COMPUTER SOFTWARE REVIEWS

AccuModel vl.1 for Windows 95

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1. Introduction. AccuModel 1.1 is a new product developed by MicroSimulations (New Jersey). The mission of the company is stated to be the development of accurate, powerful, automated, and intuitive software products targeting a broad user base through innovative adaption of powerful methods from modern computational chemistry and computer technology. AccuModel vl.1 is an attempt not only in this direction with some nice features but also with drawbacks and pitfalls which should be corrected in future versions of the program.

The program was employed for 2 months in an introductory course on Molecular Modeling for Biology. The students had little if any exposure to Quantum Theory but were conversant with General and Organic Chemistry as well as with basic principles of biochemical organization. The group of 10 students was divided into five subgroups of two students each. Individual tasks were proposed to each one of the subgroups, and the lectures were complemented with 6 h of computing work per week. The comments about the program stem mainly from that course.

2. Presentation and Manuals. AccuModel vl.1 is well presented, with enough descriptive material and a step-by-step tutorial through a series of experiments that demonstrate the basic operations. The program has an online help which implements the full manual. Therefore there is little need of the printed manual after the first use of the program. The printed manual is full of hype, especially concerning the accuracy of the calculations performed, which I personally find slightly disturbing. A more sober description of the capabilities of the program would be beneficial.

The tutorials are simple and fast to perform. The explanation of the different options and completion of the six tutorials by the students took about 2 h with the computers. Since the emphasis of this program is on the accuracy of the calculations (besides its simplicity), the manual could be of more lasting value if some comparisons were included in the form of tables. Thus, comparison of results obtained with AccuModel with experimental data and with the results calculated with other popular desktop molecular modeling programs (Hyperchem, Spartan, etc.) would be welcomed.

3. Installation. Installation of the program is extremely easy and without glitches. Double-clicking on the *Setup.exe* icon invokes the *InstallShield Wizard* which performs the installation after a few typical questions. Two modifications would improve the procedure. The window that offers the possibility of installing the ISIS/Draw addin files would benefit from a *browse* option, so that the user that does not remember where the ISIS/Draw files are installed can find them without leaving the installation procedure. The second improvement would be that the program is asking whether or not to install its icon directly in the Windows 95 taskbar, a thing it does at present without warning.

4. Main Window. The program shows most of its options in task bars located around one or more drawing windows, where molecules can be sketched. The program adopts the point of view that the user will feel more comfortable with all the available tools displayed. It produces a crowded screen if low resolution monitors are employed (although it is easy to examine at a resolution of 800×600). The icons are in general understandable. Short help labels are produced when the cursor is on top of an icon (except in certain curious cases, like if the graph box is still open when a molecule has been closed). One, at least, of these labels, that for changing the torsion angle, displays a truncated text. A somehow surprising way of coloring the background of some of the icons was adopted. The effect is most striking for the icons representing the atoms.

Auxiliary windows are produced from the main one in case a geometry optimization is performed. It would be beneficial if the windows containing important information stay on top of the screen unless the user chooses to close them.

5. Building Molecules. Molecules are built from individual atoms or fragments. This is one of the poorest features of this program. No periodic table is provided (a common feature of other programs of comparable price), and the atoms available are limited to H, C, O, N, S, P, B, Si, F, Cl, Br, and I. Most noticeable is the lack of metals of any type. Therefore, the program is mainly directed toward organic chemists, leaving behind a large part of the chemical community. Only the most usual functionalities are provided, although most others can be built with some manipulation of the fragments and residues provided.

The program does have the ability to draw several cycles and fused cycles, from which derivatives can be obtained by substitution. If the substituted atom has free valences or hydrogens on it, the program adjusts the molecular structure automatically to take into account the type of substituent atom. This is not true however when the substituted atom is bound to all non-hydrogen atoms. The multiplicity of the bond can be augmented or diminished by a special tool. When the multiplicity of a bond is increased, the program does well in suppressing the now incorrect hydrogens bound to the atoms involved in the multiple bond. However, if the multiplicity of a bond is increased and later decreased again, the H's are not added automatically. Anyway, a

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special tool allows one to saturate with H's the free valences of the atoms.

The program has an *Undo* feature which is handy for correcting mistakes. Strikingly, the *Undo* tool has a cyclic behavior. One click leads to the original structure, two clicks again to the one being undone. This is not a problematic behavior once it is understood. However, the *Undo* command also proceeds to destroy all the changes done with a single tool. For instance, let us assume that we draw a tetrahedral carbon atom and then we attach a pentadiene ring to each one of the free valences. Now we want to rotate, but forgetting that we have to select the rotation tool, we click inadvertedly on the drawing field. A "floating" pentadiene is created there, which of course we do not need. Thus, when we try to Undo, surprisingly not only the floating pentadiene disappears but also the other four which were bound to the original tetrahedral carbon. This behavior will be undoubtedly corrected in future versions of the program. It would be nice if multiple Undo levels are then added as well as the ability to select a whole molecule (only atoms can be selected at the present time).

Another drawback with respect to the building of molecules is the lack of any specific capability for drawing macromolecules. Thus, no amino acids, DNA bases, or sugar fragments are provided. Although these fragments can be built by the user and saved in a private library, it would be much better if the functionality were provided by the program itself.

Notwithstanding the above mentioned drawbacks, the building procedure is fast. The molecules appear well centered on the screen after each addition or deletion, and there seems to be no obvious geometrical problem with the construction algorithm.

6. Visualization. The program allows for a basic "wire" representation of the molecules, plus ball-and-stick and shaded CPK models. The algorithms are fast, so that rotation or displacement of the molecule on the screen (even if done with the CPK model) have no appreciable delay. The drawing of the CPK model involves a memory bitmap of the size of the window. Therefore, if large windows are used, the procedure is very memory-intensive.

A minor glitch of the program is evident in the ball-and-stick model. The "sticks" representing the bond between atoms do not point to the center of the balls representing the atoms. The appearance is amusing, especially with respect to the hydrogen atoms.

The program allows for rotation (around the three axis with two different tools), displacement and zooming of the molecules on the screen. A nice feature of the program is that it allows simultaneous displaying of four different views at one time. Stereoview is possible, displaying side-by-side images of the molecule on the screen. Labeling is provided, either by element type, atom identificator, atom type, or atomic *z*-coordinates.

One disturbing problem is that the algorithm for rotation seems to be screen based and not molecule based. Thus, if one translates the molecule and then attempts a rotation, the molecule is translated back to the center of the screen before rotating. This algorithm has some problem that results in rotations not being smooth when done around a different axis than one of the principal axes of the molecule.

7. Computation. AccuModel does not provide any other method of calculation than Molecular Mechanics with the MM3 force field of Allinger and co-workers.[1] For those elements not covered by this force field, AccuModel uses the Universal Force Field of Rappe *et al*.[2] The force field includes the usual harmonic terms for stretching and bending, truncated Fourier for rotation, and van der Waals and electrostatic terms (charge−charge, charge−dipole, and dipole−dipole). Cross-interaction terms (stretch-bend, etc.) are also included. The user can choose whether to allow the UFF to be employed together with MM3 or not.

The program can calculate the total energy (single point calculation) and optimize the energy as a function of the coordinates of the atoms. Two different optimization algorithms are included, steepest descent and conjugated gradients. No Newton-Raphson is available. The optimization is global and complete, with no restrictions possible. Therefore, curves of the energy as a function of one internal coordinate can be done only with fixed geometries; it is not possible to optimize the remaining degrees of freedom. Since there is no checking of the second derivative, no identification of the saddle points on the conformational potential energy surface is possible. On the other side, the algorithms do converge toward the structure of a saddle point if the starting geometry is forced to have the appropriate symmetry. For instance, *cis*-butane can be optimized in addition to the two minima (gauche and trans). Of course, since the program does not include any quantum chemical method at all, AccuModel is almost useless for the study of reaction pathways.

To test the accuracy of the calculations, we tried several geometry optimizations (CH_3NH_2, H_2CO, CH_3OH, CH_3F, CH_3SiH_3, CH_3PH_2, SiH_3Cl, P_2H_4, Si_2H_6, cylopentadiene, benzene, F_2CCH_2, CCl_4 and CH_3Cl). In all cases the optimizations were extremely fast. The geometries were compared with the experimental ones and with those provided by other programs and force fields (the programs PC-Spartan Plus and Hyperchem 5.0 were employed for the comparison). Both types of comparisons showed that the force field in AccuModel is well coded and that the geometries are as good or better than those afforded by other force fields. A similar comparison was performed with respect to the relative energy of different conformations of those same molecules. The results were again accurate. All in all, one can say that the accuracy of the force field and the speed of the algorithm that is implemented in the program are the strongest points in AccuModel vl.1.

The results of energy calculations and optimizations are informed in two windows, one with textual information and the other with a graph of the total energy as a function of the optimization step. This graph box is useless and should be taken away from the program. Much more useful would be to have an algorithm of rotation around single bonds which automatically calculates the energy and places it in a graph of the energy vs the value of the rotation angle. This feature could be truly used for conformational analysis.

8. Import/Export Capabilities. AccuModel vl.1 allows import of molecules in some few formats (besides their propietary one). MDL.MOL files, MM3 input files, Macromodel.dat files, and PDB files are understood by the program. Probably this is not a major drawback, provided the existence of free programs like BABEL which allows

for easy format interconversion. However, being also a simple task, it would be nice to see a larger selection of input formats in future versions of AccuModel. AccuModel provides also the means for importing 2D structures from a variety of file formats or from SMILES strings.

AccuModel provides for an addin to ISIS/Draw, such that a 2D structure drawn with this program can be displayed automatically by AccuModel. Conversely, AccuModel provides a tool that exports the 3D structure as a 2D sketch back to ISIS/Draw. The displayed structure can also by copied to the clipboard and transferred to other documents.

9. User Friendliness. One of the most important features of any molecular modeling program that targets chemists at large as potential customers must be its user-friendliness. Researchers usually lack the time required by the learning curve of a new tool. More serious, they usually lack the mathematical and physical background necessary for making a meaningful choice among many options presented to them by a molecular modeling program.

AccuModel vl.1 is satisfactory in the sense that practically all the options the program has are iconized in the task bars. Learning to use the program requires about 1 h for any average student. Some modifications of the actual default actions however would improve the program. An outstanding example is the default behavior of the mouse. Since there is no active-molecule selection procedure, the mouse "remembers" the last action performed. Thus, if one has added a fragment to a molecule and wants now to have a different view of the molecule, one needs to select the rotation tool (forgetting this and clicking in any part of the drawing area leads to the creation of a floating fragment). It would be much more user-friendly if the mouse had rotation as its default action whenever the click is not on a free valence of the active molecule. Similarly, although the program has the ability to save user-defined fragments for later use, it would be much better if amino acids, sugars, DNA bases, and other such common building blocks were already programmed. Obviously, this would imply that not all the information available could be displayed as it is now, therefore adding some complexity to the program.

10. Conclusions. AccuModel vl.1 is a limited, easy-to-use program, generally user friendly, with some few glitches which will be undoubtedly corrected in future versions. In its present form, the program is more adequate for teaching than for performing serious research. Although its lack of optional force fields or more sophisticated methods is in principle a serious disadvantage, it is also true that this same lack of complicated options may make the program more appealing for people lacking the mathematical and physical training necessary to grasp the tougher concepts in advanced molecular modeling. As a teaching tool, AccuModel vl.1 is extremely valuable, since the students establish a very positive rapport with the program. The experience with biology students showed that molecular modeling concepts were easily understood and remembered with the help of the program.

In summary, AccuModel vl.1 is a program that does not live up to its claim of being the ideal tool for the research chemist. However, it is a useful tool for teaching and probably adequate for research in which only very few molecular modeling functionalities are needed.

AccuModel vl.1 is available from MicroSimulations, 478 Green Mountain Road, Mahwah, NJ 07430, Fax (201) 512-0489, e-mail info@microsimulations.com, web site at www.microsimulations.com. AccuModel has a retail price of $499, with good discounts for Government (25%), Faculty (50%), and students (80%).

REFERENCES AND NOTES

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