JOURNAL OF CHEMICAL EDUCATION

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Development of a Broadly Accessible, Computationally Guided Biochemistry Course-Based Undergraduate Research Experience

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Cite This: J. Chem. Educ. 2021, 98, 400−409 Read Online

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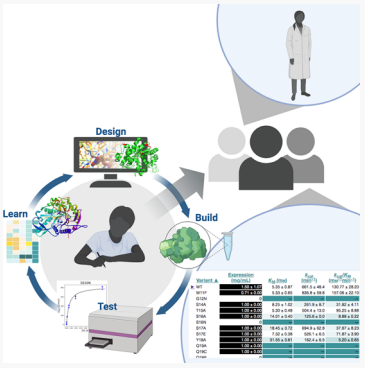
ABSTRACT: Including undergraduate research in STEM education is a well-supported and growing high-impact practice that has been made much more scalable through integrating these experiences into the classroom. Here we describe a new biochemistry Course-based Undergraduate Research Experience (CURE) that follows a design-to-data workflow with a strong connection to a worldwide community of protein modeling software developers. Analysis of psychosocial developments in association with participating in this CURE from the first set of students formally participating in the course suggest a beneficial effect on attributes associated with STEM persistence. To increase successful propagation, the design of the CURE's curriculum, supporting learning materials, and instructor resources are provided to make it facile for faculty at any institution to join this network and implement the CURE. With this foundation, we expect student participation and the data set to continue to grow.



KEYWORDS: *First-Year Undergraduate/General, Upper-Division Undergraduate, Biochemistry, Laboratory Instruction, Hands-On Learning/Manipulatives, Inquiry-Based/Discovery Learning, Amino Acids, Enzymes, Professional Development, Proteins/Peptides, Quantitative Analysis, Undergraduate Research*

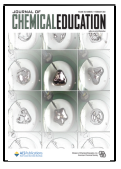
INTRODUCTION

In 2012 the President's Council of Advisors on Science and Technology called for 1 million more STEM (Science, Technology, Engineering and Math) professionals than projections estimate the current training programs will produce.[1] To compound the challenge, the demographics of the STEM labor force are inequitably distributed,[2−5] with women and certain ethnic/racial minorities (Black, Latinx, Native American) comprising just 29% and 13.6%, respectively, of workers in science and engineering occupations in 2017.[6] Higher education is positioned to address these gaps, and efforts in education reform have specifically focused on incentivizing practices that level the playing field for students of all backgrounds to encourage STEM retention.[7,8]

Undergraduate research has been established as a high-impact practice in education, and there have been national calls from the highest levels for the inclusion of research in STEM curriculum.[7−10] There is a fundamental challenge in making traditional, faculty-advised research opportunities available simply because of student−faculty ratios. Additionally, students who are predicted to benefit the most from Undergraduate Research Experiences (UREs) are the least likely to gain access to them.[11,12] Integrating hands-on research experiences into the classroom setting addresses both these issues: courses are a scalable means to impart experiences, and students do not need to allocate outside time or tap into social capital to access components of a class.[11,13] Such research-integrated classes—dubbed as "CUREs" (Course-based Undergraduate Research Experiences)—have multiplied as a national trend in education.[13]

CUREs have become a sweeping national movement in higher education; Dolan's 2016 review reports that, although there are exceptions, CUREs typically fall into one of two geographically based formats: (1) national programs with common research goals, technologies, or frameworks and (2) local programs or independent courses that are hosted by single institutions.[14] From a current, informal, and preliminary review of the CURE Network Web site—the CUREnet Collection—there are several large, well-established, multi-institutional CURE programs currently available in which faculty may participate.[15] However, there are only a few published courses in CUREnet that explicitly explore molecular structure−function relationships—one of the five core concepts recommended by the American Association for the Advancement of Science and the National Science

Received: August 11, 2020
Revised: November 9, 2020
Published: December 30, 2020



Foundation's seminal report: *Vision and Change in Undergraduate Biology Education*.[10]

Over the last year, four early adopter institutions have been incubating and building out the D2D CURE that involves students in an investigation of the sequence−structure−function relationship of enzymes for which the data is relevant to a community of protein modeling stakeholders.[16−19] Using the lens of protein biochemistry and the Design2Data (D2D) workflow, students in the CURE have the opportunity to expand their knowledge and develop skills by using computational modeling tools to design novel enzyme variants, after which they move into the wet lab to synthesize novel genes encoding the designed mutant, express and purify the corresponding protein, and finally biophysically characterize them (Figure 1).

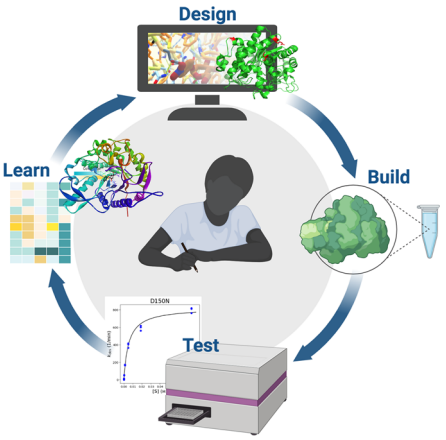


Figure 1. Design2Data workflow overview. Step 1: Design. Using Foldit,[20] students investigate and manipulate molecular interactions of designed variants, selecting a design they are interested in studying. Step 2: Build. Students create a synthetic gene encoding the designed mutant, from which the corresponding protein is expressed in *E. coli* using IPTG-induction and purified with immobilized metal-ion affinity chromatography. Step 3: Test. Data from kinetic and thermal-stability colorimetric assays performed on purified enzymes are fitted into Michaelis−Menten and temperature-to-activity relationship models, respectively. Step 4: Learn. Data are uploaded into a publicly accessible data set being used to develop new enzyme modeling algorithms. In addition, students re-evaluate their variants in Foldit and compare their experimental outcome with original predictions to redevelop their hypothesis about the protein's structure−function relationship. Graphic created with BioRender.com.

Variations of the D2D wet-lab workflow comprise national CUREs: Biochemistry Authentic Scientific Inquiry Laboratory (BASIL),[21] Biology Laboratory Education (BioLED),[22] and Malate Dehydrogenase CUREs Community (MCC);[23] however, the workflow's seeming ubiquity is unsurprising as it is representative of much protein biochemistry research and enables broad, equitable access to cutting-edge biotechnology training that is in high demand by employers.

A feature that makes D2D unique among other multi-institutional protein biochemistry CURES is it is connection to the protein modeling research community: Rosetta Commons, which uses the D2D student-generated data to improve functionally predictive enzyme-design algorithms.[24,25] Over 100 institutions comprise the Rosetta Commons, and the software suite developed by the group has been licensed over 35 000 time.[25] A grand challenge that faces the Rosetta and other protein engineering communities is a lack of functional data for software benchmarking.[26] Before 2016, the largest data set that probed the effects of enzyme gene mutation on soluble protein expression, thermal stability (T_{50} or T_M), turnover number (k_{cat}), and response to varied substrate concentrations (K_M) consisted of only 30 data points,[27−30] precluding the use of any advanced computational methods without risk of overfitting to the training data set. In 2016, the Siegel Lab published the largest data set of its kind with ∼100 enzyme mutants, where each of these parameters were explicitly measured, and the data set was expanded upon in 2017.[18,19] Based on these early scouting data, a critical result from the analysis of Carlin et al. (2017) indicated that more data are required before advanced computational methods can be used to start quantitatively predicting function. Given the vast potential sequence space of proteins (e.g., for β-glucosidase there are ∼10 000 single-point mutations and $>10^{500}$ combinatorial mutations), the project is ideal for the work of many hands and many minds.

The underlying research goal of the D2D CURE is to facilitate "academic crowd-sourcing" to rapidly address questions that would normally take isolated laboratories decades to answer and, as such, is well positioned to expand to a multi-institutional, national program. In 2019 we initiated the D2D Network and engaged four faculty from institutions across the country who beta-tested teaching D2D or made significant steps in planning their course; this team's insight and collective wealth of teaching and research knowledge, along with a small group of expert advisors, have been the guiding force of program development. In the 2020−2021 academic year, we plan to expand the program to serve a total of 12 institutions.

Herein, we will describe the curricular and programmatic components (i.e., workflow modules and learning objective) of the D2D CURE and faculty network and will assess preliminary student attitudinal shifts that have been linked to STEM persistence, a small but key first step in examining this CURE's efficacy in meeting the national calls for an expanded STEM labor force. We aim to provide suitably detailed course and network information for prospective instructors and preliminary evidence of the course's success to warrant expansion of the program and guide that development.

METHODS

D2D Workflow Modules: Activities and Learning Objectives

The workflow of the D2D is broken into four distinct modules, Design, Build, Test, and Learn, that engage students in activities common to molecular biology and biochemistry research (Table S1); the full lab manual can be access through the program's static Web site https://d2d.ucdavis.edu/. Six D2D faculty network members rated their perception of the alignment between the modules and the American Society of Biochemistry and Molecular Biology (ASBMB) certification test published learning objectives.[31,32] These learning objectives were selected because they integrate concepts that bridge between biology and chemistry disciplines and are organized by the Vision and Change core competencies.[10] The 5-point Likert-scale response data means for each learning objective-to-module alignment were translated to the connection thicknesses in Figure 2. The full set of items is

https://dx.doi.org/10.1021/acs.jchemed.0c01073
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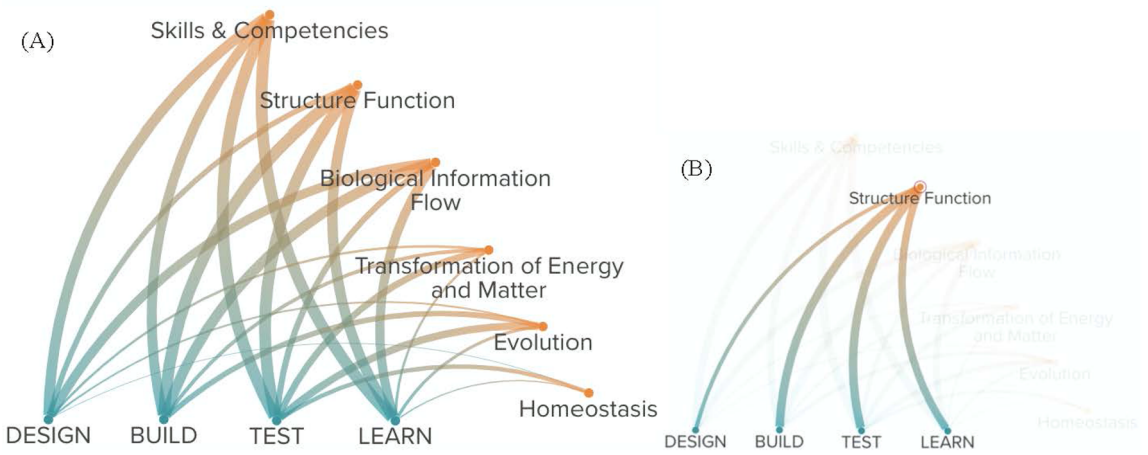

Figure 2. Design2Data (D2D) module and ASBMB learning outcome alignment map. Map shows the relationships between learning outcomes and modules where connection line thickness represents the relationship strength. Module nodes (teal) are organized left to right to capture the workflow progression. Learning outcomes (orange) are organized vertically and spread out in space with the uppermost node having the strongest connections to the modules descending to the lowermost node with the weakest connections. (A) Data for all outcomes and modules shown. (B) Highlighted structure−function data shown by "focus" feature that allows viewers to examine elements in isolation. Figures created in Kumu.io.[41]

provided in the Supporting Information. These questions were not validated; the very preliminary, rudimentary analysis seeks to begin to address the question: "how might we visualize the complex and often overlapping alignments between standard, relevant learning outcomes and the D2D CURE modules?"

D2D Course Variation Descriptions

In the 2019−2020 academic year, the D2D network produced two courses that completed the workflow and were included in the study's evaluation methodology (Table 1). These two courses were both offered by large, R1 institutions on the Eastern and Western Coasts; however, one served as a senior capstone molecular biology and biochemistry course and the other was offered as a nonmajor's, first-year, elective class, with other notable variations described in Table 1. Other planned courses were halted in spring 2020 by COVID-19 pandemic. Course 2 made it nearly to the end of the workflow, but students were given mock data to analyze for their final presentations, as they were also barred from wet-lab activities because of health and safety restrictions. Course 1 was first piloted in 2017 and initially broken up into a two-course series that stretched the workflow over a 20-week period, but in the 2019 iterations, it was compacted into a single 10-week quarter. These adaptations exemplify the range of possibilities for structuring the class. All courses were led by a faculty instructor and had some degree of graduate student or staff support for both instruction and class preparation.

Table 1. Summary of D2D CURE Courses Offered from 2017 to 2020[a]

Variable	Course 1	Course 2
Terms offered[a]	Spring 2017, summer 2017, fall 2017, spring 2019, fall 2019	Spring 2020
Institution region	West Coast	East Coast
Institution type	R1	R1
Term length	10-week quarter	16-week semester
Average number of students served/term	20	48
Course level	Lower division	Upper division
Course units/credits	2-credit (quarter)	1-credit lab course (semester)
Course descriptor	First-year seminar	Senior capstone
Modules completed	Design, Build, Test, Learn	Design, Build, Test, Learn

[a]More than one section was offered in some terms.

Summary of Inaugural D2D Faculty Network

The first year of the D2D multi-institutional research team was supported from an NSF Research Coordination Network grant. The network activities included: a cornerstone, week-long immersive professional-development workshop; monthly remote meetings for troubleshooting, maintaining connection, guiding program developments, and sharing learning materials and resources; and shipment of a "care package" of in-house reagents like plasmid template single-strand DNA and competent cells. The 2019−2020 network members included four tenured and tenure-track faculty. The network was coordinated by a staff scientist, and technical web application and database development was performed by a research faculty member.

Student Psychosocial Assessments

Between 2017 and 2020 the D2D CURE program hosted 11 sections of the course. In all but three of these sections, students were surveyed to investigate course-related shifts in psychosocial factors associated with STEM persistence, and their response data were included in this study. We selected this metric for analysis because our overarching student learning goal is to increase the likelihood of student matriculation into STEM careers, with STEM major persistence being a key and measurable midpoint stepping-stone. However, as we are in the early phases of the program, we do not yet have graduation data to analyze. In the interim, we are investigating attitudinal shifts that influence social integration, which include self-efficacy and identification as a scientist.[33] Throughout all courses, we used the Scientific Identity and Scientific Self-Efficacy question sets validated in Robnett et al., 2015, with small language variations (Supporting Information). In Fall 2019, we added question sets exploring (1) scientific community values and (2)

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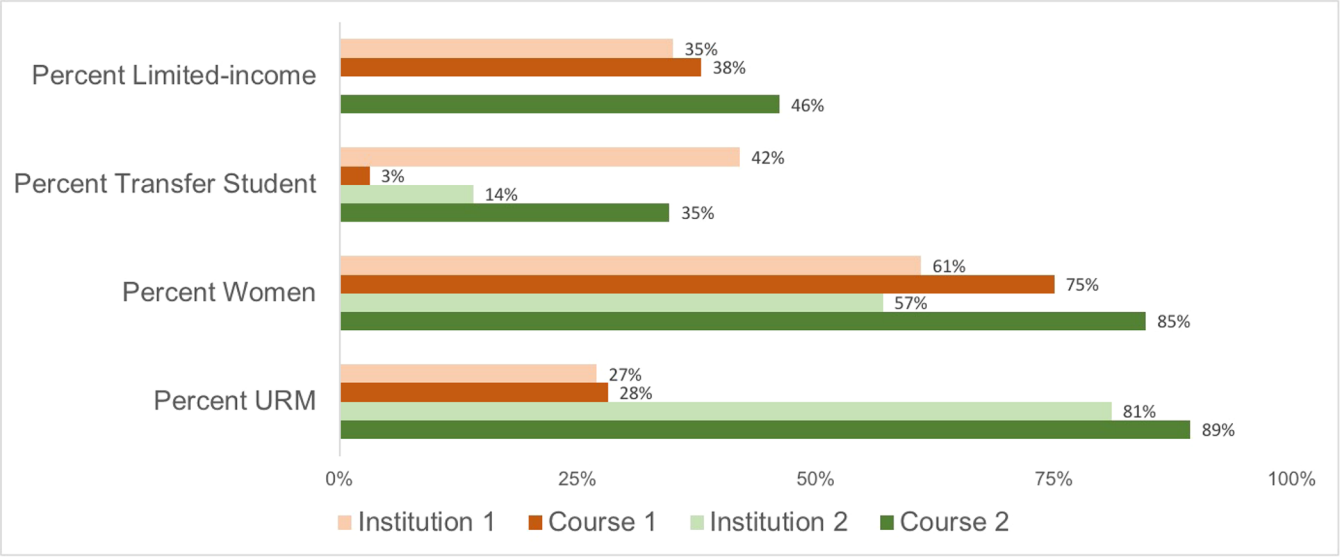

Figure 3. D2D Student body demographic composition of courses and of each course's institution. URM student percentages align with student bodies of each participating institution, as does limited-income at Institution 1; note, these data are not reported publicly for Institution 2. Both courses attracted a high percentage of women students relative to their respective institutions' student bodies. Transfer student participation in Course 1 fails to represent the institution's student body, while in Course 2 it exceeds it.

networking behaviors, instruments validated separately for predicting STEM persistence by Hanauer et al. and Estrada et al.[3,34] For the purposes of this study, we will refer to the networking question set as "Networking & Engagement" because the questions ask students about behaviors that indicate engagement in the project, perhaps more so than behaviors that create a research network. We matched students' pre- and postcourse responses using unique identifiers and omitted unmatched responses from the sample set with a total of 76 paired responses for the final analysis. A full breakdown of response data is listed in Table S2.

In 2017, our study design protocol involved Family Educational Rights and Privacy Act (FERPA) data-release consent, and survey response data were matched with registrar admission data for demographic analysis. In 2019, we began asking students to self-report these data instead. Institutional student body demographics used for demographic representation comparative analysis were obtained from publicly available reports.[35,36] We did not include a control group of students for comparison who were not enrolled in a D2D CURE, as such only inferences about associations are appropriate to draw from these data. The methods in this study were approved by University of California, Davis, Institutional Review Board, IRB protocols: 983274 &1289158.

Statistical Analyses

Pre- and postcourse responses were aggregated as a mean score for each psychosocial factor question set and differences were compared by the Wilcoxon sign rank test. Score differences pre- and postcourse were calculated between independent variable groups and were assessed by the Student's t test; pooled or unpooled methods were selected depending on sample variance.[37] Statistical significance was interpreted as differences between groups where p-values were calculated to be less than 0.05. Concurrently, normalized gains (g) were assessed for independent variable groups; gain (g) interpretation follows: high, $0.70 < (g)$; medium, $0.30 < (g) < 0.70$; low, $(g) < 0.30$.[38] Effect sizes based on the difference between means (d) were measured and interpreted following Cohen's 1988 analysis: high, $0.80 < (g)$; medium, $0.20 < (g) < 0.50$; low, $(g) < 0.20$.[39] All statistical analyses were done in R version 4.0.0.[40]

RESULTS

The D2D workflow modules and their relative learning objective alignments are shown in Figure 2, which previews the interactive visualization tool capable of highlighting the varying strength of relationships between the activities and learning objectives (https://d2d.ucdavis.edu/goals-and-activities-students).

From this first-pass, very limited analysis, we observe the strongest perceived connections are between *Skills and Competencies* objectives across all four modules; *Structure Function* objectives appear most strongly aligned with the Build, Test, and Learn modules; and *Biological Information Flow* most aligned with Design and Build modules. *Transformation of Energy and Matter*, *Evolution*, and *Homeostasis* are all weakly linked to all the modules, with an average response score indicating "The module touches upon the concepts but will not facilitate any level of proficiency of the learning objectives".

Student survey data were collected from Institution 1 and Institution 2. The self-reported demographic data suggest that the course participants well represent the student body from the respective institutions (Figure 3), with two exceptions: transfer students at Institution 1 (~35% of student body) and women students at both institutions. For example, nearly 80% of Institution 2 students are either or both of Latinx or African American descent, and at Institution 1 Underrepresented Minority (URM) students comprise about 25% of the undergraduate student body. While there are more women than men students at both institutions, women do not exceed 61%, making the high percentage of women student participants in these classes striking.

We surveyed students for social−psychological attributes that have been associated with STEM persistence in other studies.[3,34] The overall pre- and postcourse response analysis

https://dx.doi.org/10.1021/acs.jchemed.0c01073
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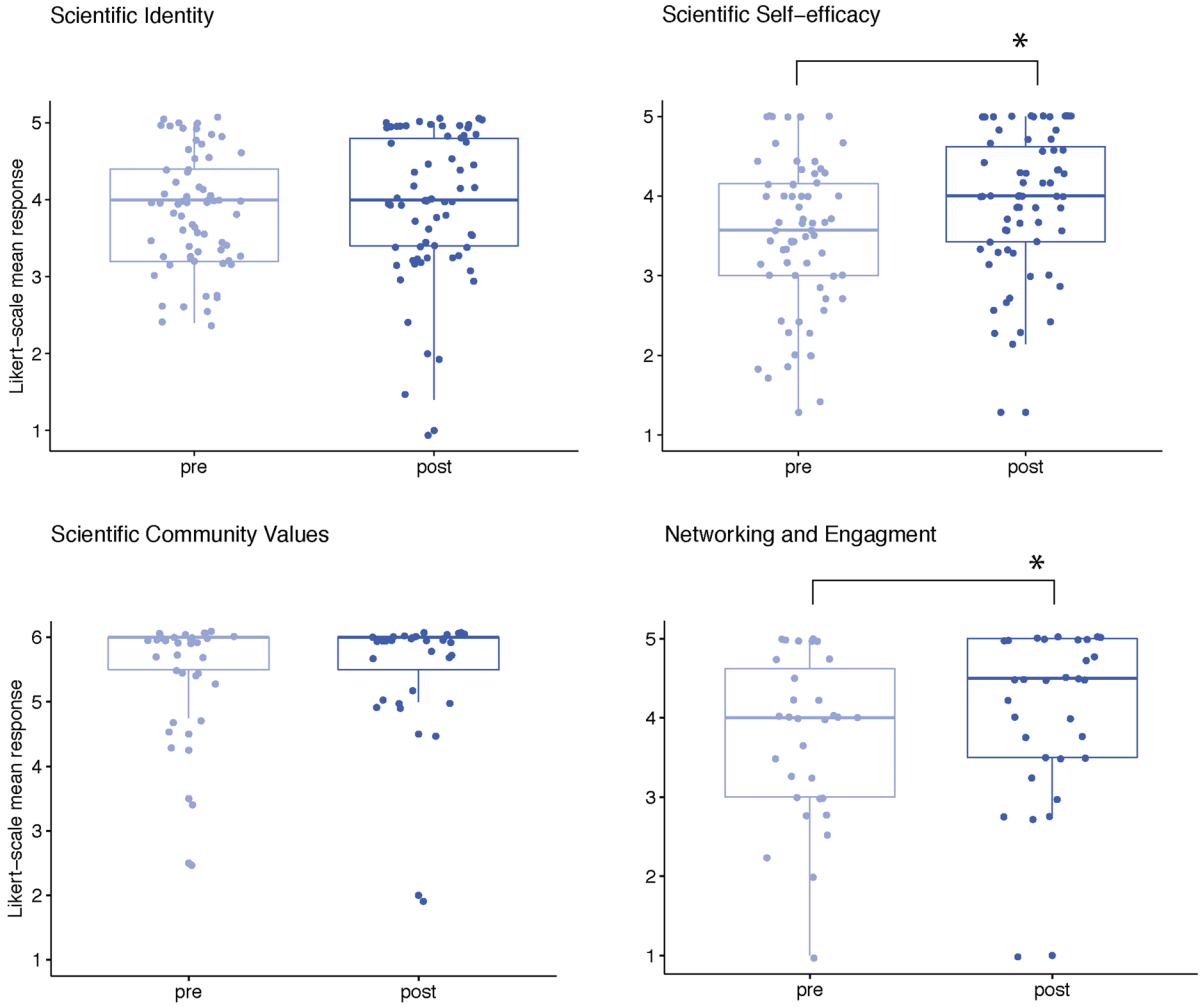

Figure 4. Pre- and postcourse survey responses for the 5-point Likert scale question sets: Scientific Identity (N = 67, p-value = 0.081); Scientific Self-efficacy (N = 67, p-value = 5.87×10^{-5}), and Networking & Engagement (N = 31, p-value = 0.01). Six-point Likert scale question set: Scientific community values (N = 31, p-value = 0.62). *p-value < 0.05. Quartiles (Q_1 (25th percentile) and Q_3 (75th percentile) show the median of the lower and upper halves of the data sets, respectively; the data median is shown at Q_2(50th percentile). The whiskers extend to the most extreme data points, which are no more than 1.5 times the length of the interquartile range.[42] Likert scale defined: the strongest supportive response (i.e., strongly agree) for instruments' questions/prompts is represented as 5 or 6, depending on scale, and strongest rejective response (i.e., strongly disagree) is represented as 1.

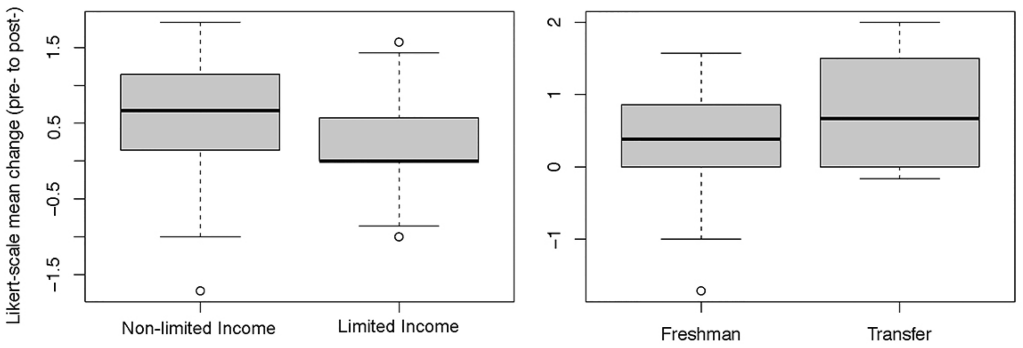

Figure 5. Demographic variables: Income level and admission level (first-year, transfer) have a small but likely meaningful difference (p-value < 0.10) on Scientific Self-efficacy response outcomes. Limited-income students (N = 24) show reduced gains compared to students of other income levels (N = 37). Transfer students (N = 13) have increased response gains in comparison to freshman-admit students (N = 54). Quartiles (Q_1 (25th percentile) and Q_3 (75th percentile) show the median of the lower and upper halves of the data sets, respectively; the data median is shown at Q_2 (50th percentile). The whiskers extend to the most extreme data points, which are no more than 1.5 times the length between Q_1 and Q_2 from the box.[42]

shows negligible gains in students' researcher identity, a ceiling effect in scientific community values, but significant gains in students' self-reported Scientific Self-efficacy as well as Networking & Project Engagement (Figure 4). This analysis

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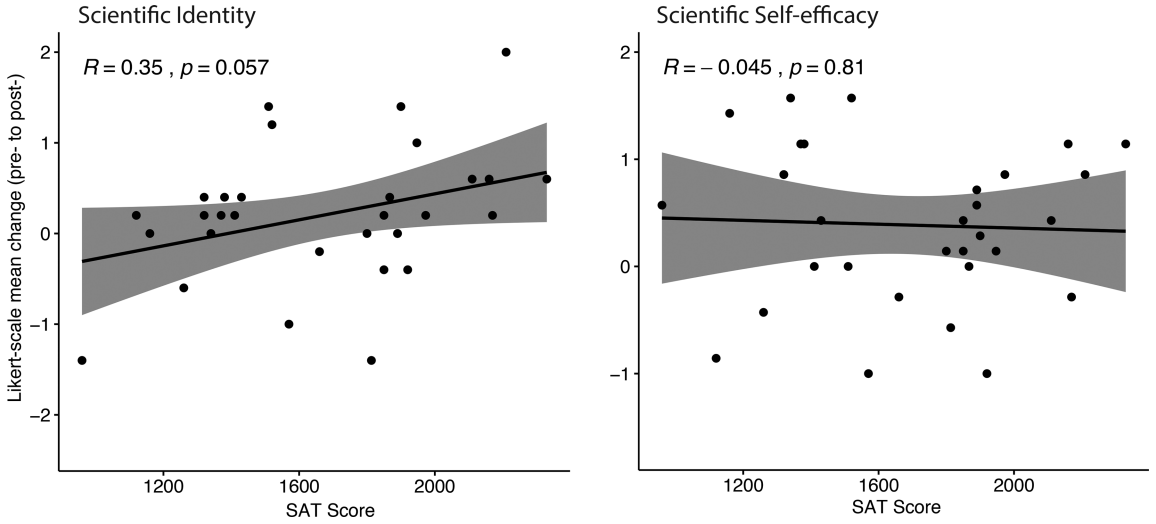

Figure 6. SAT score is predictive of gains/reductions in Researcher Identity but not Scientific Self-efficacy. SAT score data was provided by the registrar and matched to student response data for Institution 1 courses in 2017−2019 (N = 31).

aggregates survey data from both participating institutions. We next investigated breakdowns by school and demographic factors that may contribute to students' experiences.

We evaluated pre- and postcourse Likert scale response score variations in each of the four psychosocial factors surveyed, broken out by underrepresented minority (URM), first in family to attend college, and limited income statuses, as well as transfer or first-year admission level, gender identity, and institution (Table S2). We did not observe significant differences in response data between any of the investigated variables; all p-values exceeded 0.049 (Table S2). We observed modest differences ($0.05 \leq p$-value ≤ 0.1) in self-reported scientific self-efficacy in association with limited income status and transfer admission (Figure 5). Small to medium size normalized gains and effect sizes paralleled the larger pre- to post- increases we observed in Scientific Self-efficacy and Network & Engagement responses.

In addition to the demographic variables, for which we collected data from all surveyed students, we collected admission data in 2017—with student's FERPA data release consent—from the institution's registrar, which allowed us to link students' survey response data to their SAT scores (Figure 6). We found a positive relationship between SAT score and gains in researcher identity but not in gains in scientific self-efficacy.

Given the development of materials to support implementation, variations between (a) upper and lower division course offerings and backgrounds and (b) preparatory experiences of the student participants and the course-associated psychosocial gains point to overall program functionality and open the doors to avenues for further evaluation and expansion.

DISCUSSION

The developments of the logistical components of the D2D course and benefits of student participation support readiness for—and will serve as a guide to—program expansion. The design−build−test−learn workflow approach to studying the β-glucosidase B enzyme system was first conceived as an undergraduate training and research experience by Siegel in his graduate program, and it has developed into the current program at a steady and sustainable rate that has afforded the time to benefit from many contributors as it has evolved. The course-support materials, particularly the learner-centered laboratory manual, now stand as resources that make adopting this course (in both partial and full-form) more feasible for new network faculty. The following discussion aims to (1) supplement the technical instructions in the lab manual by sharing the salient recommendations about teaching students through the workflow, (2) describe successes and obstacles in assessing student learning objectives and goals, and (3) propose future directions of the course and network.

Workflow Module Implementation Insights: Opportunities and Challenges

In considering the workflow progression, the "Design" module is the section where student's creativity most comes into play. Here students explore their enzyme mutation in virtual 3D space using a simplified yet representative version of the Rosetta Molecular Modeling software suite. We have found that this is a truly accessible entrée into the world of computational protein design; however, it can be challenging for novice students make reasonable interpretations about their mutant designs. Recently, Miller et al. produced a new version of Foldit, *Foldit Education Mode*, that not only leads students through the mechanics of the game but also supplements essential biochemistry concepts in a playful and friendly format that serve as just-in-time teachings to support this workflow module.[43] The current versions of Foldit work well on Mac and PCs, but Chromebooks remain a challenge; we recommend working with your campus IT to provide remote access (i.e., virtual box) or a computer lab to support students who may not have access to Windows or MacOS machines. When students are ready to reverse-translate the amino acid sequence of their protein variants to codon-optimized DNA oligos to take forward into Kunkel mutagenesis, instructors may choose to have students do this by hand, but we also provide an interactive, dynamic application on our Web site that performs this task (https://www.d2dcure.com/resources/oligo_search/) Instructors and students can interface with resources as best fits their course's level and learning goals.

In the "Build" module, students venture into the wet lab and explore the translation between theoretical and experimental research, while quickly developing their technical skills. We

https://dx.doi.org/10.1021/acs.jchemed.0c01073
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include a full session on the basics of pipetting, which we've found to be essential for subsequent experiment success in the workflow. When Kunkel fails, we find the most common culprits are old molecular biology reagents, sensitive to freeze−thaw cycles; we recommend making single-use aliquots for small groups or pairs of students. The combination of (a) students with very novice-level lab experience and (b) a workflow that requires samples to matriculate through a building, term-long progression exacerbates any inconsistencies in students' labeling techniques. At the start of the term, assigning students a number, which they must use to label all of their tubes, has made a huge impact on reducing "sample attrition". With these tools, we've found kick starting the wet lab sequence with Kunkle mutagenesis and transformations to be straightforward. When analyzing gene sequence data to verify success of the mutagenesis, we've designed our lab manual instructions to guide student in using Benchling, which is free, intuitive, web-based software that works on any machine with access to the Internet.[44]

The research activities in the "Test" module engage students in an exploration of enzyme dynamics and experimental design. Students learn the basics of engineered expression systems and purification techniques and then carry those forward into the functional assays, which are the culmination of their efforts and which generate contributable data toward the main research goal of this CURE. β-Glucosidase B is a robust enzyme that is easily expressed in small cultures (i.e., five milliliter volumes); further, it works with a stable and inexpensive colormetric substrate making it ideal for novice hands. When no significant protein is obtained after expression and purification, we recommend repeating the protocols but replicating the nonsolublely expressed and isolatable protein is a viable result and one with considerable importance as part of the data set. Mutant characterization should always be done in parallel to a positive control of the wild-type β-glucosidase B to ensure all reagents and methods performed by the student were correct. The "Test" component of the workflow is the most resource intensive, requiring multichannel pipettes and a plate reader. We provide assistance to institutions with limited research resources by mailing a loaner plate reader as well as partnering with biotech vendors for educational discounts on equipment. Further, should network institutions prefer, they can do any of the modules independently. For example, a course might only include the modules "Design" and "Build" and would ship sequence-verified plasmids to another institution to integrate them into their "Test" and "Learn" sample pool. Thus, the network facilitates flexibly to accommodate different curricula and varying resources.

While the wet-lab modules have natural stopping points, in which samples can be stored safely, there are sets of protocol that are time sensitive and require students to progress rapidly through the workflow. The "Learn" module is an opportunity for students to slow down, reflect on, and synthesize their results and to go deeper into the scientific concepts that are applied in technical activities they have engaged in. Registered D2D students interact with the program's dynamic, online data analysis apps (https://www.d2dcure.com/submit/), which allows any student, regardless of coding experience, to use curve fitting software to examine data (1) using the Michalis Menton model and (2) for loss of enzymatic activity in relation to temperature increase. Students learn to evaluate their hypothesis and to present their results with a scientific poster.

In summary, each of the modules has opportunities and challenges for implementation and for student learning; the D2D faculty network and the program facilitators have become increasingly better equipped to share resources and support new implementers.

Meeting Student Learning Objectives and Goals

Published CURE assessments have primarily focused on investigating student *competencies* and the degree to which students experience the defining features of CURES.[15,45,46] In contrast to these assessment practices for CUREs, we are interested in taking a deeper dive into formally coding and analyzing how D2D activities facilitate increased *concept* knowledge core to biology and chemistry curricula such that we can expand our very preliminary evaluation of these relationships in Figure 2. Anecdotal reports from collaborating faculty support this idea, describing calls from administrators to "check the box" by using evidence-based practices to teach conceptual learning outcomes included in course descriptions; we would like to understand if and to what degree the D2D course is accomplishing this. However, we have focused our current assessment efforts on our overarching student learning goal: to motivate student to stay in STEM.

Of the psychosocial factors we assessed in this study, the Scientific Community Values instrument was the only one to show a "ceiling effect", meaning that no growth was observable because most students strongly agreed with the Likert-scale questions prior to taking the course. It is not clear why this is occurring; though there are small variations related to the demographic variables, none are significant (Table S2). Further, variations between the two institutions, which we might expect to produce considerable differences in psychosocial outcomes, appear to not have an effect. For example, Institution 2's course served senior students, who may have had previous research experiences, while Institution 1's course targeted incoming freshman. Additionally, the breakdown by institution captures the variable COVID-19 effects in that Institution 2 did not complete characterizing their mutants due to COVID related shutdowns and relied on mock data. While we did not observe an effect in our quantitative data, we did capture students' anecdotal accounts of much disappointment. Otherwise, we observed negligible and modest gains across the other factors with Scientific Self-efficacy being the most pronounced; this is supported by the results of effect size and normalized gain analysis. Deeper analysis of this result in the context of the relationship between pre- to postcourse gains and academic preparation—as proxied by incoming SAT score, particularly in contrast to the Researcher Identity results—is encouraging and indicates that the Scientific Self-efficacy instrument might be the best suited psychosocial factor for predicting programmatic benefits for students of different backgrounds and levels of academic preparation. In other words, from these initial data, the D2D experience may be helping students of all levels of preparation feel more confident about their ability to carry out scientific work.

From the network's first academic year, we were able to report success in offering the course in upper- and lower-division formats. The courses attracted student participants demographically representative of the respective institutions' student bodies with two exceptions. Institution 1 has a large transfer population that is not well-represented, but that is likely because the course is marketed through the first-year

https://dx.doi.org/10.1021/acs.jchemed.0c01073
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seminar program, and while it is open to transfer students, it has generally low transfer-student enrollment. Anecdotally, transfer students do not identify as first-year students, and this likely influences their enrollment in classes advertised as such. However, we are unable to propose a clear reason for the high rate of female participation in these classes; this unexpected and pronounced variation warrants further investigation.

The student research activity—contributing quantitative results to an open access, stakeholder-relevant database—is a feature of D2D that makes it stand out from other similar protein-engineering and characterization CUREs. This provides students with an activity that captures a research milestone in a way that has been shown to motivate students.[47] While there is debate regarding the necessity of publication as a research outcome for CURE legitimacy, unpublished reports from those teaching CUREs and a few published examples point to the difficulty of producing finalized, peer-reviewed research products.[48,49] Given this, it is encouraging to consider the results of the Wiley and Stover study[47] and their recommendation that dissemination of student results directly to a user audience as part of the course has positive student outcomes. The D2D database is in an early beta-test phase of development and has built-in functionalities that assist students in analyzing how and whether their initial design hypotheses were supported. The overall design of the project is optimal because, regardless of whether a student's hypothesis is supported, the data are of interest and important for protein-design algorithm development while still giving students the opportunity to independently explore a scientific question.

Thinking Forward

As we move into the second year of producing networked D2D CUREs, we look forward to continuing the associated student-outcomes research. We expect that differences in outcomes related to demographic variables will emerge as our participant population grows; however, results that continue to show limited differences will be equally interesting, thus further supporting benefits to students from all backgrounds. We also look forward to expanding our analyses of the D2D CURE to the student-generated database itself. We intend to investigate data replicates from different institutions, complete characterization of particular residues, and eventually integrate new enzyme systems and the comparison of results across systems. Our network aims to annually grow in size at a rate that both aligns with the biochemistry and molecular biology teaching community's needs and with our capacity for coordination and to host professional development opportunities. We will to continue to analyze and report on faculty network participant perceptions, student learning and attitudinal outcomes, and research progress.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available at https://pubs.acs.org/doi/10.1021/acs.jchemed.0c01073.

Table S1: Research tasks students complete in modules through progression of the workflow (PDF)

Table S2: Breakdown of surveyed psychosocial factors by demographic variables to investigate variations between sample groups (i.e., research identity response differences of URM versus non-URM students) (PDF)

Pre- Post- Psychosocial Question Set D2D-CURE Student Survey (PDF)

D2D Module & ASBMB Learning Outcome Alignment Questionnaire (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors acknowledge Erin Dolan for providing critical support and consultation on this project's development and particularly the assessment design. Special thanks to Marc Facciotti and Andrew Yao of the MPBIL space for their efforts in supporting these classes. Thanks to the D2D team of faculty members for sharing perceptions of learning outcome alignment with student research activities. Thanks to many members of the Siegel Lab, particularly Peishan Huang, Ryan Caster, Morgan Connelly, and Alex Carlin who helped develop the original protocols for the D2D workflow and to the team of undergraduates who continually provided feedback on the materials. We thank the UC Davis Center for Educational Effectiveness team for assistance with data management. We acknowledge support from the National Science Foundation award #1827246.

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