TEXAS A&M UNIVERSITY

NMR NEWSLETTER

No. 398

November 1991

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D-14							543 (20)
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D-130							
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FORTHCOMING NMR MEETINGS

Scientific Conference on the Application of Magnetic Resonance to the Cardiovascular System, Atlanta, Ga., **December 15-18, 1991**; Sponsored by the American Heart Assoc., 7272 Greenville Ave., Dallas, TX 75231-4596.

Eighth Australian NMR Conference, Lorne, Victoria, Australia, **February 2-6, 1992**; See Newsletter 391, 38.

33rd ENC (Experimental NMR Conference), Asilomar Conference Center, Pacific Grove, California, **March 29 - April 2, 1992**; Contact: ENC, 750 Audubon, East Lansing, MI 48823; (517) 332-3667

Sixth Washington University-ENI/Emerson Electric Co. Symposium on NMR, St. Louis, Missouri, **May 8, 1992**; Contact: Karen Klein at (314) 935-6405.

Third Annual Workshop on Magnetic Resonance Microscopy and Materials Imaging, Charlestown (Boston), Massachusetts, **May 11-12, 1992**; Contact: J. L. Ackerman or L. Garrido, Mass. General Hospital, NMR Center, 149 13th St., Charlestown, MA 02129; Tel. (617) 726-3083 or -5820; Fax: (617) 726-5819.; See Newsletter 398, 8.

Sixth International Symposium on Magnetic Resonance in Colloid and Interface Science, Florence, Italy, **June 22-26, 1992**; Contact: Prof. Giacomo Martini, Department of Chemistry, University of Florence, Via G. Capponi 9, 50121 Firenze, Italy.

ISMAR 92, the XIth Meeting of the International Society for Magnetic Resonance, Vancouver, B.C., Canada, **July 18-24, 1992**; Contact: Dr. C. A. Fyfe, Department of Chemistry, Univ. of British Columbia, Vancouver, BC, Canada V6T 1Z1.

Eleventh Annual Scientific Meeting and Exhibition, Society of Magnetic Resonance in Medicine, Berlin, Germany, **August 8-14, 1992**; Contact: S.M.R.M., 1918 University Ave., Suite 3C, Berkeley, CA 94704; (415) 841-1899, FAX: (415) 841-2340.

XV International Conference on Magnetic Resonance in Biological Systems, Jerusalem, Israel, **August 16 - 21, 1992**; Contact: Prof. Gil Navon, XV ICMRBS, P. O. Box 3190, Tel Aviv 61031, Israel.; Tel. (972-3) 5271111, Fax: (972-3) 5239099.

High Resolution NMR Spectroscopy (a residential school), University of Sheffield, England, **April 1993**[*sic*]; Organizer: Dr. B. E. Mann (Sheffield); For information, contact Ms. L. Hart, The Royal Society of Chemistry, Burlington House, Piccadilly, London W1V 0BN, England; Tel.: 071-437-8656.

Additional listings of meetings, etc., are invited.

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All Newsletter Correspondence

Should Be Addressed To:

Dr. Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303, U.S.A.

(415) 493-5971

DEADLINE DATES

No. 400 (January) - * 13 December 1991 *
No. 401 (February) -------- 24 January 1992
No. 402 (March)----------21 February 1992
No. 403 (April) ----------20 March 1992

* *Please note that this date is somewhat earlier in the month than usual !!*

* * * * *

Congratulations

to

Richard R. Ernst

for the award of the

Nobel Prize

in

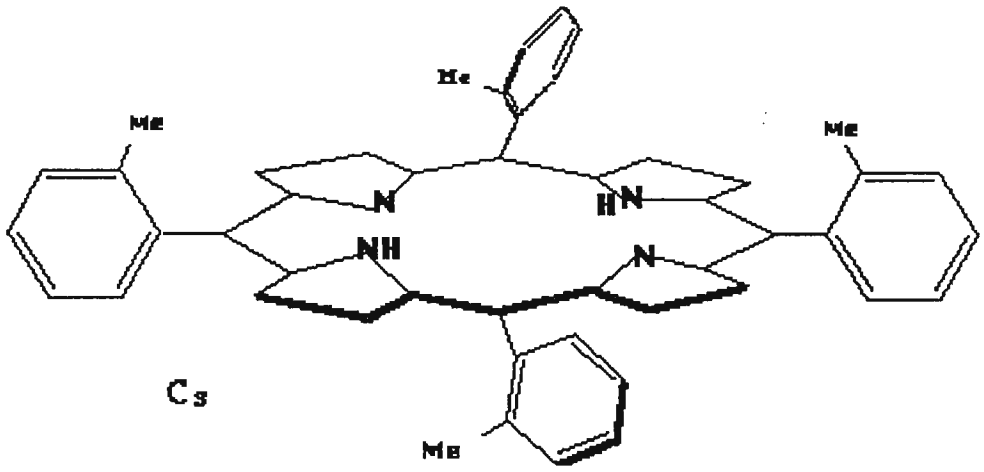
Chemistry

October 1991

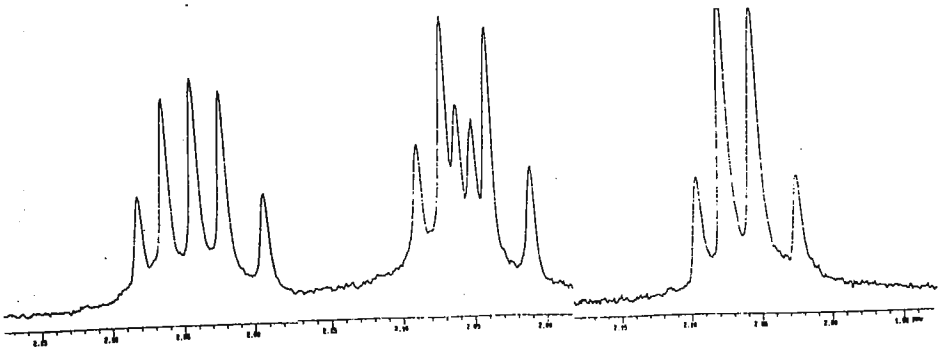
Unusual Temperature Dependent Chemical Shifts for 5,10,15,20-tetrakis(2-methylphenyl)-21H, 23H-Porphine

(received 10/8/91)

The title compound exists in solution as a mixture of four atroposiomers, differing in the orientation of the four 2-methylphenyl rings held perpendicular to the porphyrin plane.



When rotation of the aryl rings is slow but the proton exchange among the central nitrogens is fast on the NMR time scale, the four isomers have C_s, C_{2h}, D_{2d} and C_{4v} symmetry respectively. Based on symmetry considerations these isomers should be in relative abundance of 4:2:1:1 respectively. In $CDCl_3$ at -20° the methyl proton region of the NMR spectrum of the mixture of four isomers features five resonances with intensities 1:2:2:2:1. Upon increasing the temperature from 0° to 40° the central line separates into two lines, one moving upfield and one downfield with increasing temperature. The resulting 1:2:1:1:2:1 six line pattern can be rationalized in terms of the four atropoisomers: three lines in a 1:2:1 pattern arise from the C_s species, a single line of double amplitude corresponds to the C_v species, and the other two diastreomers appear as singlets. Above 40°, the two internal singlets have merged with the two tall lines for C_s and C_{2h} to yield a 1:3:3:1 "quartet." These four resonances are temperature independent over the range 40°C to +75° in $CDCl_3$, indicating that this effect cannot be attributed to rapid rotation of the aryl groups. Only at temperatures well above 100° in the higher boiling solvent $C_6D_5NO_2$ does the aryl group rotation become rapid on the NMR time scale so that the remaining lines merge to a single line. To our knowledge unusual o-methyl chemical shift changes at temperatures well below those favoring rapid aryl group rotation have not been reported. These shift changes are occuring over the same temperature range as when proton exchange among the central nitrogens is frozen out. We would appreciate suggestions from readers regarding the explanation of the methyl proton behavior.



Michael J. Minch
Department of Chemistry
University of the Pacific
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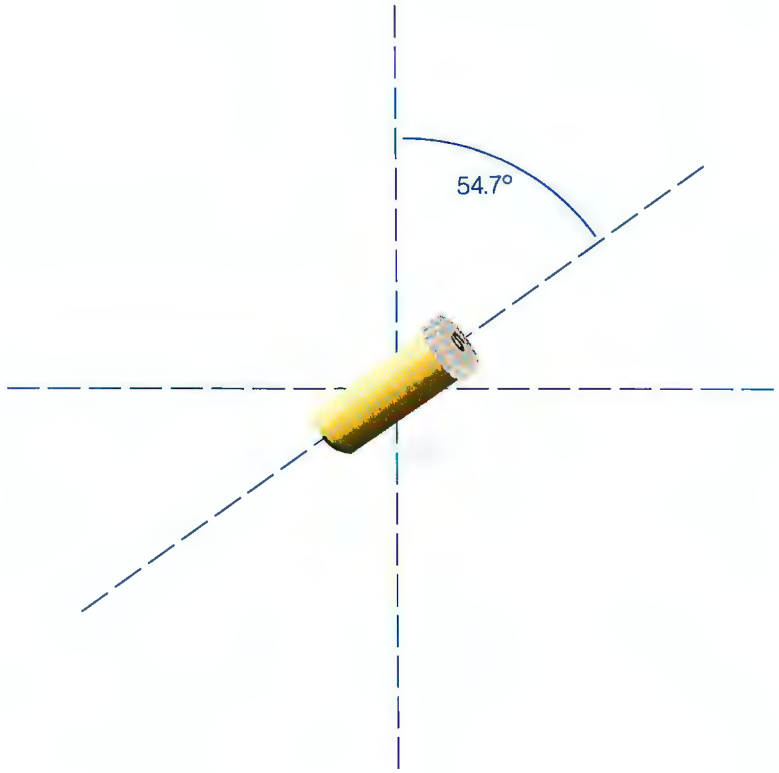

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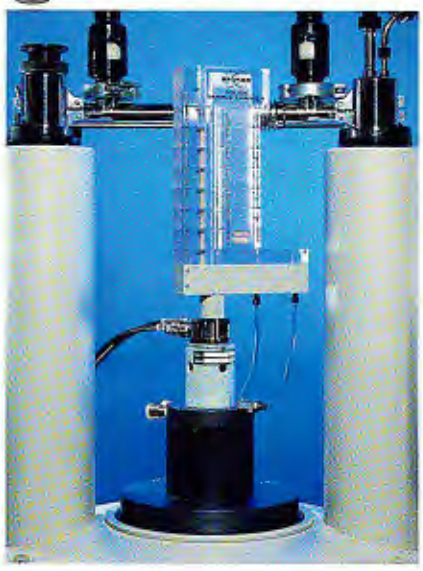

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Dr. B. L. Shapiro
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October 11, 1991
(received 10/16/91)

The first persistent 750 MHz/5 cm superconducting NMR magnet

Dear Barry:

Bruker is proud to announce that about 3 months ago we succeeded, in collaboration with the Kernforschungszentrum Karlsruhe, in energizing a superconducting magnet to 17.63 Tesla, corresponding to an NMR frequency of 750 MHz. The magnet is designed for high-resolution NMR, and operates in the persistent mode with a 5 cm room-temperature bore. We believe that with this accomplishment we are the first to have reached this goal, which these days is discussed so much in the NMR community.

However, the production of further magnets will still require some time. Due to the fact that with this 750 magnet we had to push the limits of technology to 25 % higher field values, advanced and specialized materials had to be developed, which cannot be produced very rapidly at the moment. Moreover, it is also quite a task to engineer a smooth transfer from our prototype 750 MHz magnet to series production.

We still are some time away from a first AMX 750 high-resolution NMR spectrometer, and some years away from small series production. Eventhough our SE 451 AMX receiver was designed from the beginning to work up to 1,000 MHz proton frequency, the development of high-quality probeheads, transmitters, preamplifiers, etc., for an AMX 750 will take some time to guarantee a successful introduction.

Our NMR division managers can provide preliminary site planning guidelines in order to assist those who wish to reserve a facility for an AMX 750. We appreciate the support and feedback from the high field NMR community, and hope that this letter is of significant interest to TAMU readers.

With our best wishes !
Sincerely yours,

Günther Laukien

Prof. Dr. Günther Laukien

Gerhard Roth

Dr. Gerhard Roth

Preliminary Announcement and Call for Papers

Third Annual Workshop on Magnetic Resonance Microscopy and Materials Imaging

A Tutorial and Workshop Devoted to Microscopy, Nonmedical, Industrial and Biomedical Solid State Applications of Nuclear Magnetic Resonance Imaging

Massachusetts General Hospital
NMR Center
Charlestown (Boston), Massachusetts
May 11 - 12, 1992

The purpose of this workshop is twofold. First, it is intended to acquaint industrial and academic newcomers to the field with the principles and practice of magnetic resonance imaging, especially as applied to potential problems in materials analysis, industrial R & D, quality control and nondestructive testing. The second, equally important, purpose is to bring together NMR researchers at the cutting edge of this technology to discuss the latest methods and applications. This workshop should provide an excellent forum for the discussion of novel ideas for adapting MRI technology in many areas of interest to academic and industrial scientists and engineers.

There will be opportunity to present a number of contributed papers. Please submit a camera-ready 15 cm wide by 10 cm high abstract on plain white paper, showing title, authors, affiliation and abstract text to the address shown below by ***April 1.*** Mark the envelope "Materials Workshop."

For more information contact:

	Jerome L. Ackerman	or	Leoncio Garrido
Phone:	617-726-3083		617-726-5820
Internet:	jerry@nmr-r.mgh.harvard.edu		garrido@nmr-r.mgh.harvard.edu

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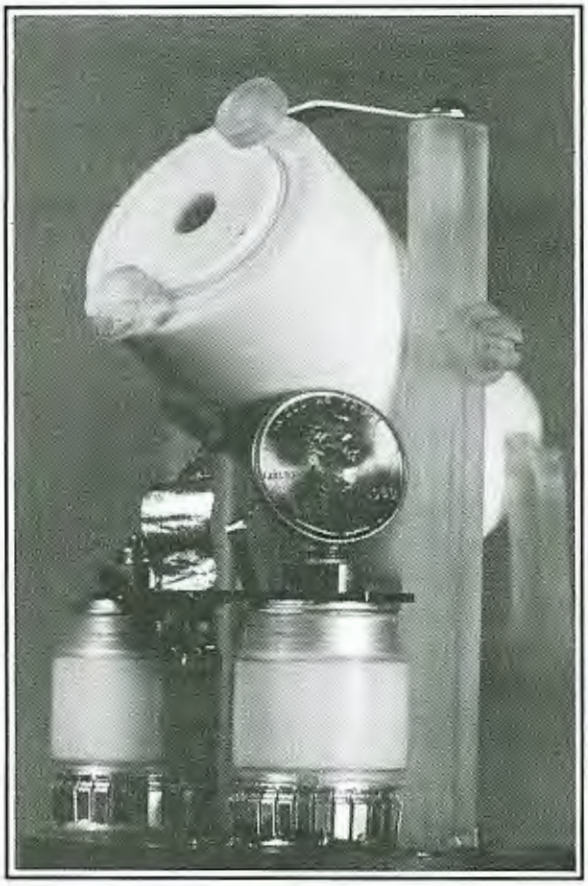

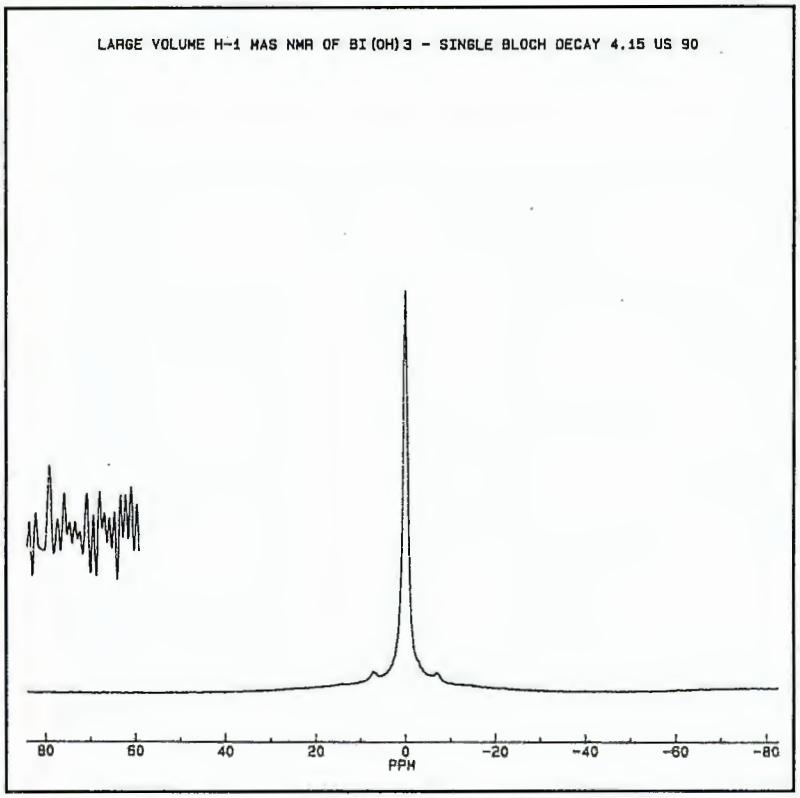

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September 18, 1991
(received 9/23/91)

A MAGIC (ANGLE) WAND FOR LOCKING

Bernard L. Shapiro
966 Elsinore Court
Palo Alto, CA 94303

Dear Dr. Shapiro:

Recently, while doing melt NMR of a polypropylene sample (at 230°C) with one of our Doty VT-MAS probes we were able to achieve sufficient resolution to easily see the series of peaks of the methyl carbon due to the tacticity of the propylene monomer units.

Typically, we do routine polyolefin (PP, PB) tacticity analyses by high-temperature solution NMR which necessitates long sample preparations. The ability to do this analysis without dealing with the time-consuming sample dissolution step (i.e. just load a MAS rotor with powder, spin, and apply heat) is thus very appealing.

One problem that we have found the need to overcome so that we can use our VT-MAS probes to do such a "high-resolution" measurement is that with such line-narrowing capability (mainly thermally induced motion of the polymer chains plus MAS and decoupling protons) we actually need the ability to lock the field when using the VT-MAS probes. We have therefore built a single resonance deuterium lock circuit that actually can be easily inserted into our VT-MAS probes from Doty. We utilize the "wand port" that many broadband Doty probes have for installation of extra capacitors to change the observe tuning range. Our "lock wand" is simply the lock circuit mounted on a small piece of PC board that is attached to a length of 1/4" diameter copper coax. A BNC connector is soldered to the end of the coax coming out the bottom of the probe to enable connection to the lock circuit of our spectrometer. The external lock sample is about 3 cm below the center of the coil around the MAS stator, and about 2 cm radially out from the center of the field.

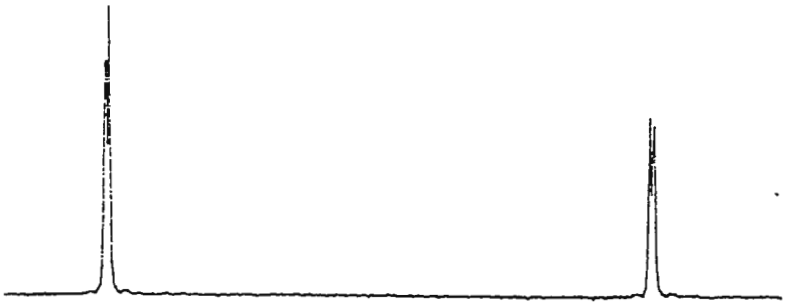
We have found that on our MSL-200, it is not too difficult to use this external lock to lock the field when doing long acquisitions. Below is an example showing that the circuit works. In this example, we have "faked" a drifting field by simply perturbing the Z0 setting with our RT shims. We moved Z0 to emulate a 200 MHz Oxford magnet at the maximum of its within specification drift rate over a ten hour acquisition. The spectrum of adamantane was collected under conditions of "simulated drift" with the lock off (peaks split due to field drift) and with the lock on (no splitting). A drawing of the lock wand is also shown.

Sincerely,

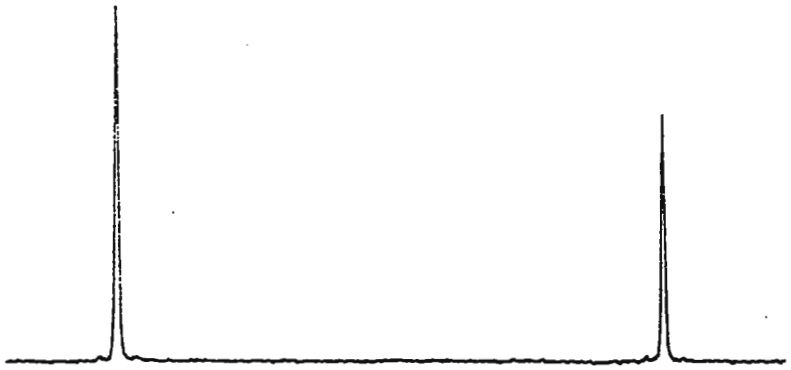
Grant W. Haddix
Research Engineer
Shell Development Co.
Westhollow Research Center

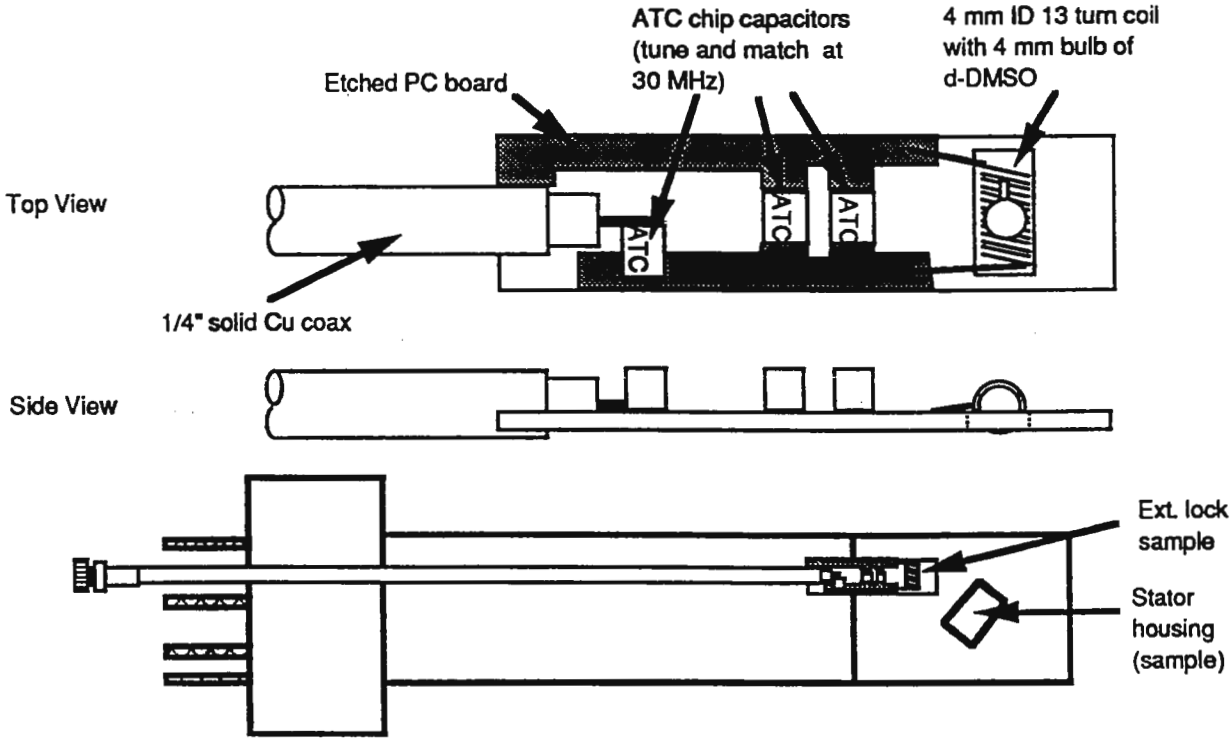
Figure 1, CP/MAS Spectra of Adamantane

a) Unlocked, simulated drift

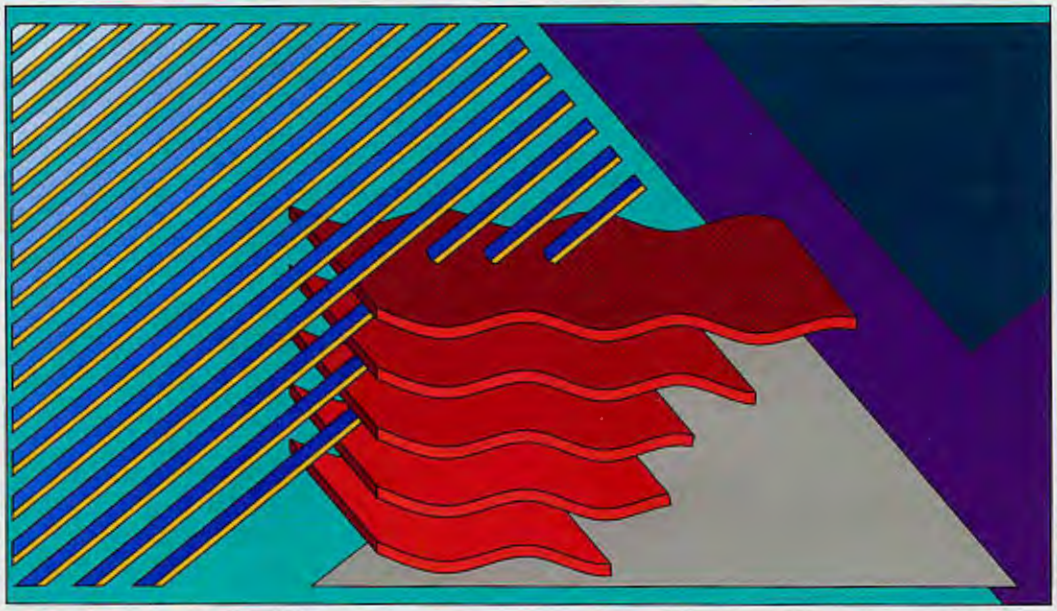


b)Locked using external ^{2}H lock





What's the difference between the new CMX spectrometer and the competition?



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NMR AND DATA PROCESSING LABORATORY

OFFICE OF THE DIRECTOR

10/04/1991
(received 10/7/91)

Multi-Dimensional Correlations with HOMQC Involved

Dear Dr. Shapiro,

Among other applications in multi-dimensional NMR, currently we are playing around combining homonuclear multiple-quantum correlation (HOMQC) with both coherent and incoherent magnetization transfer steps in a 3D experiment. We have found such 3D spectra to be highly dispersive and informative, especially when applied to crowded spectral areas. We have used such experiments to complete assignments in the strongly overlapping spectral regions of our nucleic acid samples.

In Figure 1, selected slices from a 3D NOE/2QC spectrum are shown for an RNA 24-mer hairpin structure, which we are investigating extensively.[1] F3-F1 NOE slices are sorted out in F2 by 2Q-frequencies of the spins involved. The slices shown represent a correlation region between base and base/1' protons. Due to extensive aliasing (using first point at half dwell time acquisition method[2]) the F1 dimension shows two, while the double quantum dimension represents three resonance frequencies.

Data processing has been accomplished on an Alliant FX-80 computer with our SDFT software.[3] Only the selected "brick" was reconstructed in one step in *ca.* 20 minutes (elapsed time). Input size for the time domain data was t1-t2-t3: 64 x 32 x 1024 (x 8; all complex) points, output size of the "brick" was only F1-F2-F3: 64 x 64 x 240 (real) points, which is smaller than a usual 2D data size. A similar increase in digital resolution would end up with overall output size of 256 x 64 x 2048 (real) points (which is more than 130 MBytes!) by conventional FFT processing.

Yours sincerely,

István Pelczer Sándor Szalma[4] KeYu Wang Phil N. Borer George C. Levy

(1) Borer, P. N. *et al.* Poster (No. CG202), Frontiers of NMR in Molecular Biology-II, Keystone, Colorado, April 8-14, 1991
(2) Bax, A., Ikura, M., Kay, L. E. Zhu, G. *J. Magn. Reson.*, 91(1991)174
(3) Szalma, S., Pelczer, I., Borer, P. N., Levy, G. C. *J. Magn. Reson.*, 91(1991)194
(4) present address: J. W. Goethe-Universität Frankfurt, Frankfurt am Main, Germany

CENTER FOR SCIENCE AND TECHNOLOGY / SYRACUSE, NEW YORK 13244-4100

315-443-1021 / FAX 315-443-1022

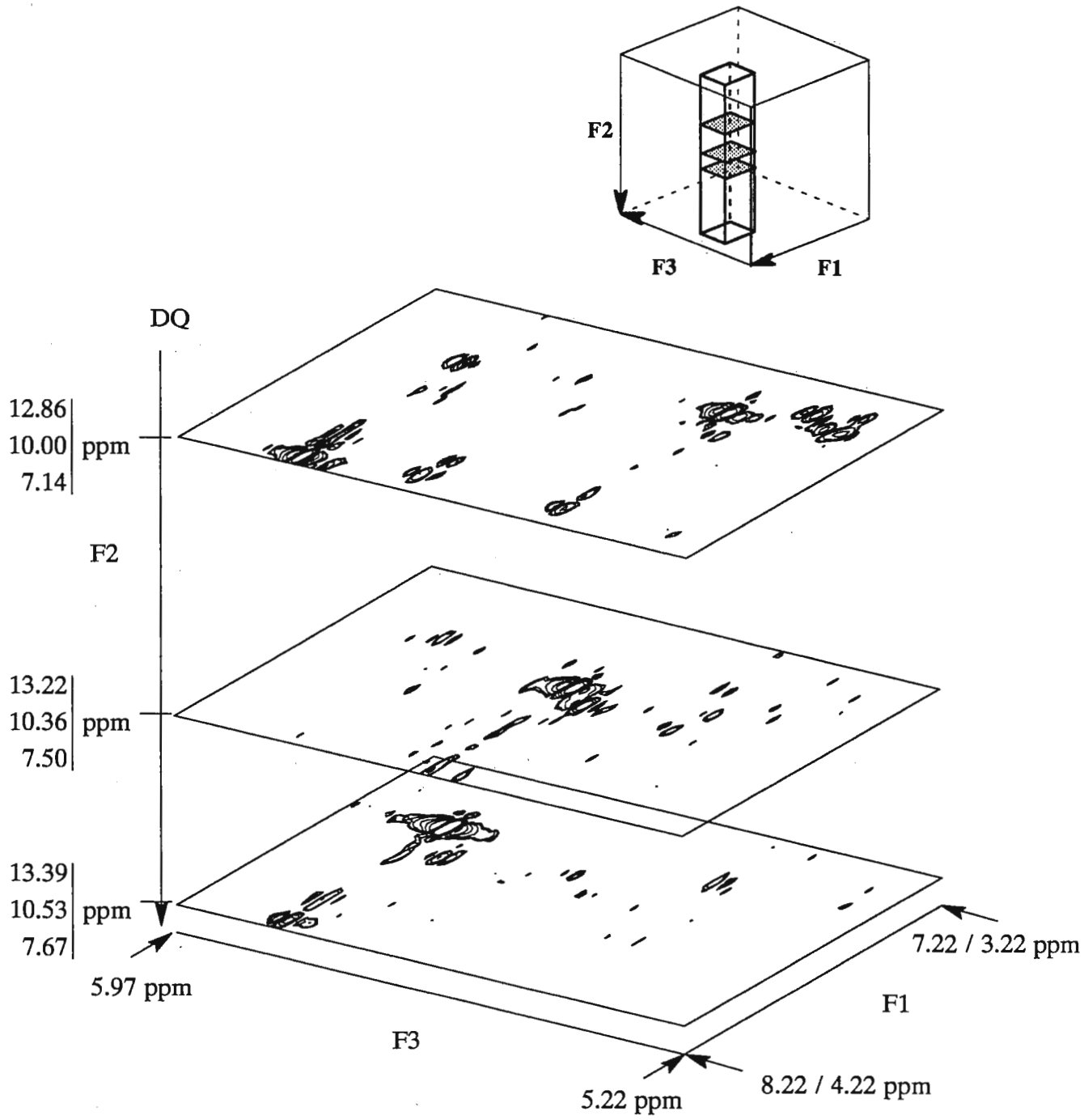
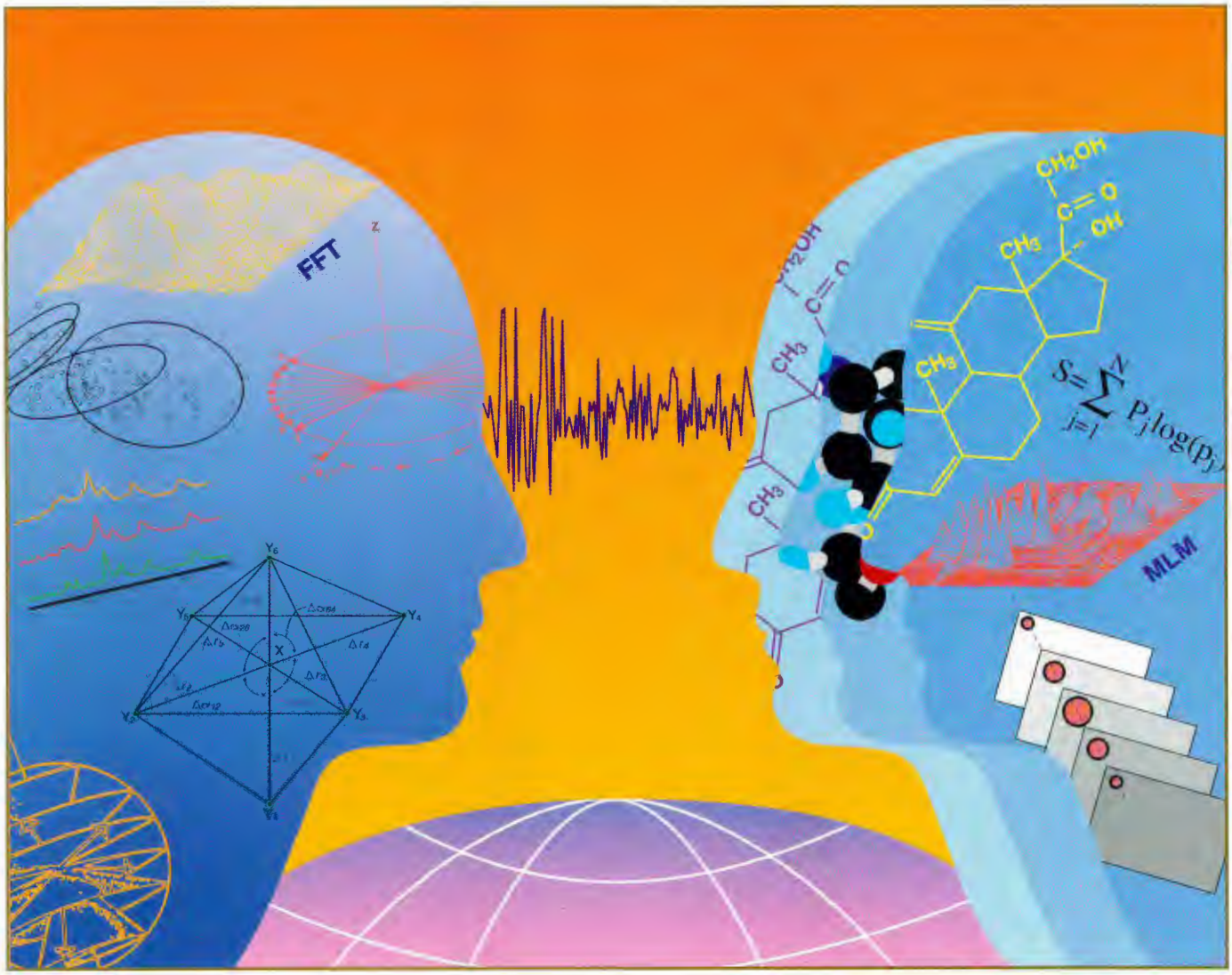

F2
F3
F1
DQ
12.86
10.00 ppm
7.14
F2
13.22
10.36 ppm
7.50
13.39
10.53 ppm
7.67
5.97 ppm
F3
5.22 ppm
8.22 / 4.22 ppm
F1
7.22 / 3.22 ppm

Figure 1

THE NMRZ™ SYSTEM

Advanced Software for All Dimensions of NMR Data Processing and Analysis



NEW METHODS
IMAGINATION TRANSFORMING INFORMATION

Introducing the NMRZ System

Today's laboratory demands versatile 3-D visualization for the determination of complex structures. Multidimensional NMR analysis and NMR-based distance constraints can now provide the basis for 3-D molecular structures.

New Methods' global commitment to customer support includes intensive training programs and workshops.

New Methods proudly presents the NMRZ System for NMR data reduction and analysis to solve ever-more complicated spectral challenges. The NMRZ System incorporates many important new products into a problem-solving system that can significantly improve the productivity of our customers. Incorporating all the features of NMR1™ and NMR2™, New Methods introduces the modules NMRZ, NMRZ/MODEL™, DISNOE™, MARDIGRAS+™ and SpecExec™ to form a totally integrated solution to the complex structural challenges of today and tomorrow. New Methods' focus on NMR processing and analysis provides the scientist unprecedented power and ease of operation.

The new point-and-click Graphics User Interface (GUI) simplifies operation of the NMRZ System for both local and remote network execution. The GUI, together with the macro language, provides both novice and advanced users with easy access to all of the features of the NMRZ System. These features include multidimensional processing and analysis, NMR-based structure determination, Relaxation Matrix NOE-based distance constraints and structures determined by New Methods' DISNOE Distance Geometry module. One can now choose from a selection of meaningful 1-D, 2-D and 3-D displays of multidimensional spectra. Window display modes and user-directed grouping of windows and cursors are flexible, permitting customization of the graphics display to create unique environments to solve specific problems in spectral assignment. The novice is no longer required to learn Unix or VMS to manage data files.

The NMRZ System includes advanced spectral optimization and characterization algorithms incorporated within a highly automated macro processing environment. The NMRZ System goes beyond NMR data reduction and analysis to include initial calculation and refinement of molecular structures. Reliable network data transfers are provided from NMR instrumentation using Ethernet or economical RS-232 serial connections. Data from most models of NMR spectrometers are translated into the standard LAB ONE® file format for optimal data archiving and information management. The NMRZ System takes advantage of highly developed computer algorithms for one, two, three and higher dimensional processing and analysis, making it easier to solve increasingly complex structures. The NMRZ System will remain the most advanced software for the processing and analysis of NMR spectra of any dimension.

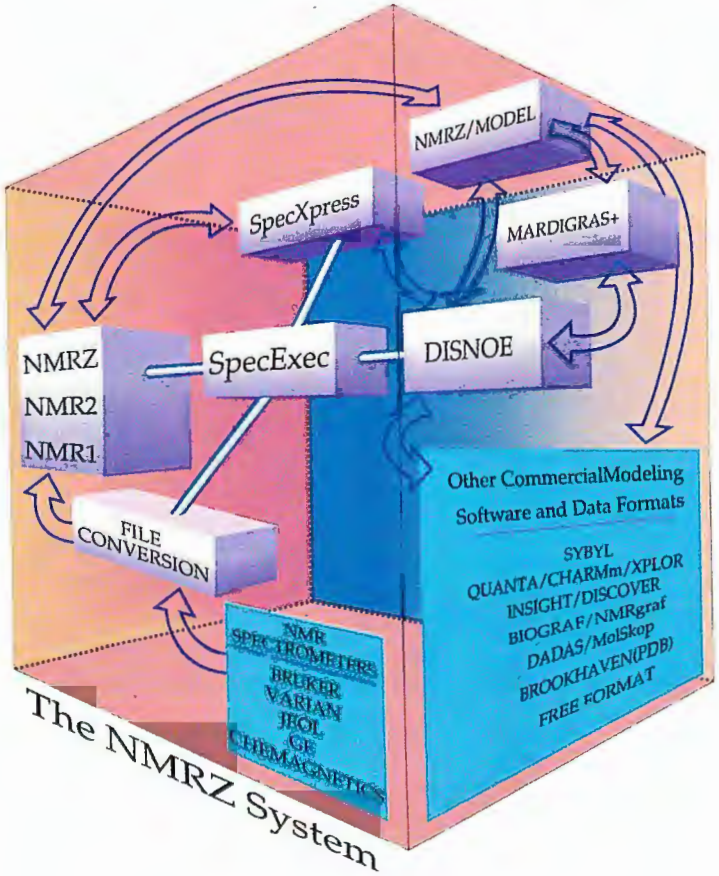
SpecExec: Gateway to the NMRZ System

SpecExec, New Methods' laboratory computing manager, features automated data transfer, file conversion and processing for one or more NMR spectrometers communicating to a single workstation, or within a heterogeneous computer network. SpecExec allows the user to transfer files without having to learn the different commands necessary for each transfer protocol, spectrometer type and operating system. SpecExec helps the user select: module-specific options, display format, graphics display placement, as well as which module to operate and what machine will execute it. As a laboratory computing manager, SpecExec facilitates the effortless transfer of data from the instrumentation to any networked platform, and concurrently invokes data processing modules on all platforms in the network.

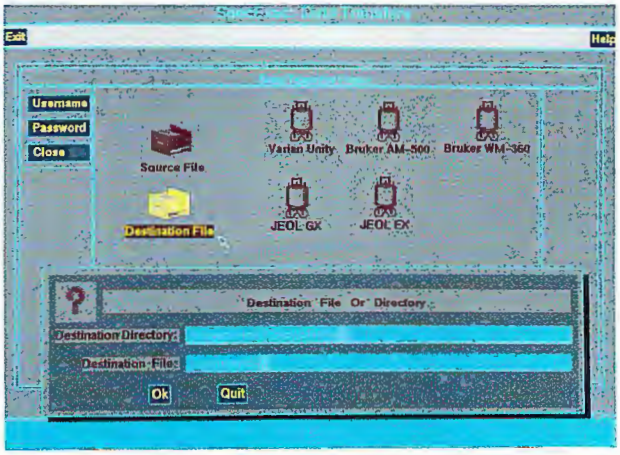
Network, transfer, file conversion and processing manager

SpecXpress

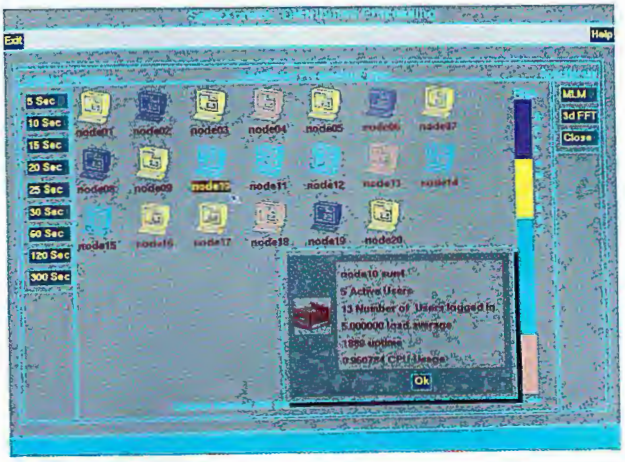
SpecXpress, New Methods' distributed and parallel computing module, can significantly reduce the time required for data reduction and spectral optimization of multidimensional NMR through the efficient use of existing computing resources in your laboratory. These functions operate automatically and can be monitored graphically on any networked display.



SpecExec features user execution and control of all NMRZ System modules. Multiple modules can be launched on any platform in the network.



SpecExec automates data transfer and file conversion for most models of NMR instruments. Choice of spectrometer, file name and directory is selected by clicking on icons.

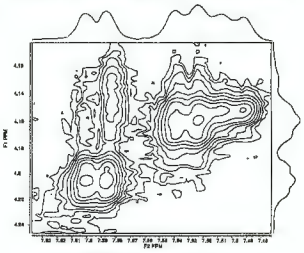


SpecXpress features the ability to monitor computer usage throughout the network. This figure displays a 20-node network and the current system loading at each node. (The color bar at the right indicates the level of system loading). Also displayed is information about a specific networked workstation, which is used by the software to optimize network distributed processing.

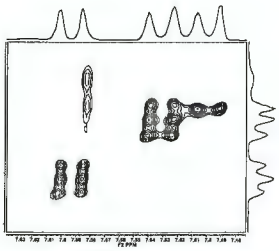
2-D Processing and Analysis

The NMRZ module processes all types of 2-D spectra. Versatile processing modules provide advanced user-friendly techniques, including:

- Phasing of hypercomplex and TPPI 2-D spectra in both dimensions
- Effective solvent and noise ridge suppression
- Automated and interactive baseplane corrections
- Linear Prediction extrapolation
- Resolution and contrast enhancement by the Maximum Likelihood Method and related techniques
- Effective peak table editing, including multiplet recognition and consolidation
- Capability of running sequentially on a single workstation or, via SpecXpress, in parallel on a network of workstations (transparent to the user).

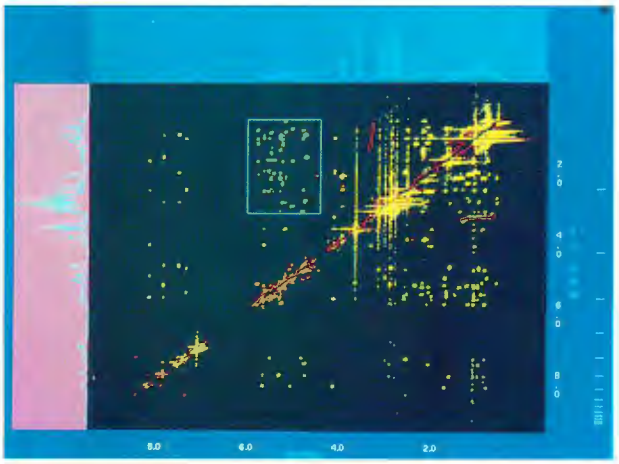


FFT Processing

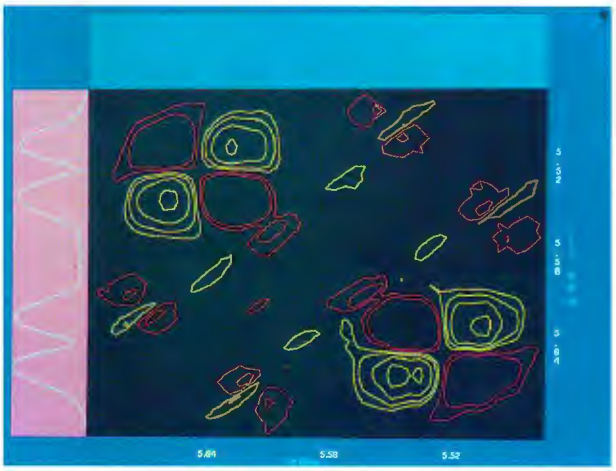


MLM Deconvolution

(Above) Features derived from NMR2 include tools for peak location and refinement which allow automated detection and quantitative evaluation of partially resolved peaks. Spectral features can be determined accurately, even in severe overlap, using automated 2-D surface fitting or powerful non-linear 2-D spectral deconvolutions to produce reliable NOE volumes and coupling constants.



NMRZ includes 2-D NMR spectral displays. Here a contour plot of a small protein is displayed, along with projections in both dimensions, and a zoom box around the alpha-to side-chain protons.

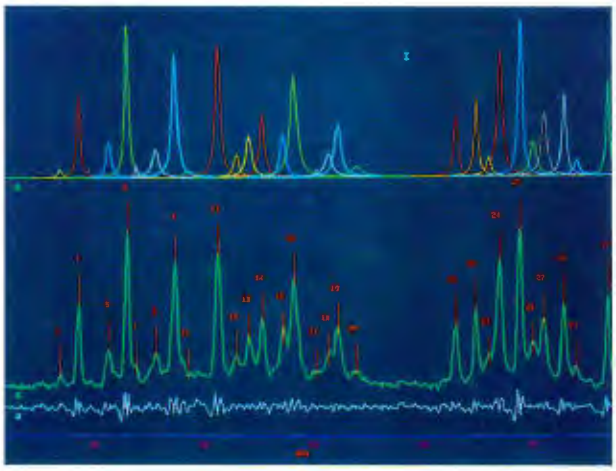


(Right Image) In 1991, a new "Simple COSY" experiment was reported (I. Pelczer, J. Am. Chem. Soc., 113, 3211), which greatly simplifies phase correction in phase-sensitive COSY spectra. Hilbert transformations supported the introduction of S. COSY, the simplest implementation of phase-sensitive COSY processing. The S.COSY processing scheme is easily implemented via automated macros. Since 1989, New Methods' 2-D Processing and Analysis software included Hilbert transforms; an example of New Methods providing the most advanced tools possible.

1-D Processing and Analysis

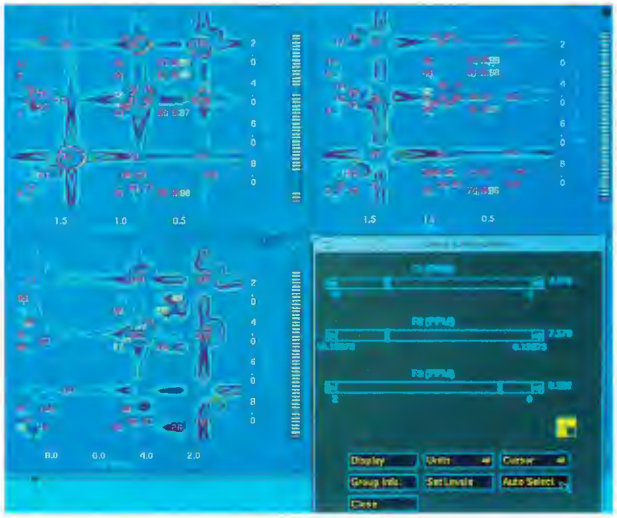
The NMRZ module incorporates all of the algorithms previously contained in NMR1 for automated processing and classification of 1-D spectral data, while minimizing bias through advanced numerical and statistical analysis. Features include:

- Automatic baseline evaluation and correction
- Rapid peak analysis
- Curve-fitting of overlapping, low signal-to-noise peaks with complex lineshapes and non-linear optimization methods
- Regression Analysis for T_1 ,T_2, kinetic measurements
- Resolution enhancement by maximum entropy and linear prediction

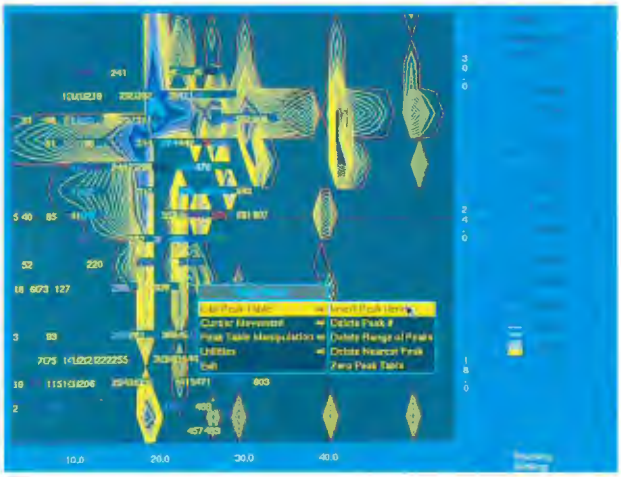


A section of a Carbon-13 spectral analysis following fully automated curve fitting. Shown in the figure are the experimental spectrum (green) indicating the updated peak information, the difference spectrum (white) and the individual modeled peaks (top trace). The raw information from the peak analysis module served as the initial data for this automatic curve fit. With the 33 peaks shown, this is a 99 dimensional surface that has been minimized.

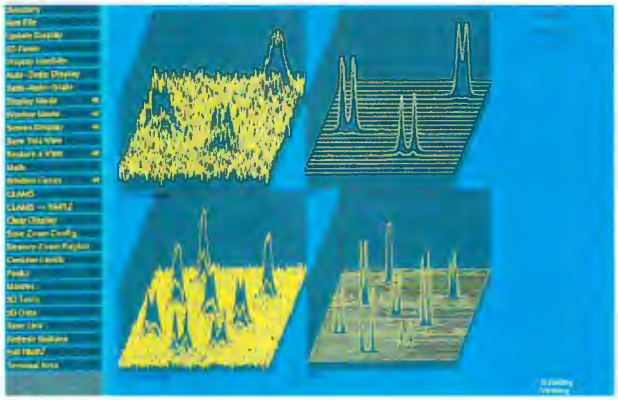
Multidimensional Processing and Analysis: NMRZ



The NMRZ module utilizes extensive real-time graphics analysis of slices in multidimensional spectra for practical and efficient visualization and analysis. Windows can be grouped so that spectral features can be tracked in each dimension using grouped cursors.



Automated peak location and refinement tools facilitate detection and quantitative evaluation of partially resolved peaks.



Four stacked plots of 2-D spectral regions are displayed: at left, processed by conventional apodization and FFT; the right side shows maximum likelihood reconstructions calculated without need for user interaction.

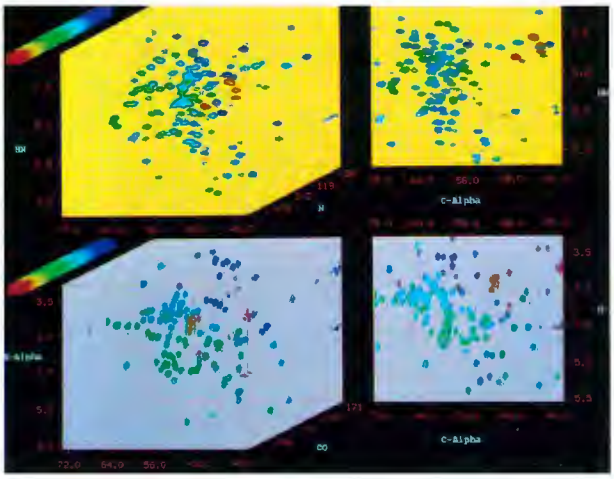
New Methods' Multidimensional Processing and Analysis module, NMRZ, includes standard and advanced options for phase-sensitive Fourier processing and transformation schemes. Hilbert transformation can be used to reconstruct imaginary data for phasing, as well as for suppression of diagonal and solvent peaks or for data compression with large 3-D data sets. New Methods application scientists can assist you to implement these and other sophisticated techniques in your lab:

- ***LINEAR PREDICTION (LP) EXTENSION*** – A feature which facilitates the extension of interferograms, especially for indirectly detected dimensions, to produce better definition of crosspeaks in multidimensional spectra without increasing the experiment time.

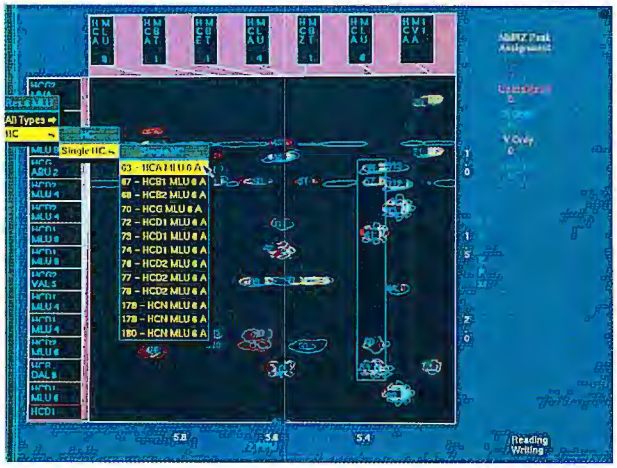
- ***MAXIMUM LIKELIHOOD METHOD (MLM) DECONVOLUTION*** – This feature enhances peak picking and assignment, and preserves crosspeak volumes, producing accurate distance estimates from individual or multiple NOE spectra. MLM deconvolution improves data visualization and quality by improving spectral resolution up to threefold while effectively suppressing spectral noise.

- ***PEAK PICKING AND EDITING*** – NMRZ advanced peak picking and editing routines are reliable and time-saving because many editing features operate on the reduced data format in the peak table rather than on the entire frequency-domain data set.

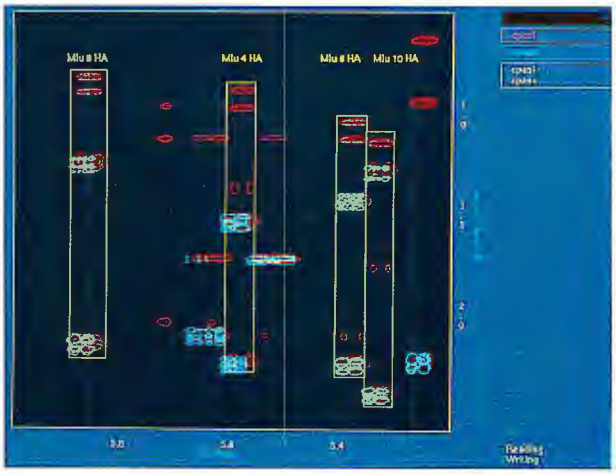
- ***VOLUME DETERMINATIONS*** – NMRZ, together with NMRZ/MODEL, provides facilities for summation of points within a specific region, local baseplane corrections, surface fitting, and regression analysis of integrals as a function of mixing time.



NMR-Based Structure Determination: NMRZ/MODEL



General-purpose spectral assignment modules take advantage o molecular structure file information to generate atom lists targeted specifically to the spectrum at hand.

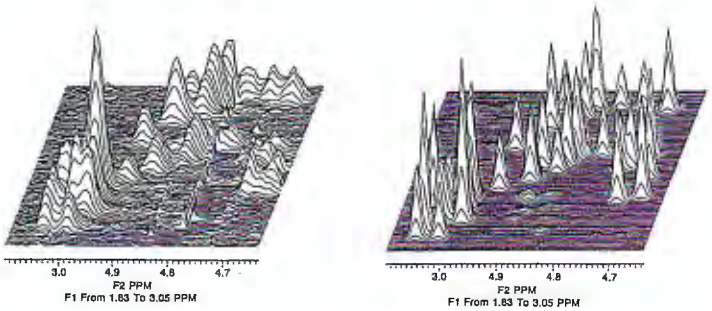


Many forms of assisted analysis are available, including bitmap overlays for peak picking and side-chain assignments. Shown is a COSY/TOCSY overlay for a crowded part of the alpha-to side-chain proton connectivities in cyclosporin A. The characteristic patterns of the four leucines are labeled. The two spectra do not have the same spectral widths or digital resolution, yet can be easily overlaid.

The NMRZ/MODEL module provides the power to solve assignment problems quickly, determine distance and torsional restraints, and simulate NOE and COSY crosspeaks. Choose assignments from button tools customized to interface with DISNOE-New Methods' Distance Geometry program, and most other modeling programs. Button tools are automatically arranged in sensible order to simplify the bookkeeping tasks associated with complex molecules. Overlays of related spectra are easy to prepare for assistance in assigning amino acid side-chains. In addition, connectivities and plane-to-plane correlations facilitate sequential assignment. Spectral assignments are stored in the NMRZ peak table, easy to access and ready to use in calculating distance and dihedral angle constraints.

NMRZ/MODEL analyzes spectral data to record structural information which can be used by virtually any molecular modeling system. NMR-based structure determination is tightly integrated into the NMRZ System environment utilizing all of the multidimensional processing and presentation advantages. NMRZ/MODEL provides a complete set of tools for assigning spectra and extracting structural information accurately and quickly. Facilities include:

- Multiplet recognition techniques
- Automated and interactive connectivity analysis
- General-purpose assignment module suitable for recording assignments of any type of spectrum or molecule
- Estimation of distances from NOE intensities
- Regression analysis of NOE buildup curves
- Simulation of NOE spectra from candidate structures



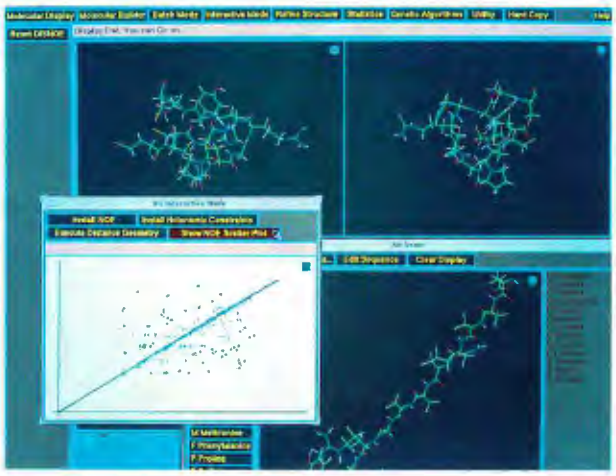
Experimental (left) and simulated NOE (right) spectra for a dodecamer DNA molecule. Part of the sugar proton crosspeak region is shown. The calculated spectrum utilizes complete relaxation matrix theory. Differences between the simulated and experimental spectra can reflect structural deviations, or variation in molecular motions. (Experimental data provided by Professor T. Krugh, University of Rochester).

Distance Geometry and Structure Refinement: DISNOE

The DISNOE module includes standard distance-geometry as well as simulated annealing and genetic algorithms, automated builders for peptide and nucleotide conformations, and molecular display capabilities. You'll like the way it is integrated into the NMRZ System via the new Graphics User Interface–all in the same X-windows environment.

DISNOE refines structures and it also will coordinate with molecular modeling systems from other vendors through NMRZ/MODEL. DISNOE includes:

- Metric matrix distance geometry algorithm
- Enhanced optimization, including simulated annealing and genetic algorithms
- Versatile automated molecule builder
- Optimization of various target functions, including full relaxation matrix NOE calculations, distance matrix and bonding parameters
- Capable of operating on a single workstation or, via SpecXpress, in parallel on a network of workstations (transparent to the user)

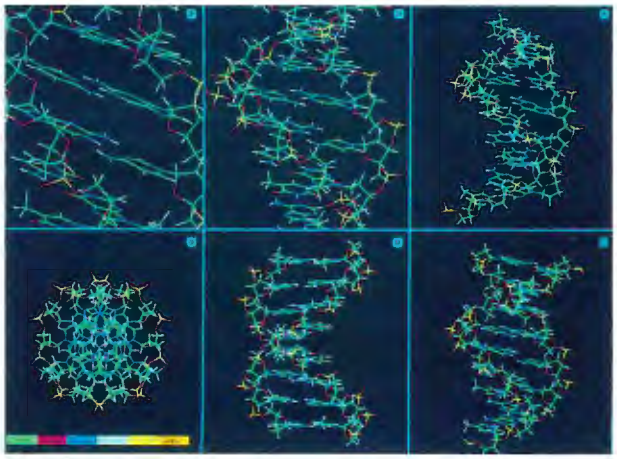


A DISNOE screen displaying features of the module and the NMRZ graphics user interface. At the top of the screen the module option menu bar is displayed and just below this row of buttons, the graphics window displays two views of the peptide conotoxin. The lower portion of the display has two additional windows: at left, a scatter plot of calculated versus experimental NOE's for a partially refined structure and at right, an extended structure in the molecule builder module of DISNOE.

Relaxation Matrix NOE-Based Distances

New Methods' newly-licensed MARDIGRAS+ calculates NOE-based distances that satisfy the full relaxation matrix. The MARDIGRAS+ module features calculation of distance constraints from NOE data that correct for spin diffusion. It also calculates the effect of specific spectral densities on NOE spectra. MARDIGRAS+ eliminates the need for multiple NOESY experiments and for reliance on low S:N spectra at short mixing times. One or two spectra at intermediate mixing times will yield superior distance constraints from complete relaxation matrix calculations. MARDIGRAS+ incorporates the NMRZ advanced Graphics User Interface complete with macro commands and direct communication to and from NMRZ/MODEL.

MARDIGRAS+ was adapted from programs developed at the University of California at San Francisco by Professor T. James and co-workers. This product is another example of New Methods' commitment to increase your power and accuracy in determining complex structures.



Visualization of molecular structures and distance comparisons facilitate analysis of the results. Six views of a DNA octamer are shown in the DISNOE graphics window which the user can configure.

The NMRZ System is available on a wide variety of computers, including New Methods' SpecStation computers and networks based on advanced workstations, as well as VMS and Unix departmental computers and servers from Sun, DEC, IBM, Silicon Graphics and other manufacturers.

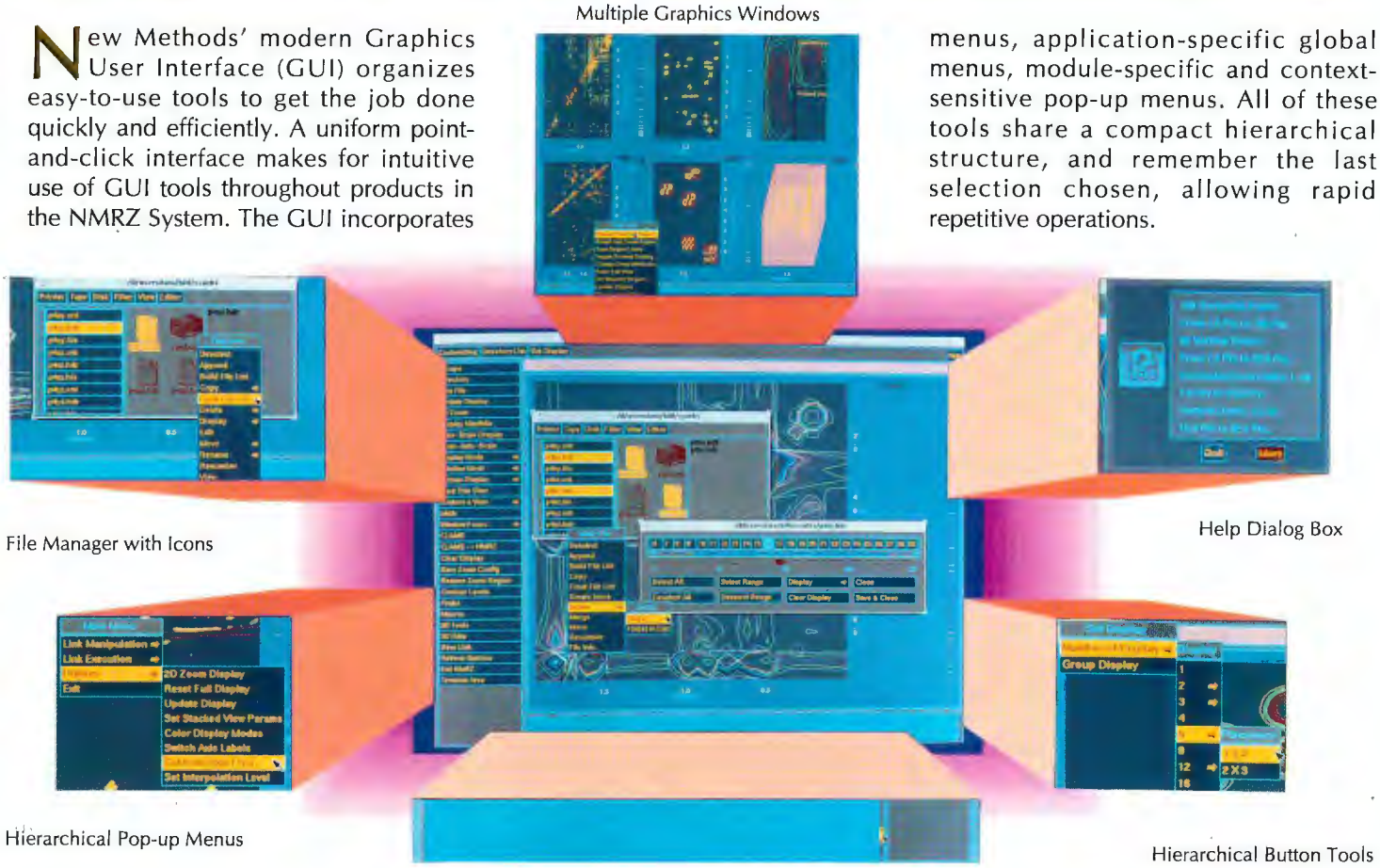
Standard protocols, UNIX/VMS environments, and the X-window system allow SpecStations to operate other software applications including molecular modeling and theoretical calculations. SpecStation systems make available literally thousands of applications.

You see the advantages that the NMRZ System will provide for your applications. A demonstration of the NMRZ System's data processing power can be provided by our trained sales and applications specialists either in our laboratory or your applications environment.

New Methods' NMRZ System has the power and flexibility for tomorrow's experiments.

Features of New Methods' GUI

New Methods' modern Graphics User Interface (GUI) organizes easy-to-use tools to get the job done quickly and efficiently. A uniform point-and-click interface makes for intuitive use of GUI tools throughout products in the NMRZ System. The GUI incorporates menus, application-specific global menus, module-specific and context-sensitive pop-up menus. All of these tools share a compact hierarchical structure, and remember the last selection chosen, allowing rapid repetitive operations.



many convenient and flexible productivity features.

The spectrum window is large. It can be configured into a multiple window display allowing side by side comparison of as many as 16 different experimental results. This is exploited in the NMRZ module by coupling the cursor positions and the zoom regions for groups of windows, to coordinate data set manipulations in all dimensions.

The terminal window is resizable in either a tiling or overlapping mode with the spectrum window. The terminal window is also scrollable.

User-definable button tools can access commands and macro functions. The button tools include system and display pull down

GUI input functions are supported by pop-up dialog boxes that provide a standard forms style interface. This same dialog box interface displays context-sensitive on-line help.

Incorporated into the GUI is a standardized interface to the platform operating system. Utilities such as file copying, moving, deleting, and listing are all available to the user from within the program. The file manager uses the same point-and-click style interface and remembers previous selections. The user can keep track of important or commonly used files by generating icons to be used as an alias for file names. The GUI provides a unified operating environment for the entire NMRZ System.

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September 8, 1991

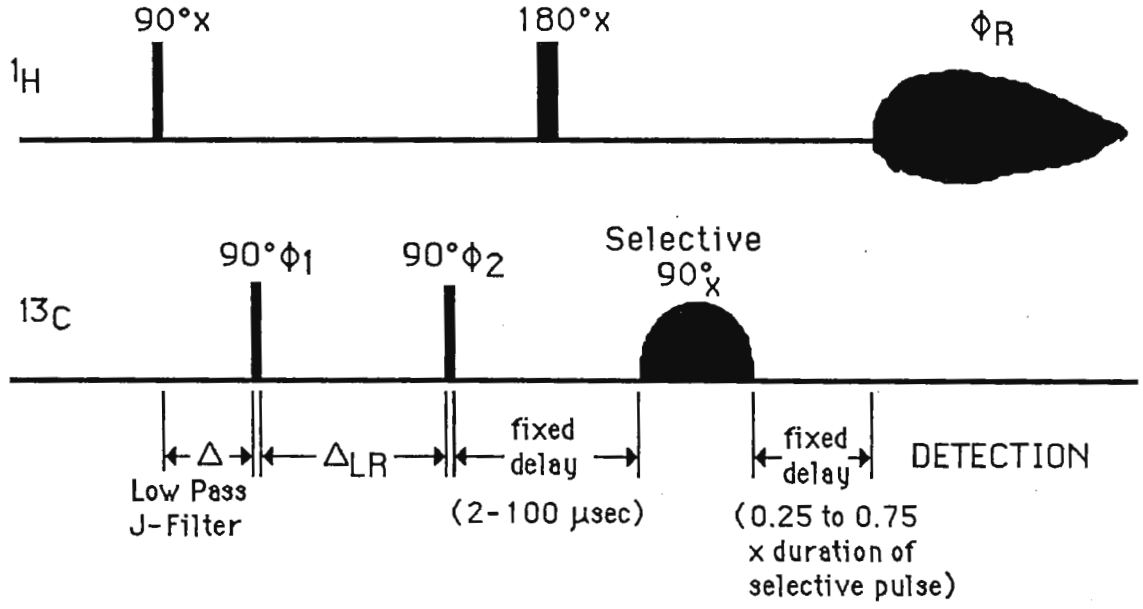
(received 10/12/91)

Bernard L. Shapiro, Ph.D., Editor
Texas A&M NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Further Refinement of SIMBA

Dear Barry,

A few months ago, we published a report[1] describing a selective one-dimensional analogue of the familiar HMBC experiment of Bax and Summers.[2] Our paper followed shortly after a similar but simpler description of a selective HMBC experiment by Keniry and Poulter.[3] Our experiment, SIMBA (selective inverse multiple bond analysis), or the variant described by Keniry and Poulter, has obvious advantages if only a few long-range connectivities to quaternary carbon resonances are required. When we first developed the method, we were interested in putting a technique into the literature that the owners of older spectrometers could also implement and use. Thus, we implemented the experiment with square rather than shaped selective pulses. While later exploiting the selectivity benefits which accrue from the use of shaped pulses with the SIMBA experiment, we found that further beneficial improvement in the quality of the spectral data obtained could be obtained by inserting a fixed delay following the shaped, final pulse of the sequence. We have found that iterative adjustment of the duration of the fixed delay seems to be a necessary evil but that best results are generally obtained when the delay is set at 0.6 times the width (duration) of the shaped pulse. Setting this delay for square pulses may require iterative optimization. However, since the experiment runs in a relatively short period of time, optimization of the delay hasn't represented much of a problem. The modified SIMBA pulse sequence is shown schematically below.



On another front, we have now essentially completed the movement of five of our supercons over the course of the summer, coupled with the installation of a new Varian Unity 300. As with all such moves, we did have some small problems but, in general, everything has gone reasonably smoothly. We now in the process of completing the installation of several new Sun workstations on our nmr computer network. The nmr computer network, however, will be the subject of a later contribution to the newsletter.

Best regards,

Gary E. Martin

Ronald C. Crouch

1. R.C. Crouch and G.E. Martin, *J. Magn. Reson.*, **92**, 189 (1991).
2. A. Bax & M.F. Summers, *J. Am. Chem. Soc.*, **108**, 2093 (1986).
3. M.A. Keniry and G.A. Poulter, *Magn. Reson. Chem.*, **29**, 49 (1991).

STANFORD MAGNETIC RESONANCE LABORATORY
STANFORD UNIVERSITY
STANFORD, CALIFORNIA 94305-5055

Director: Oleg Jardetzky, M.D., Ph.D.
Professor of Pharmacology

(415) 723-6153
(415) 723-6270

Postdoctoral Positions Open

Under the terms of a new NIH grant we have immediate openings for two postdoctoral fellows interested in NMR studies of protein dynamics and the implications of dynamics for protein structure determination by NMR.

We are looking for bright, well-trained, energetic individuals with a serious interest in science. A good background in the exact sciences is essential. Some experience with protein chemistry, protein structure, NMR and/or computer programming are highly desirable.

Candidates should apply to: Dr. Oleg Jardetzky, Stanford Magnetic Resonance Laboratory, Stanford University, Stanford, CA 94305-5055. Phone: 415/723-6270; Fax: 415/723-0010. Stanford University is an Equal Opportunity/Affirmative Action Employer.

University of Arkansas for Medical Sciences
Departments of Radiology and Pathology
Biomedical NMR Center

Professor B. Shapiro,
TAMU NMR Newsletter
966 Elsinor Court,
Palo Alto, CA 94303

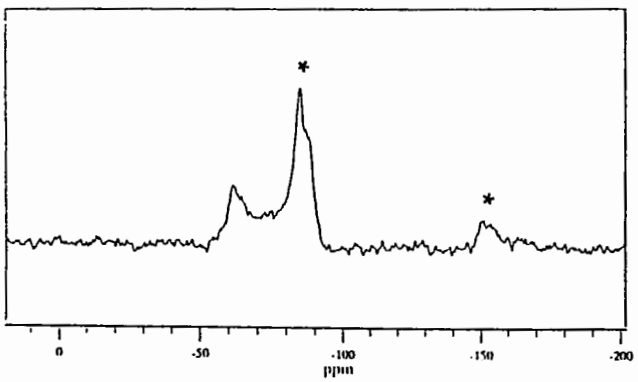
(received 10/10/91)

Problems With Coil Materials

Dear Barry:

We recently constructed a birdcage coil for use on our GE CSI 4.7T imager. The coil was to be used for ^{19}F experiments. The in vivo ^{19}F spectrum from the rat head after multiple dose treatment of fluoxetine obtained using this coil contained resonances in addition to the ^{19}F resonance expected for fluoxetine . Our first suspicion was the adhesive on the copper tape used to make the coil. We dissolved the adhesive in chloroform and recorded the ^{19}F spectrum on our high resolution GE GN300 instrument. The spectrum did not show the presence of any fluorine compounds. The next suspicious component was the variable capacitor. We contacted Voltronics, the manufacturer of the capacitors, to find out if they used any fluorine containing materials. Unfortunately the lubricant used in these capacitors contains fluorine. This was confirmed by acquiring a spectrum of a whole capacitor. The solution to the problem was to use a capacitor of the same value (but with less "Q") manufactured by Johansen, and the extra resonances were gone.

The figure below shows the typical in vivo ^{19}F spectrum from a rat head recorded on our Omega 4.7T instrument. The peaks indicated by * are from the variable capacitors and the remaining peak is from fluoxetine in rat head.



Sincerely,

David Cardwell S. Ramaprasad R. A. Komoroski

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DAVIS, CALIFORNIA 95616

September 17, 1991
(received 9/18/91)

Dr. Bernard L. Shapiro
TAMU Newsletter
966 Elsinore Court
Palo Alto, CA 94303

RE: More on GE–Ω Pulse Repetition Rates; Sequel Sequences Solve Problem.

Dear Dr. Shapiro:

We reported previously (TAMU 387, pp. 25-6) on the repetition rate problems we had experienced on our GE–Ω spectrometers. On the Ω spectrometers equipped with 293 pulse programmers using the APPL pulse sequence language, the actual pulse sequence recycle time was longer than the value set by the user. An additional amount of "recycle delay" was added to each pulse sequence, ranging from 20 msec for 1-Pulse or COSY, to 30 msec for NOESY, and 160 msec for TOCSY. We notified GE-NMR, and they immediately set to work on correcting the problem. Recently they shipped us a Beta version of software utilizing their new Sequel pulse sequence language. We have tested several pulse sequences with the following results: 1-Pulse, COSY, and NOESY all have recycle delays of only ca. 3 msec, thus enabling recycle times of < 10 msec. With TOCSY the recycle delay is ca. 5 msec and recycle times < 40 msec are possible. The increased repetition rates now possible have already proven valuable for aiding our investigations of paramagnetic iron model porphyrin complexes with extremely short T_2s. We thank the programming group at GE-NMR and Jerry Dallas of their Applications group for their diligent work in correcting the repetition rate problem.

Sincerely,

Elizabeth Boyle
Elizabeth Boyle

Jeff de Ropp
Jeffrey S. de Ropp

Gerd
Gerd N. La Mar
Director

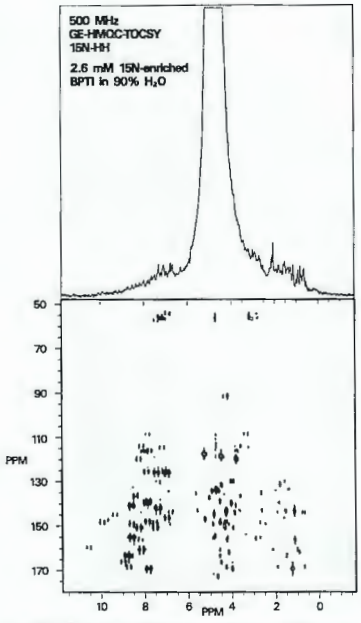
NMR UPDATE

Gradient Enhanced Spectroscopy: a new, practical answer

By Frank Huang, PhD, Paul Calderon, MS, and Boban John, PhD

Making Gradient Enhanced Spectroscopy (GES) a viable method for high resolution spectroscopy has long been of interest to researchers. The obvious benefits in speed and information content were too often overshadowed by the drawbacks of signal loss and distortion.

Technology developed at GE NMR Instruments has overcome these challenges. The S-17 Gradient Enhanced Spectroscopy Accessory with integrated inverse probehead makes GES practical for a broad range of applications in 1D, 2D, 3D and 4D experiments.



Gradient Enhanced Spectroscopy technique applied to an HMQC-TOCSY experiment demonstrates excellent water suppression without the need for presaturation or selective excitation.

Research Implications

- ► Speed without phase distortion or signal loss.
- ► Practical for 1D, 2D, 3D and 4D experiments.
- ► Accommodates proton and heteronuclear GES techniques.

A better design

The use of a three-axis, actively-shielded gradient set allows GE to overcome the inherent drawbacks of previous GES technology —most notably, phase distortion and signal loss:

Active shielding. Eddy current effects are the major source of phase distortion in GES spectra. Active shielding prevents interaction of strong gradients with magnet and shim components—the source of eddy current effects.

Fast, strong gradients. Short gradient pulses in excess of 20 G/cm minimize signal loss during pulse sequences.

Applications advantages

With its integral inverse probehead, the S-17 Accessory can accommodate proton as well as heteronuclear GES techniques.

Gradient fields in excess of 20 G/cm are able to suppress water in aqueous samples and to improve performance in heteronuclear experiments. Other applications advantages:

- ► Eliminates phase cycle requirements and subtraction error.
- ► Reduces T1 noise.
- ► Reduces collection times for 2D, 3D and 4D data sets.
- ► Provides lineshape independent water suppression in multiple quantum coherence selection experiments.
- ► Provides lineshape independent water suppression via diffusion differences for large molecular weight samples.
- ► Improves water suppression in experiments using selective time reversal RF pulses.
- ► Separates cross-correlation and exchange phenomena in NOESY experiments.
- ► Distinguishes chemicals inside the cell from those outside in whole cell applications.

For additional information on the S-17 GES Accessory, write to GE NMR Instruments, 255 Fourier Ave., Fremont, CA 94539.
Or call toll free:

1-800-543-5934

GE NMR Instruments

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Gradient-Enhanced ^{15}N HMQC

The pulse sequence and the coherence pathway diagram for a ^{15}N GE-HMQC are shown in Fig. 1. The pulse sequence was a standard ^{13}C GE-HMQC experiment (1) with different gradient amplitudes to account for the difference between the gyromagnetic ratios of ^{13}C and ^{15}N. The 90° proton pulse creates transverse magnetization which evolves into an anti-phase state with respect to J(NH) coupling at the end of the period Δ (where Δ = ½J (NH)). The antiphase components are converted into heteronuclear zero- and double-quantum coherence by the ^{15}N 90° pulse and the multiple quantum coherences are allowed to evolve during t_1. The 180° ^{1}H pulse in the center of the evolution period serves to eliminate the ^{1}H chemical shift evolution, yielding pure ^{15}N chemical shifts along that axis. The zero- and double-quantum signals are then *coherence-order labeled* by the gradient pulses G1 and G2. After conversion into antiphase proton magnetization by the last ^{15}N 90° pulse, the desired components are refocused by the gradient G3 and detected. The application of a gradient pulse results in a phase factor being applied to the magnetization which is dependent upon gradient strength, duration, the distance from the gradient isocenter, the gyromagnetic ratios of the coupled nuclei, and the desired coherence order. The relative amplitudes of the labeling and refocusing gradient pulses will determine the selection of a specific coherence pathway and are calculated to suppress magnetization components arising from the solvent and other protons not coupled to ^{15}N spins.

The fundamental principle of coherence selection using gradients is that for a pathway to be detected, the cumulative phase factor during the acquisition must be zero:

$$G_1p'1 + G_2p'_2 + G_3p'_3 = 0. \quad [1]$$

The subscripts denote steps in the pulse sequence where p′ defines a composite coherence order for the heteronuclear case which includes the gyromagnetic ratios of the coupled nuclei:

$$p' = {}^{p1}\mathrm{H} + (\gamma^{15}\mathrm{N}/\gamma^{1}\mathrm{H})^{p15}\mathrm{N} \quad [2]$$

and ^{p1}H and ^{p15}N are the coherence orders for the ^{1}H and ^{15}N spins respectively.

In the coherence pathway diagram, the relevant values of p' are given to the left and the relative gradient areas (gradient strength x duration) are given next to each gradient pulse. The following pathway (shown in *Fig. 1*):

$$\mathrm{H}(+1) \rightarrow \mathrm{H}(+1)\mathrm{N}(0) \rightarrow \mathrm{H}(+1)\mathrm{N}(+1) \rightarrow \mathrm{H}(-1)\mathrm{N}(+1) \rightarrow \mathrm{H}(-1)\mathrm{N}(0)$$

is detected using a 5:5:1 ratio of gradient areas, since according to Equation 2:

$$5(1.1) + 5(-0.9) + 1(-1.0) = 0 \quad [3]$$

where the numbers in the parentheses refer to the composite coherence orders. Using these relative gradient areas, protons not coupled with ^{15}N spins may pass through an alternate pathway:

$$\mathrm{H}(+1) \rightarrow \mathrm{H}(+1) \rightarrow \mathrm{H}(+1) \rightarrow \mathrm{H}(-1) \rightarrow \mathrm{H}(-1)$$

which results in a net phase factor:

$$5(1.0) - 5(-1.0) + 1(-1.0) = -1 \quad [4]$$

Thus, signals from this pathway remain defocused during the acquisition.

A 2D ^{15}N GE-HMQC spectrum of ^{15}N enriched BPTI is shown in *Fig. 2*. The spectrum was collected using a 5 mm inverse probe on an Omega™ PSG 500 spectrometer equipped with an S-17 gradient accessory. Half-sinusoid shaped gradient pulses were applied simultaneously along the X, Y, and Z axes with a maximum gradient strength of ≈20 Gauss/cm and a duration of 3.5 ms. A matrix size of 2048 × 128 resulted in 3.5 Hz resolution in the ω_2 dimension and 10 Hz in the ω_1 dimension. No decoupling was applied.

Gradient-enhanced experiments provide a viable alternative to traditional phase-cycling methods for the selection of coherence pathways. In cases where the sensitivity is adequate, gradient selection can substantially reduce the collection time in multi-dimensional experiments. The ^{15}N GE-HMQC data presented here has none of the t_1-noise from cancellation artifacts usually present in phase-cycled versions of the HMQC experiment. In addition, since the suppression of the single-quantum signals is done prior to acquisition, the receiver gain may be increased, which results in a substantial increase in signal-to-noise. For these reasons, gradient pulses should be the method of choice for coherence selection in HMQC experiments.

Reference

1. R.E. Hurd and B. K. John, *J. Magn. Reson.* **91,** 648 (1991).

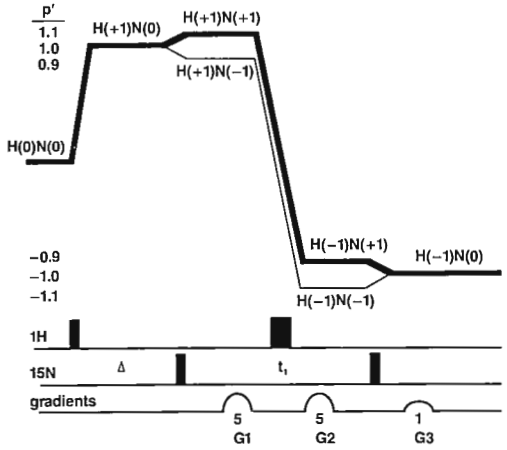


Fig. 1

Pulse Sequence and the coherence pathway diagram for a 15N GE-HMQC experiment.

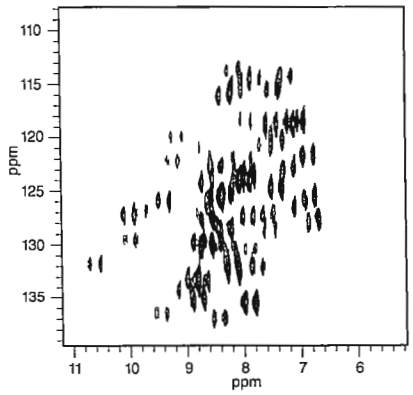


Fig. 2

A 2P Ge-HMQC spectrum of 15N enriched BPTI. The sample was 2.6mM in 90% H2). The data collection time was 2.6 hours.

Abbott Laboratories
D-47G, AP9
Abbott Park, IL 60064

Dr. B. L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, California 94303

(received 9/28/91)

RE: SOLVENT EXPOSED REGIONS OF ENZYME-BOUND LIGANDS

Dear Barry,

In order to aid in the design of clinically useful enzyme inhibitors, it would be helpful to distinguish between those portions of the ligand that interact with the enzyme from those that are exposed to solvent. This information is important for identifying the functional groups of the ligand that could be modified to improve the physical properties (e.g., water solubility) of the inhibitor without affecting binding affinity. Towards this end, we have been developing and applying NMR methods for identifying the solvent exposed regions of enzyme-bound ligands using the paramagnetic relaxation reagent, 4-hydroxy-2,2,6,6-tetramethylpiperidinyl-1-oxy (HyTEMPO). The approach that we have employed relies on the distance-dependent change in T_1 measured in the presence and absence of HyTEMPO using a pulse sequence (T_1-HMQC) that consists of a 180° proton pulse and variable delay (t) followed by a heteronuclear multiple quantum correlation (HMQC) experiment. The method is easy to implement, highly sensitive, and can rapidly yield important structural information on enzyme/inhibitor complexes.

We have applied this approach in the study of the immunosuppressant cyclosporin A (CsA) bound to its putative target protein, cyclophilin (CyP). For the most part, those CsA residues that were close to the protein as evidenced by CsA/CyP NOEs (1) were those residues that were the least affected by the addition of HyTEMPO (2).

We have also applied this technique to the study of an FK506 analog, ascomycin, bound to FKBP. Analogous to our work on the CsA/CyP complex, those portions of ascomycin close to the protein as evidenced by ascomycin/FKBP NOEs (3) were those residues that were the least affected by the addition of HyTEMPO and those portions of ascomycin exhibiting no NOEs to the protein were found to be the most solvent exposed (4).

(1) Fesik et al., Biochemistry 30, 6574-6583 (1991).

(2) Fesik et al., J. Am. Chem. Soc. 113, 7080-7081 (1991).

(3) Petros et al., J. Med. Chem. 34, 2925-2928 (1991).

(4) Petros et al., J. Biomol. NMR (in press).

Sincerely,

Stephen Fesik Ed Olejniczak Andrew Petros David Nettesheim, Tim Logan

Gerd Gemmecker Rob Meadows Placido Neri Andrew Hansen Robert Xu

September 17, 1991 (received 9/18/91)

Professor Barry Shapiro
966 Elsinore Ct.
Palo Alto, CA 94303

Dear Prof. Shapiro:

Carbon-13 NMR of Phenyl Sulfide

During recent investigations into the applicability of carbon-13 NMR to the analysis of poly(phenylene sulfide), PPS, we examined the chemical shifts of the carbons of phenyl sulfide, **1** (structure and numbering system shown in the attached table) in several different solvents as a model for the phenylthio end group of PPS and in an iodine charge transfer complex. In the table are shown the chemical shifts for the carbons of **1** neat and in acetone, sulfolane, chloroform and 1-cyclohexyl-2-pyrrolidinone (CHP). Spectra were collected at room temperature. For the neat sample or solvents without deuteration, field/frequency stabilization was accomplished with the deuterium of glyme-d_6 held in a concentric capillary while, for acetone (10% acetone-d_6) and chloroform-d, field/frequency stabilization was accomplished with the deuterium in the solvent. Dissolved samples were prepared so that the solvent was in excess relative to **1**. For the charge transfer complexes, neat **1** was saturated with iodine and in chloroform-d the molar ratio of iodine: **1** was 1.42:1. Chemical shift assignments for the carbons were accomplished by examining the proton-coupled spectrum relative to the decoupled spectrum. Over the concentration range of 2.0 to 0.01 M in chloroform-d, C1, C2, C3 and C4 exhibit no more than 0.16 ppm variation in chemical shift.

Carbon resonance assignments for **1** in the iodine charge transfer complexes were accomplished in a similar manner. From the accompanying graph, it is clear that the solvent-induced chemical shifts exhibit no unexpected effects. Iodine complexation of **1** has been studied by carbon-13 NMR (M. J. Shapiro, J. Org. Chem., 43(4), 742-3 (1978)) and provides results similar to these for C1 and C4 chemical shifts, that is, diamagnetic shifts (increased shielding) for C1 and paramagnetic shifts

(decreased shielding) for C4. From this work, C2 exhibits a small diamagnetic shift while C3 exhibits a slightly larger paramagnetic shift.

These results will be of value as we continue to evaluate NMR as a tool for the analysis of PPS.

Sincerely yours,

Doug

Douglas W. Lowman
Senior Research Chemist
Research Laboratories
P. O. Box 1972
Telephone: (615) 229-4728
Internet Address: dwlowman@kodak.com

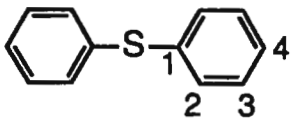
Position Available

The Research Laboratories of Eastman Chemical Company has an opening for a PhD NMR Spectroscopist with a background in organic, analytical or physical chemistry. Experience with NMR relative to polymer chemistry would be beneficial. Working knowledge of state-of-the-art solution-state high-field NMR techniques, including both 1D and 2D homo- and heteronuclear NMR, and hardware and software trouble-shooting skills are necessary. The successful candidate must be interested in working in a problem-solving environment, exhibit good communications skills, and be a self-starter with a desire to work both as a contributing member of a team and as an individual contributor.

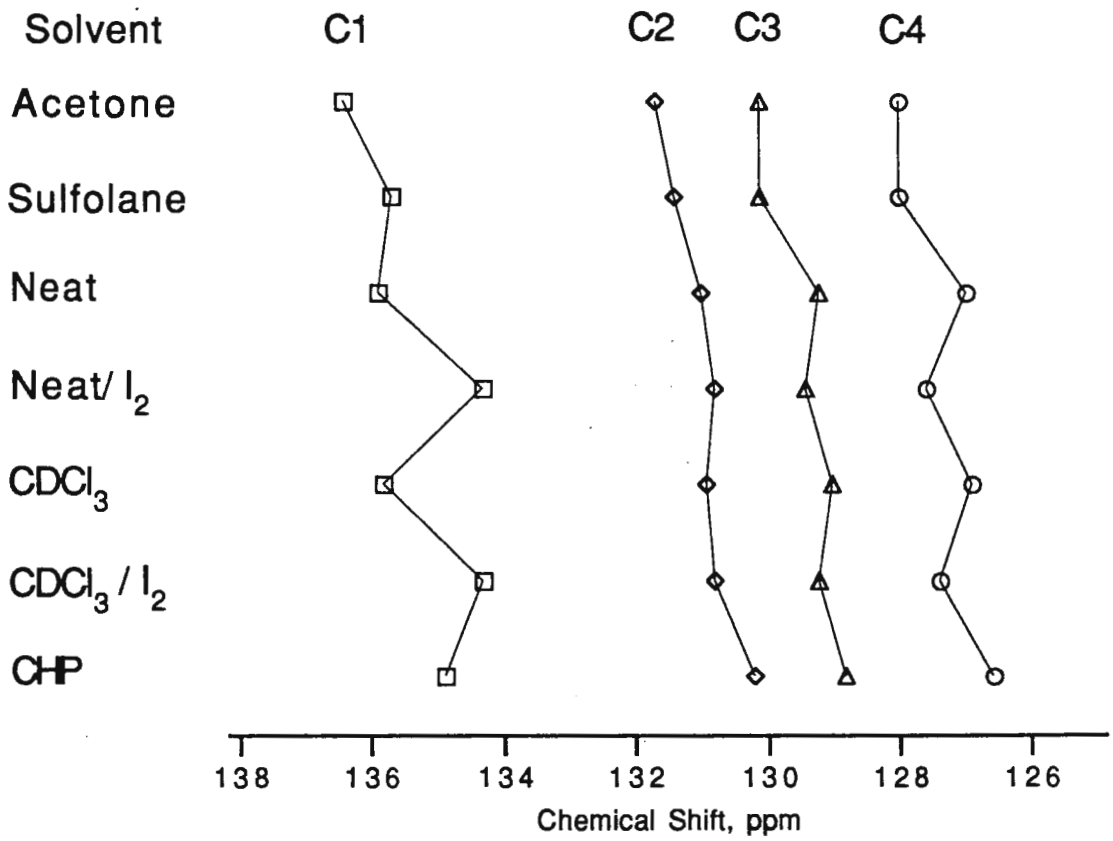
Eastman Chemical Company, which employs approximately 300 PhD scientists and engineers, is one of the largest chemical and fiber manufacturing facilities in the U. S. Interested candidates should send resume to: EASTMAN CHEMICAL COMPANY, P. O. Box 1975, Kingsport, TN 37662

AN EQUAL OPPORTUNITY EMPLOYER

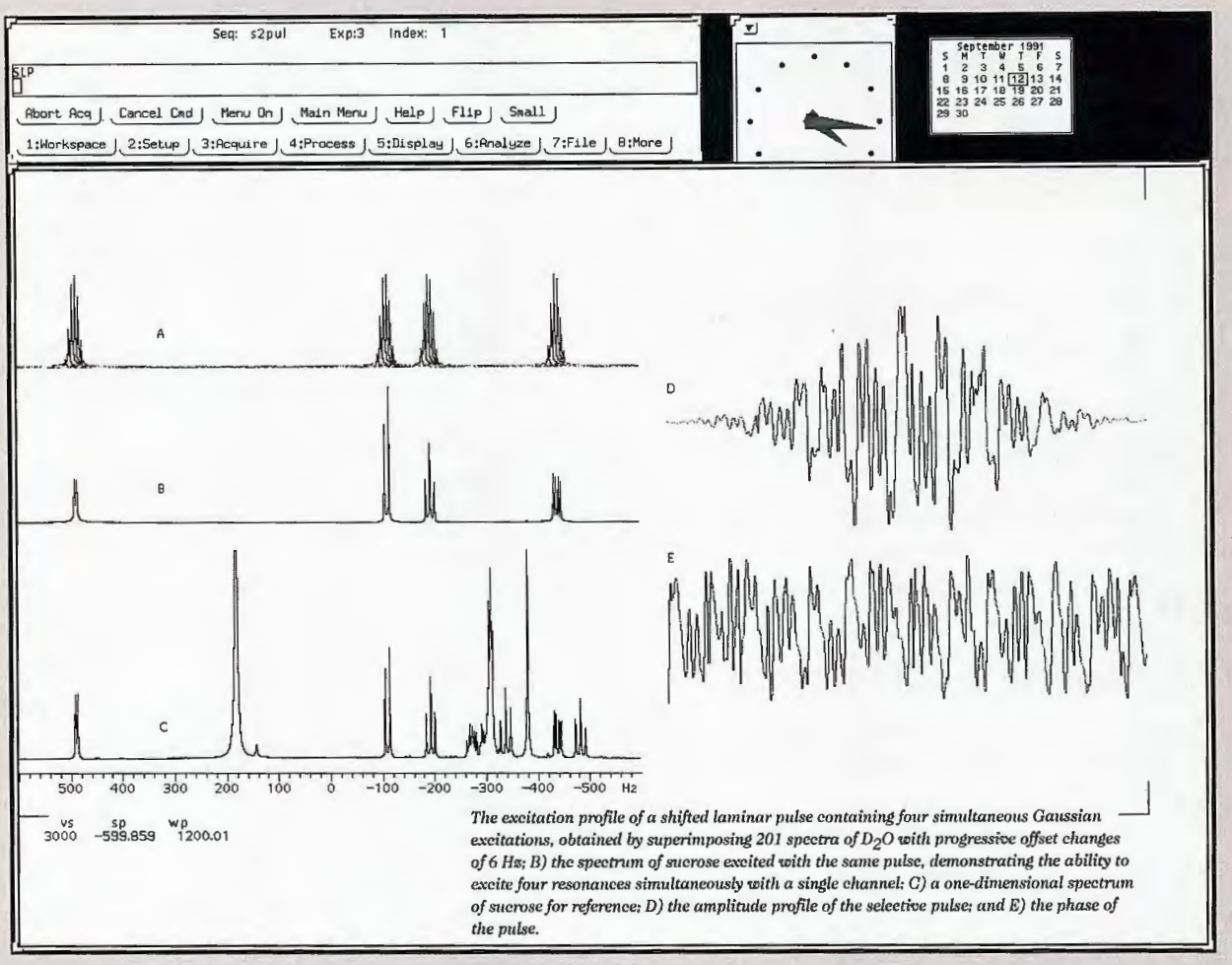
Carbon-13 NMR Chemical Shifts for Phenyl Sulfide



Solvent	C1	C2	C3	C4
Acetone	136.4	131.7	130.1	128.0
Sulfolane	135.7	131.4	130.1	128.0
Neat	135.9	131.0	129.2	127.0
Neat/I_2	134.3	130.8	129.4	127.6
$CDCl_3$	135.8	130.9	129.0	126.9
$CDCl_3/I_2$	134.3	130.8	129.2	127.4
CHP	134.9	130.2	128.8	126.6



Excite Four Resonances Simultaneously with Shifted Laminar Pulses.



The excitation profile of a shifted laminar pulse containing four simultaneous Gaussian excitations, obtained by superimposing 201 spectra of D_2O with progressive offset changes of 6 Hz; B) the spectrum of sucrose excited with the same pulse, demonstrating the ability to excite four resonances simultaneously with a single channel; C) a one-dimensional spectrum of sucrose for reference; D) the amplitude profile of the selective pulse; and E) the phase of the pulse.

Need to excite three isotopes and three, four, or even more resonances simultaneously? Many of the experimental results in the published literature have been obtained on modified spectrometers. These experiments can now be executed on Varian's standard UNITY® 3-channel NMR spectrometer with the shifted laminar pulse (SLP[1]) technique.

Don't waste valuable time and money on unnecessary hardware or modifications. Buy a UNITY NMR spectrometer and get results instead.

1. Steven L. Patt, Journal of Magnetic Resonance (in press).

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varian

What does it take to do quadruple resonance experiments?

• An ultra-high performance NMR spectrometer with three rf channels...

Varian's UNITY NMR spectrometer is modularly configured with either a lowband or an industry-unique fullband 3rd rf channel for these demanding triple and quadruple resonance applications.

• An optimized application-focused triple resonance probe for superior sensitivity...

Varian's $^{1}H\{^{13}C/^{15}N\}$ Triple•nmr™ Probe gives stellar performance under the lossy sample conditions required to carry out a myriad of biomolecular NMR experiments. The excellent rf homogeneity results in efficient transfer of magnetization for optimal sensitivity and high quality solvent suppression. The probe's robust high-power handling circuit design makes full use of the power output from Varian's 3-channel UNITY NMR spectrometers.

• Waveform generators...

Varian's programmable pulse modulators provide advanced pulse shaping capabilities for these complex biomolecular applications. Proper execution of the experiments mandates fast and accurate phase control within the shaped pulses. The programmable pulse modulators also maintain a linear response throughout the amplitude range.

• Shifted laminar pulses...

Varian's new shifted laminar pulse technique allows a single rf channel to apply excitation at more than one frequency simultaneously, thus allowing multiple resonance experiments to be performed with only a single channel per isotope.

• 3-D software...

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Dr. Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

September 30, 1991
(received 10/14/91)

Some Observations on Linear Prediction

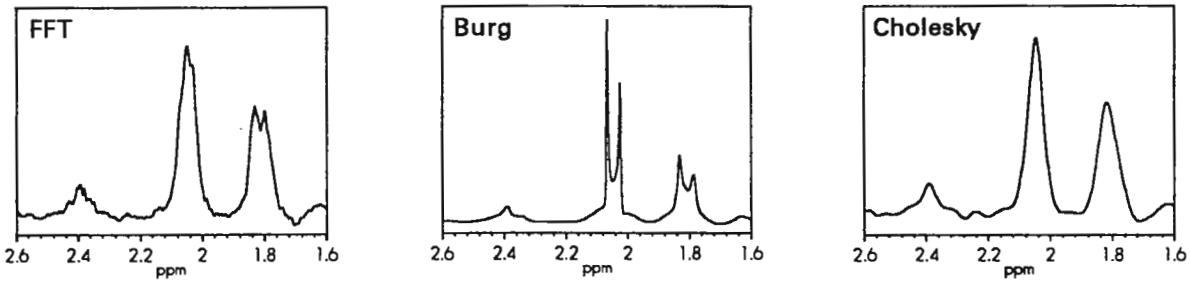
Dear Barry,

We have been working on the application of linear prediction (LP) to NMR problems for more than 3 years now and, as our annual contribution is due, it seems that it might finally be an appropriate time to share some of our results and opinions on this subject. The use of LP to extend data, a method popularized by economists as "time series forecasting" (*1*), and first used in NMR by Marion and Bax (2), is becoming more prevalent - particularly the forward extension of multi-dimensional data, so we tested our favorite algorithms for calculating LP coefficients at this task. The algorithms used were a Burg method (*3*), our linear least squares (LLS) method using Cholesky decomposition, and Marple's COVAR and MODCOVAR algorithms (*4*). Selected T1 traces containing some signal from a half-transformed NOESY 2-D spectrum and a half-transformed TOCSY 2-D spectrum were used. The algorithms were evaluated by using 20 LP coefficients determined from the first 64 points of each FID to predict the next 64 data points. The forward error variance of data points 21-64 (we call this "in the LP window") was calculated, along with the forward error variance of the 64 "out of the LP window" data points. The average results with 9 TOCSY traces and 15 NOESY traces are shown in the table below.

Experiment	Method	In Window σ^2 (x10^8)	Out of Window σ^2 (x10^8)
NOESY	Burg	1.11	1.20
	Cholesky (LLS)	0.89	1.24
	COVAR	0.78	1.10
	MODCOVAR	1.02	1.16
TOCSY	Burg	2.12	4.20
	Cholesky (LLS)	1.47	3.53
	COVAR	1.29	3.08
	MODCOVAR	1.97	4.51

It is apparent from the results shown, as well as numerous other tests we have performed, that Marple's COVAR algorithm is superior for predictions in one direction using a small number of coefficients and data points. Also, the observation that the Cholesky algorithm gave the worst NOESY predictions nicely illustrates the sometimes erratic behavior that can occur with these LP methods. We have found that our Cholesky least squares method is generally as good or better than the COVAR algorithm when using a large number of parameters or especially a lot of data points. There are other advantages (and disadvantages) to each of the methods we used, so I'll comment on all of them.

The well-known Burg method uses the Levinson recursion to calculate LP coefficients and minimizes the forward and backward error variance over the data set with respect to each coefficient as it is calculated. This constrained least squares approach of minimizing over each coefficient as it is determined, rather than over all coefficients, is known to produce coefficients that can cause line splitting when doing spectral estimation with methods such as maximum entropy (MEM) (*5*). As the problem in this case is with the LP coefficients, not the MEM frequency domain estimation, it might be expected that line splitting will also be observed when doing data extension as described above with coefficients calculated from the Burg method. In fact, we have observed this problem on quite a few instances, and it seems to be the most severe when using high S/N noise data sets with the number of coefficients approaching half the number (the maximum) of data points. An example is shown in the figure below. In this example one of the 1K complex point NOESY T1 traces was used. For the FFT, the FID was zero-filled to 4K. For the Burg prediction the first 128 points were used with 64 coefficients to predict points 129-4096. The other three algorithms calculated coefficients that produced diverging predictions under the same conditions, so the "prewhitening" method described below was used with our Cholesky routine to form stable coefficients. There was little change in the Burg prediction with the same "prewhitening". The Burg method is not



without its charms however. It is by far the least sensitive algorithm to data conditioning (S/N of the covariance matrix), and it is the only method that constrains the coefficients to be in the z-space unit circle, so that a forward extension of data will always converge. For these reasons, the Burg method can often produce usable LP coefficients and data extensions, especially with high S/N data, when the other methods blow up.

Our LLS method uses an otherwise hard-to-come-by vectorized, complex Cholesky decomposition routine (*4*), to determine LP coefficients from the covariance matrix. We actually calculate "npar+1" coefficients, and use the last one as an offset. As the offset is usually minuscule, it can just be discarded. This method has the overhead of creating and storing the covariance matrix that can take longer than the Cholesky decomposition, and the decomposition takes more calculations to perform than the other three "fast" algorithms. Nevertheless, this method will produce the best coefficients when calculating a large number of coefficients with a large number of data points from a well-conditioned data set. We and others (*6*) have calculated 2000 or more coefficients from 6000 or more data points successfully with a Cholesky decomposition LLS. This method minimizes the error variance in both directions with respect to all coefficients over the data set.

Marple has taken advantage of special substructures of the LP covariance matrix to create two "fast" algorithms, COVAR and MODCOVAR that rival the Burg method in efficiency and produce very accurate LP coefficients, but that are much more sensitive to data conditioning. His COVAR algorithm calculates two sets of coefficients, one with the error minimized in the forward direction with respect to all coefficients, and one with the error minimized in the backward direction. For some reason it does much better in the forward direction, so much so that, when back predicting, it is advantageous to just load the data in backwards and do a "forward" prediction on it. This algorithm is a good one to use with small well-conditioned data sets as shown above. Marple's MODCOVAR routine seeks to minimize the error in both directions with respect to all coefficients, and produces one set of coefficients. Marple suggests this method as an alternative to the Burg or other Levinson recursion based methods for spectral estimation as it is immune to the line splitting problem of the Burg algorithm.

Finally, we have found that when working with poorly conditioned data, for example, high S/N ^{1}H spectra, it can occasionally be useful to remove the mean from the data and normalize it before calculating LP coefficients, but it is somewhat more useful to add a small amount of noise to the data, a process engineers call "prewhitening," to better condition the data. An example is mentioned above in association with the figure shown above. The best amount of noise to add varies depending on the data, but halving the S/N of the data is a good place to start. With either of these methods, once the LP coefficients are calculated, they can be used with the original data set for data extensions.

1. Box and Jenkins, "Time Series Analysis: Forecasting and Control," Holden-Day, San Francisco, 1976.
2. Marion and Bax, *J. Magn. Reson.*, **83**, 205 (1989).
3. Burg, *Proceedings of the 37th Meeting of the Society of Exploration Geophysicists* (1967).
4. Marple, "Digital Spectral Analysis With Applications," Prentice-Hall, Englewood Cliffs, NJ, 1987.
5. Fougere, Zawalick, and Radoski, *Phys. Earth Planet. Inter.*, **12**, 201 (1976).
6. Gesmar and Led, *J. Magn. Reson.*, **76**, 183 (1988).

Sincerely,

Doug

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(415) 750-2146

September 16, 1991 (received 9/20/91)

Professor Bernard L. Shapiro
Texas A&M University NMR Newsletter
966 Elsinore court
Palo Alto, CA 94303

Dear Barry:

3-Dimensional Spatial Encoding Proton Spectroscopic Imaging

For over the past year we have been performing two-dimensions of phase encoding to obtain spectroscopic imaging results of protonated metabolites (primarily N-acetyl aspartate, creatine, choline, and lactate when it is elevated) in human brain (1). To accomplish this, we use a PRESS (90-180-180) localization experiment (2) to select a slice of 17 to 20 mm thickness within the brain, and perform phase encoding over the selected slice. The slice must not extend to the skull or our results are swamped by lipid signal originating from the scalp. Water suppression is accomplished by a double WEFT sequence ahead of the PRESS localization (1,2).

We have recently extended this experiment to provide three dimensions of spatial encoding (3). This enables selection of a much thicker (60 mm) region of brain, and display of several spectroscopic imaging slices through the selected region. To further suppress lipid contamination and enable extension of the PRESS-localized region closer to the skull, we have also added sinc cosine outer volume suppression pulses to the experiment (Fig. 1). Typically, we use an echo time of 272 ms, and a TR of 1700. The times t_1 and t_2 are adjusted to minimize the water signal; 16 encodings are used in the x and y directions, and 12 in the z direction. However, a reduced k-space sampling scheme is utilized to enable the run time to be just under 45 minutes. Field of views are chosen to obtain a nominal voxel volume of approximately 1 cc. Figure 2 shows results of N-acetyl aspartate (NAA) spectroscopic images from a normal volunteer. Figure 2A shows a transverse MR image with an inner box indicating the region selected by the PRESS sequence, along with a single voxel spectrum showing the large, upfield NAA resonance. Figure 2B contains a series of conventional MR image slices along with the corresponding NAA spectroscopic images obtained from a single experiment.

Sincerely,

Jeff Duijn Gerald B. Matson Michael W. Weiner

MR Unit, Department of Veterans Affairs Medical Center, San Francisco, and
Departments of Medicine, Radiology, and Pharm. Chem., UCSF.

References:

1. J.H. Duijn, G.B. Matson, J.W. Hugg, A.A. Maudsley, and M.W. Weiner. Proton magnetic resonance spectroscopic imaging of human brain infarction, Radiology (Submitted, 1991).
2. P.R. Luyten, A.J.H. Marien, W. Heindel, et al. Metabolic imaging of patients with intracranial tumors: H-1 spectroscopic imaging and PET. Radiology 176:791 (1990)
3. J.H. Duijn, G.B. Matson, and M.W. Weiner. 3D phase encoding methods for ^1H spectroscopic imaging of human brain (Abs). Society of Magnetic Resonance in Medicine, p. 1005 (1991).

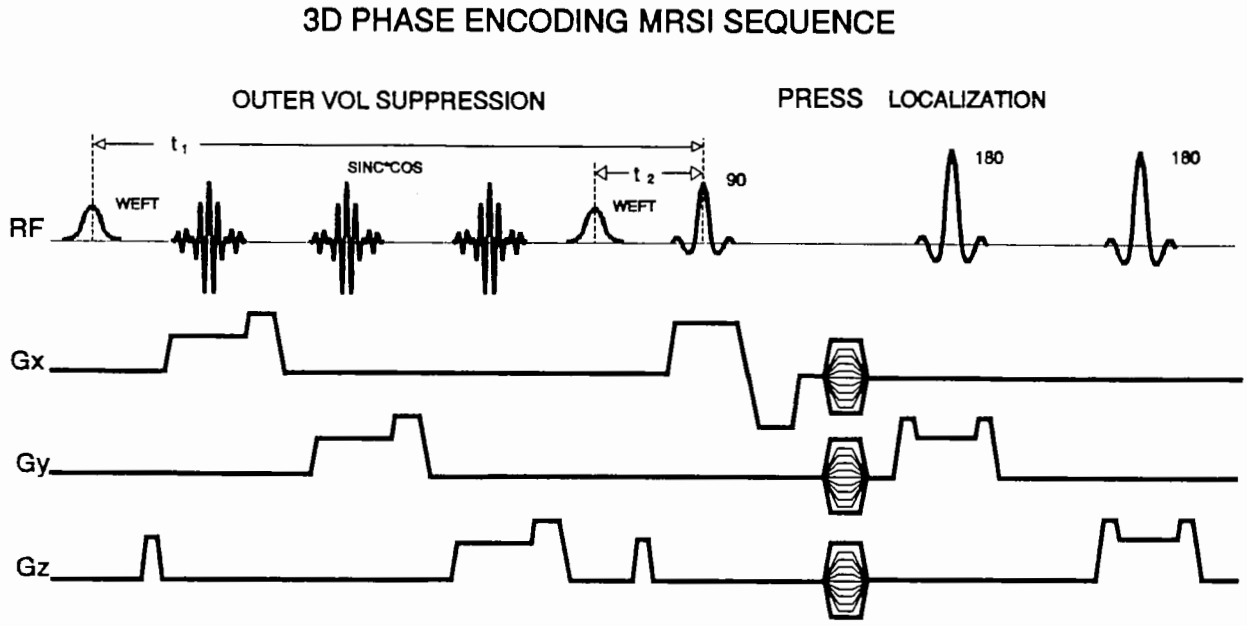

Fig. 1. 3-D MRSI sequence.

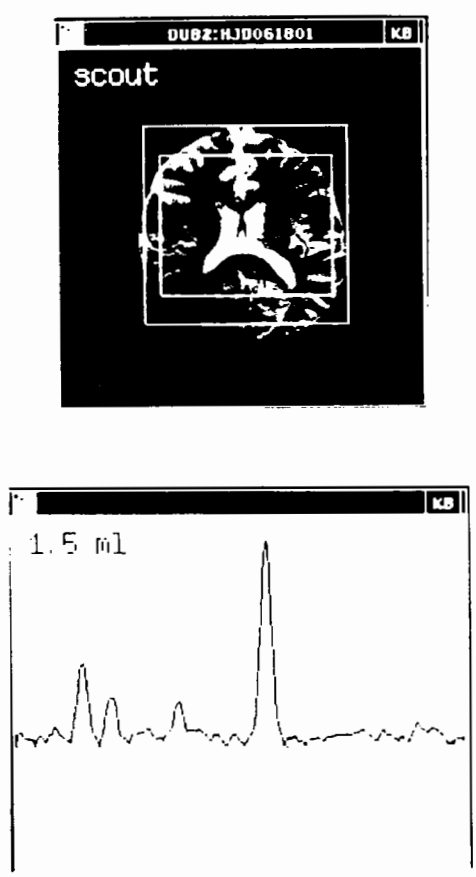

Fig. 2A. MR image with pre-localization volume (upper) and single voxel spectrum.

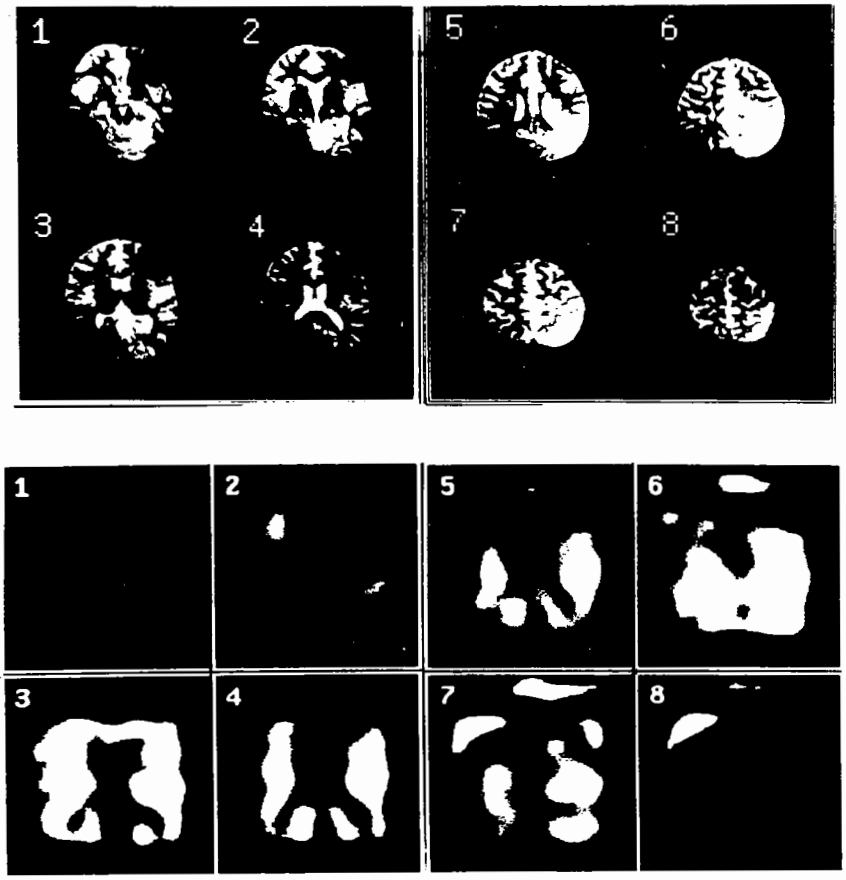

Fig. 2B. Transverse MR images (upper) and corresponding NAA MR spectroscopic images (lower).

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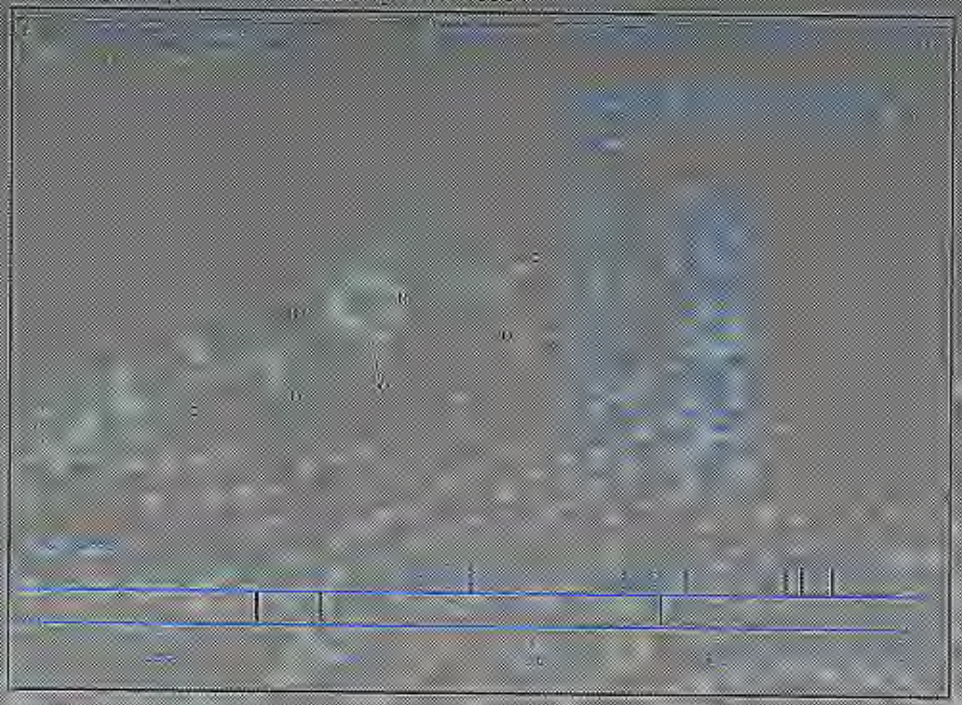

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Dr. Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

October 1, 1991
HvH 91-A-162
(received 10/3/91)

Measuring very small carbon-proton coupling constants in oligosaccharides

Dear Dr. Shapiro:

While searching for long-range carbon-proton coupling constants in oligosaccharides, we found that measurement of coupling constants that are smaller than the natural line widths is experimentally difficult. As has been shown before [1], this task is best accomplished by recording exclusive-type (E.COSY) proton-carbon correlation spectra.

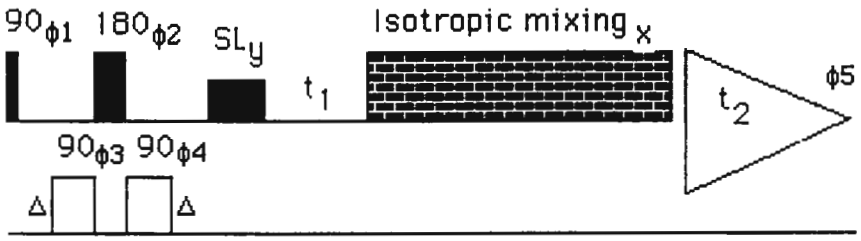
Figure 1 shows a pulse sequence for the selective 2D analogue of the 3D E.COSY $\{^1H,^{13}C\}$ experiment described in [2]. The carbon 90° pulses were selective; the delay $\Delta+0.6t_{90(^{13}C)}$ was taken as $1/2^1J_{CH}$. The phase cycling was as follows: ϕ_1=x, ϕ_2=4x,4y,4(-x),4(-y), ϕ_3=x,-x, ϕ_4=x,x,-x,-x, ϕ_5=2(x,-x,-x,x),2(-x,-x,x,x). Retaining t_1 evolution allows separation of proton multiplets corresponding to molecules with different carbon spin polarization. Figure 2 shows H2 to H6 proton multiplets of β-(1-^{13}C)-glucose split in the vertical dimension by $^1J_{C1H1}$ and in the horizontal dimension by $^nJ_{C1H}$. The spectral resolution in the ω_2 domain was 0.055 Hz/pt and allowed us to determine the C1-H6R and C1-H6S couplings to be +0.2±0.05 and 0.4±0.1 Hz, respectively.

Sincerely,

Leszek Poppe John Glushka Herman van Halbeek

[1] G.T. Montelione, M.E. Winkler, P. Rauenbuehler & G. Wagner; *J. Magn. Reson.* **82**, 198-204 (1989).
[2] A.S. Edison, W.M. Westler & J. Markley; *J. Magn. Reson.* **92**, 434-438 (1991).

Fig. 1:


90φ1
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t1
Isotropic mixing x
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90φ3
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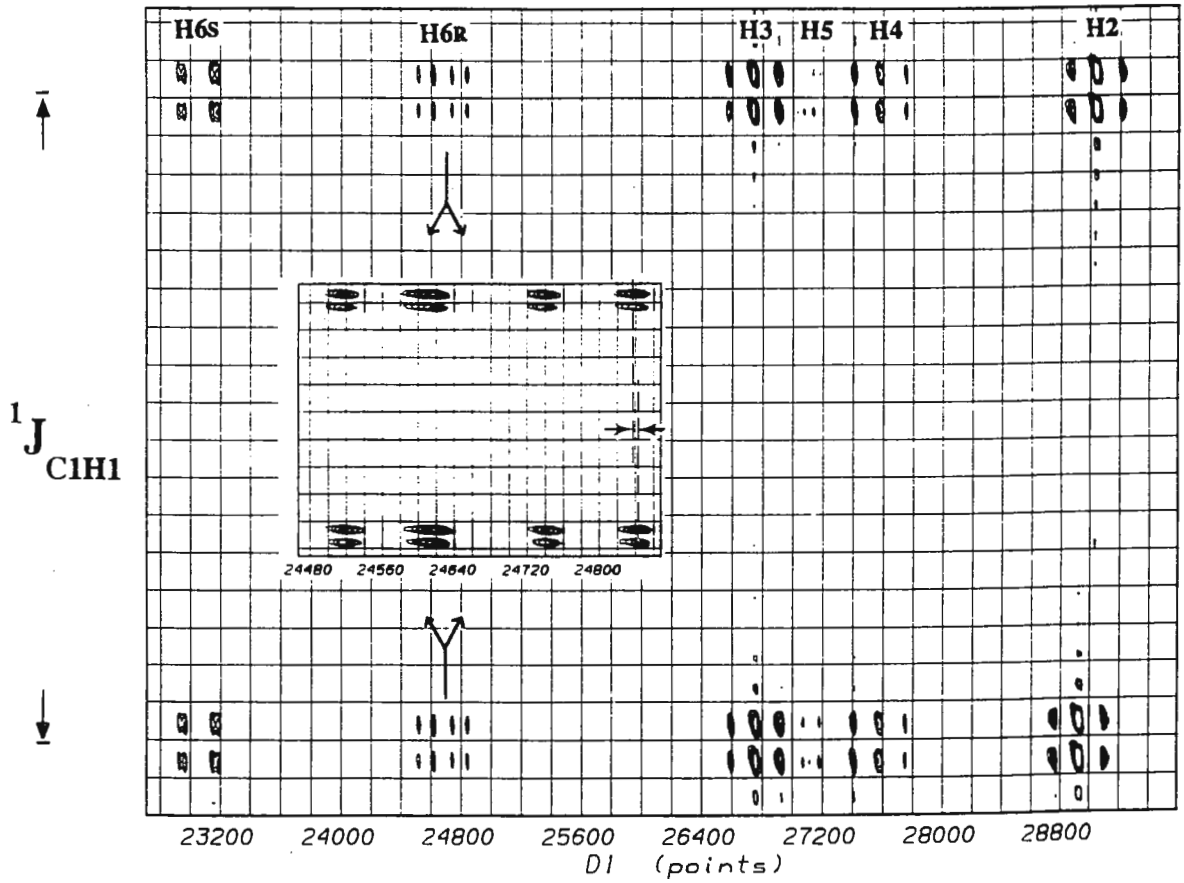
Δ

Fig. 2:


H6S
H6R
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24480
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24800
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VARIABLES CONTRIBUTING TO ACCURATE SIGNAL TO NOISE MEASUREMENTS

We recently had the opportunity to make signal to noise measurements for the Bruker dynamic range test sample under a variety of conditions. It is clear that careful optimization of acquisition parameters and a judicious choice of the amount of noise used for the calculation can lead to a huge increase in the values obtained. As a result of these measurements, we concluded that it is critical to standardize methods for measuring sensitivity under these conditions.

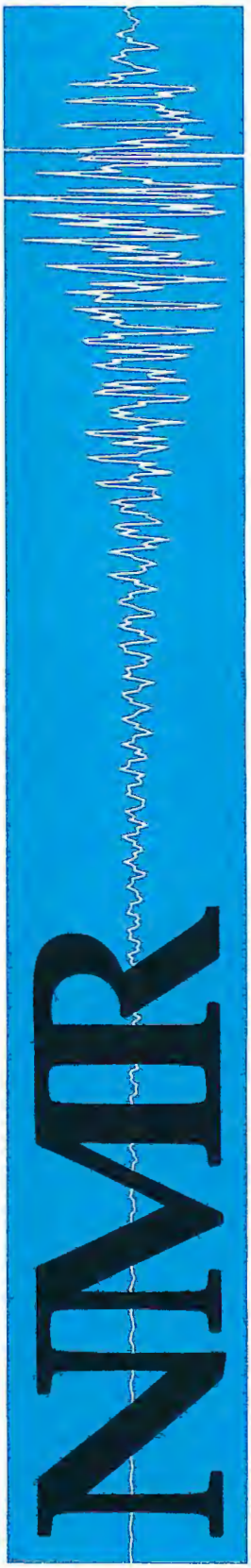
SIGNAL:NOISE VALUES FROM AMX300 WITH 5 MM BROADBAND PROBE

	SW[1]	RG[2]	NOISE[3]	S/N[4]
1	**3731**	not full	300 Hz	38
2	**6024**	not full	300 Hz	60
3	6024	**not full**	300 Hz	60
4	6024	**full**	300 Hz	104
5	6024	full	**300 Hz**	104
6	6024	full	**100 Hz**	203

[1] Acquisition parameter: sweep width
[2] Acquisition parameter: receiver gain, should be optimized for full digitization
[3] Amount of noise used for S/N calculation
[4] The dynamic range test sample consists of a mixture of water, methanol, acetonitrile and t-butanol at proton molar ratios of 10,000, 100, 10, and 1 in D2O (8.8% gram/gram). The conditions for measuring sensitivity are to apply a 90 degree pulse to the non-spinning sample, and measure the height of the t-butanol signal relative to the height of noise.

Several conclusions are obvious from this study (see Bruker Report 1/83 for a detailed exposition of this problem). First, absolute values for sensitivity measurements can be meaningless without careful standardization of the measurement conditions. Second, relative comparisons of values are only valid when conditions are meticulously duplicated for each measurement. And third, it is clear how easily parameters can be manipulated to artificially enhance apparent performance in a test spectrum.

As a result of this comparison, we propose the following standard procedure for measuring sensitivity under conditions of high dynamic range.



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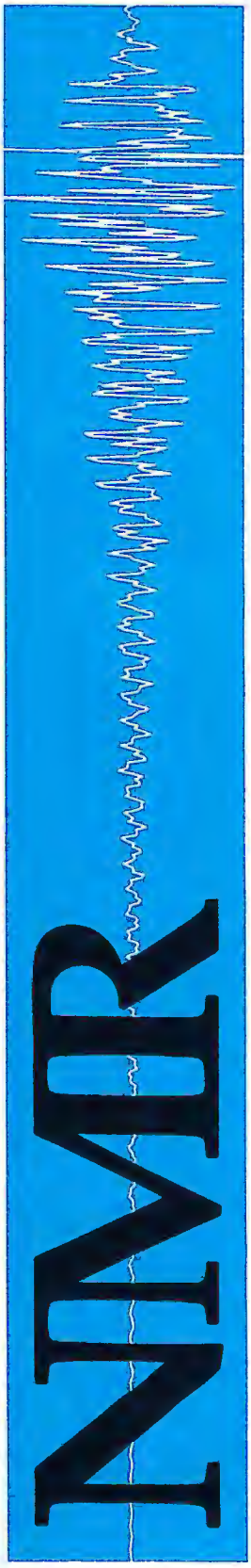
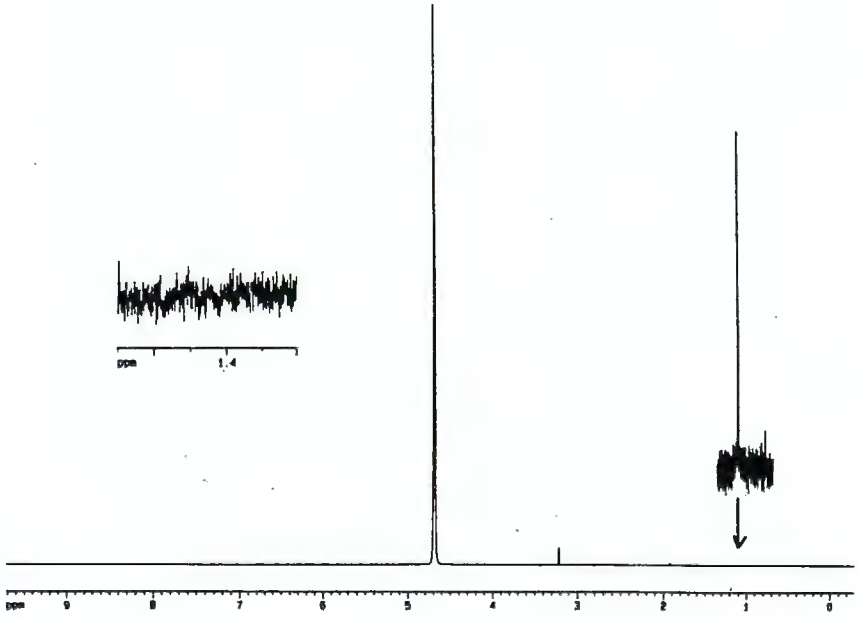


TEST CONDITIONS FOR MEASURING SENSITIVITY UNDER CONDITIONS OF HIGH DYNAMIC RANGE

sample:	mixture of water, methanol, acetonitrile and t-butanol at proton molar ratios of 10,000, 100, 10, and 1 in D2O (8.8% gram/gram)
number of scans:	1
pulse width:	90 degree
sweep width:	10 ppm, with carrier offset positioned at the water resonance
filter width:	10 ppm
acquisition time:	2.0 seconds
receiver gain:	optimized to fill the digitizer
presaturation:	none
processing:	no apodization
noise:	a region of 0.5 ppm plotted in the region between acetonitrile (1.9 ppm) and t-butanol (1.1 ppm) peaks.



9/91, CAJ/SSP

Position Wanted

Dr. **Mario F. Simeonov** wishes to make his availability for, and interest in, a position in NMR spectroscopy known. Dr. Simeonov received his Ph.D. degree in 1980 at the Institute of Organic Chemistry, Bulgarian Academy of Sciences, Sofia, under the direction of Prof. Stefan Spassov. He has also worked in the laboratories of Profs. H. Duddeck, H. Kessler, K. Pihlaja, and E. Randall. In addition he also lists Prof. G. Snatzke as a reference. Dr. Simeonov has extensive experience involving modern NMR techniques on a wide variety of NMR instruments.

I will be happy to send a copy of Dr. Simeonov's letter to me, his curriculum vitae, list of publications, his references, etc., to potentially interested persons and organizations. Please call or write me. I am also sending Dr. Simeonov copies of a few recent Newsletters, in which quite a number of Positions Available are advertised.

B. L. Shapiro
17 October 1991

FOR SALE, VARIAN XL200. Beckman Instruments, Inc., Research and Applications Department, Palo Alto, offers for sale a VARIAN XL200. Price--best offer. Purchased new in 1985, currently in use, the instrument is in good working order. The probe is broadband/switchable (20-80/200 MHz), the magnet has rubber (adjustable) seals, and the host and acquisition computer systems are stock issue. The instrument includes a Topaz Power Conditioner and HP7475A Plotter (6-pen). Please contact Mr. Jeffrey Smith, Beckman Instruments, Inc., 1050 Page Mill Road, Palo Alto, California, 94304; (415)859-1565.

POSTDOCTORAL/OPERATOR POSITION

A Postdoctoral position in NMR is available at Clark University. The position involves a collaboration between the Chemistry Department of Clark University and Genetics Institute, an established biotechnology company in the area. The position involves responsibility for the operation and management of a newly acquired Varian Unity 500 MHz, three channel NMR system and includes the participation in collaborative research projects with research groups in the biomolecular structure area. It's anticipated that the candidate will spend approximately 50% of his time in each of these two endeavors. A knowledge of new high field, high resolution techniques and a familiarity with UNIX is required. Salary is in the range of $26-30K depending on qualifications and the initial appointment is for two (2) years. Please send a resume and three letters of recommendation to: **Dr. Paul Inglefield, Director, NMR Facility, Chemistry Department, Clark University, Worcester, MA 01610.**

Clark University is an Equal Opportunity/Affirmative Action Employer

Macromolecular NMR Spectroscopist

The Lilly Research Laboratories, a division of Eli Lilly and Company, has an opening for a postdoctoral fellow who will collaborate with established groups from several disciplines to study the structure of DNA duplexes and their interactions with drug molecules.

Candidates for the position should have a Ph. D. and experience in determining DNA structures by NMR spectroscopy. This also includes computational methods used in refining structures. A strong background in biological sciences would also be desirable.

The Lilly NMR laboratory is well equipped for macromolecular studies and includes a UNITY-500 NMR spectrometer with triple-resonance capabilities, a Silicon Graphics workstation, and the necessary software for advanced NMR processing and molecular calculations. These facilities are housed in a newly completed suite of laboratories which also include x-ray crystallography, vibrational spectroscopy and computational chemistry. There is also access to a Cray 2S supercomputer running numerous computational programs.

Qualified candidates should send a curriculum vitae to:

Dr. Allen D. Kline
Lilly Research Laboratories
Lilly Corporate Center
Indianapolis, Indiana 46285-0403

Position Available

Postdoctoral Associate

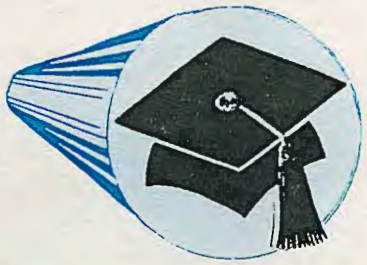
An opening for a Postdoctoral Associate is available in the pharmaceuticals division of **CIBA-GEIGY Corp.** Candidates should possess a Ph.D. in Chemistry, Biochemistry or closely related dicipline and should be fully conversant with the application of NMR theory and practice to the solution of peptide/protein structures. Experience in the preparation of peptide/protein samples for NMR evaluation is required and knowledge of data processing software (eg. FELIX or New Methods Research) and molecular modeling software (eg. MacroModel, DSPACE, INSIGHT/DISCOVER, or X-PLOR) is essential. Candidates should possess a high degree of innovative and practical skills and be willing to work closely with biochemists, medicinal chemists and molecular modeling/computational chemists in a multidiciplinary environment.

The NMR facility is equipped with a Bruker AMX-500 MHz NMR spectrometer containing a multi-channel interface and triple resonance probe for multinuclear/multidimensional experiments. The spectrometer also possesses shaped pulse capability. Off line data processing is conducted on a silicon graphics 4D/35GT computer. NMR data processing and molecular modeling software programs include: FELIX, MADNMR, MacroModel, DSPACE, DIANA, INSIGHT, and DISCOVER. The Computer-Assisted Molecular Modeling/Computational Chemistry group is equipped with a variety of graphics workstations and mainframe computers including the IBM 3090/200E with vector processors.

The position could become available as early as January 1, 1992. Interested persons should direct their inquires to: Dr. Nina Gonnella, CIBA-GEIGY Corp., 556 Morris Ave., Summit, N.J. 07901. Tel. (908) 277-7265

INTRODUCING

the NMR Graduate™ No. 509-UPG, Ultraprecision NMR Sample Tube with 0.01ml graduations!



PRICE

1-99 tubes .. $10.00 ea.
100 - 299 ..... 9.00 ea.
300 plus ..... 8.00 ea.

SPECIFICATIONS:
Standard Tube length: 178 mm (7 in.)
o.d. 4.97 mm ± 0.006 mm (0.00025 in.)
i.d. 4.20 mm ± 0.012 mm (0.0005 in.)
Camber: ± 0.0006 mm (0.00025 in.)

ADVANTAGES? Too many to list! Can you imagine working in the lab without a standard graduate cylinder or a pipette. You'll wonder why it took so long to introduce the NMR Graduate™. We are the first to bring it to you (patent pending).

HERE'S A SPECIAL OFFER THAT CAN'T BE BEAT!

(Offer No. 1231T, expiring December 31, 1991)

1. **Order 100 XR-55 5 mm Precision NMR Sample Tubes at $2.00 each, and receive 5 of our New NMR Graduate™ (No. 509-UPG) Tubes FREE OF CHARGE ($50.00 value).**

2. **Order 50 of our NMR Graduate™ (No. 509-UPG) Tubes at a discount price of 50% - you pay only $5.00 per tube, instead of $10.00, which is our regular price.**

3. **SELECTED DEUTERATED SOLVENTS AT 50% DISCOUNT (packaged in special glass sealed MINIPULS™ of 0.4 ml and 0.7 ml. Teflon* link sleeve, for transfer into NMR tubes, is provided). Order the solvents below (before December 31, 1991) and SAVE 50%!**

→ Chloroform-d, $CDCl_3$,
99.99% D, Catg. No. DC1084
10 x 0.4ml ... $30.00, you pay only $15.00/lot
10 x 0.7ml ... $52.50, you pay only $26.25/lot

→ Pyridine-d_5, C_5D_5N,
99.5%D, Catg. No. DC1280
10 x 0.4ml ... $42.00, you pay only $21.00/lot
10 x 0.7ml ... $73.50, you pay only $36.75/lot

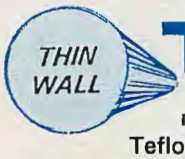
→ Toluene-d_8, $C_6D_5CD_3$,
99.9%D, Catg. No. DC1334
10 x 0.4ml ... $57.00, you pay only $28.50/lot
10 x 0.7ml ... $99.00, you pay only $49.50/lot

→ Acetonitrile-d_3, CD_3CN,
99.7%D, Catg. No. DC1025
10 x 0.4ml ... $34.00, you pay only $17.00/lot
10 x 0.7ml ... $59.50, you pay only $29.75/lot

*Teflon is a Registered Trademark of DuPont

IMPORTANT!
To get these low prices, you must refer to Offer No. 1231T

THIN-WALL-TRANSPARENT



TUBING OF TEFLON*

manufactured exclusively by Norell, Inc. from special grade DuPont thermoplastic Teflon*. Unlike PTFE, tubing from this material can be sealed by application of heat. This property offers extremely large possibilities for packaging and/or storage of samples (corrosives, liquids, solids, etc.). Our tubing of Teflon* can be also used where snug and tight fit over glass or metal tubing is required.

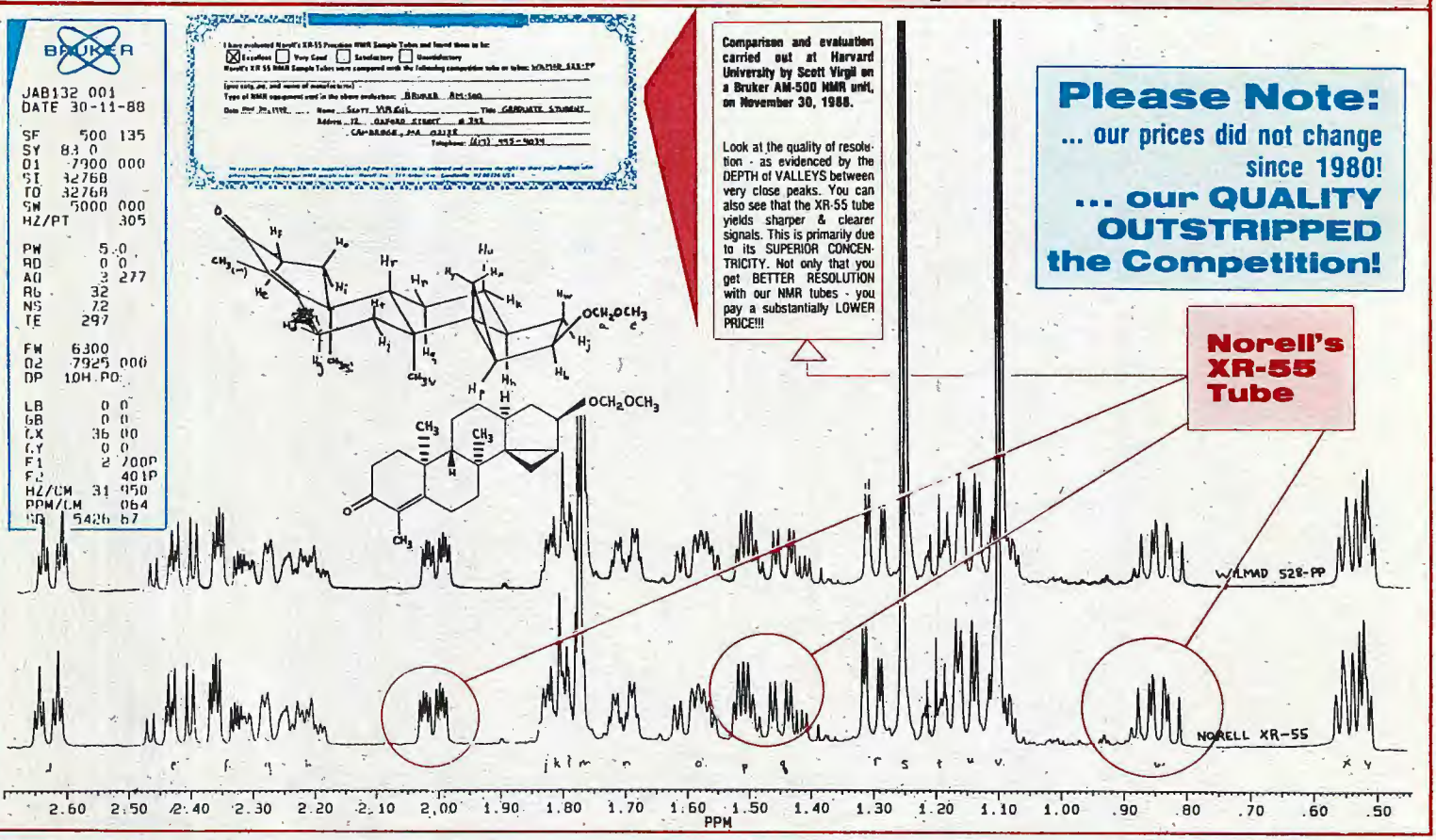
Sold in standard packaging of 12 inch sections, 4 sections per package, Catg. No. TWT-3, or 5, etc.

SIZE, i.d., mm	3	4	5	6	7	8	9	10	12
PRICE	$9.00	$9.50	$10.00	$11.00	$12.00	$14.00	$16.00	$18.00	$20.00

Single package one of each size (9 tubes).... $30.00/package of 9 Tubes, Catg. No. TWT3-12.
Other sizes and lengths available upon request.

Norell, Inc. 22 Marlin Lane, Mays Landing, NJ 08330 USA
Tel. 609-625-2223, Fax: 609-625-0526; toll-free in USA 800-222-0036; Telex: 5106006283

INDEPENDENT EVALUATION OF NORELL'S NMR Sample Tube



MOST WIDELY USED NMR Sample Tubes

PRECISION *THIN WALL*® 5mm o.d. NMR SAMPLE TUBES

No. 508-UP ULTRA PRECISION for ultra high resolution NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.013mm (0.0005 in.);
i.d. 4.20 ± 0.025mm (0.001 in.);
camber ± 0.013mm (0.0005 in.).
For additional length, add $0.24 per cm ($0.60/in.).

1-99 tubes ..... $4.50 ea.
100-299 ..... $4.25 ea.
300 + ... $4.00 ea.

Our Top Quality Tube

No. XR-55 PRECISION for medium and high resln. NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.025mm (0.001 in.)
i.d. 4.20 ± 0.025mm (0.001 in.);
camber ± 0.03mm (0.0015 in.);
For additional length, add $0.08 per cm ($0.20/in).

1-99 tubes ..... $2.20 ea.
100-299 ..... $2.00 ea.
300 + ... $1.90 ea.

No. 507-HP HIGH PRECISION for high resolution NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.013mm (0.0005 in.);
i.d. 4.20 ± 0.025mm (0.001 in.);
camber ± 0.025mm (0.001 in.).
For additional length, add $0.21 per cm ($0.50/in.).

1-99 tubes ..... $3.00 ea.
100-299 ..... $2.95 ea.
300 + ... $2.90 ea.

No. 505-P PRECISION for medium and high resln. NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.03mm (0.001 in.);
i.d. 4.20 ± 0.03mm (0.001 in.);
camber ± 0.04mm (0.002 in.);
For additional length, add $0.08 per cm ($0.20/in).

1-99 tubes ..... $1.80 ea.
100-299 ..... $1.75 ea.
300 + ... $1.70 ea.

No. 506-P PRECISION for medium and high resln. NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.025mm (0.001 in.);
i.d. 4.20 ± 0.025mm (0.001 in.);
camber ± 0.025mm (0.001 in.).
For additional length, add $0.16 per cm ($0.40/in.).

1-99 tubes ..... $2.50 ea.
100-299 ..... $2.45 ea.
300 + ... $2.40 ea.

No. 502 DISPOSABLE TYPE ["Throwaway Type"]

Standard tube length: 178mm (7 inches)
o.d. 4.97 ± 0.05mm (0.002 in);
i.d. 4.20 0.05mm (0.002 in);
camber ± 0.07mm (0.003 in);
For additional length, add $0.08 per cm ($0.20/in).

1-99 tubes ..... $0.80 ea.
100-299 ..... $0.75 ea.
300 + ... $0.70 ea.

NOTE: Other tube sizes available, please inquire

LARGE VOLUME NMR SAMPLE TUBES

10mm o.d. *THIN WALL* NMR SAMPLE TUBES

No. 1008-UP ULTRA PRECISION for ultra high resolution NMR

Standard length: 178mm (7 inches);
o.d. 10.00 ± 0.013mm (0.0005 in.);
i.d. 8.76 ± 0.025mm; (0.001 in.)
camber ± 0.007mm (0.0003 in.).
For additional length, add $0.20 per cm ($0.50/in.).

1-5 tubes ..... $14.50 ea.
6-25 ..... $13.75 ea.
26 + ... $12.95 ea.

No. 1005-P PRECISION for medium and high resln. NMR

Standard length: 178mm (7 inches);
o.d. 10.00 ± 0.013mm (0.0005 in.);
i.d. 8.76 ± 0.025mm (0.001 in.);
camber ± .013mm (0.0005 in.).
For additional length, add $0.20 per cm ($0.50/in.).

1-5 tubes ..... $9.50 ea.
6-25 ..... $9.25 ea.
26 + ... $9.00 ea.

20mm o.d. *THIN WALL* NMR SAMPLE TUBES

No. 2005-P PRECISION for medium and high resln. NMR

Standard length: 178mm (7 inches);
o.d. 20.00 ± 0.01mm;
i.d. 17.70 ± 0.02mm;
camber ± 0.03mm.
For additional lenght, add $1.00 per cm ($2.50/in.).

1-5 tubes ..... $38.00 ea.
6 + ... $37.25 ea.

PTFE VORTEX PLUGS

All sizes - specify tube size ... $40/lot of 5
Rods for all Vortex Plugs ..... $10.00 each.

PTFE Machined Tube Caps

5mm ..... $40/25 caps; $75/50 caps
10mm ..... $43/25 caps; $80/50 caps

For 5mm HIGH PRECISION and ULTRAPRECISION work, we recommend our No. 507-HP and No. 508-UP NMR Sample Tubes. For 10mm tubes, most widely used is our No. 1005-P.

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1-800-222-0036

Norell, Inc., 22 Merlin Lane, Mays Landing, NJ 08330 USA Tel: 609-625-2223, Fax: 609-625-0526; Telex: 5106006283(Norell UD)

NMR Spectroscopist at the Molecular Spectroscopy Laboratory, School of Chemical Sciences, University of Illinois-Urbana. Requirements for this position include a Ph.D. in chemistry, or extensive equivalent experience with state-of-the-art NMR spectrometers; a thorough familiarity with modern FTNMR spectroscopy; and the ability to work independently and collaboratively in a stimulating research environment. Experience in devising or implementing new FTNMR experiments (e.g., new 2D NMR pulse sequences), a working knowledge of FT solid state NMR and EPR, as well as experience with General Electric (Nicolet) and Varian FTNMR instruments (General Electric GN300WB with solids, Varian Unity 400) and Bruker ESP300 EPR spectrometer is desired. Duties will include the supervision of instrument operators, and the instruction of graduate students and postdoctoral fellows in NMR techniques.

The starting date is January 6, 1992, but other starting dates could be negotiated. This is a regular, full-time position. The starting salary is commensurate with experience. To ensure full consideration, submit resume and three letters of recommendation by December 4 to Dr. Vera V. Mainz, School of Chemical Sciences, Box 34 Noyes Laboratory, University of Illinois, 505 S. Mathews Avenue, Urbana, IL 61801 (Tel: 217/244-0564). The University of Illinois is an affirmative action/equal opportunity employer.

POSTDOCTORAL POSITION

A postdoctoral position is currently available in the Chemistry Division at Argonne National Laboratory applying multinuclear solid-state NMR spectroscopy and imaging to the study of heterogeneous catalysts, polymer composites and blends, and fossil fuels. NMR methods are to be developed for structure studies of heterogeneous systems, for regioselective enhancement of nuclear spins and to quantitative approaches for structure elucidation.

The Chemistry Division NMR laboratory is equipped with Bruker CXP-100 (solids/imaging), Bruker AM-300 (ultra-fast MAS probe), Nicolet NTC-200, and GE Omega-300 NMR spectrometers. Excellent resources in macromolecular modeling, computing and imaging graphics visualization are available.

Competitive salary and benefits package is offered. Those interested should contact:

Dr. Robert E. Botto
Chemistry Division
Argonne National Laboratory
9700 South Cass Avenue
Argonne, IL 60439

Phone: (708) 972-3524
FAX: (708) 972-9288

NMR Spectroscopist Position **Georgetown University**

A position is available for an NMR spectroscopist (MS, or PhD preferred) to be in charge of two 400 MHz spectrometers in the laboratory of Dr. Jack S. Cohen, Cancer Pharmacology Section, Pharmacology Department, Georgetown University. One spectrometer is equipped with a gradient accessory allowing localized spectroscopy and gradient-enhanced high resolution work. Two main areas of research are being pursued; metabolic studies of trapped cancer cells using 31P and 1H NMR, and high resolution studies of DNA duplexes and proteins. The successful applicant should be experienced in at least one of these areas, preferably both. The responsibilities include maintaining spectrometers, running spectra, preparing samples, growing cells, and research, allowing a great deal of growth for the successful individual. Salary will depend on experience. Georgetown University is an equal employment opportunity employer. Send cv and three letters of recommendation to:

Dr. Jack S. Cohen, Georgetown University Medical Center
Cancer Pharmacology Section
4 Research Court Rockville MD 20850

SYRACUSE UNIVERSITY
NMR INSTRUMENTATION SPECIALIST

Syracuse University seeks an individual, preferably at the PhD level, to oversee our NMR facilities, consisting of three NMR spectrometers (250-500 MHz) and an associated graphics workstation computer network. Candidates should have knowledge of NMR hardware and maintenance, the implementation of modern pulse sequences and related techniques, as well as versatility with associated computer software. NMR operator training and collaborative research activities are included.

Send resume by January 1, 1992 to: **Office of Human Resources, SYRACUSE UNIVERSITY, Skytop Office Building, Syracuse, NY 13244-5300.** Applications from minority and women candidates are encouraged. Syracuse University is an Affirmative Action/Equal Opportunity Employer.

Gradient Enhanced Spectroscopy SWAT

GE introduces the use of Switched Acquisition Time (SWAT) gradients to achieve pure phase 2D spectra with quadrature detection in both the acquisition (ω_2) and evolution (ω_1) dimensions without any phase cycling and without an additional set of t_1 data.

One example of a pure phase gradient enhanced COSY spectrum of a solution of 2,3-dibromopropionic acid in benzene-d6 is shown in Fig. 1. SWAT gradients and a single acquisition per block were used. Data was collected on an Omega 300WB with Microstar actively-shielded gradients. A 5mm inverse probe was built for use within the gradient coils.

Digital resolution of 1.2 Hz in ω_1 and 2.4 Hz in ω_2 was achieved by collection of a 512 x 512 matrix with t_1 evolution time of 840ms and a t_2 acquisition time of 420ms. A single acquisition per t_1 evolution data block and an average recycle time of 1.84s resulted in a 15 minute total collection period.

Since the SWAT gradient method encodes the necessary information in a single t_2 acquisition time, it avoids the collection of additional data blocks required by traditional pure phase methods. This time efficiency is especially important for collection of large multidimensional data sets.

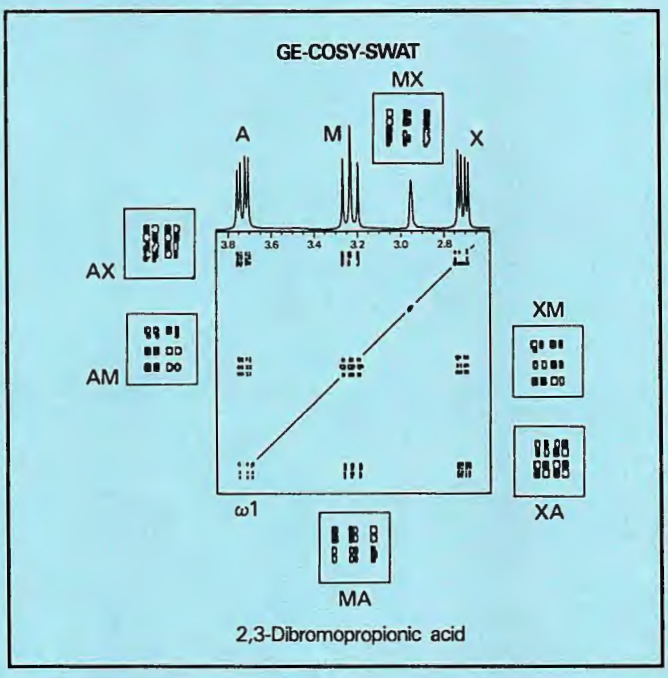

Fig. 1

Contour plot of a 300 MHz pure-phase COSY spectrum of a solution of 2,3-dibromopropionic acid in benzene-d6 acquired with only a single acquisition per t_1 evolution time increment using the GE-COSY-SWAT method. Cross peaks are shown in expanded insets with positive peaks as darkened contours and negative peaks as open contours. A one dimensional spectrum is plotted across the top of the 2D spectrum.

GE NMR Instruments

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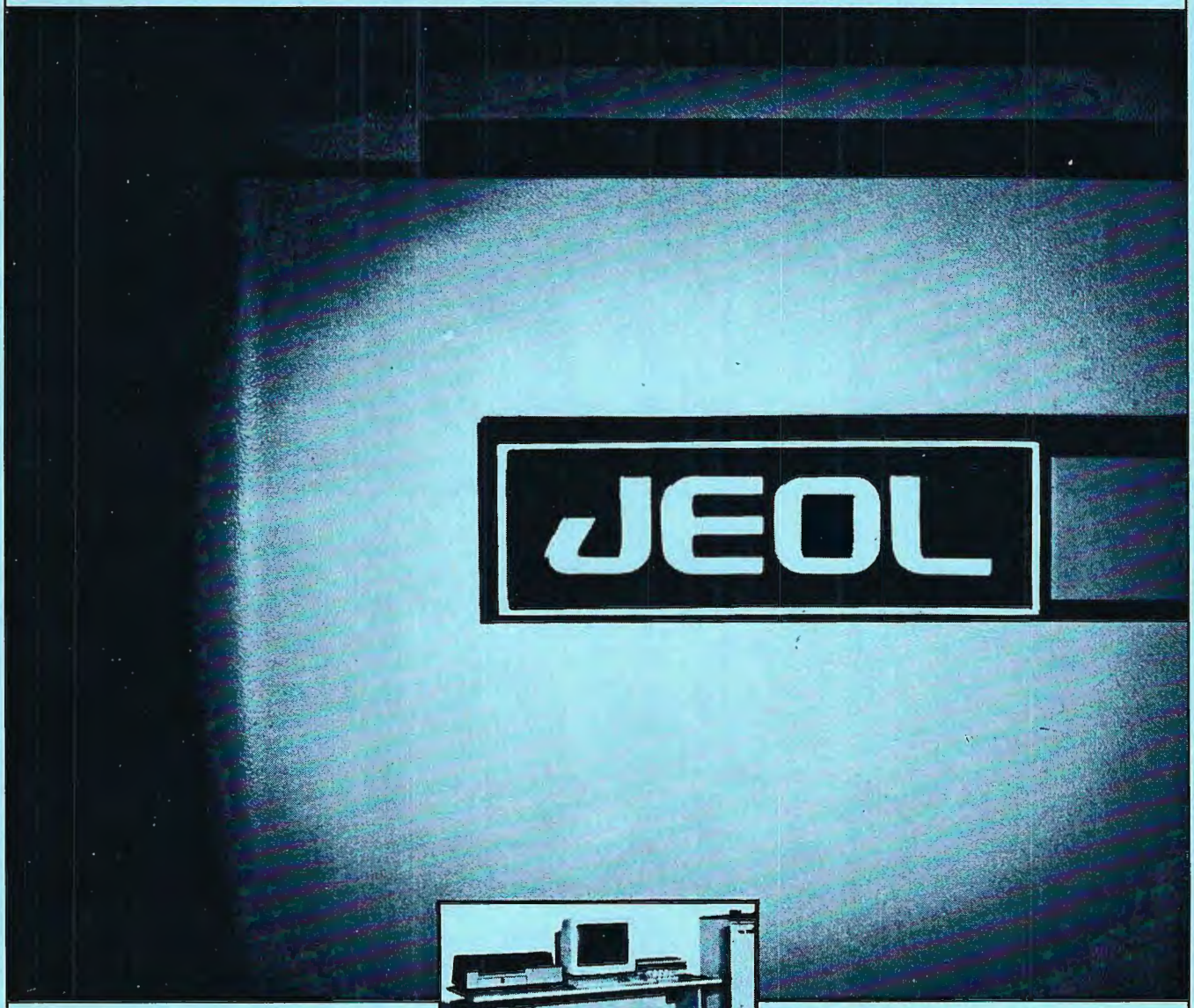
Of all the advanced technology on this research-level NMR, this may be the most important piece of hardware.



JEOL's Alpha series FT NMR system offers a research-level NMR spectrometer that sets a new standard of performance and reliability.

The Alpha combines event bus architecture, experiment definition language, dynamic RF control, pulse shaping and matrix shims into an extremely flexible, high speed precision machine with exceptional sensitivity.

One of the Alpha's most important features isn't listed on a technical data sheet, however. It's the reputation for quality and service that JEOL has earned over the years.

All of our machines are designed for reliability, flexibility and durability. And the outstanding service and applications support provided by our customer service staff makes sure that our high-performance equipment always performs to your satisfaction.

For a demonstration or more information about the JNM-A400/A500/A600 Alpha series of FT NMR systems and JEOL's customer service organization, call 508-535-5900 or write to JEOL USA, 11 Dearborn Rd., Peabody, MA 01960.

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