ChemPlus for Windows

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Received March 19, 1996

INTRODUCTION

ChemPlus is a new software product of Hypercube, consisting of a set of extension modules for HyperChem, which augment and enhance the functionality of HyperChem. Each distinct module of ChemPlus interacts with HyperChem, bringing to the user eight new functionalities for HyperChem: RMS Fit, a module for overlaying molecules by minimizing the distances between atoms; Molecule Presentations, a module which provides a number of renderings for molecules and molecular orbitals not available in HyperChem; the Sequence Editor, which creates from a one-letter amino acid sequence the three-dimensional structure which can be sent to HyperChem; Crystal Builder, a module for reading, creating, and viewing crystal structures with HyperChem; Sugar Builder, a module which allows the user to build polysaccharide structures; the Conformational Search module which may be used for finding low energy conformations of molecular systems by varying user-defined dihedral angles; QSAR Properties, a module which allows several properties commonly used in QSAR (Quantitative Structure−Activity Relationships) studies to be calculated; Script Editor, a module which provides an environment for developing and editing HyperChem scripts; ChemPlus contains also PhiPsi, an Excel 4 for Windows macro, that can be used with HyperChem to produce an energy surface as a function of two dihedral angles.

ChemPlus offers useful extensions to HyperChem and allows one to investigate new areas of theoretical chemistry, like crystal chemistry or empirical QSAR parameters.

SYSTEM REQUIREMENTS

The equipment requirements of ChemPlus are the same as for HyperChem: an IBM PC 386, 486, Pentium, or compatible with math coprocessor, 4 MB of RAM, 4 MB of free hard disk space, a VGA or SuperVGA video display, a mouse, Microsoft Windows 3.1 or higher version, and DOS 5 or a later version. The evaluation of ChemPlus presented in this review is based on installation and testing on an IBM PC 486 DX2 computer at 66 MHz with 16 MB of RAM and with HyperChem 4.5 installed on.

INSTALLATION AND DOCUMENTATION

In order to use ChemPlus, one must have a version of HyperChem installed on the computer. The installation of ChemPlus is easy to perform and follows the usual procedure of Windows-based programs. In the installation process, the ChemPlus Setup program places a ChemPlus icon in the HyperChem Program Manager group. Double clicking on this icon attaches the ChemPlus modules to appropriate menus in HyperChem, and also it will start HyperChem if it is not already running. The modules of ChemPlus are launched from the HyperChem menus. Once launched, each module communicates with HyperChem using Windows Dynamic Data Exchange. The ChemPlus modules can be launched individually from the Program Manager, by double clicking on the icon of the appropriate module. The ChemPlus modules may not work properly if there is more than one copy of HyperChem active at a time.

The printed documentation of ChemPlus consists in a manual of 174 pages which includes 11 chapters. The first one is a short introduction, Chapter 2 describes the installation procedure, while each of the remaining chapters describes a specific ChemPlus module independent of any of the other extensions. Each chapter gives an overview of the module, a tutorial to help the user to learn how to use the module, a background on the new capability that the extension adds to HyperChem, and a reference section that details the menus and commands.

THE CHEMPLUS MODULES

We will present a short description of the modules of ChemPlus, and their use in interaction with HyperChem.

RMS Fit. The RMS Fit module can be used for overlaying molecules by minimizing the distance between atoms. The RMS value of the residual distance (in Å) is reported on the status line as a measure of the similarity of the two molecules. The RMS Fit module is compatible with the selection mode of operation of HyperChem. If there are atoms selected, only these atoms will be overlayed. Otherwise, if no atoms are selected from the two molecules, then all atoms are considered in the RMS fitting process. The residual RMS distance is reported on the HyperChem status line. The RMS Fit overlay by molecule numbering is used when overlaying two conformations of the same molecule, while overlay by selection order is appropriate for comparing a series of structurally related molecules.

Molecule Presentations. The Molecule Presentations module provides some new renderings of molecules and molecular orbitals which are not available in HyperChem. In Molecule Presentations atoms can be rendered as either disks or shaded spheres, and bonds can appear as sticks, unshaded cylinders, or shaded cylinders. This can yield the ball and stick rendering of molecules that is not available in HyperChem. Also, the three-dimensional envelopes of molecules can be displayed as wire meshes or solid surfaces. When atoms are rendered as sticks the user can specify text labels which are displayed with each atom.

After computing the molecular wave functions of a molecular system by a quantum chemical method, the user can select an orbital and display it in Molecule Presentations. There are three rendering methods for orbitals: wire mesh, flat surface, and shaded surface. The module has a number of options for the display of orbitals: the user can change

the isosurface value at which the orbital is displayed, can modify the colors for orbital lobes and contour lines, can adjust the number of points in the mesh used to render the orbital, or can modify atom colors or radii. The molecular orbital can be viewed by rotating the molecule.

The printed output from the Molecular Presentations module is superior to that available for HyperChem spheres rendering.

Sequence Editor. The Sequence Editor module can be used to create a one-letter amino acid sequence or to read it from a sequence database. To the primary structure of the sequence the user can assign a secondary structure: α helix, β sheet, β turn, or random coil. The three-dimensional structure of a protein can be imported in HyperChem for molecular modeling. The Sequence Editor can also be used to view certain properties of a sequence of amino acids, such as the percentage of individual residues, the hydrophobic character of residues, to view two sequences and compare them. The probability of substitution of one amino acid with another can be obtained by the use of the Dayhoff Matrix option.

Crystal Builder. The Crystal Builder module offers important features for the inorganic chemists, allowing one to read, create, and view crystal structures. With HyperChem the user can save or edit the crystal structure or can apply various molecular and quantum mechanics calculations to it. With Crystal Builder it is easy to generate crystals having one of the basic crystal types: cubic, tetragonal, orthorhombic, rhombohedral, hexagonal, monoclinic, triclinic, face-centered cubic, body-centered cubic, and hexagonal close-packed. The module has some basic crystal structures, enabling one to use them or to modify them in order to generate related crystal structures. The sample crystal structures contained in Crystal Builder are as follows: NaCl, CsCl, CaF_2, diamond, PbS, MgO, CuZn, RbCl, ZnS (zincblende and wurtzite), AgI, CuCl, Ar, Cu, Au, Na, NbO, Zn, TiO_2, $MgAl_2O_4$, $CaTiO_3$, and PtS. The module can read and write files in the Cambridge Structural Database format as well as HyperChem's HIN format.

Sugar Builder. The Sugar Builder module allows the user to build polysaccharide structures in a manner similar to the use of amino acids and nucleic acids databases of HyperChem. Also, the user can define new residues, which need not be saccharides, and use Sugar Builder to link them together. The module contains 32 templates of monosaccharides including aldoses and ketoses, in different forms: D, L, α, β, and acyclic forms. The user can select from a set of 11 saccharide residues, like glucosamine, galactosamine, inositol, fucose and apiose, and a number of common blocking groups, like NH_2, =O, Me, −OMe, *O*-acetyl, and *N*-acetyl. Two chains can be connected together so as to form branched oligosaccharides. The module contains special AMBER parameters for polysaccharides.[1]

Conformational Search. The Conformational Search module can be used for finding low-energy conformations of molecular systems by varying selected dihedral angles. The method implemented involves random variation of dihedral angles to generate new structures and then energy minimizing each of those. Low-energy conformations are stored, while high-energy or duplicate structures are discarded. New conformations are generated by rotation for acyclic bond dihedral angles, while for dihedral angles in a ring the module uses the "torsional flexing" method of Kolossvary and Guida.[2] The goal of a conformational search is to identify the global minimum of the potential energy surface and to determine all conformations that are close to the global minimum. In the process of global minimum identification the selection of the initial structure is done by a "random walk" scheme, which uses the last accepted conformation, or by the "usage directed" scheme,[3] which uses all previously accepted conformations (in order from lowest energy to highest) when selecting each initial structure. When the generated structure is minimized, the module uses two types of criteria to decide when to accept the new conformation, geometric and energetic criteria, respectively. The geometric comparison is made with previously accepted unique conformations, by a superposition of the conformers. When the comparison indices fall within a specified tolerance, then the new conformation is discarded. The energetic tests for accepting a new conformer are of two types: a cutoff relative to the lowest energy previously found or a Metropolis rule where higher energy structures are accepted with a probability determined by the energy differences and the temperature of the system.[4] The results of a conformational search are stored in a Hypercube Conformational Search file which is a text file that contains all search options, a HIN description of the molecule, the chosen torsions, the defined rings, and the results of the search including the coordinates for all conformations that are accepted.

QSAR Properties. The QSAR Properties module can be used to calculate a number of structural descriptors used in QSAR analysis. Some important quantum descriptors can be computed by HyperChem alone, but with this module one can use fast empirical models to compute important QSAR parameters: atomic partial charges, van der Waals and solvent accessible surface areas and volumes, hydration energy for peptides, log *P*, the molar refractivity, polarizability, and mass.

Partial Charges. This section computes the atomic partial charges by using the Partial Equalization of Orbital Electronegativity (PEOE) empirical method of Gasteiger and Marsili.[5] Because this method considers only the molecular graph, the PEOE charges are not sensitive to conformational changes.

Surface Area (Approximate). This option can be used to compute the van der Waals and solvent-accessible surface areas by an approximate method introduced by Still.[6] This fast method is parameterized for organic molecules and is accurate to within 10%, but in some cases we have obtained results with a larger error, e.g., in the case of fullerenes.

Surface Area (Grid). This second method to compute the van der Waals and solvent-accessible surface areas is more accurate for a given set of atomic radii but slower than the previous one. The grid algorithm[7] is recommended for a precise molecular surface area calculation, which can offer also the atomic contributions to the total surface area. The type of surface (van der Waals or solvent-accessible) and the density of grid points can be specified by the user. The grid method uses the atomic radii determined by Gavezotti.[8]

Volume. This module can be used for the calculation of the van der Waals or solvent-accessible molecular volume using a grid algorithm. Its precision depends on the number of points in the grid. The user must specify the type of

surface (van der Waals or solvent-accessible) and the density of grid points.

Hydration Energy. The hydration energy is an important factor for determining the stability of different molecular conformations. The method used in ChemPlus was developed by Scheraga[9] for peptides and uses the surface computed by the approximate method, weighted by atom type.

Log *P*. The octanol−water partition coefficient (log P) is one of the most important QSAR parameters. ChemPlus allows one to compute it with the atomic parameters developed by Ghose.[10,11]

Refractivity. Also of great importance as a QSAR parameter is the refractivity. The method and parameters developed by Ghose[10,11] are implemented in ChemPlus. Like log *P*, the parameters for the refractivity were parameterized for a large set of organic molecules with a variety of heteroatoms.

Polarizability. In ChemPlus, the polarizability is computed with an additivity scheme developed by Miller,[12] which contains parameters for different atom types.

Mass. This option can be used to calculate the mass of a molecular system.

With the QSAR Properties module the user can perform batch calculations on a set of molecules stored in HIN files. The batch calculations are controlled by an external program or macro. A convenient way to perform batch calculations is offered by Excel, which has a macro language which can interact with the QSAR Properties module.

Script Editor. The Script Editor module provides an easy to use environment for developing and editing HyperChem scripts. The editor can be used also for sending script messages to HyperChem without creating a script file, acting as a command-line interface to HyperChem.

PhiPsi. ChemPlus offers an Excel macro, PhiPsi, which can be used by HyperChem to produce an energy surface as a function of two dihedral angles. In the case of peptides, the macro can be used to generate Ramachandran plots. PhiPsi requires that both HyperChem and Excel be running and that the molecule is in the HyperChem workspace and has two dihedral angles as named selections.

The installation of ChemPlus was straightforward, and the modules were ready-to-run after installation. With a little practice to become familiar with the interface of the modules I was able to explore the extentions to HyperChem offered by ChemPlus. As a whole, the modules are very easy to use; there functionality corresponds to the description from the documentation, and, as far as we have tested them, they are free from numerical problems.

SOFTWARE DISTRIBUTION

ChemPlus for Windows is produced and distributed by Hypercube, Inc., 419 Phillip St., Waterloo, Ontario, Canada N2L 3X2; Tel. (519)-725-4040; Fax: (519)-725-5193; information hot-line: (800)-960-1871; E-mail information requests: info@hyper.com; E-mail support questions: support@hyper.com. The price of ChemPlus release 1.5 is $495 for academic and $795 for commercial users.

To obtain ChemPlus, contact one of the Hypercube dealers; the address of the nearest dealer can be obtained from Hypercube. Hypercube maintains a World Wide Web site at http://www.hyper.com.

CONCLUSIONS

ChemPlus contains modules which enhance the functionality of HyperChem, and the usual user of HyperChem will find it remarkably easy to use, enabling him to explore new areas of computational chemistry.

ChemPlus is well documented, and after testing all its modules we can conclude that there are no numerical problems. I use HyperChem regularly in my undergraduate and graduate courses, and I found some extensions offered by ChemPlus very useful in designing new classroom experiments, mainly in crystal and sugar chemistry. I consider very useful the option of the Sugar Builder module which allows the user to define and link together new residues, which need not be saccharides. This option opens the possibility to explore organic polymer chemistry. Also, the important topic of finding the low energy conformations of a flexible molecule is efficiently solved by Conformational Search module.

In summary, ChemPlus offers interesting and useful extentions to HyperChem, and we recommend it for all users of HyperChem, either for teaching or research.

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CI960442N