COMPUTER SOFTWARE REVIEWS

HyperNMR for Windows

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Received March 19, 1996

INTRODUCTION

HyperNMR for Windows is a new software product of Hypercube which enables the user to compute with an original semiempirical quantum mechanical approach the ^{1}H, ^{13}C, ^{15}N, ^{19}F, or ^{31}P NMR spectra of a molecular system containing the elements from hydrogen through argon (the elements potassium through xenon could also be present in the investigated molecule but are treated at a nonquantum level).

Starting from the three-dimensional structure of a molecule HyperNMR computes the chemical shifts and coupling constants for selected atoms followed by the determination of the frequencies and intensities of the one-dimensional NMR absorption spectrum. After the computation of the NMR spectrum, HyperNMR displays it, and the user can select and integrate peaks or can copy the spectrum via the Windows clipboard to other Windows applications in order to obtain a hard copy. HyperNMR provides also several rendering options for the molecules: disks and shaded spheres for atoms and sticks, unshaded cylinders, and shaded cylinders for bonds. Molecules can be rotated and translated, and atoms can be selected or deselected by using the mouse.

HyperNMR is easy to use and provides user-friendly tools and pull-down menus. This software can be used both for teaching basic elements of NMR spectroscopy or for research as an aid in structure elucidation of organic compounds.

SYSTEM REQUIREMENTS

HyperNMR requires an IBM PC 386, 486, Pentium or compatible with math coprocessor, 4 MB of RAM (8 MB of RAM recommended), 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. This evaluation of HyperNMR is based on installation and testing on an IBM PC 486 DX2 compatible computer at 66 MHz with 16 MB of RAM and with HyperChem 4.5 installed on.

INSTALLATION, HELP, AND DOCUMENTATION

The installation of HyperNMR follows the usual procedure of Windows-based programs and is very easy to perform. If a copy of HyperChem is detected by the setup program, then the HyperNMR icon is inserted into the HyperChem group. Otherwise, if HyperChem is missing from the computer, HyperNMR will be installed in a new group, the HyperNMR group. Although the NMR spectrum simulation program can be used without having a HyperChem copy on the computer, we recommend the frequent user of HyperNMR to use HyperChem to generate the three-dimensional structure of the molecule whose NMR spectrum is to be computed and to save it in a HIN (Hyperchem INput) file.

By double-clicking the HyperNMR icon (either from the HyperChem group or from the HyperNMR group) the NMR spectrum simulation software is launched and is ready to read a molecule from a molecular structure file and to compute its NMR spectrum. The user has access to an extensive on-line help available from the "Help" menu located on the menu bar.

The printed documentation of HyperNMR consists in a manual of 215 pages which includes six chapters. The first one is a short overview, Chapter 2 describes how to install HyperNMR, Chapter 3 is a short introduction to the basic ideas of HyperNMR, and Chapter 4 contains four tutorials on the basic operation of the HyperNMR program. The first tutorial is an introduction to the menus and tools of HyperNMR, and the second is a description of the computation of shielding constants, chemical shifts, and nuclear spin−spin coupling constants. The third tutorial gives the steps for the computing of the NMR spectrum, and the fourth tutorial is a guide for a HyperNMR calculation for a portion of a protein. Chapter 5 is the reference manual for HyperNMR, illustrated with many reproductions of screens and dialog boxes. It gives extensive information, with examples, for the use of the NMR spectrum simulator. For the advanced user there is a description on how to modify the atom typing rules together with information on the structure of the NMR files. Chapter 6 gives a full description of the theory used in NMR spectrum simulation program, namely the Typed Neglect of Differential Overlap (TNDO) method.

OPERATING THE SOFTWARE

Theoretical prediction of NMR spectra can be very helpful both for chemists and biochemists in structure elucidation of organic or bioorganic compounds, but usual semiempirical quantum chemical methods lack the generality needed to treat a wide range of chemical compounds. On the other hand, *ab initio* calculations provide accurate predictions for the NMR spectra, but their use is restricted to small systems due to the large computational time consumed.

HyperNMR uses a new semiempirical quantum mechanical methodology, the Typed Neglect of Differential Overlap (TNDO) method. The parameters used in the usual semiempirical quantum chemical methods treat each element with unique parameters independent of their hybridization state or chemical environment. HyperNMR uses a classification of atom types, according to their chemical environment,

which is used in molecular mechanics methods. As a result, in the TNDO method there are, for example, a set of parameters characterizing the carbon atom in different chemical environments.

HyperNMR contains two TNDO versions: TNDO/1, which uses atom types with the CNDO method, and TNDO/2 which derives from INDO. TNDO can be considered as a hybrid between a molecular mechanics method (from which it takes the concept of atom types) and a quantum chemical method (from which it uses the LCAO SCF MO treatment). The names and definitions of atom types are derived from the AMBER molecular mechanics method. Using the information from the HyperNMR manual the user can define new atom types and can add new parameters in the semiempirical parameter files.

Because the three-dimensional coordinates of a molecule represent the starting point for a TNDO computation, HyperNMR requires a source of molecular structure files. HyperNMR can transfer molecular structures directly from HyperChem via Dynamic Data Exchange or can read a molecular structure from a file, either in HIN format (produced by HyperChem) or in Z-matrix format (provided by MOPAC).

After loading a molecular system into HyperNMR, the user must assign atom types by using the "Calculate Atom Types" menu item from the "Edit" menu.

Before starting a TNDO computation, the user must perform various selections in the molecular system, either with HyperChem before getting the molecular system in HyperNMR or by using the tools offered by HyperNMR.

All atoms that are included in the TNDO quantum chemical calculation must be selected as "NMR atoms". Only elements hydrogen through argon can be included as "NMR atoms", while the elements potassium through xenon, if present in the moleclar system, are treated in a nonquantum chemical fashion.

By default, HyperNMR considers the atoms as the isotope with the highest natural abundance. If an atom is selected as an "labeled atom", then its nuclear spin will be equivalent with that of the next most abundent isotope, i.e., a labeled hydrogen atom will have a deuterium nucleus and a labeled carbon atom will have a ^{13}C nucleus, for example. This option allows the user to simulate ^{13}C or ^{14}N spectra or spectra of deuterated compounds.

Because the TNDO method computes the shielding constants and spin−spin coupling constants at a fixed nuclear geometry, equivalent atoms by conformational changes, for example, will not all have equal shielding constants. The user can specify sets of atoms whose shielding constants and spin−spin coupling constants are to be averaged prior to producing a spectrum.

After preparing the molecule by assigning atom types and by selecting quantum, NMR, and equivalent atoms, one can use the TNDO quantum method to calculate shielding and nuclear spin−spin coupling constants.

In the last step HyperNMR computes and displays the one-dimensional NMR spectrum for the type of nucleus and simulated spectrometer frequency specified by the user.

HyperNMR can be used to calculate a ^{1}H, ^{13}C, ^{15}N, ^{19}F, or ^{31}P spectrum of a molecular system. HyperNMR may compute only one type of NMR spectrum at a time, but from the same set of shielding and coupling constants the user can calculate multiple spectra. Also, the user can introduce a set of shielding and coupling constants which were not computed by HyperNMR and then compute the NMR spectrum using the new shielding and coupling constants.

Spectra can have peaks displayed as separate vertical lines, as an envelope, or both of them. The envelope of a peak is formed by applying a Gaussian or Lorentzian curve to each peak. The user can zoom a specific region in a spectrum, select a peak, integrate peaks to determine how many nuclei they represent, and display in a table the spectrum information.

For large organic or bioorganic compounds, such as polymers, proteins, or nucleic acids, it is not possible to carry out a complete TNDO quantum chemical calculation for the whole system. For such cases HyperNMR offers the mixed model option, in which the user selects the part of the system to treat at the quantum level with an electrostatic background generated by the unselected part of the molecular system.

The user can can copy a molecular representation or NMR results to the clipboard and import them in other Windows applications.

HyperNMR is a robust software and very fast in computing the shielding and spin−spin coupling contants of fairly large molecules. In order to appreciate the computing power of HyperNMR, we have to note that the shielding contants of small to medium organic compounds are computed in a few minutes. With the computer used for this review, the shielding constants for the C_{60} fullerene were computed in 18 min. The software operation conforms to the description from the printed documentation of HyperNMR, and in a short time we were able to perform the computation of the NMR spectra of interesting organic compounds.

SOFTWARE DISTRIBUTION

HyperNMR 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 the software is $695 for academic and $995 for commercial users.

To obtain HyperNMR, 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. From this site one can obtain information concerning the new products and releases.

CONCLUSIONS

HyperNMR introduces a new quantum chemical method for the simulation of the NMR spectra which can be applied to various molecules, from small organic compounds to biochemical macromolecules. The software is very easy to use, and with a little practice one is able to investigate the NMR spectra of a molecule starting from its three-dimensional structure. To fully benefit from the features of HyperNMR the user needs some practice with a molecular modeling software, and HyperChem is a good companion for HyperNMR, both for generating the three-dimensional structure and for making the various selections used by HyperNMR.

HyperNMR is an excellent program for learning NMR spectroscopy, and the teacher can use it for computational experiments or as an aid in interpreting real spectra. For

the students, the software operation is easy to learn, and they can concentrate on the interpretation of the results. Experimental chemists or biochemists can use HyperNMR as an additional tool in structure elucidation, while for theoretical chemists this is an opportunity to investigate large molecular systems, a task which is not feasible with the *ab initio* calculations of the NMR spectra.

The program is well documented, and its installation is easy. After extensive use of HyperNMR we have encountered no convergence or other numerical problems. The system is open for improvement, in the sense that the user can add new atom types or new sets of parameters for use with the TNDO quantum method.

HyperNMR is an excellent software, and we recomend its use both for teaching and research.

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