrect.

In some instances, identical or nearly identical questions appeared on both an LO and on the final exam. Student success on these questions was measured to gauge retention of course material over time (Table 2). Across all identical questions and all student answers, those students who answered a given question correctly on an LO also answered that identical question correctly on the final exam 70% of the time. On the other hand, among all students who answered a question incorrectly on an LO, the identical question was answered correctly 61% of the time. These numbers can be compared to an overall correct answer rate on the final exam of 61%. The higher percentage of correct answers from the group that originally answered a question correctly on the LO suggested retention of the associated course material.

TABLE 2
Retention of material, assessed using identical or nearly identical questions on the LOs and the cumulative final exam[a]

| LO answer | No. (%) of students whose final exam answer was: Correct | Incorrect |
|---|---|---|
| Correct ($n = 321$) | 224 (70%) | 97 (30%) |
| Incorrect ($n = 261$) | 158 (61%) | 103 (39%) |

[a]Answers to these questions were first sorted into LO correct ($n = 321$) if the question was answered correctly on the LO or LO incorrect ($n = 261$) if the question was answered incorrectly. The values reported represent comparison of LO responses to those on the final exam that were then either answered correctly or incorrectly.

In addition to performance on course assessment materials, student attitudes toward the specs grading approach were measured at two points during the semester (Fig. 4). Students were surveyed on the first and last days of the course, and they were asked to indicate their preference toward specs grading or their preference for traditional exams on a five-point scale. The questions were: (1) which method is best for a science course, (2) which method is best for a biochemistry course, (3) which method helps you to learn more, (4) which method most accurately reflects your learning, (5) which method best fosters collaboration, and (6) which method is most likely to lead to academic dishonesty. In each of the first five questions, the students showed a preference for specs grading at both time points. The preference was stronger earlier in the course for questions 1, 2, 4, and 5. There was very little change in the preference for question 3. For question 6, early in the course students indicated they thought a traditional exam approach would more likely lead to academic dishonesty. This moved to a more neutral attitude by the end of the semester. It is unclear whether opportunity, temptation, or other factors associated with potential acts of academic dishonesty affected these responses.

The quantitative data on student attitudes were supported by qualitative data in the form of four open-ended survey responses administered at the beginning and end of the course (Table 3). The first two questions asked students to compare this course with their experiences in traditional, exam-based courses. Their responses to the first question indicated their belief that a specs grading approach promoted mastery of the course content more than an exam-based approach. While most students indicated they review their mistakes on previous assessments, regardless of whether the assessment is a traditional exam or an LO, 100% of the students in this study attended office hours at some point in the semester to look over their

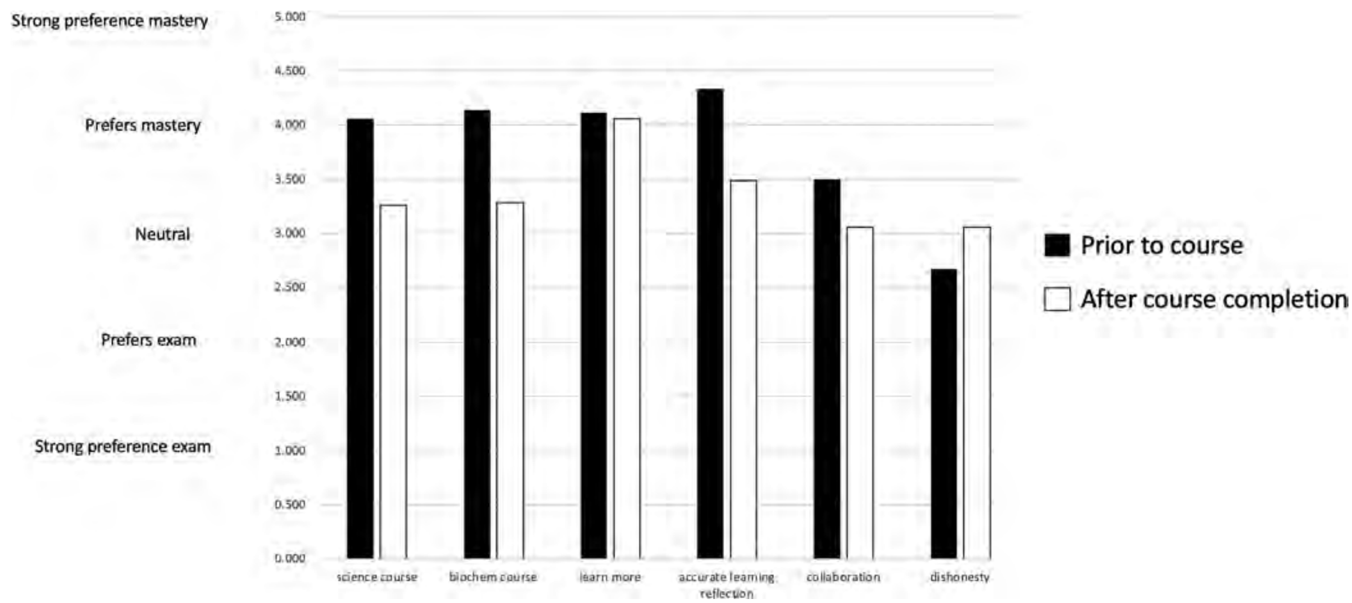


FIG 4. Likert scale of student-reported attitudes ($n = 35$) on the specification grading assessment LOs (strong preference = 5) versus a traditional exam format (strong preference = 0). Solid bars represent attitudes at the start of the course (before taking assessments), and empty bars represent student attitudes at the completion of the course.

past performance(s) on an LO(s). This indicated the LO system used here resulted in an increase in student's reviewing their mistakes compared to those in traditional, exam-based offerings of the course. The data on aspects of the system that students liked revealed the students appreciated the opportunity to meet often with their instructors and to have multiple attempts at demonstrating mastery. Conversely, the students reported they struggled most with fitting in 12 LOs with potentially two reattempts during the course of the semester.

To assess the success of the specs grading approach in comparison to a traditional exam-based approach, student performance on the cumulative final exam was plotted for representative cohorts (Fig. 5). The median performance in the semester where specs grading was employed was higher than in most semesters where exam-based assessment was used, and it was comparable to the highest medians for semesters where exam-based assessment was used. These data indicated that the specs grading approach is at least as good as the traditional approach in this respect. However, the scores in the specs grading semester were more tightly distributed than those in semesters where traditional exams were used. The significance of this difference in distribution was measured using the F test of variance. At the 95% confidence level, the variance in the scores in the cohort being assessed with the specs grading system was significantly smaller than that for six of the seven cohorts that were assessed with a traditional exam-based approach. Although the remaining exam-based cohort also had a larger variance than the specs grading cohort, the result was not significantly different at the 95% confidence level. The distribution of variances suggested the specs grading approach is a tool that more uniformly fosters learning across the entirety of the students in each class.

## DISCUSSION

Student's perceptions of learning are very impactful on their overall attitude toward a course and the content associated with that course. If students perceive that they are learning, it enables them to value the experience more, and it helps them to continue to be successful in applying the course material (19). In this study, students reported a perception of having increased their knowledge of every topic taught in the course. The largest reported learning gains were seen in topics where the students had little knowledge of the topic when they entered the course. Conversely, the students reported more modest learning gains on topics that they had seen in multiple previous courses, indicating that the students were likely closer to mastery of these topics when they entered the course, leaving less room for perceived learning gains on those topics.

In two of the three instances where student perception of mastery was higher than their actual mastery as measured by performance on the corresponding LO, the material was heavily quantitative (LO 5, Michaelis-Menten kinetics, and LO 7, Thermodynamics and redox chemistry). Future work could elucidate whether this performance discrepancy is a result of the need to solve quantitative problems. Success on these types of problems necessitates students practicing solving similar problems on their own. It is common for students to simply look over problems they've solved in class so that they recognize the right answer; however, without working problems on their own, they are unable to solve similar problems on an LO. It is possible this recognition without the ability to solve the problem would account for the differences between performance and perception.

Student performance on identical questions suggested that students who answered questions correctly on the LO

TABLE 3

Qualitative data containing student perceptions, collected in surveys administered on the first and last days of the course[a]

| Topic and bin | No. in bin | Representative comment |
|---|---|---|
| Ultimately your goal is to learn course content and develop problem solving skills. Thinking about prior chemistry and biology courses you've had, how well do you think taking hour long unit and or midterm exams helps you succeed in mastering essential and important learning objectives? | | |
| Positive | | I think they help because it allows me to easily connect topics and think of the course as a whole. It gives continuity for me. |
| Pre | 4 | |
| Post | 7 | |
| Neutral | | I think it helped me to remember a lot of topics in the moment, but didn't help me long term. |
| Pre | 10 | |
| Post | 9 | |
| Negative | | I would say large exams caused more stress and anxiety than seemed worth it. I never really mastered topics for long, seemed the information didn't get into long-term memory. |
| Pre | 22 | |
| Post | 20 | |
| How frequently do you review mistakes you've made on an exam to see if you can correct them before the next exam? | | |
| Positive | | All of the time, I want to know what I got wrong and why. |
| Pre | 20 | |
| Post | 22 | |
| Neutral | | Sometimes, but the class keeps moving so I would feel like learning the new chapters was more important. |
| Pre | 10 | |
| Post | 9 | |
| Negative | | Rarely ever. I feel like once an exam is over it's just time to move on to the next one right away and not even look at the previous. |
| Pre | 6 | |
| Post | 5 | |
| Are there aspects of this course you especially appreciated and would like to see retained for the future? If so, please list them here. | | |
| Meeting | 12 | I liked the aspect that you needed to meet with your professor to obtain your quiz so that you could get a detailed review with them. |
| Attempts | 5 | Three attempts allows for improvement. |
| Mastery | 4 | The LO system was good in my opinion and helped with mastering one topic at a time. |
| Engagement | 4 | I liked that I was essentially "forced" to study every night which I think helped me in learning the material |
| Logistics | 2 | I enjoyed having multiple attempts at the LOs and being able to do them at my own pace (there were lots of slots available). |
| Do you have suggestions for how this course could be improved? | | |
| Time | 10 | I would maybe offer more time in class to take the quizzes. |
| LO rules (e.g., no partial credit) | 14 | More than 1 LO/day if 2nd LO is going 4 to 5 |
| Logistics | 3 | It would be better to have tighter deadlines for quizzes. |

[a]Comments were binned by theme, and representative comments for each bin have been included.

were more likely to retain that information when asked the identical question on the final exam. The increased percentage of correct answers on the final exam among those who answered the identical question correctly on an LO (70%) over those that answered the question incorrectly on the LO (61%) likely underestimated the difference between these two groups. Within the group that originally answered the questions incorrectly and then answered correctly on the final exam, some students would have learned from their mistakes and retained the information. However, that group also included students who got the question correct because they simply remembered the correct choice after having a conversation about their errors on the LO with their instructor but who had not truly mastered the underlying course content.

After attempting an LO, students regularly met with their instructor to go over their mistakes so that they could improve their performance on subsequent attempts. During this study period, office hour attendance was tracked. Those data revealed

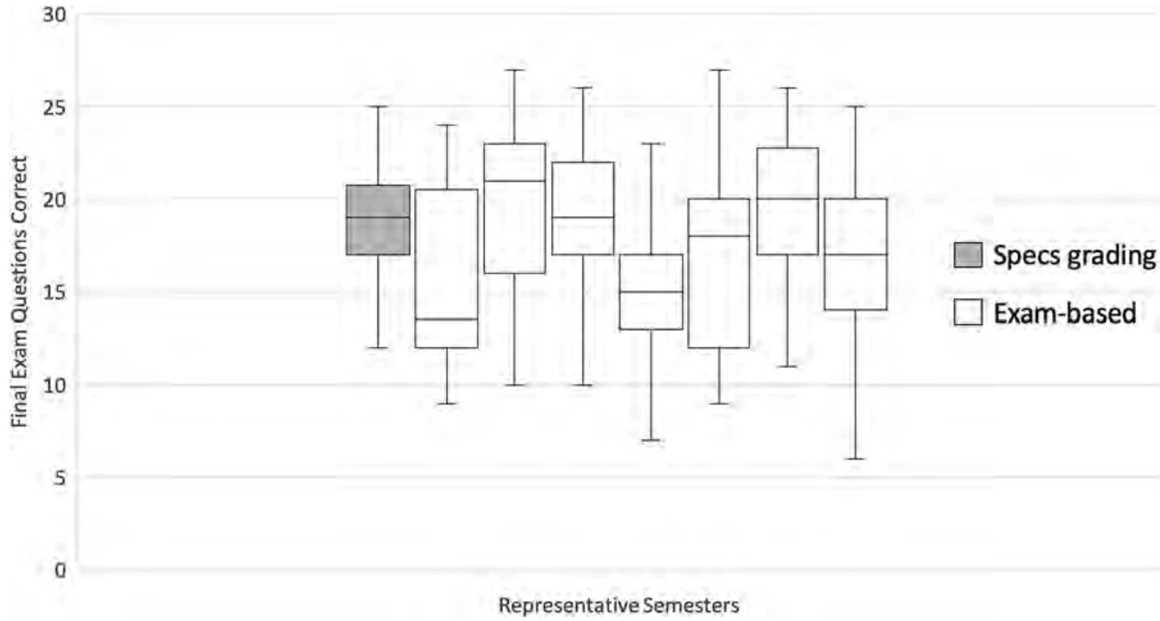


FIG 5. Final exam questions answered correctly were plotted as a box-and-whisker plot for representative semesters. Data shaded gray represent the semester where specs grading was used. Data in white represent semesters where an exam-based approach was used.

that every student enrolled in the course met with their instructor at least once to discuss LO performance and strategies for improvement. The one-on-one consultations with the instructor included discussions of learning strategies employed by the student. Metacognitive engagement by students has significant positive impact in their retention and depth of knowledge (20). The one-on-one consultation strategy ensured all our students were engaged in assessing their learning strategies. The logistics of a rapid feedback and consultation mechanism for a large enrollment class size would necessitate structural changes to the course to make the time commitment more practical. These changes would likely include teaching assistants who could hold regular office hours for LO attempts and discussion of previous attempts. This would offer the students more potential times outside regular course meetings to attempt LOs, thus increasing flexibility. Formatting this approach for larger classes would also require an alternative way of integrating a metacognitive component to the course design (21). The benefits of metacognitive engagement in introductory courses like general chemistry have been well studied, and it would be interesting to how see how they persist in student study habits in advanced courses (21).

The attitudinal data highlighted important changes in student perception between the beginning and the end of the course. Student attitudes were first surveyed at the beginning of the course, when very few, if any, of the students had any experience with a course taught using specifications grading. The description of a course without traditional exams, where the majority of the grade is determined by short quizzes with multiple attempts, bolsters student enthusiasm. This can be seen in Fig. 4, where the average attitude toward this approach was >4 (on a 5-point scale). A similar outcome of an overall positive perception toward specification grading has been reported for introductory to advanced courses (6, 14, 22, 23). Although this attitude waned over time, the final attitudes toward specs grading remained positive. The decrease in positive scores may have reflected an overinflated expectation prior to taking the course that the mode of grading would make the course less rigorous. Alternatively, given that course points are tied to the LOs and thus have a direct and meaningful impact on the students' grade in the course, the distribution of student perceptions could be based on mastery-oriented or grade-oriented attitudes, though this remains an area for further investigation (24). Once students experienced the grading approach, they were able to report a more realistic perception of how effective this approach to learning was for them.

Teaching always presents an opportunity for learning and making changes to pedagogical approaches. The introduction of a specs grading approach to this course has changed with each subsequent offering. The approach presented here was implemented after multiple pilot semesters. In the first offering, the course was split into 14 LOs instead of 12. The increased number of assessments seemed to require too fast a pace and not enough time for students to engage and reattempt the LOs, prompting the move to a system with 12 LOs. Early on, different LOs were given different weighting in the final grade. This made those LOs that impacted the grade more heavily feel like exams. Therefore, in recent semesters, all LOs were given equal weighting. Finally, due to the asynchronous nature of the LO offerings, the success of this strategy requires students to honor the confidentiality associated with each LO and each office visit. To facilitate that, a strict academic integrity statement has been introduced, which all students must sign, that clearly explains the expectations regarding maintaining confidentiality throughout the process of attempting and discussing LOs with the instructors.

Overall, the experience gained from the pilot offerings and the beneficial outcomes from the course model we implemented give us confidence for continued use of the specs grading model for assessment.

## SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

**SUPPLEMENTAL FILE 1**, DOCX file, 0.02 MB.

## ACKNOWLEDGMENT

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