

Using augmented reality in molecular case studies to enhance biomolecular structure-function explorations in undergraduate classrooms

Didem Vardar-Ulu,¹ Saif Eldeen Ragab,¹ Swati Agrawal,² Shuchismita Dutta³

AUTHOR AFFILIATIONS See affiliation list on p. 5.

ABSTRACT Molecular case studies (MCSs) are open educational resources that use a storytelling approach to engage students in biomolecular structure-function explorations, at the interface of biology and chemistry. Although MCSs are developed for a particular target audience with specific learning goals, they are suitable for implementation in multiple disciplinary course contexts. Detailed teaching notes included in the case study help instructors plan and prepare for their implementation in diverse contexts. A newly developed MCS was simultaneously implemented in a biochemistry and a molecular parasitology course at two different institutions. Instructors participating in this cross-institutional and multidisciplinary implementation collaboratively identified the need for quick and effective ways to bridge the gap between the MCS authors' vision and the implementing instructor's interpretation of the case-related molecular structure-function discussions. Augmented reality (AR) is an interactive and engaging experience that has been used effectively in teaching molecular sciences. Its accessibility and ease-of-use with smart devices (e.g., phones and tablets) make it an attractive option for expediting and improving both instructor preparation and classroom implementation of MCSs. In this work, we report the incorporation of ready-to-use AR objects as checkpoints in the MCS. Interacting with these AR objects facilitated instructor preparation, reduced students' cognitive load, and provided clear expectations for their learning. Based on our classroom observations, we propose that the incorporation of AR in MCSs can facilitate its successful implementation, improve the classroom experience for educators and students, and make MCSs more broadly accessible in diverse curricular settings.

KEYWORDS molecular case studies, hands-on learning, molecular visualization, augmented reality, biochemistry, structure-function, molecular parasitology

Molecular case studies (MCSs) use a storytelling approach to offer active learning opportunities for exploring biomolecular structure-function relationships (1). These ready-to-use, modular, open educational resources (OERs) are available from the Molecular CaseNet website (<https://molecular-casenet.rcsb.org/>) and adaptable to various curricular settings. Through MCSs, students can apply biology and chemistry concepts to authentic contexts, visualize case-relevant biomolecular three-dimensional (3D) structures, integrate information from various bioinformatics data resources, and synthesize new knowledge. Answer keys and teaching notes accompanying the MCS, help educators with limited prior knowledge about the case theme, plan and prepare successful classroom implementations.

Implementing a new MCS in two different curricular settings revealed the need to improve educator preparation and support for students while integrating structure-function discussions into the course objectives. This case study, titled "Maria vs Malaria" (2),

Editor Dave J. Westenberg, Missouri University of Science and Technology, Missouri, USA

Address correspondence to Didem Vardar-Ulu, dvardar@bu.edu.

The authors declare no conflict of interest.

Received 1 February 2024

Accepted 15 March 2024

Published 16 April 2024

Copyright © 2024 Vardar-Ulu et al. This is an open-access article distributed under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International license](https://creativecommons.org/licenses/by-nc-nd/4.0/).

examines the structure of a metabolic enzyme lactate dehydrogenase, as an antiparasitic drug target (3, 4) for treating the tropical disease, malaria. It was written as a partial course-based undergraduate research experience in a biochemistry course at Boston University (BU) (5). In Spring 2022, as part of a faculty mentoring network activity (6), this MCS was implemented in a large biochemistry course at BU (~150 students) and a smaller molecular parasitology class at the University of Mary Washington (UMW) (~15 students) (Fig. 1, blue boxes). Discussions following these implementations highlighted the importance of finding effective ways to bridge the gap between the MCS authors' vision and implementing the instructor's interpretation of the case-related molecular structure-function discussions.

Augmented reality (AR) technology has emerged as a powerful and accessible educational tool for enhancing visuospatial learning experiences in diverse fields (7–9). Classroom interventions have reported that the use of AR technology is effective in visualizing macromolecular structures (10–12), exploring metabolic pathways (13), and increasing student engagement, and motivation for learning (14–16). Herein, we describe the integration of AR technology to create an MCS adaptation and its implementation in a large classroom (Fig. 1, yellow boxes). Using AR technology in this context may apply to other molecular case studies with similar effects.

PROCEDURE

Implementation of the MCS “Maria vs Malaria” in diverse course settings in Spring 2022 identified two areas for improvement. First, instructors teaching different disciplinary contents needed additional teaching notes to prepare them for the MCS implementation. Second, students with limited prior experience in biomolecular visualization needed easily accessible, interactive tools to engage with and complete the MCS-related molecular structural explorations. In Summer 2022, the two instructors from BU and UMW collaborated on incorporating AR into the MCS (Fig. 1, yellow box). Saif Ragab, an undergraduate chemical education research student at BU, tested a variety of molecular representations for pre-determined molecular scenes (checkpoints) in the MCS, using

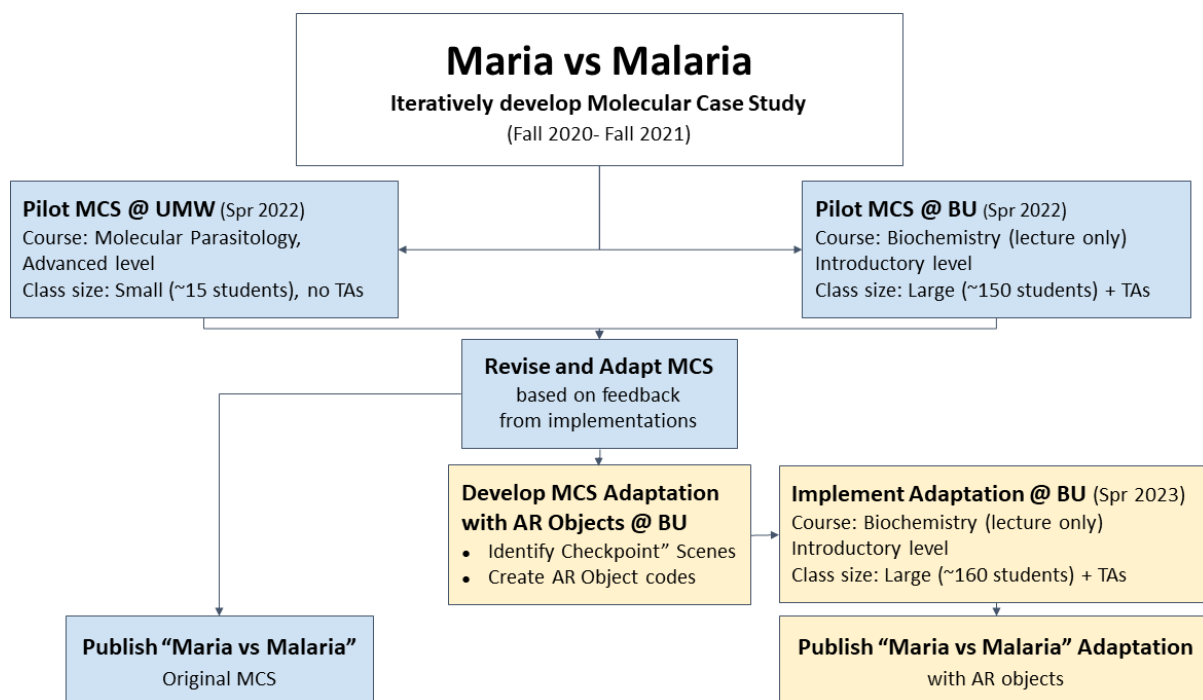


FIG 1 Development of molecular case study (Maria vs Malaria) with augmented reality (AR) adaptation. Details of the two curricular settings for piloting of the original MCS are shown in blue text boxes, while the development and implementation steps of the AR adaptation are shown in yellow text boxes.

3D structural data from the Protein Data Bank (17, 18) and the visualization tool, Mol* (19). He converted these scenes into AR objects [see Supplementary Material (20)] for visualization with a free “Merge Object Viewer” app on smart devices (Merge Labs Inc.). The AR objects were included in an adaptation of the MCS and published as an OER (21). While integrating AR in the MCS, both technical aspects (e.g., choice of 3D representations, colors, structural features) and the pedagogical issues (e.g., curriculum alignment, usability in diverse settings) were carefully considered.

Traditional molecular visualization (Fig. 2A) requires students to learn to use the tool, which takes time, and can often overwhelm novice users. The AR objects allow students to directly interact with the molecular scenes on a touch screen, as free-standing objects placed on flat surfaces, or captured in a hand-held physical cube (Fig. 2B). AR objects for checkpoints in the MCS help implementers see the molecular details the author intended to highlight. They also provide students with clear expectations and direct access to case-relevant molecular scenes, without the need to learn a visualization tool to create the scenes (Fig. 3).

In Spring 2023, the MCS adaptation with AR objects was implemented in a biochemistry course at BU with ~160 students and two teaching assistants (TAs) leading 10 discussion sections (~16 students each). The TAs were introduced to the use of AR technology for the MCS adaptation in ~15 minutes and received the teaching notes as part of their preparation. Students used handmade paper Merge cubes for a tactile experience of the AR objects through the “Merge Object Viewer” app on smart devices (Fig. 3).

Despite the similarity between the biochemistry knowledge and interest of both the students and the TAs in the 2022 and 2023 implementations, notable improvements were observed when using the MCS adaptation with AR: (i) the TAs self-reported feeling more prepared and were more effective in leading the class through the MCS, (ii) students completed more questions from the MCS during the class period and spent more time discussing their molecular explorations, (iii) students used more discipline-specific vocabulary in their explanations and created more detailed figures, and (iv)

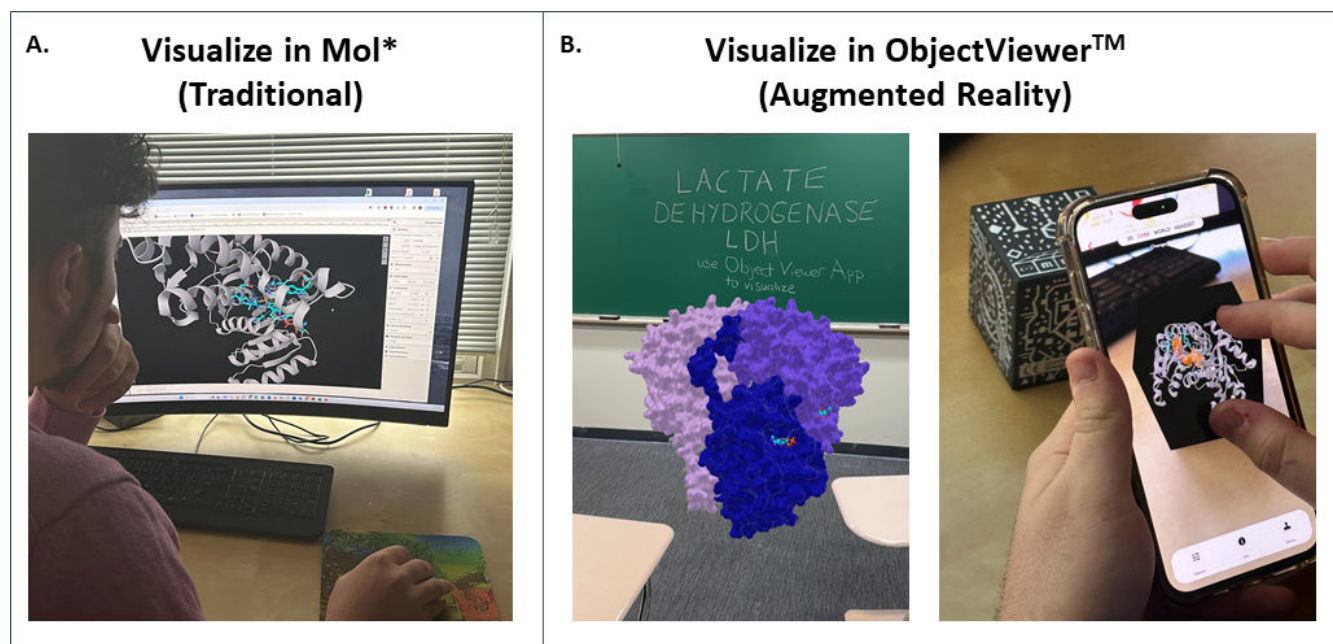


FIG 2 Comparison of molecular visualization using traditional and AR technology. (A) A biochemistry student exploring one of the MCS checkpoint structures on their computers using Mol*. (B) Biomolecular structure viewed by students using ObjectViewer App on the phone as free-standing objects placed on flat surfaces or captured in a hand-held physical cube.

A.

Q19. Insert a screen capture of the *pf*LDH and *h*LDH-B active site residues interacting with NADH below.

- Label all the residues that are directly interacting with NADH on your figure.
- Identify and label the conserved Histidine residue in the active site.
- Do you see any other interactions that play an important role in orienting NADH in the active site?

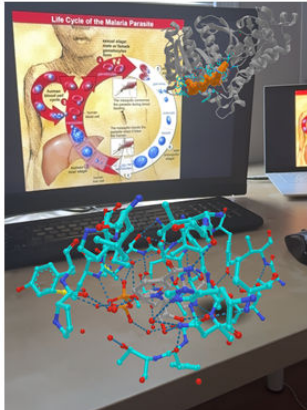
PDB ID: 1T2C



PDB ID: 7DBK



B. Engage with the molecule on your desk



C. Hold the molecule in your hand

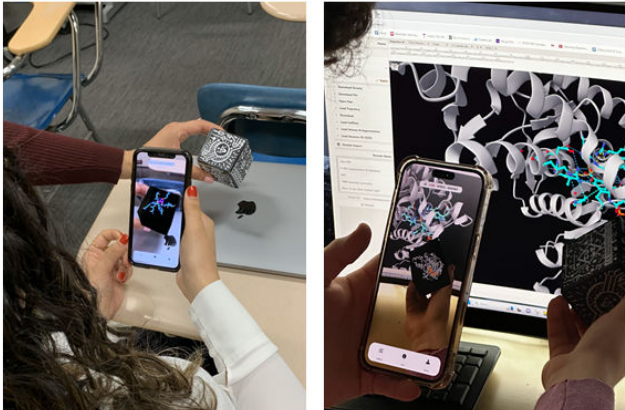


FIG 3 Use of AR objects in the MCS adaptation. (A) Sample question from the MCS with AR object codes included. (B) Students answering the question while viewing the AR object codes (for PDB ID 1T2C) shown in panel (A) with the malaria life cycle shown on the computer screen. (C) Students interacting with the AR objects (PDB ID 1T2C) to explore the molecular details of the MCS-related scenes using the hand-held cube and smartphones.

several students voluntarily engaged with the MCS AR object codes after class time, some even several weeks after the assignment (based on Bitly Analytics, bitly.com).

CONCLUSION

The cross-institutional collaboration between BU and MWU created an MCS adaptation that includes AR objects. This adaptation provides educators and students a robust visual roadmap of the author's vision of the case-related 3D structure-function discussions. This innovative approach was piloted in 10 small discussion sections of a large class (~160 students). Instructor and TA observations from preparation to post-implementation suggest that the AR objects helped less experienced educators become more confident in leading the MCS discussions. AR objects also enhanced user experience by encouraging students with limited experience in using visualization tools to engage more deeply in structure-function discussions. By providing rapid visual confirmation and/or allowing a quick "catch up" with their classmates, AR objects allowed students to have more time to focus on the disciplinary-specific learning goals. For students still developing molecular visualization skills, the AR objects also served as guides both in and out of class. These findings suggest that this MCS adaptation can be beneficial in a variety of classroom settings (small/large, in-person/remote) when limited time is available and direct guidance or support opportunity is limited.

Our study indicates that AR objects can be used by any educator as a highly needed alternative visualization tool, especially with students who have limited experience using traditional biomolecular visualization programs. By providing free and rapid access to checkpoint scenes, AR objects promote independent molecular exploration through increased student engagement, confidence, and motivation for learning. A broader integration of AR objects into additional molecular case studies in the future will facilitate a robust assessment of students' learning gains in the biomolecular structure and function discussions.

ACKNOWLEDGMENTS

Most importantly, we would like to thank the students at BU and UMW for their hard work and perseverance during the piloting of the different versions of this MCS (22). We would also like to thank the teaching assistants Matthew Vince, Favian Lui, Arisdelsy Cervantes, and Mike Susoeff at Boston University for their contributions to the associated teaching materials of the MCS, as well as their dedication during the pilot implementations. Molecular CaseNet is funded by the National Science Foundation (DBI-1827011 and DBI-2018884).

All authors have approved the manuscript for submission. On behalf of all authors, the corresponding author states that there is no conflict of interest. The enclosed manuscript is an original work and is not under review at any other publication.

AUTHOR AFFILIATIONS

¹Boston University, Boston, Massachusetts, USA

²University of Mary Washington, Fredericksburg, Virginia, USA

³Rutgers, The State University of New Jersey, Piscataway, New Jersey, USA

AUTHOR ORCIDs

Didem Vardar-Ulu  <http://orcid.org/0000-0003-3793-0124>

ADDITIONAL FILES

The following material is available [online](#).

Supplemental Material

Supplemental material (jmbe00019-24-S0001.docx). Information about the specific AR platform used and on alternatives.

REFERENCES

- Goodsell DS, Dutta S, Voigt M, Zardecki C. 2021. Molecular storytelling for online structural biology outreach and education. *Struct Dyn* 8:020401. <https://doi.org/10.1063/4.0000077>
- Vardar-Ulu D, Yu S, Lau A, Szpakowski M. 2023. Maria vs malaria. <https://qubeshub.org/publications/4551/1>.
- Cameron A, Read J, Tranter R, Winter VJ, Sessions RB, Brady RL, Vivas L, Easton A, Kendrick H, Croft SL, Barros D, Lavandera JL, Martin JJ, Risco F, García-Ochoa S, Gamo FJ, Sanz L, Leon L, Ruiz JR, Gabarró R, Mallo A, Gómez de las Heras F. 2004. Identification and activity of a series of azole-based compounds with lactate dehydrogenase-directed anti-malarial activity. *J Biol Chem* 279:31429–31439. <https://doi.org/10.1074/jbc.M402433200>
- Menting JG, Tilley L, Deady LW, Ng K, Simpson RJ, Cowman AF, Foley M. 1997. The antimalarial drug, chloroquine, interacts with lactate dehydrogenase from *Plasmodium falciparum*. *Mol Biochem Parasitol* 88:215–224. [https://doi.org/10.1016/s0166-6851\(97\)00095-9](https://doi.org/10.1016/s0166-6851(97)00095-9)
- Riley KJ, Vardar-Ulu D, Pollock E, Dutta S. 2021. Students authoring molecular case studies as a partial course - based undergraduate research experience (CURE) for lab instruction. *Biochem Mol Biol Educ* 49:853–855. <https://doi.org/10.1002/bmb.21578>
- Rook D, Donovan S, Eaton C, Jenkins K, LaMar D, Wojdak J, Chodkowski N, Crisucci E, Fagen A, Hamerlinck G, Hamman E, Orndorf H. 2019. Faculty mentoring networks: community professional development for the digital age (1.0). <https://doi.org/10.25334/EEEE-R150>
- Quintero J, Baldiris S, Rubira R, Cerón J, Velez G. 2019. Augmented reality in educational inclusion: a systematic review on the last decade. *Front Psychol* 10:1835. <https://doi.org/10.3389/fpsyg.2019.01835>
- Alzahrani NM. 2020. Augmented reality: a systematic review of its benefits and challenges in E-learning contexts. *Appl Sci* 10:5660. <https://doi.org/10.3390/app10165660>
- Parekh P, Patel S, Patel N, Shah M. 2020. Systematic review and meta-analysis of augmented reality in medicine, retail, and games. *Vis Comput Ind Biomed Art* 3:21. <https://doi.org/10.1186/s42492-020-00057-7>
- Peterson CN, Tavana SZ, Akinleye OP, Johnson WH, Berkmen MB. 2020. An idea to explore: use of augmented reality for teaching three-dimensional biomolecular structures. *Biochem Mol Biol Educ* 48:276–282. <https://doi.org/10.1002/bmb.21341>
- Safadel P, White D. 2019. Facilitating molecular biology teaching by using augmented reality (AR) and protein data bank (PDB). *TechTrends* 63:188–193. <https://doi.org/10.1007/s11528-018-0343-0>
- Sung R-J, Wilson AT, Lo SM, Crowl LM, Nardi J, St. Clair K, Liu JM. 2020. BiochemAR: an augmented reality educational tool for teaching macromolecular structure and function. *J Chem Educ* 97:147–153. <https://doi.org/10.1021/acs.jchemed.8b00691>
- Galembeck E. 2018. Augmented reality metabolic pathways (ARMET). <https://doi.org/10.25334/Q4Q420>
- Fombona-Pascual A, Fombona J, Vicente R. 2022. Augmented reality, a review of a way to represent and manipulate 3D chemical structures. *J Chem Inf Model* 62:1863–1872. <https://doi.org/10.1021/acs.jcim.1c01255>
- Schmid JR, Ernst MJ, Thiele G. 2020. Structural chemistry 2.0: combining augmented reality and 3D online models. *J Chem Educ* 97:4515–4519. <https://doi.org/10.1021/acs.jchemed.0c00823>
- Agrawal S. 2020. Augmented reality in undergraduate biology classroom. *Adv Biol Lab Educ*. <https://doi.org/10.37590/able.v41.art1>
- Berman HM, Westbrook J, Feng Z, Gilliland G, Bhat TN, Weissig H, Shindyalov IN, Bourne PE. 2000. The protein data bank. *Nucleic Acids Res* 28:235–242. <https://doi.org/10.1093/nar/28.1.235>
- Burley SK, Bhikadiya C, Bi C, Bittrich S, Chao H, Chen L, Craig PA, Crichlow GV, Dalenberg K, Duarte JM, et al. 2023. RCSB protein data bank

- (RCSB.org): delivery of experimentally-determined PDB structures alongside one million computed structure models of proteins from artificial intelligence/machine learning. *Nucleic Acids Res* 51:D488–D508. <https://doi.org/10.1093/nar/gkac1077>
19. Sehna D, Bittrich S, Deshpande M, Svobodová R, Berka K, Bazgier V, Velankar S, Burley SK, Koča J, Rose AS. 2021. Mol* Viewer: modern web app for 3D visualization and analysis of large biomolecular structures. *Nucleic Acids Res* 49:W431–W437. <https://doi.org/10.1093/nar/gkab314>
 20. Agrawal S, Austin S. 2023. An idea to explore: augmented reality and LEGO® brick modeling in the biochemistry and cell biology classroom - two tactile ways to teach biomolecular structure—function. *Biochem Mol Biol Educ* 51:439–445. <https://doi.org/10.1002/bmb.21734>
 21. Vardar-Ulu D, Ragab SE, Agrawal S. 2023. Maria vs malaria - AR adaptation. <https://qubeshub.org/publications/4554/1>.
 22. Agrawal S, Vardar-Ulu D, Yu S, Dutta S. 2022. Collaborative case writing and field testing with molecular caseNet brings together discipline specific expertise for innovative pedagogical tools in the classroom (1.0). <https://doi.org/10.25334/HZGX-MF51>