Integrating protein visualization in the classroom with StarBiochem

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Abstract - Teaching about proteins, how their structure is specified, and how in turn this influences their function has become an integral curriculum component for both introductory biology and biochemistry undergraduate courses. To understand how proteins work, students first learn about protein structure and its relationship to protein function. StarBiochem is a protein visualization tool that is used to assist in teaching key structural biology concepts in an interactive manner. StarBiochem allows for the visualization and manipulation of PBD (Protein Data Bank) molecules in a 3D environment. In this manuscript, we provide examples of StarBiochem usage within high school and undergraduate curricula. Specifically, we will highlight how StarBiochem is currently used in undergraduate courses at the Massachusetts Institute of Technology (MIT), Brandeis University, and in high school outreach programs at the Broad Institute of Harvard and MIT, and at the MIT Museum.

I. INTRODUCTION

Teachers of biology and biochemistry courses at both the high school and college levels are charged with the task of making the exciting developments in these fields accessible and interesting to students. One major curriculum component of introductory biology and biochemistry courses is the understanding of how proteins work, in particular how protein structure determines function. It has been observed that students often have a difficult time visualizing and grasping three-dimensional structures in a two-dimensional environment. Even simple three-dimensional structures, such as DNA, can be difficult to represent with the two-dimensional non-interactive constraints of traditional educational tools. This often leads to insurmountable difficulties in understanding protein function and in explaining how their function relates to their shape. To overcome these difficulties, teachers and faculty can use technology to help teach these fundamental concepts in biology and biochemistry.

MIT Professor Graham Walker and Brandeis University Professor Melissa Kosinski-Collins and their colleagues led the development of the StarBiochem [1] protein visualization tool to address the difficulty experienced in using existing protein visualization tools in the classroom to teach about protein structure (unpublished correspondence). Existing protein visualization tools are difficult to use, and require installation on a student's computer. In developing StarBiochem, MIT's Software Tools for Academics and Researchers (STAR) group sought to address these issues. In addition, the STAR group focused on producing a tool that could be used by a large cohort of students at the same time on multiple computers and in different locations.

The StarBiochem software is freely available. In addition to the software, the STAR web site features lesson materials that help in incorporating StarBiochem into classrooms around the world.

II. THE STARBIOCHEM APPLICATION

StarBiochem is a tool that visualizes protein structures. The application's user interface revolves around key concepts of protein structure. The simplicity and usability of StarBiochem's user interface are the result of developing novel and flexible methods for selecting and manipulating elements of protein structure visualization. It allows the user to control the rendering of protein structures found in protein databank (PDB) files by providing the user control of the resulting visual experience. The result is that users are able to manipulate the protein's snapshot until it emphasizes areas of the protein's structure that are of interest. These snapshots are important for formulating, communicating, and visualizing important aspects and properties of a protein's structure.

The key design principles behind StarBiochem were to simplify how to:

• Select protein structural components
• Control the rendering of selected components
• Introduce higher-level protein structural elements in the same order in which they would be encountered in the classroom

These enhancements over existing protein visualization tools allow StarBiochem to be used in classrooms and workshops. Additionally, StarBiochem features the ability to search and download approximately 54, 000 molecules from the Protein Data Bank [2]. This allows students and researchers to access up-to-date information as new structures are discovered and published.

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The software is based on the TEALsim simulation framework [3] developed by MIT Professor John Belcher. TEALsim was implemented in Java and thus StarBiochem runs on most popular platforms (including Linux, Windows, and Mac OS X). StarBiochem and TEALsim images are rendered with Java3D; a Java package for creating three-dimensional visualizations that takes advantage of hardware acceleration on a user's graphics card.

III. STARBIOCHEM IN THE CLASSROOM

A. Introductory Biology at MIT - How does a heme group dock on hemoglobin?

StarBiochem has been used in MIT's "Introductory Biology" course since the fall of 2006 [4]. In this required course, students learn fundamental biology concepts, including determinants that govern protein structure. The faculty and instructors of this course use StarBiochem to present complex structural information to the students in an understandable, visually rich, and intuitive manner.

In the "Introductory to Biology" course students are given homework assignments that explore a protein structure without prior training on this software or other protein modeling applications. For example, one of the proteins that students are asked to explore is human hemoglobin. Hemoglobin is responsible for carrying oxygen through the bloodstream, which it does through a non-protein heme group that contains iron. In examining the molecule, students find that hemoglobin has four heme groups. By focusing on hemoglobin's secondary structure, students can observe that each heme group is attached to one of hemoglobin's helix motifs (Figure 1). StarBiochem allows students to select certain structural elements, such as the four heme groups and their subsequent helices, and hide the unselected parts of the protein. The ability to select specific molecular components and make the unselected ones partially or completely transparent is unique to StarBiochem's user interface. This process allows students to formulate questions about the nature and function of the-highlighted structural elements.
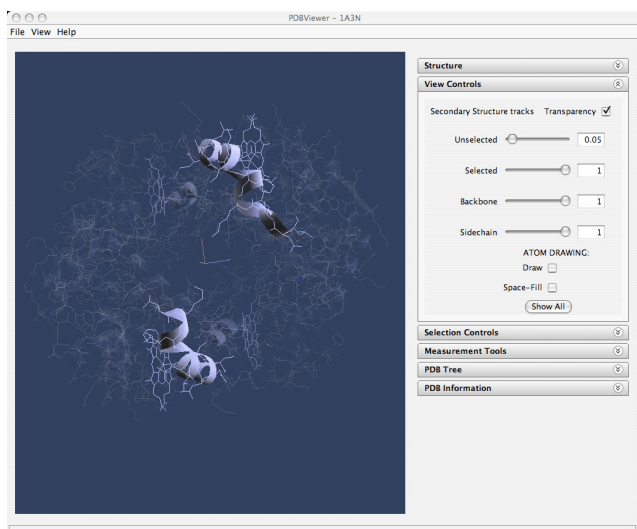

Fig. 1. Highlighted heme groups in deoxy human hemoglobin.

B. Introductory Biology at Brandeis University - Understanding protein stability and cataracts

StarBiochem has been used at Brandeis since 2007 in the Introductory Biology Laboratory course (Biol18). This course enrolls mainly sophomores pursuing either primary or secondary degrees in the life sciences. The students in this course have never used a protein modeling software program before and have no training on StarBiochem.

In the fall semester of Biol18, students are asked to study the structure of a human eye lens protein called Human γD Crystallin (HγD-Crys). Changes in the structure and stability of HγD-Crys lead to protein aggregation and are thought to be involved in cataract formation in the human eye. In this condition, the lens becomes clouded due to changes in crystallin's structure. The students of Biol18 use StarBiochem to explore the structure of HγD-Crys in three dimensions. After examining HγD-Crys's structure in StarBiochem, students are asked to make hypotheses as to which amino acids and elements of structure are important to maintaining the shape and stability of the molecule. The students then specifically explore the interactions made by these residues with other aspects of the protein. Based on this exercise, students design a mutation that they make in the crystallin gene. They then purify their mutant protein and study its stability and structure as compared to the non-mutated version, to assess whether their new protein forms an aggregate that has cataract-like qualities.

C. Educational Outreach Program at the Broad Institute of MIT and Harvard – High school lessons combining lab experiences and structural analysis

The Broad Institute of MIT and Harvard has been using StarBiochem in its Educational Outreach Program since its inception in January 2007. Since then, hundreds of high school students and teachers in the Boston area have used the software to examine the structures of different proteins. The Educational Outreach Program allows high school students and teachers to visit the Broad Institute on organized field trips that involve an array of educational experiences. Before each field trip, teachers are allowed to customize their visit by selecting various activities from a menu of educational experiences that includes wet-lab experiments, computer labs, lab tours and small group discussions with scientists. One of the computer lab options involves using StarBiochem to explore the structure of a protein. This exercise can be combined with a complementary activity, such as a wet-lab experiment, to create a multi-disciplinary lesson. For instance, students may examine the structure of a protein such as hemoglobin using StarBiochem and then purify that protein in the lab from a mixture. Alternatively, students might genetically engineer bacterial cells so that they are capable of producing the Green Fluorescent Protein (GFP), which is produced in nature by glowing jellyfish. StarBiochem can then be used to understand why this protein glows.

Another example of how StarBiochem can be paired with a laboratory exercise relates to the genetics of the roundworm *C. elegans*, a common model organism in biological research. This field trip experiment involves the

students learning to set up genetic crosses (or matings) between a mutant and a non-mutant worm. The students then examine the offspring from this cross to determine the mode of inheritance of the mutant trait (e.g. is it recessive or dominant and is it a sex-linked trait or not). In this lab exercise students are separated into groups. Each lab group receives a different mutant trait that they must first identify before setting up the crosses and analyzing the offspring. This classic genetics experiment can be combined with StarBiochem by assigning the students the task of examining the structure of the protein that is changed in their mutant. For instance, one of the mutants available for this lab experience is a worm that has multiple vulva (i.e. multiple egg-laying organs). The mutated protein responsible for this trait is E2F. This protein is particularly interesting because it is often mutated in multiple cancers. By exploring E2F using StarBiochem, students can learn how its mutated form can lead to the mutant trait they examined and to cancer.

In addition to the high school field trips, the Educational Outreach Program staff has also presented StarBiochem to high school teachers during Professional Development Days and summer workshops. During these workshops, teachers learn to use and incorporate the software in their classroom curriculum. For this purpose, the staff uses a "training" version of a StarBiochem problem, which demonstrates the major functions of the software, so that teachers can pick and choose the functions most interesting to their students. This training problem examines the structure of lysozyme, a protein found in human tears, that degrades the cell walls of bacteria. This lysozyme exercise is simple enough that the Outreach Program staff has also successfully used it with 7th grade students.

D. Outreach program at the MIT Museum – Protein building with LEGO® molecules

The MIT Museum's "Learning Lab: the Cell" [5] utilizes both LEGO bricks and StarBiochem to teach how proteins are built. MIT Museum's Learning Lab: the Cell is a classroom space that represents a cell by using different-sized tables for the nucleus and for several ribosomes. The lesson for high school students includes a sophisticated simulation of protein synthesis that is played out on these tables utilizing LEGO molecules specially designed for teaching molecular processes. In the simulation, a gene for a membrane channel protein is transcribed into mRNA and translated into a protein. In the final step, protein subunits come together to create the transmembrane helices that form a passageway through the membrane. Overall, the lesson demonstrates how a single DNA nucleotide replacement can modify the 3-D shape of a protein and the lesson clearly illustrates the molecular basis of a genetic disease, such as cystic fibrosis.

However, while the LEGO models created for this experience are unique and kinesthetically helpful, by necessity the molecules must be greatly simplified. Therefore this lesson is significantly enhanced by viewing membrane protein structures with the StarBiochem software. A small adjacent computer gallery at the museum is utilized by the high school students to discover the details of proteins, such as the protein water channel aquaporin, a molecule that allows water to pass through cell membranes. Overall, teaching with both a simplified

physical model and the full virtual presentation of a protein is an effective approach that allows proteins to come alive for students.

IV. RESULTS

As of December 2008, StarBiochem has been successfully used by approximately 2000 MIT students in the Introduction to Biology course, 600 students at Brandeis University, and hundreds of high school students. StarBiochem is freely available on the STAR web site: http://web.mit.edu/star/biochem.

V. CONCLUSION

StarBiochem is a classroom-tested protein visualization tool. StarBiochem's web site features guided questions and user manuals that help faculty integrate it into their existing curriculum. StarBiochem has proven that it can be integrated in a wide range of educational experiences, from high school biology outreach programs, to museum exhibits and undergraduate courses.

VI. ACKNOWLEDGEMENTS

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