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Undergraduate Biology Student Ideas about Biochemical Pathway Dynamics

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Abstract

We seek to tackle imperfect teaching methods in life science majors by revealing student ideas about concepts in the core classes for many of these majors. In particular, the study focuses on the way students understand metabolic pathway dynamics and regulation (MPDR)—relevant to classes in low- and upper-level biology, anatomy and physiology, biochemistry, and more—through visual representations and existing foundational knowledge. We collected think-aloud interview data from beginner-level undergraduate biology students and intermediate-level undergraduate biochemistry students, and catalogued trends in those students' ideas about an assessment dealing with MPDR. The primary trends observed are as follows: visuals heavily influence student ideas about a metabolic pathway, final products of a pathway take precedence in student solutions, and accurate student ideas about negative feedback are often limited by difficult-to-detect gaps in understanding or alternate ideas. We recommend the development and implementation of intuitive scientific visuals and accompanying teaching materials that focus on exploring MPDR ideas, and that educators consciously expand their perspective on student ideas beyond simple categories of "correct" and "incorrect". Students hold a variety of subtle and difficult-to-detect alternate ideas about feedback inhibition which educators should seek to find and address. Students would also benefit from teaching which places an increased emphasis on the holistic perspective in MPDR education.

Keywords: Metabolic Pathway Dynamics, Student Ideas, Biochemistry Education

1. Introduction

Life sciences education continues to face the challenge of imperfect teaching methods and suboptimal scientific comprehension among undergraduate students in the United States[2]. To facilitate student success in the life sciences, we approach the central subject of biochemistry from an idea-oriented perspective. Since the publication of the American Association for the Advancement of Science's (AAAS) *Vision and Change* report in 2011, biology and biochemistry education research has shown intensified focus on understanding the way students think about life science concepts[1, 13]. As part of the revitalized focus on student ideas, this study seeks to reveal student ideas and improve teaching for biochemistry. Biochemistry teaching and learning have an especially wide impact because most science undergraduates and all pre-health professionals take the course.

The new focus on understanding student ideas comes with the challenge of accurately representing the complexities of student thought. Existing bodies of research reveal a depth and breadth of nuance to students' thought processes that cannot be categorized in simple terms of "correct" and "incorrect". Many students have accurate ideas with naive facets, and alternate conceptions that incorporate accepted scientific knowledge. Truly understanding and addressing these ideas requires intentionally setting aside attempts to categorize ideas based on superficial and dichotomous descriptors, such as correctness[11, 16, 20, 21, 22, 23].

We recognize the biochemistry concepts identified by Loertscher and colleagues[8] as the primary set of ideas students must grasp to be successful in the biochemistry course. These concepts include steady state, physical basis of interactions, thermodynamics of macromolecular structure formation, free energy, and metabolic pathway dynamics and regulation (MPDR). In particular, this study focuses on MPDR, a field vital to understanding human nutrition and improving medical treatments for diabetes, obesity, and cancer[7]. Biochemistry students learn MPDR by building upon their prior knowledge of homeostasis and catalysis from biology and reaction favorability from chemistry[10]. Students also learn MPDR by studying and using visual representations designed to convey information about the concept.

Students first learn about aspects of MPDR—such as reversible reactions, enzymes, and homeostasis—in introductory biology and general chemistry, which they take prior to biochemistry, so studying MPDR enables probing of the development that occurs as students build expertise[17]. The way students understand MPDR's essential ideas in these early stages directly influences the way they build expertise in the concept over time. If foundational ideas are not fully understood, the subsequent lack of understanding poses a roadblock to success in biochemistry and therefore also the real-world application of MPDR—as detailed above—to physical fitness treatments and medicine[8]. Even as students develop their understanding of MPDR, alternate ideas established in these early courses may still exist in their reasoning. Both beginner biology and intermediate biochemistry students are investigated in an attempt to understand student ideas about MPDR from several levels of experience, search for persistent alternate ideas, examine potential interplays between student ideas in both courses, and answer our research question: what ideas do biology and biochemistry students express when solving MPDR problems?

MPDR instruction also enables and requires consideration of the centrally important, but often neglected, topic of scientific visuals. Most specifically, this entails investigation of how students understand and interact with visual representations of metabolic pathways. Students learn better from a combination of visuals and text than from text alone—and MPDR instruction almost always makes use of visual representations[9, 19, 24]. Prior research in the life sciences recommends expanded investigation into students' ability to use visual representations like those for MPDR, and points out the conspicuous absence of that skill as an explicit objective of scientific teaching, despite its central importance to the field and student learning[2, 6, 14]. Additionally, visuals in biology have been shown to be highly inconsistent—there is no significant linkage between style and meaning of schematic arrows used in textbooks[14]—and development of an intuitive and standardized system of representations based in student ideas would greatly assist the effectiveness of life science education.

2. Methodology

This study centers on verbal data collected from undergraduate students at a large, selective state university with beginner- and intermediate-level experience in biochemistry. We administered a well-defined problem set—referred to as the "BioSTEPS assessment"—on MPDR in two variations of the pathway that shows the biosynthesis of dimethylacryloyl-coenzyme A (see Figure 1) to 22 beginner-level biology students (11 male and 11 female; given pseudonyms beginning with the letter "B") and 22 intermediate-level biochemistry students (3 male and 19 female; given pseudonyms beginning with the letter "C"). The equal gender divide of the biology student cohort could not be replicated for the biochemistry student cohort, due to a much smaller pool of available student interviewees for the latter group. The biology course in question was the level generally taken by first- and second-year students in life science majors, which would require them to take the introductory biochemistry course later on (generally in their second or third year). All biology sections were taught by a single professor, while a different professor taught each section of the introductory biochemistry course.

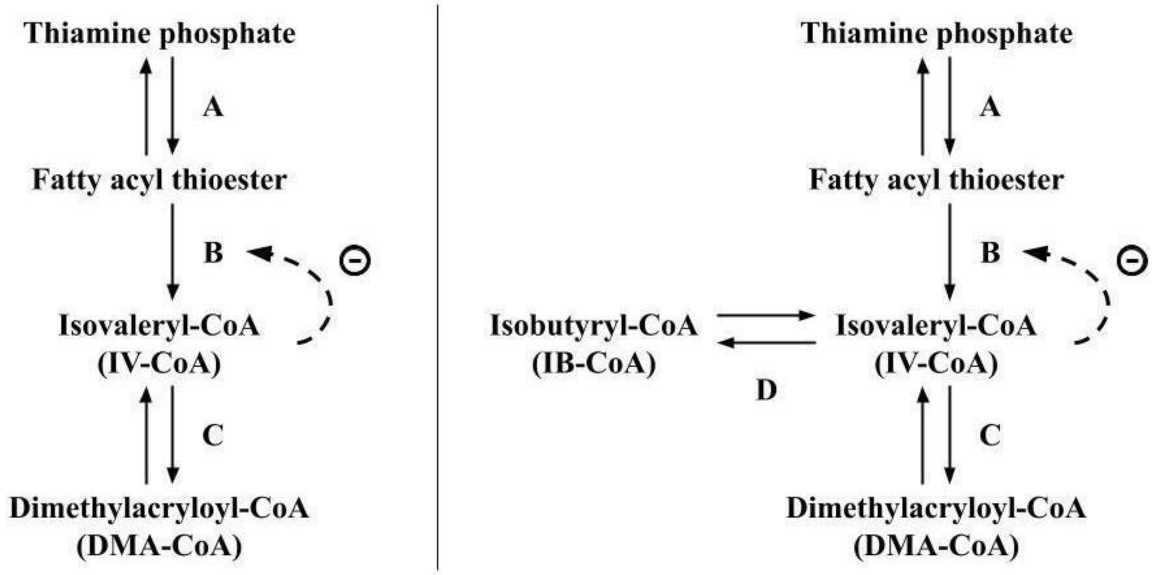

Figure 1. The two variations of the metabolic pathway presented to student subjects in the BioSTEPS assessment

In the pathway shown—the biosynthesis of dimethylacryloyl-coenzyme A—thiamine phosphate is converted over several steps to dimethylacryloyl-coenzyme A (DMA-CoA) by enzymes A, B, and C. If there is an excess of the intermediate compound isovaleryl-coenzyme A (IV-CoA), some IV-CoA can bind to enzyme B to prevent the enzyme from working via negative feedback inhibition. Feedback inhibition slows the rate of IV-CoA production to keep the pathway under control. In the variation of the pathway pictured on the right, the enzyme D—with the ability to convert the intermediate IV-CoA to the compound isobutyryl-coenzyme A (IB-CoA)—is introduced, and less of the IV-CoA is used for DMA-CoA production.

The MPDR portion of the BioSTEPS assessment consists of 9 total items: 3 multiple-choice items, 3 multiple true-false items, and 3 constructed response items. The pathway shown in Figure 1 was chosen because the molecules involved are likely to be unfamiliar to students based on their classes—ensuring that student ideas about the pathway were generated from consideration of the visual rather than knowledge of the substances involved. The problem set described was administered via Qualtrics (Qualtrics, Provo, UT). The students solved the problems in the assessment during a recorded think-aloud interview[12, 16]. In a think-aloud interview, participants are instructed to verbalize all of their thinking while they solve the problem. The interviewers serve as neutral investigators who only prompt participants to keep stating what they are thinking. For the MPDR interviews, the interviewers spoke only to guide students through the assessment software or to invite them to elaborate on specific scientific terms or ideas the students mentioned.

Following the completion of these interviews, the interview recordings were examined using qualitative content analysis as previously described by Halmo and colleagues[26]. We catalogued student thought based on the trends in ideas observed within and between the two groups.

3. Data

The following analysis of student responses focuses on what students' problem-solving descriptions reveal about their understanding of the problems presented in the BioSTEPS assessment. The analysis also accounts for students' use and interpretation of the visual representations within BioSTEPS. For ease of understanding, the interview transcripts below do not include vocal fillers ("um", "like", etc.). Beginner-level students were given pseudonyms beginning with the letter "B", and intermediate-level students were given pseudonyms beginning with the letter "C".

3.1 Visuals Influence Student Ideas About A Metabolic Pathway

The dashed arrow/circled bar symbol (see Figure 1) conveys IV-CoA binding to enzyme B in order to allosterically inhibit the enzyme and counteract any potential buildup of IV-CoA. Although scientific textbooks are frequently inconsistent in their visual representation of allosteric inhibition[14], this choice of symbolism for the assessment matches one of the most popular depictions. Yet, most students did not completely grasp the intended meaning. The two most common ideas students displayed were that IV-CoA was inhibiting enzyme B, or that IV-CoA was being "recycled" in the pathway.

Beginner-level students most often interpreted the dashed arrow and circled bar shown in the metabolic pathway (see Figure 1) as a "recycling" process. Students believed the symbol indicated IV-CoA serving as a component of the reaction catalyzed by enzyme B, in order to facilitate the conversion of fatty acyl thioester into more IV-CoA—an idea detailed below by Bernard:

> Bernard: "[IV-CoA is] being added back in right here to B, so that it can somehow bond with the fatty acyl thioester and make some more of itself."

The idea that IV-CoA is "recycled" or reused to produce more of itself frequently impacted students' discussion of the pathway throughout the assessment. Beginner-level students who identified the arrow as both recycling and negative feedback nearly always explained their answers in terms of the former interpretation, rather than the latter.

Rarely, some beginner-level students accurately identified the arrow as representing feedback inhibition. When they did so, they often cited the presence of the circled bar—the negative sign—as the reason for their choice. Take Ben's statement below:

> Ben: "I feel like the circled bar would have something to do with it being negative. So, in that thinking, I would say that this would be negative feedback or inhibition, and it would not be positive. And I'm only saying that because I see this as being a negative sign."

When beginner-level students made such a choice, however, they often were even less successful in their application of the negative feedback concept than the intermediate-level students—frequently displaying naive understanding of the idea or failing to consider the phenomenon's influence on the pathway later on in the assessment. For example, Barrett described feedback inhibition as follows:

> Barrett: "Each letter represents the enzyme as it facilitates the metabolism, and the dashed arrow is negative feedback… It's helping the reaction process to continue, kind of like sending more signals or enzymes out to facilitate the metabolism."

Several beginner students identified the dashed arrow as representing feedback inhibition, but never referred back to feedback inhibition at all in their later discussion unless specifically prompted by the assessment or the interviewer. This was true whether or not they also identified the arrow as representing "recycling" as well.

Nearly all intermediate-level students identified the dashed arrow as representing feedback inhibition. Chloe's statement below is an example.

> Chloe: "So, the dashed arrow implies regulation of some sort of the metabolic compound on the activity of the enzyme. And the circled bar, since it's a negative—a minus sign—it would be negative inhibition."

Some of the intermediate-level students did express alternate ideas about the phenomenon of inhibition, such as the idea that feedback inhibition functioned as an "alternate pathway". Yet, despite these naive explanations of the concept, these students often successfully deciphered the intended meaning of the visual to be "negative feedback". In contrast, most beginner-level students exhibited alternate interpretations of the dashed arrow.

3.2 Student Difficulties With Feedback Inhibition Are Difficult To Detect

Both beginner and intermediate-level students were able to come to conclusions about feedback inhibition deemed "correct" by the assessment parameters, but their thought processes were limited by the application of alternate ideas and reasoning. While these students were able to arrive at some accurate conclusions during the BioSTEPS assessment, these hidden limitations still led to incomplete understanding of MPDR. Take Barry's statement below as an example.

> Barry: "If [IV-CoA] was binding to [enzyme B], then it would have some effect on both [branches], just because some of this IV-CoA would not go to these two enzymes right here," <he indicates enzymes C and D> "So … if none of this [IV-CoA] could bind to this enzyme B right here, then I think there would be more movement across enzymes C and D."

Note that Barry accurately predicted an increased amount of movement across enzymes C and D if IV-CoA lost the ability to bind to enzyme B, by reasoning that the IV-CoA that would otherwise have bound to enzyme B would then be free to move across enzymes C and D. Yet, Barry's reasoning—while accurate—is insufficient. He came to his conclusion without realizing or discussing the fact that the phenomenon described would also prevent the production process of IV-CoA from regulating itself—which was the idea the assessment aimed to probe. He does not know about the inhibitory interaction happening between enzyme B and IV-CoA.

We also encountered students who applied a logical sequence of reasoning to a feedback inhibition problem, but arrived at the opposite answer to the one expected. Take Chelsea's discussion below.

> Chelsea: "So if [enzyme C] is inhibited, [IV-CoA] won't be converted to [DMA-CoA] as much. … I think [the activity of enzyme B] would increase still, with that reasoning."

Chelsea successfully predicts the changes in the amounts of compounds in the pathway based on the inhibition of enzyme C, but selects a final answer that is counter to these conclusions. Clearly, Chelsea holds limiting ideas about feedback inhibition that caused her to select that answer. Those limiting ideas could not be gleaned from her think-aloud interview. Notably, both Chelsea and Barry accurately identified the dashed arrow and circled bar as signifying negative feedback.

In some cases, limiting ideas caused students to arrive at "incorrect" final answers. However, many limiting ideas did not affect students' multiple choice or multiple true-false assessment performance and were therefore undetected until the students were probed for their reasoning during interviews.

Ideas like those shown here by Barry and Chelsea cannot be faithfully represented and understood through the use of simple categories of "right" and "wrong". Taking a more nuanced analytical perspective[11, 16, 20, 21, 22, 23] revealed that capable students frequently held varying, but specific, limiting ideas about negative feedback.

3.3 Final Products Take Precedence In Student Solutions

Students in the sample focused primarily on the end products of the pathway rather than the interconnectedness of pathway components. Chelsea encapsulated this idea in the following statement.

> Chelsea: "I'm thinking … what is the point of [this pathway]? And I would think the conversion to the DMA-CoA is the main product of this pathway—is what its main goal is."

There were some students in both groups that consciously acknowledged—like Bryanne does below—that the pathway elements were all interconnected.

> Bryanne: "What controls how much DMA-CoA is made by this pathway? I think everything would kind of affect it. 'Cause it's one big pathway."

Yet, most students still had difficulty engaging with the BioSTEPS pathway as a unified whole, in which all parts of the pathway affected one another. Some beginner-level students interpreted the pathway as being divided into subsections that did not cause changes in one another. As Booker stated during his interview:

> Booker: "[Enzyme C not working anymore] would affect only this pathway," <he indicates the pathway from thiamine phosphate to DMA-CoA> "So it wouldn't affect the whole system. It would affect this way because if [enzyme C] stops working, then it's gonna stop working to produce the dimethylacryloyl-CoA, but it won't be affecting this one…" <he indicates the pathway from IV-CoA to IB-CoA> "…since it's using a completely different enzyme."

In particular, students rarely discussed the effects of pathway phenomena on the compounds at the beginning of the pathway—thiamine phosphate and fatty acyl thioester. Even when specifically asked by the interviewer whether or not those compounds would be affected by a given change to the pathway, intermediate-level students were divided over whether any change would occur. Their two differing interpretations are exemplified by Clara and Chloe below.

> Interviewer: "Once we've introduced this branch point … does that affect the flux of the pathway prior to the branch point? …"
> Clara: "… since the isovaryl-CoA [*sic*] is now being distributed amongst two branches, there's less of that in general, so there's less of it to inhibit enzyme B. … So it's not changing anything about the thiamine phosphate to the fatty acyl thioester, but it could be decreasing their concentrations, if anything.

> Interviewer: "When you introduce a branch point to a pathway, is it going to affect any steps prior to that branch point? …
> Chloe: "No, it would only affect the concentration of DMA-CoA and IB-CoA, because it's just working with how much IV-CoA is available at this predetermined place."

Even when students believed there might be some change in the amounts of thiamine phosphate and fatty acyl thioester, they often minimized the importance of that change. Clara suggests a decrease in concentrations as an afterthought—a side effect that may or may not occur, and that would have no groundbreaking significance either way.

4. Conclusion

Our findings confirm the significance of visual understanding and suggest more research is needed on the relative intuitiveness of standard visual representations of metabolic pathways. Subjects' interpretations of the visual heavily impacted their conceptual discussions of the pathway. This trend further emphasizes the importance of scientific visual understanding to student success. Placing a greater conscious emphasis on visual interpretation in life science courses such as biochemistry could greatly improve student ability to successfully reason through pathway dynamics and other concepts. Yet, simply expanding visual instruction efforts for students is not enough. The tendency of beginner-level students to interpret the dashed arrow as "recycling" despite the presence of the negative sign suggests that visual representations for particular concepts may be less intuitive to students than educators believe. We recommend researchers also work to optimize the intuitiveness of MPDR visuals, by designing a variety of visuals for MPDR concepts and comparing student understanding among them. Sets of teaching materials, produced as companions to those visuals, could also be created. Contrasting cases[5] or guided-inquiry[4] questions might probe ideas such as the "recycling" interpretation and help students explore whether negative feedback truly fits these definitions.

When discussing the result above, it is important to consider the potential for the assessment design to have primed students to form these alternate ideas about the pathway. One of the first multiple true-false questions in the MPDR portion of the BioSTEPS assessment asked students to interpret the meaning of the dashed arrow and circled bar. Each of these alternate interpretations discussed, including "IV-CoA is being recycled", were included as potential answer choices for students alongside feedback inhibition. However, these answer choices were developed from recurring interpretations of the arrow and bar that were observed in student pilot interviews, and as such remain rooted in student ideas. Notably, students tended towards the naive “recycling” interpretation as opposed to the intended “negative feedback” interpretation, even with the circled bar—the negative sign—present in the visual.

These data also provide additional support for the existing recommendation, based on prior findings[11, 16, 20, 21, 22, 23], that educators and assessments of student knowledge shift focus towards analyzing student ideas and reasoning as opposed to making judgments based on “correctness” of student conclusions. As shown, the use of simple “right” and “wrong” categorizations for student answers can cause educators to misrepresent student levels of understanding. In particular, we recommend that educators pay close attention to students’ discussion of feedback inhibition, as these data show that even an apparently strong grasp of the concept may conceal significant alternate ideas.

Lastly, we recommend that biochemistry instructors place a greater emphasis on the holistic consideration of metabolic pathways. While these subjects displayed a consistent ability to reason about the pathway in localized areas, they rarely discussed the pathway as a unified entity and occasionally even declared the pathway segments to be divided from one another.

The tendency of the students to focus their discussions on the final products of the pathway requires further investigation. The specific pathway used in the BioSTEPS assessment may perhaps have encouraged such a phenomenon, as many of the more complicated elements (the feedback inhibition arrow, the branch point, the irreversible reaction) were situated in the latter half of the pathway. Investigating this trend with a different metabolic pathway—one in which the more complicated elements are present at the beginning of the pathway or absent entirely—may be beneficial to understanding the degree to which the trend persists across different situations.

The small sample of subjects in our study limits the generalizability of these results to beginner biology and intermediate biochemistry students as a whole. All students in the study attended a single Southeastern university. The sample is demographically non-representative of the introductory biology and biochemistry populations at large—eg. 19 of the 22 students in the biochemistry student cohort were female. The purpose of the study was to perform a focused examination of student ideas from a qualitative perspective in order to identify areas for further research and development in the field of biochemistry education—and the teaching of metabolic pathway dynamics in particular.

Further ongoing research on these results is exploring the potential correlations between the student ideas observed and way the teaching materials they encountered—including lectures, textbooks, and homework—presented the relevant concepts. We intend to move forward in further research by designing and testing educational materials that address the concerns detailed above. By creating accessible visuals embedded within lessons for evidence-based pedagogies like worked examples with practice[18] or guided inquiry[3, 25], educators can help students understand nuanced concepts in MPDR and use the observations made here to produce tangible resources for improved biochemistry education.

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