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NSF Highlights
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Teaching and Assessing Three-Dimensional Molecular Literacy in Undergraduate Biochemistry

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Chemists have long understood the influence of structural geometry on the reactivity and specificity of molecular interactions. Molecular geometry is taught using a variety of tools, including paper sketches, physical models, and computer graphics. The visualization of molecular structures in three dimensions becomes more difficult for the biochemist, who must grapple not only with lipids and amino acids, but also with large biopolymer structures such as RNA and proteins. Because of the central role of structure in all aspects of biochemistry, it is essential for the biochemistry student to achieve some level of "three-dimensional molecular literacy".

The modern biochemistry textbook, therefore, typically comes with a CD or Web site containing animations and illustrations of biochemical procedures, processes, and structures. In addition, many biochemistry instructors incorporate assignments utilizing one of the free molecular graphics programs—Rasmol (*1*), Chime (*2*), Protein Explorer (*3*), CN3D (*4*), Deep View (*5*), Mage (*6*)—into their courses. These assignments typically involve lessons in which the student views a previously prepared series of three-dimensional images while being guided by a written narrative, sometimes also accompanied by questions requiring more minds-on interaction with the images. Undoubtedly these lessons help students to visualize the complex structure–function relationships of biochemical systems, but there have been few attempts to rigorously assess their usefulness.

We have taken a different approach to teaching three-dimensional molecular literacy (*7*) in the typical undergraduate biochemistry course. Rather than have students concentrate on previously prepared lessons using animations or graphic images, we use such lessons as an introduction to the course material and the software. We then go deeper by having each student complete a semester-long project that consists of choosing a biochemical topic, learning about the important structural features of this topic by finding and reading a small number of structure-based papers, and finding appropriate coordinate files from the Protein Data Bank. From this information the student develops an annotated, three-dimensional "molecular story" to communicate that information to anyone who views it. Students are therefore actively involved in constructing their own knowledge of structural details and structure–function relationships. We are using kinemages (*6*) for this project, which are plain text scripts generated from Protein Data Bank coordinate files with the program Prekin, and viewed with the program Mage. Kinemages (pronounced "kin-images", with the accent on the first syllable) were originally designed for the journal *Protein Science* to allow authors of structure-based papers to communicate their important conclusions in a three-dimensional manner (*8*, *9*).

Our Constructivist Approach

An example schedule from a typical project is given in the timetable in the first semester of a two-semester senior-level biochemistry course at the University of Southern Mississippi (USM). After a brief review of introductory material, the instructor (RCB) begins to use kinemages in class to illustrate nucleic acid structure and explain the basics of the kinemage-viewing program, Mage. Students are then given a homework assignment utilizing a series of nucleic acid kinemages in which they must explore each kinemage to generate questions about it. At this point the students are learning to manipulate the view of the structure (zoom, center, rotate, etc.) as well as how to obtain atomic and distance information from a structure. In class the instructor discusses nucleic acid and protein sequence information, including how to obtain this information from the sequence databases such as Genbank. This is combined with a demonstration of how to search PubMed, the Web interface to the National Library of Medicine. As the class moves into a discussion of tertiary and quaternary structure, students are introduced to the Protein Data Bank (PDB) and how to extract information from PDB files.

After this background in use of electronic databases, students are given guidance in selecting possible topics for their individual projects and asked to explore the literature to find a topic that interests them. They must come back with an abstract and brief list of structure-based references on their topic of interest. The class is now beginning to discuss protein structure: students are given a homework assignment requiring an analysis of a piece of protein secondary structure. For example, an alpha helix kinemage was distributed and each student required to measure all dihedral angles and sequential alpha carbon distances, tabulate the results, generate a Ramachandran plot, and discuss their results in the context of what they knew about protein secondary structure.

An example structure-based paper, in this case the structure of glucose oxidase (*10*), is also discussed in class as a model to help students learn to extract the pertinent structural information from the literature associated with their topics. During this section of the course the students are asked to complete a tutorial on kinemage authorship using castor bean ricin as the example structure. The tutorial and all authorship materials are freely available online (*11*, *12*). With this thorough introduction to protein structure, each student is then required to turn in a one-page outline of a project, and the project is refined upon discussion with the instructor. The last part of the semester is then devoted to actually constructing a series of kinemages to bring their outline into three dimensions. Because the project is spread over the entire course and involves considerable time outside of class, it is given the grading equivalent of a regular examination. We have developed a grading rubric, which is given to the students at the outset, and students are encouraged to discuss drafts of their kinemages as they progress. Since kinemages are plain text files, they can easily be attached to email and viewed by the instructor.

Assessment—Strategies and Results

Assessment of the effectiveness of the authorship project has focused on determining the differences between students performing assignments with previously prepared kinemages (control group) and students actually constructing their own kinemages (experimental group). Quantitative assessment instruments included an attitudinal survey, which was given at all test sites, and a performance assessment. This latter instrument was a kinemage-based examination given as half of the final exam by a single class at USM during the fall of 2000. This particular class of 40 students had been randomly divided in half before the start of the semester, with the control half writing term papers instead of constructing kinemages to equalize the workload. Preliminary results from the first round of testing showed no statistically significant difference in the performance evaluation between experimental and control groups.

The third assessment strategy was to formally interview eight students from the USM class as a complement to the attitude survey. The interviews and other anecdotal evidence confirmed the attitude survey results that indicated the students thought the project was worthwhile, motivated them to learn biochemistry, and would benefit them in their future careers. They also felt that authorship had given them a deeper understanding of higher-level structure, particularly quaternary structure and conformational changes. Perceived difficulties were the time investment required, and a wide variety of attitudes toward learning new software.

Project Outcomes

What deliverables have come from the student kinemage authorship project? A manual has been developed that is designed to guide instructors and students in both the pedagogy and the practice of kinemage authorship. The next edition of the manual will emphasize inquiry, with authors encouraged to go beyond the literature and attempt to discover or propose something new about the structure that is being built. A portion of this manual is a Kinemage authorship tutorial; this manual is available separately on *JCE Online* (*12*). We are also developing a suite of assessment tools, both performance and attitudinal, for judging the effectiveness of molecular visualization in teaching biochemistry (*13*). Finally, the project has driven the rapid evolution of the kinemage authoring and viewing/editing programs Prekin and Mage, respectively. New features including text editing capability, mutation and rotation of side chains, and a superposition/docking feature highlight this round of program improvements, which can be freely downloaded (*14*).

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WSupplemental Material

A guide for instructors and students in the use of Kinemage is available in this issue of *JCE Online.*

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13. Interested parties should contact RCB at the address below for information on the status of these assessment tools.
14. Those interested can freely download the most current software at the Richardson laboratory Web site, ref. *6*.

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