Article

Anticipated Learning Outcomes for a Biochemistry Course-Based Undergraduate Research Experience Aimed at Predicting Protein Function from Structure: Implications for Assessment Design[S]

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Abstract

Several course-based undergraduate research experiences (CUREs) have been published in the literature. However, only limited attempts have been made to rigorously identify the discovery-type research abilities that students actually develop during such experiences. Instead, there has been a greater focus on technical or procedural-type knowledge or general CURE skills that are too comprehensive to effectively assess. Before the extent of discovery-type learning outcomes can be established in students (termed verified learning outcomes or VLOs), it is important to rigorously identify the anticipated learning outcomes (ALOs) and to then develop student assessments that target each ALO to reveal the nature of such student learning. In this article we present a matrix of 43 ALOs, or course-based undergraduate research abilities (CURAs), that instructors anticipate students will develop during a recently-developed biochemistry CURE focusing on the prediction of protein function from structure. The CURAs were identified using the process for identifying course-based undergraduate research abilities (PICURA) and classified into seven distinct themes that enabled the characterization of the CURE and a comparison to other published inventories of research competencies and CURE aspects. These themes and the CURE protocols aligning to the CURAs were used to form the ALO matrix that was, in turn, used to inform the design of an assessment that revealed evidence that a student had developed some of the targeted CURAs. Future research will focus on further assessment development that targets other identified CURAs. This approach has potential applications to other CUREs both in biochemistry and other science disciplines. © 2018 International Union of Biochemistry and Molecular Biology, 46(5):478–492, 2018.

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Introduction

As the field of biochemistry continues to advance, it has become increasingly important to clarify what students should be learning from their undergraduate biochemistry coursework. As emphasized by Caldwell *et al.* [1], students will be better prepared and more competitive when applying to graduate programs or entering industry, if undergraduate programs focus on the mastering of relevant technical and problem-solving skills and key content knowledge. White *et al.* [2] extends this argument by stating that students should be given the opportunity to develop more

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than just the fundamentals of biochemistry; they should also be taught communication and technical skills, which can often be overlooked within a curriculum. Toward this goal it is essential for students to partake in some sort of biochemical research experience [3]. Furthermore, there is a general consensus that when students have more authentic research experiences they will learn more about scientific inquiry which will, in turn, promote their attitude toward science [4]. In this article we extend this thinking to focus more specifically on some of the scientific discovery skills (rather than technical skills or procedural knowledge), that are essential for the performance of sound research.

At many institutions it is not possible for students to take part in undergraduate research [4], but it is possible for them to participate in laboratory experiences that provide opportunities to experience research and to develop research and problem solving abilities [3,5]. This is in line with recent reform efforts [6–11] aimed at incorporating more authentic practices within the sciences, such as course-based Undergraduate Research Experiences (CUREs) [12]. CURE activities have demonstrated positive impacts on many different factors, across academic levels and scientific disciplines, ultimately leading to student persistence in science [5]. Some recently published protein biochemistry CURE examples include: studying protein mutations in tumor and cancer-related proteins [13,14], investigating the effect of mutating non-conserved protein regions [15], and characterizing proteins of known structure but unknown function [16–18]. Some CUREs have been purposely designed in a modular fashion to allow for different implementation strategies [16,17,19]. One such example is the biochemistry CURE developed by the Biochemistry Authentic Scientific Inquiry Laboratory (BASIL) as a multi-institutional collaborative project, described by Craig *et al.* [16,17]. The BASIL CURE is a modular CURE focused on assigning function to proteins of known structure but unknown function. The BASIL CURE serves as the context for this study.

As advocated by various authors (e.g. Brownell & Kloser [20] and Bell *et al.* [21]) the learning objectives that students are expected to achieve during a particular CURE need to be identified before a CURE can be evaluated. Such learning objectives can then be used to inform assessment design to confirm to what extent students are achieving these objectives [22,23]. More recently, we published an article [22] in which we suggest the use of the phrase, "Anticipated Learning Outcomes" (ALOs) instead of learning objectives. In so doing we distinguish between ALOs proposed by instructors and Verified Learning Outcomes (VLOs) based on evidence of students demonstrating that they have achieved an outcome through appropriate assessments [22]. This is in line with the tenets of sound assessment design [23–25] as well as those relating to the assessment triangle [26], which states that the three key elements of assessment are concerned with: *cognition,* identifying the set of knowledge important to measure (i.e. the Process for Identifying Course-based Undergraduate Research Abilities, used as part of this study [22]); *observation*, specifying elements to be incorporated into assessment items to elicit responses about that knowledge from students (i.e. goal of this article); and *interpretation*, reasoning from evidence provided by students in response to knowledge being assessed (i.e. VLOs [22] confirmed from student responses to assessments).

Publications describing various CUREs do not always specify the related ALOs. For example, on the CURE database, CUREnet [27], authors are required to outline what they believe are the student goals and research goals of their CURE but few discovery-type ALOs are specified. Instead, when ALOs are reported for CUREs they tend to be either too general or not clearly defined, often based on the aspects of what defines a CURE [12], or are similar to the broad potential CURE outcomes reviewed by Corwin *et al.* [5]. In addition, some of the listed ALOs focus more on technical or procedural-type knowledge. Even when CUREs present a set of ALOs, it is often not clear how the outlined ALOs were identified or if any steps were taken to confirm if they are VLOs. Such confirmation is dependent on well aligned student assessments, which are often lacking from the literature. To address some of these issues, Irby *et al.* [22] developed a data-driven, five-step, Process for Identifying Course-based Undergraduate Research Abilities (PICURA) that instructors of our BASIL CURE anticipate students will develop during the course. We termed the identified ALOs, CURAs, after Course-based Undergraduate Research Abilities. The identification of ALOs (CURAs) by a robust process, such as PICURA [22], is an important component of course evaluation and assessment frameworks [26] for determining the extent of student learning and the VLOs for a course [22]. The CURAs identified using PICURA and presented in this article are aimed at informing the design of assessments that will allow us to confirm to what extent students actually develop the specific research abilities that instructors anticipate students will learn during the BASIL CURE, compared with more general assessment measures that have been disseminated to assess CUREs [28].

In addition to identifying ALOs to determine what should be assessed for a particular CURE, ALOs can also be used as a way to characterize a CURE. For CUREs, this has previously been done by situating courses within the five aspects of CUREs [12,29], which are a set of features or activities that have been proposed by Auchincloss *et al.* [12] to characterize a typical CURE. Another more general effort by the Advancing Competencies in Experimentation-Biology (ACE-Bio) network has involved the identification of a set of competencies for biological experimentation (also referred to as "ACE-Bio competencies") [30]. Though developed in the context of the biological sciences, many of the identified experimental competencies [30] are skills applicable to many fields of research and should be present in courses, such as CUREs, that focus on integrating authentic scientific practices. Thus, one way to characterize the unique

features of a CURE could involve identifying and aligning ALOs to more general competencies of experimental research [30] and the aspects that should be incorporated into a CURE [12,29], an approach used in the current article.

Thus, the goal of the present study was to identify the ALOs or CURAs for the BASIL CURE which, in the future, could be used to develop assessments in order to measure actual student leaning outcomes or VLOs [22]. Toward achieving this goal, we addressed the following research question: "Which CURAs do the instructors of the BASIL CURE consider the most relevant learning outcomes and how do these compare to other published descriptions of CURE objectives and experimental competencies?" To address this research question, we chose to collect data from the course instructors and lead course designer using the PICURA approach [22]. In this article we present the resulting CURA statements (Table I) which we then organized as an ALO matrix (Table II). We also illustrate by means of one specific example how readers might use the matrix to inform the design of a student assessment to measure the development of various CURAs by a student.

Description of the BASIL CURE and the Study Participants

This study focuses on a novel biochemistry CURE, developed as part of the BASIL project [16,17] and implemented at multiple institutions. The BASIL CURE consists of 10 protocols (listed in Table II, Column 1 and described in detail in references [16,17]) which involve a combination of computational and wet lab biochemical techniques to elucidate the function of proteins whose structures have been solved but their functions have not been confirmed. The CURE was modeled after the work done by researchers in the field to elucidate the function of proteins deposited in the Protein Data Bank [e.g. [31]] and is described in more detail elsewhere [16,17,22]. There were 10 participants in this study, including one lead designer and nine instructors who also contributed to the development of the BASIL CURE [22]. The participants are either tenured (n = 8) or tenure-track (n = 2) faculty members at a range of US institutions who all maintain active research groups, have two or more years' experience teaching lab courses, and whose expertise is in either computational chemistry, biochemistry, or both. This study was approved by the Purdue University IRB (#1503015825 and #1604017549).

Description of PICURA

The PICURA approach as described by Irby *et al.* [22] was used to identify the CURAs that instructors anticipate students would develop from this CURE. PICURA consists of a five-step process that, in sequence, includes: (i) Step 1 a content analysis of course protocols, (ii) Step 2 an open-ended survey with instructors and course designers from the CURE, (iii) Step 3 an interview with the lead designer, (iv) Step 4 an alignment check to refine verb-noun CURA statements, and finally, (v) Step 5 a two-tier Likert survey to establish the final list of CURAs that participating instructors and designers consider to be the most important ALOs for the CURE. PICURA is informed by the conceptual-reasoning-mode (CRM) model [32–34] to guide coding of the data sources for the range of concepts (C), modes of representations (M), and reasoning skills (R) associated with them (RC and RM). The CURA statements were generated by first identifying instances where the lead designer discussed (Step 3) reasoning with concepts (RC) or representations (RM) while explaining the research associated with the CURE. A thought experiment guided by the CRM model [32–34] was done to identify specific RC and RM verb-noun CURA statements [22,34]. For a full description of the five steps of PICURA with respect to their inputs, analytical approach, and achieved outputs, see Irby *et al.* [22].

Identification and Refinement of Technical- and Discovery-type CURAs

Table I lists all of the final 43 CURAs that were identified as a result of the PICURA process, after generation, refinement, and alignment of 66 initial CURA statements (Steps 3–5 of PICURA). An alignment check (Step 4) was performed to check for consensus with Steps 1 and 2 (content analysis and open-ended survey). The CURA statements were subsequently member checked with the lead course designer and revised according to the lead designer's feedback and to ensure that there was no significant overlap between CURA statements.

CURA statement TR6, *Design an enzyme assay to elucidate protein function* (Table I), will be used as an example of how initial CURA statements were determined and refined through the alignment check (Step 4). TR6's original wording was *Analyze kinetic data, properly, to elucidate an understanding of protein function,* which came from an interview quote when the lead designer talked about "having students generate enzyme kinetic data and then look at the 3D structure of a protein and see what are the parts that contribute to that process" (Step 3). Here the lead designer was discussing how students generate and interpret kinetic data and make connections between a protein's structure and its function. However, when the lead designer member checked the CURA statements, the wording of TR6 got changed to its final wording (Table I) because the lead designer said "it is unlikely that students will get as far as formal enzyme kinetics (Km, Vmax, turnover number, etc.), but they will be assessing activity with some screening [of] substrates". In fact, the final wording of TR6 came directly from the lead designer, during the member check.

TABLE I ***Finalized list of the 43 course-based undergraduate research ability (CURA) statements grouped together by weighted relevance (WR)***

Identified CURA Statements	*WR**
Top-rated†	
TR1: Explain how the colorimetric enzyme assay works to allow detection of protein function	+18.0
TR2: Identify an enzyme active site using appropriate computational programs	+17.5
TR3: Determine the appropriate factors to consider when optimizing or interpreting an enzyme assay	+17.5
TR4: Determine using computational software whether and where a ligand may be binding to a protein	+17.0
TR5: Compare enzymatic results with those computationally predicted	+17.0
TR6: Design an enzyme assay to elucidate protein function	+16.5
TR7: Explain how the purification of tagged proteins works and ways the process can be optimized	+16.5
Middle-rated†	
MR1: Assess the quality of data and how data gets altered when computationally manipulated (e.g. if going from a raw plot of data to a reciprocal plot)	+16.5
MR2: Demonstrate whether a particular substrate binds to an active site	+16.0
MR3: Consider how to minimize protein denaturation when planning/performing experiments	+16.0
MR4: Optimize the reaction parameters (e.g. substrate and enzyme concentration, pH, temperature, etc.) that are essential for the occurrence of an enzyme-catalyzed process.	+15.5
MR5: Connect the data from an enzyme assay to what the enzyme is actually doing	+15.5
MR6: Compare results of different computational methods to determine if they agree with each other	+15.0
MR7: Use SDS-PAGE gels for interpreting information about a protein and its expression from a plasmid	+15
MR8: Understand the effect of a residue's charge on substrate interactions with an enzyme	+14.5
MR9: Recognize parameters that will impact protein substrate interactions	+14.5
MR10: Propose modifications to ligand molecules to increase their binding affinity for a protein	+14.0
MR11: Determine and interpret kinetic rates in light of saturation effects	+14.0
MR12: Recognize the different types of atoms and/or number of atoms present in a representation of a molecule	+14.0
MR13: Identify which ligands bind specifically to members of a particular protein family	+13.5
MR14: Relate a graphical representation of data from an enzyme assay to what can happen biologically with that enzyme	+13.5
MR15: Grasp the limitations of research methods based on homology	+13.0
MR16: Determine using computational software where enzymatic activity may cause bond breaking	+12.5
MR17: Relate structurally conserved protein regions to their function	+12.5
MR18: Distinguish between the different components of an enzyme including amino acids; secondary, tertiary and quaternary structure and any non-proteinaceous components	+11.5
MR19: Recognize a bad data point on a graph of research data	+11.5
MR20: Recognize the different symbols used in a graph and their meaning	+11.5

(Continues)

TABLE I *(Continued)*

Identified CURA Statements	*WR**
MR21: Compare conditions to determine a binding interaction between a substrate and a protein	+11.5
MR22: Distinguish between molecules that are good at binding to an enzyme versus those that could also be a substrate for that enzyme	+10.5
MR23: Translate or map features between 2D and 3D representations of proteins	+10.5
MR24: Use kinetic data to determine important parts of a protein's structure (e.g. binding pockets and/or catalytic residues)	+10.5
Lower-rated[†]	
LR1: Recognize the types of bonding interactions between an enzyme and its substrate	+10.0
LR2: Use protein and substrate electrostatic information to propose ways to improve binding	+9.5
LR3: Explain the relationship between a concept or a phenomenon and a mathematical equation representing that concept	+9.5
LR4: Identify the hydrogen bonds in a protein based on the properties of the atoms and their interatomic distances	+9.0
LR5: Recognize how proteins that are closely related by evolution can have dramatically different functions	+9.0
LR6: Explain the strengths and weaknesses of a Michaelis–Menten plot and a Lineweaver-Burke plot and explain when each one is easier to use	+8.0
LR7: Recognize that the factors that determine protein structure and function happen from interactions throughout the protein and not just from neighboring residues	+8.0
LR8: Explain how secondary and tertiary structure is influenced by intramolecular forces within a protein	+8.0
LR9: Relate a biochemical representation of a structure or process to its real life practical meaning or interpretation	+7.0
LR10: Determine biochemically relevant constants (such as Vmax or Km) from a Lineweaver-Burke plot	+7.0
LR11: Determine the presence and nature of a transition state analog	+6.0
LR12: Relate a data point in a Michaelis–Menten plot to one on a Lineweaver-Burke plot	+3.5

**Current weighted-relevance (WR) scores for the identified CURAs from the 10 participants.*

[†]The weighted-relevance (WR) scores (table 1), which indicate the amount of consensus among participants doing the Likert survey [22], were used to rank the CURAs into top-rated (TR) items (meaning that there was consensus about their importance to this type of research as well as their importance to different instructors' courses), middle-rated (MR), and lower-rated (LR) statements (meaning there was less consensus; see also Supporting Information, Tables S1, S2A, and S2B, for detailed rankings and how cutoffs were assigned).

Some examples in support of TR6 during the open-ended survey (Step 2) can be seen by the following quotes, "My goals for this project were to see if students could actually design their own experiment, analyze their results, and figure out what to do next" and "They [students] should have to consider what the possible outcomes of their experiments (computational or wet lab) are and what they should do next in the case of each outcome", thus demonstrating the expectation for students to be learning how to design experiments. Lastly, CURA statement TR6 is supported by the BASIL CURE enzyme activity protocol (Table II, [16,17]), where students design and conduct assays to evaluate the function of their protein. As the last phase of the alignment check (Step 4), overlap between CURA statements was remedied by fine-tuning the wording and/or merging statements. This procedure narrowed the list of CURA statements from 66 to 44; but after the CURA statements were rated (Step 5) one more CURA statement was removed due to its similarity to a higher-rated CURA statement, resulting in 43 final CURA statements (Table I).

The final step of PICURA, Step 5, deployed a Likert scale to gauge participants' rating of the importance of each CURA statement to this type of research and to a specific instructor's course. The Likert survey also had open-ended

TABLE II ***ALO matrix organizing the CURAs into seven themes and ten BASIL CURE protocols***

CURE Component	*CURE Protocol*	*1. Hypothesize the location and function of an enzyme active site*	*2. Propose a particular method based on considerations of the pros and cons of different methods*	*3. Interpret data to understand a biochemical meaning*	*4. Rationalize the design of candidate substrates*	*5. Visualize and determine key components of protein structure*	*6. Relate multiple types of data to reach a singular conclusion*	*7. Understand the biochemical theory behind methods*
Biochemical Modules	Protein Expression							
	Protein Purification							TR7
	Protein Concentration							
	SDS-PAGE			MR7				
	Enzyme Activity		TR3, TR6, MR4	MR11, LR10	MR21		LR6, LR12	TR1
Computational Modules	BLAST		MR15					
	Dali		MR15			MR17		
	Pfam	TR2	MR15		MR13			
	ProMOL	TR2, MR2, MR22			MR13			
	PyRX	TR2, TR4, MR2, MR9, MR16, MR22			MR8, MR10, MR13, LR1			
Contained in both computational and biochemical modules or does not pertain to any singular protocol but to the CURE as a whole		LR11	MR3,	MR1, MR5, MR14, MR19, MR20, LR3, LR9	LR2, LR5	MR12, MR18, MR24, LR4, LR7, LR8	TR5, MR6, MR23	

response boxes for the participants to comment whether any CURA statements should be added, removed, or altered. There was no consensus to add or remove any CURA statements, but the wording of TR7 was changed from "His-tagged proteins", to just "tagged proteins" because students may encounter other tagging purification methods in this CURE (Table I).

The weighted-relevance (WR) scores (Table I), which indicate the amount of consensus among participants doing the Likert survey [22], were used to rank the CURAs into top-rated (TR) items (most consensus about their importance to this type of research as well as their importance to different instructors' courses), middle-rated (MR), and lower-rated (LR) statements (less consensus; see also Supporting Information, Tables S2A and B, for detailed rankings and how cutoffs were assigned). This was done to prioritize CURAs for assessment development, since the top-rated statements would be a target for assessment by different instructors implementing the BASIL CURE at various institutions. Note that the WR rankings of each CURA may fluctuate as the BASIL CURE evolves over time, because rankings vary across individuals and institutions [22]. In other words, a CURA with a lower WR score does not mean that it is less important to every instructor who implements the course. In fact, in this study with 10 participants, the calculated WR scores could have ranged from −20 to +20 [22], but instead all of the identified CURA statements showed a WR score of +3.5 or greater (Table I). This indicates that on average most of the instructors rated all the CURAs to be important and relevant to their BASIL CURE courses. But it is important to realize that if the BASIL CURE were implemented at other institutions, the participant instructors may rate the CURAs differently and may even suggest alternative CURAs not identified in this study.

On close scrutiny of the listed CURA statements in Table I it is clear that they require the same technical and procedural research abilities that are commonly taught in most traditional biochemistry laboratory courses, underpinned by the necessary biochemistry conceptual knowledge. For example, TR1 requires technical knowledge of the use of positive and negative controls to detect enzyme function as indicated by the presence or absence of a colored product, while MR7 requires the performance of SDS-PAGE to isolate and characterize the target protein relative to appropriate standard proteins. TR3, in contrast, is concerned with determining the important factors to consider and to optimize when designing an enzyme assay to elucidate enzyme activity. In addition to the above biochemical techniques, the computational biochemistry in the BASIL CURE requires other technical aspects such as the need to learn how to use computational software for determining ligand binding (TR4) or for identifying an enzyme active site (TR2). These CURAs that are focused on the use of computational methods are a unique feature of the BASIL CURE and are not commonly found in traditional biochemistry labs. Furthermore, most of the listed CURAs require biochemistry conceptual knowledge to master them. For example, LR10 requires students to understand the meaning of enzyme kinetics constants, Vmax and Km, and how Lineweaver-Burke plots are constructed to characterize a specific enzyme. Other examples include LR4, which requires conceptual knowledge of H-bonding and interatomic distances within proteins, and MR11 that requires understanding of the meaning of enzyme saturation as a limiting factor in enzyme kinetics.

In contrast to some traditional labs where students may be graded according to how well they purify a protein, determine constants, perform SDS-PAGE, or recite relevant biochemical principals or parameters, most of the CURAs in Table I do not simply address technical skills associated with the procedures of a protocol. Instead, they are also focused on the types of reasoning and problem solving needed for the discovery of new knowledge. To achieve this each of these discovery-type CURAs requires students to integrate a wide range of technical, procedural and conceptual knowledge and to apply their cognitive abilities to solving problems. For example, TR5 requires students to compare enzymatic results with those computationally predicted to discover the function of a protein of known structure but unknown function, while MR22 requires students to discover the substrate of a protein by distinguishing between ligands that simply bind the enzyme and those that can also be processed by the enzyme. Thus, the CURAs in Table I constitute a wide range of discovery skills that researchers deploy when doing this type of research. This require the integration of technical, procedural and conceptual knowledge in ways that are not usually developed in traditional student labs and which can lead to novel research findings.

In conclusion, the data in Table I suggest that the BASIL CURE, just like most traditional biochemistry labs, covers the development of students' technical/procedural and conceptual knowledge, but in addition it also targets the integration of such knowledge and the development of discovery skills that characterize good research. Of course, no training in research should be without the essential technical skills but good research training also needs to focus on students' abilities to use such knowledge to solve novel problems and to discover new knowledge—the goal of this study and of the BASIL CURE.

An ALO Matrix of the CURAs

After the CURA statements were ranked and the wording was finalized (Table I), the statements were grouped into categories according to common themes. Patterns emerged by looking across the groupings of CURA statements and identifying the common theme underlying a particular group. This was done first with the middle-rated CURAs because this group contained the most ALOs. Subsequently,

the top-rated and lower-rated statements were placed into the themes already generated and new themes were added if needed. After all of the CURA statements were organized into their underlying theme or, in some cases, themes (see columns in Table II), they were then further organized by aligning them with one or more BASIL protocols (rows, Table II) [16,17]. Protocols were aligned with CURAs that pertained to specific experiments and activities covered by the protocol.

The grouping of CURA statements resulted in six initial themes: (i) Hypothesizing the location and function of an enzyme active site, (ii) Proposing a particular method based on considerations of the pros and cons of different methods, (iii) Interpreting data to understand a biochemical meaning, (iv) Rationalizing the design of candidate substrates, (v) Visualizing and determining key components of protein structure, and (vi) Relating multiple types of data to reach a singular conclusion. When the top- and lower-rated CURAs were sorted into these themes, a seventh theme, "Understanding the biochemical theory behind methods," was needed to accommodate all the CURAs, specifically TR1, and TR7 (Table I). When the new theme was checked to see if any of the middle- or lower-rated CURAs should be moved to this new theme there were no such cases. These classifications were used as the first dimension of the ALO matrix (Table II, columns).

The CURA statements were then organized according to the protocols of the BASIL CURE (Table II, rows). As mentioned previously, CURAs were only aligned with a specific protocol if the activities of a protocol specifically utilized a particular CURA. For example, MR7 is related to protein expression, because information from the SDS-PAGE gel will give insight into how well the expression worked. However, only during the SDS-PAGE protocols are gels and the types of information you can get from them discussed in detail. Thus, MR7 is associated only with the SDS-PAGE protocol and not the expression protocol, even though MR7 will produce information about the expression (Table II). Additionally, several CURAs were not aligned with any protocol specifically. Instead, they were aligned as being *Contained in both computational and biochemical modules or does not pertain to any singular protocol but to the CURE as a whole.* Examples are TR5 because it is concerned with comparing enzymatic results with computational results; MR3 that is concerned with keeping a protein from denaturing which pertains to all biochemical protocols; and, LR9 which corresponds to the ability to make a connection between a representation and what is actually happening, as this can relate to any BASIL CURE protocol that produces a representation like a gel image or a graph of the findings.

Table II shows how all the CURA statements were organized into an ALO matrix. Note that two protocols, protein expression and protein concentration, were not specifically associated with any of the CURA statements. This is not to say that there were no CURAs related to these protocols. For example, MR3, LR3, and LR9 (Tables I and II) are related to both of these two protocols and to every other biochemical protocol. Instead, rather, this finding suggests that protocols like protein expression and protein concentration were focused on procedural training that would be insufficient on their own at addressing the research goals of the BASIL CURE, which are aimed at developing students' competence to do discovery-type research. Thus, there was a need for the row of ALOs that cover both computational and biochemical modules or the CURE as a whole (bottom row in Table II). The nature of a CURE is to resemble authentic research practices, and not to merely follow or repeat steps in a protocol. Therefore, CURAs focus on the reasoning abilities scientists employ when conducting similar research activities and not just simply the procedural steps in the protocols [22]. In other words, the CURAs encompass all aspects of the CURE and focus on the CURAs most pertinent to addressing research questions about determining the function of a protein with unknown function but known structure, not just what was specifically detailed in the protocols. For this reason, the computational protocols and the enzyme activity protocols have the most CURAs specifically aligned to them because these protocols are directly related to the goals of the research being conducted in the BASIL CURE, whereas more preparatory protocols (e.g. protein concentration) did not receive any specifically aligned CURAs (Table II).

The ALO matrix (Table II) shows the spectrum of coverage of CURA statements, as well as their current relevance to this CURE. In addition, the ALO matrix allows for the characterization of the unique features of this CURE and how it may fit into an institution's or a program's curriculum aimed at developing students into scientists.

How the BASIL CURE Themes Compare with Experimentation Competencies and Other Aspects of CUREs

The generation of the seven themes used to construct the ALO matrix (Table II), also provided the opportunity to characterize the BASIL CURE relative to other published work in the field. For example, further analysis of our BASIL CURE themes revealed that they align well with the list of ACE-Bio competencies of biological experimentation put forth by the ACE-Bio network [30], as well as with the aspects that define a CURE identified by Auchincloss *et al.* [12] and Corwin *et al.* [29] (Table III).

These alignments were initially based on the specific CURE themes, and then checked against the CURA statements that comprise them. The association between the themes and the ACE-Bio competencies and the CURE aspects were not mutually exclusive, meaning that multiple ACE-Bio competencies and/or CURE aspects can be

TABLE III ***A comparison of the CURE themes for the BASIL with other documented experimental competencies and CURE aspects.***

CURE Themes for the BASIL CURE Based on Identified CURA Statements	*ACE-Bio*[*†] Competencies of Biological Experimentation Pelaez* et al. *[30]*	*CURE Aspects*[*†] Proposed by Auchincloss* et al. *[12] to define what a CURE is. Definitions of the aspects came from Corwin* et al. *[29].*
1. Hypothesize the location and function of an enzyme active site	Analyze: The ability to analyze and process data. Question: The ability to generate a research question and formulate hypotheses.	Use of science practices: The degree to which students engage in asking questions, building and evaluating models, proposing hypotheses, designing studies, selecting methods, gathering and analyzing data, and developing and critiquing interpretations and arguments. Students are likely to engage in several but not all scientific practices during a single CURE.
2. Propose a particular method based on considerations of the pros and cons of different methods	Plan: The ability to plan feasible and ethical experiments to answer research questions or test hypotheses.	Use of science practices Iteration: The degree to which students have opportunities to revise or repeat aspects of their work to fix problems, improve validity of their own and others' results, understand variation in data, or further test hypotheses.
3. Interpret data to understand a biochemical meaning	Analyze	Use of science practices Discovery: The degree to which students have opportunities to generate new scientific knowledge.
4. Rationalize the design of candidate substrates		
5. Visualize and determine key components of protein structure		
6. Relate multiple types of data to reach a singular conclusion	Analyze Conclude: The ability to conclude about data with inferences that are limited to the scope inherent in the experimental design.	Use of science practices Discovery
7. Understand the biochemical theory behind methods	Identify: The ability to identify gaps or limitations in current research knowledge through the review, filtering and synthesis of relevant literature.	Use of science practices
	Conduct: The ability to conduct an investigation to achieve research goals.	Use of science practices Iteration
	Communicate: The ability to communicate research work in professionally appropriate modes, including visual, written, and oral formats.	Broad relevance: The degree to which students' work is of interest to a community beyond the classroom, which can manifest as authorship on a scientific article or presentations or reports to stakeholders.
	Communicate	Collaboration: The degree to which students are encouraged to work together, help each other, build off one an- other's work, and provide and respond to feedback.

**Definitions for the ACE-Bio competencies [30] and CURE aspects [29] were copied verbatim.*
†In cases where there is more than one ACE-Bio competency or CURE aspect, the item is only defined the first time it appears.

associated with a singular theme and vice versa. For instance, the ACE-Bio competency of "analyze" and the CURE aspect of "use of scientific practices" both have to do with processing and making decisions about data, which is a prominent theme associated with many components of the BASIL CURE (Table III). For example, students propose a hypothesis for their protein's function, but they produce and analyze data to do so [16,17,22]. Thus, the theme of *Hypothesizing the location and function of an enzyme active site* was associated with the ACE-Bio competencies of "analyze" and "question" as well as the CURE aspect of "use of scientific practices" because it covers asking questions as well as processing data (Table III). Interestingly, the BASIL CURE themes 3–5 (Tables II and III) that only contain the ACE-Bio competency of "analyze" did not contain any top-rated CURAs. However, the themes that combined "analyze" with "question" (theme 1) or "conclude" (theme 6, Tables II and III) contain top-rated CURAs, which implies that the participants valued those CURAs, that require students to use their analytical and questioning skills, as a key part of the course for learning how to conduct scientific research. It also suggests that competent researchers only perform data analysis with reference to a purpose such as to answer a research question or to draw conclusions. Thus, assessments should link across areas of competence and not simply focus on one area such as data analysis.

The fact that all of these efforts align is unsurprising because they have similar goals, but this alignment adds merit to the themes identified for this CURE. It was also not a surprise that no themes of this CURE aligned with the ACE-Bio competencies of conduct and communicate [30] (Table III). This is because in this study the CURAs were generated by focusing on the reasoning abilities pertaining to this type of research [22], and did not explicitly target technical skills or research communication. Additionally, for the same reason, the CURE aspects [12,29] of broad relevance and collaboration were also not associated with a BASIL CURE theme (Table III). This is not to say that students do not engage in such activities. On the contrary, the ability to communicate, collaborate, and conduct experiments to collect novel data are important aspects built into the course [16,17].

The seven ACE-Bio competency areas (Table III) are big picture ideas that are too complex to easily assess in students. For this reason, the authors Pelaez *et al.* [30] unpacked each competency area to identify numerous subcompetencies that are readily assessable. A similar problem exists regarding the identified CURE aspects [12,29] in that they too are higher level abilities, composed of numerous sub-abilities, which still need to be unpacked before effective assessments could be designed. In an analogous manner, in the present study, we have identified themes that because of their complexity will be more difficult to thoroughly assess but, as shown in the next section, the constituent CURAs can be readily assessed.

In our view, the above discussion provides an explanation for why the vast majority of published research competencies lack adequate assessments and, therefore, a strong motivation for why assessment development should be an important target for future research in this area. Toward this end, we are actively engaged in developing and validating assessments that target our identified CURAs. An example of such an assessment task is presented in the next section.

Use of the ALO Matrix to Inform Assessment Design

In this section we demonstrate how the ALO matrix could be used by instructors in different ways to inform the design of student assessment tasks for the BASIL CURE. For example, if instructors wish to develop assessment tasks for any particular protocol, they can look along the corresponding rows in the matrix and design questions that focus on the listed CURAs. Similarly, if they wish to develop assessment tasks for any particular theme, all they need to do is look down the relevant column and focus their efforts on the listed CURAs. The ALO matrix also allows simultaneous comparison of both dimensions to guide the development of cross-protocol and/or cross-theme assessments. In all cases, the ultimate challenge is to design assessment tasks that specifically require and stimulate students to use the targeted CURAs in their answers. This can only be fully confirmed by reciprocal analysis of student answers and modification of the tasks till the task achieves its desired goals. The detail of such assessment validation is beyond the scope of this article. Instead, the assessment example provided below is intended to illustrate to what extent selected ALOs can be confirmed as VLOs through analysis of a student answer. But it is important to mention at this stage that students frequently include far less in their answers than they actually know about the problem which requires modifications to the task to facilitate more comprehensive answers. This problem is often resolved by including statements in the question like, "Include the following words or terms in your answer…".

To illustrate the use of the matrix for assessment design we provide here an example of a student task, that was designed to incorporate CURA statements TR1, TR3, TR5, and TR6 (Fig. 1). In so doing, the question is intended to focus on three themes of the BASIL CURE (themes 2, 6, and 7, Table III) as well as the enzyme activity protocol while also requiring both computational and biochemistry knowledge (See last row of Table II).

In the assessment task (Fig. 1), students are asked to compare the results of an enzyme assay (Fig. 1*A*, graph) with outputs from various computational programs and databases to predict the enzyme class (EC) of the protein of interest (Fig. 1*A*, table). The data provided is similar to data

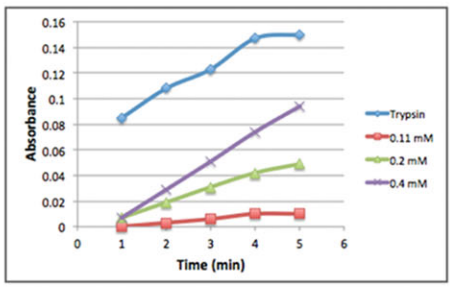
A

Compare the graph and computational outputs for a protein of interest, 3H04. The graph shows a constant concentration of 3H04 with different concentrations of p-nitrophenyl acetate (PNPA) and a positive control (Trypsin).

How does the computational prediction and the results from the assay compare? In your explanation provide justification for whether there is evidence that this protein interacts with this substrate, or not. In so doing describe:

- **the relevant biochemical concepts used when interpreting these results, and**
- **the process you used when comparing them.**

Additionally, be sure to cite the specific information you used to reach your conclusion, as well as any additional information you would have liked to have to help you reach your conclusion. Explain your reasoning in every case.



3H04	
ProMOL	**EC** 3.4.11.5, 3.7.1.8, 3.4.21.26 Hydrolase
BLAST, Dali, and Pfam common function	**EC** 3 or 3.1.1 Alpha/beta hydrolase or esterase

B

Examples of key points expected in student answers:

1. The computational results agree with one another; they all give the same EC class (EC3) which suggests the protein is a hydrolase.
2. If PNPA is hydrolyzed there will be a color change, which can be detected at a specific wavelength.
3. Trypsin is said to be a positive control, as it is a known hydrolase. However, it is necessary to know if PNPA (the substrate) was used in the trypsin assay, because the positive control should measure trypsin activity.
4. There were interactions between the protein and PNPA as can be seen by the increase in absorbance.
5. Higher concentrations of PNPA with 3H04 give corresponding higher absorbance values.
6. Increasing the concentration of PNPA increased the rate of product production.
7. Like for trypsin, for 3H04 there was an increase in absorbance over time suggesting it behaves like a hydrolase.
8. The assay appears to confirm the predictions made from the computational software results.
9. This assay does not include a negative control, which is needed to prove that these are true positives. A better study would include measures of absorbance over time (the rate of product accumulation) with the same 3 PNPA concentrations in the assay, but without any 3H04.
10. Other useful information that would help with this comparison would be: concentration of 3H04 and trypsin, optimizing the assay with constant PNPA concentration but different 3H04 and trypsin concentrations, determine why the trypsin rate of product accumulation is similar to 3H04 yet background absorbance is above zero, define the wavelength, for each curve find a best-fit straight line, etc.

C

Example of an actual student answer:

Just glancing over the data there seems to be activity occurring since there is an increase in absorbance as the reaction proceeds showing that assay was reacting with the product which would correlate to a higher absorbance when recorded.[4,7] The data is also linear as it should be because as the protein works on the substrate the concentration of the product would steadily increase.[2] There is also a correlation between the absorbance and the concentration of the protein as the concentration increases the rate of change of absorbance also changes drastically so we see three separate lines.[5,6] Since there is no crisscrossing of the lines there is nothing to worry about protein stability and the rate at which the reactions are occurring so good data is being obtained. Since all of these things are present I can say that this protein definitely interacts with this substrate.[7] Since it reacts with this substrate then the computational data was correct in assessing this as a hydrolase.[8]

FIG 1

Example of an assessment task developed to cover four CURA statements, TR1, TR3, TR5, and TR6. The assessment item (panel A) is accompanied by the expected key points for students to include (panel B) and an example of a student answer (panel C). In panel C superscripts indicate where the student incorporated one of the corresponding numbered anticipated key points from panel B. The prompt (panel A) includes data from an instructor who was teaching students to identify if there is evidence that a protein of interest is acting like a hydrolase and to compare the assay results to computational results, and not to do a formal kinetic analysis of their protein of interest, which in this example is 3H04. The item includes some ambiguity that gives the opportunity to see how a student deals with real-life messy data which a scientist might gather to answer their research question. [Color figure can be viewed at wileyonlinelibrary.com]

that students would have generated and used as evidence when they were investigating a possible function of their assigned proteins as part of the BASIL CURE. In contrast, a discipline-based educational researcher (DBER) might have independently drafted a novel assessment task (termed a research probe) in the context of a real-life research situation that might differ from the CURE context. Appropriate background information would be provided to give all of the conceptual subject matter knowledge required to answer the question. The research would involve validating how

well the item would measure research competence (and not confounding subject matter knowledge) by conducting case study oral interviews about the novel assessment. Data could have been gathered to optimize the probe for measuring research abilities in general, and then to determine how well the assessment reveals the nature of expert knowledge and visualizations that are critical to research competence, using expert responses to the assessment for comparison to establish a measurement scale for the development of expert-like research behaviors in students [35]. In contrast, the case example discussed here is based on a graph that was provided by an instructor for a particular course context. Thus, the data analysis expected of students is limited to the context of the BASIL CURE, where the research goal was for students to answer a question about enzymatic activity of a protein. The students were doing research to identify if there is evidence that the protein of interest is acting like a hydrolase and to compare the assay results to computational results and not to do a formal kinetic analysis of their protein. This is also evident in the example of the CURA statement that was changed in the member check step to focus on activity and not on formal kinetics. The scope of activities that are typically done in the BASIL CURE involves assessing whether or not their protein of interest shows evidence of activity, since the students do not have enough time for a formal study of the enzyme kinetics. A few great students might respond to the item in Fig. 1*A* by suggesting that the slopes could be used for a Michaelis–Menten plot, if this enzyme had been purified, by graphing these velocities on the y-axis against each substrate concentration on the x axis (LR6 in Table II), As these lines might represent initial velocities. But for the BASIL CURE, the expected response from students who completed the course would be for the student to recognize that each curve could be aligned with best-fit straight lines where each slope represents a different rate of product production for each substrate concentration (Fig. 1*B* items 6 and 10).

The ALOs that this question is targeting involve the ability to identify and use evidence from an activity assay to determine the function of the protein of interest. If the student has truly developed the ALOs covered by this assessment (i.e. the ALOs qualified as VLOs), he or she would be expected to be able to discuss how the assay works (TR1), interpret important data about the protein's function (TR3), be aware of what experimental information is included or needed to make a conclusion (TR6), and relate the enzyme assay (Fig. 1*A*, graph) and computational data (Fig. 1*A*, table) to see if they support each other (TR5) in predicting the function of the enzyme.

Fig. 1*B* lists 10 key points which instructors expected students to include in their answers to demonstrate whether they have achieved the applicable ALOs. Of course, the open-ended nature of the assessment task means that students may come up with other acceptable responses not listed here. This supports the idea that there can often be multiple paths to resolving or addressing a research question, which typifies part of the nature of research abilities that we are attempting to develop in our students. The expected answer within the context of the BASIL CURE combines "analyze" with "question" (theme 1) or "conclude" (theme 6, Tables II and III) as top-rated CURAs, which confirms that to do competent research in this program, students are expected to combine use of their analytical and questioning skills or their analytical and concluding skills, and not to simply "analyze" the data in terms of enzyme kinetics, which would not be a first step for characterizing proteins of known structure but unknown function.

One student response to the question (See Fig. 1*C*) from a biochemistry junior who had previously completed the BASIL CURE gives some initial evidence to support the fact that the ALOs are at least being partially achieved in this student (i.e. the ALOs are being partially confirmed as VLOs). The student included six of the anticipated key points listed, indicated by the superscripts (Fig. 1*B* and 1*C*). The student's response is primarily focused on the data presented about the protein of interest, primarily eliciting CURAs TR1, TR3, and TR5, and to a lesser extent TR6. For example the student makes several connections to data trends saying things like "there is also a correlation between the absorbance and the concentration of the protein" (Fig. 1*C*), but the student does not mention experimental parameters such as what wavelength the measurements were done or which controls (either present or not present) were used in the enzyme assay. In fact, there is some ambiguity in the item regarding the trypsin curve, which gives the opportunity to see how the student will deal with real-life issues. The assessment prompt identifies "trypsin" as "a positive control." Trypsin is a positive control because it is a known hydrolase, but trypsin is a protein thus it can only give "positive control" measures if p-nitrophenyl acetate (PNPA) had been included as a substrate for the trypsin curve assay. A competent research student might express concerns about the raised trypsin curve absorbance or the failure of a best-fit line to indicate zero absorbance at the zero time point for the trypsin curve. Under Fig. 1 part B for point nine, there is mention of a negative control. An expected response would identify the need to show that PNPA on its own does not show any change in absorbance, which happens only when its hydrolysis is catalyzed by an enzyme. A response from a great student might identify the need to measure the change in absorbance over time (the rate of product accumulation) with an assay that uses the same three different PNPA concentrations but without any 3H04 or with some protein like BSA in place of 3H04 in the solution. However, instead of identifying the need for better positive and negative controls, the following phrases in this student's response suggests some difficulties. In line two, "the assay was reacting with the product" suggests that this student does not know what "assay" means, and lines

four to five "a correlation and the concentration of the protein" suggests that the student does not know that 3H04, and not PNPA, is the protein in the assay solution. Lastly, in the student response (Fig. 1*C*), there is an underlined passage that raises questions about the protein's stability and the quality of the data. This was an unanticipated response but is a significant observation made by the student that demonstrates their ability to think about the data presented, showing signs of developing scientific thinking.

Although at this stage only one example of an assessment is presented with only one student response, there is clearly partial evidence that a well-designed assessment task based on data from an instructor and within the research context for a particular CURE could successfully confirm that some of the CURAs identified by instructors as ALOs could be considered as VLOs [22], whereas previously unsuspected student difficulties may need to be addressed. But in line with the tenets of sound assessment (e.g. [23]), in the case of all assessment development for the BASIL CURE, instructors will find that several different assessment tasks will be required to cover the full range of CURAs with any one theme or protocol. Furthermore, they will likely find that a single task will seldom just assess one CURA but rather more than one related CURA of importance to a particular protocol. Thus, instructors will find that a range of assessment tasks will be required to achieve a comprehensive and more complete assessment of student learning during the BASIL CURE. In addition, it will be important to develop a range of assessment types (e.g. open-ended, scenario-type, multiple choice questions) to assess different types of knowledge and also to consider for whom the measures are valid as different students might answer different types of questions more competently [23]. As a result of assessment responses, more pertinent ALOs may emerge as the CURE progresses as students begin spending less time troubleshooting and assigning the type of function to focus more on specific substrates and formal kinetics. The focus currently is not to answer research questions that compare the kinetics of trypsin and 3H04 directly to determine which is a better enzyme. Rather, the current research goal is to detect the presence of hydrolase activity, as PNPA is likely not the preferred substrate for the protein of interest, in this case, 3H04. Thus, some of the CURAs that pertain to explicit kinetics were not rated highly at this time (LR6, LR10, and LR12 in Table II), but this also provides a good example of the point that a different set of CURAs may become more relevant as the nature of the research advances and the focus of the research questions shifts. Given the potential for ALOs that change over time, a detailed discussion of more generalized assessment validation for CUREs is beyond the scope of this article but will be the focus of future work as novel assessment tasks are developed and validated around the identified CURAs.

Summary and Conclusions

In our view, the results of this study successfully addressed our research question: Which CURAs do the instructors of the BASIL CURE consider the most relevant learning outcomes and how do these compare to other published descriptions of CUREs and experimental competencies? We used PICURA to successfully identify 43 CURAs (Table I) which were categorized by instructors as either top-, middle- or low-rated using a previously reported weighted-relevance scoring approach [22]. The CURAs were then organized into a two-dimensional (2D) ALO matrix with each ALO mapped to 10 lab protocols as well as seven "big idea" themes of importance to the BASIL CURE (Table II). By means of a specific example, we illustrated how the matrix might be used to inform the design of a cross-theme assessment task within one probing task that focuses on revealing student development of four top-rated CURAs. We also demonstrated with an example student answer how one might begin to validate the assessment task by checking whether the CURAs that instructors anticipated students will learn (ALOs) are actually being developed in students (i.e. VLOs), as demonstrated by their use of the targeted CURAs in the answer. We also emphasized that for optimal validation of the task, the task should reveal evidence of both sound student knowledge and a range of difficulties with the CURA, and that with a much larger sample of student responses, the information gathered might suggest a need to change a CURA or to refine the research instruction. We also illustrated how ambiguity in an assessment item might prompt deeper thinking in a student response about the research process. On the other hand, the data may reveal flaws in the probing task itself, necessitating modification of the task and its retesting until good alignment is achieved between the CURAs, the assessment task and the student answers that confirm that the targeted CURA is being thoroughly assessed in the students.

A key achievement of this project has been to identify CURAs that constitute a shift in focus from just typical procedural or technical knowledge, which is commonly found in most biochemistry lab courses, toward a greater emphasis on the discovery part of research competence, which involves alignment of data analysis to a research question and conclusions based on evidence from that data. That is not to say that technical skills and procedural knowledge are not important. On the contrary, as discussed above, none of the discovery-type CURAs listed in Table I can be mastered by students without also developing the technical competence that allow them to achieve such goals. Thus, the nature of the identified CURAs support the fact that instructors believe/anticipate that their students are developing discovery skills and research abilities that require students to reason about knowledge and to solve novel problems within the themes of the research project, much like authentic research practice. This contention is

supported by the fact that our CURAs compare well (Table III) to those identified in various other projects including the ACE-Bio network [30]. By presenting preliminary evidence that our CURAs are assessable we also expose the need to unpack the various complex CURE aspects or "big idea" competencies published by Auchincloss *et al.* (2014) and Corwin *et al.* (2015) [12,29] into more specific sets of connected abilities that could be assessable. Clearly, though, we believe that our work has further emphasized the urgent need to develop more validated assessments of the various research discovery abilities currently being published in the CURE literature, and how to accomplish that task. Whereas, technical and procedural-type abilities are more directly and easily assessable by simply observing students in the lab, or grading their lab notebooks, to see if they have mastered such abilities, discovery-type CURAs are far more complex and require specially designed assessment tasks to gauge whether students have developed the desired research competence. Assessments of this nature will also enable better evaluation and characterization of CUREs which is an important future step for CURE projects [20–22,26,28].

Although this study has successfully identified the ALOs or specific CURAs that instructors teaching the BASIL CURE consider important for students to learn, until such a time when we have developed a full range of assessments to target those CURAs and obtained student responses to them, we will not be in a position to claim with any surety that our students are actually developing such research knowledge and abilities (i.e. VLOs). This will require a longer-term study involving the meticulous development, validation, and testing of assessments that target all the CURAs and any other CURAs that may be identified by future instructors at the same or other institutions. We do, however, believe that through this study and the research published elsewhere (see Irby *et al.* [22]), and the initial analysis of a response on a singular assessment item (Fig. 1), we have taken the essential first steps toward achieving our goals.

The CURA statements generated by PICURA [22] are intended to guide researchers' investigations into student learning within this specific BASIL CURE. The ranked CURAs serve as a way to focus attention on the CURAs that in the opinion of the instructors, currently teaching this course, have the most consensus of relevance to the CURE. The AOL matrix of CURAs presented in this article constitutes the consensus opinions of 10 instructors at this point in time, following implementation of our biochemistry CURE at specific institutions for a limited number of semesters. It is likely that the list of CURAs will change as instructors gain more experience and the labs are modified or improved to stay current. Additionally, we do not claim that this list of CURAs is exhaustive as it is likely that other instructors in the future will come up with other CURAs that they consider more important. Thus, we recommend that the PICURA process should be repeated when deemed necessary [22].

Readers could benefit in multiple ways from the results of this study. Firstly, by implementing the BASIL CURE [16,17,22] at their own institution, their students would stand to develop the wide range of CURAs identified here that could have a significant impact on their future performance as researchers. Secondly, instructors of other CUREs, whether in biochemistry or other discipline areas, could use PICURA and the weighted relevance approach [22] we have presented in this article to identify their own CURAs. Thirdly, instructors and researchers participating in CURE projects could take our idea of focusing more on discovery-type research abilities rather than only technical and procedural type knowledge that characterizes so many of our traditional undergraduate biochemistry labs. Fourthly, in view of the dearth of good available assessments for CUREs, we strongly recommend that all participants in CURE research and instruction consider embarking upon extensive assessment development and validation projects, which target identified CURAs, on similar lines to what we advocate in this article. Finally, in so doing, future instructors will focus their assessment tasks on assessable research abilities that emerge from unpacking the big CURE ideas.

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