

THE
NMR
NEWSLETTER

No. 488
May 1999

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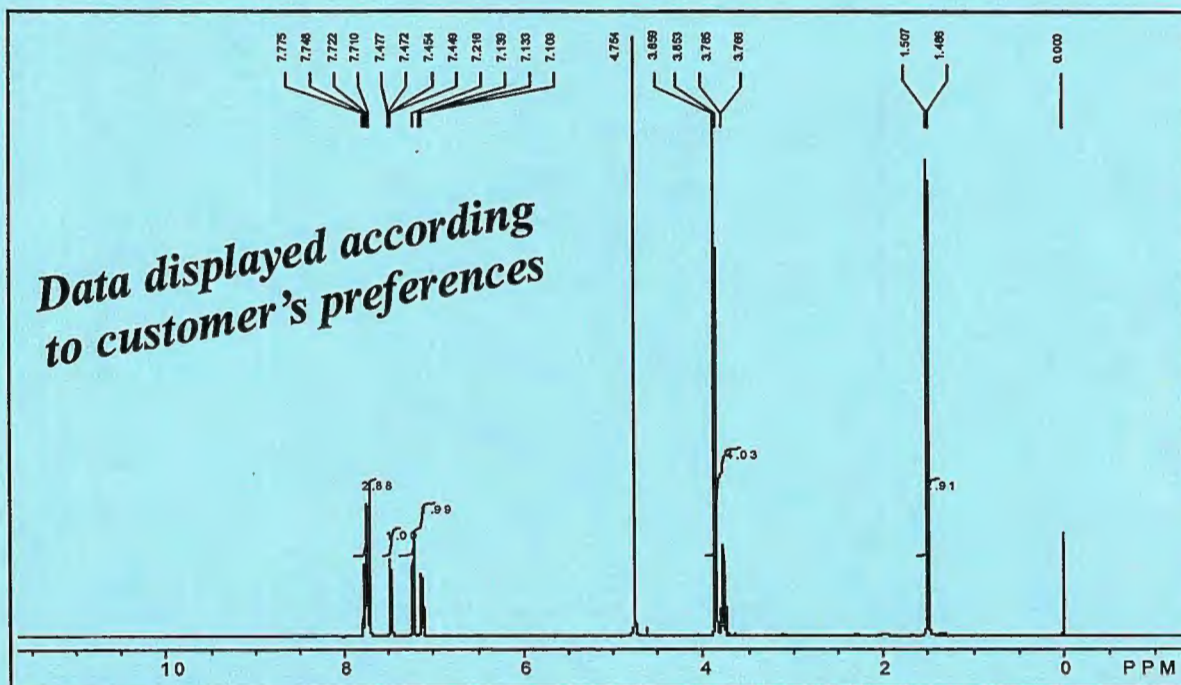
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FORTHCOMING NMR MEETINGS

Seventh Scientific Meeting and Exhibition of the Intl. Soc. for Magnetic Resonance in Medicine (ISMRM), Philadelphia, PA, **May 22 - 28, 1999**; Contact: International Society for Magnetic Resonance in Medicine, 2118 Milvia St., Suite 201, Berkeley, CA 94704.

International School of Structural Biology and Magnetic Resonance, 4th Course: Dynamics, Structure and Function of Biological Macromolecules; Erice, Sicily, Italy; **May 25 - June 5, 1999**; Contact: Ms. Robin Holbrook, Stanford Magnetic Resonance Laboratory, Stanford University, Stanford, CA 94305-5055; (650) 723-6270; Fax: (650) 723-2253; Email: reh@stanford.edu. See Newsletter 483, 8.

Gordon Conference on Magnetic Resonance, Henniker, NH, **June 27 - July 2, 1999**. Contact: the chairperson: (Regitze Vold, rvold@ucsd.edu) or vice-chairperson (Robert Tycko, tycko@helix.nih.gov. See Newsletter 487, 37.

Royal Society of Chemistry: 14th International Meeting on NMR Spectroscopy, Edinburgh, Scotland, **June 27 - July 3, 1999**; Contact: '99NMR14' c/o Mrs. Paula Whelan, The Royal Society of Chemistry, Burlington House, London W1V 0BN, England; +44 0171 440 3316; Email: conferences@rsc.org\

Rocky Mountain Conference NMR Symposium, Denver, CO, **August 1-5, 1999**. See Newsletter 487, 36 and <http://india.cchem.b4rkeley.edu/~rmc/>

SMASH No. 1 (Small Molecules Are Still Hot), Argonne, IL, **August 15-18, 1999**; Contact: Ms. Karen McCune, (mccune_karen_a@lilly.com, 317-276-9783) or S. R. Maple (maple_steven_r@lilly.com) or G.E. Martin (gary.e.martin@am.pnu.com) or A. G. Swanson (alistair_swanson@sandwich.pfizer.com. See Newsletter 487, 17.

Applications of NMR to Complex Systems, Symposium at the American Chemical Society Meeting, New Orleans, LA, **August 22-26, 1999**; Contact: R. E. Botto, Symposium Chair, Chemistry Division, Argonne National Laboratory, 9700 South Cass Ave., Argonne, IL 60439; 630-252-3524; Fax: 630-252-9288; E-mail: robert_botto@qmgate.anl.gov

continued on inside back cover

Regitze R. Vold

Regitze R. Vold, a leading figure in the magnetic resonance community and a close friend and valued colleague to many of us, passed away on April 11 in Cambridge, England. Her death resulted from an accidental fall.

Gitte received her Ph.D. from the Technical University of Denmark in 1962. Following postdoctoral work at the University of New Mexico and the National Institutes of Health, she moved to the University of California at San Diego in 1971. She was appointed to the faculty in 1982. At the time of her death, Gitte was a full professor in the Department of Chemistry and Biochemistry at U.C. San Diego.

Gitte made many fundamental contributions of magnetic resonance spectroscopy. She is perhaps best known for her work on deuterium NMR spectroscopy, including the development and application of techniques for studying the dynamics and structure of liquids, liquid crystals, solids, and inclusion compounds. Gitte was an accomplished and innovative experimentalist, adept in the design, construction, and troubleshooting of all manner of NMR equipment. She was also one of the world's experts on the theoretical analysis of NMR lineshapes and relaxation rates in terms of molecular dynamics. In recent years, Gitte's research focused on deuterium NMR spectroscopy of paramagnetic solids and on NMR studies of membrane-bound peptides and proteins. Investigations by Gitte and her coworkers of magnetically aligned phospholipid bicelles, including detailed studies of the structure and phase diagrams of bicelle-forming phospholipid mixtures and demonstrations of the effects of paramagnetic ions on the alignment of bicelles, had a large impact on current applications of bicelles in biomolecular NMR spectroscopy.

Gitte's many activities on behalf of the magnetic resonance community included two terms as Chair of the Experimental NMR Conference, in 1983 and 1998, and membership on the editorial board of the Journal of Magnetic Resonance. She was Vice-Chair of the Gordon Research Conference on Magnetic Resonance in 1997, and Chair in 1999.

When not teaching and working on her research, Gitte enjoyed athletic pursuits, including tennis, skiing, and swimming. She had a great fondness for cats. In all respects, she was a very classy individual.

Gitte's insatiable appetite for new scientific exploration, her courageous approach to scientific and non-scientific problems, and her devotion to the magnetic resonance community set a standard that few can match. She was taken from us much too soon, and she will be sorely missed.

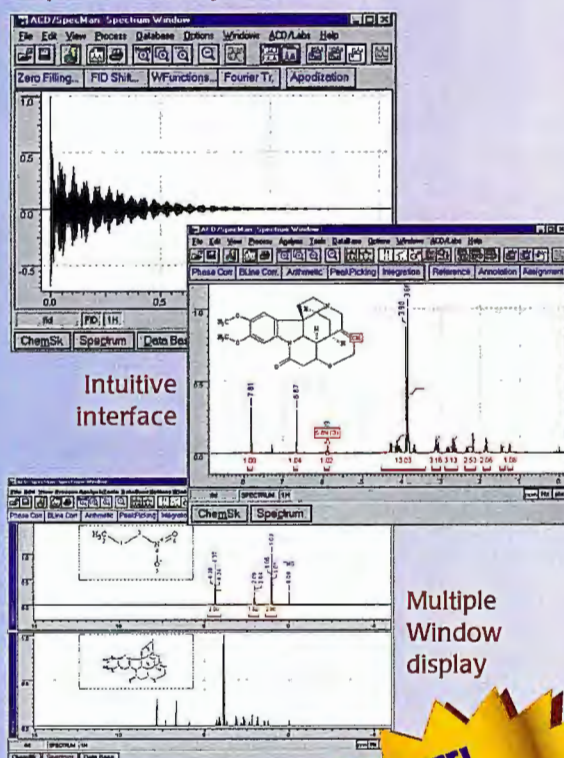
Robert Tycko
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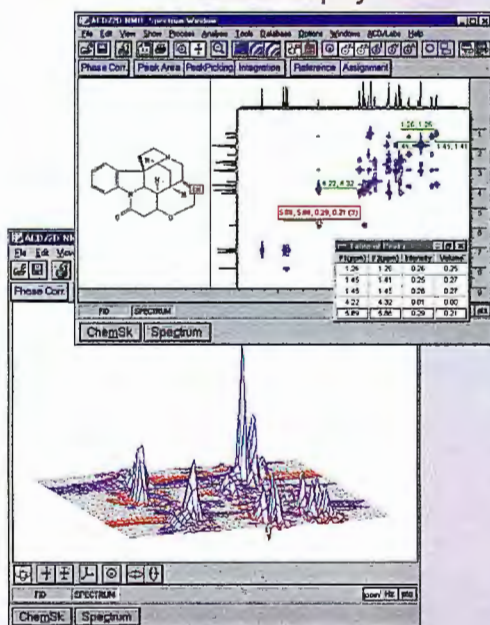
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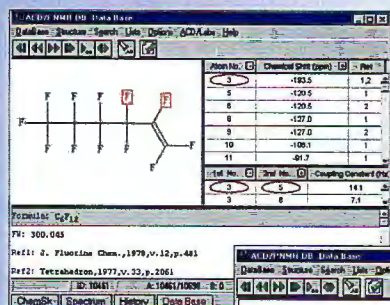


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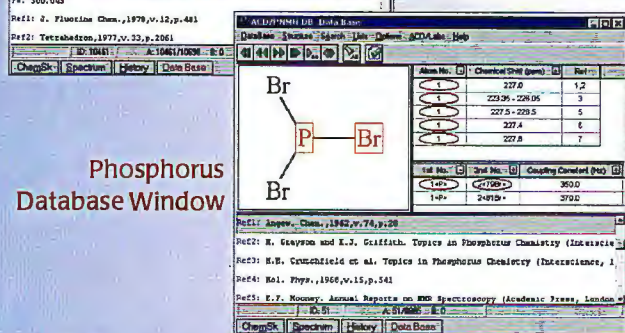
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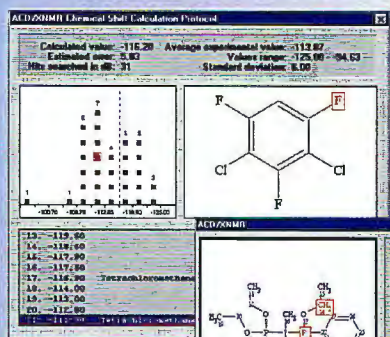
Look up or predict the ^{19}F or ^{31}P NMR spectrum for almost any drawn organic structure at the click of a button!



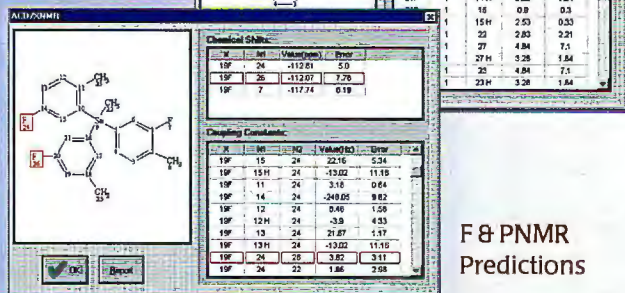
Fluorine Database Window



Phosphorus Database Window



View fragments contributing to each prediction



F & P NMR Predictions

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- If the structure is missing or some of its shifts are not reported, predict the values you need—ACD/XNMR contains an internal ^{19}F data file with over 25,200 chemical shifts and 15,300 coupling constants.

Similarly, ACD/XNMR handles phosphorus compounds:

- For database look-up, it contains an internal database of ^{31}P NMR spectra for over 19,000 structures.
- For prediction, it uses an internal ^{31}P NMR data file with over 23,300 chemical shifts and 8,600 coupling constants.

Each database includes original literature references, molecular formula, molecular weight and IUPAC names which can be searched and viewed. Search capability also includes structure and substructure, and searching by exact value or range of values for chemical shifts and coupling constants.

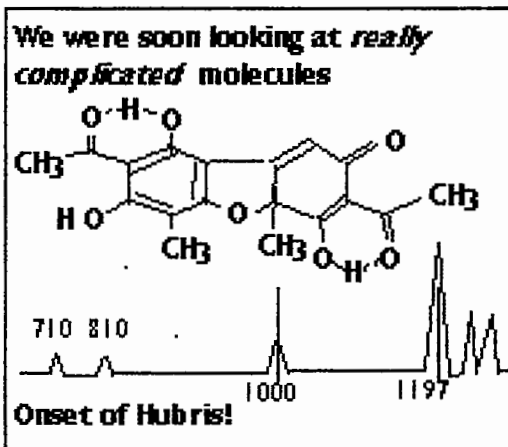
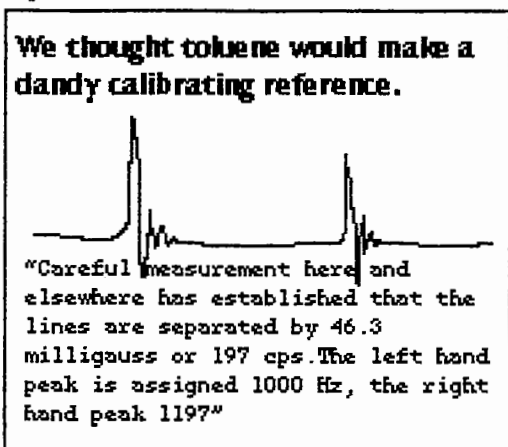
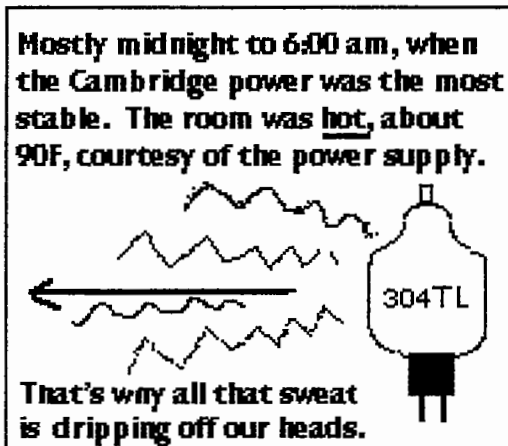
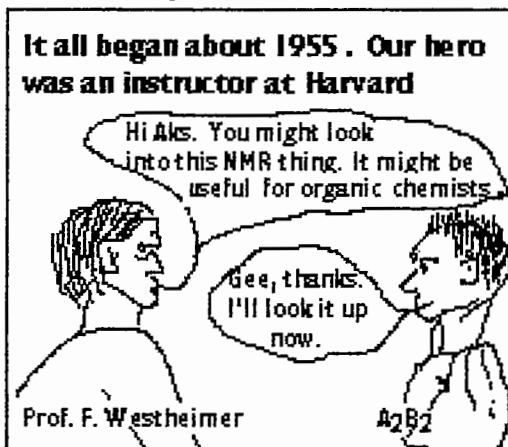
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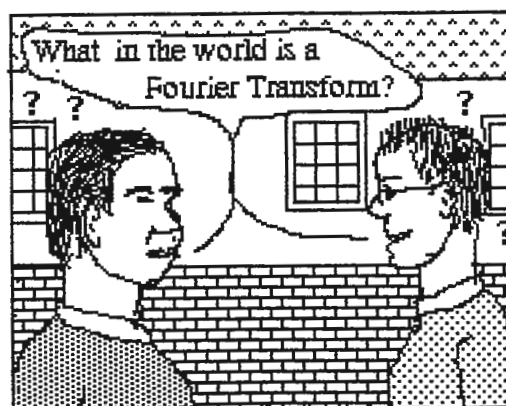
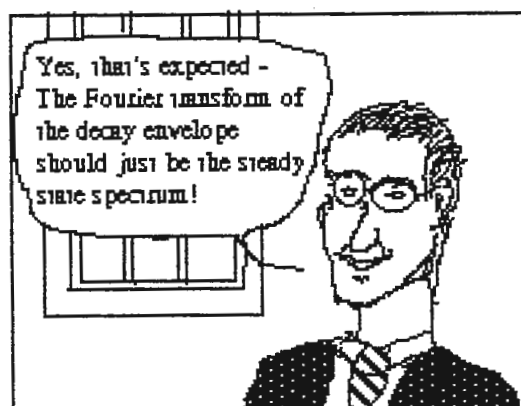
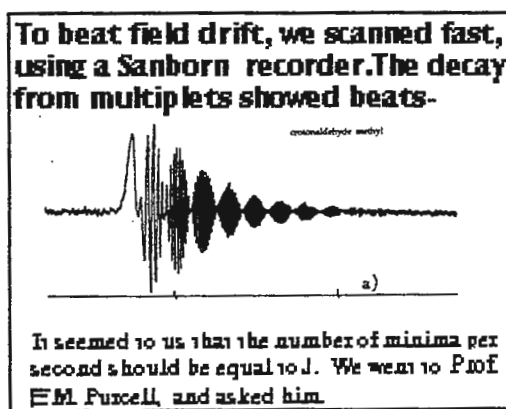
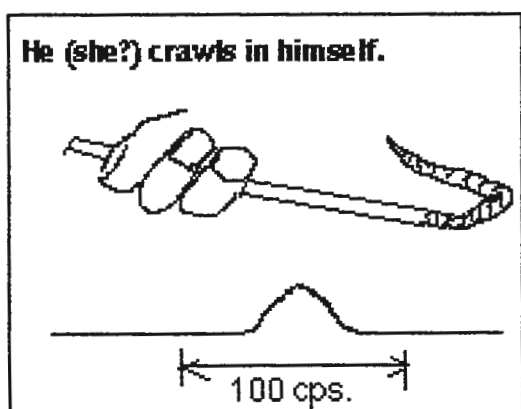
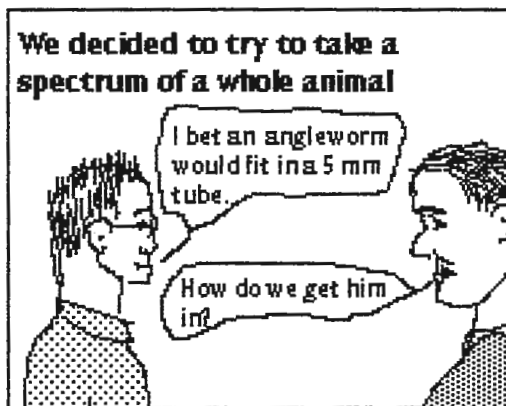
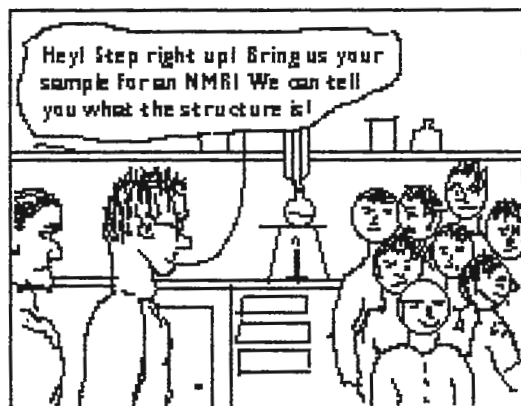
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40 YEARS IN SHOW BUSINESS

Yo, Barry! - At the 40th ENC I reminisced about my 40 years in NMR, ('55-'95), 40 years of the newsletters, ('58-'98), and 40 years of ENCs ('60-'99). Here is some of the nostalgia for you- It's going to come in some number of installments



40 YEARS IN SHOW BUSINESS



To be continued --

Aksel
Aksel A. Bothner-By

Dr Bernard L. Shapiro
The NMR News Letter
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Palo Alto, CA 94303

(received 4/12/99)

Simulation of NMR Diffusion-Coherence Effects in Erythrocyte Suspensions

Dear Barry,

In our last communication, we reported that the ^1H NMR diffusion-coherence effects (see Fig. 1A) evident in the q -space plots of water in erythrocyte suspensions are caused by the diffusion of water in two essentially different regions, namely, the intracellular region and the extracellular region. By using appropriate chemical compounds, we were able to separate these two coherence effects and relate the unique positions of their respective maxima and minima to the cell dimensions in the suspension (1,2,3).

Although mathematical expressions for the q -space plots of molecules trapped in planar, cylindrical, and spherical pores have been presented (4), expressions describing the q -space plot for erythrocytes are difficult to derive analytically as a consequence of their considerably more complex geometry (biconcave disc). We recently conducted random walk simulations to confirm the assignment of coherence features in q -space plots of water in erythrocyte suspensions (3). The Monte Carlo method followed the approaches described previously in simulating q -space plots for samples composed of molecules diffusing in restricted geometries (5). "Virtual" discocytes were modelled to have typical erythrocyte dimensions, and were arranged in a hexagonal lattice with a packing density of 0.5. The intrinsic diffusion coefficient in both intra- and extracellular regions was set to $2.0 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ and membrane permeability could be adjusted by specifying a transition probability between 0 and 1.

Selected results of the computer simulations are presented in Figures 1B to 1D. The positions of the coherence features in q -space plots for water diffusing in the intracellular region alone (Fig. 1B) differ markedly from those in the q -space plot for water restricted to diffuse in the extracellular region; both plots correlate closely with those obtained from experimental data. The choice of packing density (0.5, i.e., intra- and extracellular water volumes equal) allowed for these results to be "added" together (Fig. 1D) resulting in a q -

space plot for water diffusing in both the intra- and extracellular regions (no exchange). In terms of the positions of the coherence features this plot correlates closely with that obtained from experimental data (Fig. 1A).

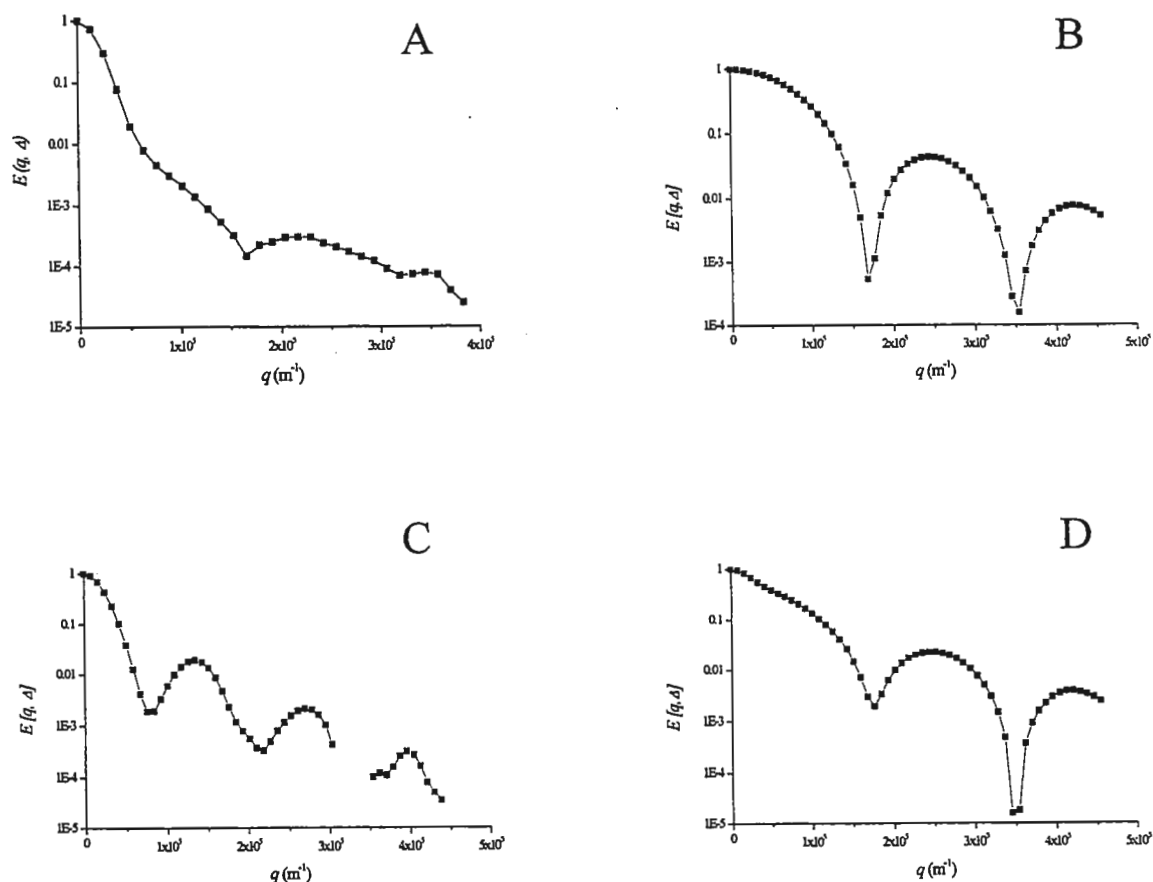


Figure 1. Experimental and simulated q -space plots of water in an erythrocyte suspension. Experimental q -space plot at 0.30-Ht and 298K (A); simulated q -space plot for water diffusing in the intracellular (B) and extracellular (C) regions of the cell suspension; and the sum of the two simulated curves (D).

References

1. P.W. Kuchel, A. Coy, P. Stilbs, *Magn. Reson. Med.* **37**, 637 (1997).
2. A.M. Torres, R.J. Michniewicz, B.E. Chapman, G.A.R. Young, P.W. Kuchel, *Magn. Reson. Imaging* **16**, 423 (1998).
3. A.M. Torres, A.T. Taurins, D.G. Regan, B.E. Chapman, P.W. Kuchel, *J. Magn. Reson.* in press (1999).
4. P.T. Callaghan, *J. Magn. Reson. A* **113**, 53 (1995).
5. A.J. Lennon and P.W. Kuchel, *J. Magn. Reson. A* **111**, 208 (1994).

Yours Sincerely,

David Regan Allan Torres Bob Chapman Andrew Taurins Philip Kuchel

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Family Matters



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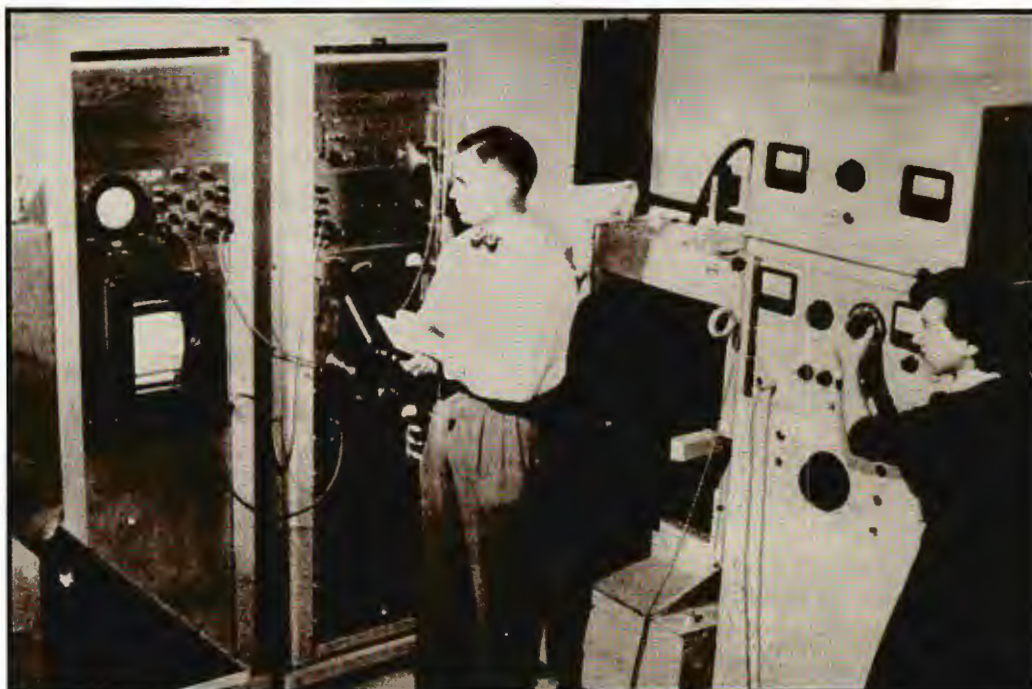
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(received 4/26/99)
 April 22, 1999

Bernard L. Shapiro, Ph.D.
 Editor, The NMR Newsletter
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 Palo Alto, CA 94303

IMPEACH - IMproved Performance ACCordion Heteronuclear Spectroscopy

Dear Barry,

The ACCORD-HMBC experiment of Wagner and Berger¹ which we discussed in our last contribution to The NMR Newsletter^{2,3} represents a powerful new way of sampling a potentially wide range of long-range heteronuclear couplings in a single experiment. The single major drawback of sampling a wide range of potential long-range couplings is that to keep the scaling factor, N , which governs the F_1 modulation or "skew" in ACCORD-HMBC spectra to a manageable level, a large number of increments of the evolution time, t_1 , must be accumulated. We would like to now report a new experiment, to which we have given the acronym IMPEACH⁴ (IMproved PERFORMANCE ACCordion Heteronuclear spectroscopy -- for the record, the acronym arose during the Starr investigation of the President but doesn't represent our position on any of that issue!).

The IMPEACH experiment replaces the variable delay, vd , of the ACCORD-HMBC experiment with a new pulse sequence element which we term a constant time variable delay. Despite the rather oxymoronic sound of the name for this pulse sequence element, its function is really quite simple. In the modified version of the pulse sequence (mIMPEACH) presented in Figure 1, the variable delay interval of the experiment is subdivided into two segments. The first portion of the constant time variable delay is an interval, D , which is split by a 180° ^{13}C pulse. The second portion of the pulse sequence element is a variable delay, vd , analogous to that in the ACCORD-HMBC experiment. F_1 modulation in ACCORD-HMBC experiments arises as a function of homonuclear ^1H frequency modulation during the variable delay, vd , which serves as a pseudo-evolution period for this process.^{2,3} By keeping the overall delay duration constant, ^1H frequency modulation, obviously, can be suppressed. To allow the sampling of a range of potential heteronuclear long-range couplings, however, the duration of time interval during which this process is sampled must be of variable duration. To achieve these seemingly conflicting objectives, the constant time variable delay first maintains the overall time constant to suppress ^1H frequency modulation. As the duration of vd is decremented with successive increments of the evolution time, t_1 , the overall duration of the delay, D , is incremented by the same amount. To sample heteronuclear couplings using a variable duration delay, the 180° ^{13}C pulse at $D/2$ decouples these process at D . Hence, heteronuclear couplings evolve only during the portion of the delay represented by vd . In this fashion, as the duration of vd is successively decremented in successive increments of the evolution time, t_1 , the sampling of a range of long-range couplings is facilitated in a manner analogous to the ACCORD-HMBC experiment.⁴

To illustrate the differences between the ACCORD-HMBC and (m)IMPEACH experiments, two panels showing the aliphatic region of the spectrum of strychnine (1) are presented in Figure 2. The left panel shows the data for a 2 to 25 Hz optimized ACCORD-HMBC experiment digitized by 512 increments of the evolution time to minimize the scaling factor, N . Despite the large number of increments of the evolution period, there is still a substantial F_1 modulation or "skew" associated with the individual long-range responses. In contrast, in the IMPEACH spectrum shown in the other panel of Figure 2, which was acquired using the same 2 to 25 Hz optimization with 512 increments of the evolution time, the F_1 modulation is suppressed or "decoupled." To better illustrate the differences in the responses in the two experiments, expansions of the H23a/C12 long-range correlation from both experiments are shown in Figure 3. As is clearly shown in

the left panel, the response from the ACCORD-HMBC experiment still shows significant F_1 modulation with a width of >800 Hz in F_1 . In contrast, the data from the IMPEACH spectrum shows that the F_1 modulation is suppressed, improving resolution and reducing the likelihood of response overlap in congested regions of the spectrum which can be a problem with ACCORD-HMBC spectra when limited numbers of increments of the evolution time are used in digitizing the second frequency domain.³

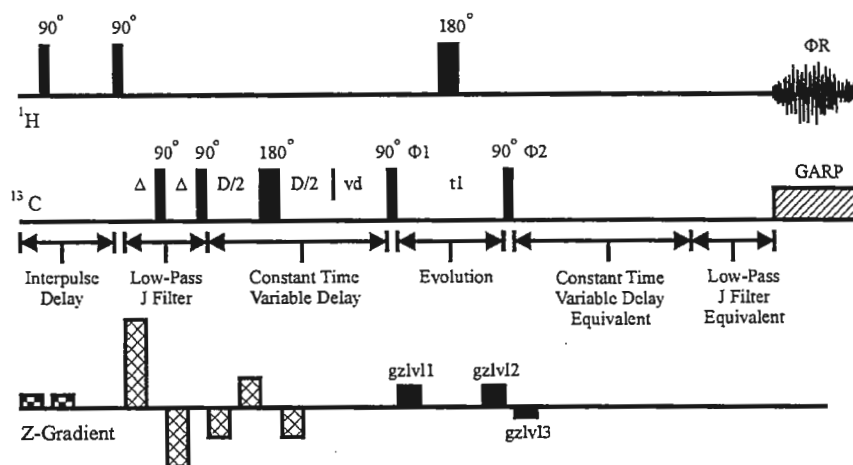


Figure 1. Modified IMPEACH pulse sequence.⁴ All pulses and gradients following the reconversion of multiple quantum coherence to proton single quantum coherence with the application of the final 90° X-pulse are eliminated, affording an $\sim 25\%$ improvement in the sensitivity of the experiment relative to the variant in our original report.⁴ The constant duration of the constant time variable delay suppresses F_1 modulation characteristic of the ACCORD-HMBC experiment. Heteronuclear long-range couplings are allowed to evolve only during the variable, vd, portion of the

constant time variable delay. In this fashion, a range of long-range couplings can be sampled in the experiment despite the constant duration of the time interval. The phase of the unlabeled pulses in the sequence was held constant at 0. The cycled phases were: $\Phi_1 = 0202$; $\Phi_2 = 0202$; $\Phi_R = 0220$. Gradient ratios were $2 : 2 : 27 : -18 : -9 : 9 : -9 : 2 : 2 : -1$ G cm^{-1} .

The version of the pulse sequence shown in this contribution to The NMR Newsletter (shown above) differs somewhat from the pulse sequence contained in our original report.⁴ Specifically, the 180° ^{13}C pulse and gradients from the constant time variable delay are omitted in the segment of the experiment following the 90° X-pulse used to recreate ^1H single quantum coherence after the evolution period. By eliminating all pulses and gradients following the last 90° X-pulse, roughly a 25% gain in sensitivity is realized relative to what is offered by a completely symmetric pulse sequence. Similar gains can also be realized by eliminating the pulses of the dual stage low-pass J-filter and the attendant gradient pulses in the ACCORD-HMBC pulse sequence, replacing them with a fixed delay of equivalent length.

Overall, we feel that the utilization of the accordion principle as a means of sampling a wide range of potential long-range heteronuclear couplings, as pioneered by Wagner and Berger¹ has opened an exciting new chapter in the development of new long-range, inverse-detected heteronuclear shift correlation spectroscopy. It will be interesting to watch as new applications of ACCORD-HMBC or the IMPEACH experiment described in this contribution begin to be reported in the context of the elucidation of complex new chemical structures.

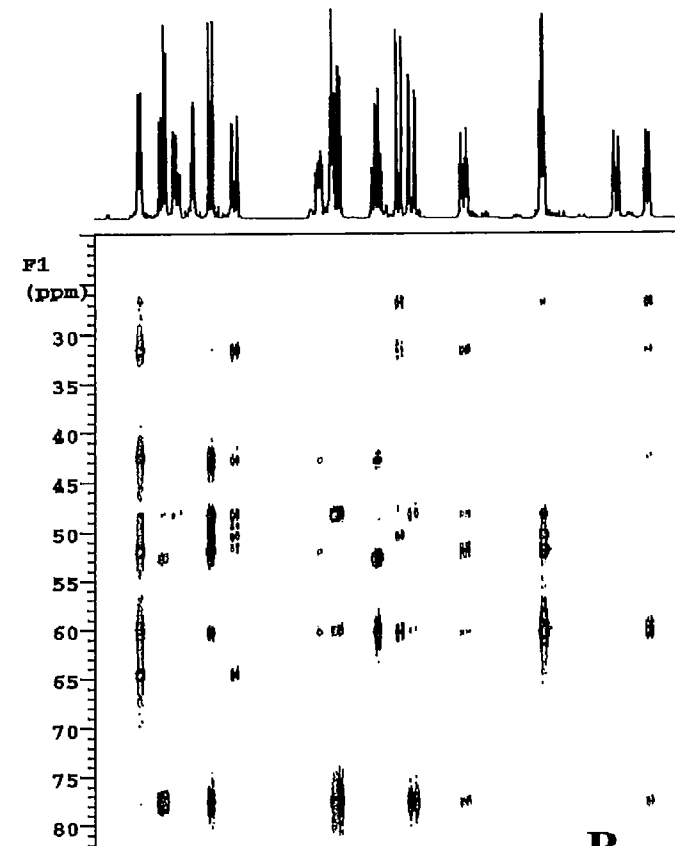
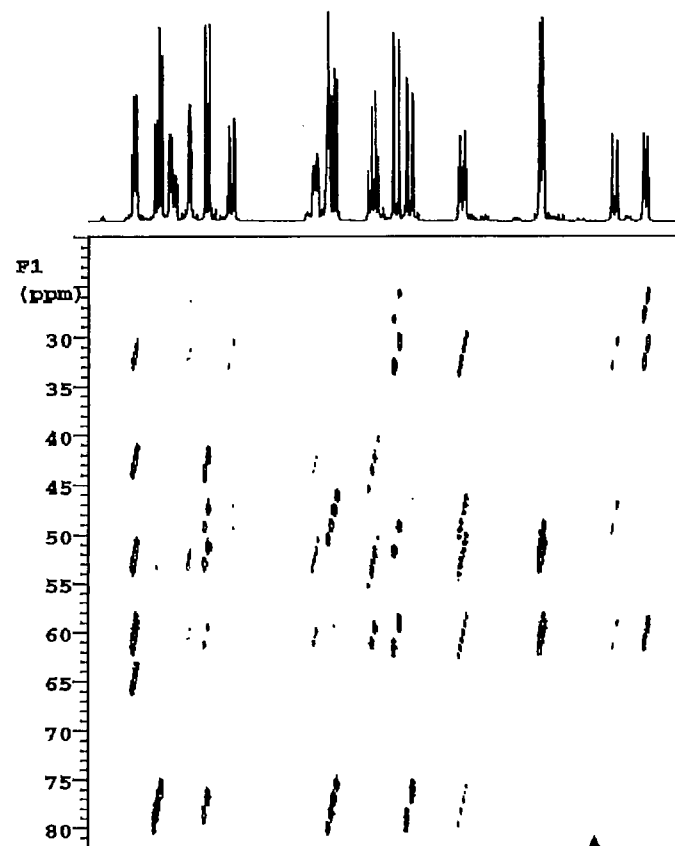
Gary E. Martin

Chad E. Hadden

V. V. (Krish) Krishnamurthy
Varian, Inc.

References

- 1) R. Wagner and S. Berger, *Magn. Reson. Chem.*, **36**, S44 (1998).
- 2) G. E. Martin, C. E. Hadden, R. C. Crouch, and V. V. Krishnamurthy, *The NMR Newsletter*, No. 478, pp. 11-13 (1999).
- 3) G. E. Martin, C. E. Hadden, R. C. Crouch, and V. V. Krishnamurthy, *Magn. Reson. Chem.*, **37**, in press (1999).
- 4) C. E. Hadden, G. E. Martin, and V. V. Krishnamurthy, *J. Magn. Reson.*, submitted (1999).



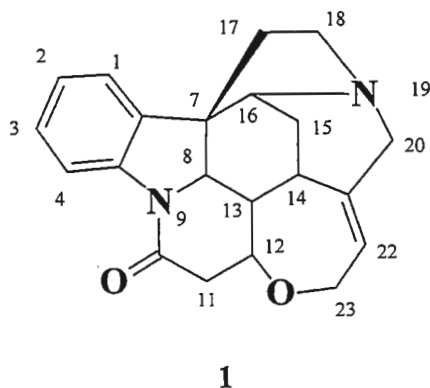
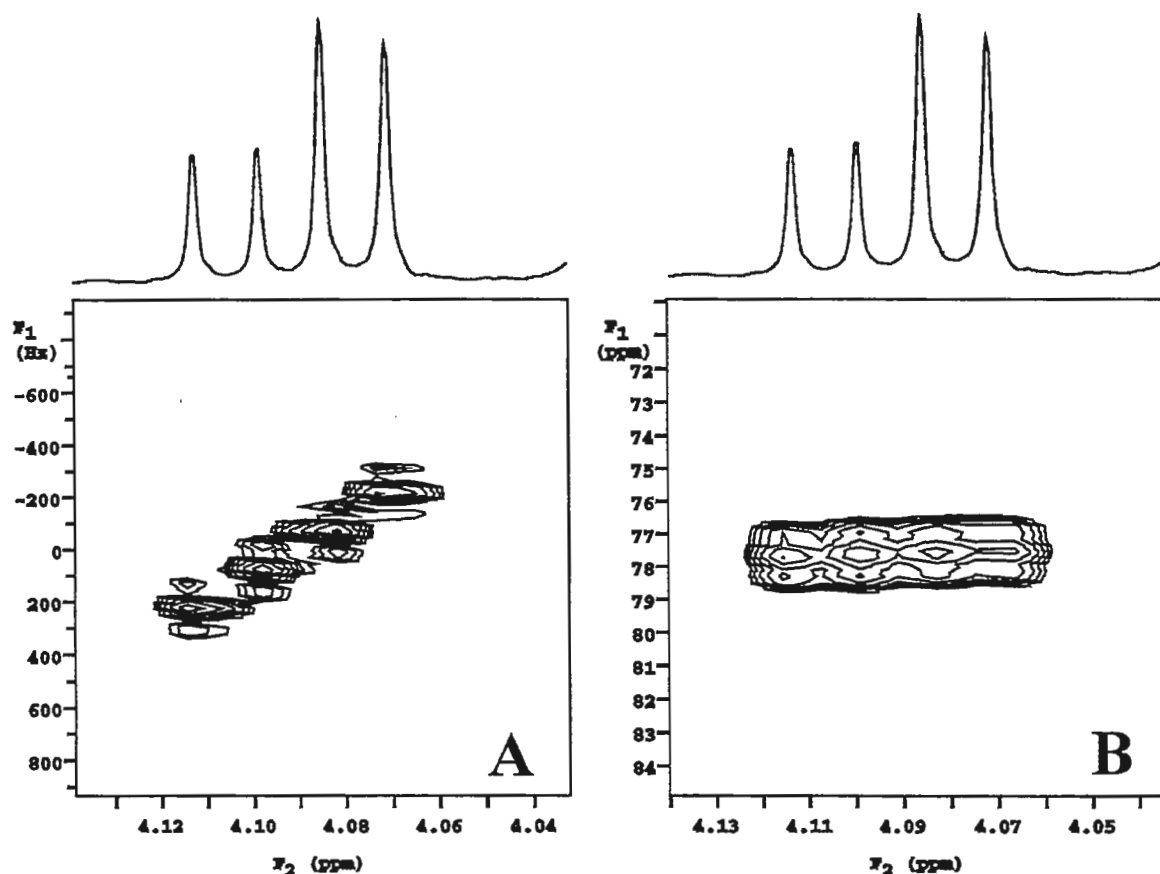


Figure 3. H23a-C12 long-range correlation responses from the 2 to 25 Hz ACCORD-HMBC (A) and IMPEACH (B) spectra of strychnine (**1**). Panel A shows the F_1 modulation or “skew” characteristic of long-range correlation responses in ACCORD-HMBC spectra. The modulation is the result of the variable delay, vd , which serves as a pseudo-evolution time for ^1H frequency modulation during the variable delay. Despite acquiring the data using 512 increments to digitize the second frequency domain, the scaling factor, N , still has a value >20 .³ In contrast, the constant time variable delay employed in the IMPEACH pulse sequence (see Figure 1) suppresses ^1H frequency modulation by keeping the overall duration of the variable

delay constant. In contrast, heteronuclear couplings are refocused during the first part of the constant time variable delay by the 180° ^{13}C pulse located $D/2$ after the beginning of the period. Heteronuclear couplings are sampled during the variable portion of the delay, vd , which allows the desired range of potential long-range couplings to be sampled. The suppression or “decoupling” of ^1H frequency modulation during the variable delay has the beneficial effect of improving F_1 resolution and preventing possible response overlap in congested regions of the spectrum.³ Unfortunately, the IMPEACH experiment does prevent the use of F_1 modulation as a criterion for the verification of the authenticity of weak, long-range couplings.³



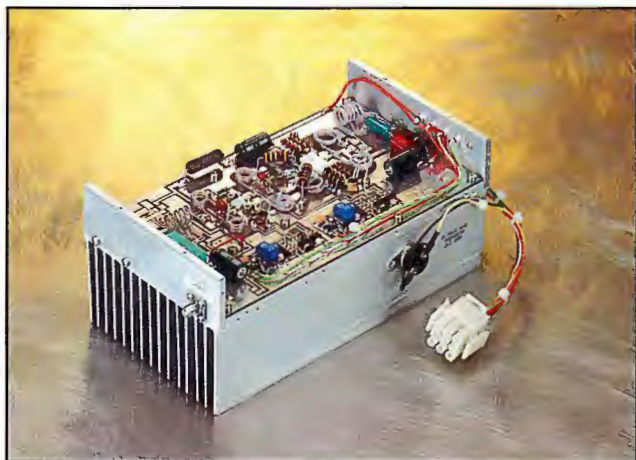
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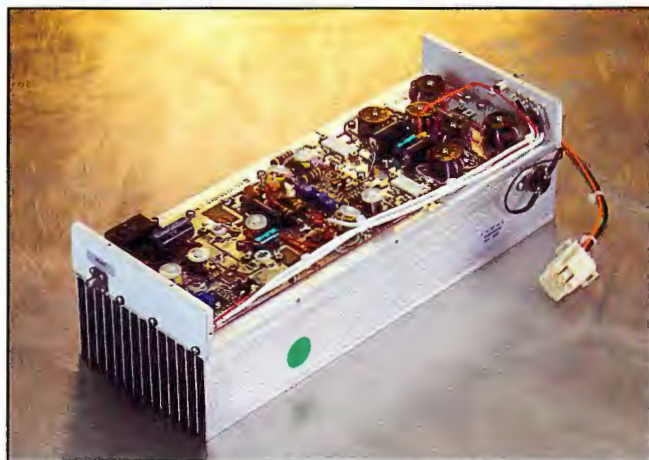
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April 6, 1999
(received 4/12/99)

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Converting Chemagnetics m100S Files for NUTS

Dear Barry:

I am happy to announce that Dr. Shi (Steve) Bai has become the NMR spectroscopist/facility manager at the University of Delaware. Steve came to Delaware in September, 1998, and promptly began to make a significant mark on the facility. First, he created a Web site for NMR service [<http://www.nmr.udel.edu>] including on-line sign-ups, on-line requests for training and service, information and administration of the facility. This site has become very popular with users, because they can now check usage and sign up for time without going down three flights of stairs or across campus.

For many years, we have used our Chemagnetics m100S, an original spectrometer (!!!), to obtain CPMAS data on solid, carbon-containing materials. It has provided excellent service. However, I have always wanted to be able to export the data for analysis with NUTS, but the format of the Chemagnetics export utility's files (an old FELIX format) is not recognized by NUTS. Steve has recently written a program in C, called CONV, that converts the exported data into NUTS Common Data File Format. Use of this program allows us to analyze data with NUTS, from which we can use the data in other Windows-compatible programs routinely.

So you can clearly see that we look forward to continuing development of the facility at the University of Delaware with Steve as the manager.

Yours truly,

A handwritten signature in cursive script that reads 'Cecil'.

Cecil Dybowski
Professor



University of Berne

Department of
Chemistry and Biochemistry
NMR-Laboratory

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Dr. B. L. Shapiro
The NMR Newsletter
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april, 7th 1999
(received 4/23/99)

$C(NO_2)_4$: A New NMR Reference Standard?

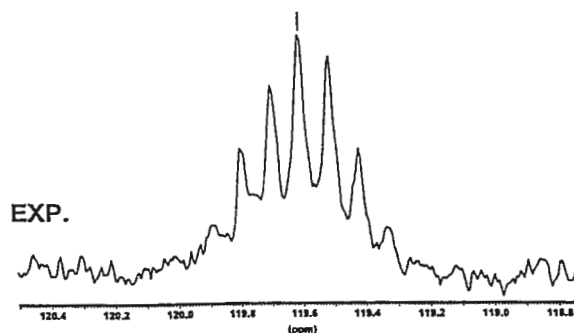
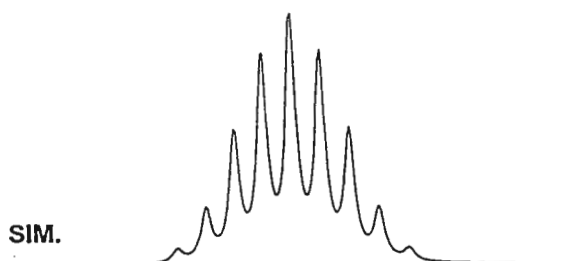
Dear Dr. Shapiro

recently we got a sample of tetranitromethane from one of our customers working in the field of explosives and measured the corresponding ^{15}N - and ^{13}C - spectra of the neat liquid. The ^{15}N chemical shift of 47.0ppm (relative to Nitromethane as the external reference) agrees well with the value (46.6ppm) found in the literature. Measuring the ^{13}C spectrum we expected a singlet but surprisingly obtained a multiplet centered at 119.6ppm (relative to TMS dissolved in $CDCl_3$ as the external reference). It is obvious that the splitting of the carbon signal originates from the coupling with the four ^{14}N nuclei. Although ^{13}C scalar relaxation induced by the four quadrupolar ^{14}N nuclei was expected to be most efficient, giving rise to a single broadened carbon signal, this seems not to be the case and the individual multiplet lines could be resolved (see Figure).

Tetranitromethane, belongs to the class of explosive compounds and should be handled very carefully. It will therefore certainly not replace TMS and its derivatives as a new NMR reference standard for most of us. Its use could be however a valuable alternative to get rid of your decrepit spectrometer in case other more common ways to modernize your equipment fail.

C-SHIFT: 119.610

J_{C-N} : 9.33 Hz



Yours sincerely

Peter Bigler

The NMR Newsletter - Book Reviews

Book Review Editor: István Pelczer, Dept. of Chemistry, Princeton University, Princeton, NJ 08544

**" Protein NMR Spectroscopy
Principles and Practice"**

by

**John Cavanagh, Wayne J. Fairbrother, Arthur G. Palmer III,
and Nicholas J. Skelton**

*Academic Press (www.apnet.com), 1996. 587 pages,
\$63.00 (Case Bound); ISBN 0-12-164490-1*

There are things which were born to be classics of their kind. Some are creatures of Nature, while others are results of hard and thorough work by dedicated individuals, such as the authors of this book. It has been a pleasure to see the appearance of several good volumes on NMR spectroscopy over the last years, but the present publication stands out as one of the very best. Although it was published almost four years ago, it remains an excellent source of knowledge, information, and reference in this rapidly developing field of high-resolution NMR studies of large biomolecules – and beyond.

The book starts with a very useful Table of Symbols, followed by eight chapters with a well-selected, yet moderate, list of references for each, a couple of pages of suggested reading, and almost thirty pages of Index. This structure already suggests the goal of the authors, to provide an extensive handbook to students, researchers, and all who are interested in this methodology.

Each of the eight chapters reflects the same highly educational approach and presentation: classical NMR principles are introduced in Chapter 1, followed by theoretical description, quantum mechanics, density matrix analysis, and introduction of product operator formalism. Chapter 3 discusses basic experimental aspects of NMR spectroscopy from hardware through quadrature detection, various pulse techniques, water suppression (so important for biomolecular studies), and basic data processing.

General aspects of multidimensional NMR spectroscopy are summarized in Chapter 4, including clear explanations of coherence pathways, phase cycling procedures (citing the excellent lecture of James Keeler) and gradient applications. The next chapter is a similar high point of the book, discussing relaxation and dynamic processes.

Experimentalists will especially enjoy the following two chapters which talk about ^1H homonuclear and heteronuclear methods, respectively. These two chapters present a wealth of information, both practical and theoretical, about pulse sequences, comparative analysis of their variants, data processing and presentation. There is somewhat less about gradient versions (which are better used in moderation anyway), but that does not reduce the value of the insightful analysis of the various methods. The final chapter is a compressed, yet well organized, summary of the assignment protocol, with hints on the subsequent structure calculation.

This book has an exceptional value for teachers and students, for experimentalists and for those looking for thorough and exhaustive theoretical analysis of methodologies and principles. I believe that it will be one of the most extensively used handbooks, and not only for protein studies, for years to come. And it is a bargain at the price.

István Pelczer
Department of Chemistry
Princeton University
Princeton, NJ 08544

QUEEN'S UNIVERSITY
CHEMISTRY DEPARTMENT
KINGSTON, ONTARIO
CANADA
K7L 3N6

April 14, 1999
(received 4/23/99)

Dr. B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

"NMR course on the WEB"

Dear Barry:

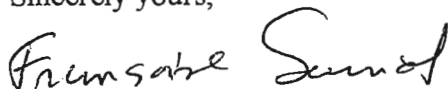
I have been involved in teaching NMR for a few years first at McGill and now here at Queen's University and I thought that creating an NMR course for the WEB containing a few animations (without using any mathematics) would be a good idea. The course I have been teaching focusses on practical analysis of spectra and gives an overview of various NMR techniques so that the student by the end is in a position to decide which technique to use in which situation.

The Web site I created is still in its infancy but I thought I would share with you its existence. One of the animations for example presents the periodic table. When the user clicks on a nucleus, the program displays the NMR properties of the various stable isotopes for that nucleus and in the next pages the chemical shift ranges of various compounds (relative to the accepted reference) and in the next page the size of various coupling constants. There are also some basic animations on the pulse, the composite pulse, the APT and INEPT sequences and on the use of field gradients in the spin echo experiment {with animated vectors to give the student an idea on how NMR works with pulses, delay and refocusing block (τ -180- τ)}. There is also an animation that illustrates how to analyze various 2D data sets (COSY, NOESY, TOCSY, Homo-2DJ, HMQC, HMBC). The compound selected for that animation is a disaccharide (sufficiently complex to justify those 2D experiments and sufficiently simple for the student to follow the analysis). You can also find in the 3D-homonuclear page, an animation that describes how to analyze a 3D-NOESY-TOCSY experiment. For more in depth treatment, there are a few pages on phase cycling (in 1D and 2D NMR) using the vector model and the coherence pathway and on the use of field gradients in NMR spectroscopy (to simplify phase cycling)

For those interested, I created these animations using a program called "Director" from "Macromedia". The animations can be played using a plug-in from Macromedia. The instructions to get the plug-in are embedded in the animation pages. The address of the introductory page for this NMR course is:

<http://www.chem.queensu.ca/nmr/nmr/webcourse/index1.htm>

Sincerely yours,



Françoise Sauriol
Manager of the Instrumentation Facility
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NMR-Sim (numerical simulation of NMR spectra)

NMR-Check (diagnostic software).

These programs run on a PC with Microsoft's Windows NT operating system, the same as they also run on a Silicon Graphics Inc (SGI) workstation under the IRIX operating system.

Q: Can NMR Suite for Windows NT control the spectrometer?

A: Yes! NMR Suite for Windows NT running on a PC has full control of the spectrometer and also does the data processing and data manipulation.

Q: Can I import spectra generated in NMR Suite for Windows NT into Windows programs such as MS Word or MS PowerPoint?

A: Yes! Our programs can write the plots into the Windows Clipboard or into a Windows Enhanced Metafile. From there the files can be imported into Word, PowerPoint and other Windows programs.

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A: No! Bruker continues to support the SGI/IRIX platform. NMR Suite for Windows NT is an option, and the choice is yours!

Q: Is special hardware required for the PC to control the spectrometer?

A: No! The PC is connected to the spectrometer by a standard ETHERNET card. We require a second ETHERNET card to connect the PC to the INTERNET/INTRANET.

Q: Is NMR Suite for Windows NT "Year 2000 compliant"?

A: Yes! To learn more, please check our Year 2000 homepage at www.bruker.com/y2000.

Q: What minimum configuration do I need for the PC to run NMR Suite for Windows NT?

A: The following hardware is recommended:

- Pentium II/266 MHz
- 64 MB ram (128 MB recommended)
- 4 GB disk (SCSI recommended)
- PCI graphics card, 2MB, minimum 256 colors and 1024 x 768 pixel resolution
- 3.5" floppy, 1.44 MB
- CD ROM
- 3 button mouse for PS/2 port
- Keyboard
- 2 ETHERNET cards, 10/100 Mbit 3COM 3C905 PCI bulk
- Windows NT 4.0 workstation installed on NTFS file system, including service pack 3

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UCD NMR FACILITY

DAVIS, CALIFORNIA 95616

April 9, 1999

(received 4/14/99)

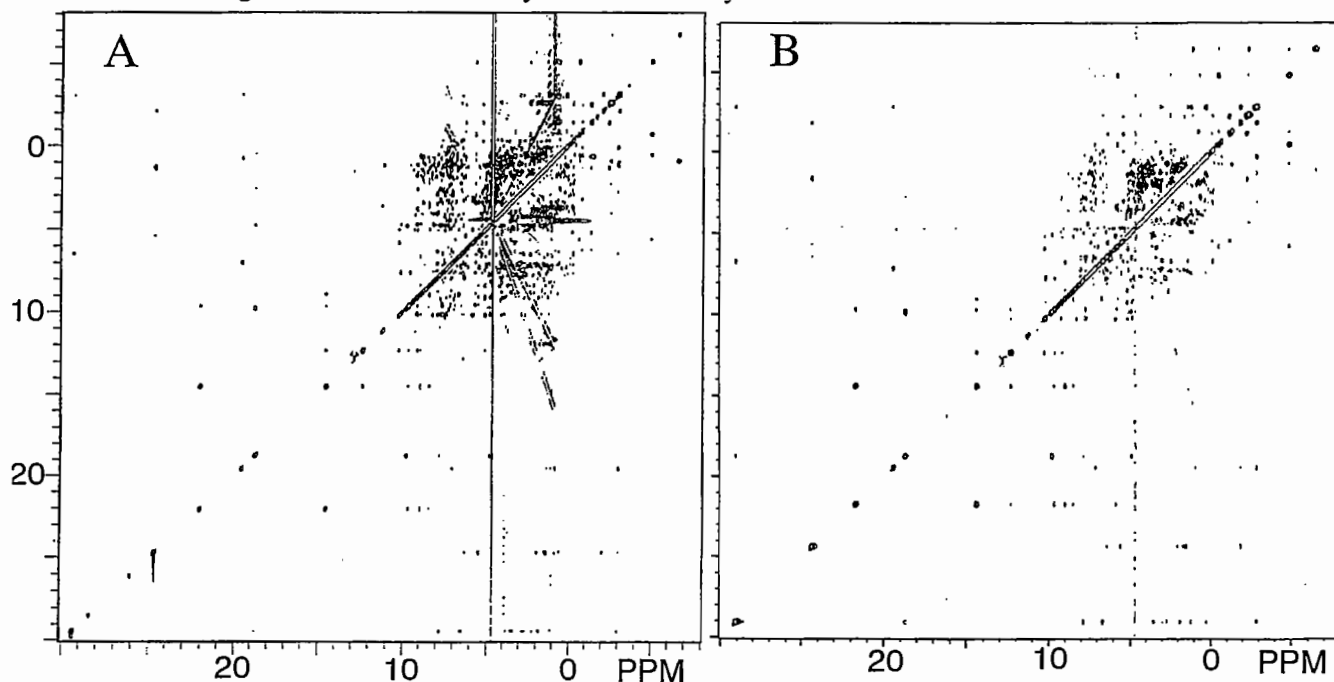
B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto CA 94303-3410

Fast, Faster, Fastest

Dear Barry,

We are the delighted owners of new 600 and 500 MHz Bruker Avance spectrometers. One of the long-standing areas of study here at UCD is NMR of paramagnetic metalloproteins, under the leadership of Professor G.N. La Mar. Naturally it was of great interest to us to see if the Avance spectrometers could collect data over large bandwidths at high repetition rates needed for paramagnetic biomolecules. Our previous systems, GE-NMR Omega consoles, suffered from a) various "hidden" pulse timing delays that slowed the nominal repetition rates and b) 2D maps collected at high rep rates had various artifacts.

We are happy to report both of these problems trouble us no longer with the Avance spectrometers. Figure A shows a fast rep NOESY on the Omega-500. Figure B shows a much cleaner NOESY dataset collected with essentially identical parameters on the Avance-500. The data in Figure 1 was collected in four hours with a 10 mm sample, while the data in Figure 2 was collected in a 5 mm sample tube (1/4 the sample of A) in just 24 minutes, illustrating the excellent sensitivity of the Avance system.



Figures A and B: 500 MHz NOESY datasets of 3 mM horseradish peroxidase cyanide complex in D₂O at 40 C, pH 7.0. Data collected with 200 ms recycle time and 20 ms mixing time. (A) is GE-NMR Omega data and (B) is Bruker Avance data.

In addition to better 2D data at high rep rates, the Avance is able to execute 1D spectra at very high rep rates with <1 msec of timing overhead, using a sequence sent to us by Bruker's Gerhard Eber as shown below.

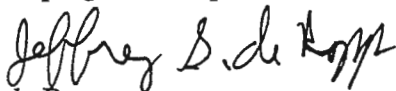
```
;zg.explicit
;avance-version
;1D sequence
;XWIN-NMR version 2.5
#include <Avance.incl>
define delay rde1
define delay rde2
"rde1=de3-de1"
"rde2=de3-de2"
"de1=1u"

1 ze
2 d1
  p1 ph1
  (de1 rde1 adc ph31 syrec) (de2 rde2 ph0):f1 (de3)
aq
  d31 rcyc=2 ;d31 may be adjusted
  wr #0
exit

ph0=0
ph1=0 2 2 0 1 3 3 1
ph31=0 2 2 0 1 3 3 1
;p1 : f1 channel - power level for pulse (default)
;p1 : f1 channel - high power pulse
;d1 : relaxation delay; 1-5 * T1
```

We wish also to express our appreciation to Mark O'Neil Johnson of the Bruker Fremont office for helping us to implement fast rep sequences on the Avance.

Sincerely,



Jeffrey S. de Ropp

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Laboratorium für Physikalische Chemie
Prof. Dr. Beat H. Meier

Zürich, 17.2.1999

(received 4/20/99)

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Dr. B.L. Shapiro
The NMR Newsletter
966 Elsinore Court

Palo Alto, CA 94303-3410
U.S.A.

Decoupling at High MAS Spinning Speeds

Dear Dr. Shapiro,

the standard way of obtaining high-resolution ^{13}C solid-state NMR spectra under magic-angle spinning (MAS) is the combination of high-speed spinning and high-power proton decoupling. With the recent availability of spinning speeds of $\omega_r/(2\pi) > 30$ kHz we were interested in the question whether one could combine high-speed spinning with low-power decoupling in order to obtain well resolved solid-state NMR spectra. Using TPPM decoupling one can achieve even higher resolution in many cases. Here we are only looking at CW decoupling.

Figure 1 shows the ^{13}C spectrum of uniformly labeled Tyrosine at a spinning speed of 30 kHz (^{13}C resonance frequency of 100 MHz) a) under high-power CW decoupling ($\gamma B_1/(2\pi) \approx 160$ kHz), b) under low-power decoupling $\gamma B_1/(2\pi) \approx 5$ kHz, and c) without any decoupling. The spectra were recorded using a Varian/Chemagnetics 2.5 mm double-resonance MAS probe. It is clearly visible that the α -carbon at 57 ppm and the β -carbon at 38 ppm show the narrowest lines under high-power decou-

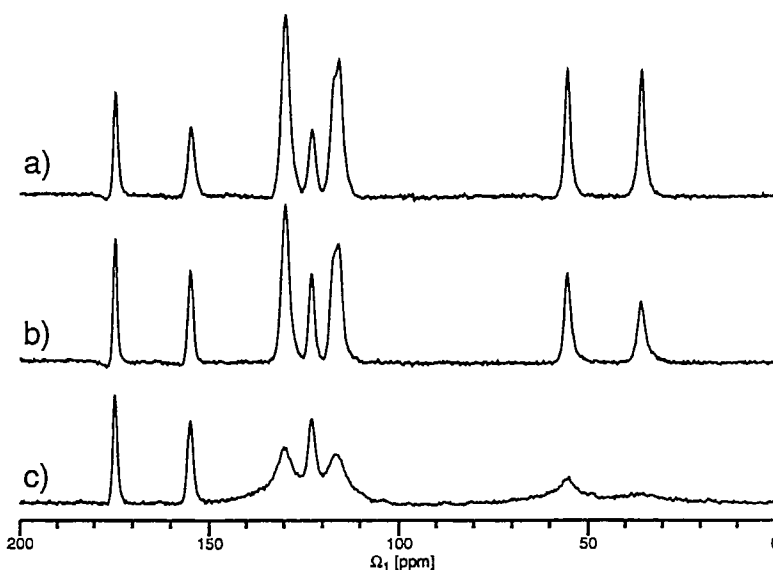


Figure 1

pling. The carbonyl at 175 ppm and the C-OH at 156 ppm show narrower lines under the low-power decoupling. Without any decoupling the carbonyl and the C-OH show also narrow lines but all the protonated carbons are quite broad due to the J coupling and magnetization exchange processes between the different multiplet lines.

Figure 2 shows the spectrum of Tyrosine over the full range of decoupling field strengths from $\gamma B_1/(2\pi) \approx 5$ kHz up to $\gamma B_1/(2\pi) \approx 140$ kHz. It can clearly be seen that for fields lower than the HORROR condition ($2 \cdot \gamma B_1 = \omega_r$) the decoupling is quite good. Around the rotary resonance conditions ($\gamma B_1 = \omega_r$ and $\gamma B_1 = 2 \cdot \omega_r$) the decoupling is very poor and we observe broad lines. Above the second rotary resonance condition the decoupling improves and the line width decrease with increasing field strength.

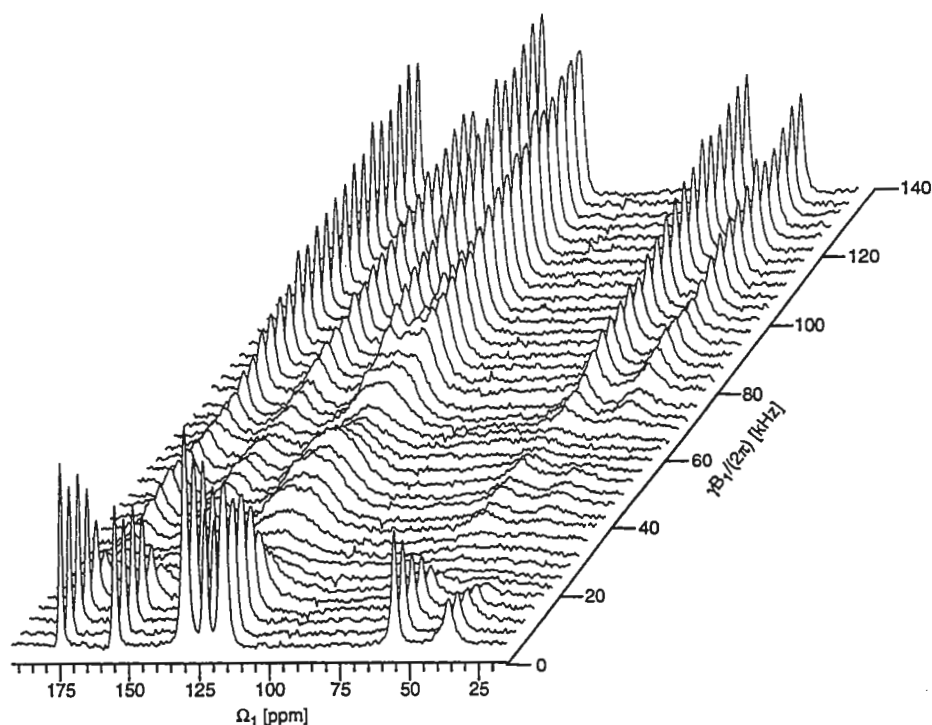


Figure 2

For certain applications and classes of substances low-power decoupling combined with high-speed MAS spinning can provide a viable alternative to high-power decoupling.

Sincerely,

Matthias Ernst

Beat

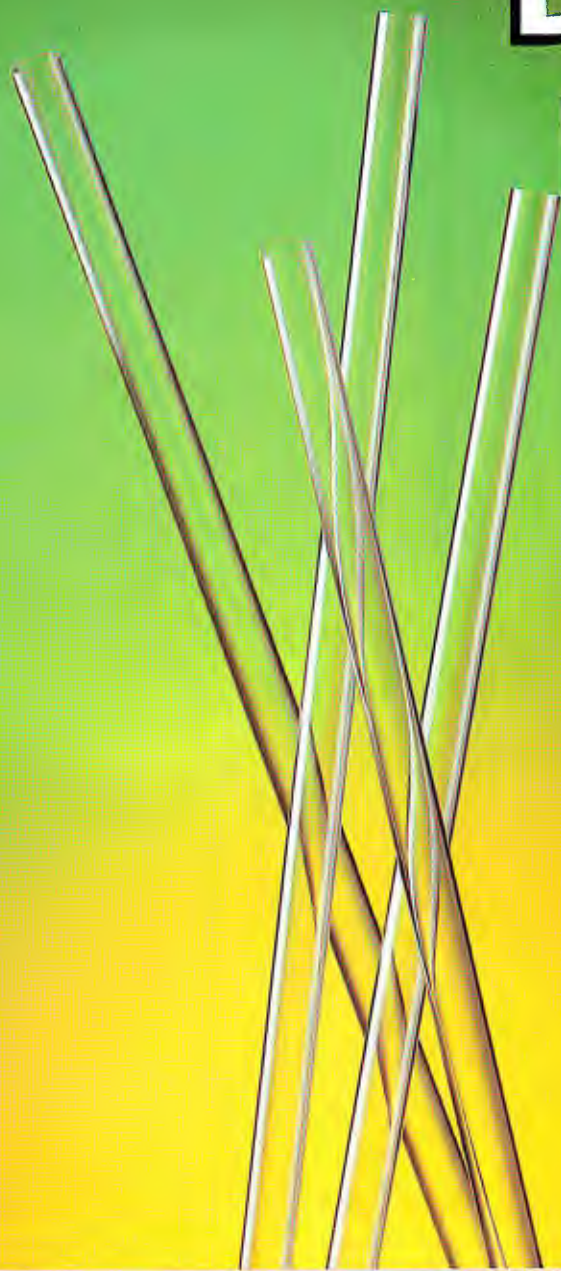
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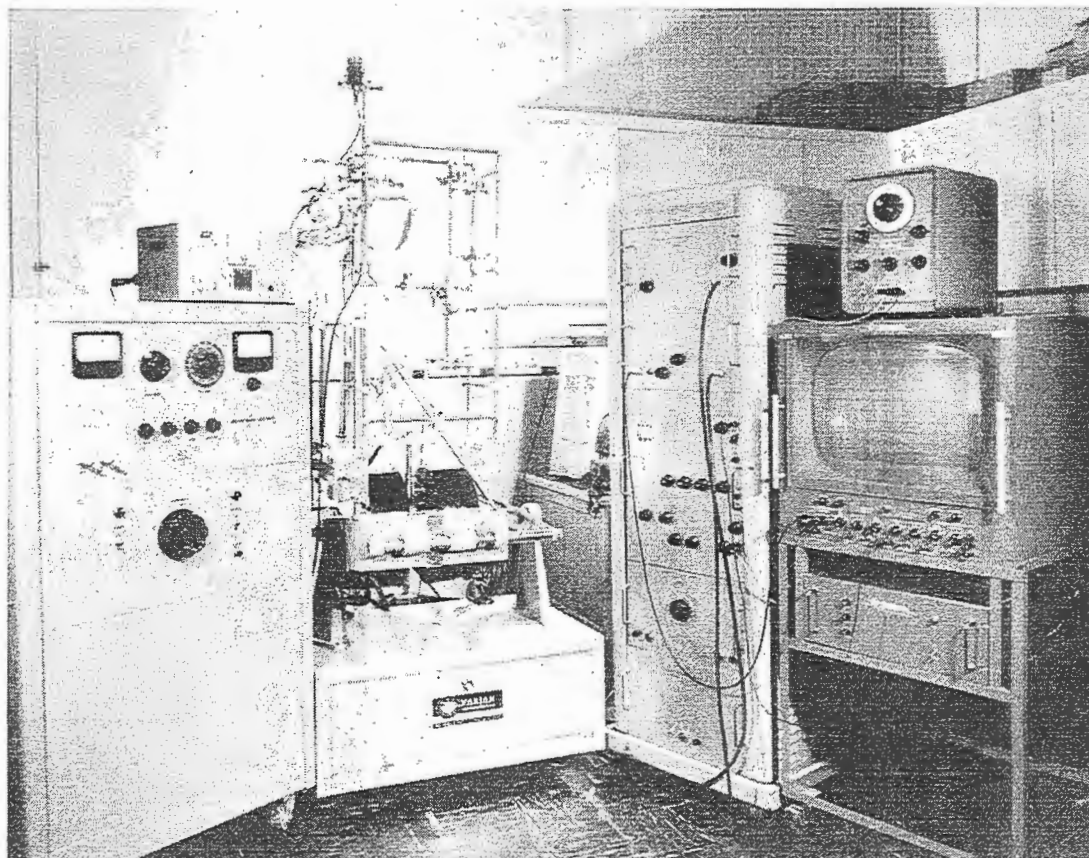
Dr. B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
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**Early Days of NMR in the Southwest:
Third Installment**

Dear Barry,

I continue the story of the early days of NMR at Magnolia/Mobil in Dallas, starting with the second NMR machine that arrived from Varian. It was the first commercial pulse spin-echo machine (Serial No. 1, made in San Carlos, CA), shown below.

Fig. 2. The first commercial pulse NMR machine.



The electromagnet had 6-inch diameter pole faces with a two-inch gap and operated at approximately 25 MHz. The assemblage mounted on top of the magnet is the vacuum apparatus that was used to apply various vapor pressures of water vapor to the sample. The unit at the right is a special large oscilloscope on which the transient FID's were displayed. The screen was covered with a fine, detailed graticule that allowed the spectroscopist to observe and measure visually the fleeting signal. On top of the oscilloscope is a Hewlett-Packard 200-CD vacuum tube analog audio oscillator that generated an alternating voltage that was adjustable continuously from 6 Hz to 600 kHz. It was the time base that was used to set the pulse intervals in the pulse sequences that were generated by the pulse programmer housed in the console to the left of the oscilloscope.

This instrument was both the *first* commercial pulse NMR machine, and the *last* one that Varian built for many years. Evidently, the construction of this machine led to the later visit to Gutowsky in Urbana to determine whether to market such pulse NMR machines, as mentioned in the first installment. (This was long before the development of Fourier Transform NMR.)

Soon afterwards, the NMR research at the Field Research Laboratory (FRL) was combined into a single research group. Dr. John R. Zimmerman of the University of Colorado was hired by Mobil for the summer of 1953; he also had the idea of using relaxation in NMR well logging. A few months later, Zimmerman considered an attractive offer from Schlumberger, but he accepted Mobil's offer of a permanent position. When he returned to Mobil in the first half of 1954, he became manager of a new research group called "Radio Frequency Spectroscopy" that included all of the NMR research at FRL. In continuing exploration research aimed at interpreting NMR well logs, around 1953-1954 Zimmerman carried out high-field pulse NMR experiments on liquids in contact with solid surfaces. He found that the silica gel surface greatly shortens the proton relaxation times of water and that two-component relaxation curves can be observed (because of proprietary considerations, Mobil delayed publication of this research for several years). Zimmerman and Ely filed a well logging patent application on May 20, 1954; the patent was granted on January 17, 1961.

In this general period of time, many patent applications were filed by many different companies; Chevron, with R. J. S. Brown, was especially active. As might be expected, there was considerable litigation and negotiations. In litigation between Mobil and the California group, the Mobil application of 1952 was assigned (1957) to Chevron. (It is not clear whether other Mobil patent applications were involved.) In the settlement, Mobil received \$100,000 and agreed to help the California group fight a suit filed by Texaco to support its own patent applications. In this suit, Zimmerman maintained that the Texaco idea would not work. Dr. Charles P. Slichter of the University of Illinois was an expert witness for Texaco. He carefully considered the idea from a fundamental scientific basis, enlisting the aid of Robert T. Schumacher, one of his students, and concluded that it could not be proved that the Texaco idea would not work. Also, in 1970 Slichter filed for a U.S. patent on nuclear magnetism logging, assigned to Texaco.

In 1958, I joined Zimmerman's group to carry out new research to understand the NMR relaxation phenomena of liquids on surfaces which would support the interpretation of NMR well logs in terms of quantities useful to the log analyst. This was shortly after publication of the famous NMR exchange paper [J. Phys. Chem., **61**, 1328 (1957)] by Zimmerman and Brittin that quantitatively explained the two-component observations on silica gel in terms of exchange between sites with different relaxation times. (In 1991, the Institute for Scientific Information sent a letter stating that this paper ranks as the 16th most-cited paper in the Journal of Physical Chemistry.) I extended the previous research on silica gel surfaces and prepared to expand the research to clay surfaces because most of the pore surface area in sandstones is provided by extremely high surface area clays such as montmorillonite, illite, and kaolinite.

Seeking to exploit the advantages of spin-echo measurements in inhomogeneous magnetic fields, Gustave L. Hoehn, Jr., Woessner, and Zimmerman filed a well logging patent application on March 1, 1960. This application described the use of a pulse to refocus the protons and form a spin echo. The use of the spin echo would overcome (a) the effects of inhomogeneity in the earth's field and (b) the effects of the long deadtime of the electronics caused by the transients at 2 kHz induced by the cut-off of the large polarizing magnetic field. The patent was issued on August 23, 1966. Also, I developed the idea that spin-echo measurements can be used to measure restricted diffusion [J. Phys. Chem., **67**, 1365 (1963)] and that such measurements could be used to measure the average pore size in rocks. The patent application, filed on April 6, 1962, was granted on October 19, 1965.

The basic philosophy that I followed was to carry out fundamental research to understand NMR relaxation phenomena in liquid water and hydrocarbons and also in water at surfaces to best interpret the NMR signals from logging tools. To do this, I needed to understand relaxation phenomena of water in electrolyte solutions, of nonspherical liquid hydrocarbon molecules, and nonspherical molecules at silica and clay surfaces. This entailed much theoretical work on anisotropically reorienting molecules in the bulk liquid and in surface layers. Experimental data on various systems were needed. To obtain data on clays, the performance of the spin echo equipment was upgraded. Hoehn did early work on improving the response of the NMR receivers. Robert A. McKay then extended this work and also developed successful Q-switching NMR probes to greatly decrease the deadtime so as to allow observation of weak signals with short T_2^* values.

During all this time, I was looking for new commercial equipment so that we could minimize our in-house efforts in equipment development. In the early 1960's a new company (Bruker) sent us a brochure on their pulse NMR equipment. Then, in 1963, Bruker had a booth at the Pittsburgh Conference and I asked Dr. Guenther Laukien about details of pulse response. Although he assured me that their equipment was the best available, it was clear to me that the equipment we had at Mobil was superior for our research. We continued with our in-house development and gradually replaced all of the original Varian components except the high voltage power supply for the pulse transmitter. McKay then developed the first automated pulse programmer and data acquisition system. Previously, the pulse intervals had to be set manually and the pulse NMR signals had to be collected by visually observing them on an oscilloscope and manually recording them. Now, the pulsing procedure was automated and the signals were automatically integrated and recorded on paper tape to be read by computer key punch operators (in those days, data and computer programs were entered on punched cards).

The ultimate goal of being able to analyze NMR well logs led to another instrumentation effort. We realized that the NMR relaxation times of liquids in rocks at 2 kHz could be different from those obtained from high-field spin echo measurements at 25 MHz and that laboratory measurements on representative rocks in the earth's field at 2 kHz were needed to calibrate the high-field experiments for use in well log interpretation. For such measurements, in 1963-64 McKay constructed an earth's field machine for measurements on fluids in 3.5 inch diameter rock samples. He made such measurements over the next few years. In the meantime, the uninspiring performance of the commercial earth's field NMR well logging tool during field tests that I attended caused Mobil to gradually lose interest. However, NMR was still deemed to be the potentially most useful tool to detect permeable zones on rock formations.

Going back in time, I return to oil production research. The third NMR machine ordered from Varian arrived about the same time that Zimmerman formed the Radio Frequency Spectroscopy group. It was a 40 MHz high resolution, continuous wave spectrometer. Parenthetically, Varian's first high resolution spectrometer (30 MHz) had been sold to Exxon in Baytown, TX. The second Varian high resolution spectrometer went to Dr. Charles A. Reilly at Shell Development Company in Emeryville, CA. Mobil received the third such spectrometer that Varian sold.

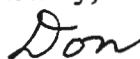
One of Zimmerman's major efforts was to develop high resolution NMR for analyzing petroleum and other liquids. Because the highest possible resolution was needed, Zimmerman began development of sample spinners and uniform sample tubes soon after the machine arrived. With W. F. Mueller, an excellent mechanical instrument maker at Mobil, he designed several prototype spinners. They soon ran into materials problems because sample spinning requires a high degree of dimensional uniformity for the glass sample tubes. Also, some batches of glass gave magnetic susceptibility artifacts because of variations in glass purity and composition. To solve these problems, he invited representatives from a glass products company in Landisville, NJ, to Dallas to discuss his needs. This visit was the start of Wilmad in the NMR sample tube business. Referencing of NMR spectral peaks was another problem. Zimmerman worked with Wilmad in developing the coaxial tube external referencing system in which the reference is located in the thin cylindrical shell between the two tubes. (This was before the time that TMS was universally adopted as an internal sample reference.) External referencing was used because of initial concerns that intermolecular interactions might occur between a dissolved reference and the sample and thus cause a shift in the Larmor frequency of the reference so as to render it unreliable.

To obtain even better spectral resolution for NMR methods of hydrocarbon analysis, Zimmerman sought to obtain the highest magnetic field possible. He received information about a Swiss company, Traub-Tueber, that had developed a new 90 MHz high resolution spectrometer and attempted to negotiate a purchase. However, Traub-Tueber informed him that they would not sell their instrument in the U. S. (Traub-Tueber later became the high resolution component of Bruker). Then, Varian proposed to upgrade the 40 MHz spectrometer to 100 MHz with new electronics and new magnet pole faces. Mobil purchased this conversion for about \$8,000. It was delivered in 1964, but Varian supplied a whole new magnet because they had found that the magnet conversion for high resolution spectroscopy was too difficult. This was an early Varian HR-100 NMR spectrometer. Later on, Varian introduced an NMR lock and marketed the HA-100 spectrometer.

Again, I solicit comments, corrections, additional material, etc. on the topics covered in the first three installments.

More in the next installment. I plan to cover more academic laboratories, industrial laboratories, biomedical research laboratories, and independent contract research institutions.

Sincerely,



Donald E. Woessner, Ph.D.

Adjunct Assistant Professor of Radiology

dwoess@mednet.swmed.edu



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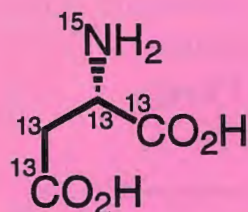
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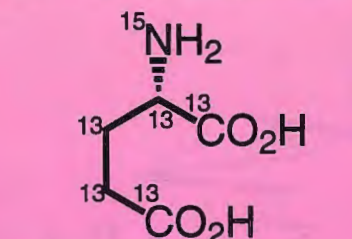
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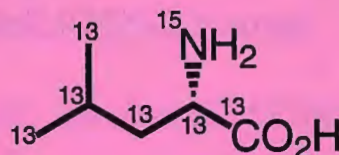
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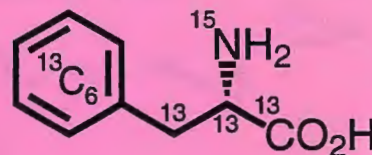
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03 April 1999
(received 4/23/99)

Adiabatic Fast Passage Inversion in Deuterium Single Crystal NMR Spectroscopy

Dear Dr. Shapiro

In a recent paper, Speier et. al [P. Speier, A. Müller, C. Meinel and U. Haeberlen, *Molec. Phys.* **95**, 1153 (1998)] have shown how to selectively mark specific doublets in deuterium single crystal spectra by Zeeman and/or Quadrupolar order. Such experiments are useful for the study of spin exchange phenomena in solids. They demonstrated their method in an investigation of the various spin exchange processes (chemical exchange and spin-diffusion) in a single crystal of deuterated bischlorophenylsulphone. Specific marking was affected by selective saturation and/or selective adiabatic fast passage (AFP) inversion. For their experiments, Speier et. al used a home built spectrometer augmented with a PC-controlled external frequency source, coupled to the regular rf line.

Here we demonstrate the implementation of the method on a commercial solid state spectrometer (Bruker DSX 300). To produce the chirp pulses for AFP a "do-loop" command was used, which generates a series of N back to back, constant-phase, frequency incremented pulses of duration t_p (separated by $0.05\mu\text{s}$) and strength γB_1 . The incremented frequencies were stepped by constant increments Δ , and were read from a pre-prepared "fqlist". In our experiments, pure Zeeman order was induced by a set of three sequential AFP's (see Fig. 1, top), first (for example) through the low-frequency component of the selected doublet ν_l , then through its high-frequency component ν_h , and finally again through ν_l . In exchange experiments, this preparation period is followed by a mixing time τ_m , during which spin exchange is allowed to take place. To overcome the spectrometer dead time, the detection was affected by the usual Quadrupole echo sequence, $\pi/2)_x - \tau - \pi/2)_y - \tau - \text{acqu.}$ For Quadrupolar order exchange experiments, we chose to induce a mixed Zeeman/Quadrupolar order state by AFP inversion of one peak, and monitor exclusively the Quadrupolar order using the read out detection sequence, $\pi/4)_x - \tau - \pi/2)_x - \tau - \text{acqu.}$, for detection (Fig. 1, bottom).

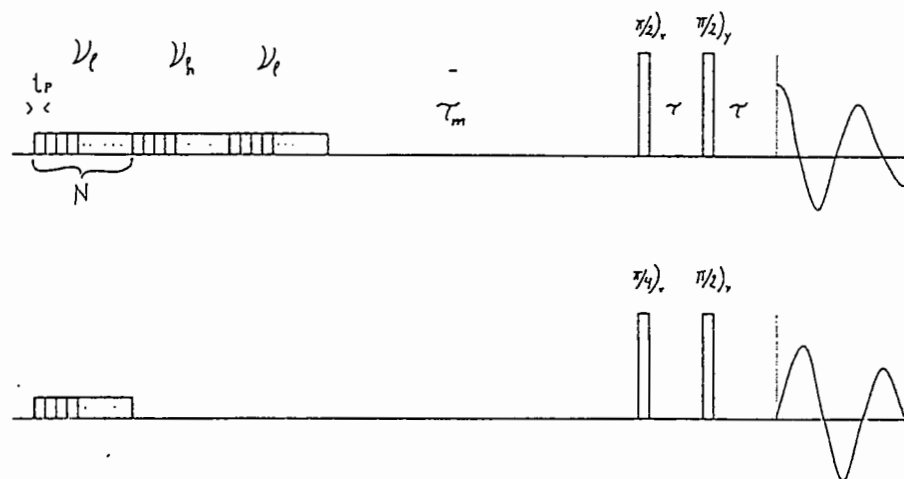


Fig. 1: RF pulse sequences and detection schemes used to monitor deuterium Zeeman (top) and Quadrupolar (bottom) order exchange.

In Fig. 2 we show results for a nematic liquid crystalline solution of cyclohexane- d_{12} (C_6D_{12}). The two doublets in the spectra correspond, respectively, to the axial (outer) and equatorial (inner) deuterons. Zeeman (left) and Quadrupolar (right) marking of the outer doublet were induced and detected as explained above. The bottom spectra were recorded shortly after preparation, while the upper ones were obtained after the indicated mixing times. The transfer of magnetization due to ring inversion is clearly observed. Note, in particular, the preservation of the sign of the Quadrupole interaction in the Quadrupolar order exchange experiment.

In Fig. 3 are shown deuterium NMR results for a more demanding experiment on a single crystal of azulene-1,3- d_2 . The magnetic field lies in the monoclinic plane and the two signals correspond to the magnetically inequivalent deuterons 1 and 3, in the molecule. The bottom spectrum was recorded immediately after selectively marking the outer doublet by Zeeman order, while the others were recorded after the indicated mixing times. The effect of spin exchange is again clearly observed.

Sincerely

T. Bräuniger

Thomas Bräuniger

Christoph Meinel

Christoph Meinel

Raphy Poupko

Raphy Poupko

Z. Luz

Zeev Luz

Fig. 2: Deuterium Zeeman (left) and Quadrupolar (right) order exchange experiments in a solution of C_6D_{12} (4%) in the nematic solvent ZL2452 (Merck) at -35°C . For the AFP inversion sequences we used, $N=250$, $t_p=0.95\mu\text{s}$, $\Delta=35\text{Hz}$, $\gamma B_1=1.5\text{kHz}$. The bottom spectra were recorded immediately after preparation; the top ones after the indicated mixing times.

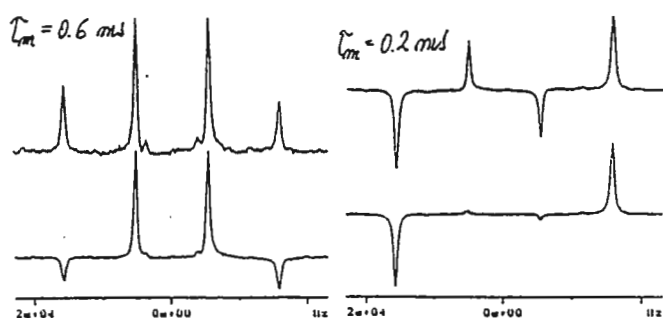
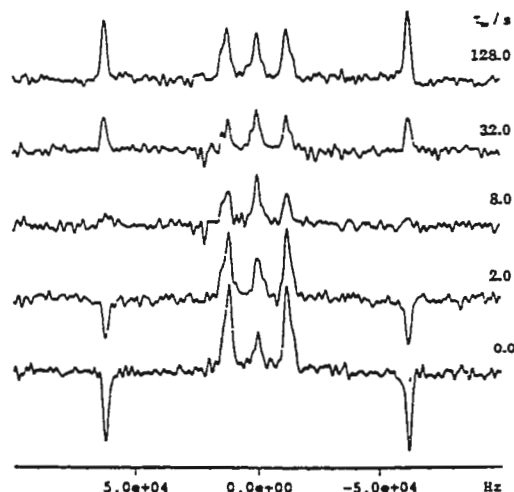
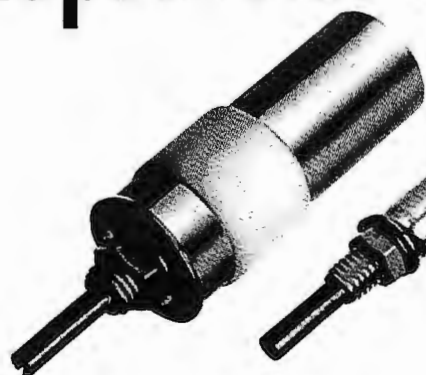


Fig. 3: Deuterium Zeeman order exchange spectra of a single crystal of azulene-1,3- d_2 at 57°C and the indicated mixing times. The AFP conditions were, $N=500$, $t_p=1.95\mu\text{s}$, $\Delta=60\text{Hz}$; $\gamma B_1=3\text{kHz}$. The magnetic field is in the monoclinic plane and the two doublets correspond to the two magnetically inequivalent deuterons in the molecule.



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**LABORATOIRE DE RESONANCE MAGNETIQUE NUCLEAIRE
METHODOLOGIE ET INSTRUMENTATION EN BIOPHYSIQUE
CNRS UPRESA 5012**

Dr. B.L. SHAPIRO
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303-3410
(USA)

March 29th, 1999

MEDICAL IMAGING : NMR AND NUCLEAR TRACERS

Dear Dr. Shapiro,

A special colloquium on recent bioengineering NMR methods will be held during the 12th Entretiens Jacques Cartier (Rhône-Alpes-Canada-Québec research organization) in Lyon 5-8 december 1999.


This meeting will emphasize the use of new nuclear markers such as hyperpolarized gases, electrons to nuclear magnetization transfer, and their prospective use for clinical applications.

You may find the meeting programme and the scientific committee on the following web site :

<http://jade.univ-lyon1.fr/JacquesCartier/>

The end of the meeting coincides with the most popular festivities in Lyon, the 8 december day. During the evening, lot of lighting candelas are set on the window-sills and people invade all the streets.

Yours sincerely,


Marie-Josée BEURIN


André BRIGUET

**Université Claude Bernard Lyon 1 et
Ecole de Chimie, Physique et Electronique de Lyon**
Bâtiment 308 - 43, Boulevard du 11 novembre 1918 -
69622 Villeurbanne cédex

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BICELLE PREPARATION

Buffer: An effective and convenient method for preparing bicelles makes use of a buffer solution containing 10mM phosphate buffer, pH 6.6, 3.0 mM sodium azide, 93% H₂O (HPLC-grade), 7% D₂O (99.9%). Below, this solution will simply be referred to as buffer.

Bicelle Formation: DMPC/DHPC stock solutions containing a total of 15% w/v (150mg lipid/ml) are prepared as follows:

Add buffer to the lyophilized lipid mixture

50mg lipid mixture, 280µg buffer

200mg lipid mixture, 1130µg buffer

Let the mixtures hydrate at room temperature (18-22°C) for several hours.

Lipid mixtures with a "q" of 2.8 - 3.0, the hydration is complete in 2 - 3 hours.

Lipid mixtures with a "q" of 3.25 - 3.5 require 24 hours for complete hydration.

Accelerated hydration (one hour) may be effected by heating any mixture to 40°C for 10 minutes and cycling to 18°C twice, then briefly vortexing.

Protein-Bicelle Mix: Two volumes of protein solution are added to one volume of bicelle solution.

Tjandra, N., & Bax, A., "Direct Measurement of Distances and Angles in Biomolecules by NMR in a Dilute Liquid Crystalline Medium" *Science* (1997) **278**:1111-1113.

Ottiger, M., & Bax, A., "Characterization of Magnetically Oriented Phospholipid Micelles for Measurement of Dipolar Couplings in Macromolecules" *J. Biomol. NMR* (1998), in press.

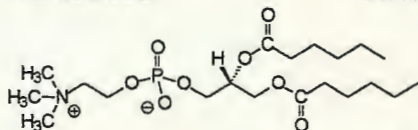
BICELLE FORMING LIPIDS

1,2-dihexanoyl-*sn*-glycero-3-phosphocholine

(DHPC)

Cat No. 850305

MW 453.51

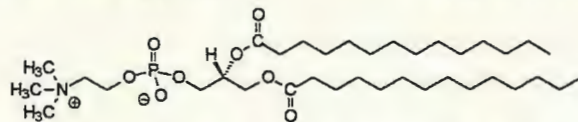


1,2-dimyristoyl-*sn*-glycero-3-phosphocholine

(DMPC)

Cat No. 850345

MW 677.95



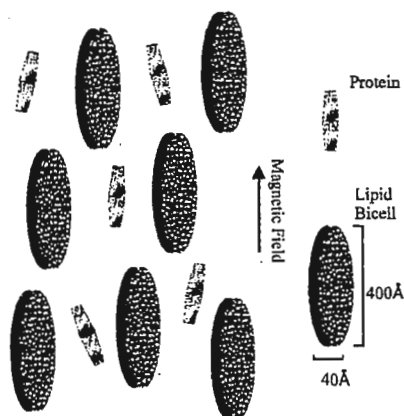
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The Phospholipid People
Research Chemical Division

Discotic Phospholipid Particles (Bicelles) Revolutionize Structural Analysis of Macromolecules by NMR

A new **NMR technique** gently **aligns protein molecules** in a bath of liquid crystals, allowing researchers to determine how each bond between neighboring atoms is oriented with respect to the rest of the molecule. By compiling all such orientations between atoms, a **precise map of the protein can be derived**. In aqueous solution, just above room temperature, the lipids switch from a gel to a Liquid Crystal (LC) phase, where they form **disc-shaped particles**, often referred to as **bicelles**, with diameters of several hundred angstroms and thicknesses of ~40Å. The lipids are diamagnetic, and, as a result, the bicelles orient with their normal orthogonal to the magnetic field.

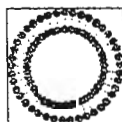


Two of the most common phospholipids used for bicelle formation are **1,2-Dimyristoyl-*sn*-Glycero-3-Phosphocholine (DMPC)** and **1,2-Dihexanoyl-*sn*-Glycero-3-Phosphocholine (DHPC)**. Preparation of defined mixtures of these lipids can be technically difficult and time consuming. Also, specialized equipment is required for handling the materials due to the hygroscopic nature of DHPC. To assist researchers in utilizing this technique, Avanti now offers these components in **pre-mixed units ready for hydration**. Just add buffer and protein solution and you can be ready to take measurements in less than 1 hour.

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Pre-mixed Lipids for Bicelle Formation

DMPC:DHPC Ratio (g)	Pricing Information			Catalog #
	50mg / 200mg	5 x (50mg / 200mg)	10 x (50mg / 200mg)	
2.8	\$50 / \$150	\$195 / \$625	\$325 / \$1000	790590
3.0				790573
3.25				790574
3.5				790575



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April 11, 1999
(received 4/22/99)

THE COLLEGE OF STATEN ISLAND
THE CITY UNIVERSITY OF NEW YORK



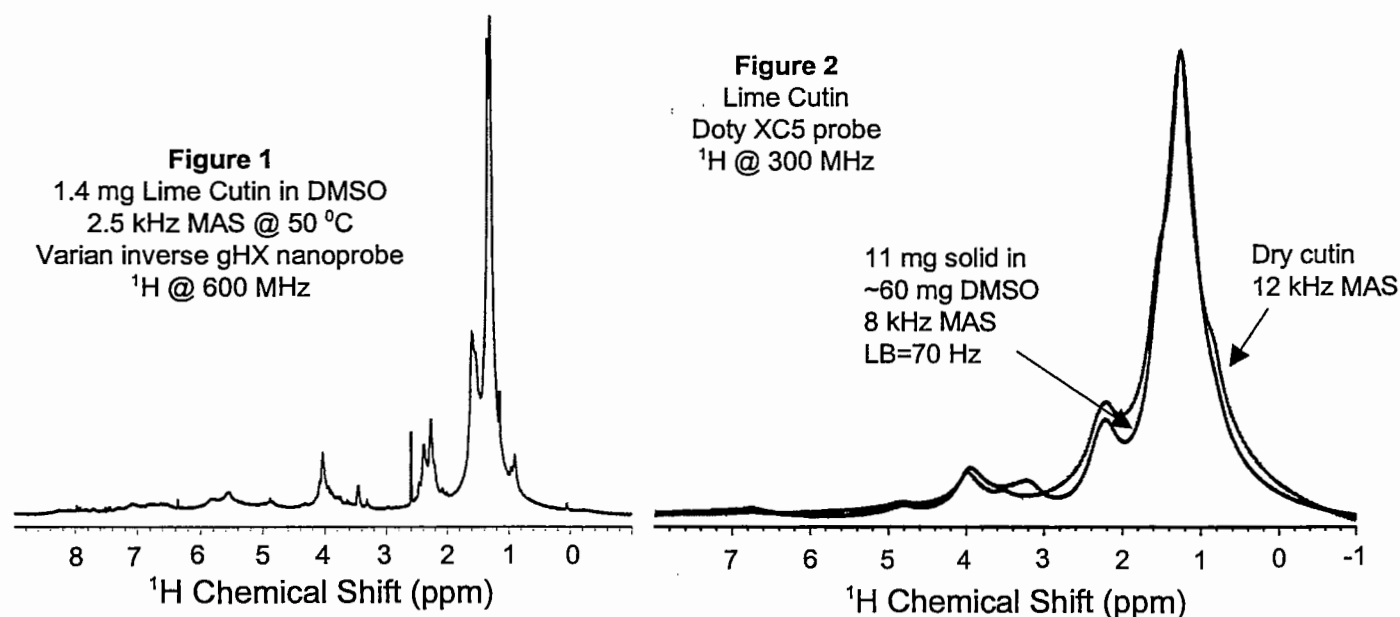
Dr. Bernard Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Re: Squeezing the Juice Out of Solvent-Swollen Plant Polymers

Dear Barry,

Since we reported on MAS NMR spectroscopy of solvent-swollen potato suberin last year ^[1], we have been extending this fruitful investigative approach to other plant polymers. As noted previously, the partially averaged dipole-dipole interactions in many polymer gel, phospholipid membrane, and cell samples make them challenging to cross polarize, but their relative motional freedom and disorder facilitate the acquisition of well-resolved NMR spectra using just MAS and modest recycle delays. ^[2,3,4] Cutin, an insoluble polyester purified in the present instance from the skin of limes, is a particularly good candidate for such studies, since it has rather flexible hydrocarbon chains and can be swelled effectively in many organic solvents. MAS-assisted ¹H and ¹³C NMR experiments on the intact polymer can potentially reveal its molecular architecture directly, avoiding the loss of time and information associated with chemical or enzymatic depolymerization procedures. That being said, it was important for us to examine the limits of attainable spectral resolution, the fidelity with which solvent-swollen spectra represent the polymeric material, and the similarities between its ¹H-¹³C HMQC "fingerprint" and that of a typical oligomeric constituent of cutin.

The high-field ¹H MAS NMR spectrum of swollen cutin (Fig.1) is sufficiently well resolved to assign and quantify many proton types; it exhibits all of the resonances expected from its monomeric and dimeric constituents ^[5,6] plus additional resonances in the aromatic region.



¹ B. Yan and R.E. Stark, *NMR Newsletter*, June 1998.

² H.D.H. Stöver and J.M.J. Fréchet, *Macromolecules*, 24 (1991) 883.

³ J. Forbes, C. Husted, and E. Oldfield, *J. Am. Chem. Soc.*, 110 (1988) 1059.

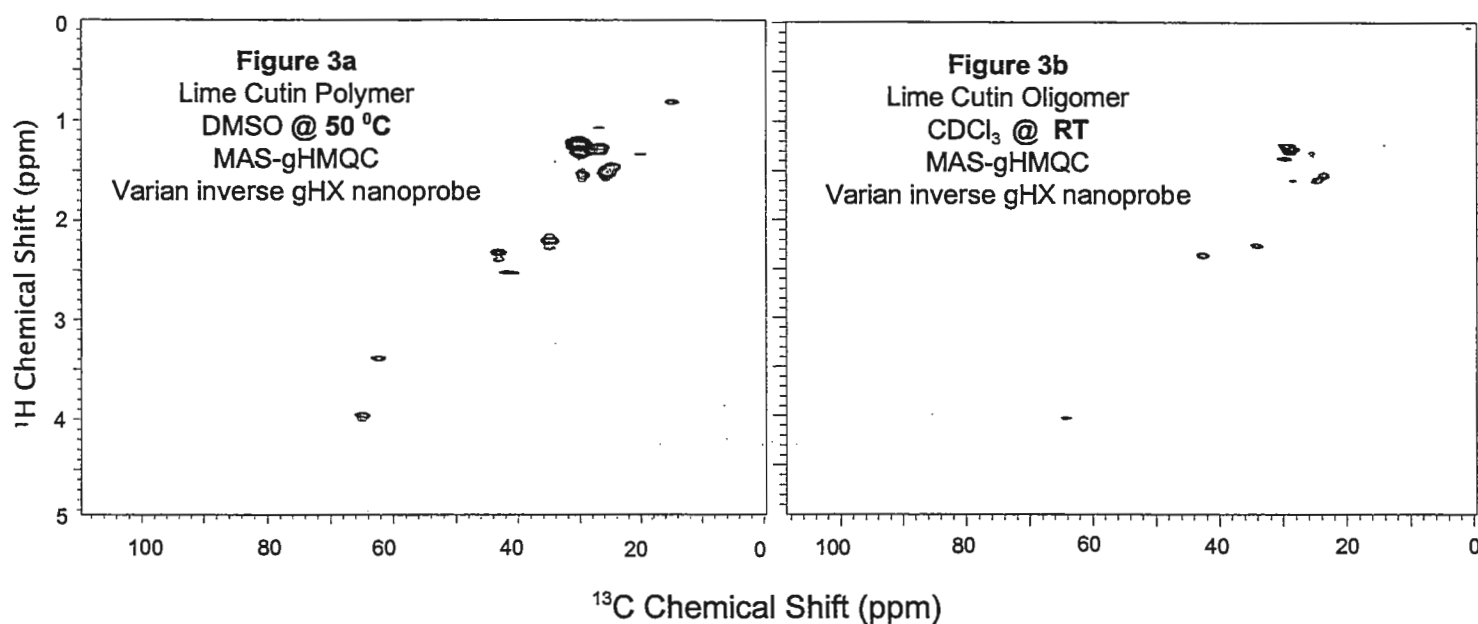
⁴ L.L. Cheng, C.L. Lean, A. Bogdanova, S.C. Wright Jr., J.L. Ackerman, T.J. Brady and L. Garrido, *Magn. Reson. Med.*, 36 (1996) 653.

⁵ A.K. Ray, Y.Y. Lin, H.C. Gerard, Z. Chen, S.F. Osman, W.F. Wett, R.A. Moreau and R.E. Stark, *Phytochemistry*, 38 (1995) 1361.

⁶ A.K. Ray, Z. Chen and R.E. Stark, *Phytochemistry*, 49 (1998) 65.

Moreover, a quantitative ^1H MAS-NMR comparison of dry and wet cutin samples (Fig.2) confirms that all of the polyester has been swelled and no functional groups are under- or over-represented. This type of method validation has also been conducted successfully for heavily crosslinked suberin, a related plant material that consists of an aliphatic-aromatic polyester embedded within a matrix of cell-wall polysaccharides (data not shown).

Finally, comparison has been made of HMQC contour plots for swollen lime cutin (Fig. 3a) and a soluble tetramer isolated from the low-temperature HF cleavage of neutral sugar linkages in this material (Fig. 3b). The superior spectral resolution achieved for the tetramer may be attributed to its chemical homogeneity and rapid reorientation in solution, but the polymer spectrum nevertheless reveals a more complete set of hydrocarbon, hydroxylated, and esterified functional groups within the cutin architecture.



With these encouraging results in hand, our next experiments will aim to augment the molecular information content and extend the chemical applicability of MAS NMR in swollen biopolymers.

Sincerely yours,

Bin Yan
Postdoctoral
Research Associate

Xiuhua Fang
Postdoctoral
Research Associate

Hsin Wang
NMR
Facility Manager

Ruth E. Stark
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UNIVERSITY OF ILLINOIS
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600 South Mathews Avenue
Urbana, IL 61801

March 24, 1999

(received 4/5/99)

¹³C Mass Sensitivity: Two Probes Compared

Dear Barry,

Our recent equipment upgrade has led to questions concerning sensitivity and measurement of probe performance for mass limited samples. We would like to share the results of this exercise with you. Our current probe inventory includes two probes that by design will maximize mass sensitivity for carbon-13 NMR, a 3mm ¹³C{¹H} standard high resolution probe for our 750MHz instrument and a Varian 4mm ¹³C{¹H} Nano-Probe tuned for a 500MHz instrument. The exercise was to determine which probe is better for acquiring carbon spectra of mass limited samples. The Nano probe is a high resolution, slow spinning (2-3kHz) MAS probe developed for mass limited samples and combinatorial chemistry studies. For combinatorial chemistry, the magic angle spinning averages the effect of magnetic field inhomogeneities near the solid supports. The sample is positioned entirely within the coil (without the problem of line broadening cause by field inhomogeneities at the sample ends) thus a good choice for mass limited samples.

We started with available data, signal to noise ratios (S/N) for the benzene triplet of a standard 40% dioxane in C₆D₆ sample. The 3mm probe gives an S/N of about 220:1 compared to 80:1 for the Nano probe. First the data was adjusted to account for the differences in sample volume, 200uL for the 3mm and 40uL for the Nano probe. When the factor of 5 difference in sample volumes (total amount of analyte) is considered the Nano probe is favored, giving an adjusted S/N of 400:1.

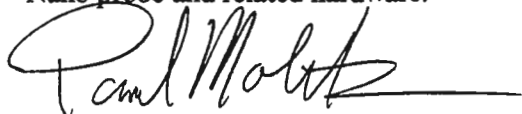
As is standard practice, the 3mm sample extends beyond the coil (observe region) of the probe to avoid irregularities due to magnetic field inhomogeneities at the ends of the sample. In the above comparison the 3mm sample is approximately three times the probe's coil length or about 4.5 to 5 cm long, thus only one third of the sample, about 75uL, is detected. The total sample volume can be reduced, increasing the concentration of analyte, the amount of analyte observed and hence the signal. We have been able to achieve comparable lineshape with samples as small as 110 uL with the 3mm probe. If the volume is reduced to 110μL the volume factor is reduced to 2.75 and the Nano probe and 3mm give comparable mass sensitivities. Further reductions in sample size make it very difficult to achieve optimal line shape and hence do not increase S/N substantially.

With a 110 μL sample in the 3mm tube about 50% of the analyte is within the observe region of the probe. Susceptibility matched plugs, Shigemitsu tubes and cylindrical or spherical sample cells, are all designed to restrict the sample to the observe region of the probe with a minimum of line broadening due to field inhomogeneity. If the analyte is restricted entirely to the observe region of the 3mm probe, without a notable degradation of lineshape, the mass sensitivity should increase by about a factor of two from the 110μL sample. At best this will give the 3mm probe a 2:1 advantage over the Nano probe. A 2:1 increase is about what would be expected due to the increase in field strength. Our experience with these is limited and lineshape may or may not be an issue. From what we have heard from other users, these susceptibility matching methods work well if the sample ends are outside of the coil region, which will decrease the mass sensitivity slightly for a given line shape.

Routinely achievable lineshape values are 0.2/3/4 for the 3mm and 0.4/7/8 for the Nano probe (50%/0.55%/0.11% linewidth of the proton decoupled dioxane peak, no line broadening applied). This difference results in lines of different widths for the C_6D_6 triplet, thus for lines of comparable width, the homogeneity differences are included in the measured S/N values. However, most research samples give narrower linewidths. As the linewidth narrows, (assuming minimal line broadening is applied and shimming, is good) the 3mm probe's advantage may increase somewhat.

There are other practical considerations as well. The 3mm probe is a standard probe and as such requires a minimum of additional user training, changing samples is routine and sample tubes are available from standard suppliers. The Nano probe is a high resolution, slow spinning MAS probe thus additional hardware is required, sample changing is less routine, sample tubes are currently available only from Varian for a price greater than most 3mm tubes and additional user training is required.

Of these two probes, the 3mm probe for the 750MHz instrument is generally the better choice for mass limited ^{13}C liquid samples. The S/N is comparable for sample volumes of 110 μ L in the 3mm probe and likely better depending on lineshape. The advantage could be as high as 2:1 if any of the techniques mentioned above for restricting the sample to the observe region are viable. The Nano probe's performance is still very good and it is the only choice for molecules tethered to solid supports. Of course the above discussion assumes access to a 750MHz instrument and the cash outlay for such an instrument with a room to house it is much greater than the price of a Nano probe and related hardware.



Paul Molitor

Please credit this contribution to the subscription of Vera V. Mainz.

MAGNETIC RESONANCE SPECTROSCOPIST

Princeton University has an immediate opening for a Ph.D. level magnetic resonance spectroscopist with experience in liquid-state small molecule structural studies, and solid state NMR spectroscopy. At least two years of postdoctoral or industrial experience is preferred. Additional expertise in EPR spectroscopy and Unix system management are highly welcome. Experience with structure calculations and spectral simulations is a plus. Primary duties involve maintenance and troubleshooting of related instrumentation (hardware) and associated peripherals, including all spectrometer components, computers (Unix, PC and Mac platforms), and plotters; training of new users on basic as well as more advanced 1D and 2D techniques; scheduling and bookkeeping of multi-user instruments, educating students and faculty in new magnetic resonance methods and instructor for lectures on the theory of instrument operation; drafting of instrumentation proposals. The spectroscopist will fill one of two Professional Technical Staff positions with complementary skills and overlapping instrument responsibilities in the NMR/EPR facility (5 NMRs, 2 EPRs, 1 ENDOR). Send resume to: **Prof. Robert A. Pascal, Jr., Operations Committee, Dept. of Chemistry, Princeton University, Princeton, NJ 08544.** *Princeton University is an Equal Opportunity/Affirmative Action Employer*

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only between 8:00 am and
10:00 pm, Pacific Coast time.

Deadline Dates

No. 489 (June) 21 May 1999
No. 490 (July) 25 June 1999
No. 491 (Aug.) 23 July 1999
No. 492 (Sept.) 20 Aug. 1999
No. 493 (Oct.) 24 Sept. 1999

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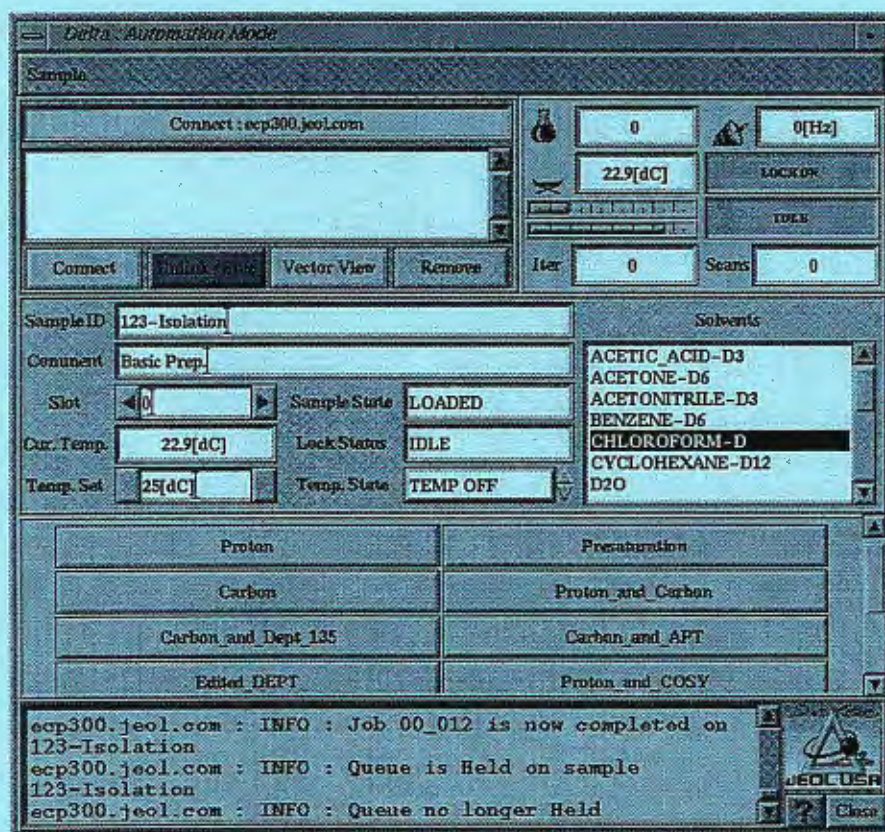
Forthcoming NMR Meetings, continued from page 1:

Medical Imaging: NMR and Nuclear Tracers, colloquium at the 12th Entretiens Jacques Cartier, Lyon, France, **December 5-8, 1999**; See <http://jade.univ-lyon1.fr/JacquesCartier/> and Newsletter 488, 38.

41st ENC (Experimental NMR Conference), Asilomar Conference Center, Pacific Grove, CA, **April 9-14, 2000**; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87505; (505) 989-4573; Fax: (505) 989-1073; E-mail: enc@enc-conference.org.

XIX International Conference on Mag. Res. in Biological Systems, Florence, Italy, **August 20-25, 2000**. Contact: Profs. Ivano Bentini or Lucia Banci, Chem. Dept., Univ. of Florence, Via G. Capponi 7, I-50121, Florence, Italy; Phone: +39-055-2757600; Email: icmrbs@lrm.fi.cnr.it; Fax: +39-055-2757555; <http://www.lrm.fi.cnr.it/icmrbs.html>.

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