Using Physical Models of Biomolecular Structures To Teach Concepts of Biochemical Structure and Structure Depiction in the Introductory Chemistry Laboratory

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As part of an effort to introduce beginning students to concepts of biomolecular structure in their first university chemistry course, we have developed a laboratory exercise in which students handle and study 3D physical models of biochemical structures. The exercise is designed both to teach the students about *how* biochemical structures are portrayed in models (both physical and computer animated) and to help them learn about the features of these structures. Some of the models use uncolored backbones, omit side chains, or confine CPK coloring to only the parts of the molecule that the student is expected to study. The twofold goal of the exercise is for students to

- Recognize the structural features they have encountered when they look at 2D or 3D depictions of other proteins
- Be able to select a specific protein from among a number of possible depictions (as supplied in a Chime file, for example) in order to see particular details within the complex whole

This university has seen considerable growth of interest in the biological sciences among the incoming students throughout the latter part of the 1990s and into the 2000s. The growth of both interest and importance of biochemical concepts in a chemist's education has also been recognized by the American Chemical Society Committee on Professional Training in its insistence that biochemistry be an integral part of all ACS-certified degree programs. This department has chosen to integrate concepts of biochemistry into courses throughout its curriculum as a means of addressing this need. A major restructuring of our accelerated general chemistry course for mathematically well-prepared students was implemented in the fall of 2001. This first chemistry course for science students now includes significant examples taken from biochemical systems and specifically teaches fundamental concepts of protein and DNA structure and of enzyme action. For two years prior to the change in focus of the 800-student accelerated course, we had been experimenting with prototype models supplied by the Center for BioMolecular Modeling (CBM) in a 220-student second-semester general chemistry class. This had allowed us to build a framework of instructional materials and exercises and to learn some important lessons about how much material students could reasonably work through in a three-hour lab period and in what order certain concepts ought to be taught. One of our faculty in second-semester general chemistry (teaching a section of 350 students) continues to use this experiment in his class.

Previous Work on Use of Models

The use of models to provide simplified representations of complicated systems is well-documented *(1)*. With the recent increase of interest in biologically-active molecules, the chemist's use of molecular models has taken on a new dimension. Physical and computer graphical molecular models afford a unique mode of representing biomolecular structure. By allowing the visualization of complex biomolecular structures, molecular models overcome many of the limitations of 2D graphical representations *(2)*. The clearest advantage of *physical* models is that they can be easily manipulated by any user to explore the various facets of the molecules in question *(3)*.

Presenting the Material

The week before the lab exercise, students are assigned three sets of preparatory online tutorials (see the Supplemental Material[W]) to work through. These tutorials combine text, line-art diagrams, still images, manipulable Chime or JMol images, and self-test questions that must be answered correctly to progress. The first two tutorials introduce the structure of proteins by examining amino-acid structure, sequencing, and formation of α-helices and β-sheets as well as their role in the tertiary structures. The third tutorial provides an introduction to the structure of DNA.

On the week that the models lab takes place, two hours of lecture time are devoted to reviewing and expanding on the material in the tutorials. This maximizes the connection between lab and lecture and permits students to apply and extend their "book" knowledge through examination and construction of the biochemical models.

Logistics of Exposing Many Students to Limited Numbers of Models

Each static model costs between $400 and $700 to manufacture. The construction kits are (in the case of DNA) or soon will be (α-helix) available as injection-molded pieces at ~$100 each. This high capital cost means that the CBM cannot lend unlimited copies of models. The laboratory exercise is divided into four stations. Three of these stations involve protein structure while the fourth involves DNA structure. Experimentation has shown that students gain the most from each station when the three protein stations are done "in order", whereas the DNA station stands on its own to some extent. Since there is a limited number of models,

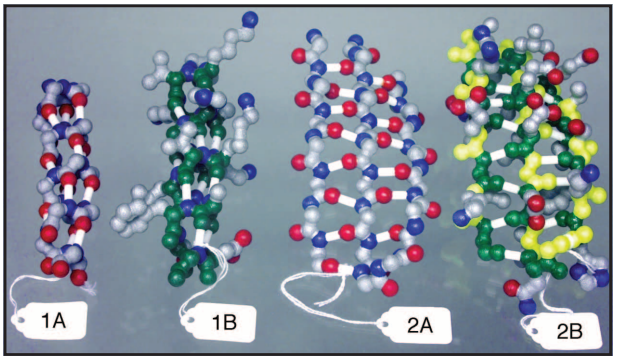

Figure 1. The four models in station A (photo by Jerry J. Jacobsen).

we endeavor to keep group size to 3–4 students. The logistics for a lab section of ~22 students involve two groups arriving at the formal start of the lab period and beginning with the first protein station, station A. The remaining two groups arrive 35 minutes later and begin with station A, while the first two groups move on to station B. After another 35 minutes, the groups again move on to the next station. Rotation among stations continues at 35-minute intervals.

The Models and Stations

Station A concentrates on α-helices and β-sheets. Models of both the backbone of these secondary structures (Figure 1, models 1A and 2A) and the same backbones with side chains attached (Figure 1, models 1B and 2B) are used. These latter models use the CPK color scheme for the side chains while the amino-acid components in the backbone are either green with blue nitrogen backbone atoms or alternating green and yellow. These color schemes demonstrate how one can facilitate identification of the individual amino acids for sequencing purposes. Among other exercises, students are required to identify the N-terminal end and to partially sequence each structure. The complete exercise is reproduced in the Supplemental Material.[W]

Station B uses a series of models depicting the zinc finger motif (Figure 2). This tertiary structure contains an α-helix, a short section of β-sheet, and a zinc ion coordinated to two cysteine and two histidine molecules in the protein chain. Students examine six depictions of the motif, answer questions on what is portrayed and how, and attempt to mark on 2D color pictures in their worksheets some of the features that are visible in the models. This exercise clearly demonstrates the superiority of the model over a 2D picture.

Station C consists of two models—the "green fluorescent protein" and β-globin structure (Figure 3). The latter has a backbone composed of multiple α-helices while the former's backbone is a β-barrel. The only side chains shown on either model are those bound to or comprising the active site, and the amino acid glu-6 on β-globin that, when replaced by valine, is responsible for the sickle cell mutation.

Station D requires the students to build structures with kits. They construct several layers of DNA using the DNA modeling kit. Each piece of this kit comprises a phosphate, a sugar, and a particular base (Figure 4). Pieces attach via magnets set into sockets keyed to prevent incorrect assembly of the backbone. The most practical method of construc-

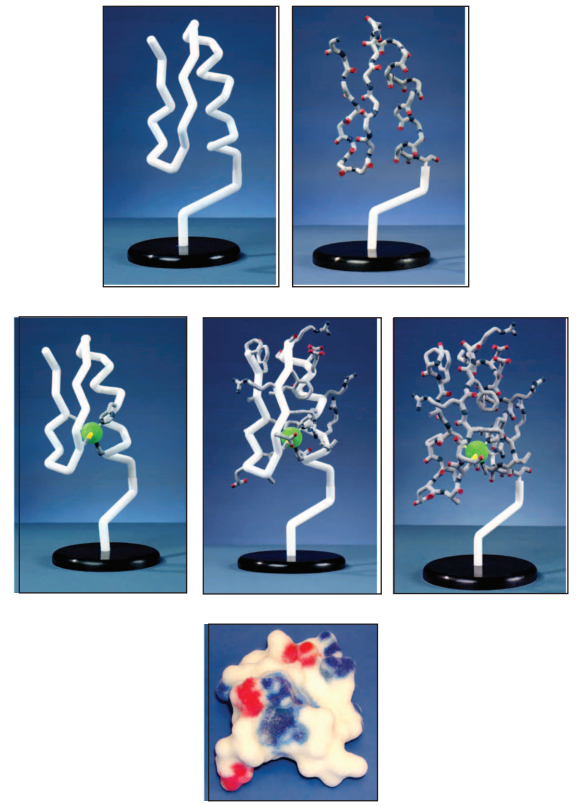

Figure 2. Models used in station B. The models are presented to students without stands. (Photographs by the Center for BioMolecular Modeling.)

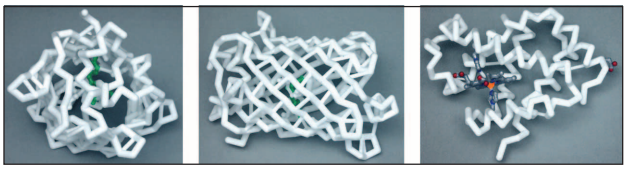

Figure 3. Models used in station C: (left and center) green fluorescent protein, a β-barrel, and (right) β-globin (photo by Jerry J. Jacobsen).

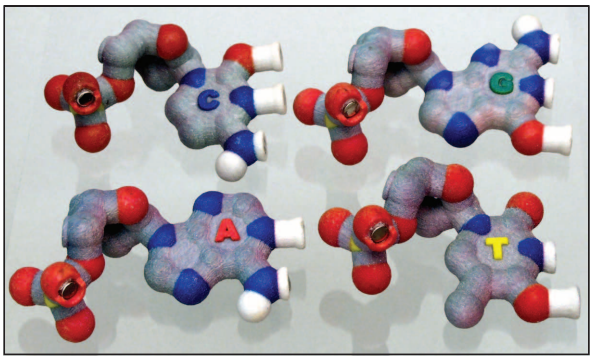

Figure 4. Components of the DNA modeling kit (photo by Jerry J. Jacobsen).

tion is to make layers (Figure 5) and then stack them to form the double helix (Figure 6). It *is* possible to form certain "disallowed" base pairs, but the error of this is seen when the student attempts to place the layer, as the backbone connections will not match up. A larger model depicting a full turn of β-DNA is supplied at this station for the students' reference.

α-Helix and β-sheet construction kits have also been obtained from the CBM. Kits consist of amino-acid backbone units with detachable side chains. Pieces are held together by magnets, and the structures are stabilized by 3-mm diameter steel wire "hydrogen bonds" between appropriately placed magnets on the nitrogen and oxygen atoms. We have tested the α-helix kit as part of this station, requiring students to build a certain sequence (helix E of β-globin). Those students who attempted to build the helix backbone first and then place the hydrogen bonds received an object lesson in the importance of hydrogen bonds to the stability of such structures.

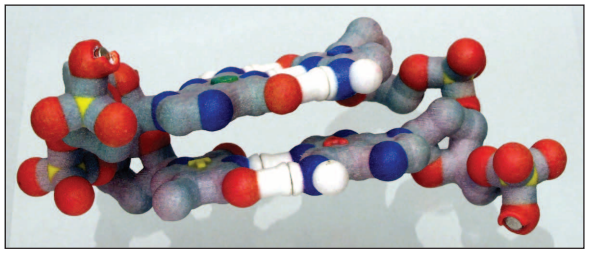

Figure 5. Two layers of DNA made up of the bases shown in Figure 4 (photo by Jerry J. Jacobsen).

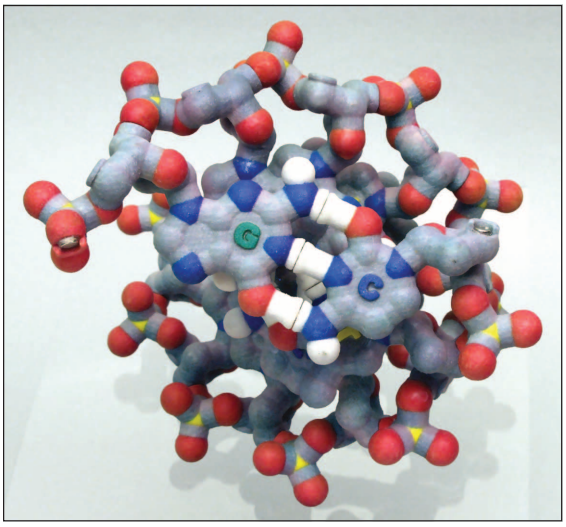

Figure 6. Six layers showing a half turn of DNA. Note that the 2D picture cannot show the double helix nearly as well as the 3D model does (photo by Jerry J. Jacobsen).

Efficacy of the Models as a Teaching Tool

Over the course of four years teaching with these models, we have developed a survey instrument and a pre- and post-test covering some of the material taught in the lab. A full discussion of these results will be presented in a separate article *(4)*. We can report here, however, that the most comprehensive data available (> 400 individuals in fall 2004) provide clear evidence that a large majority of students react positively to the models and believe that their understanding is improved by doing the exercise. Further, these students performed demonstrably better (improved scores statistically significant at the 95% confidence level) on the post-test than on the pre-test covering the same concepts. We interpret this as clear evidence of the success of the exercise in improving student comprehension of the concepts tested.

Adaptation to Other Institutions

The CBM operates a lending library of biomolecular models. Available models and checkout forms can be accessed online *(5)*. We operated with loaned models for three years before opting to buy our own set with grant funds. Our experience suggests that others would have no difficulty replicating our exercises or developing and implementing their own using these models. The CBM also maintains a database of instructional materials developed by model users that is expected to be made available at their Web site *(6)*.

Hazards

There are no hazards associated with this exercise.

Acknowledgment

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[w]Supplemental Material

Instructions for the students, notes for the instructor, a guide for the teaching assistants, and the preparatory tutorials are available in this issue of *JCE Online*.

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