be changed easily to take advantage of the output medium.

This work was performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under contract number W–7405–Eng–48 and was partially supported by an Institutional Research and Development grant.

## An Educational Molecule-Building Simulation Using Interactive Computer Graphics

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A microcomputer simulation is presented that allows students to build molecules from the first 18 elements of the periodic table. Ball-and-stick representations of atoms and molecules can be manipulated to produce colored three-dimensional structures. This is accomplished by "breaking the bonds" of on-screen molecules and recombining the parts to form a new molecule. A total of 144 different molecules can be created in this way.

The Lewis structure is also shown for each atom and molecule involved. A "three-dimensional" picture of each individual atom can be viewed, showing all its nucleons and electron orbitals. Finally, the physical properties of the component elements and the completed molecules are presented pictorially (and with sound effects) to indicate color, state, melting and boiling points, acid/base properties, heat of reaction and toxicity.

Approved by the Ontario Ministry of Education as exemplary lessonware for high school chemistry classrooms, this microcomputer program with its extensive database is also being used in undergraduate instruction at the University of Toronto.

## Applications of Artificial Intelligence Techniques in Conformational Analysis

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There are a number of different ways to describe a molecule's conformation. Numerically based techniques, such as energy calculation and molecular fitting, usually require the specification of the atomic coordinates and sometimes the atomic connectivity. However, this method is largely impractical for the chemist, who uses a more abstract description based upon groups of connected atoms (conformational units) about whose behavior he has some knowledge (e.g., "chair" cyclohexane). An important role of computer graphics is to provide the chemist with a means of interconverting between the numerical and the abstract descriptions.

We are developing an expert system, WIZARD–II, that aims to link these two approaches in the field of conformational analysis. The system generates high-level descriptions of a molecule by recognizing conformational units and the way in which these units are joined together. This then enables it to reason at an abstract level about the conformational possibilities available to the molecule. One application of such a system is in searching the conformational space of a molecule. If desired, the conformations it generates can then be minimized using a program such as MM2. However, in many cases, the initial conformations suggested by WIZARD lie very close to the structures obtained by energy minimization or by experimental methods such as X-ray crystallography. WIZARD can therefore be used on its own to generate structures that are good approximations to the minimum energy conformations.

This is in contrast with many of the alternative methods used to search conformational space. Such methods (e.g., torsion angle driving or random search techniques) generate an initial structure that is then driven to an energy minimum. There is frequently a significant difference between the structure initially suggested and that eventually obtained, and the minimization is therefore an integral part of such methods. Some important classes of molecules cannot yet be tackled by these techniques, as the necessary energy calculations cannot be performed (for example, because the molecular mechanics force field lacks some of the required parameters).

The conformational properties of many inorganic complexes and organometallic compounds have not been investigated for this reason, yet the ability to generate low-energy conformations for such molecules would be of use in a wide variety of fields. We are therefore investigating how the techniques employed in WIZARD can be applied to this class of molecules. We initially chose to examine transition metal coordination complexes because these show some similarities with the molecules previously investigated using WIZARD. We are now extending the system to cover a wider variety of similar molecules.

## A New Approach to Rational Drug Design: Automated Structure Generation at Specified Binding Sites

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The goal of rational drug design is to construct *de novo* therapeutically useful ligands. This aim can be achieved only by a thorough understanding and description of the forces involved in molecular recognition and binding. Molecular graphics programs display regions of putative binding on protein surfaces; possible ligand binding sites can be found so that a profile of the active site can be constructed. This type of information could guide an automated structure generator; it is hoped that candidate molecules will be produced that match the hydro-