COMPUTER SOFTWARE REVIEWS

ALCHEMY

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ALCHEMY is an interactive, three-dimensional, real time, menu-driven molecular graphics and editor program package running on a PC/XT or AT with an enhanced graphic adaptor graphics card, at least 512 kbytes of processor memory, and an MS mouse. Plotter is very desirable. Hard disk is recommended. ALCHEMY is a user-friendly program package. Help is available online.

ALCHEMY is designed to build models of small molecules (Figure 1) rather than large ones like biopolymers, for example. It offers to the user a "filling" for a three-dimensional model of a generated molecule.

A molecule in ALCHEMY is a set of atoms generated by using a Build and Edit mode (Figure 2) from atoms (C3 is, for example, C sp^3 hybridized, tetrahedral carbon), groups of atoms (COOH), and fragments (phenyl) or a molecular data file read from disk and later updated. All functions with the exception of those referring to the screen manipulation can be activated on one molecule at a time only.

ALCHEMY enables the user to build molecules from atoms and fragments interactively using the electronic form of Dreiding model construction (ring fusion is possible as well), modify a molecular conformation by redefinition of the appropriate bonds and bond and dihedral angles or by optimization of molecular structures using an energy minimization procedure, change the position of atom centers of molecules either by translation and rotation in three dimensions with the mouse or by superimposition of two molecules using the least-squares fitting routine, download generated molecular data ASCII files to disk and later on to retrieve them, and write down and retrieve a molecular data file in SYBYL format. (SYBYL is a computer program for molecular mechanics designed by Tripos Associates, Inc.)

Brief Description of Functions. The user's action results in an immediate modification of the molecule's image on the screen. All molecules present in the program are displayed on the screen as long as they do not drop out of the visible area. The number of atoms in a molecule is limited only by the user's ability to trace them in the image. The number of atoms that can be resolved depends on the distances among the atom centers in the molecules. In a comparison study we were able to work simultaneously with 6 molecules (all together around 150 atoms) with their atom centers quite close together using different coloring for each molecule and stereo projection. When atom centers are well separated, not coming closer than the sum of their van der Waals radia, molecular models of a few hundred atoms can be resolved; hence, models of small proteins can be treated. By use of mono images only, the number of atoms in observed molecules is approximately quartered. Of course, while the number of atoms is increasing, the program's response time is increasing, especially for the functions transforming atom center coordinates.

The user can choose between 15 different colors for the entire molecule or select the default atom type coloring. The user cannot define colors for atom types or parts of the molecule or change the definition of colors in the video look-up table. The generated molecule models can be presented as a space-filling model of spherical atoms with van der Waals radia. Spheres are not shaded.

Optimization of a molecular structure model assumes the molecule to be in the gas phase. ALCHEMY uses the empirical energy force field parameters for energetic optimization of generated molecular conformations. In general, the construction of a molecular model based on geometrical properties in combination with the empirical energy force field does not yield very reliable results. When the user has access to other more reliable sources of molecular structures (X-ray, NMR, molecular or quantum mechanics programs, etc.), it makes sense to connect different formats of molecular data files. The ALCHEMY molecular data file contains a list of atoms with their coordinates and bond connections. The ALCHEMY molecular data file cannot be easily created with a text editor. ALCHEMY does not warn the user for reading in wrong atom coordinates. For example, if instead of a coordinate value of 1.2345 a string 1.2G45 has been written, ALCHEMY interprets this as 1.2000. It would be easier for the user to detect this type of error if the coordinate were interpreted as 0.0000 or 9999.999. When there is an atom missing in the molecular data file, the user obtains an avalanche of messages, quickly disappearing one after another from the screen. It would be much better for the user if at the point where a mistake is detected, the interpretation were interrupted and the appropriate message displayed. Because editing errors can sometimes be hard to detect, additional computer programming is recommended to avoid them.

From the standpoint of many research areas it seems inconvenient to work only with one molecule at a time. Generating a molecular complex with ALCHEMY is rather complicated. The relative positions of atoms in the molecule can be changed only when they are connected via covalent bonds from the Build and Edit mode. Relative positions of atoms in different molecules can be changed by using relative translations and rotations governed by the mouse. Usually, a molecule is a group of atoms connected via a net of covalent links. A molecular complex is a set of such molecules. In order to generate and optimize a structure of a molecular complex, the user ought to overcome ALCHEMY's concept of allowing the functions to act only on one molecule. This can be achieved by generating the molecular complex as one ALCHEMY molecule. Using the Build and Edit mode, the user builds the molecular complex with all the atoms, including linking ones as dummies. In order to disconnect different atom groups, the dummy atoms are later deleted. From the manual and from the built-in force field parameters, it is not clear whether these parameters were optimized for application on molecular complexes or not.

ALCHEMY as a stand-alone program can be very useful for chemists needing fast and reasonably reliable three-dimensional models of molecules, for pedagogical use, and for those eager

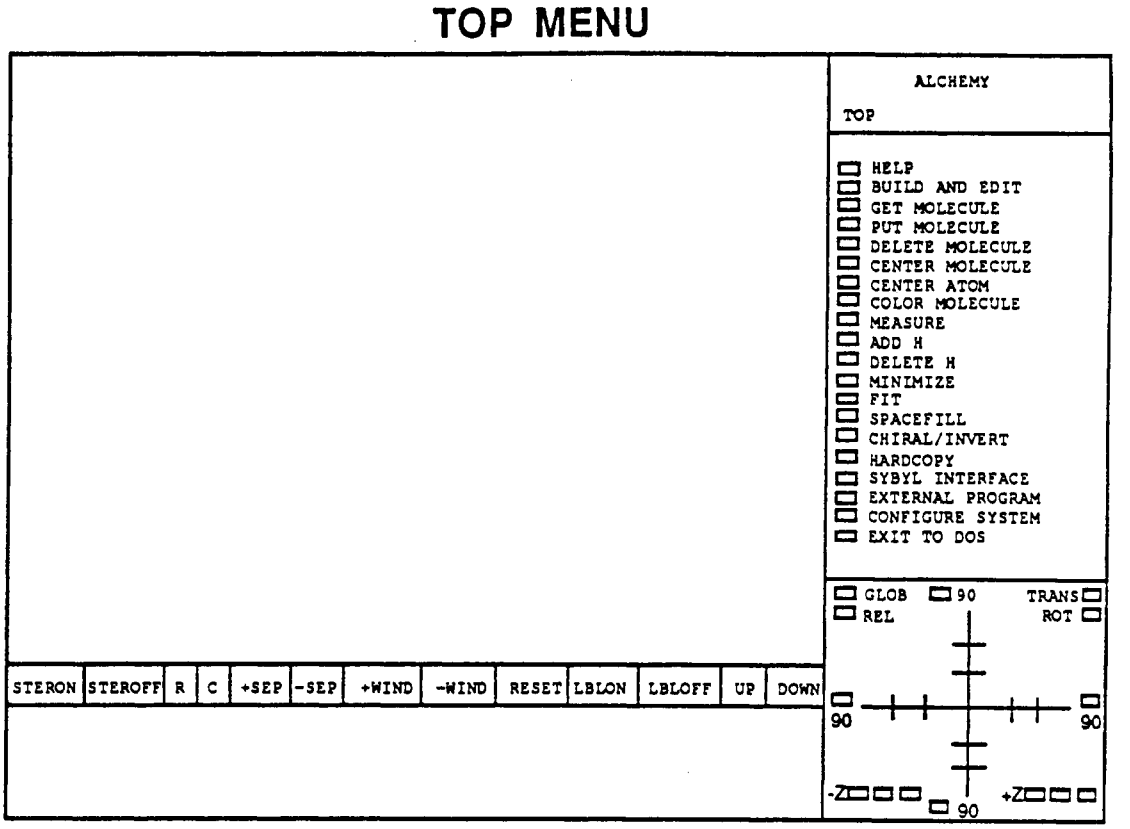

Figure 1. Scheme of ALCHEMY's top menu from the manual.

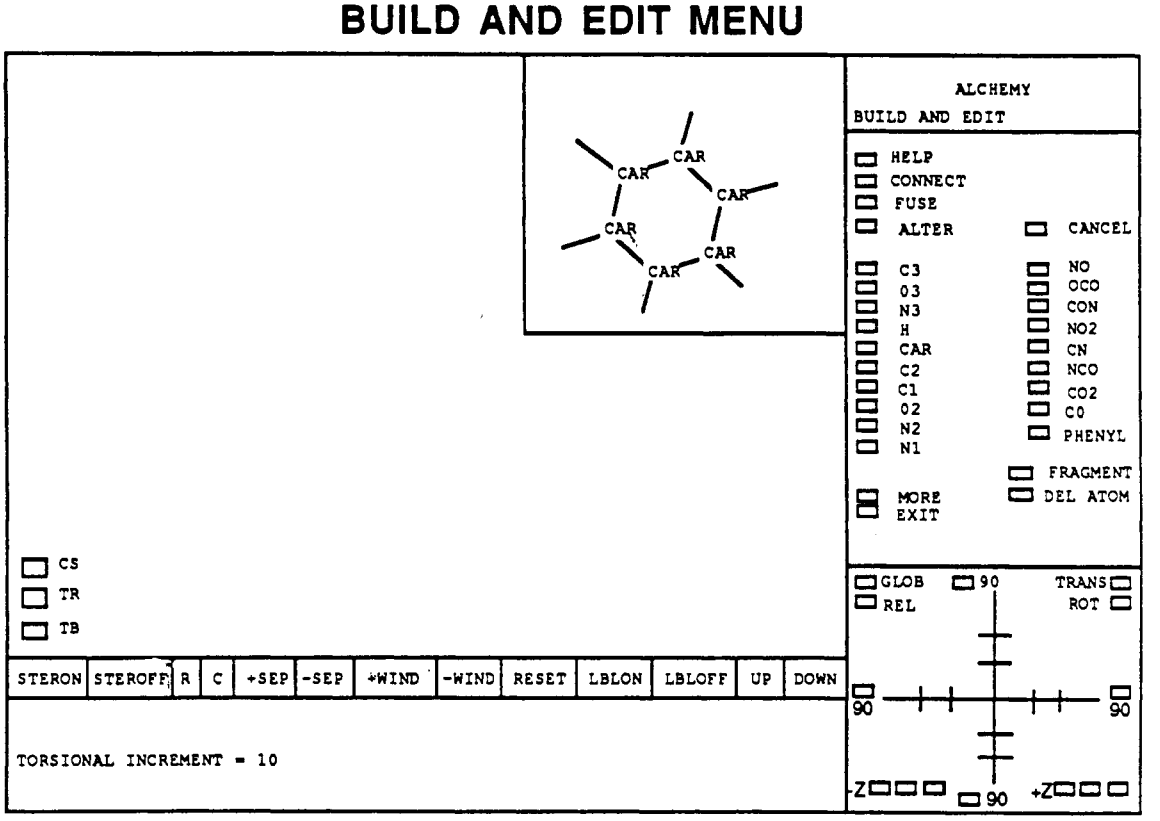

Figure 2. Scheme of ALCHEMY's Build and Edit menu from the manual.

to handle molecular structures but disliking or having no possibility to access large computer or powerful graphics systems.

Manual. The manual is appropriate, clearly written, well organized, well printed, and easy to read. It is written as a user's and as a reference manual, so it gives instructions on how to install and use the program. The latter can be mastered within a few hours. Our suggestion is that the producers should add a few words about the general goals of ALCHEMY. ALCHEMY does not and cannot cover all the areas of molecule structure research, and the addition of comments on most prospective areas of its use could give the potential user a better

feeling of why he or she should buy it.

Comments. In order to test the general concept and "psychology" of the program, we first tried to use ALCHEMY without reading the manual. The use of functions and their mnemonics seems to be natural. We were able to use most of ALCHEMY's functions as they were intended. It can be said that ALCHEMY is a user-friendly package. When the user's action is not in agreement with ALCHEMY's demands, an appropriate message is usually given.

We appreciate the concept that the user can start from atoms and later on generate atom groups and fragments of his or her own in order to effectively apply ALCHEMY to a specific area of research. It should be said, however, that as a consequence of this flexibility electrostatic potential as an additional energy term cannot be included in the energy calculations.

We also appreciate that the time-consuming processes (minimization and space-filling imaging) can be interrupted within ALCHEMY.

The rectangles to be hit with the mouse in order to govern ALCHEMY's commands are too small to allow rapid communication. The areas in Figure 1 are relatively larger on the scheme than they are on the screen.

Orientation of unfilled valence bonds of the last appended atom can be changed interactively by step rotation. It would be nice to extend this interactive real time rotation on any bond.

Applying an energy optimization procedure to a molecular conformation results in a conformation with low energy and small forces acting on atoms. On a few occasions the conjugated gradient method built into ALCHEMY did not succeed in improving the conformation of a molecule, in spite of the fact that the energy of conformation was extremely high and very large forces were acting on atoms. The number of atoms that could be efficiently used in the molecule is not very large; hence, some other optimization method might work better, although not that fast (for example, the Newton–Raphson method). The user would like to have a choice among more methods.

ALCHEMY's editing concept is not consistent throughout the program. If there is more than one molecule contained on the screen, the user entering the Build and Edit mode should pick the molecule he or she wants to edit. All the functions except the one for deleting atoms can be activated only on the chosen molecule. Atoms can be deleted on any molecule.

We were not able to crash ALCHEMY and could not make the program get lost by using built-in data files, but we did lose the molecule structure. When the user is changing the dihedral angle of the atoms for which the bond angle is set close to zero, atom centers in a molecule are fused into a straight line. Such a molecule could not be put to the coordinate center with the command "Center molecule" or "Center atom" any longer.

If the user saves a molecule with all filled valences as a fragment, it cannot be connected to already existing molecular structures. The user should get an appropriate message but not one saying "Sorry, but the bond types are not of the same".

If atom labels are excluded from the image, this should apply as well for a molecule appended to already existing ones from a disk file.

Conclusion. Due to the fact that intensive handling of chemical structures is an everyday occupation for many chemists, spectroscopists, pharmacologists, and others, ALCHEMY implemented on a PC can be of very good help for many of them. Apart from some minor shortcomings that could easily be corrected in following versions, ALCHEMY is a package that should be seriously considered as a part of accessible software for many laboratories.

ALCHEMY is copy protected. No source code is available. A special license for updates of ALCHEMY would be recommended. The user can return ALCHEMY within a 3-day period if he or she is not satisfied with the program.

Product: ALCHEMY

Price: Tripos Associates, Inc., 6548 Clayton Road, St. Louis, MO 63117 [(314) 647-1099].

Hardware requirements: IBM-PC/XT/AT or compatible; at least 512 kbytes of processor memory; one 1.2-Mbyte floppy disk drive or two 360-kbyte floppy disk drives; serial port; mouse from either Mouse Systems, Inc., or Microsoft Corp., enhanced graphic adaptor (EGA) or compatible with at least 256 kbytes of graphic memory; appropriate EGA monitor.

Hardware recommendations: hard disk drive; floating point coprocessor.

Plotters supported: plotter that uses the HPGL plotter commands as defined by Hewlett-Packard, Inc., with a serial interface connected to a second serial port on PC.

GRAPH X

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GRAPH X is a library of subroutines (procedures) for generating graphics on screen (0–719, 0–347 pixels) and on dot-matrix printers if the PC is equipped with a Hercules graphics card. The library consists of 15 on-screen programs and a hardcopy program for printing the generated graphic images (both pages, 0 and 1, in normal or reverse video form) on a dot-matrix printers (see Table I). The routines (procedures) can be used in FORTRAN, Pascal, Turbo Pascal, BASICA, Compiled BASIC, and Assembly language. Although C language is not mentioned in the manual, the software supplied to us contained the graphics library for C language as well.

GRAPH X is a well-defined and concise set of routines that programmers (with the exception of Turbo Pascal users) of PC's are waiting for. I like the easiness of implementation and linking with already compiled programs as well as the possibility to include the graphics library into the existing high level language libraries (FORTRAN, Pascal, etc.). The manual is clearly written and easy to follow. There are few typographical errors in the programming guidelines, and some of them are already corrected on the supplied floppy disk. The hardcopy routine can be activated from the program or executed on the system prompt.

The assortment of routines is parsimonious, although it must be admitted that the existing set is sufficient to program far more than meets the eye. However, the lack of any "comfort" keeps the programmer very busy. Even only a slightly complicated task (as, for example, deleting a line) must be pro-