COMPUTER SOFTWARE REVIEWS

Alchemy 2000 Version 1.00 for Windows: A Review

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Introduction. Developing tools for the next millenium. The new version of the Alchemy Tripos program is being called 2000. Like its older brother, Alchemy III, Alchemy 2000 is a molecular editor that offers some computational capabilities. The step into XXIst century is characterized by new graphics possibilities, openings to comprehensive file formats, and use of Windows 95 features. Thus, Tripos is investing again in "general audience" software, this kind of software that may be defined as cheap, working on a personal computer and with an easy-to-use interface. This review is intended to explore the capabilities of Alchemy 2000. It will try to be as objective as possible, but the opinion of the author may be influenced by his personal needs[1] in this software and previous relations with Hyperchem,[2] and Spartan,[3] even though it should be quite clear that the goals of Alchemy 2000 are rather different from those softwares.

System Requirements. The minimum hardware configuration as advised by Tripos[4] is a 486 processor, 8 Mb of RAM (16 Mb recommended), a hard disk with at least 40 Mb of free space, VGA graphics capabilities (800 × 600 pixels recommended), and a mouse. The system must run MS-DOS version 6.00 or higher and Windows version 3.11 or 95. As Alchemy 2000 relies on high definition graphics, the higher the performance of the computer graphics, the better. This study has been performed on a PC compatible with a Pentium processor (120 MHz) and 16 Mb of RAM, SVGA graphics, and 256 Kb of VRAM, running under Windows 95.

Installation, Help, and Documentation. The installation is as straightforward as any Windows program. A local code, depending on the actual computer it is run with, must be provided by the distributor the first time the program is launched. The Alchemy 2000 program is Windows 95 compatible, although it will automatically reduce more-than-eight-letters-long filenames, like Windows version 3 software does. Alchemy 2000 is a multiwindow software and is customizable. The Help menu can provide useful information using the index command. This is appreciated, because the documentation manuals are not very thick and contain no index. The first manual, called Getting Started, presents an overview of the Alchemy 2000 capabilities and functions as a tutorial. It contains 18 chapters: Introduction (8 pages), The Desktop (9 pages), Opening and Closing Files (9 pages), Movement of Molecules (6 pages), Selection Tools (10 pages), Displaying Small Molecules (12 pages), Displaying Proteins (12 pages), Multiwindow Environments (7 pages), Building Small Molecules (27 pages), Building a Protein (12 pages), Small Molecule Energy Minimization (12 pages), Semiempirical Methods (8 pages), Batchmode (11 pages), RMS Fit (3 pages), Determining Bond Lengths and Angles (8 pages), The Presentation Pane (15 pages), Preferences (6 pages), and Auxiliary Programs (4 pages). The second manual, called Technical Reference Manual, presents the functionalities of Alchemy 2000 (10 chapters: Introduction (2 pages), The Desktop (12 pages), Working with Small Molecules (8 pages), Working with Proteins (6 pages), Molecular Dimensions and Properties (4 pages), Basics of Molecular Calculations (9 pages), Batchmode and the Log (4 pages), The Presentation Pane (6 pages), Files Types (4 pages), and Customizing Alchemy 2000 (7 pages)) and details each menu command (15 chapters). Some commands are not available in version 1.00 (for example, the Set Bond length, Bond Angle, Dihedral commands, or the Charge menu in the 2D sketcher), but an upgrade will be provided soon free of charge. The manuals are especially brief when describing scientific techniques, such as molecular mechanics or semiempirical methods. Furthermore, Tripos provides 60 days of support free of charge.

Building Molecules. Building molecules is one of the best features in Alchemy 2000. One can choose to sketch a 2D structure with the 2D sketcher (formerly known as ChemPrint in the earlier versions of Alchemy). In this case, the user is presented with templates featuring most commonly drawn substructures and most commonly written functional groups. Those can be modified. The 2D structures may then be constructed in a simple drag and drop way. The 3D structure of the molecule is reached with the 2D-to-3D builder. Aromatic bond orders and chirality are taken into account, but the charge menu appears not to work. Also the 2D-to-3D builder can import Chemdraw and Isis draw files.

The other possibility is to build directly in a 3D mode, which can be more convenient if one is concerned with different conformations. The user is presented with a list of atom types corresponding to the Tripos force field. From this, the molecule can be built atom by atom (in which case each bond created can be rotated before a new atom is set) or from a fragment library. This library is comprehensive and, furthermore, can be edited, and substructures can be minimized, and then saved as a new fragment in the library. Also, a special builder can be utilised for peptides. Each amino acid sequence can be simply defined with its one letter code. Each sequence can be assigned a specific secondary structure and a specific rendering.

Displaying Molecules. Alchemy 2000 can read a very large number of file formats (Brookhaven pdb, SCIvision seq, MDL mol, Alchemy III mol, Sybyl mol2, Hyperchem, Tripos sybyl line notation, Swissprot/gcg, pir/nbrf pir,

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Chemdraw, Chemdraw connection table, Chemprint, Molecular presentations graphics, PC Model, Beilstein's institute rosdal, Softshell scf, MDL sd, MDL isis skc, Smiles, Kekule str file, MDL isis tgf, X-ray cartesian data) and moreover can export to cgm metafile, postscript, hp-gl, bioCAD catalyst tpl, windows metafile, and wordperfect graphics. The opening and displaying procedure is rather fast. For instance it took 25 s to open and display a Brookhaven PDB file of a rhinovirus coat protein (pdb4rhv.ent), whereas the same operation took 99 s with Hyperchem[2] but only 2 s with Rasmol.[5] The rendering of the molecules can be mixed in a variety of ways. The different chains of a protein can be separated easily, and a secondary structure determinator is provided. Furthermore, molecules can be saved in various image file formats with parameterized definition of the image. Last, a "presentation pane" is a tool that can mix 3D or 2D structures, texts, and images, for presentation exports.

Performing Calculations. Alchemy 2000 can perform properties calculations (volume, surface, ovality, dipole moment via a Gasteiger Marsili charge calculation) and RMS fit. It can also list bond distances, angles or dihedrals, and export them to a Excel file, which can be a rather straightforward way of plotting a crystallographic Ramachandran map.

Alchemy 2000 can do molecular mechanics calculations. The two force fields provided are the Tripos force field[6] and the MM3(94) force field. Single point or geometry optimization can be performed, but the former force field can only yield a (total) steric energy, while the latter yields a typical MM3 text output. Atom types can be chosen for the Tripos force field, but they are automatically assigned for the MM3 force field. The MM3 energy terms can be saved as an Excel file. A batchmode process can be used to perform a series of calculations on several files. The graphing capability associated with it is useless for dihedral driving because it automatically sorts the files by decreasing order of one of the properties displayed. This can be bypassed with an Excel export.

Alchemy 2000 also has semiempirical capabilities. As for molecular mechanics, single point energy and geometry optimization are available with the PM3 method. Only total energies, eigenvalues, and point charges are yielded with this calculation. They can be exported to Excel. An access to a MOPAC 6 code is also provided, as an external program like MM3, and like MM3, the output is a MOPAC text file. No graphing capabilities such as orbital displaying are provided. In order to compare calculation velocities, a PM3 single point energy calculation of coronene ($C_{24}H_{12}$) with an SCF convergence limit of 0.01 was performed. It took 18 s for Alchemy and 9 s for Hyperchem[2] to complete the task.

Conclusions. The powerful capabilities of molecular editing (especially the numerous file imports and exports and the fragment library) as well as the customizable multiwindow environment and the rendering capabilities make Alchemy 2000 a new generation software in molecule manipulation. Unfortunately, the computational part of the software is too limited, especially in the utilization of results. Also, the computational engine appears to the user as a black box, with very scarce explanations about the calculations undertaken. This is prejudiciable in a teaching utilization perspective. Alchemy 2000 is currently running version 1.00. New plans for computational chemistry (such as molecular dynamics, conformational search or dihedral driving) are foreseen for a next version. This software has the potentiality of growing into a widely accepted tool in the research and teaching area. It still has to grow to reach this goal.

Software Distribution. Alchemy 2000 is distributed by Tripos (Tripos Inc., 1699 South Hanley Road, St. Louis, MO, U.S.A.). This company maintains a world wide web site (http://www.tripos.com) with a worldwide distributors list, a frequently asked questions page, information about training courses, and a description of support available. Some auxiliary programs, that were not tested here, can be purchased. There are four of them, apparently coming from Scivision. SciQSAR creates structure−activity or structure−property relationships. SciProtein provides additional tools for handling peptides, such as homology searching, motif identification, sequence property maps, and prediction of secondary structures. Scipolymer predicts structure−property relations for polymers. SciLogP calculates lipophilicities.

REFERENCES AND NOTES

(1) Hocquet, A. Teaching molecular mechanics in the chemistry curriculum. *L'actualité Chimique*. Submitted for publication.
(2) Hyperchem version 4.5, for Windows; Hypercube Inc., 419 Phillip St., Waterloo, Ontario, Canada.
(3) Spartan version 3.1, for Silicon Graphics; Wavefunction Inc., 18401 Von Karman #370, Irvine, CA, U.S.A.
(4) Alchemy 2000 version 1.0, Getting Started manual; Tripos Inc., 1699 South Hanley Road, ST Louis, MO, U.S.A.
(5) Rasmol version 2.5; Sayle R., Glaxo: Greensford, Middlesex, UK.
(6) Clark, M.; Cramer, III R. D.; Van Opdenbosch, N. Validation of the general purpose Tripos 5.2 force field. *J. Comput. Chem.* **1989**, *10*, 982−1012.

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