Enhanced Learning in Biochemistry Using the Protein Data Bank and 3D Molecular Modeling in ChimeraX

Christopher Arias, Ezekiel Buchert, Johana Cruz Lopez, Cesar Fernandez, Elizabeth Kowalski, Elisabet Tesla Nichols, Gabrielle Onnenga, Kellie Pierson, Jenny A. Cappuccio, and Frank E Cappuccio
Department of Chemistry,Cal Poly Humboldt, Arcata, CA, USA

Cal Poly Humboldt.

Department of Chemistry
Biochemistry

Introduction

- RCSB PDB (RCSB.org) is the US data center for the global Protein Data Bank (PDB) archive of 3D structure data for large biological molecules (proteins, DNA, and RNA) essential for research and education in fundamental biology, health, energy, and biotechnology. (3)
- The Protein Data Bank (PDB) was the first open access digital data resource in biology and medicine.(3)

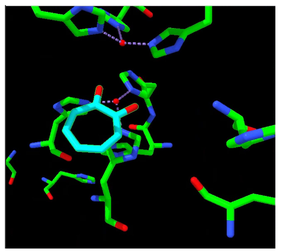
RCSB PDB PROTEIN DATA BANK

- Macromolecular structures are used in biotechnology, medicine and environmental studies to develop new cures for disease, and better biofuel production for example.
- Molecular visualization software ChimeraX was developed by UCSF faculty as a free program funded by the National Institutes of Health. (1, 2)

Methods

- Faculty developed hands-on student tutorial curriculum to demonstrate how to utilize PDB data.
- Students learned how to make 3D molecular representations of this data using UCSF ChimeraX software.
- A threaded curriculum biotechnology related protein (tyrosinase) was chosen to connect with previous knowledge in other courses.

Figure 1. Excerpt of student submissions for the hands-on PDB tutorial. This student utilizes their knowledge of charge to interpret the binding of an inhibitor to the tyrosinase enzyme active site, an enzyme causing browning in mushrooms. PDB 2Y9X. (5)



Inhibitor is the 7-membered cyan ring ^^. It seems to be attracted to the Cu+ ions – which makes sense given the resonance and more negative Oxygen atoms in the ring being attracted to the Cu+.

- Students applied their knowledge to a protein of their choice creating both a Quad Chart presentation and a 3D printed surface model of the protein (4)
- Quad Chart presentations are used to pitch an idea or quickly and inform the audience for funding or further studies.

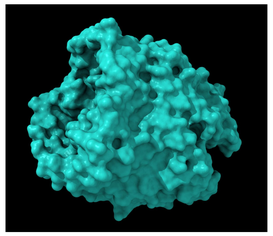
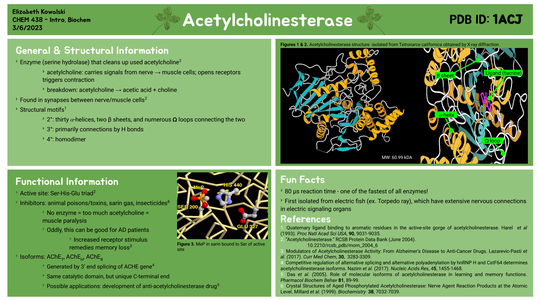
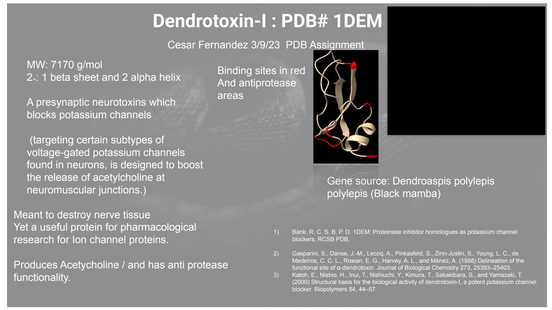
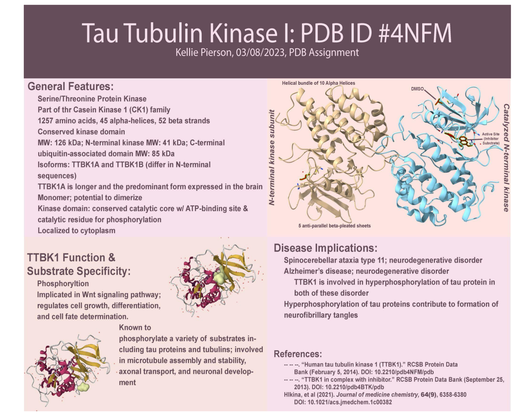


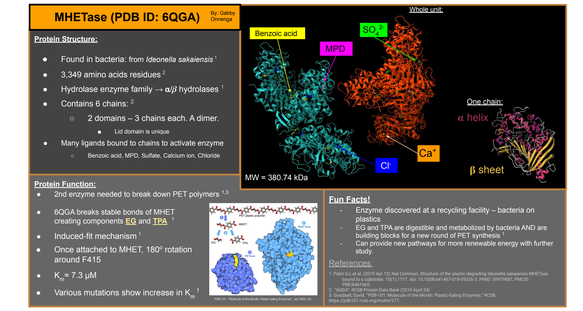
Figure 2. Student surface model submissions .stl file for the 3D printing of their protein choice, cobalamin (vit B12) transporter BtuB from the bacterium *E. coli* PDB 1NQH. (2003) Nat Struct Biol **10**: 394-401

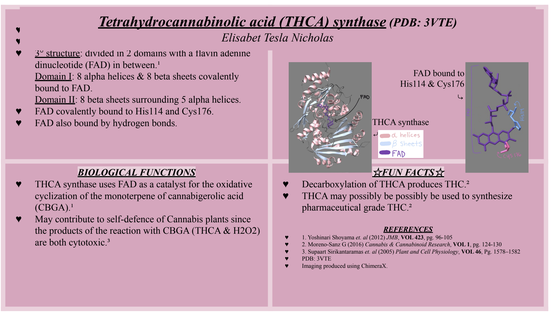
Student Products

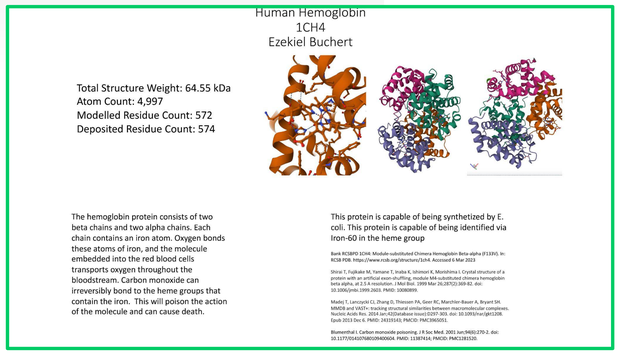


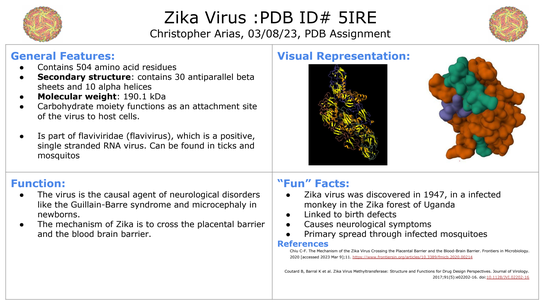












Conclusions

- 3D modeling is a valuable interactive tool to understand the complexity of biological macromolecules informing function.
- Student displayed in-depth understanding of protein structure and binding in hands-on activities and presentations of protein structures
- The knowledge of biological molecular structure in drug design and biotechnology is an essential skill set for modern scientists to meet the grand challenges of the future.

Acknowledgments

We would like to thank Tim W. Miller the Cal Poly Humboldt Digital and Media Librarian for assistance in printing the 3-D surface models.

We would like to acknowledge funding from a CSU Program for Education and Research in Biotechnology (CSUPERB) curriculum development grant.

Molecular graphics and analyses performed with UCSF ChimeraX, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from National Institutes of Health R01-GM129325 and the Office of Cyber Infrastructure and Computational Biology, National Institute of Allergy and Infectious Diseases.

References

1. UCSF ChimeraX: Structure visualization for researchers, educators, and developers. Pettersen EF, Goddard TD, Huang CC, Meng EC, Couch GS, Croll TI, Morris JH, Ferrin TE. *Protein Sci.* 2021 Jan;30(1):70-82.
2. UCSF ChimeraX: Meeting modern challenges in visualization and analysis. Goddard TD, Huang CC, Meng EC, Pettersen EF, Couch GS, Morris JH, Ferrin TE. *Protein Sci.* 2018 Jan;27(1):14-25.
3. The Protein Data Bank H.M. Berman, J. Westbrook, Z. Feng, G. Gilliland, T.N. Bhat, H. Weissig, I.N. Shindyalov, P.E. Bourne (2000) *Nucleic Acids Research*, **28**: 235-242. https://doi.org/10.1093/nar/28.1.235
4. PDB-101: Educational resources supporting molecular explorations through biology and medicine. Christine Zardecki, Shuchismita Dutta, David S. Goodsell, Robert Lowe, Maria Voigt, Stephen K. Burley. (2022) *Protein Science* **31**: 129-140 https://doi.org/10.1002/pro.4200
5. Crystal Structure of Agaricus Bisporus Mushroom Tyrosinase: Identity of the Tetramer Subunits and Interaction with Tropolone. Ismaya, W.T., Rozeboom, H.J., Weijn, A., Mes, J.J., Fusetti, F., Wichers, H.J., Dijkstra, B.W. (2011) Biochemistry **50**: 5477