COMPUTER SOFTWARE REVIEWS

ALCHEMY III, Three-Dimensional Molecular Modeling Software

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The word "Macintosh" is enough to make some hard-core DOS-box enthusiasts turn crimson. On the other hand, most computer science undergraduates scoff at DOS-boxes but will still use a Macintosh if their favorite UNIX machine is unavailable. For the inspiration of zealotry, computer preference is in the same category as religion and politics. Until recently, molecular modeling using personal computers has been restricted primarily to DOS-boxes because of the perceived better price/performance ratio of these machines as compared to the Macintosh. There are also many more DOS-boxes than Macintoshes so that the potential market is greater. At colleges and universities the Macintosh is often significantly less expensive, so the relative number of Macintoshes compared to DOS-boxes is higher. Macintoshes can also be seen in surprising places in industry, debatably because in absolute terms people using them are more productive. This may change as DOS-boxes become more like Macintoshes due to Windows-based software. However, there are now a significant number of desktop molecular modeling programs for the Macintosh, and a chemist with access to a Macintosh should be able to find a program, comparable to those available for DOS-boxes, which serves his or her needs.

A great service has recently been provided by J. Philip Bays[1] in his evaluation of five desktop modeling programs for the Macintosh: ALCHEMY II, Nemesis, PC-Model, MacMimic, and Chem3D Plus. Anyone wishing a side-by-side comparison of these programs is encouraged to consult this very worthwhile summary. The review by Bays has a note added in proof concerning the recent update of ALCHEMY II to ALCHEMY III with a paragraph devoted to the revision.

ALCHEMY III[2] is a good implementation of the Macintosh interface, and a user with prior Macintosh experience will feel comfortable using the program. Documentation is of high quality (about 200 pages) and indexed. The documentation is at an appropriate level—neither too skimpy nor overwhelming. A good feature of the program and documentation is the clear explanation (with an example) of how to add a new atom type to the force field. There is nothing more frustrating for a new user than to find that a needed parameter is not available and then not to be told in a clear fashion how to go about remedying the situation.

The virtual trackball method of manipulating an image is implemented in this update of the software. This method allows the user to readily obtain any view of the molecule in an interactive fashion. The gadget box from previous versions is retained, and although this seems redundant, it is also quite useful. One can rapidly and exactly obtain a new view which is 90° away from the previous one along some axis. It is possible to view stereo pairs on the monitor in either relaxed or cross-eyed stereo mode. The stereo separation is conveniently adjustable.

There is an interface to an MM2 program, which is marketed by TRIPOS, and runs on a variety of computers. There is also an interface to the Chemical Abstracts Service (CAS), which allows one to upload ALCHEMY files to STN for searching. One can also download 3D CONCORD 3D coordinates from the CAS Registry File for use in modeling. Provision is also made for communication with the SYBYL and Labvision products of Tripos. Structures can be written to an HP-Plot file, and a stand-alone utility is provided which allows the plot file to be dumped to a plotter at a later time outside the main ALCHEMY program.

Although ALCHEMY includes a number of good features, there are also some drawbacks. The library of structures provided with the system is rather small. Also, for applications of interest in biochemistry, the "build" options for peptides are inconvenient. It would be much more useful if the user could specify φ and ψ for a growing peptide chain, or at least specify that sequential amino acids be added in a helical or β-sheet geometry. An output file suitable for use in MOPAC or Gaussian calculations would be very useful. The ability to write output files in pdb format would be a worthwhile additional feature. Currently, bond lengths and angles are selected one at a time and *have to be written down*! Laser printer output of structures is disappointing.

Default options of the program are sometimes annoying. Prior to printing or copying to a word processor, one must remember to toggle the screen color from black to white or the subsequent output will have a black background. Deep purple is very difficult to see against a black background, and this contributed to making some of the examples in the tutorial difficult to follow. A lack of control of the front to back intensity when using depth-cueing (it only toggles on and off) also contributed to difficulties in following the tutorial.

Some of these problems may be due to the fact that ALCHEMY III is a member of a family of programs from TRIPOS. Improving its functionality may be tricky because this could undercut the "big brother" programs. This may explain why some of the useful and obvious features of competitive programs are missing.

Some aspects of the program cannot fairly be described as either good or bad. For example, ALCHEMY III does not compute molecular energies as accurately as "real" MMX programs.[1] However, this is of great importance only if you take these calculations very seriously and if you do, you probably should not be using most microcomputer-based programs. If you use the energy minimization routines only to "touch up" your molecular creation, then exact correspondence with energies derived from an authentic MMX program is probably not important. For comparable calculations, the ALCHEMY III minimizations have been reported to be rather slow. We checked this for a few of the same examples on the same machine using PC-Model[3] and ALCHEMY III, and it appears to be true. If rough structures are usually adequate for the problems at hand, then this is not a serious drawback.

National advertising for this program touts the Macintosh Quadra as a suitable platform. Considering the cost of a Quadra, this seems like a questionable marketing strategy because a humbler Macintosh (a IIci was used primarily for this review) seems adequate. Attempts to run the program on a Macintosh Powerbook 170 were foiled by the requirement for a color monitor. Considering the quality of the force field and the tailoring of the program to be used to prepare for MM2 calculations to be done on *another* machine, pushing an expensive piece of hardware like the Quadra for use of the program is puzzling.

A variety of interesting and useful desktop modeling programs is currently available for the Macintosh. Of these no single one will do all that a user might like. The usual advice about buying software applies here. The questions to ask are: What exactly do you want to do with this software? Are all of these things possible with the software being considered? If a special feature (such as the ability of ALCHEMY III to interface to STN Express) is important, then this unique feature alone may dictate purchasing ALCHEMY III.

If a user already has access to other members of the TRIPOS suite of programs, then ALCHEMY III is an excellent choice. It is also quite useful as a set of electronic Dreiding models for structure building, inspection of stereochemistry, and evaluation of geometry. However, if the user wants a stand-alone program for research-quality moleculer mechanics calculations, then it is inadequate. Such a user might look into MacMimic.[4] The program is weak in file interconversions, and it would not be suitable for the chemist interested in a front-end for computational chemistry programs such as MOPAC or the Gaussian Series. Here PC-Model or Chem-3D[5] might be worth investigating. If one wishes to prepare illustrations of three-dimensional structures for publication, then the hardcopy output of Chem-3D is superior.

Finally, it should be recognized that, just as with computers, software evaluation depends a great deal on personal preference. From personal experience we can state that the Macintosh programs—ALCHEMY III, PC-Model, and Chem-3D—are all extremely useful. To pick any one of them as "best" is not possible without considering the exact use to which they would be put. Someone obviously likes the ALCHEMY III package very much because during the course of preparing this review our copy of the manual was stolen.

REFERENCES AND NOTES

(1) Bays, J. P. *J. Chem. Educ.* **1992**, *69*, 209.
(2) ALCHEMY III is available from TRIPOS Associates, Inc., 1699 South Hanley Rd., Suite 303, St. Louis, MO 63144. Phone: 314-647-1099.
(3) PC-Model, Serena Software, Box 3076, Bloomington, IN 47402.
(4) MacMimic, Instar Software AB, Research Park IDEON, S-22370 Lund, Sweden.
(5) Chem3D, Cambridge Scientific Computing, Inc., 875 Massachusetts Ave., Suite 41, Cambridge, MA 02139.