

Using Molecular Visualization as a Tool for Culturally Competent and Culturally Relevant Teaching: A Guided-Inquiry Biochemistry Activity

Pumtiwitt McCarthy
Department of Chemistry
Morgan State University
Baltimore, MD
Pumtiwitt.McCarthy@morgan.edu

Richard Williams
Department of Chemistry
Morgan State University
Baltimore, MD
rjwilms3@gmail.com

Cleo Hughes-Darden et al.¹
Department of Biology
Morgan State University
Baltimore, MD
Cleo.HughesDarden@morgan.edu

ABSTRACT

The central dogma is a key foundational concept in biochemistry. The idea that DNA mutations cause change at the protein level can be abstract for students. To provide a real-world example of the effect of mutation on protein function, a molecular visualization module was developed and incorporated into two biochemistry courses. This inquiry-based activity explored the molecular basis and cultural relevance of sickle cell anemia. Hemoglobin structural changes from the disease were examined. Participants used free tools including NCBI, RCSB PDB, LALIGN and Swiss PDB DeepView protein visualization software from EXPASY. This module was an active, engaging exercise which exposed students to protein visualization and increased cultural awareness.

Keywords

Biochemistry, Computer-Based Learning, Inquiry-Based/Discovery Learning, Internet/Web-Based Learning, Proteins/Peptides, Underrepresented Minorities, Culturally-Relevant Pedagogy

1. INTRODUCTION

Effective teaching of biochemistry often uses computational tools for students to visualize and analyze macromolecular structure [1, 2]. Numerous science education articles describe addition of bioinformatics to the chemistry/biochemistry curriculum [3]. Many exercises use free stand-alone or web-based tools [4] making incorporation of bioinformatics achievable. Students used bioinformatics to investigate multiple topics such as drug design [5, 6, 7, 8, 9], visualization of protein structure [10, 11, 12, 13, 14], homology modeling [15, 16, 17], genomics/proteomics [18, 19] and genetic diseases [20]. The work described here is distinct because students use bioinformatics to investigate a genetic disease and explores the racial disproportionality of this disease. The goal of this activity was to provide students an engaging experience in protein visualization in a culturally relevant way.

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The term culturally relevant or culturally responsive pedagogy was first described over twenty years ago [21, 22]. In short, this describes a teaching approach that embraces students' different cultural perspectives to further the learning experience. One aspect of this pedagogy is cultural competence. Culturally competent pedagogy allows a teacher to impart knowledge that allows students' to appreciate their own culture and learn about the culture of others [23]. Sickle cell anemia afflicts African-Americans disproportionately. This activity provides an opportunity for a diverse set of students to research the epidemiology of the disease thereby increasing cultural awareness [24].

Genetic diseases arise from changes in DNA which leads to changes at the protein level [25]. Sickle cell anemia is caused by a point mutation in the gene message encoding hemoglobin [26]. The most prevalent mutation is a change of glutamic acid to valine in the beta subunit. Hydrophobic "sticky" patches are produced that associate with the beta subunit of other hemoglobin molecules [27]. One result of this aggregation is a decrease in iron binding and fibril formation leading to sickle-shaped red blood cells [28]. The DNA, mRNA and amino acid sequence of both types of hemoglobin are known. This activity uses free bioinformatics software and tools (Table 1) to increase student engagement with computational analysis and cultural awareness.

2. ACTIVITY INFORMATION

2.1 Software Used

Freely available software and tools were used in this activity. These are described in Table 1.

2.2 Learning Goals

There are five student learning goals each with specific outcomes. **Learning Goal 1.** Students will understand the relationship between DNA, RNA and protein sequence. Outcomes from Goal 1. If given an RNA sequence, students should be able to: a) derive the original strands of DNA; b) manually translate into amino acid sequence; use bioinformatic tools to translate into amino acid sequence. **Learning Goal 2.** Students will understand the effects of amino acid change on protein structure and function. Outcomes from Goal 2. Students should be able to: a) compare two amino acid sequences; b) classify and predict the severity of amino acid substitutions based on the chemical properties of amino acids; c) to highlight and label amino acids at both termini of a protein. **Learning Goal 3.** Students will understand how to use molecular visualization software to display and modify protein structures.

¹ Additional authors under "Author List"

Outcomes from Goal 3. Students should be able to: a) highlight and label amino acids that interact with a ligand during binding; b) to report the racial incidence of sickle cell anemia. **Learning Goal 4.** Students will understand the cultural relevance of sickle cell anemia. Outcomes from Goal 4. Students should be able to: report the global incidence of sickle cell anemia. Summative assessments were used for each outcome with specific problems within the assignment.

Table 1. Software and tools used in activity [29, 30, 31]

| Name | Provided by | Address | Function |
|-------------|--|---|--|
| NCBI | NIH National Library of Medicine | http://www.ncbi.nlm.nih.gov | -Provides access to biomedical and genomic data |
| RCSB PDB | The Research Collaboratory for Structural Bioinformatics | http://www.rcsb.org/pdb/home/home.do | -Repository of protein structural data |
| LALIGN | ExPASy SIB Bioinformatics Resource Portal | http://embnet.vital-it.ch/software/LALIGN_form.html | -Aligns two sequences to determine matching segments |
| DeepView | ExPASy SIB Bioinformatics Resource Portal | http://spdbv.vital-it.ch/refs.html | -Protein visualization software |
| Translate | ExPASy SIB Bioinformatics Resource Portal | https://web.expasy.org/translate/ | -Translates nucleotide sequence to protein sequence |
| Google Docs | Google | http://docs.google.com | -Web-based word processing tool |

2.3 Tenets of Culturally Sensitive Teaching Adopted

This activity was developed as one part of a wider inter-department goal of increasing culturally sensitive teaching in STEM courses [32]. A cohort of faculty from the departments of Mathematics, Computer Science, Chemistry, Biology, Physics, Industrial Engineering and Information Sciences and Systems developed five tenets for culturally-sensitive pedagogy in our courses. These were: 1) to incorporate physical and hands on activities in instructional practice, 2) to incorporate physical and hands on activities in instructional activities, 3) to become conscious of biased judgements about students based on limited perceptions of them and be willing to change these perceptions, 4) to have student apprenticeships that foster empowered learning communities and 5) to use students' lived experiences as content for course content and activities.

2.4 Activity Information

2.4.1 Participants and Materials

Students in CHEM 202 Biochemistry for Health Majors are second-year undergraduate Medical Technology majors and upper-division undergraduate Nutrition majors. Students in CHEM 304 Biochemistry are upper-division level Chemistry and Biology majors. These students anticipate entering graduate or medical school after graduation. Activities were performed during consecutive laboratory periods. CHEM 202 has 2 hr 50 min allotted for lab each week while CHEM 304 has 3 hr 50 min allotted.

Ten laptop computers were provided by the Chemistry Department. Groups of 2-4 students performed the activity. One computer was provided per group.

2.4.2 Pre-laboratory Activities

Students were assigned a pre-lab activity about the Protein Data Bank (PDB) and hemoglobin structure and function. A YouTube video [32a] about the PDB was made available on the online course management system. An article from the Molecule of the Month on the PDB website [33] about hemoglobin and sickle-cell anemia was assigned and students answered instructor-supplied questions.

2.4.3 Overview of Laboratory Activity

Modules were performed over two course laboratory periods. In the first week, students learned crystal structure basics and how to use computer software to visualize them. Targeted questions discuss cultural relevance and impact. The assignment called for students to download the crystal structure of normal hemoglobin from the PDB (PDB ID: 1hho [34]) and visualize its structure in Swiss DeepView. Next, they examined the secondary structure elements present in the protein. Students identified and labeled the N- and C-termini and the histidine residues that coordinate the heme group. The amino acid position that will be changed in the sickle cell variant was also identified and labeled by students. At the end of the exercise students are asked to answer questions related to rate of occurrence, racial incidence, symptoms and cure for the disease.

In the second week, students compare the 3-dimensional structure of sickle cell hemoglobin (PDB ID: 2hbs [35], **Figure 1**) to normal.

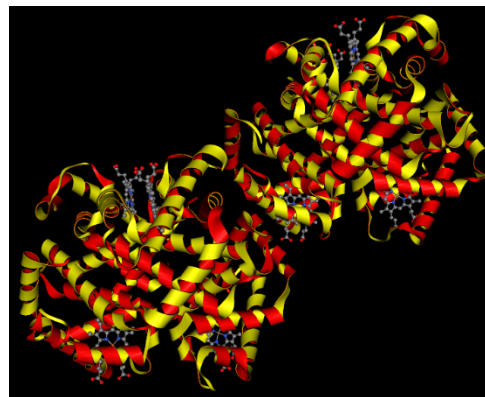


Figure 1. Crystal Structure of Sickle Cell Hemoglobin (2hbs)

They also engage with the central dogma by analyzing the DNA, RNA and amino acid sequence manually and with online bioinformatics software. As before, students use Swiss DeepView to label pertinent histidine residues. Students are also asked to discuss changes in the crystal structure between the normal and sickle hemoglobin. A portion of mRNA from wild type and sickle cell hemoglobin are given to students to translate into amino acid sequence manually. They also derive the original DNA sequence for both variants of hemoglobin. Next, the entire mRNA sequence of both types of hemoglobin is provided and online tool is used to translate sequences. LALIGN was used to compare similarity. All answers went into a Google document shared with group members and the instructor.

3. RESULTS AND DISCUSSION

3.1 Impact of Activity on Student

Engagement and Cultural Awareness

This activity was developed over two summers and implemented in Spring 2016 for CHEM 202. It was used in both courses the following academic year. Over 70 students have been exposed to this activity over this time. This activity is student-centered with very little instructor interaction. The instructor offers a brief introduction to the activity and the students begin following the step-by-step instructions for each week. When questions arise, the instructor clarifies for students. They also have access to the internet during this time. This activity was successful in engaging students. During implementation of the module in CHEM 202 in Spring 2016, a team of evaluators observed the class and scored the activity on the level of student engagement and use of computational tools. The scale runs from 1 (lowest) to 7 (highest). Evaluators found that the module scored high on all aspects. Specifically, the module “incorporated engaging team-based, real world projects” (score = 7), “used computational tools for modeling and simulations” (score = 7), students “understood why they were using computational tools” (score = 6) and “student’s interest in the class” (score = 7).

Sickle cell anemia was chosen for its cultural relevance and because students were introduced to it earlier in the semester. Morgan State University is becoming increasingly diverse. Morgan State University is a Historically Black College or University (HBCU) located in Baltimore, MD. In 2016-2017, 22 participants identified themselves as African-American (64%), 6 as Caucasian (18%), 5 were international (15%), and 1 was multiracial (3%). Therefore, many cultural backgrounds learned about this disease and its incidence.

3.2 Alignment with Developed Tenets of Culturally Sensitive Teaching

This exercise was developed keeping five main culturally-sensitive goals in mind. These were 1) to incorporate physical and hands on activities in instructional practice, 2) to incorporate more student-led discussions and teaching opportunities in class, 3) to becoming conscious of biased judgments about students based on limited perceptions of them and be willing to change these perceptions, 4) to have student apprenticeships that foster empowered learning communities and 5) to use students’ lived experiences as content for course content and activities. All five of these goals were achieved. This was primarily a student-led protein visualization project. There was a very brief introduction to the students by the instructor about what they will be doing, but the students discussed within their group and across groups how best to complete assignments (Tenets 1, 2, and 4). All students were treated in an equitable fashion and resources were made available to all students (Tenet 3). During the activity, one student was also able to offer a personal perspective as they had a family member that has the disease (Tenet 5).

3.3 Activity Outcomes

At implementation of this activity, students have already learned about the different levels of protein structure and are starting to learn the details of the central dogma. Hemoglobin and sickle cell hemoglobin had been discussed. Relevant concepts such as quaternary structure, protein-ligand binding and allosterism had also been discussed. This activity was designed to integrate early course material with new material that they are learning.

Learning goals and outcomes are described in Section 2.2. In the Bloom’s taxonomy hierarchy [36], these integrated questions range from lower level “knowledge” to higher level “evaluation” and “synthesis”. One example of an integrated question asks students to look at the amino acid sequences of the proteins and label the N- and C-termini of each subunit and determine whether the structure is the oxygen-bound form. Students must recall their knowledge of amino acid codes, protein directionality, and hemoglobin subunits. An example of an “evaluation” type is when students are asked to translate both types of hemoglobin into amino acid sequence. During alignment of the two sequences students must determine which alignments are correct and the number of sequence positions where they differ. Overall, the module successfully introduced students to protein visualization, reinforced knowledge of the central dogma and increased cultural awareness.

4. CONCLUSIONS AND FUTURE WORK

Genetic diseases can serve as tractable examples of the central dogma’s importance. A mutation in sickle cell anemia leads to hemoglobin structural changes that students were able to investigate using free resources. This module explored the molecular basis and cultural relevance of sickle cell anemia to help increase cultural competency. Future versions of this module will better assess student engagement with protein visualization.

Student handouts with step-by-step instructions and laboratory questions, Student pre-lab activity; mRNA sequence of normal and sickle-cell hemoglobin chain A, and example student data are available from the authors by email request to Pumtiwitt.McCarthy@morgan.edu.

5. AUTHOR LIST

Additional authors in order are: Roni Ellington², Paminas Mayaka², Monica Jackson³ and Asamoah Nkwanta⁴

²Advanced Studies, Leadership, and Policy, Morgan State University, 1700 East Cold Spring Lane, Baltimore, MD 21251,

³Department of Mathematics and Statistics, American University, 4400 Massachusetts Avenue, NW, Washington, DC 20016,

⁴Department of Mathematics, Morgan State University.

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