MOLECULAR MODELING WITH MOBY

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For several years, students at Bridgewater State College have used PCMODEL (Serena Software, Box 3076, Bloomington, IN 47402-3076) as a part of the laboratory in the introductory organic chemistry course. We have found that PCMODEL helps students to visualize molecules in three dimensions; the program also serves as an excellent introduction to the use of molecular mechanics to calculate molecular geometry and NMR coupling constants.

Recently we have obtained a copy of a new molecular modeling program, MOBY, and a CD-ROM containing all of the structure files in the Brookhaven Protein Data Bank (both MOBY and the CD-ROM are available from Springer-Verlag NY, Inc., 175 Fifth Avenue, New York, NY 10010). This year we used MOBY to teach protein structure in a senior biochemistry course. MOBY is a powerful tool for helping students get a feel for the complexity of biopolymers.

Each student was given the amino acid sequence of a fairly small protein. First the student used the protein secondary structure prediction program, PROTYLZE (Scientific & Educational Software, P. O. Box 440, State Line, PA 17263-0440), to predict the presence of alpha helices and beta pleated sheets in the protein. PROTYLZE uses both the Chou-Fasman and Garnier-Osguthorpe-Robson algorithms to predict secondary structure. Then the Brookhaven Protein Data Bank x-ray crystallography data file of the same protein was used with MOBY to examine the actual structure and look for alpha helices and beta pleated sheets. The fact that MOBY can represent the structure of a protein in terms of a line drawing connecting the alpha carbon atoms makes it very easy for students to recognize the two types of secondary structure. Students can selectively color helices and sheets and rotate the molecule to get a better view of them. Comparing the predicted secondary structure with the actual allows students to get some feeling for the accuracy of the predictions.

Students can then represent the same molecule with increasing degrees of complexity

- Backbone only (line drawing)
- Complete structure (line drawing)
- Ball and stick model
- van der Waals radii.

It has been our experience that students have extreme difficulty in recognizing features of secondary structure in any of the latter three representations.

The software used runs on IBM PCs and compatibles and the total software cost is less than $1000. An 80X87 math coprocessor, 640 K ROM, VGA and a hard disk are essential; a 386 or 486 cpu and a mouse are strongly recommended. If you have a SUPER VGA card, such as the Paradise, MOBY supports both HIGH (800x600) and SUPER (1024x768) VGA. We have been using a NEC Multisync 3D monitor, but any system which supports VGA graphics is acceptable. MOBY uses over 500K of memory to run and requires 1MB of hard disk space.

A tutorial for students on the use of MOBY to visualize protein structures has been prepared and tested. Copies of the tutorial and a list of small proteins by their Protein Data Bank identifier are available by writing to one of the authors (WBC). We have used PROTYLZE, MOBY and the CD-ROM on one computer which was reserved for biochemistry students.

We are planning to use MOBY to allow students to investigate the active sites of enzymes and to study how restriction endonucleases interact with DNA, using files from the Protein Data Bank. MOBY uses the AMBER force field to do force field calculations on molecules of up to 150 centers in the presence of another larger molecule of up to 2000 centers. The structure predicted for the small molecule reflects all interactions, including those with the large molecule. For this reason, MOBY can be used to predict the conformation of substrates in the vicinity of the active site of an enzyme. We are investigating the use of an inexpensive reflecting stereoscope (Aldrich, Z15,675-2) to view the stereo representations that can be produced with MOBY. MOBY can do molecular dynamics simulations like the denaturation of a short protein alpha helix, and it can simulate the rotation of the side chain of an amino acid like tyrosine in a protein.

MOBY will do both MNDO and AM1 quantum mechanical calculations for molecules as large as glucose. The resulting charge distributions can be represented in user-selected colors. MOBY can read and write files that are compatible with many other molecular modeling and quantum mechanics programs and also supports a user-definable format. The next version of MOBY, now in beta testing, will be able to display the molecular vibrations that correspond to the peaks in the IR spectrum of a molecule. (Access to a version of MOPAC on a minicomputer or workstation is necessary to calculate the nature of the vibrations.) The new version will also have extended capabilities for doing very rapid rotations of molecules under control of the mouse.