

**Traditional, Mixed-Mode, and Online Instruction for Microbial Metabolism
Before and During COVID-19**

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Abstract. As COVID-19 restrictions are removed, instructors are faced with two questions: should the course be taught online, via mixed-mode, or through traditional methods, and what effect did online instruction have on students in the course in regards regarding enrolled across eight semesters of metabolism courses using traditional, mixed-mode, and online methods. Post-hoc analysis of a repeated-measures ANOVA determined that while mixed-mode outperformed traditional methods on metabolism exams involving introductory concepts on the first exam (4.47 ± 4.24 , $p = 0.012$) and on the cumulative final exam (8.15 ± 4.24 , $p = <0.001$), traditional methods were superior to both mixed-mode (9.21 ± 4.24 , $p = <0.001$) and online methods (6.37 ± 5.76 , $p = 0.006$) at teaching alternative pathways of metabolism and lipid, nucleotide, and amino acid synthesis pathways. All methods showed poor student scores on glycolysis, TCA cycle, oxidative phosphorylation topics. Online methods performed nearly equally to mixed-mode, though there was not a significant difference on the first exam's content as was found with mixed-mode. It is evident that, based on this study, a different approach to teaching basic central metabolic cycles such as glycolysis, the TCA cycle, and the electron transport chain is necessary to improve student understanding of these topics.

Keywords: mixed-mode; COVID-19; online; metabolism; microbial

With regulations on instruction during COVID-19 relaxing, instructors of upper-level undergraduate science courses like microbial metabolism are faced with two major questions: how did COVID-19 impact the education of students and how should teaching transition from online instruction now that COVID-19 no longer requires instruction to be fully online?

It is no surprise that COVID-19 has had dramatic effects on instructor perception and teaching approaches: teachers are often not seeing online instruction as beneficial, there are increased feelings of burnout, and there are difficulties in transitioning to online teaching (Abdelmola et al., 2021; Daumiller et al., 2021; Dietrich et al., 2020). This difficulty was similarly felt by students, with questions of accessibility for students with disabilities, psychological health, and the influence of diverse backgrounds on learning all making teaching STEM a challenge (Gin et al., 2021; Yu, 2021; Hasan & Bao, 2020; Lynn et al., 2020). Undergraduates have been shown to have decreased participation and engagement in college science courses before the pandemic; this has only gotten worse during the pandemic (Wester et al., 2021; Perets et al., 2020). Even with attempts to adapt biochemistry and metabolism courses to novel online instruction, there are reports that some

methods have not been effective or have been inconclusive to improving student outcome (Ossai et al., 2020).

Despite these negatives, however, there have been multiple successes with instruction for biochemistry and metabolism courses switching to online formats (Kapil et al., 2021; Contreras-Rodríguez et al., 2020). With effective preparation and successful activities to apply biochemistry course content, there is research showing that students can perform just as well online as face-to-face instruction (Keppetipola & Patchen, 2021). Even the laboratory content of biochemistry was shown to effectively be performed in online formats without having students experience gaps in knowledge (Costabile, 2020; Zewail-Foote, 2020). Successful strategies have included instructors and teaching assistants being available for students to assist in biochemistry, encouraging participation and collaboration amongst the students, and being prepared with strategies adapted to online teaching (Procko et al., 2020). Despite the negatives introduced by the COVID-19 pandemic, there is evidence supporting that metabolism and biochemistry courses may be viable in an online format.

Conflicting ideas presented here call for an investigation as to how student scores were affected in metabolism courses when taught fully online versus different instructional methods of the past. This question is important for instructors as they transition away from the online-only courses during COVID-19. Instructors are faced with either continuing to teach online-only, going back to traditional methods of instruction, or trying less commonly used mixed-mode approaches. This scenario offers a prime opportunity for instructors to explore different teaching methods. Unfortunately, the conflicting research surrounding each method of instruction (traditional, mixed-mode, and online instruction methods) as well as the lack of studies concerning online instruction for such high-level undergraduate sciences makes this question a difficult one for an instructor to make.

While instructors may be familiar with online methods of instruction due to the recent pandemic or traditional teaching methods using lectures before the pandemic, the term mixed-mode may be less known. Mixed-mode is a method of instruction which provides approximately half of class time online and half of class time in person, acting as a sort of mix between traditional in-person instruction and online methods of teaching. Though there are several approaches to this method of instruction, arguably the most common structure is that of a flipped classroom: students learn lecture material delivered online, read their textbooks or readings, and listen to videos outside of class while in class, students apply the information using active learning collaborative activities (Sajid et al., 2016). Flipped classroom mixed-mode designs have shown gains in student problem-solving skills in upper-level sciences, higher scores, and more preparation of students (Klegeris, 2020; Styers et al., 2018; Gross et al., 2015). Regarding metabolism and biochemistry courses specifically, students have higher grades, difficult concepts have been better understood by students, and students have improved upon their cooperative learning abilities (Ren et al., 2020; Francis et al., 2020; Jafarkhani & Jamebozorg, 2020; Ojennus, 2016). With research supporting mixed-mode approaches like this,

a switch to mixed-mode instruction methods for teachers of metabolism courses stands as a valid choice.

Traditional lecturing also is a method many instructors are used to, and most certainly will be a comfortable pick for instructors returning to teaching in classrooms without COVID-19 restrictions. One may argue that this method has been the most used form of teaching biochemistry and metabolism courses, and thus, it makes little sense to change what has been used in the past. For instructors wishing to branch off from lectures alone, beneficial results have been seen when instructors using traditional lecture teaching give short activities between lectures to check for student understanding (Ghorbani & Ghazvini, 2016; Miller et al., 2013). Instructors of metabolism courses can use online technology to enhance their traditional lecture content, allowing students to further increase understanding of lectures without requiring a change to another teaching method (Henly & Reid, 2001). Traditional lectures combining technology may best for metabolism education post-COVID-19, but this is ultimately something future research will examine.

Ultimately, instructors are left confused as to which instruction method to use as more questions arise from research than answers. One problem concerning research in different methods of instruction is that of consistency, as an overall increase in student gains from mixed-mode methods does not in itself mean that all metabolism topics are best taught in that format. Another problem arises choosing between traditional or online instruction: how does online instruction differ from the traditional lecture-based approach of the past, and is it viable to continue teaching metabolism courses online?

This study wishes to answer these questions. First, this study wishes to evaluate multiple semesters of data of students enrolled in undergraduate metabolism courses to understand which instructional method produces better scores for students. Second, the effect of COVID-19 online-only instruction will be evaluated to see if scores differ markedly from mixed-mode and traditional instructional methods; this will help instructors understand the effect COVID-19 had on student understanding of metabolism concepts. Finally, this study explores whether each teaching method is consistently better or worse for teaching metabolism topics based on performance on exams.

Methodology

Student participants from eight semesters of microbial metabolism were chosen for analysis. All eight semesters were taught by the same instructor at the same university. By choosing multiple semesters, data from both spring and fall was included, therefore limiting influence of the time of the course as a factor in student scores. Two of the eight semesters were taught using a traditional teaching method (N= 367), three semesters were taught with a mixed-mode method (N= 429), and three semesters were taught using an online method of instruction during the COVID-19 pandemic (N= 152). In total, 948 students' scores on each of the four exams were used for analysis.

The semesters used for analysis included fall semester and spring semester metabolism courses to help eliminate time of semester instruction as a factor in student score. Additionally, students were only included if there was an exam score available for all four exams, meaning that students who withdrew from the course were not included for analysis. Semesters taught during COVID-19 had markedly lower student enrollment and smaller class sizes in an online environment. More semesters would have been used for analysis to help balance the number of students being compared to be more equal across the three instruction method groups if possible, however, online-only education during COVID-19 was restricted to those semesters alone.

All microbial metabolism semesters had four exams covering the same learning objectives. The same question bank was consistently used across all semesters to preserve comparability. Each exam had the same number of questions in every semester to make the scores more comparable as well. In person exams were proctored by the instructor and teaching assistants and online exams were proctored by proctoring software that locks down the exam takers browser and video monitors them during the exam. Exam 1 content covered basic microorganism introductory material and review content from prerequisite science courses. Exam 2 content covered central metabolism including enzymes, reactions, and substrates involved in glycolysis, the TCA cycle, and oxidative phosphorylation. Exam 3 covers alternative pathways of metabolism as well as pathways for lipid, nucleotide, and amino acid synthesis. Exam 4 is the final, cumulative exam of the course with content from all previous exams as well as additional metabolic pathway content and quorum sensing not covered in exam 3.

All student grade data was collected with approval by an IRB, with grade data being de-identified before analysis. All data analysis and interpretation was performed by a separate researcher than the instructor to limit bias in interpretation. The course instructor always included an extra-credit question on each exam, allowing the total score on each exam to be slightly above 100%; this was consistent across all semesters. Beyond this, the lowest exam score (except the final exam, exam 4) was always dropped from a student's final grade calculation in each semester. This lowest score dropping caused students to ultimately get a zero on some exams on purpose as they were aware of the dropped score. These zeroes were viable grades for statistics and as such were still included in the analysis.

To consistently teach each instructional method, the curriculum for each method was developed and used the same way for each semester. At the university where this study was conducted, the metabolism course used one of two schedules: classes on Monday, Wednesday, and Friday for a 50-minute periods, or classes on Tuesday and Thursday for a 75-minute periods. The course was taught using one of these two options depending on the semester that the course was taught. The traditional method used every class time for lectures taught by the instructor of the course. For the mixed-mode method semesters, a flipped classroom approach was used modeling previous research (Johanson, 2017). There would be one day in which class was online where students would watch pre-recorded lectures and take

a quiz on the content. The following day of the class was taught in person in which students applied the learned material from online to scenarios and activities.

Instruction during COVID-19 was entirely online. Students had online lectures on half of the days and online collaborative activities applying the material on the other half. As COVID-19 progressed, literature on effective methods of instruction for biochemistry education online were considered (Lapitan Jr. et al., 2021). This approach also included the collaborative aspect to improve student biochemistry outcomes, increase positive perception of the course, and make the online environment more akin to what it would be like if the course were in person (Wilson, 2021; Fernández-Santander, 2008). Lecture content for the online course was mainly pre-recorded videos, allowing them to start or pause the videos according to their needs. This also gave students a resource to refer to when studying the material.

A repeated measures ANOVA was performed comparing grades on each of the four exams across each of the students enrolled in traditional, mixed-mode, and online semesters. Results compared between the groups provides evidence supporting whether a difference exists between the teaching methods as well as whether that difference is consistent across all exams in the course. The repeated measures ANOVA was checked for assumptions with Mauchly's test, and a type III sum of squares design was used when performing the repeated measures ANOVA. Regarding post-hoc analysis, the Holm method was used.

In addition, a separate average for each exam was found to see how students perform on metabolism exams. This analysis was designed to highlight the topics most missed by students overall, making it easier for instructors to identify necessary changes.

Results

Upon analysis of the results via repeated measures ANOVA, Mauchly's test of sphericity indicated a violation, $X^2(5) = 405.60$, $p = <0.001$. To compensate for this, a Greenhouse-Geisser correction was applied. The repeated measures analysis of variance with a within-subjects factor of semester instruction method (traditional, mixed-mode, online) and a between-subjects factor as exam (exam 1, exam 2, exam 3, exam 4) summarized in table 1 and table 2 showed semester instruction method had an effect on exam score $F(2, 4.89) = 29.13$, $p = <0.001$, $\eta^2 p = 0.06$. Descriptive statistics are summarized in table 3 and represented in boxplots in figure 1.

Table 1*Between Subjects Effects*

Cases	Sum of Squares	df	Mean Square	F	p	η^2	η^2_p
Semester	1079.69	2	539.84	0.83	0.44	8.38e -4	0.002
Residuals	614478.22	945	650.24				

Note: Type III Sum of Squares.

Table 2*Within Subjects Effects*

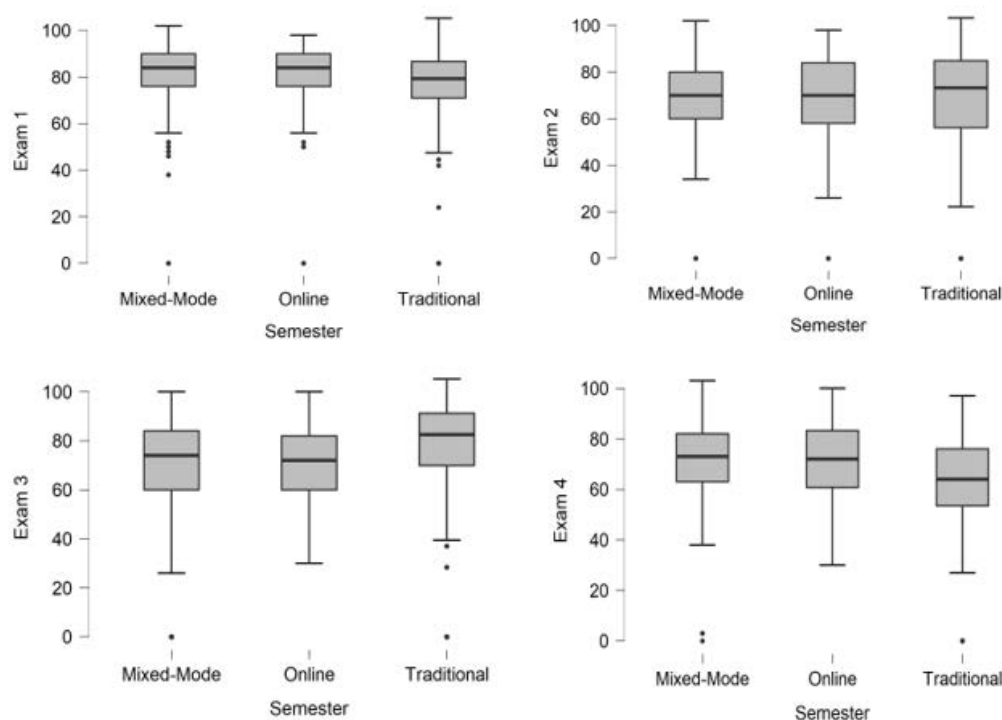
Cases	Sphericity Correction	Sum of Squares	df	Mean Square	F	p	η^2_p
Exam	Greenhouse-Geisser	67551.68	2.44	27657.84	112.05	< .001	0.11
Exam * Semester	Greenhouse-Geisser	35119.17	4.89	7189.46	29.13	< .001	0.06
Residuals	Greenhouse-Geisser	569697.58	2308.07	246.83			

Note: Type III Sum of Squares. ^a Mauchly's test of sphericity indicates that the assumption of sphericity is violated ($p < .05$).

Table 3*Descriptive Statistics by Instruction Method*

Exam	Semester	Mean	SD	N
1	Mixed-Mode	81.59	12.92	429
	Online	80.88	14.25	152
	Traditional	77.13	15.95	367
2	Mixed-Mode	67.66	19.29	429
	Online	68.16	19.20	152
	Traditional	67.81	23.98	367
3	Mixed-Mode	68.63	20.57	429
	Online	71.47	14.92	152
	Traditional	77.84	19.14	367
4	Mixed-Mode	71.78	14.26	429
	Online	71.82	14.33	152
	Traditional	63.63	16.26	367

Figure 1

Boxplots

Note: Data is divided based on exam number and compares the different results of each method of instruction.

Post hoc analysis results are summarized in table 4. A post hoc analysis with Holm correction showed that exam scores on exam 1 were higher for participants taught using mixed-mode instruction versus traditional instruction (4.47 ± 4.24 , $p = 0.012$), but exam scores did not differ significantly between traditional and online instruction nor between mixed-mode and online teaching. No significant differences were found with exam 2 scores between semesters. Exam scores on exam 3 were lower for participants taught using mixed-mode instruction versus traditional instruction (9.21 ± 4.24 , $p < 0.001$) and were lower for participants taught using online instruction versus traditional instruction (6.37 ± 5.76 , $p = 0.006$). Exam 3 scores did not differ significantly between mixed-mode and online instruction ($p = 1.000$). Exam scores on exam 4 were higher for participants taught using mixed-mode instruction versus traditional instruction (8.15 ± 4.24 , $p < 0.001$) and were lower for participants taught using online instruction versus traditional instruction (8.19 ± 5.76 , $p = 0.006$). Exam 4 scores did not differ significantly between mixed-mode and online instruction.

Table 4

Post Hoc Analysis

			95% CI: Δ Mean				
Group 1	Group 2	Δ Mean (Group 2- 1)	Lower	Upper	SE	t	p _{Holm}
Exam 1							
Mixed-Mode	Online	0.71	-4.92	6.34	1.67	0.43	1.00
	Traditional	4.47	0.22	8.71	1.26	3.55	0.01*
Online	Traditional	3.76	-2.00	9.51	1.71	2.20	0.50
Exam 2							
Mixed-Mode	Online	-0.49	-6.13	5.14	1.67	-0.30	1.00
	Traditional	-0.14	-4.39	4.10	1.26	-0.11	1.00
Online	Traditional	0.35	-5.40	6.11	1.71	0.21	1.00
Exam 3							
Mixed-Mode	Online	-2.84	-8.47	2.80	1.67	-1.70	1.00
	Traditional	-9.21	-13.45	-4.97	1.26	-7.32	<0.001*
Online	Traditional	-6.37	-12.13	-0.62	1.71	-3.73	0.006*
Exam 4							
Mixed-Mode	Online	-0.04	-5.67	5.59	1.67	-0.02	1.00
	Traditional	8.15	3.90	12.39	1.26	6.47	<0.001*
Online	Traditional	8.19	2.43	13.94	1.71	4.80	<0.001*

Note: * $p = <0.05$

To determine how students overall performed on each exam all 948 students were combined into a single group, and an average exam score and standard deviation for each exam was found. Findings are summarized in table 5. Overall, students performed worst on exam 2 ($M = 67.80$, $SD = 21.20$). Exam 4 scores were overall low as well ($M = 68.63$, $SD = 15.58$). This lower score may be due to the cumulative nature of the exam, as it covered all content of the course. Students who already failed a previous test or who did not understand a section previously most likely struggled with those same subjects when they appeared on the final, exam 4. Exam 1 had the highest overall average ($M = 79.75$, $SD = 14.51$) which is unsurprising considering the prerequisite information included on this exam. Exam 3's average score was 72.65% ($SD = 19.65$). Overall class grades were not used for statistical analysis; while the exams were graded the same way during all eight semesters, there were additional pre and post quizzes, extra assignments, and other differences in grading the course during mixed-mode and online semesters which may have artificially inflated the final grades of the students. By comparing exams rather than final grade in the class, this variable is eliminated, and only the exams that were consistent across all semesters were considered.

Table 5:*Descriptive Statistics with All Students Combined*

	Exam 1	Exam 2	Exam 3	Exam 4
N	948	948	948	948
Mean	79.75	67.80	72.65	68.63
Std. Deviation	14.51	21.20	19.65	15.58

Discussion

To answer the central questions of this study, an examination of two ideas was necessary. Firstly, which instructional method or methods achieved higher scores compared to others on each exam of the microbial metabolism course? Secondly, did students consistently get higher scores in that instructional method across the different exams of the course compared to other methods, or was the instructional method inconsistent in generating better scores across the four exams of the microbial metabolism course?

Results indicate that, rather than being consistently higher in score across all exams, instruction using mixed-mode methods produced higher scores on two of the four exams of the microbial metabolism course when compared to traditional instruction. Mixed-mode instruction outperformed traditional instruction on exam 1, the test covering basic microorganism introductory material and review content from previous science courses, and exam 4, the cumulative final exam with additional metabolism concepts not covered in exam 3. Interestingly, online instruction was closer to the average score found with traditional teaching, though it was not significantly different from either traditional instruction ($p = 0.50$) or mixed-mode instruction ($p = 1.00$). This establishes evidence towards mixed-mode teaching being effective at introducing basic microbial metabolism concepts in exam 1 as well as being a positive influence on reviewing past prerequisite material covered on the first exam of the course in comparison to online or traditional teaching. Exam 4, which reviewed all content of the course with a final exam plus additional metabolic processes, similarly showed that mixed-mode teaching produced better results on exams compared to traditional teaching. Exam 1 and exam 4 were both associated with reviewing past content (either from before the course as is the case with exam 1 or the entire semester's content with exam 4), so results may support mixed-mode teaching serves a beneficial purpose in reviewing content.

Although mixed-mode teaching overall outperformed traditional instruction on half of the exams of this study, the other exams show a problematic result. Regardless of method, students performed the same on exam 2 (central metabolism including enzymes, reactions, and substrates involved in glycolysis, the Krebs's cycle, and oxidative phosphorylation). This was the only exam with an average score of between 60-69% for all three methods. Results suggest one of two conclusions as

to why teaching method did not change student score. Firstly, the mixed-mode approach to teaching basic metabolic cycles may not be effective in the form it is being taught and if it were modified, it could possibly show higher scores. Another possible conclusion is that central metabolism cycles are consistently difficult to teach regardless of teaching method.

Exam 3 showed the inverse of what occurred with exam 1 and exam 4, with traditional teaching methods leading to higher scores compared to the scores found when teaching with mixed-mode methods ($p = <0.001$). Exam 3 covered topics including alternative pathways of metabolism as well as pathways for lipid, nucleotide, and amino acid synthesis; this raises a question as to what made the traditional teaching more effective compared to mixed-mode teaching when teaching these topics. As these metabolic processes are complicated with many steps, it may be that more guidance from instructors is necessary. The self-directed active learning of the mixed-mode course may either not be effectively applying these concepts, or the approach of mixed-mode teaching may not have enough teacher guidance to be effective with students.

Online teaching during the pandemic produced approximately the same scores as mixed-mode, performing better than traditional methods on exam 4 and performing worse than traditional methods during exam 3. Strangely, exam 1 did not show a large enough difference in mean score to be substantially different from traditional methods ($p = 0.502$) despite the mean average online score on exam 1 being higher. Regardless of this finding, online instruction managed to have students with higher scores than student scores during traditional methods on exam 4 by 8.19% ($p = <0.001$). Despite the forced transition to online instruction, students were able to perform on-par or better than students who were taught by traditional and mixed-mode methods (except in exam 3, which students had higher scores when taught with traditional methods). Students taught with online methods performed most like those taught with mixed-mode methods. Though it may be due to the similarity with mixed-mode and online instruction which led to their close results, an alternative explanation may be the increased withdrawals from the semesters taught online during COVID-19. With a higher-than-normal withdrawal rate from the microbial metabolism course, some of the lowest scoring students never completed the course and therefore did not have exam results available to compare in this study; this may have influenced the results in the online semesters.

Synthesizing the data from this study, one sees that despite mixed-mode instruction outperforming other methods on half of the exams of the microbial metabolism course, it is inconsistent in its effectiveness for certain exam topics. An alternative explanation may be that the approach used by the instructor was a poor way of adapting that teaching method. For example, the mixed-mode and online teaching may have both been taught in a similar, ineffective way for the material covered on exam 3. Changes to the activities performed in the mixed-mode courses or modifications of online instruction may be necessary to improve the results. The opposite issue may have made the traditional method of teaching less effective on exam 1 and exam 4: traditional instructional methods may just have been poorly performed by the instructor rather than being the traditional method itself being

problematic. As this study used 948 students across eight semesters, this problem was hopefully mitigated.

Exam 2, which covered basic central metabolism cycles and topics, produced the same results across all teaching methods. Combining all student scores across all teaching methods together and finding the average score of students, exam 2 had the lowest average score as well (67.80%). It is evident that a different approach to teaching basic central metabolic cycles such as glycolysis, the TCA cycle, and the electron transport chain is necessary to improve student understanding of these topics.

Conclusion

Mixed-mode instruction for upper-level sciences for undergraduates is commonly seen as the more effective method of teaching compared to traditional teaching regarding overall student achievement, but just having an overall better outcome does not mean that mixed-mode is consistently better throughout an entire semester of teaching. The results of this study suggest that while mixed-mode instruction produced the strongest scores of students in the first and last exams of the microbial metabolism course, it was not effective at teaching alternative pathways of metabolism and pathways for lipid, nucleotide, and amino acid synthesis compared to traditional teaching methods during the two exams in the middle of the course. Rather than suggesting that mixed-mode instruction is the optimal teaching method for microbial metabolism, results of this study suggest either changing the method of instruction from mixed-mode to traditional depending on the subject material of an exam or improving on the teaching approach when covering topics of metabolic cycles such as glycolysis, the Krebs cycle, and alternative metabolic pathways to change the average or poor results seen in scores on exam 2 and exam 3. There is merit to using traditional instruction for certain metabolism concepts that should not be disregarded. An approach to teaching which embraces traditional teaching at some points, such as when alternative pathways are taught, and mixed-mode teaching at other points, such as at the start and end of the course, should be explored in future research.

With central metabolism cycles being so challenging for students, research prevents several novel approaches to help students learn the material more effectively. Some research-supported approaches have included interactive arts-and-crafts type activities to learn steps of metabolism, metabolic cycle board games, or interactive physical games (França & Campos, 2021; Fishovitz et al., 2020; Rose, 2011). Alternatively, a case-based approach may work, as it connects the individual steps of metabolic cycles to real-world medical conditions and has been shown to be effective for learning biochemistry and metabolism (Thibaut & Schroeder., 2022; García-Ponce et al., 2021; Joshi et al., 2014; Kulak & Newton, 2014; Nair et al., 2013). Beyond this, additional media and representation methods can help cement student understanding of metabolic cycle content (Long et al., 2021; Wikandari et al., 2021). While it is unclear why students performed the worst on the exam covering these metabolic cycles, there may be individual student factors which can be explored to improve understanding of processes like the electron transport chain.

(Darabi et al., 2015). Perhaps game-based learning, different active learning methods, or other ideas may be explored for this purpose. The proposed ideas here offer different approaches for instructors to pursue in their transition back to normal teaching after the COVID-19 pandemic.

While the online semesters during COVID-19 managed to still do better than traditional instruction methods on the final exam, the same effect that mixed-mode instruction had compared to traditional was not as apparent on exam 1. The cause of this remains a question, though this study provides some evidence supporting that online teaching of microbial metabolism did not substantially lower student scores. It is possible that students performed worse in the prerequisite courses for microbial metabolism during COVID-19, with their foundational knowledge covered on exam 1 less than that of students in other semesters. While not effecting the first semester of online instruction, it influenced the other semesters of online instruction.

Regardless of these results, it is the instructor's decision as to how different teaching methods are used in the classroom. Whether traditional methods or mixed-mode methods are adopted, an approach bringing in active learning, technology, or fun methods of approaching metabolism should be explored. Giving up on traditional methods or fully switching to mixed-mode is not what this study suggests; instead, there is a need to be more open to adaptability. Twenty-first century skills are expected from students, and it is up to instructors to bridge the gap in their science courses and use mutability in instruction to supply that need.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

References

- Abdelmola, A. O., Makeen, A., Hanafi, H. M., & Ageeli, E. (2021). E-learning during COVID-19 pandemic, faculty perceptions, challenges, and recommendations. *MedEdPublish*, 10, 112. <https://doi.org/10.15694/mep.2021.000112.1>
- Contreras-Rodríguez, L. E., Sandoval-Hernández, A. G., Maya-Hoyos, M., & Soto, C. Y. (2020). Remote learning of biochemistry during the COVID-19 pandemic: case of undergraduate students in Bogota, Colombia. <https://doi.org/10.21203/rs.3.rs-72902/v1>
- Costabile, M. (2020). Using online simulations to teach biochemistry laboratory content during COVID-19. *Biochemistry and Molecular Biology Education*, 48(5), 509–510. <https://doi.org/10.1002/bmb.21427>
- Darabi, A., Arrastia-Lloyd, M. C., Nelson, D. W., Liang, X., & Farrell, J. (2015). Learning how the electron transport chain works: Independent and interactive effects of instructional strategies and learners' characteristics.

Advances in Health Sciences Education, 20(5), 1135–1148.

<https://doi.org/10.1007/s10459-015-9592-2>

Daumiller, M., Rinas, R., Hein, J., Janke, S., Dickhäuser, O., & Dresel, M. (2021). Shifting from face-to-face to online teaching during COVID-19: The role of university faculty achievement goals for attitudes towards this sudden change, and their relevance for burnout/engagement and student evaluations of teaching quality. *Computers in Human Behavior*, 118, 106677. <https://doi.org/10.1016/j.chb.2020.106677>

Dietrich, N., Kentheswaran, K., Ahmadi, A., Teychené, J., Bessière, Y., Alfenore, S., & Hébrard, G. (2020). Attempts, successes, and failures of distance learning in the time of COVID-19. *Journal of Chemical Education*, 97(9), 2448–2457. <https://doi.org/10.1021/acs.jchemed.0c00717>

Fernández-Santander, A. (2008). Cooperative learning combined with short periods of lecturing: A good alternative in teaching biochemistry. *Biochemistry and Molecular Biology Education*, 36(1), 34–38. <https://doi.org/10.1002/bmb.20141>

Fishovitz, J., Crawford, G. L., & Kloepper, K. D. (2020). Guided heads-up: A collaborative game that promotes metacognition and synthesis of material while emphasizing higher-order thinking. *Journal of Chemical Education*, 97(3), 681–688. <https://dx.doi.org/10.1021/acs.jchemed.9b00904>

França, V., & Campos, W. F. (2021). Interactive metabolism, a simple and robust active learning tool that improves the biochemistry knowledge of undergraduate students. *Advances in Physiology Education*, 45(2), 353–364. <https://doi.org/10.1152/advan.00042.2020>

Francis, N., Morgan, A., Holm, S., Davey, R., Bodger, O., & Dudley, E. (2020). Adopting a flipped classroom approach for teaching molar calculations to biochemistry and genetics students. *Biochemistry and Molecular Biology Education*, 48(3), 220–226. <https://doi.org/10.1002/bmb.21328>

García-Ponce, Á. L., Martínez-Poveda, B., Blanco-López, Á., Quesada, A. R., Suárez, F., Alonso-Carrión, F. J., & Medina, M. Á. (2021). A problem-/case-based learning approach as an useful tool for studying glycogen metabolism and its regulation. *Biochemistry and Molecular Biology Education*, 49(2), 236–241. <https://doi.org/10.1002/bmb.21449>

Ghorbani, A., & Ghazvini, K. (2016). Using paper presentation breaks during didactic lectures improves learning of physiology in undergraduate students. *Advances in Physiology Education*, 40(1), 93–97. <https://doi.org/10.1152/advan.00137.2015>

Gin, L. E., Guerrero, F. A., Brownell, S. E., & Cooper, K. M. (2021). COVID-19 and undergraduates with disabilities: Challenges resulting from the rapid transition to online course delivery for students with disabilities in

- undergraduate STEM at large-enrollment institutions. *CBE—Life Sciences Education*, 20(3), ar36. <https://doi.org/10.1187/cbe.21-02-0028>
- Gross, D., Pietri, E. S., Anderson, G., Moyano-Camihort, K., & Graham, M. J. (2015). Increased preclass preparation underlies student outcome improvement in the flipped classroom. *CBE—Life Sciences Education*, 14(4), ar36. <https://doi.org/10.1187/cbe.15-02-0040>
- Hasan, N., & Bao, Y. (2020). Impact of “e-Learning crack-up” perception on psychological distress among college students during COVID-19 pandemic: A mediating role of “fear of academic year loss”. *Children and Youth Services Review*, 118, 105355. <https://doi.org/10.1016/j.childyouth.2020.105355>
- Henly, D. C., & Reid, A. E. (2008). Use of the web to provide learning support for a large metabolism and nutrition class. *Biochemistry and Molecular Biology Education*, 29(6), 229–233. <https://doi.org/10.1111/j.1539-3429.2001.tb00129.x>
- Jafarkhani, F., & Jamebozorg, Z. (2020). Comparing cooperative flipped learning with individual flipped learning in a biochemistry course. *Journal of Medicine and Life*, 13(3), 399. <https://doi.org/10.25122/jml-2019-0149>
- Johanson, K. E. (2017). A topic-based approach for teaching metabolism in a flipped classroom. *The FASEB Journal*, 31, 751.13. https://doi.org/10.1096/fasebj.31.1_supplement.751.13
- Joshi, K. B., Nilawar, A. N., & Thorat, A. P. (2014). Effect of case based learning in understanding clinical biochemistry. *IJBAR*, 5(10), 516–518. <https://doi.org/10.7439/ijbar.v5i10.920>
- Kapil, A., Gonzalez, L., & Sikora, A. (2021). Analysis of student learning gains in a biochemistry CURE course during the mandatory COVID-19 shift to online learning. *The FASEB Journal*, 35. <https://doi.org/10.1096/fasebj.2021.35.S1.03494>
- Keppetipola, N., & Patchen, T. (2021). Titrating teaching: An interdisciplinary case study of online and face-to-face undergraduate biochemistry instruction. *Journal of Microbiology & Biology Education*, 22(1), ev22i1–2603. <https://doi.org/10.1128/jmbe.v22i1.2603>
- Klegeris, A. (2020). Mixed-mode instruction using active learning in small teams improves generic problem-solving skills of university students. *Journal of Further and Higher Education*, 1–15. <https://doi.org/10.1080/0309877X.2020.1826036>
- Kulak, V., & Newton, G. (2014). A guide to using case-based learning in biochemistry education. *Biochemistry and Molecular Biology Education*, 42(6), 457–473. <https://doi.org/10.1002/bmb.20823>

- Lapitan Jr, L. D., Tiangco, C. E., Sumalinog, D. A. G., Sabarillo, N. S., & Diaz, J. M. (2021). An effective blended online teaching and learning strategy during the COVID-19 pandemic. *Education for Chemical Engineers*, 35, 116–131. <https://doi.org/10.1016/j.ece.2021.01.012>
- Long, S., Andreopoulos, S., Patterson, S., Jenkinson, J., & Ng, D. P. (2021). Metabolism in motion: Engaging biochemistry students with animation. *Journal of Chemical Education*, 98(5), 1795–1800. <https://doi.org/10.1021/acs.jchemed.0c01498>
- Lynn, M. A., Templeton, D. C., Ross, A. D., Gehret, A. U., Bida, M., Sanger, T. J., & Pagano, T. (2020). Successes and challenges in teaching chemistry to deaf and hard-of-hearing students in the time of COVID-19. *Journal of Chemical Education*, 97(9), 3322–3326. <https://doi.org/10.1021/acs.jchemed.0c00602>
- Miller, C. J., McNear, J., & Metz, M. J. (2013). A comparison of traditional and engaging lecture methods in a large, professional-level course. *Advances in Physiology Education*, 37(4), 347–355. <https://doi.org/10.1152/advan.00050.2013>
- Nair, S. P., Shah, T., Seth, S., Pandit, N., & Shah, G. V. (2013). Case based learning: A method for better understanding of biochemistry in medical students. *Journal of Clinical and Diagnostic Research: JCDR*, 7(8), 1576. <https://doi.org/10.7860/JCDR/2013/5795.3212>
- Ojennus, D. D. (2016). Assessment of learning gains in a flipped biochemistry classroom. *Biochemistry and Molecular Biology Education*, 44(1), 20–27. <https://doi.org/10.1002/bmb.20926>
- Ossai, P. A. U., Ogwu, C., Ichipi-Ifukor, P. C., & Achuba, F. I. (2020). Disposition and challenges of alternative to physical classroom teaching and learning in a pandemic; An appraisal of biochemistry students COVID-19 learning with WhatsApp. *Galician Medical Journal*, 27(4), E2020411-E2020411. <https://doi.org/10.21802/gmj.2020.4.11>
- Perets, E. A., Chabeda, D., Gong, A. Z., Huang, X., Fung, T. S., Ng, K. Y., & Yan, E. C. (2020). Impact of the emergency transition to remote teaching on student engagement in a non-STEM undergraduate chemistry course in the time of COVID-19. *Journal of Chemical Education*, 97(9), 2439–2447. <https://doi.org/10.1021/acs.jchemed.0c00879>
- Procko, K., Bell, J. K., Benore, M. A., Booth, R. E., Moore, V. D. G., Dries, D. R., & Provost, J. J. (2020). Moving biochemistry and molecular biology courses online in times of disruption: Recommended practices and resources-a collaboration with the faculty community and ASBMB. *Biochemistry and Molecular Biology Education*. 48(5), 421–427. <https://doi.org/10.1002/bmb.21354>

- Ren, X., Lin Sui, L., Fei Guan, Y., Kong, Y., Liu, B., Fang Ding, Y., ... & Kong, L. (2020). Flipped classroom is an approach of basic medical education for undergraduate students. <https://doi.org/10.1002/bmb.21427>
- Rose, T. M. (2011). A board game to assist pharmacy students in learning metabolic pathways. *American Journal of Pharmaceutical Education*, 75(9), 183. <https://doi.org/10.5688/ajpe759183>
- Sajid, M. R., Laheji, A. F., Abothenain, F., Salam, Y., AlJayar, D., & Obeidat, A. (2016). Can blended learning and the flipped classroom improve student learning and satisfaction in Saudi Arabia? *International Journal of Medical Education*, 7, 281. <https://doi.org/10.5116/ijme.57a7.83d4>
- Styers, M. L., Van Zandt, P. A., & Hayden, K. L. (2018). Active learning in flipped life science courses promotes development of critical thinking skills. *CBE—Life Sciences Education*, 17(3), ar39. <https://doi.org/10.1187/cbe.16-11-0332>
- Thibaut, D., & Schroeder, K. T. (2022). Design of a semester-long case-based active learning curriculum for medical biochemistry courses during COVID-19. *Journal of Chemical Education*, 99(7), 2541–2547. <https://doi.org/10.1021/acs.jchemed.1c01126>
- Wester, E. R., Walsh, L. L., Arango-Caro, S., & Callis-Duehl, K. L. (2021). Student engagement declines in STEM undergraduates during COVID-19-driven remote learning. *Journal of Microbiology & Biology Education*, 22(1), ev22i1–2385. <https://doi.org/10.1128/jmbe.v22i1.2385>
- Wikandari, R., Putro, A. W., Suroto, D. A., Purwandari, F. A., & Setyaningsih, W. (2021). Combining a flipped learning approach and an animated video to improve first-year undergraduate students' understanding of electron transport chains in a biochemistry course. *Journal of Chemical Education*, 98(7), 2236–2242. <https://doi.org/10.1021/acs.jchemed.0c01477>
- Wilson, K. J. (2021). Online discussions in biochemistry to increase peer interactions and student interest. *Biochemistry and Molecular Biology Education*, 49(2), 298–300. <https://doi.org/10.1002/bmb.21487>
- Yu, Z. (2021). The effects of gender, educational level, and personality on online learning outcomes during the COVID-19 pandemic. *International Journal of Educational Technology in Higher Education*, 18(1), 1–17. <https://doi.org/10.1186/s41239-021-00252-3>
- Zewail-Foote, M. (2020). Pivoting an upper-level, project-based biochemistry laboratory class to online learning during COVID-19: Enhancing research skills and using community outreach to engage undergraduate students. *Journal of Chemical Education*, 97(9), 2727–2732. <https://doi.org/10.1021/acs.jchemed.0c00543>