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|----------|--|-----------------------------------|--------------------|-------------------|------------|------------|---------------------------|
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## FORTHCOMING NMR MEETINGS

- San Francisco Symposium - "In Vivo Magnetic Resonance Spectroscopy II", March 31 - April 2, 1989; San Francisco, California; See Newsletter 363, 17.
- 30th ENC (Experimental NMR Conference), April 2-6, 1989; Asilomar Conference Center, Pacific Grove, California; Conference Chair: A. N. Garroway; Contact Ms. Judith A. Watson, ENC Conference Center, 750 Audubon, East Lansing, MI 48823; (517) 332-3667. See Newsletter 362, 69.
- NMR Spectroscopy In Vivo (Clinical Applications), July 10-12, 1989; Lyon France; Contact Prof. M. Amiel - see Newsletter 364, 73.
- The Society of Magnetic Resonance in Medicine - Eighth Annual Scientific Meeting and Exhibition, August 12-19, 1989; Amsterdam, The Netherlands; Contact: The S.M.R.M. Business Office, 1918 University Ave., Suite 3C, Berkeley, CA 94704; (415)841-1899, FAX (415)841-2340.
- 9th International Meeting on NMR Spectroscopy, Sponsored by the Royal Society of Chemistry, July 10-14, 1989; University of Warwick, Coventry, England; Contact: Dr. John F. Gibson; (01) 437-8656; See Newsletter 364, 72.
- 3rd Chianti Workshop on Magnetic Resonance Relaxation, May 28 - June 2, 1989; San Miniato (Pisa), Italy; Contact: L. Banci, Dipartimento di Chimica Bioinorganica, Università degli Studi di Firenze, Via Gino Capponi 7, 50121 Firenze, Italy. See Newsletter 362, 68.
- Eastern Analytical Symposium, September 24 - 29, 1989; New York City; Contact: EAS, P. O. Box 633, Monchanin, DE 19710-0633; (302) 453-0785.

Additional listings of meetings, etc., are invited.

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

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| No. 367 (April) ——— | 17 March 1989    |
| No. 368 (May) ———   | 21 April 1989    |
| No. 369 (June) ———  | 19 May 1989      |

THE UNIVERSITY OF MICHIGAN  
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BIOPHYSICS RESEARCH DIVISION

November 30, 1988  
(received 12/5/88)

2200 BONISTILLI BOULEVARD  
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Prof. B. L. Shapiro  
TAMU NMR Newsletter  
966 Elsinore Court  
Palo Alto, CA 94303

Long-Range Heteronuclear Coupling Constants from Homonuclear 2D-NMR Spectra

Dear Dr. Shapiro,

We've recently started to use a simple and accurate approach for measuring long-range heteronuclear couplings of isotope-enriched compounds (1) which may be of general interest. We record homonuclear 2D NMR spectra (e.g. NOESY, ROESY, RELAY, or TOCSY) of isotope-enriched proteins that contain cross peaks between the protons bound directly to  $^{13}\text{C}$  or  $^{15}\text{N}$  and the protons for which long-range coupling to the same enriched nucleus should be measured. Because the heteronuclei are not pulsed, these cross peaks show an ECOSY-like pattern with respect to the passive heteronuclear couplings; they are split in one dimension by the large direct heteronuclear coupling and, in the other dimension, by the long-range heteronuclear coupling of interest. The large splitting provides good resolution of the cross peak components and allows accurate measurements of both coupling constants. Similar effects have been observed previously in 2QF-COSY spectra of  $^{113}\text{Cd}$ -enriched metallothionein-2 (2).

To illustrate this approach, we have used product operator formalism to simulate an intrareidue  $\text{H}^{\text{N}}\text{-H}^{\beta}$  NOESY cross peak of the  $^{15}\text{N}$ -enriched amino acid spin system shown in Figure 1. We considered the NOESY peak at  $\omega_1 = \Omega_{\text{HN}}$  and  $\omega_2 = \Omega_{\text{H}\beta}$  for which the magnetization begins on the  $\text{H}^{\text{N}}$  proton. The relevant terms of the product operator at the end of the evolution period are:

$$-I_y \cos(\Omega_{\text{I}} t_1) \cos(\pi J_1 t_1) \cos(\pi J_2 t_1) + 2I_y K_z \sin(\Omega_{\text{I}} t_1) \sin(\pi J_1 t_1) \cos(\pi J_2 t_1) \quad [1]$$

in which  $J_1 \equiv {}^1J(^{15}\text{N-H})$ ,  $J_2 \equiv {}^3J(\text{HN-H}^{\alpha})$ , and I and K refer to the  $\text{H}^{\text{N}}$  proton and  $^{15}\text{N}$  nuclei, respectively. The additional terms which are not shown are eliminated by standard NOESY phase cycles. The second proton pulse of the NOESY sequence converts the in-phase and anti-phase terms of Eqn 1 into longitudinal magnetization ( $I_z$ ) and two-spin order ( $I_z K_z$ ), respectively.

Because the nitrogen nuclei are not affected by this second proton pulse, the  $K_z$  components of the product operator remain aligned along the z-axis. Nuclear Overhauser effects between the  $\text{H}^{\text{N}}$  and  $\text{H}^{\beta}$  protons during the mixing period next convert longitudinal magnetization and two-spin order of the  $\text{H}^{\text{N}}$  proton into the corresponding states of the  $\text{H}^{\beta}$  proton. Ignoring the diagonal peaks, the observable y-axis terms of the final two-dimensional product operator are:

$$-M_y \cos(\Omega_{\text{I}} t_1) \cos(\Omega_{\text{M}} t_2) \cos(\pi J_1 t_1) \cos(\pi J_2 t_1) \cos(\pi J_3 t_2) \cos(\pi J_4 t_2) \cos(\pi J_5 t_2)$$

$$-M_y \sin(\Omega_{\text{I}} t_1) \sin(\Omega_{\text{M}} t_2) \sin(\pi J_1 t_1) \cos(\pi J_2 t_1) \sin(\pi J_3 t_2) \cos(\pi J_4 t_2) \cos(\pi J_5 t_2) \quad [2]$$



in which  $J_3 \equiv {}^3J(^{15}\text{N}-\text{H}^\beta)$ ,  $J_4 \equiv {}^2J(\text{H}^\beta-\text{H}^{\beta'})$ ,  $J_5 \equiv {}^3J(\text{H}^\alpha-\text{H}^\beta)$ , and M denotes the  $\text{H}^\beta$  spin. The first term of Eqn. 2 is the usual in-phase homonuclear NOESY cross peak, while the second term, arising from heteronuclear two-spin order during the mixing time, is a superimposed NOESY cross peak which is in-phase with respect to all of the homonuclear couplings and anti-phase in  $t_1$  and  $t_2$  relative to  ${}^1J(^{15}\text{N}-\text{H})$  and  ${}^3J(^{15}\text{N}-\text{H}^\beta)$ , respectively. This second pathway of magnetization is converted back into observable magnetization only if the two protons associated with the NOESY cross peak are coupled to the same  $^{15}\text{N}$  nucleus (except in the special case of simultaneous  ${}^1\text{H}-{}^1\text{H}$  and  ${}^{15}\text{N}-{}^{15}\text{N}$  incoherent magnetization transfer). Schematic diagrams of the cross-peak fine structures resulting from each of these terms of Eqn 2, and their superposition, are shown in Figure 1. As in ECOSY, the sign of the long-range coupling relative to the direct heteronuclear coupling can also be determined.

Uniformly  $^{15}\text{N}$ -enriched human type- $\alpha$  transforming growth factor (hTGF $\alpha$ ) was prepared by Drs. Peter Rauenbuehler and Marjorie Winkler (Genentech, Inc.) as part of our collaboration on structure-function studies of transforming growth factors. We have recently determined a nearly complete set of sequence-specific proton resonance assignments for hTGF $\alpha$  using conventional homonuclear 2D-NMR methods (3). Examples of  $\text{H}^\text{N}-\text{H}^\beta$  NOESY cross peaks of this  $^{15}\text{N}$ -enriched protein are shown Figure 2. For the downfield  $\text{H}^\beta$  proton of Cys-34 the ensemble-averaged  ${}^3J(^{15}\text{N}-\text{H}^\beta)$  coupling is  $-5.5 \pm 0.5$  Hz (Figure 2A), corresponding to a trans orientation of these two atoms (4). For Cys-21, both  $\text{H}^\text{N}-\text{H}^\beta$  cross peaks are resolved (Figure 3B) with  ${}^3J(^{15}\text{N}-\text{H}^\beta)$ 's of  $-1.3 \pm 0.5$  and  $-1.8 \pm 0.5$  Hz for the downfield and upfield resonances, respectively. These measurements indicate that both Cys-21  $\text{H}^\beta$  protons are gauche (4) with respect to the  $^{15}\text{N}$  atom; i.e. the corresponding dihedral angle  $\chi^1$  is ca.  $180^\circ$ . Such measurements can be combined with values of homonuclear coupling constants, measured by homonuclear ECOSY or COSY45, to determine  $\text{H}_2^\beta$  methylene stereospecific assignments and  $\chi^1$  rotamer distributions. The same approach can also be used to measure vicinal  ${}^3J(\text{H}^\alpha-^{15}\text{N})$  couplings in sequential  $\text{H}^\alpha-\text{H}^\text{N}$  NOESY cross peaks and to determine long range couplings to enriched  $^{13}\text{C}$  nuclei. We are quite excited by these results because this information will be very useful for refining solution structures of proteins and characterizing subtle conformational changes which may accompany site-directed mutations.

Guy Montelione

Gaetano T. Montelione

Gerhard Wagner

Gerhard Wagner

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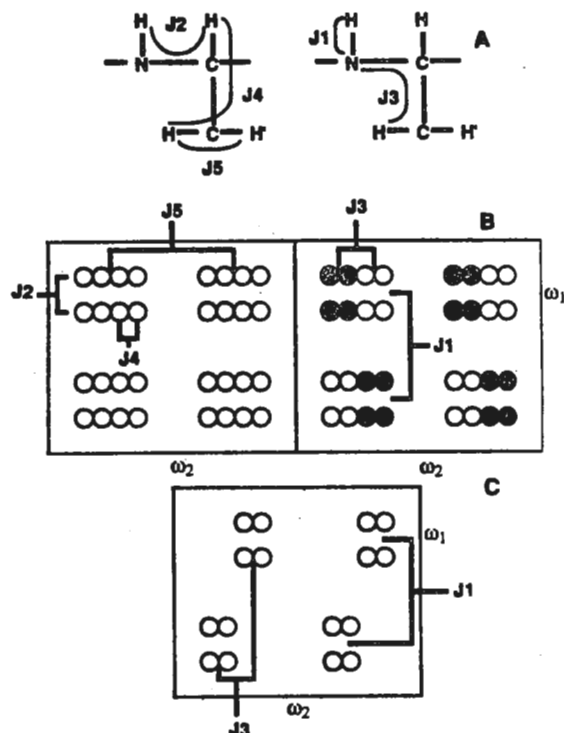


Fig. 1. Schematic drawing of a simulated  $\text{H}^{\text{N}}\text{-H}^{\beta}$  NOESY cross peak for an  $^{15}\text{N}$ -enriched protein. A) A simple amino acid spin system showing the homonuclear (left) and heteronuclear (right) spin coupling constants used for the cross peak simulation. The relevant coupling constants  $J_1$ ,  $J_2$ ,  $J_3$ ,  $J_4$ , and  $J_5$  are defined in the text. In this simulation,  $J_1 > J_5 > J_2 = J_3 > J_4$  and the product  $J_1 \times J_3 > 0$ . B) Contributions to cross-peak fine structure arising from longitudinal magnetization transfer  $I_z$  to  $M_z$  (left) and from transfer of heteronuclear two-spin order  $I_z K_z$  to  $M_z K_z$  (right) during the NOESY mixing time  $\tau_m$ . C) Superposition of these two components.

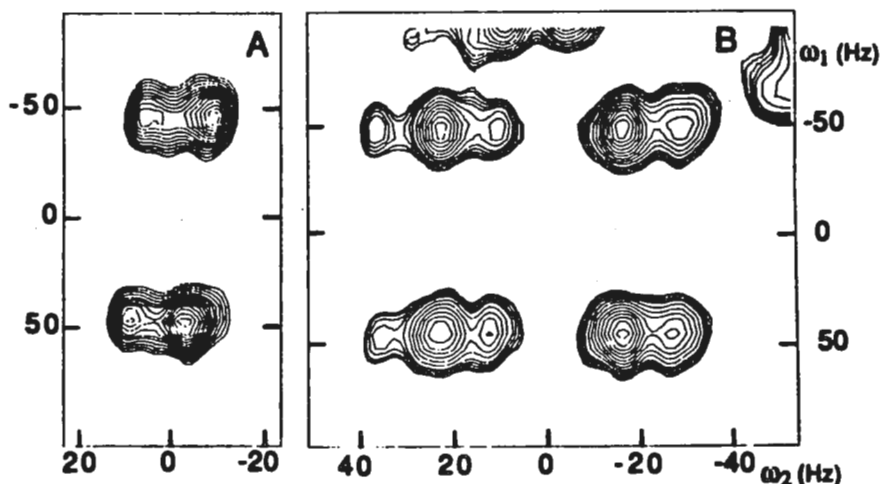


Fig. 2. Expansions of cross peaks involving methylene resonances from a NOESY spectrum of hTGF $\alpha$  at pH 3.5, temperature 30 $^{\circ}$  C. and ca 5 mM protein concentration. A) Intraresidue  $\text{H}^{\text{N}}\text{-H}^{\beta}$  cross peak of Cys-34 manifesting an  $\omega_2$  displacement due to vicinal  $^3J(^{15}\text{N}\text{-H}^{\beta})$  heteronuclear coupling of  $-5.5 \pm 0.5$  Hz. B) Both intraresidue  $^3J(^{15}\text{N}\text{-H}^{\beta})$  cross peaks of Cys-21, manifesting heteronuclear couplings of  $-1.3 \pm 0.5$  and  $-1.8 \pm 0.5$  Hz, respectively. These measurements indicate an ensemble-averaged dihedral angle  $\chi^1$  of ca 180 $^{\circ}$ .



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As part of our business charter, FMR is developing a series of hardware and software accessories based on personal computer (PC) technology. PCs are on a steep price/performance curve with the level of performance per dollar increasing daily. In addition, they are well supported by utility software and all types of mass storage devices. These characteristics make PCs an obvious choice for add-on devices. As part of the PC based hardware upgrades, FMR has developed a Software Plotting Package, a Variable Temperature Unit and a Sample Changer for existing NMR systems.

## Offline Plotting

PLOT is a software package for IBM PC and compatibles that allows you to plot off-line from your NMR instrument. PLOT supports common graphics devices, mice, plotters and printers. After you have transferred the data file by serial transfer, Ethernet or emulating the spectrometer's plotter port, the user can add any desired plot annotations and create the plot on a variety of hardcopy devices such as an Epson-compatible dot-matrix printer, an HPGL plotter or an HP-compatible laser printer. The laser produces sharp well defined plots of a convenient 8.5" by 11" size. Output files are also directly importable into common desk-top publishing software packages such as Aldus PageMaker or Xerox Ventura Publisher.

## Variable Temperature Unit

The VT Unit is available as either a stand-alone device or, optionally, as a keyboard substitute driven by an auxiliary processor (based on a MS-DOS PC) for the existing NMR system keyboard. The VT Unit has the following features:

- Graphic, mouse driven queueing software.
- -196°C to 200°C temperature range.
- 0.1° Short term temperature stability.
- Macro capability for automatic operation.

## Sample Changer

The PC based Sample Changer for new and existing NMR systems has the following features:

- Graphic, mouse driven queueing software.
- Powerful Macro capabilities for automatic operation.
- 20 sample carousel type operation for most spectrometers.

The sample changer installs into an existing spectrometer by replacing the existing keyboard with a new keyboard and auxiliary processor (based on a MS-DOS PC). A 20 sample carousel is attached to the cryostat above the sample port.



## System Noise Figure

Instrumentation Note 6

*FMR Instrumentation Note 1* described a method to determine the overall NMR system noise figure. This Note describes how to use the information extracted from these tests. To be most useful, these noise figure tests should be done routinely as part of preventative maintenance on the NMR instrument. This history of performance makes it easy to see when something goes wrong. They are still useful without this history, since most working NMR systems have noise figures typical range (1.0-2.5 dB). If the NMR system is performing outside this range, other noise tests can help determine which module of the system is at fault.

FMR markets an inexpensive noise figure meter kit with procedures for the NMR user to quickly determine the system noise figure. The test apparatus consists of a meter for displaying the noise level of the audio channel to the digitizer and a 50 ohm noise source for the preamp. The meter is calibrated with the noise source at room temperature. Then the noise source is cooled in liquid nitrogen. The system noise figure is then read directly from the meter. The entire procedure takes only a few minutes and can be repeated as a diagnostic procedure. This applications note is written for this equipment, but the procedures can be easily adapted to other methods of determining system noise figure such as those described in FMR Instrumentation Note 1.

The system noise figure is an important factor in determining the NMR instrument's overall signal to noise. The NMR instrument is designed to have the preamplifier gain and noise figure determine the total system noise figure. As a rule of thumb, a 1 dB increase in the noise figure decreases the signal to noise by 10-15%. For adequate signal to noise the overall system noise figure needs to be in the 1.0 to 2.5 dB range. If the system noise figure is outside that range, further tests are needed. Remember, if the signal to noise is low, the most common three problems are:

- Not enough signal from the probe.
- Poor system noise figure.
- Noise from other sources

### Typical Problem Areas

**Frequency dependent?** Change to another nucleus and determine the noise figure. It is best if the other nucleus uses a different preamp. If the noise figure then falls within the desirable range the preamp is suspect, but not proven guilty. Check the other test described.

**Transmitter Power Amplifier.** In some NMR spectrometers the power amplifier is linear. These amplifiers can often emit RF noise at the observe frequency. If the noise blanking circuitry is defective or inadequate this will add noise to the system. With the noise meter measuring the system noise level, disconnect the trans-

mitter cable. If the noise level (noise level *not* noise figure) drops there is noise coming from the power amplifier. This needs to be fixed before the NMR system will deliver optimal signal to noise.

**Decoupler Power Amplifier.** The phenomena is the same as above except the amplifier to be checked is the decoupler power amplifier.

**Lock.** The lock transmitter can also add noise to the system. Observe the noise level on the noise meter with the preamp connected to the probe. If the noise level increases or decreases when the lock cable is disconnected from the probe, then the lock is adding noise (meter increases) to the overall system or the lock may be overloading the preamp (meter increases or decreases). Either way is not desirable. Further filtering of the lock and/or receiver system is required. Remember the lock can be putting noise in at the observe frequency AND/OR the lock transmitter can be overloading the preamp.

**Transmitter Coupler and Directional Couplers.** Most NMR systems have some circuitry in front of the preamp to couple on the transmitter and/or decoupler. Measure the system noise figure with and without this circuitry. The difference is the loss in this circuitry. It should be less than 0.5 dB and not more than 1.0 dB.

**Filters.** Most NMR systems have some circuitry in front of the preamp to filter out the lock transmitter and/or decoupler. Once again, measure the system noise figure with and without this circuitry. The difference is the loss in this circuitry. It should be between 0.5 and 1.0 dB.

**Gain Level.** If the preamp's gain is not much larger than the console noise figure, then the system noise figure is not determined by the preamp. In many systems, the dynamic range of the NMR signal is very large. This is especially true for biological samples in water. With large signals the operating spectrometer gain settings are sometimes set low to keep the preamp and console from overloading. Overloading produces artifacts, line-shape distortion and baseline distortion in the NMR spectrum. Determine the NMR system noise figure at several settings ranging from very high to very low. If your system is forced to operate at a gain setting at which it has a poor noise figure, you need to improve the dynamic range of the preamp.

**RF Interference.** Sometimes the probe or console picks up RF interference. A good way to detect this interference is to connect an amplified speaker to the audio channel. You can hear the interference. The noise meter can also indicate the interference by a changing level reading. The speaker and noise level test needs to be done with and without the probe connected to determine the source of interference.





UNIVERSITY OF TURKU

Kalevi Pihlaja, Dr.  
Professor  
Physical Chemistry

Professor B. L. Shapiro  
TAMU NMR News Letter  
966 Elsinore Court  
Palo Alto, California 94303, U.S.A.

Turku, November 29, 1988  
(received 12/12/88)

**<sup>1</sup>H and <sup>13</sup>C NMR of Compounds 1-3**

Dear Professor Shapiro,

Compounds 1-3 are in pure state fairly high melting solids, which are believed to crystallize in one isomeric form only (A). When recording the spectra we also observed that only one form is practically exclusive in solution. Obviously this component has structure A. We like to emphasize that this type of compounds seem to be very sensitive in solution and a great care has been taken to avoid artifact peaks in the spectra (see for instance the COR peaks in the spectra of 2,3-dihydro-1,3,4-thiadiazoles in Evans et al., J. Chem. Soc. Perkin 1, 1499 (1986)).

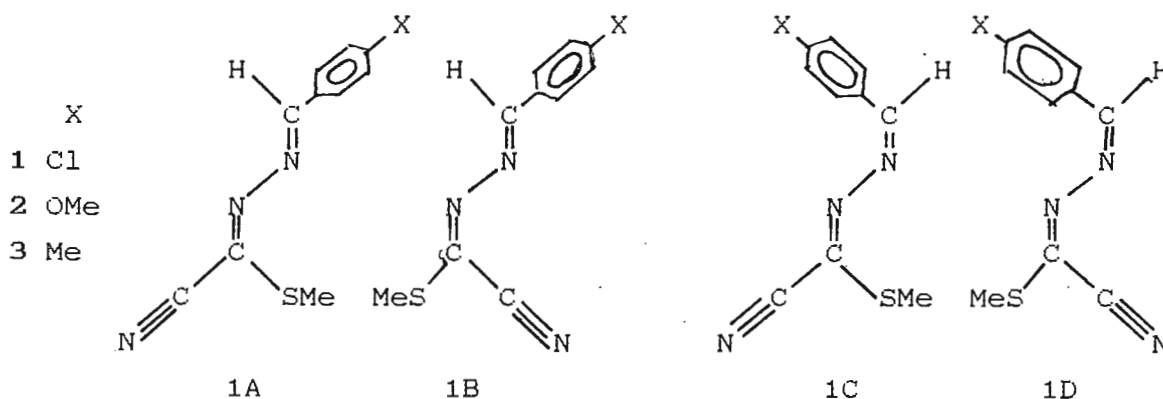


Table. Proton and carbon chemical shifts for 1-3 in CDCl<sub>3</sub> from TMS.

|    |     |       |      |       |      |                             |       |        |
|----|-----|-------|------|-------|------|-----------------------------|-------|--------|
| 1A | MeS | 2.69  | CH   | 8.40  | Ar:  | 7.79 (2H); 7.44 (2H)        | J     | 8.6 Hz |
| 1A | CN  | 161.9 | NC-C | 145.9 | C-Ar | 138.8                       | MeS   | 15.9   |
|    |     |       |      |       | Ar:  | 111.65; 128.0; 129.6; 129.6 |       |        |
| 2A | MeS | 2.67  | CH   | 8.42  | Ar:  | 7.81 (2H); 6.97 (2H)        | J     | 8.8 Hz |
| 2A | CN  | 163.4 | NC-C | 144.4 | C-Ar | 144.1                       | MeS   | 15.7   |
|    |     |       |      |       | Ar:  | 111.6; 114.6, 125.7; 131.5  | p-MeO | 55.6   |
| 3A | MeS | 2.67  | CH   | 8.42  | Ar:  | 7.74 (2H); 7.27 (2H)        | J     | 8.2 Hz |
| 3A | CN  | 163.5 | NC-C | 143.6 | C-Ar | 145.0                       | MeS   | 15.8   |
|    |     |       |      |       | Ar:  | 111.5; 129.5; 129.5; 130.35 | p-Me  | 21.9   |

Hans-Ulrich Kibbel  
Wilhelm-Pieck-Universität, Rostock

*Kalevi Pihlaja*  
Kalevi Pihlaja

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November 14, 1988  
(received 11/26/88)

Dr. Bernard <sup>L.</sup>S. Shapiro  
966 Elsinore Court  
Palo Alto, CA 94030

SUBJECT: Big structural effects in little solid molecules

Dear Barry,

Although we have been primarily interested in polymers in the solid state, I have recently spent some time looking at some smaller molecules which exhibit solid state NMR spectra that are markedly different from that of the solution spectra.

Enclosed are solution and solid state spectra of 4-Nitroanisole, a), and 4-Nitroaniline, b). Although the solution spectra shows well resolved single lines for each carbon, the solid spectrum shows multiple lines for some carbons. Some of these multiple lines are due to dipolar splitting of the quadrupolar  $^{14}\text{N}$  atoms <sup>1-3</sup>. However, the protonated carbons 2 and 6 of each molecule are split because of the orientation of the group at position 1 in the solid state. There are reports of solid state effects due crystal packing<sup>3</sup>, differences in chirality<sup>4</sup>, and due to hydrogen bonding in other small molecules<sup>5</sup>, but the splittings are not as large in general as these small simple ones. These kinds of observations point out that although simple explanations lead one to think that the isotropic value of the chemical shift of a carbon in the solid state will be the same as as in solution, the fact is that the average value in solids is not necessarily the same as the isotropic value in solutions.

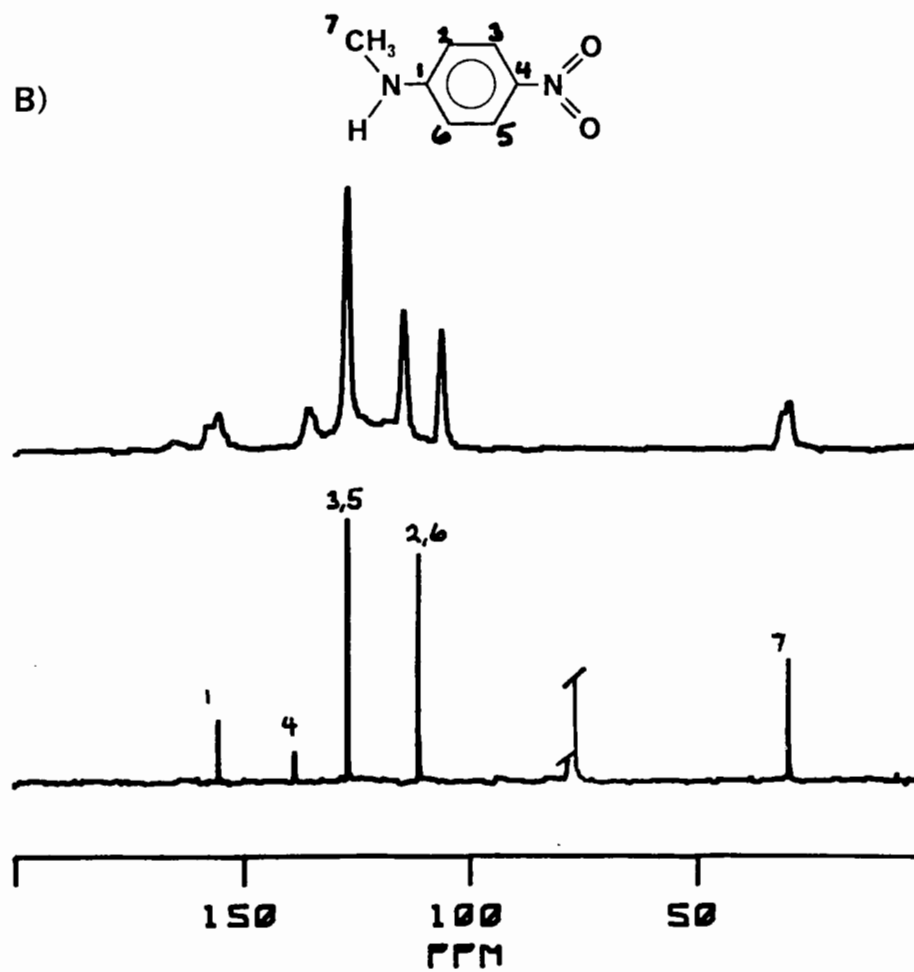
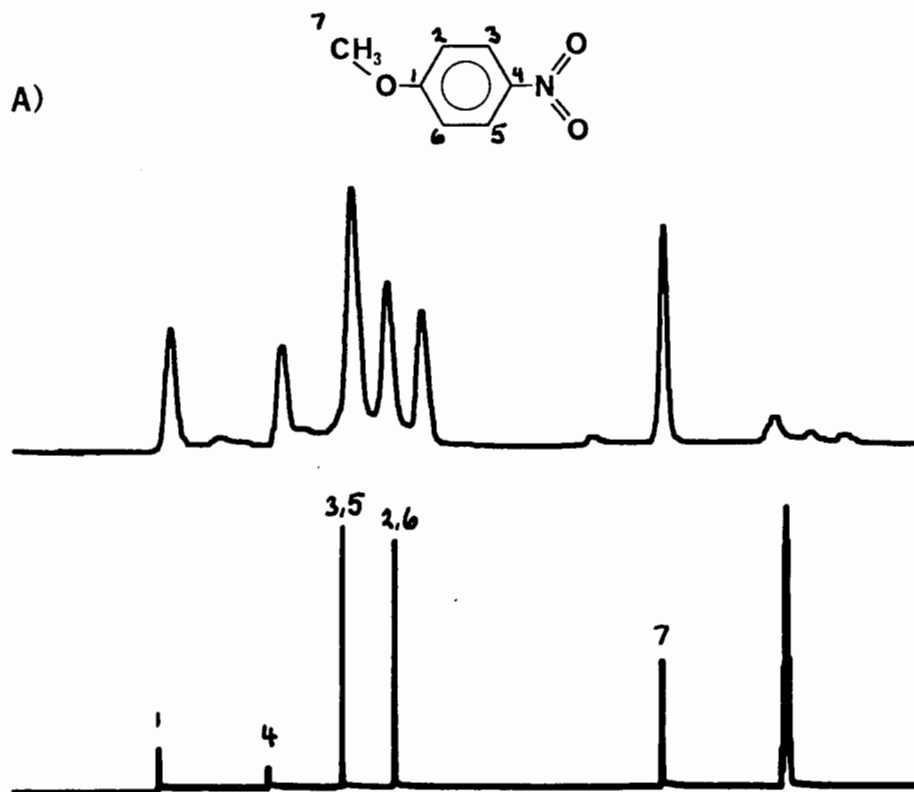
Sincerely yours,



William W. Fleming

WF/wf

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November 23, 1988  
(received 12/2/88)

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

Dear Dr Shapiro,

### Reading Between the 'Researchese' Lines

Continuing your lead in introducing some lighter aspects (and to get my new subscription onto a firmer footing!), I am offering a selection from a (rather old) article from "The Journal of Tussock Grasslands and Mountain Lands Institute" at Lincoln College in New Zealand. Much of it is surprisingly relevant – how often have you seen phrases like these recently?

Certain phrases often used in scientific research papers have varying degrees of hidden meaning. What may be "of great theoretical and practical importance" may simply mean "it's interesting to me."

So that people may better understand other 'researchese', the following explanations are offered.

1. "It has long been known that . . ." Means: I haven't bothered to look up the original reference.
2. "While it has not been possible to provide definite answers to these questions . . ." Means: The experiment didn't work but I figured I could at least get a publication out of it.
3. "Three of the samples were chosen for detailed study . . ." Means: The results of the others didn't make any sense.
4. "Accidentally filtered and purified . . ." Means: Dropped on the floor.
5. "Handled with extreme care throughout the experiment . . ." Means: Not dropped on the floor.
6. "Typical results are shown. Means: The best results are shown.
7. "It is suggested that . . . It may be that . . . It is believed that . . . Means: I think.
8. "It is generally believed that . . ." Means: a couple of other blokes think so too.
9. "It is clear that much additional work will be required before complete understanding . . ." Means: I don't understand it.
10. "Unfortunately, a quantitative theory to account for these results has not been formulated . . ." Means: Neither does anybody else.
11. "Correct within an order of magnitude . . ." Means: Wrong.
12. "Thanks are due to Bill Bloggs for assistance with the experiments and to Dr Smedley for valuable discussion . . ." Means: Bloggs did the work and Smedley explained what it meant.

In NMR papers you may additionally find statements of the following types (with their translations):

1. "No effort was made to optimize the parameters . . ." Means: I had no idea how the experiment worked, but the first time I ran it, I got some correlations that looked good.
2. "A section of the 2D contour plot is shown . . ." Means: There were some terrible artifacts in the rest of the spectrum; or: There were uninterpretable impurity peaks elsewhere in the spectrum.
3. "One compound in this series was chosen for complete spectral assignment . . ." Means: The one compound whose proton spectrum was first-order was chosen for complete spectral assignment.
4. "No resolution enhancement was applied . . ." Means: the Z<sup>2</sup> shim was so bad that, if I resolution-enhanced the spectrum, every peak looked like a doublet.
5. "Resolution enhancement was applied . . ." Means: The spectrum was plotted on good paper with a fine pen.

Cheers,

John Ralph

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|          |                             |                             | 10 g       | 14.                            |
|          |                             |                             | 5 x 10 g   | 69.                            |
|          |                             |                             | 10 x 10 g  | 135.                           |
| 82-05012 | Acetonitrile-d <sub>3</sub> | 99.8                        | 10 x 1 g   | 22.                            |
|          |                             |                             | 10 g       | 22.                            |
|          |                             |                             | 5 x 10 g   | 100.                           |
| 82-84077 | Benzene-d <sub>6</sub>      | 99.6                        | 10 x 1 g   | 18.                            |
|          |                             |                             | 10 g       | 18.                            |
|          |                             |                             | 5 x 10 g   | 75.                            |
|          |                             |                             | 10 x 10 g  | 145.                           |
| 82-80556 | Chloroform-d                | 99.8                        | 100 g      | 18.                            |
|          |                             |                             | 5 x 100 g  | 80.                            |
|          |                             |                             | 10 x 100 g | 142.                           |
|          |                             |                             | 1 kg       | 135.                           |



| CAT. NO. | PRODUCT  | ENRICHMENT<br>MIN. ATOM % D | QUANTITY*  | PRICE <sup>†</sup><br>U. S. \$ |
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| 82-70001 | Deuterium Oxide  | 99.9                        | 100 g      | 45.                            |
|          |  |                             | 5 x 100 g  | 215.                           |
|          |  |                             | 10 x 100 g | 390.                           |
|          |  |                             | 1 kg       | 375.                           |
| 82-70901 | Deuterium Oxide  | 99.8                        | min. 10 kg | 3500.                          |
|          |  |                             | 25 kg      | 8500.                          |
|          |  |                             | 50 kg      | 16250.                         |
| 82-70002 | Deuterium Oxide "100%"   | 99.96                       | 10 g       | 15.                            |
|          |  |                             | 5 x 10 g   | 50.                            |
| 84-70001 | Deuterium-depleted Water                                       | < 5 x 10 <sup>-5</sup>      | 25 g       | 25.                            |
|          |  |                             | 4 x 25 g   | 90.                            |
|          |  |                             | 10 x 25 g  | 200.                           |
|          |  |                             | 20 x 25 g  | 300.                           |
|          |  |                             | 30 x 25 g  | 400.                           |
|          |  |                             | 1 kg       | 500.                           |
| 82-00807 | Dimethyl-d <sub>6</sub> Sulfoxide                              | 99.9                        | 10 x 1 g   | 12.                            |
|          |  |                             | 10 g       | 12.                            |
|          |  |                             | 5 x 10 g   | 56.                            |
|          |  |                             | 10 x 10 g  | 115.                           |
| 82-00809 | Dimethyl-d <sub>6</sub> Sulfoxide<br>(multi-dose septum vials) | 99.9                        | 10 g       | 12.                            |
|          |  |                             | 5 x 10 g   | 56.                            |
|          |  |                             | 10 x 10 g  | 115.                           |
| 82-00061 | Methanol-d <sub>4</sub>  | 99.8                        | 10 x 1 g   | 43.                            |
|          |  |                             | 10 g       | 43.                            |
|          |  |                             | 5 x 10 g   | 171.                           |
|          |  |                             | 10 x 10 g  | 325.                           |

**\*PACKAGING:** Organic solvents are sealed in glass ampoules to maintain the high quality of the solvents. Dimethyl-d<sub>6</sub> sulfoxide is also available in multi-dose septum vials. The waters are packaged in glass screw-cap bottles, except for the "100%" deuterium oxide, which is packaged in multi-dose septum vials.

<sup>†</sup>Prices are FOB Miamisburg, Ohio for delivery in North America; please request prices for delivery to the other continents. Minimum order, \$50.

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National Center of Neurology and Psychiatry

# NATIONAL INSTITUTE OF NEUROSCIENCE

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December 6, 1988  
(received 12/10/88)

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

## H-1 NMR Detection of 2-[C-13] Ethanol in the Rabbit Brain

Dear Dr. Shapiro,

The greater sensitivity of H-1 nucleus and the ability to resolve the resonance from the C-12 and C-13 coupled protons (1) has allowed monitoring of metabolism of C-13 labeled compounds in vivo through the use of spectral editing techniques. We applied a modification of these techniques to determine the kinetics of the entry and efflux of 2-[C-13] ethanol (ETOH) from the brain and the improvement in signal to noise ratio of this proton observe/Carbon decouple pulse sequence over direct C-13 NMR spectroscopy. Female rabbits were prepared in this experiment. Either 0.5 ml/kg of 95% 2-[C-13] ETOH (92 atom% C-13) or 0.4ml/kg of 2-[C-13] ETOH and 0.6ml/kg of 99% ETOH were mixed with 9cc of 0.9% NaCl and given parenterally. A 20mm single-turn coil, double tuned to H-1 and C-13 frequencies, was placed 3mm from the skull and centered 5mm posterior to bregma. In vivo H-1 NMR spectra were acquired on a Bruker/ORS 4.7T spectrometer. The H-1 edited spectrum obtained immediately before death had a S/N ratio of 50 for the 102 sec (64 FIDs) collection. The C-13 spectrum obtained post-mortem had a S/N ratio of 13 for the 1024 sec (640 FIDs) collection. Thus, H-1 techniques gave an improvement in S/N by a factor of 12 or a factor of 4 per atom. This experiment was performed in collaboration with Dr. E. J. Novotny and Prof. R. G. Shulman at the Magnetic Resonance Center, Yale University.

### Reference

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Sincerely,

Takashi Ogino, Ph.D.

Toshio Yano, Ph.D.



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November 22, 1988

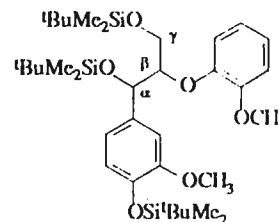
(received 12/2/88)

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

Dear Dr Shapiro,

## 2D Si-H (long-range) Correlation, Mathematica™, Positions Available

As a very practically oriented spectroscopist, I'm always slightly surprised when NMR theory proves to be invaluable in setting up a simple experiment. We have been examining the NMR spectra of t-butyldimethylsilyl derivatives of some lignin model compounds with an aim of augmenting the structural information that can be gleaned from  $^{13}\text{C}$  NMR of lignins. Some of the  $^{29}\text{Si}$  NMR assignments were assumed, without proof, and we chose 2D Si-H correlation to resolve any ambiguities.



The problem is, how do you choose delays in this experiment? Let us look at a single case, that of the  $\text{H}\alpha$  correlation. It has a  $^3J_{\text{Si-H}}$  of about 4 Hz. Setting the  $\Delta 1$  delay to  $1/2J$  (125 ms) is no problem. But how should you set  $\Delta 2$ ? My first approach to this (after some consultation with Dr V.V. Krishnamurthy, Dr Bruce Adams, and Prof. D.E. Wemmer) was to simply remove this delay. That required removing the decoupling as well, and the stripped-down pulse program that remained is presumably a simple re-invention of the FUCOUP experiment which leaves full coupling in both dimensions. This worked very well to give unambiguous correlations, with all correlation peaks present, Figures 1.

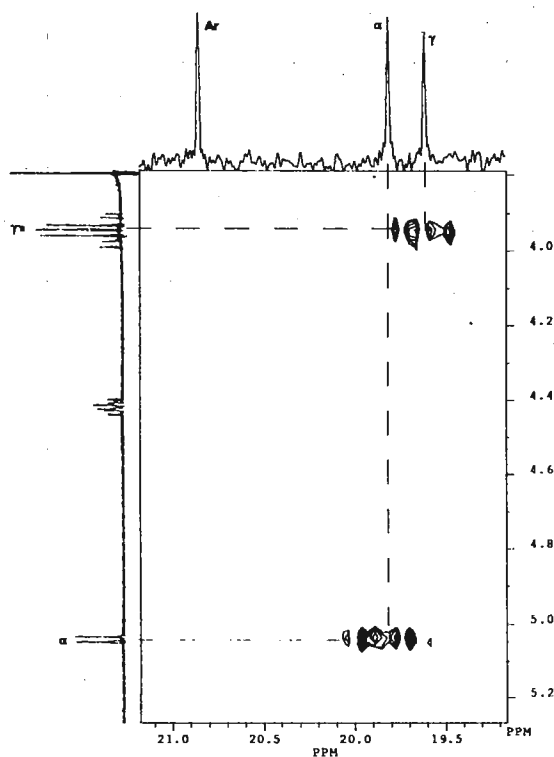


Figure 1a. Fully-coupled Si-H correlation, showing  $\alpha$  and  $\gamma$  correlations.

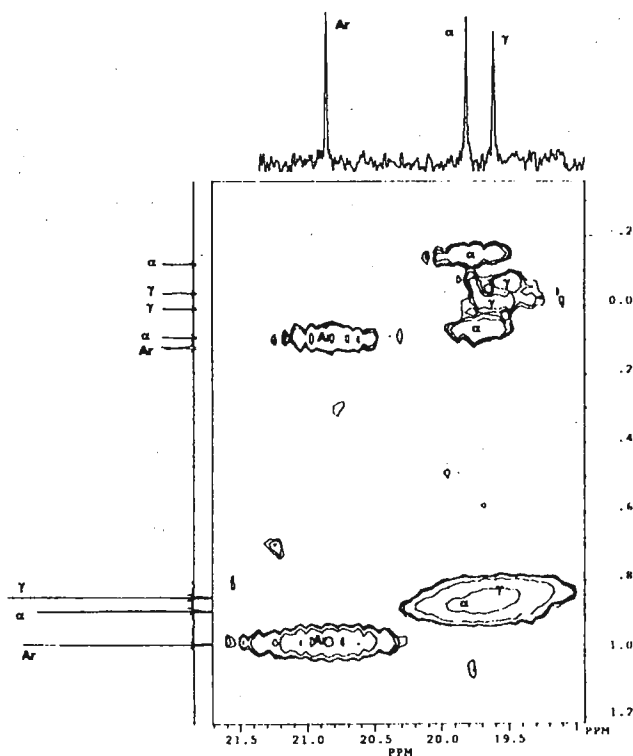
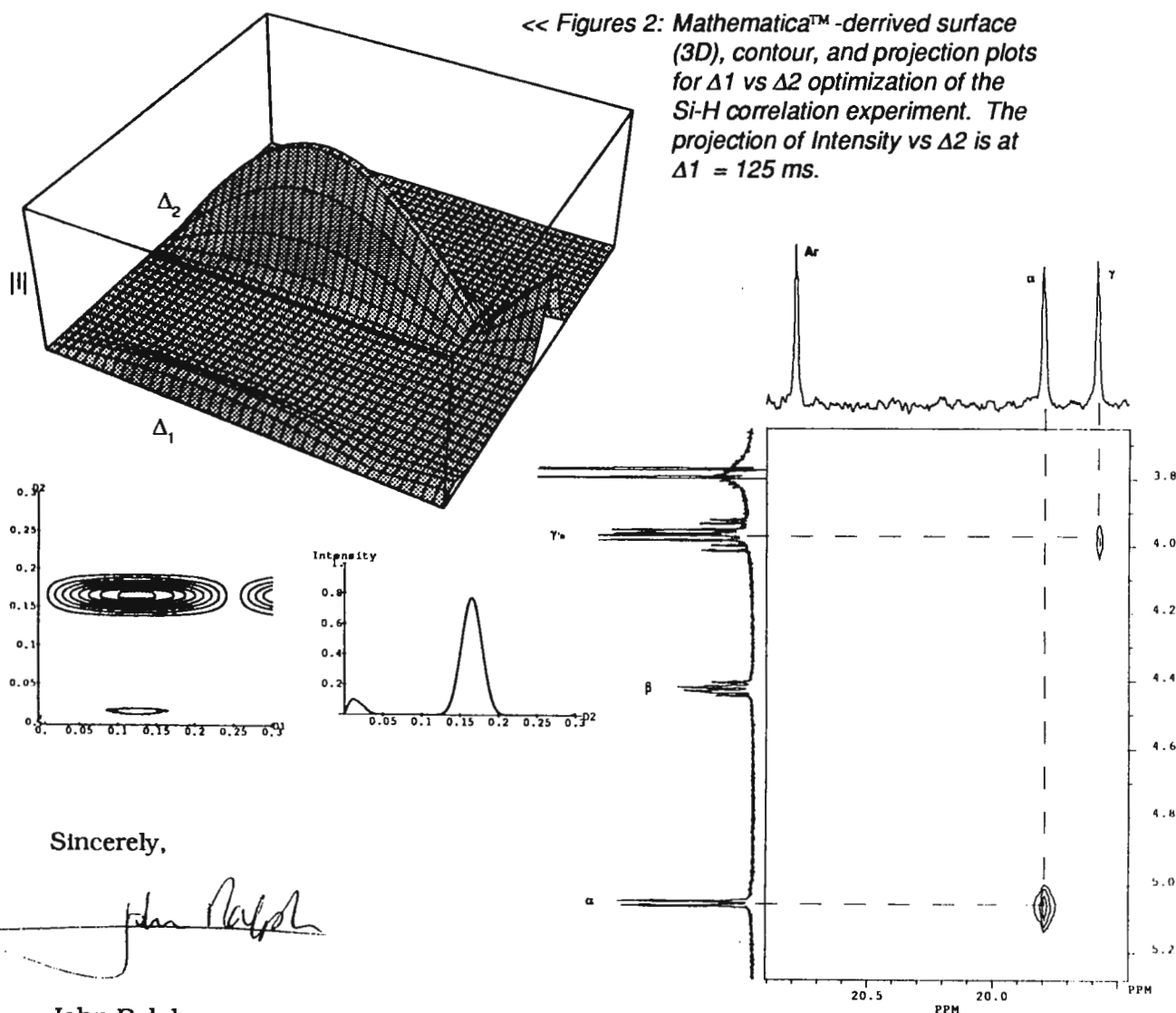


Figure 1b. Fully-coupled Si-H correlation, showing the Si-tBu and Si-Me<sub>2</sub> correlations.

The problem of course is one of sensitivity. Since the contours are spread out over a 15-tet or worse (from the 15+ coupled protons), it would seem advisable to decouple, as long as the intensity was not severely or unpredictably modulated. Examining the Intensity dependence on  $\Delta_1$  and  $\Delta_2$ :

$$I_{\text{Si-H}_\alpha} = \sin(\pi J_{\text{Si-H}_\alpha} \Delta_1) \cdot \sin(\pi J_{\text{Si-H}_\alpha} \Delta_2) \cdot \cos^9(\pi J_{\text{Si-tBu}} \Delta_2) \cdot \cos^6(\pi J_{\text{Si-Me}} \Delta_2)$$

- indicates that, if you are after the H $\alpha$  correlation peak, you had better make sure the effects of the 15 other protons, with coupling constants around 6 Hz, are minimized. That requires setting  $\Delta_2$  such that these  $\cos(\pi J' \Delta_2)$ 's are 1 (or -1) [ $J'$  is any  $J$  not involved in the correlation], i.e. that  $\Delta_2 = 1/J'$ . The intensity profile (calculated from the measured  $J$ 's) can be nicely seen using the powerful Mathematica™ program, used here on a Macintosh II, Figures 2. Obviously choosing  $\Delta_1 = 125$  ms and  $\Delta_2 = 167$  ms is the optimum here. The appropriate section of the contour plot is shown in Figure 3, with the H $\gamma$  correlation ( $J$ 's to each H $\gamma$  are about 3 Hz) also showing up, with reduced intensity.



Sincerely,

John Ralph

### PostDoc Position and PhD Assistanceships available:

I currently have the capability to hire a further postDoc and to take on 2 funded PhD students to work on aspects of lignin chemistry, highly involved with (solution-state) NMR. One project is the silicon work alluded to here. Interested individuals with a good organic chemistry background and a hankering to experience a refreshing Wisconsin winter should contact me directly.



# Spectroscopy Imaging Systems Corporation

A Joint Venture of Varian and Siemens

(received 12/2/88)

## Metabolite Mapping Using Phase Encoding

It is subscription time again, so I thought I would write another article about localized spectroscopy (last time I wrote about stimulated echo localization). A number of research groups have presented posters at SMRM on 4D chemical shift mapping of P-31 resonances in the head. This experiment has a lot of advantages compared to slice selective techniques such as ISIS or stimulated echo. First, the location of an ROI is not subject to chemical shift effect. Secondly, the phase encode method is a Fourier technique exciting the whole sample, so that S/N is gained rather than lost. Typical application in clinical MRI has involved the use of a large uniform transmitter coil tuned to the appropriate frequency. The pulse sequence is very simple (especially for P-31 where short echo times are required), consisting of an RF pulse followed by three simultaneous gradient pulses in the X, Y and Z directions, the data is collected a short while after the gradient pulses are turned off. (See diagram).

We have tried the experiment in a simplified form using a surface coil rather than a uniform transmitter to obtain metabolite maps encoded in one dimension, perpendicular to the plane of the coil. To avoid the "banding" effect that variable flip angle produces in surface coil imaging, when the surface coil is used as both transmitter and receiver, we employed an adiabatic half passage pulse of the sech/tanh type. This pulse excites with a fairly uniform flip angle over a wide range of RF field and typically excites spins up to a diameter for a circular coil. Our results are shown as the familiar contour plots of 2D spectroscopy, along with a series of spectra that have been projected out of the data matrix. The map we obtained is from the liver region of a rat, so that the phosphocreatine peak can be used as a marker to distinguish muscle from liver. The results from our preliminary experiments are quite encouraging, in that the entire map can be obtained with 1024 pulses. The length of the phase encode pulse was 2.5 ms and the TE was 5 ms. The gradients (standard Oxford 33 cm 2G/cm) seem to recover quickly enough to allow reasonably clean data acquisition.

Phase encoding compares very favourably with the competing ISIS technique. The thing I like most is that you do not need to choose your ROI before the experiment and this reduces the need for a pre experiment proton imaging scan. Needless to say we shall be extending our results to higher dimensionality and experimenting with different types of RF coils to increase penetration.

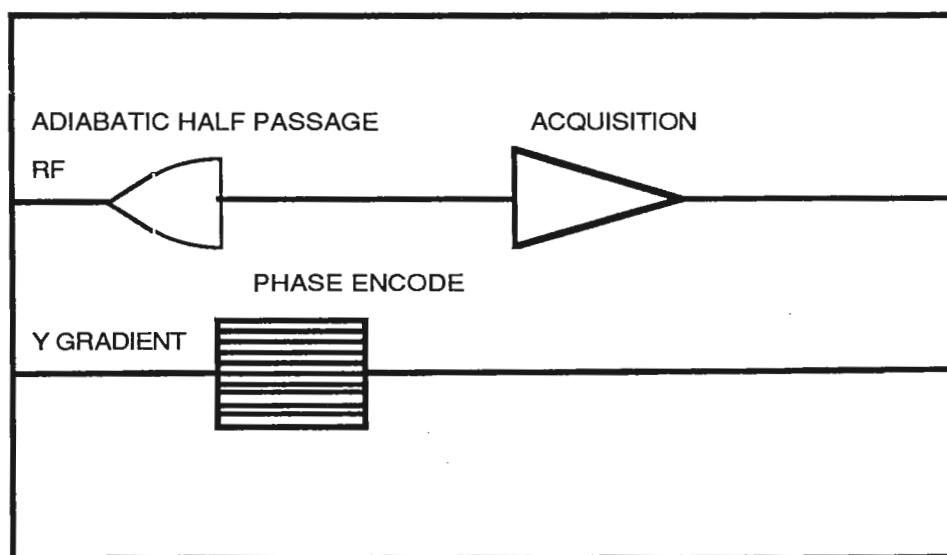


Figure 1: Shows the sequence diagram for the simplified 1D version of the phase encoding experiment.

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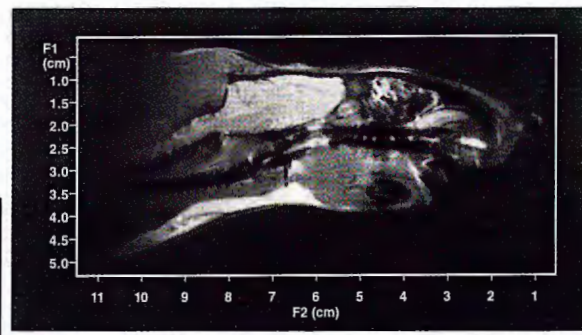
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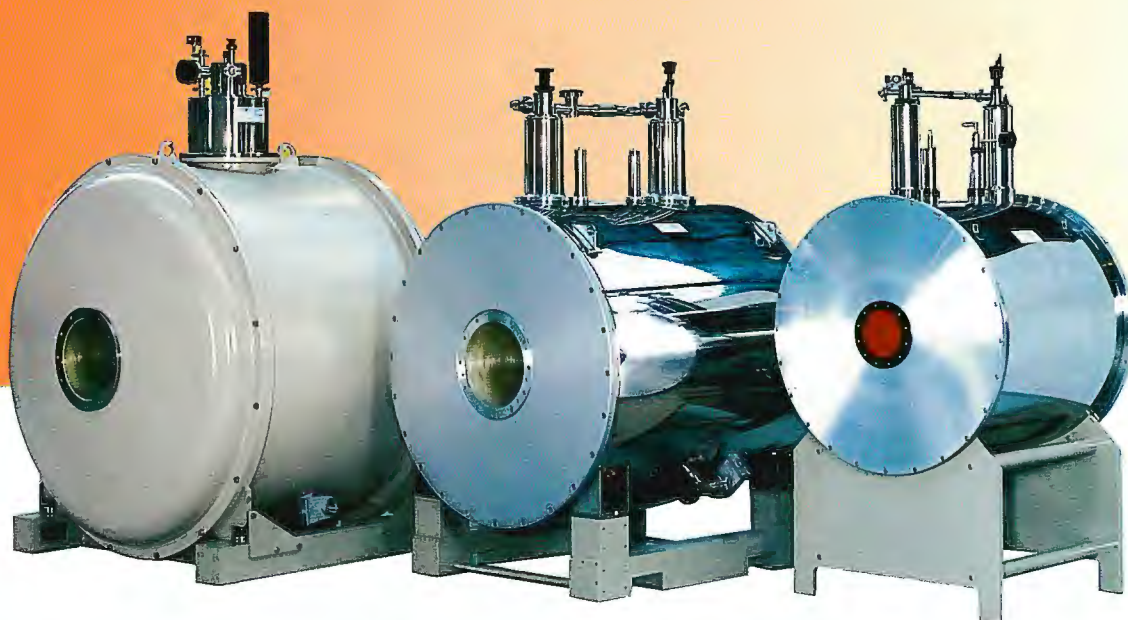
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|---------|--------------|-------------|------------|------------------|---------------------------|----------------------|-----------------|-------------------|
| 300/180 | 7.05T        | 183 mm      | 125 mm     | 4.0 G/cm         | 80 mm DSV<br>$\pm 6$ ppm  | 35 mm DSV<br>0.1 ppm | 5.60 m          | 4.45 m            |
| 200/330 | 4.7T         | 330 mm      | 254 mm     | 2.3 G/cm         | 140 mm DSV<br>$\pm 5$ ppm | 70 mm DSV<br>0.1 ppm | 6.95 m          | 5.60 m            |
| 200/400 | 4.7T         | 400 mm      | 324 mm     | 1.8 G/cm         | 140 mm DSV<br>$\pm 4$ ppm | 80 mm DSV<br>0.1 ppm | 8.50 m          | 6.75 m            |
| 85/310  | 2.0T         | 310 mm      | 225 mm     | 3.0 G/cm         | 100 mm DSV<br>$\pm 5$ ppm | 70 mm DSV<br>0.1 ppm | 4.50 m          | 3.63 m            |

DSV = Diameter Spherical Volume  
HHLW = Half-Height Line Width  
PPM = Parts Per Million



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200/400, 200/330, and 300/180 magnets for the NMR Imaging Spectrometer System.  
(Photos courtesy Oxford Instruments.)

Note: Equipment described is intended for investigational purposes, and is not approved by the FDA for clinical use.



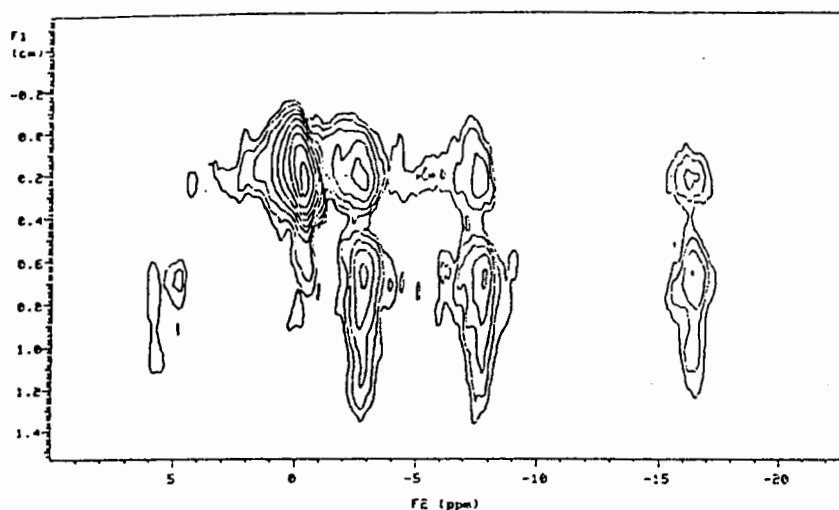


Figure 2: A contour plot of the metabolite map showing "streaks" for each metabolite resonance. The F1 axis represents distance in cm, zero reflects the position of the surface coil. The F2 axis is the spectral dimension, referenced in ppm with PCr taken as zero.

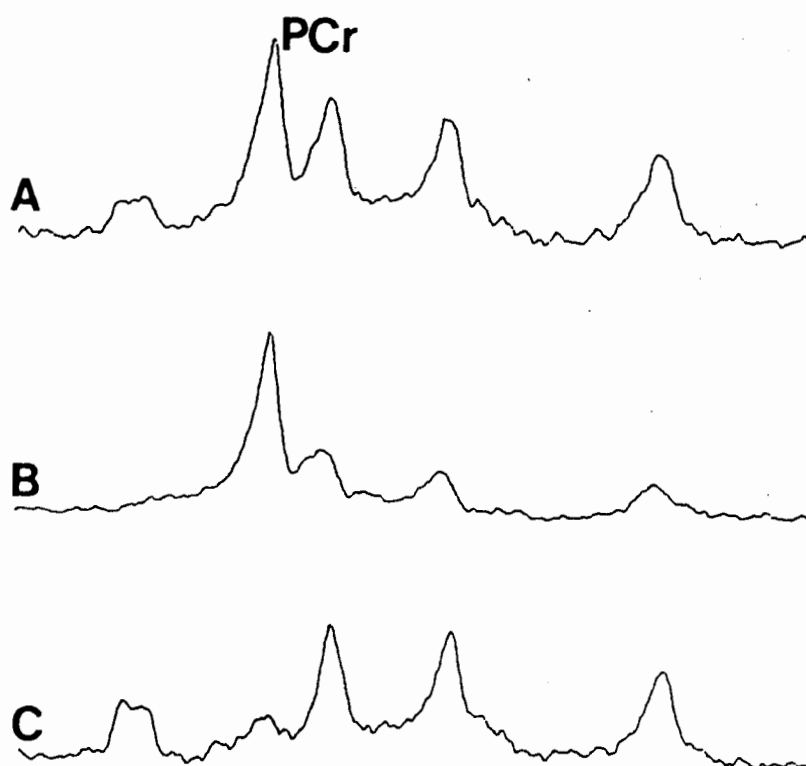


Figure 3: A series of spectra projected from the metabolite map: (A) the spectrum projected from the entire map, (B) a spectrum projected from the upper part of the map showing the PCr peak from muscle in the body wall, (C) the spectrum from the lower part of the map showing the spectrum of liver.

With kind regards,

Sincerely,

D. L. Foxall

David Foxall, D. Phil.  
Applications Scientist

Simon Chu

Simon Chu, Ph.D.  
Applications Scientist



Carleton University  
Ottawa, Canada K1S 5B6

December 6, 1988.  
(received 12/10/88)

Dr. B.L. Shapiro  
966 Elsinore Court  
Palo Alto, California  
94303, U.S.A.

Title: "Molecular Motion in Solid-18-Crown-6: Benzenesulfonamide Complexes as Studied Via Variable Temperature  $^{13}\text{C}$  CPMAS"

During his very productive sabbatical year here, Claude Morat from Grenoble prepared a series of 18-crown-6 complexes with a variety of neutral and ionic "guest" species. Among these were the 1:1 and 1:2 title systems.

The solid phase  $^{13}\text{C}$  spectra of these materials show two distinct temperatures at which broadening of the crown ether carbon resonances is observed. At ca. 298K, "dipolar washout" (1) occurs, when the correlation times for the C-H vectors are of the order of the inverse of the decoupling field magnitude, i.e. ca.  $1/2\gamma\text{H}$ , or ca.  $2.7 \times 10^{-6}\text{s}$ .

At lower temperatures, broadening is observed when the correlation times are of the order of the inverse of chemical shift differences, i.e. for a 2 ppm shift range at 45.3 MHz,  $\tau_c$  is ca.  $1/45.3 \times 2$  or ca.  $10^{-2}\text{s}$ .

Converting these correlation times to rates, and using the Arrhenius equation, yields a value of ca. 42 KJ mol $^{-1}$  as the activation energy for this motion. A similar result is found by application of the Waugh-Fedin approximation (2) as applied to the high temperature process.

We are tentatively ascribing this activation energy as that required for complete ring inversion in solid 18-crown-6. Further studies on the nature of these motions are in progress using deuterated crown ethers.

G.W. Buchanan,  
Professor of Chemistry.

References:

1. W.P. Rothwell and J.S. Waugh. J. Chem. Phys. 74, 2721 (1981).
2. J.S. Waugh and E.I. Fedin. Soc. Physics Solid State, 4, 1633 (1963).



## THE UNIVERSITY OF TEXAS AT DALLAS

BOX 830688 RICHARDSON, TEXAS 75083-0688

November 21, 1988

(received 11/23/88)

Dr. Barry L. Shapiro  
 Editor, TAMU Newsletter  
 966 Elsinore Court  
 Palo Alto, Ca. 94303

Dear Barry:

Greetings from Texas! We have been busy for the past several months stuffing perfused rat hearts into our 51 mm narrow-bore 11.75 Tesla magnet to see what we could learn about metabolism by  $^{13}\text{C}$  NMR. Now that Thanksgiving is just around the corner, we thought it might be appropriate to share some of our "stuffing" with you. Before we collected the first heart spectrum on our GN-500 using a special order 18 mm C/H probe, we anticipated the power requirements for complete proton decoupling at this field across a 140 mM aqueous salt sample might compromise the viability of the tissue. Surprisingly, this has proven to be the least of our problems as we routinely get complete proton decoupling using a WALTZ decoupling scheme with about 0.5 watt between pulses and 3 watts during a 300 msec acquisition. We detect no more than a 1-2 degree temperature increase and have found no evidence for tissue compromise as detected by heart pressure and rate recordings with and without proton decoupling. We also find that the protonated carbons of those intracellular metabolites which are detected by  $^{13}\text{C}$  NMR have full NOE's, and the  $T_1$ 's are comparable to those measured in aqueous solution at 37 °C.

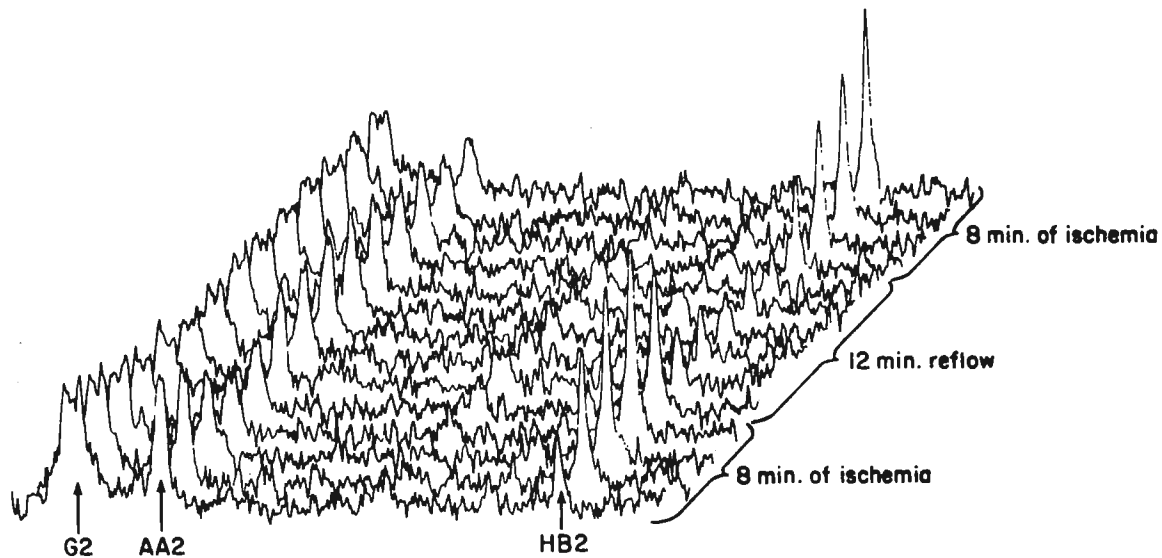
One series of  $^{13}\text{C}$  spectra obtained on a beating rat heart perfused with 2 mM [2,4- $^{13}\text{C}$ ]acetoacetate ethyl ester is shown below. The ester easily diffuses into the heart cells whereupon it is rapidly hydrolyzed to [2,4- $^{13}\text{C}$ ]acetoacetate. This ketone body is readily metabolized by heart tissue and the  $^{13}\text{C}$  is distributed into all citric acid cycle intermediate and closely related metabolite pools (G2 in the spectrum corresponds to the C2 carbon of L-glutamate) in a very predictable manner<sup>1,2</sup>. Some small portion of this ketone body also gets reduced to [2,4- $^{13}\text{C}$ ] $\beta$ -hydroxybutyrate via a dehydrogenase in the mitochondria and this offers the exciting possibility of measuring the mitochondrial redox state directly. Both metabolites are easily detected by  $^{13}\text{C}$  NMR (AA and HB in the figures) and their concentrations seem to increase and decrease in a predictable manner in response to periods of ischemia and reflow. However, if one removes the heart from the NMR tube and scans the aqueous perfusate which surrounded the heart, one finds significant acetoacetate and  $\beta$ -hydroxybutyrate in the perfusate. This makes quantitation of the intracellular signals for the redox measurement problematical. Should any of your readers have suggestions regarding this problem, we would like to hear from them.

Happy Thanksgiving! Please credit this contribution to Warren Goux. Sincerely,

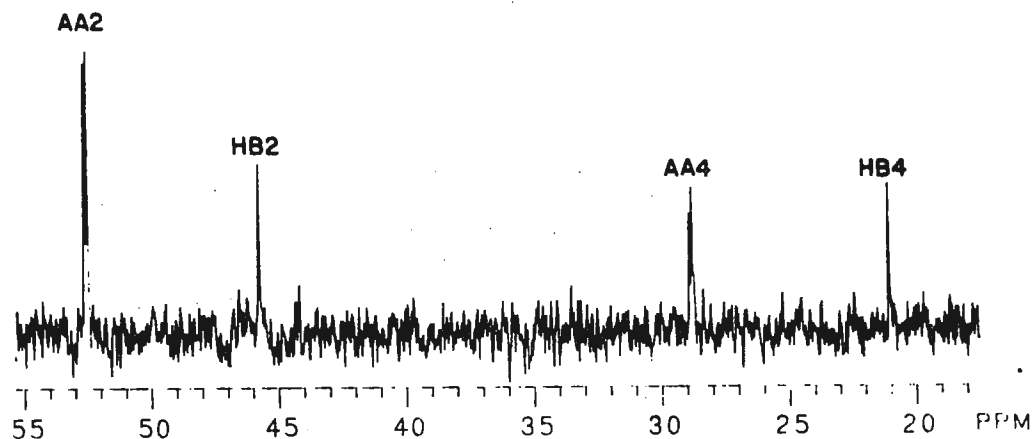
Craig R. Malloy

A. Dean Sherry

1. C. R. Malloy, et.al., J. Biol. Chem., 263, 6964 (1988)
2. A. D. Sherry, et.al., Biochem. J., 254, 593 (1988)

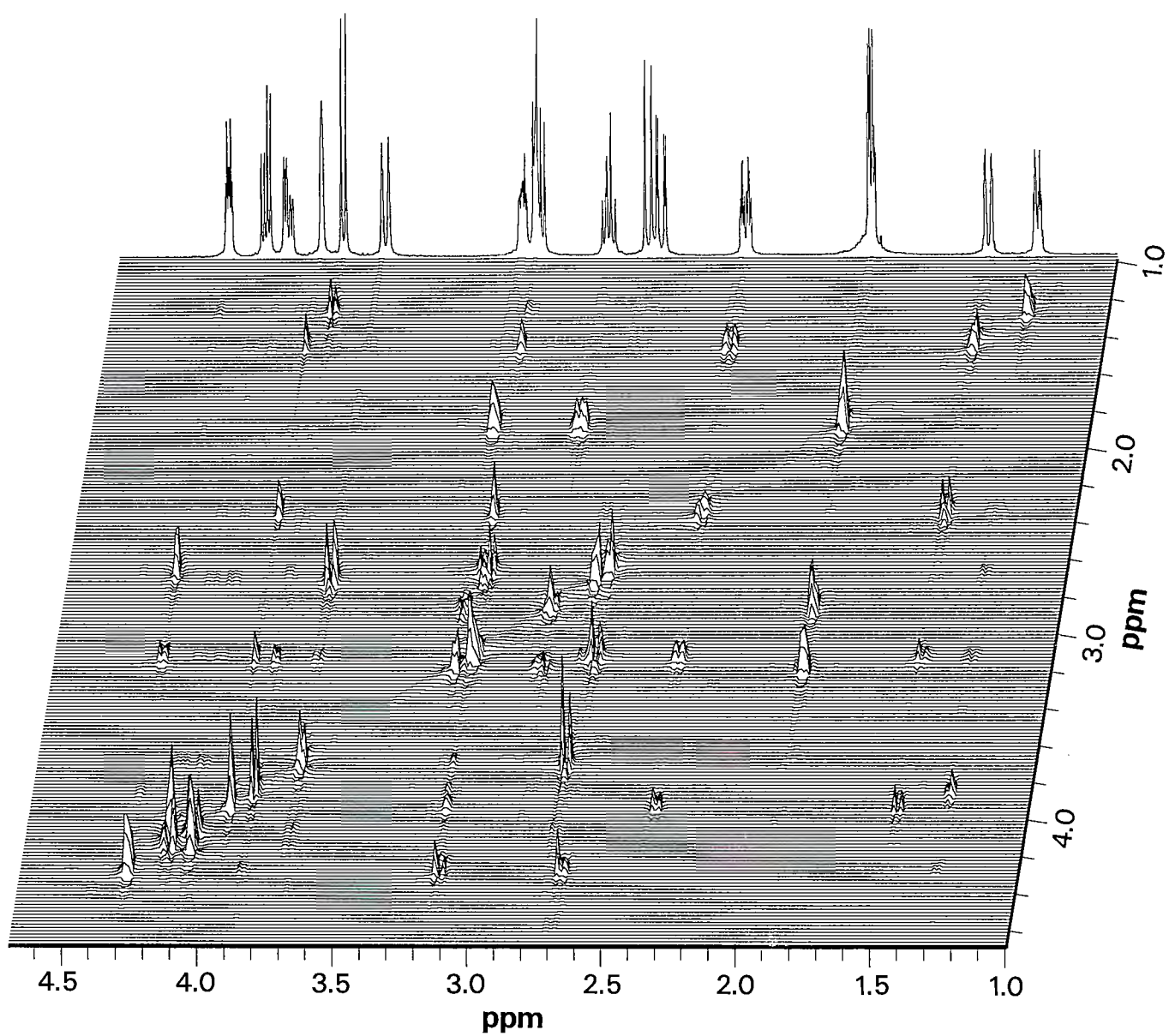


Perfusate after removal of heart.



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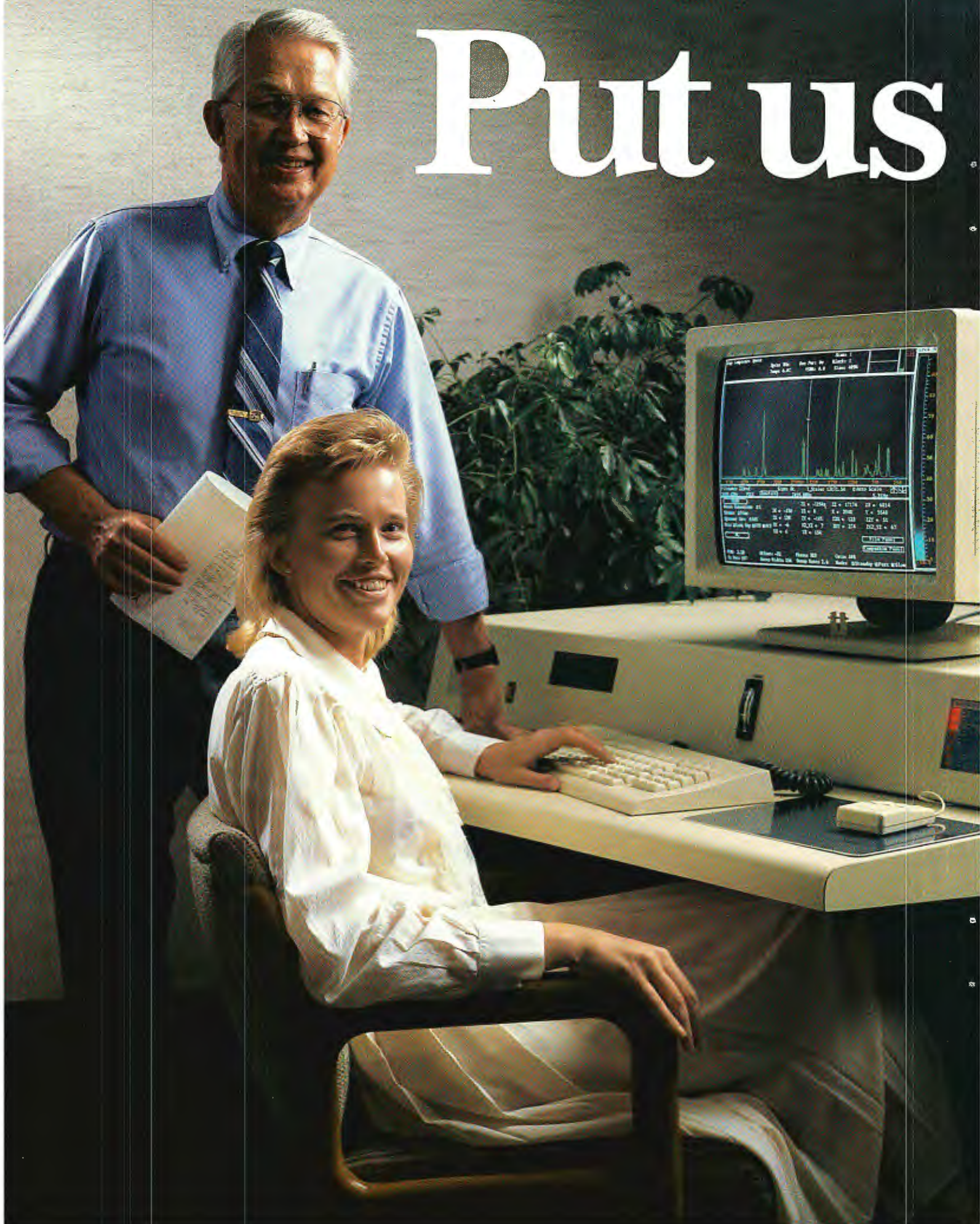
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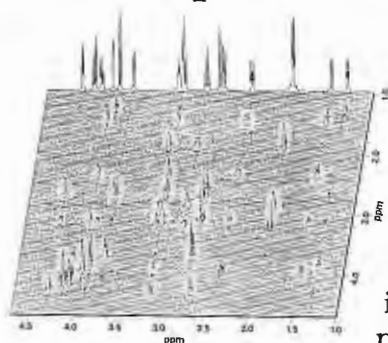


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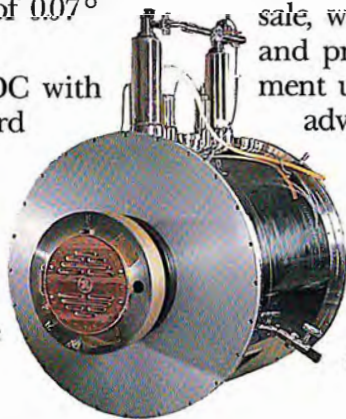
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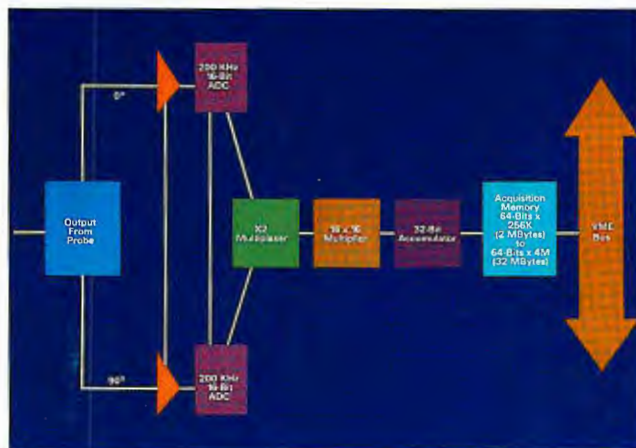


Fig. 1  
The Alpha HDR digitizer.

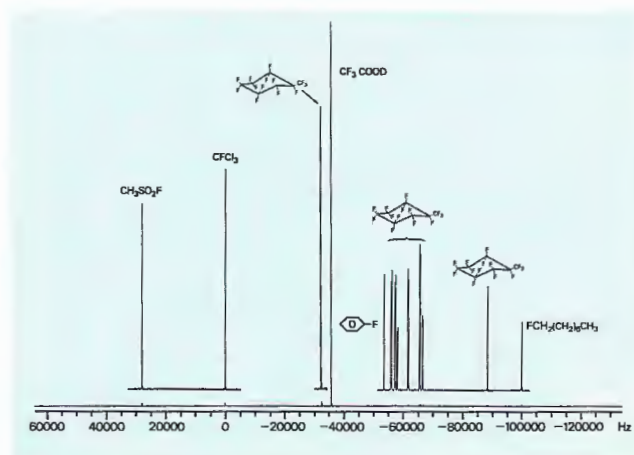


Fig. 2  
200 KHz spectral width <sup>19</sup>F spectrum acquired on a GN-500 Omega System. Note the extremely flat baseline obtained with the Alpha HDR.



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

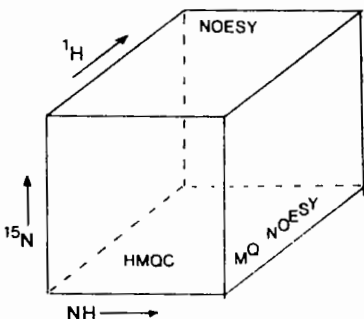
National Institute of Diabetes and  
Digestive and Kidney Diseases  
Bethesda, Maryland 20892

December 7, 1988 (received 12/10/88)

Dear Barry:

Easy 3D

The jump from 1D to 2D has extended dramatically the size of molecules that can be studied in detail by NMR. It can be speculated that recent 3D approaches developed by a number of groups may yet offer another quantum jump in the size of proteins that can be studied. One particularly promising 3D experiment combines heteronuclear multiple quantum shift correlation (HMQC) with NOESY. For practical reasons, we use a sequence that is reversed (NOESY-HMQC instead of HMQC-NOESY) relative to the one published by Fesik and Zuiderweg (1). Details will soon appear in JACS (2). When  $^{15}\text{N}$  labeling of a protein is used, this experiment enables one to separate the amide region of the regular NOESY spectrum according to the  $^{15}\text{N}$  chemical shifts of the amides. This then gives a schematic 3D spectrum as shown below:



Because the number of resonances in the amide region of the regular NOESY spectrum and in the 3D spectrum is the same, sensitivity of the 2 experiments is very similar. Figure 1 compares one of the 64 NOESY slices of the 2.5-day 3D spectrum of a 1.8 mM solution of staphylococcal nuclease with the corresponding 1.2-day 2D NOESY spectrum. The digital resolution is much lower in the 3D spectrum but resonance overlap is almost absent for this 18 kD protein; sensitivity of the 3D spectrum is at least as good. Dennis Torchia and Steven Sparks have used this 3D spectrum plus about 4 dozen "high-tech" spectra from selectively labeled nuclease samples to make virtually complete backbone assignments.

Recording of the 3D data is normally done on our old NT-500 spectrometer; the experiment is performed as a set of 64 2D experiments, executed automatically in a macro. The final resolution is largely limited by the size of 3D matrix, which is limited by the maximum number of  $t_1$  and  $t_2$  increments one can do in a reasonable amount of time. Apart from increased sensitivity there does not seem to be any urgent advantage in using our AM-600 for these time-consuming experiments.

For processing the data, Dominique and Lewis have developed a very clever approach that does not require any 3D matrix transposition and that

utilizes standard 2D processing software for doing the bulk of the work. The whole thing, including phasing, works without operator interaction and is relatively fast. Recording 3D spectra has become more or less routine now; the main remaining problem is plotting the data. Laser printers do not quite offer the size needed and our HP-draftmaster plotter requires lots of TLC plus expensive large paper to display all slices of the 3D spectrum.

*L. E. Kay*  
Lewis E. Kay

*Dominique*  
Dominique Marion

Kindest regards,

*Ad*  
Ad Bax

1. S.W. Fesik and E.R.P. Zuiderweg, J. Magn. Reson. 78:588 (1988).
2. D. Marion, L. Kay, S. Sparks, D. Torchia, A. Bax JACS, January 1989?

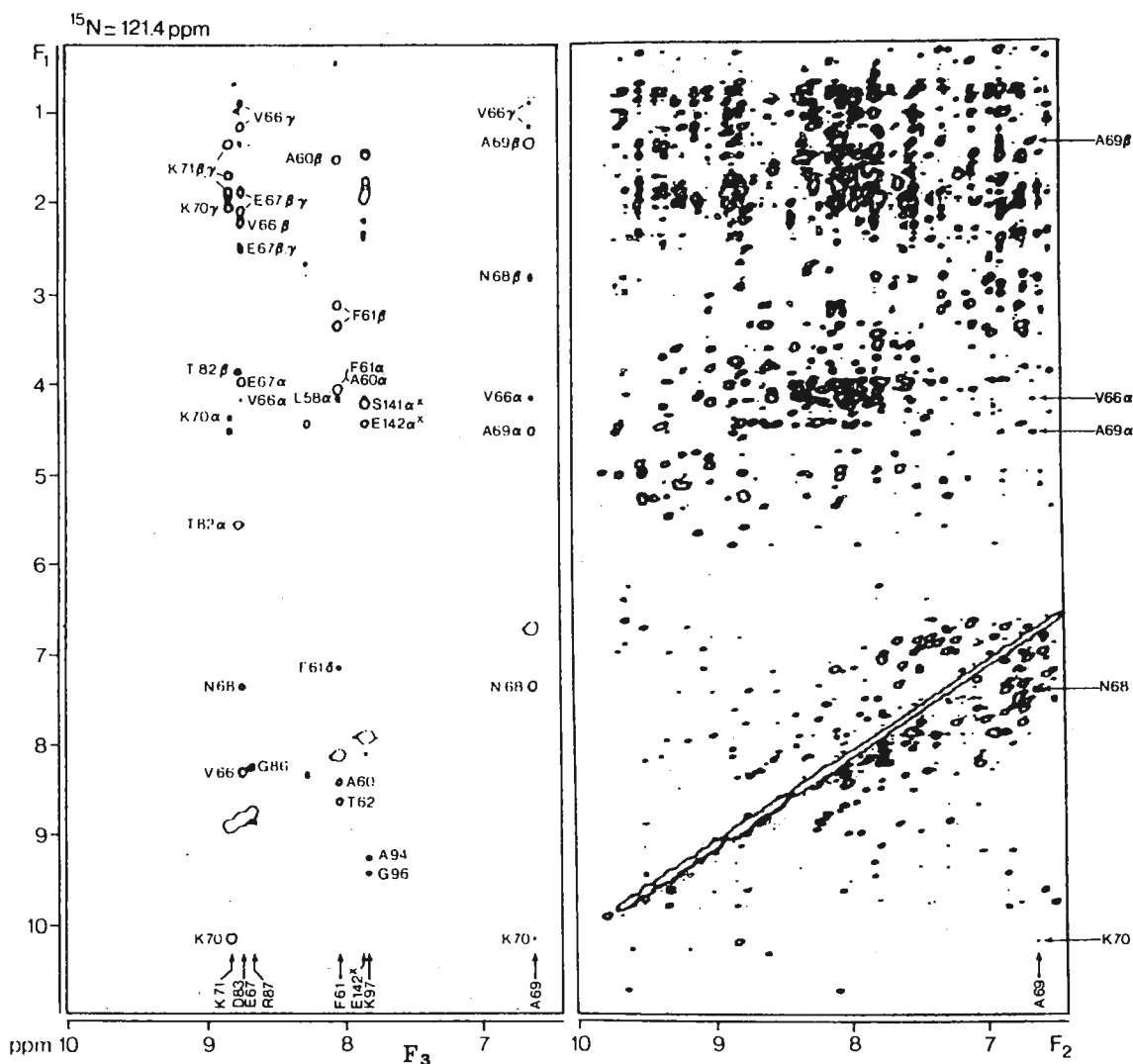


Fig.1. Comparison of a slice of the 3D spectrum (left) taken at a  $^{15}\text{N}$  ( $F_2$ ) chemical shift of 121.4 ppm with the corresponding region of a regular NOESY spectrum for 1.8 mM staphylococcal nuclease/pdTp/calcium complex (18 kD). Both spectra were recorded with a 125 ms NOE mixing time.





RESEARCH CENTER  
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(203) 271-4000

October 31, 1988  
(received 12/5/88)

Dr. B.L. Shapiro  
TAMU NMR Newsletter  
966 Elsinore Ct.  
Palo Alto, CA 94303


Dear Dr. Shapiro:

Evaluation of the Double Quantum RELAY Technique

RELAY experiments are extremely useful for determining  $^{13}\text{C}$ - $^{13}\text{C}$  connectivities and are done quite frequently in our laboratory. However, there are many cases where  $^1\text{H}$  overlaps make  $^{13}\text{C}$  -  $^{13}\text{C}$  correlations ambiguous. Philip Bolton proposed a possible solution to the problem, Double Quantum RELAY<sup>1</sup> (DQ-RELAY), which displays  $^1\text{H}$  double quantum rather than single quantum frequencies in F1. A few modifications in the pulse sequence and phase cycle were made to improve sensitivity, Fig. 1. The preparation pulses,  $\phi_1$ , were cycled in  $90^\circ$  steps while alternating the receiver,  $\Psi$ ,  $180^\circ$  in order to isolate  $^1\text{H}$  DQT. An additional phase cycle (the last  $^1\text{H}$  mixing pulse,  $\phi_2$ , and the receiver,  $\Psi$ , together in  $90^\circ$  steps) was superimposed on this to isolate a suitable coherence pathway. The last step necessary to obtain quadrature detection in F-1, was to repeat the entire sequence with a  $45^\circ$  "z-pulse"<sup>2</sup> while advancing the receiver,  $\Psi$ ,  $90^\circ$  as shown in the figure.

The resulting spectrum for an equimolar mixture of 2,5-dimethylphenol and 2,3,4-trichlorophenol taken on our Bruker AC-200 is shown in Fig. 2. Both  $t_p$  and  $t_m$  were 18 msec., and were 4 and 2 msec respectively. The signals for trichlorophenol are seen at F-2 = 115 ppm and 127 ppm, and those of dimethyl-phenol resonate at 112 ppm, 120.5 ppm and 125 ppm. Their corresponding  $^1\text{H}$  double quantum frequencies are seen along F-1, making the  $^{13}\text{C}$  connectivity determinations easy. Therefore DQ-RELAY seems to be quite useful.

However, DQ-RELAY has a serious shortcoming - sensitivity. As one would expect, the technique is far less sensitive than other RELAY methods. This becomes especially troublesome as the complexity of the spin system increases.<sup>3</sup> In Fig. 2 the signals from dimethyl phenol are about one fourth as intense as those from trichlorophenol. DQ-RELAY may be useful in cases of overlapping  $^1\text{H}$  signals, but because of its poor sensitivity the conventional RELAY technique<sup>4</sup> is a better choice for routine determinations of  $^{13}\text{C}$ - $^{13}\text{C}$  connectivities.

  
Gary Jubeau

GJ/mbt

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2. R. Freeman, T.A. Frenkiel, M.H. Levitt, J. Magn. Reson., **44**, 409 (1981)
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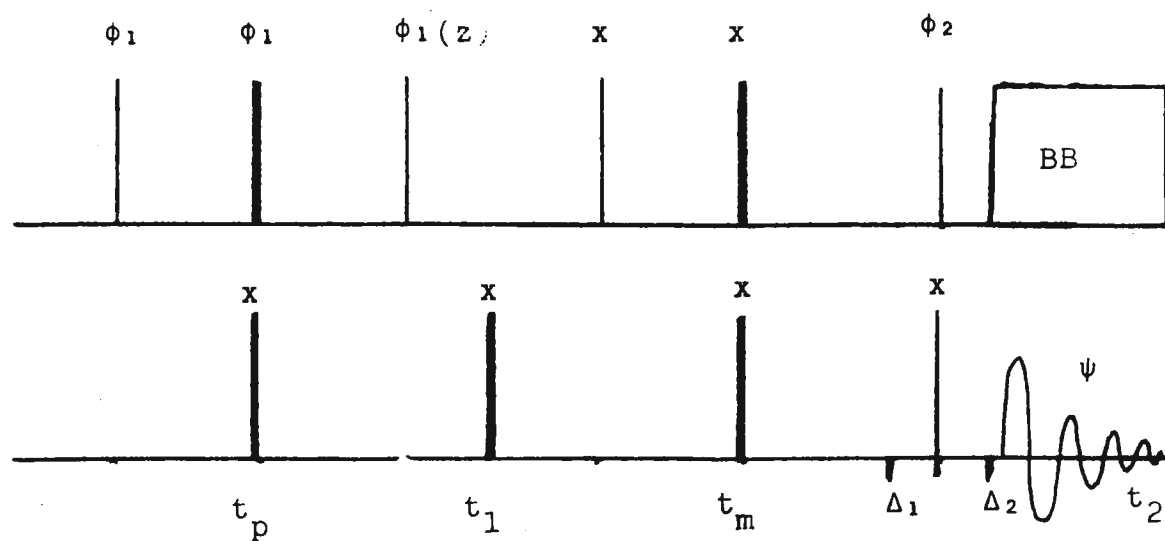


FIG. 1 Pulse Sequence - Double Quantum RELAY

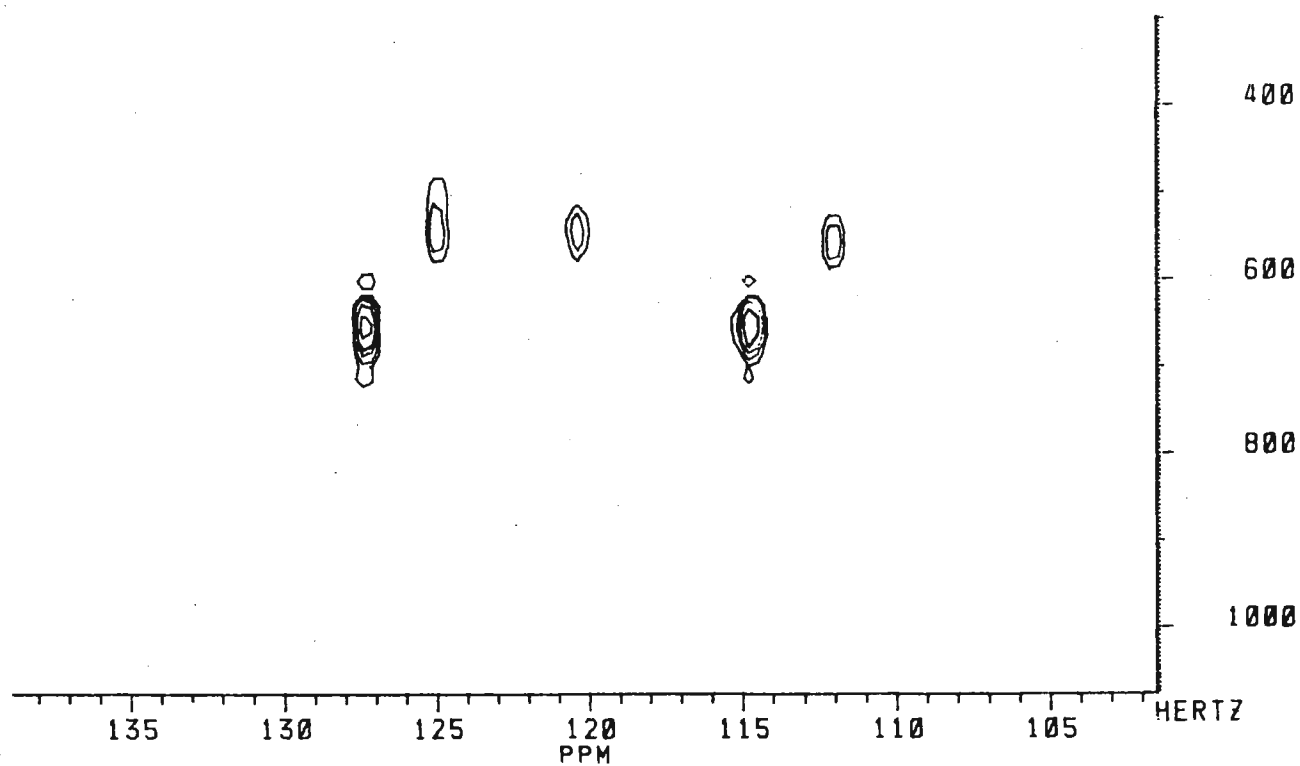


FIG. 2 Double Quantum RELAY Spectrum

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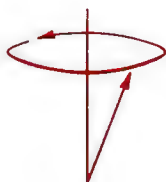
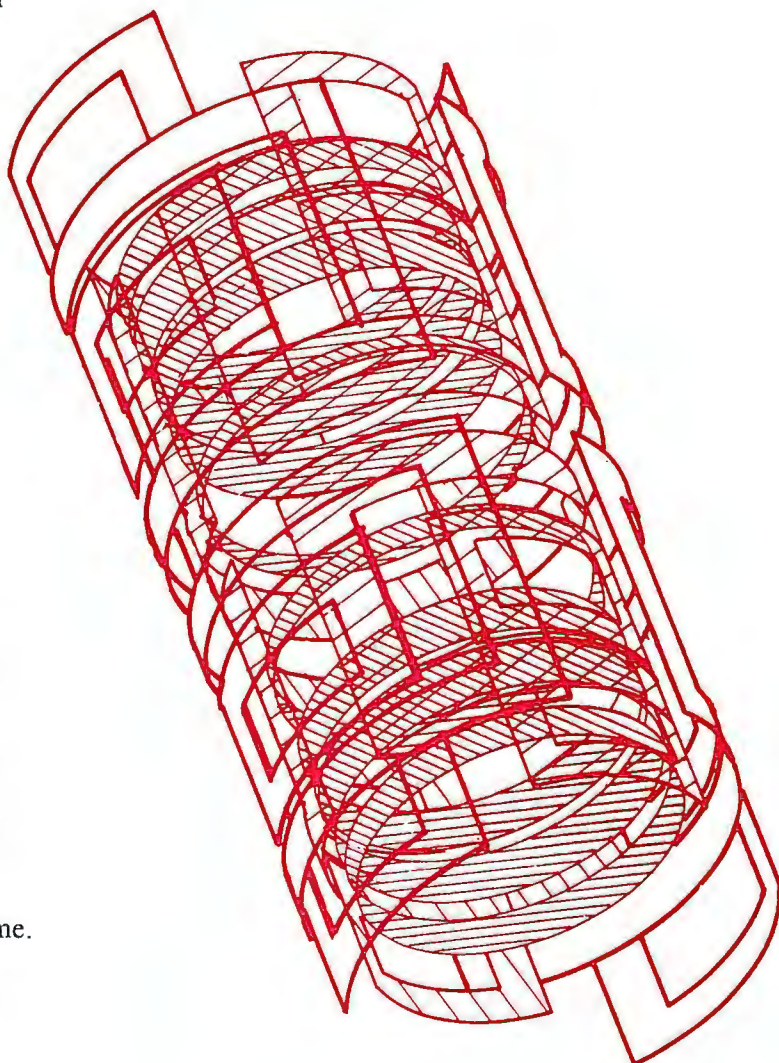
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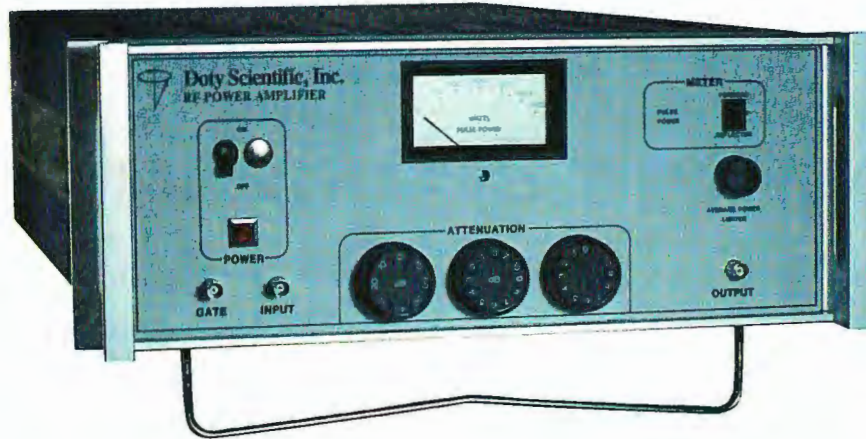


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 80dB minimum signal blanking.

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 Blanked: 25dB above thermal noise.

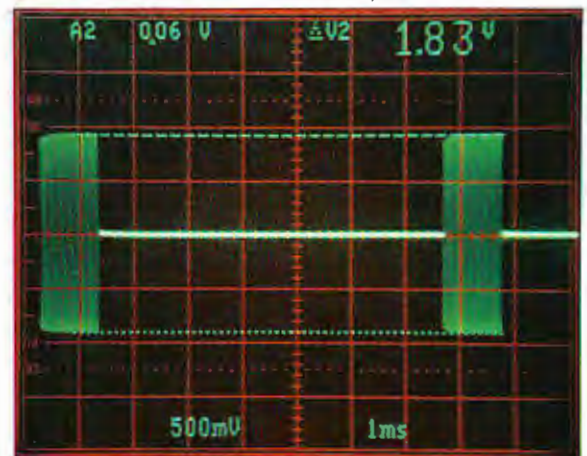
Flatness of response throughout power bandwidth:  
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THD is below 6% at any power level, any frequency.  
 Typical third order intercept is 60dBm.  
 Phase shift change (10% to 80% of rated power):  $8^\circ$  max.

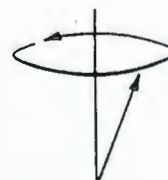
Half of rated power available to 170MHz. CW power is 20% of full pulse power.

Control panel includes three rotary decade attenuators, directional pulse power meter with 300ns response time, and adjustable average power limiter.

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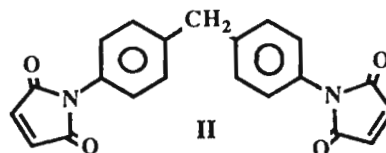
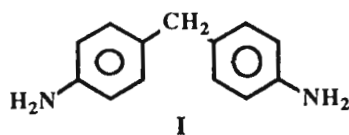
Dr. B.L. Shapiro  
966 Elsinore Court  
Palo Alto, CA 94303

November 8, 1988  
(received 12/13/88)  
[sic]

## Carbon-Nitrogen Dipolar Interactions in Epoxy Precursors

Dear Barry,

One of the early puzzles of high resolution  $^{13}\text{C}$  CPMAS NMR of solids was the observation of curious asymmetric doublets with 2:1 intensity ratios when nitrogen was present. The dipolar interaction responsible for the observed splittings has by now become a well understood phenomena<sup>1</sup>. The splittings arise because the  $^{13}\text{C}$ - $^{14}\text{N}$  dipolar interaction, while small enough to be averaged out by magic angle spinning, is in fact not removed because the  $^{14}\text{N}$  spins are not  $z$  quantized. The angular dependence for rotational averaging is therefore modified. The magic angle isn't so magic and dipolar splittings are observed. Many workers have used isotopic substitution to unravel these dipolar splittings<sup>2</sup>. The interaction is also dependent on the magnetic field strength. The splittings diminish as the field increases. We have used the field dependence to understand the observed spectrum of two epoxy precursors, methylenedianiline (I) and methylenedianiline-bis-maleimide (II).



In conjunction with Dr. Barbara Myers-Acosta of the Lockheed Missiles and Space Division in Sunnyvale, CA,  $^{13}\text{C}$  CPMAS NMR spectra of these two compounds were obtained at 50.3 MHz (4.7T, MSL200, Lockheed) and 100.6 MHz (9.4T, MSL400, Catalytica). The spectra, shown in the attached figure, contain splittings due to configurational effects in the solid state and  $^{14}\text{N}$  dipolar coupling. At 4.7T, the carbons directly bonded to nitrogen appear as triplets with intensity ratios of approximately 1:3:2. At 9.4T, the spectra are significantly simpler. The resonance at about 146ppm in the methylenedianiline spectrum is now readily recognized as a doublet with equally intense lines, each of which is split by dipolar coupling to nitrogen into doublets with intensity ratios of 1:2. In the bis-maleimide spectrum, the carbonyl carbon resonance at 170.6ppm is split into a doublet and the dipolar coupling is now reduced to the point where it cannot be observed. At any rate, we were able to sort out assignments for these two compounds by running the spectra at two fields.

Sincerely,

Charlie

C.M. Schramm

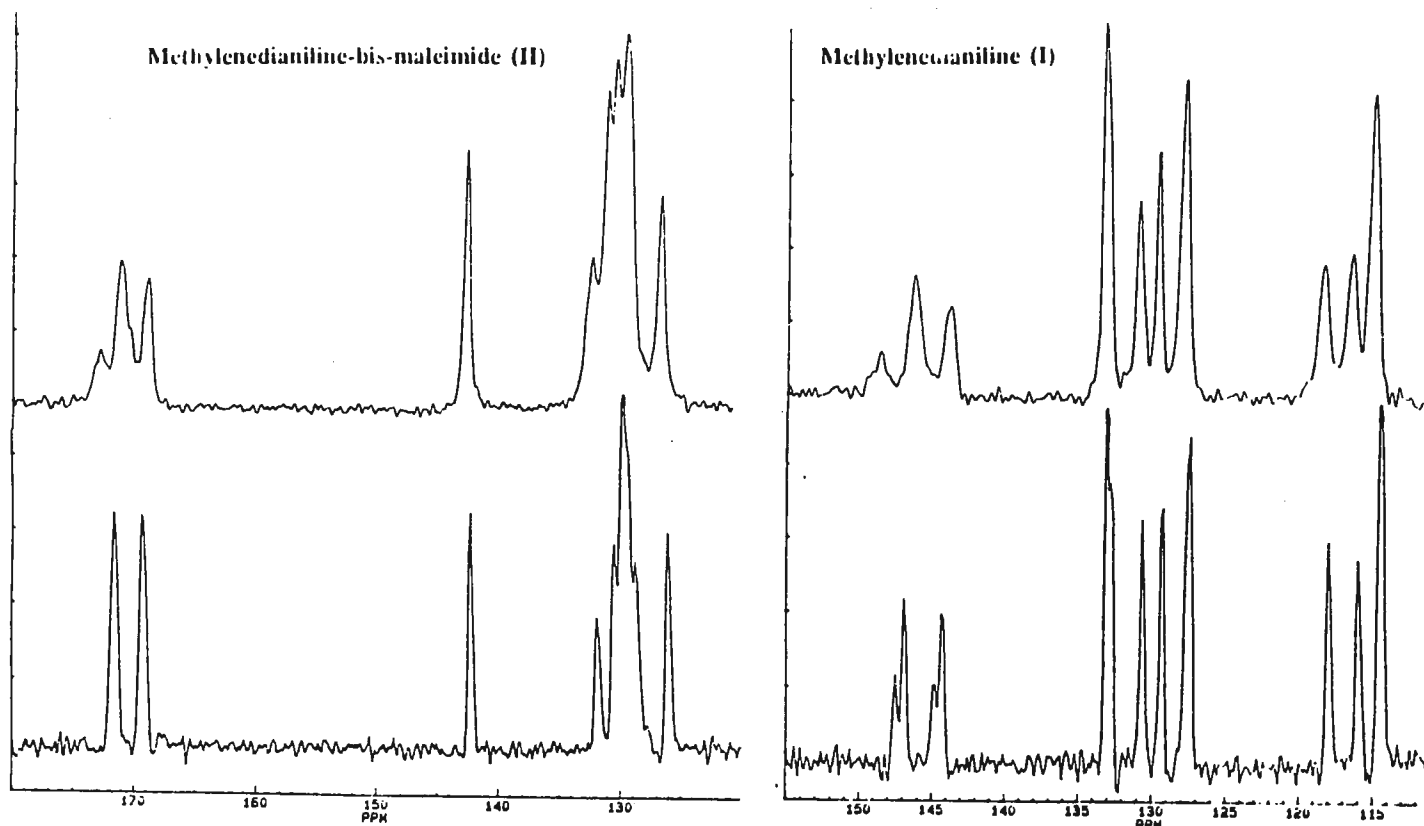
<sup>1</sup>a) Groombridge, Harris, Packer, Say, and Tanner, *J.C.S. Chem. Comm.*, **1980**, 174., b) Hexcm, Frey, and Opella, *J. Am. Chem. Soc.* **1981**, 103, 224., c) Naito, Ganapathy, and McDowell, *J. Chem. Phys.* **1981**, 74, 5393.

<sup>2</sup> a) Hexcm, Frey, and Opella, *ibid.*, 224., b) Harris, Jonsen, and Packer, *Mag. Reson. Chem.* **1985**, 23, 565.

**$^{13}\text{C}$  CPMAS NMR Spectra of Epoxy Precursors**

Upper 50.3 MHz

Lower 100.6 MHz

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- Digital Decwriter IV printing terminal
- Probes for  $^1\text{H}$ ,  $^{19}\text{F}$  and  $^{13}\text{C}$  (5mm) and  $^{11}\text{B}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$  (10mm)
- All documentation for software and hardware including complete set of schematics.
- Selection of spare parts

Interested parties should contact Tim Jones, Jack Miller or Steve Hartman at

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Prof. Bernard L. Shapiro  
Tamu Newsletter  
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October 14, 1988  
(received 12/14/88 [sic])

Dear Barry,

Recently we have combined a 1.5 T whole body Philips Gyroscan imager/spectrometer with a decoupling channel. Besides many applications for in vivo  $^{13}\text{C}$  spectroscopy, this channel may be used to improve spectral resolution in human  $^{31}\text{P}$  spectroscopy. At 1.5 T the region of interest for in vivo  $^{31}\text{P}$  spectra may be shimmed within a range from 0.1 to 0.3 ppm, resulting in 3 - 7 Hz line widths. At this point residual heteronuclear couplings with protons (5 - 10 Hz) may contribute substantially to the observed line width, deteriorating the obtained spectral resolution.

Proton decoupling of the in vivo  $^{31}\text{P}$  spectra was performed by a low power (6 micro-tesla) WALTZ-4 [1] sequence using a proton head coil with a homogeneous  $B_1$  field. In combination with surface coils, decoupling was achieved by a train of adiabatic rapid passage pulses [2,3], resulting in uniform decoupling over the entire sensitive range of the proton surface coil. This particular decoupling sequence resulted for a 16 cm diameter rectangular butterfly coil [4] in an average applied decoupling power of 3.7 W when used during a 256 ms acquisition time only and a  $T_r$  of 3 s.

Figure 1 shows the effects of  $^1\text{H}$  broadband decoupling for a  $^{31}\text{P}$  human (calf) muscle spectrum using adiabatic rapid passage decoupling pulses. Note the remarkable changes in the glycerophosphocholine (GPC) signal. Figure 2 shows a localized human brain  $^{31}\text{P}$  spectra. Proton decoupling results in clearly resolved signals in the phosphomono- and phosphodiester regions.



# PHILIPS

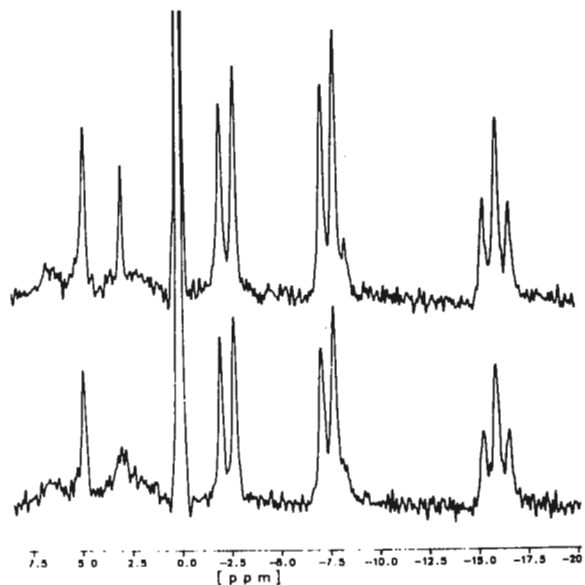


Fig. 1

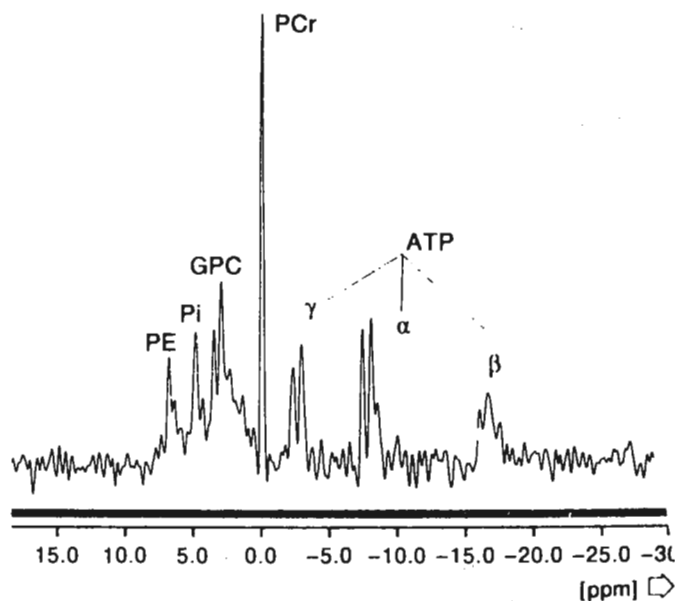



Fig. 2

Please credit this to Dr. J.A.B. Lohman's account

Sincerely

  
Peter Luyten

## References

- [1] Shaka A.J., Keeler J., Frenkiel T., Freeman R., J. Magn. Reson 52 (335- 338) 1983
- [2] Baum J., Tycko R., Pines A., J.Chem.Phys. 79 (4643-4644) 1983
- [3] Silver M.S., Joseph R.I., Hoult D.I., Phys. Rev. A 31 (2753-2755) 1985
- [4] Sobol W.T., Rev. Magn. Reson. in Medicine 1 (181-224) 1986



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Klingelbergstrasse 82, Telefon 061 - 44 22 80

CH-4056 Basel (Schweiz) Nov. 15, 88  
(received 11/19/88)

Prof. Dr. P. Diehl

Prof. B.L. Shapiro  
966 Elsinore Court  
Palo Alto, CA 94303

Program MASTER for corrections of solvent  
effects on the molecular structure as de-  
termined by NMR of oriented molecules.

---

Dear Barry,

We have developed a computer program MASTER which is able to derive solvent independent structure data for molecules dissolved in liquid crystals. The program basically consists of a combination of two modified versions of the earlier programs VIBR which calculates corrections of direct coupling constants for harmonic vibration and of SHAPE which derives molecular geometry and order parameters from the direct couplings.

The modifications take into account, that molecules dissolved in liquid crystals are deformed by the anisotropic medium and that the same interactions, which we attribute to individual bond contributions, deform and orient the molecule simultaneously.

Starting from a guessed molecular structure and guessed bond interaction parameters as well as a known molecular force field the program iteratively determines a final solvent independent structure as well as bond interaction parameters for each solvent in agreement with the observed order parameters.

The program MASTER has already been applied successfully to several molecules as eg. allene <sup>1)</sup> and is now available to anyone interested.

With best regards  
sincerely yours

Peter Diehl

Reference

- 1) P. Diehl, C. Baraldi, M. Kellerhals and R. Wasser  
J. Mol. Struct. 162, 333 (1987)

National Research Council  
CanadaConseil national de recherches  
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SciencesDivision des sciences  
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K1A 0R6November 25, 1988  
(received 11/26/88)Dr. B.L. Shapiro  
TAMU NMR Newsletter  
966 Elsinore Court  
Palo Alto, California  
USA 94303**WATANABE PLOTS ON A LASER PRINTER**

Dear Dr. Shapiro,

Our Bruker spectrometers are equipped with analog and Watanabe digital plotters, none of which are capable of producing high quality plots for publication. To circumvent this problem Watanabe plot commands are sent to a file on an IBM AT computer which is connected via its serial port COM1 to either the serial port (channel B) or the parallel port of the ASPECT 3000. A commercial parallel to serial converter is used on the parallel port. Switching the plot output from the parallel to the serial port of the ASPECT 3000 is accomplished by the CA command of DISNMR. On the parallel line, a switch box is used to send the plot commands to the plotter or the IBM AT. Hence, plot files can either be captured via the serial or parallel port of the ASPECT 3000, allowing greater flexibility of operation. When plots are sent via the serial port in one job, other plots can be sent to the Watanabe plotter in another job.

A simple BASIC program is used to capture the binary data on the COM1 port of the IBM AT. Then, Turbo PASCAL programs are used to translate the Watanabe plot commands to HPGL format, draw the plot on the screen and label it if necessary. Finally, the diagram is plotted on a Laserjet printer using the commercial program LaserPlotter (Insight Development Corp., 1024 Country Club Drive, Moraga, CA, 94556, 415-376-9451) which allows HPGL plots to be dumped on HP laser printers. The Watanabe file can also be sent to an IBM mainframe, where it is converted to DISSPLA format and plotted on a Talaris laser printer.

If you think this is easier than buying a HP plotter, send us an IBM diskette to receive a copy of the programs. A conversion program for ZETA to HPGL is also available.

Sincerely,

André Simard

Jean-Robert Brisson

*André Simard**Jean-Robert Brisson*



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School of Allied Health Sciences  
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Marine Biomedical Institute  
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DEPARTMENT OF HUMAN BIOLOGICAL CHEMISTRY & GENETICS  
Division of Biochemistry

Area Code 409  
761-2289

Phosphorus metabolism in leukemic cells.

November 28, 1988

(received 12/2/88)

Dear Dr. Shapiro,

Since the early summer of this year we have been involved in studies of phosphorus metabolism in leukemic cells by obtaining  $^{31}\text{P}$ -NMR spectra of perchloric acid cell extracts. The particular cells that we use in our studies are the wild type human leukemic CEM-C7 cells and the CEM-C1 mutant, which is resistant to the anti-tumor drug dexamethasone (1). Two areas in the  $^{31}\text{P}$ -NMR spectrum are of special importance: 1) the peaks corresponding to phospholipid metabolism, i.e. phosphomonoesters (PME's) and phosphodiester (PDE's) and 2) the peaks corresponding to the energy status of the cell, i.e.  $\alpha$ -,  $\beta$ -,  $\gamma$ -ATP and inorganic phosphate ( $\text{P}_i$ ). Two series of experiments have been performed so far. The first series was carried out to quantify changes in phosphorus metabolism while the cells multiply from early log phase into confluency. Striking differences were observed in PME concentrations between the CEM-C7 and CEM-C1 cells. CEM-C7 cells exhibit high PME concentrations in the log phase, which drop by 75% when the cells reach confluency, indicating a lower rate of phospholipid turnover. In contrast, the CEM-C1 mutant cells do not exhibit this drop in PME concentration, suggestive of a decreased degree of growth inhibition in these cells. In the CEM-C1 extracts a prominent phosphocholine (PC) peak was observed in the PME region, which was much smaller or absent in the CEM-C7 extracts. Also differences in ATP levels were observed between both cell types. In the C1 cells, the ATP levels were observed between 34% and 49% of total phosphorus, without a clear trend with respect to cell concentration. For the C7 cells ATP levels gradually increase from 23% at low cell concentrations ( $4 \times 10^5$  cells  $\text{ml}^{-1}$ ) to 51% at high concentrations ( $2.7 \times 10^6$  cells  $\text{ml}^{-1}$ ).

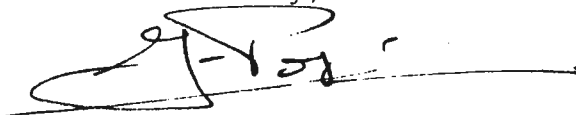
A second series of experiments was designed to follow the effect of dexamethasone. In these experiments the absolute concentrations of the metabolites, expressed as  $\mu\text{moles} / 10^8$  cells, could be determined by adding the reference Diphenylphosphate to the extracts. A major observation was that, expressed in this manner instead of a percentage of the total phosphorus intensity, in the CEM-C1 cells all metabolites occur in concentrations which are about 30% higher than in the CEM-C7

cells. 48 hours after drug addition the spectrum of the CEM-C7 cells exhibit strongly decreased ATP and PME levels and an increased level of PDE's, indicative of cell membrane breakdown and presence of non-viable cells. The spectra obtained for the C1 cells continue to show high cell viability up to 72 hours. Currently attempts are underway to embed live cells in agarose threads (2) in order to study phosphorus metabolism and effects of drug addition in-vivo.

*Erna Baum*

Erna Baum

Sincerely,



J.F.M. Post

Credit this contribution to the account of Professor L.L. Smith.

References.

1. R. Zawydwski, J.M. Harmon, and E.B. Thompson, Cancer Res. 43 (1983), 3865-3873.
2. J.S. Cohen and R.C. Lyon, Ann, N.Y. Acad. Sci. 508 (1987), 216-228.

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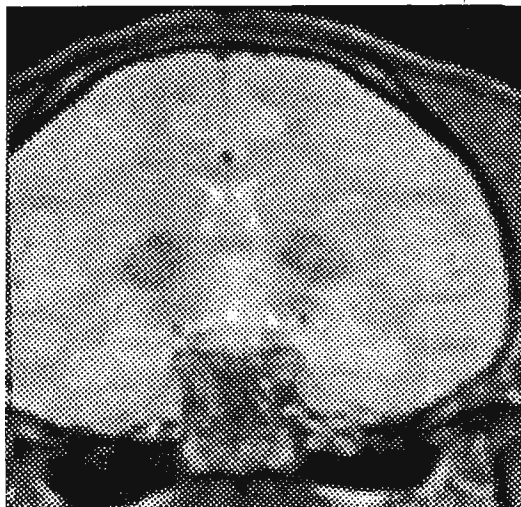
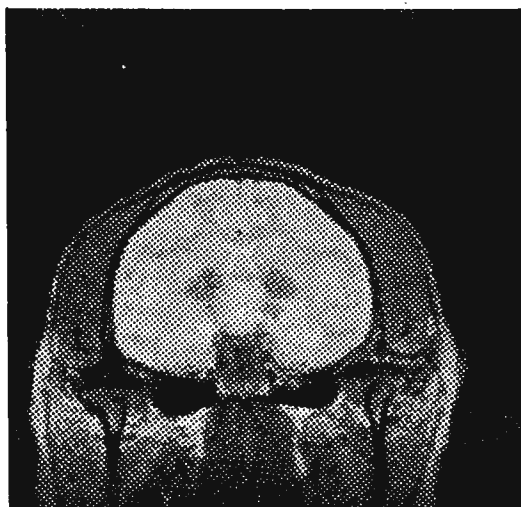
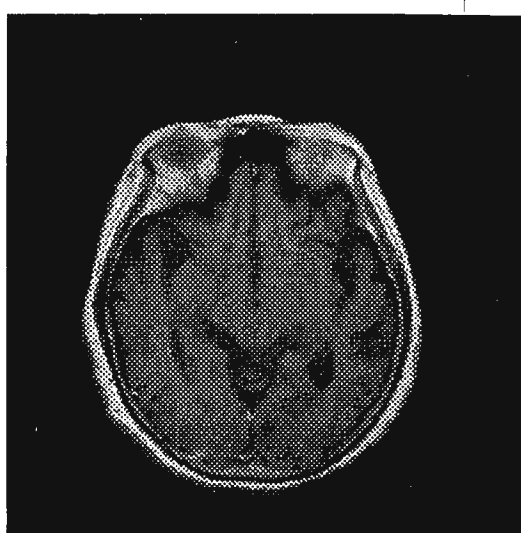
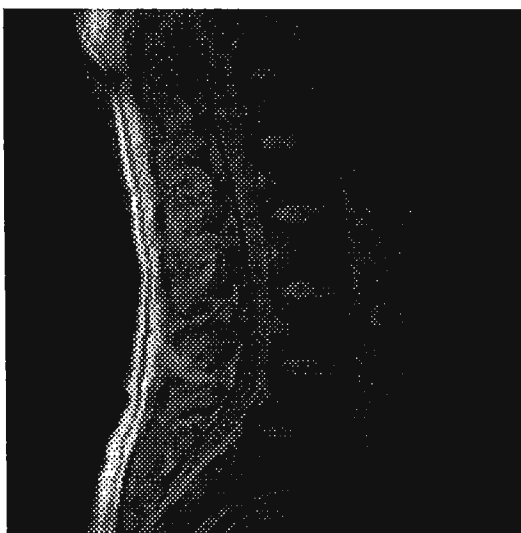
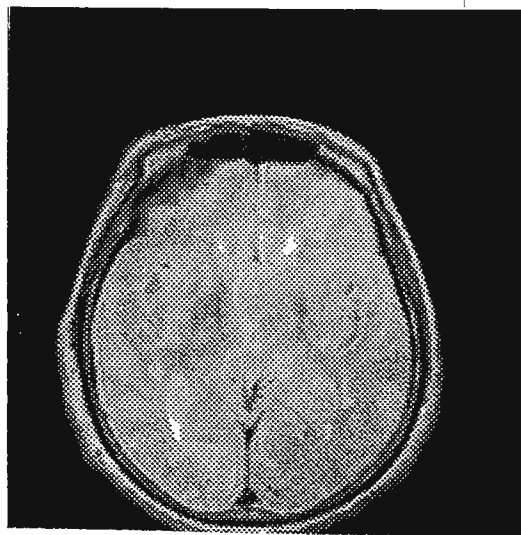


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# HMRI

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

November 21st 1988  
(received 11/26/88)

## Macintosh Computers and Mice

Dear Professor Shapiro,

In a previous contribution (TAMU NMR Newsletter #355, April 1988) a program developed for serial file transfers between Nicolet 1280 and IBM PC microcomputers was described. With the arrival of an Apple Macintosh II computer in our laboratory, we have now converted this program to allow 1280 to Macintosh II file transfers. A copy of this program is available to anybody who would like one (please send a blank floppy disk and a stamped, self-addressed envelope). Although both programs are written in Turbo Pascal, appreciable changes were required when converting the IBM PC source code to the MAC II. The serial communications ports on the MAC II are of type RS-422, so an appropriate connector is required to interface with the RS-232 output on the 1280 (see figure below); the simplest way of making this is to buy (for instance) an Apple ImageWriter cable, cut off one end, and solder on a 25-pin D-type connector.

Some frustration was generated when, after having worked reliably for a couple of weeks, all communication between the 1280 and the Macintosh came to a sudden stop. The cause of the problem was eventually traced to a badly eaten cable (!) which had been newly laid in the roof. The culprit (a small rodent) was caught a couple of days later and punished appropriately.

One of the nicer features of the Macintosh II is its graphics capabilities; these are put to good use by an excellent image processing and display program called "IMAGE.88" which I have recently come across, written (also in Turbo Pascal) by Wayne Rasband, National Institutes of Health, Bldg 36, Room 2A-03, Bethesda, MD 20892. Attached are a couple examples of standard spin echo images recorded at 200 MHz on a GE CSI spectrometer (a sagittal image of the brain of a young Macaque Monkey, and a coronal view of an isolated porcine kidney), printed on an Apple LaserWriter using "Image.88".

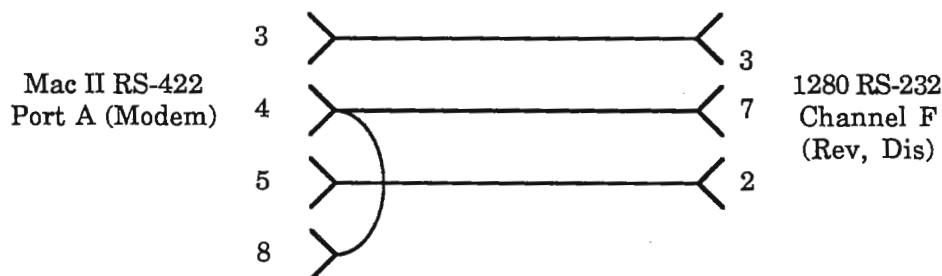
Finally, as of February 1st 1989, my new address will be; Department of Radiology, Division of NMR Research, Johns Hopkins Hospital, Baltimore, MD 21205,

yours sincerely,

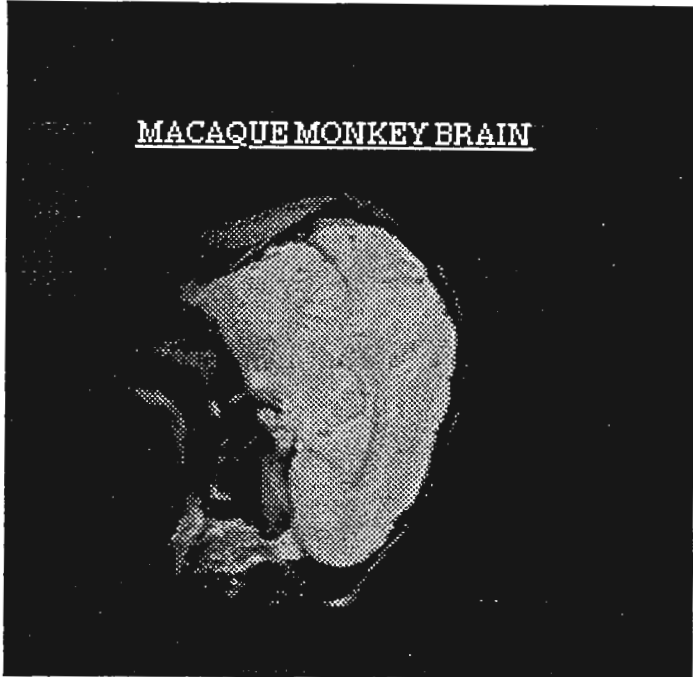
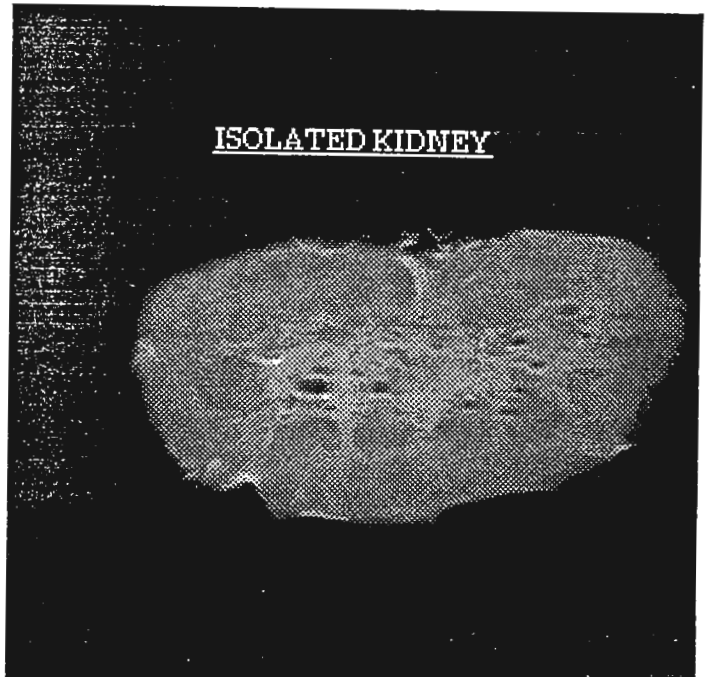
*P.B. Barker*

Peter B. Barker

## Nicolet 1280 to Macintosh II Serial Communication Cable



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TAMU NMR Newsletter  
966 Elsinore Court  
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Uw ref.:

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1949

Amsterdam, 8<sup>th</sup> December 1988  
Badhuisweg 3 (received 12/15/88)  
Tel. via telefoniste (020) 309111  
Tel. rechtstreeks (020)  
Hr/Mw

## Automated Diffusion NMR

Dear Professor Shapiro,

Recently we have started a project at SHELL Research B.V. directed towards automated diffusion NMR measurements. In the oil and chemical industry quite some applied research effort is put in the investigation of in molecular mobility type phenomena, like for example self-diffusion of micelles and polymers in solution. In this context the implementation of an automated Fourier-transform pulsed-field gradient (FT PFG) NMR diffusion facility in our research lab is very attractive.

An instrumental setup has been purchased, consisting of a narrow-bore VARIAN VXR200S spectrometer and a DOTY probe. This probe, tuned for protons, has an active shield, that reduces the gradient field (of maximally 1,000 G/cm) by a factor of at least 10,000 outside the probe. The stepping of the gradients is computer controlled.

The data-processing has been automated. After Fourier transformation from the top of the (Hahn or stimulated) echo the intensity decay ( $\ln[A(G)/A(G=0)]$  versus  $G^2$ ) is analyzed in terms of an exponential for each of the integration regions in the spectrum (see Figure). Proper phase correction is of crucial importance to obtain the correct integrated areas. Thus, a diffusion coefficient is obtained for isotropically reorientating molecules.

In the Figure the output of a typical diffusion measurement from our automated FT PFG NMR set-up is shown. The sample is 30 wt% n-C<sub>21</sub>H<sub>44</sub> dissolved in benzene. The two components are well-resolved in the spectrum, the aromatic benzene resonance at 7.4 ppm and the aliphatic n-C<sub>21</sub>H<sub>44</sub> resonances at 1.2 (CH<sub>2</sub>) and 0.9 ppm (CH<sub>3</sub>). Figure B shows the decrease in the peak intensities (with the integration regions ranging from 0-3 and 6-9 ppm for n-C<sub>21</sub>H<sub>44</sub> and benzene, respectively), which were determined from the spectra in Figure A. The mono-exponential decays yield  $D_{\text{benzene}} = 2.1 \cdot 10^{-9}$  m<sup>2</sup>/s and  $D_{\text{n-C}_{21}\text{H}_{44}} = 1.2 \cdot 10^{-9}$  m<sup>2</sup>/s.

Shell Research B.V.  
Gevestigd te Den Haag. H.reg. Amsterdam 111841

Correspondentie: Postbus 3003, 1003 AA Amsterdam  
Telex: 11224 ksla nl  
Telegram: Konshellab

It is intended to continue these experiments for the investigation of more viscous solutions and to do such analyses for solid-like samples, such as gases sorbed in zeolites,

yours sincerely,

KONINKLIJKE/SHELL-LABORATORIUM, AMSTERDAM

K.P. Date

J. A. Bolt

Alex de Groot

Klaas P. Datema Jantina A. Bolt-Westerhoff Alex de Groot

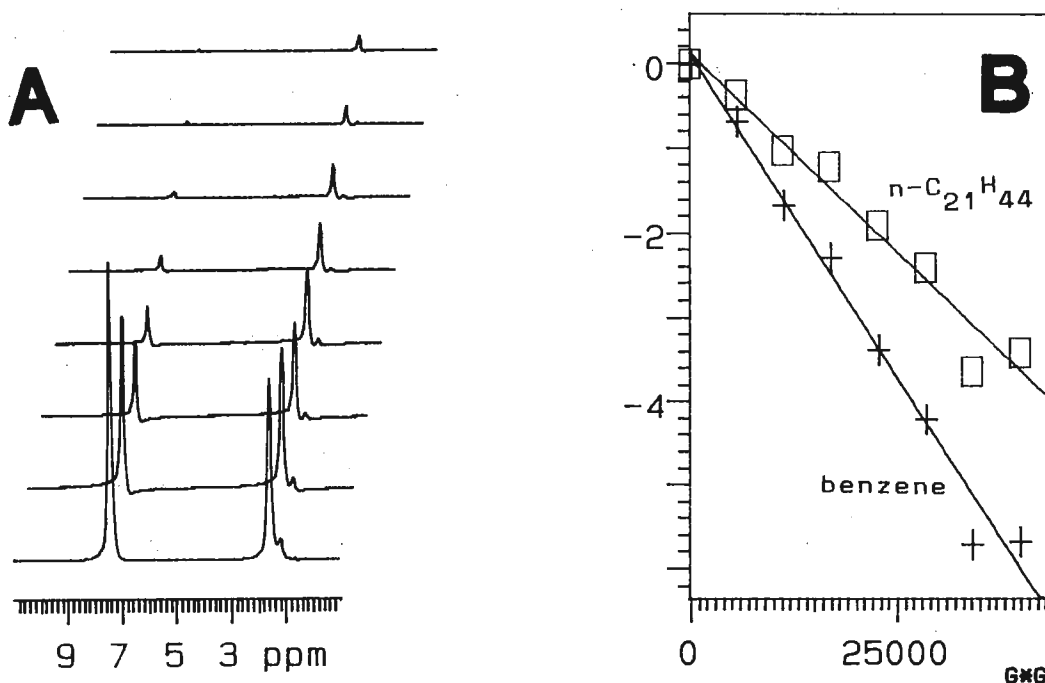


Figure. (A) 200 MHz  $^1\text{H}$ -NMR FT PFG NMR spectra of 30 wt%  $n\text{-C}_{21}\text{H}_{44}$  dissolved in benzene. The pulse sequence consists of a  $5\text{ }\mu\text{s}$   $90^\circ$  and a  $10\text{ }\mu\text{s}$   $180^\circ$  pulse (Hahn echo), in which two 1 ms gradient pulses are inserted ( $d2 = d4 = 10\text{ ms}$  and  $d0 = d3 = 40\text{ }\mu\text{s}$ ). The relaxation delay,  $d1 = 10\text{ s}$ . The gradient strength was 0, 76, 107, 131, 151, 169, 185, and 200 G/cm, respectively. The gradient was calibrated by a separate benzene measurement (298 K) with  $D = 2.3 \times 10^{-9}\text{ m}^2/\text{s}$ . (B) The frequency-resolved intensity decrease in the spectra of (A) with the integration regions ranging from 0-3 and 6-9 ppm, i.e. for  $n\text{-C}_{21}\text{H}_{44}$  and benzene, respectively.



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Professor Bernard Shapiro  
 Editor/Publisher, TAMU NMR Newsletter  
 966 Elsinore Court  
 Palo Alto, California 94303  
 U. S. A.

November 20, 1988  
 (received 11/29/88)

Dear Dr. Shapiro:

Longitudinal Triple Quantum Relaxation Studies of Supercooled  
 Aqueous LiCl-Solutions

As part of our ongoing research effort into the study of molecular dynamics, we have been studying  $^7\text{Li}$  NMR in 11 M aqueous ( $\text{D}_2\text{O}$ ) LiCl solution at 192 K by means of multiple quantum relaxations. We like to report the results of a study which utilizes one-dimensional analogue of the triple quantum 2-D experiment via the longitudinal relaxation to determine the behavior of  $^7\text{Li}$  triple quantum coherence.

The pulse sequence utilized is basically a triple quantum filter pulse sequence ( $\pi-\tau-\pi/2-\Delta-\pi/2$ ). In addition,  $180^\circ$  phase alternations in the inversion pulse are added in the phase cycling scheme in order to eliminate the transverse contribution of triple quantum coherence due to the imperfection of the  $\pi$  pulse.

The description of the relaxation processes during  $\tau$  period and acquisition period may be given in terms of the evolution of the density matrix following the formalism of Redfield theory. The creation of longitudinal triple quantum relaxation is found to be due to the non-uniform distribution between spin states  $3/2$  (or  $-2/3$ ) and  $1/2$  (or  $-1/2$ ). The longitudinal relaxation profile of the triple quantum coherence is shown in the figure. The calculated curve is obtained with a quadrupole coupling constant ( $e^2q_{\text{eff}}Q/h$ ) = 50 kHz and the correlation time  $\tau_c$  = 2300 ps. Small corrections due to the dipolar interactions between hydrated  $\text{D}_2\text{O}$  and  $\text{Li}^+$  are also considered.

Further work on transverse double quantum relaxation is underway in our laboratory.

Truly yours,

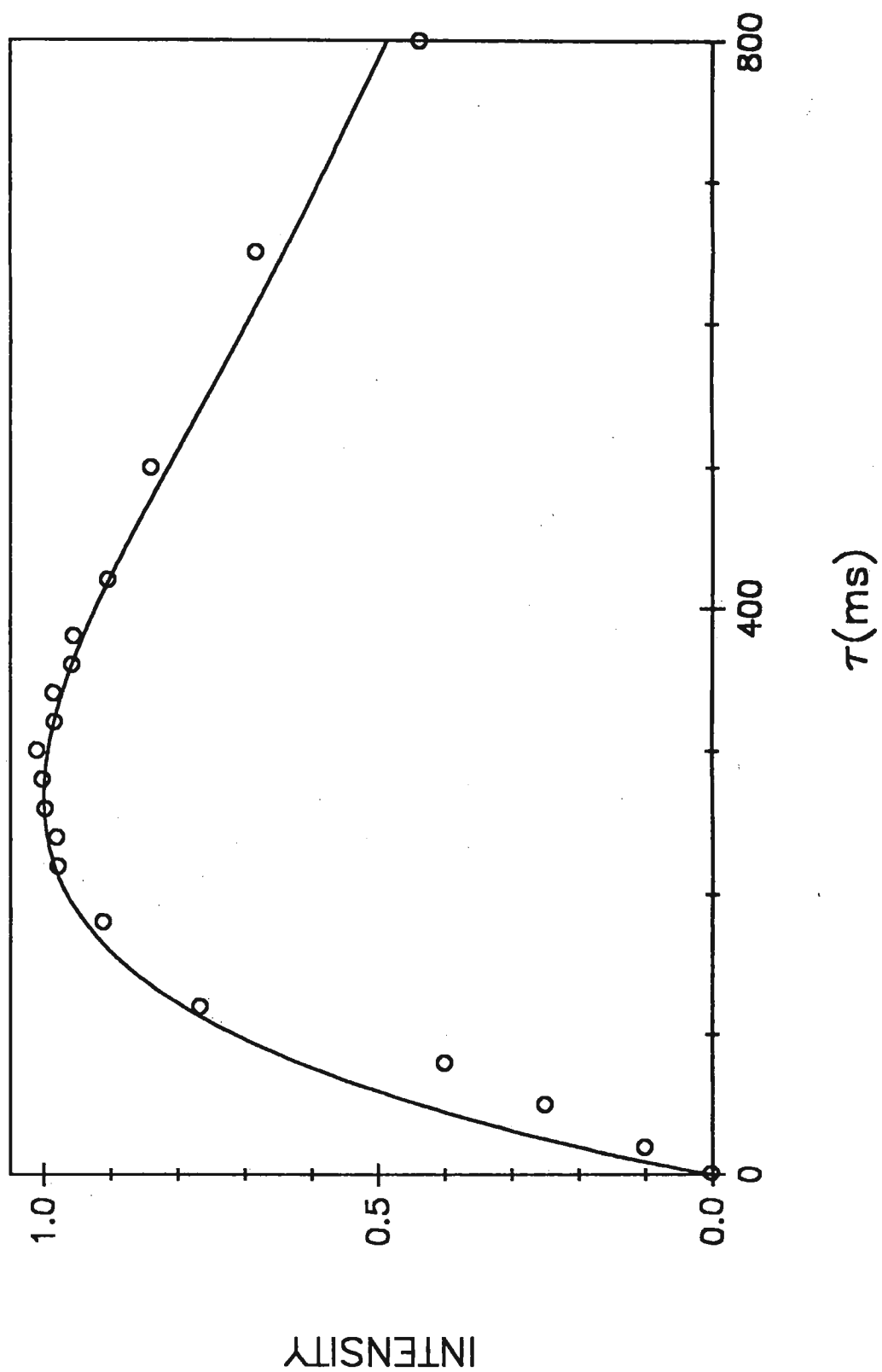
Wen-Tsung Chang

Lian-Pin Hwang

*Wen-Tsung Chang*

*Lian-Pin Hwang*

## RELAXATION OF LONGITUDINAL TRIPLE QUANTUM COHERENCE





Landbouwniversiteit **Wageningen**14 november 1988  
(received 11/28/88)

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

Dispersive waterflow in a glass bead phantom characterized by NMR.

Dear Professor Shapiro,

Flow of water and diffusion/perfusion have been our interest for more than over a decade. Recently we have been working on porous glass bead systems through which water flows continuously, as a model for flow in soil and perfusion in organs.

Working with a modified stimulated echo, MSTE (1) or SE method we are able to investigate the relation between the average flow velocity and the transversal/longitudinal dispersion coefficient with NMR.

Our spin echo NMR system consists of a Bruker Aspect 2000, a 0.5 T magnet, a Z17C pulse programmer and modified Minispec electronics. Since our Aspect 2000 computer can not really be equipped with software which can process our data, we surpassed the Aspect 2000 by doing acquisition and data manipulation with ASYST (software) on a P.C., including an DASH16 ADC. This type of data manipulation gives us an online menudriven way to view and manipulate data.

Figure(1) is showing the typical online screen information provided by the ASYST menu driven program from which the dispersion coefficient easily can be read. A typical dispersion coefficient determination takes at the moment 80 seconds.

Figure (2) shows the relation between the transversal dispersion and the velocity of water in the glass bead (diameter 1 mm) phantom (1). The negative slope above the  $2 \cdot 10^{-2}$  m/s might be due to a transition from laminar to turbulent flow in the phantom (2). Turbulence introduces vortexes in the system, this could produce a false echo attenuation which could give cause to the negative slope in fig(2). The results are in reasonable agreement with the results presented in (2), obtained with other techniques.

The values of the dispersion coefficient, as presented in fig(2) are based on preliminary results, and are presented as relative numbers. An inspection of fig(1) learns, that the first datapoint, at  $C \cdot (G \cdot \Delta t)^2 = 0$ , does not coincide with the drawn line through the other datapoints. This is due to a persistent gradient, originating from the used gradient pulse generator. We hope that with our new Bruker magnet and gradient system (0.5 T, 1500 kg, 10 cm air gap, 12 shims and 3 gradients with 80 mT/m over 10 cm) it will be quite easy to quantify the dispersion in the transversal and longitudinal direction. We also intend to perform the same kind of experiment on the flow of two or more immiscible fluids by doing data manipulation in the frequency domain. Since the MSTE and SE technique can easily be adapted for MRI pulse programs, experiments are currently being set up to obtain spatially resolved images of dispersion in glass beads/porous media, and of perfusion of blood in organ tissues.

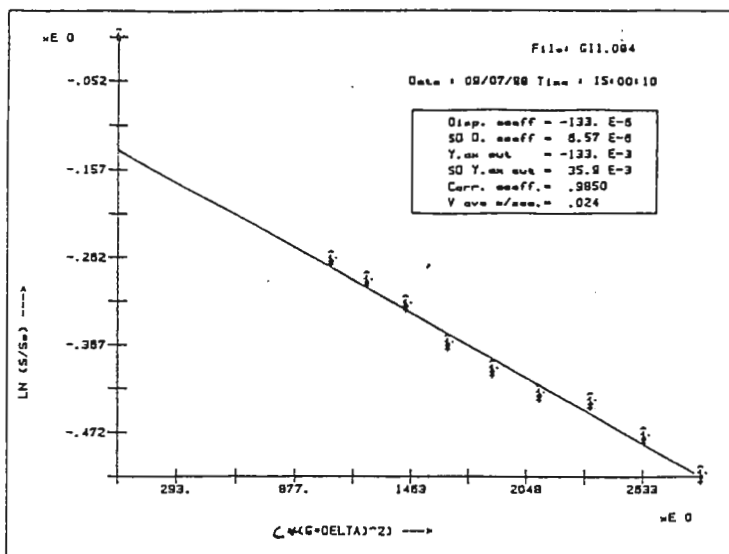


Figure (1)  $\ln(S/S_0)$  versus  $C \cdot (G \cdot \Delta)^2$  ( $\text{s/cm}^2$ ) obtained with MSTE (1).  
With  $C$  = proportionality constant.

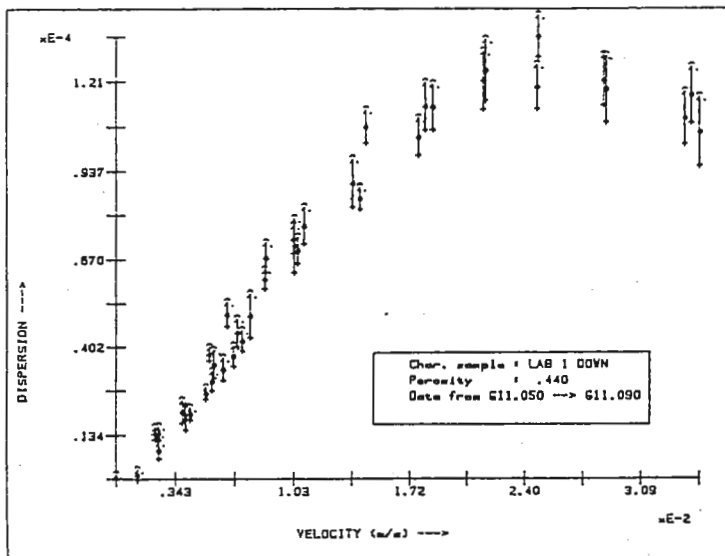


Figure (2) Transverse dispersion ( $\text{cm}^2/\text{s}$ ) versus velocity.

(1) Snaar, J.E.M.; and van As, H.; Discrimination of Different Types of Motion by Modified Stimulated Echo NMR; submitted to JMR.

(2) Bear, J.; and Yavuz Corapcioglu, M.; Fundamentals of Transport Phenomena in Porous Media.; 1984, Martinus Nijhoff Publishers, p. 249, p. 163.

Please credit this contribution to the account of the last author.

Sincerely,

Wybo Palstra

Henk van As

Tjeerd Schaafsma



# THE UNIVERSITY OF SOUTHERN MISSISSIPPI

DEPARTMENT OF POLYMER SCIENCE

Professor B. L. Shapiro  
966 Elsinore Court  
Palo Alto, CA 94303

(received 11/26/88)

## Re: Transfer and Off-line Processing of Bruker MSL FID Files

Dear Professor Shapiro:

Two years ago we purchased a Bruker MSL-200 NMR spectrometer and have experienced problems with data storage due to the large number of solution and solid-state data files generated. Although the spectrometer is equipped with a CDC disk drive unit which uses removeable 16 Mbyte platters, the platters are expensive and bulky. In addition, we also needed off-line processing capability in order to prepare documents for papers, preprints and manuals. In order to address these problems, we decided to implement data transfer from the MSL-200 to one of our PC's.

In order to transfer Bruker data files from the spectrometer to the PC, we used PC programs which implement KERMIT protocol. KERMIT is especially convenient due to its availability from public domain libraries and the existence of a limited version of KERMIT for the Aspect 3000. Initially, some file transfers in that version 880101 of Aspect KERMIT did not properly flag the PC that it was sending compressed data, resulting in unsuccessful data transfers. The new version of Aspect KERMIT has addressed this problem as well as increased the rate of data transfer by ca 30%.

We use port B located on the back of I/O board of the Aspect computer as our communication port. The baud rate is controlled by a hex switch located on the I/O board and is set to 9600. A DIP switch controls the communication status of the port and is set to "LINE BUSY" (see the Bruker KERMIT manual). After transfer from the Aspect computer, the MSL data files can be archived on 3 1/2" or 5 1/4" floppies using either high or low density format. If desired, transfer back to the Aspect can be performed as well.

The program chosen for off-line data processing was *SpectraCalc* from Galactic Industries. Although the program initially lacked NMR capability, we were impressed with its data processing and graphics capability. In addition, *SpectraCalc* can be easily modified for NMR data processing due to its ability to incorporate ARRAY BASIC programs. Working with the programmers at Galactic Industries and the support staff at Bruker, we were able to implement suitable modifications.

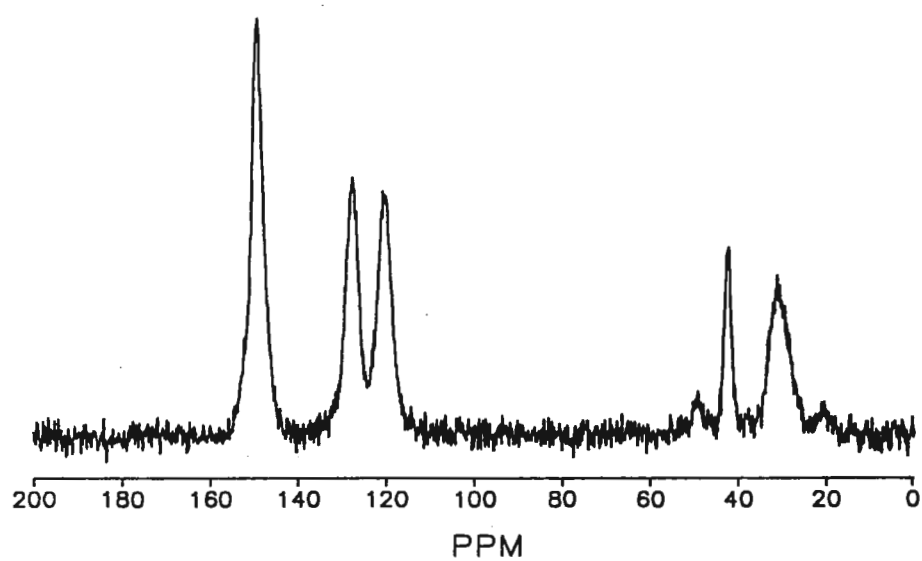
Figures 1 and 2 illustrate the results of our efforts. Figure 1 shows the solid-state  $^{13}\text{C}$  NMR spectrum of polycarbonate, while Figure 2 shows the corresponding solution  $^{13}\text{C}$  NMR spectrum. Both spectra were generated from the raw Bruker MSL FID files using *SpectraCalc*. The corresponding graphic files were also created by *SpectraCalc* and imported directly into this *Word Perfect 5.0* document (these files can also be imported into *Pagemaker* documents). Spectral processing includes application of an exponential linebroadening factor and the "Redfield trick" before the FT, and phase correction (both zero and first order) and baseline correction of the spectra after the FT. A COMPAQ DESKPRO 386/20 with 2 Mbytes of memory and a VGA monitor or an AT clone with 1 Mbyte of memory and an EGA monitor were used as the data stations. Both require a math coprocessor, and a hard disk is recommended.

Sincerely,

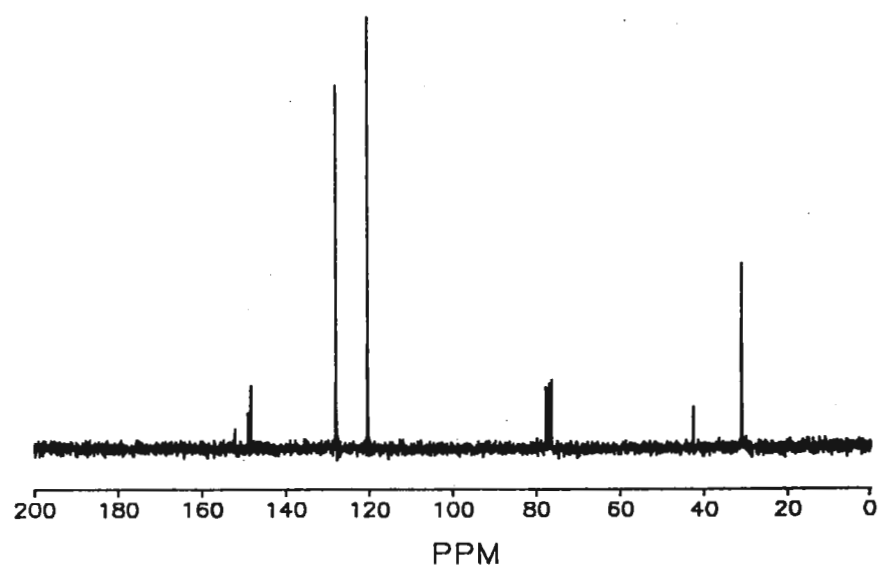
W. L. Jarrett

Paul K. Casey

Lon J. Mathias



**Figure 1. Solid-state  $^{13}\text{C}$  spectrum of polycarbonate.**



**Figure 2. Solution  $^{13}\text{C}$  spectrum of polycarbonate.**



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every experiment you've ever dreamed of, and together with its battery of distributed microprocessors, controls every function and parameter of the system.

All of this makes the MSL the ideal research spectrometer for everything from catalysts to coal, polymers to proteins, rocks to rats.

So, stop dreaming and call your nearest Bruker sales representative for more information or a demonstration. Once you've seen the MSL in action, it may even convince you that dreams can come true.

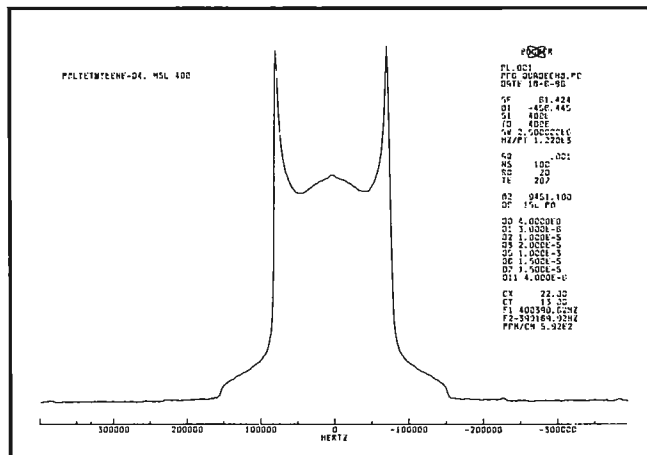


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# MSL Performance Characteristics



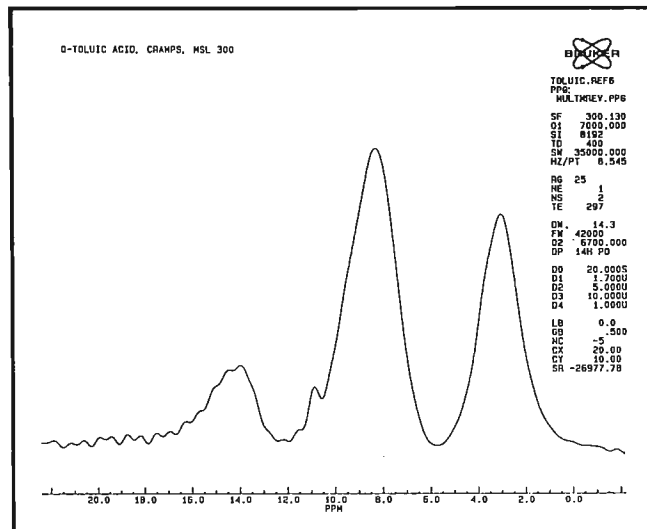
The  $^2\text{H}$  lineshape of deuterated polyethylene. This pattern is a superposition of a more or less gaussian line from the amorphous segments of polyethylene and a broad pake doublet for the crystalline  $=\text{CD}_2$  fragments.

## Wideline

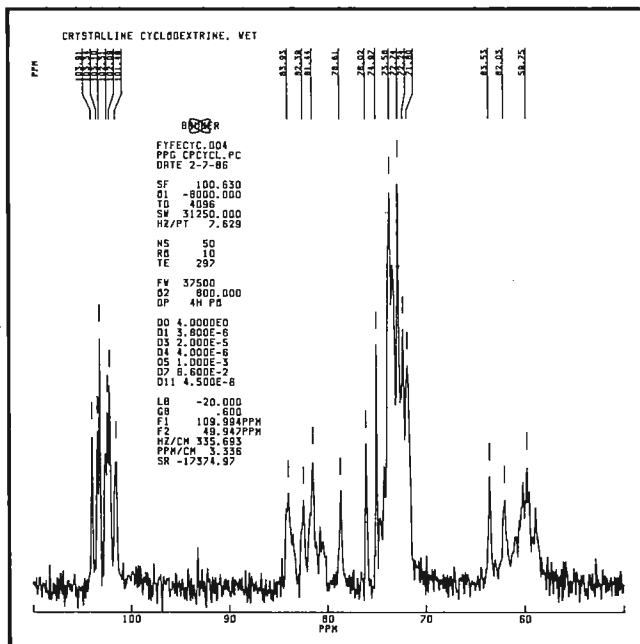
- ☐ 1 Kw RF power
- ☐ Ultra-short dead times
- ☐ Low Q solenoid probes
- ☐ 2 MHz system bandwidth

## VTMAS

- ☐ High decoupling power
- ☐ Pneumatic sample insert/eject
- ☐ Angle and tuning insensitive to VT
- ☐ Ultra-high speed spinning



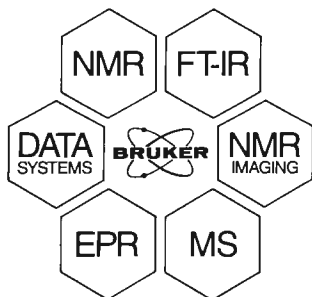
The CRAMPS spectrum of o-toluic acid. The peaks for methyl, phenyl- and carboxyl protons are clearly resolved.



Crystalline cyclodextrine. A high level of decoupling power is needed to achieve the high resolution shown in this spectrum. This is even more true when the sample is wet, as in this case, since the dielectric losses are greater.

## CRAMPS

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- ☐ Precise quadrature pulse adjustment
- ☐ Ultra-short dead times
- ☐ Sharp 90-degree pulses



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 St. Catharines, Ontario  
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 (416) 688 5550  
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Nov. 16, 1988

(received 11/26/88)

Dear Prof. Shapiro,

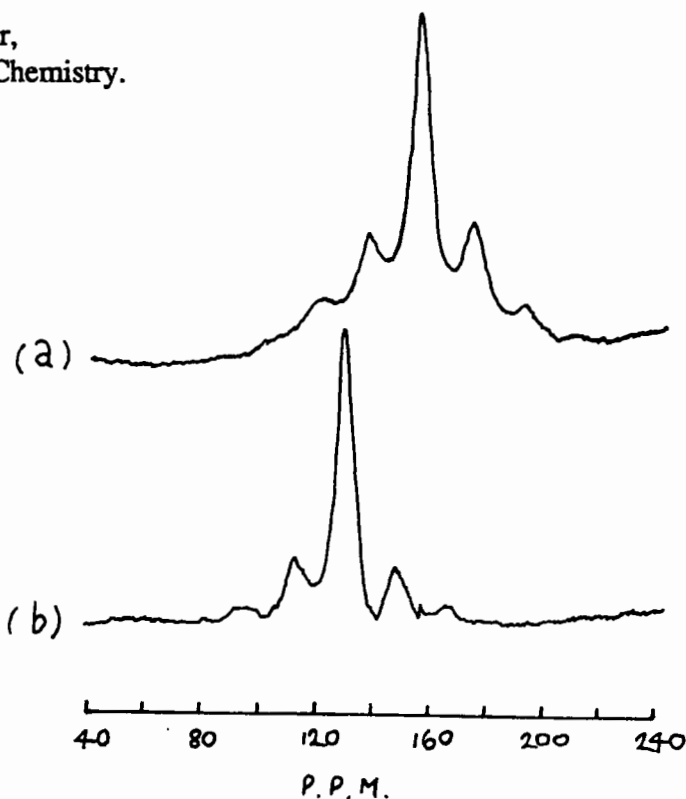
Catherine Duke and I are currently studying the surfaces of KF-alumina and KF-silica using  $^{19}\text{F}$  m.a.s. n.m.r. Although  $\text{NH}_4\text{F}$ -alumina and -silica have been studied by  $^{19}\text{F}$  n.m.r. (e.g. J.R. Schulp & R. W. Vaughan, *J. Catal.* **99** 304 (1986)), m.a.s. was not used.  $^{19}\text{F}$  m.a.s. has however been used in the analysis of fluorohydroxyapatite (Yennowski & Mobley, *JACS* **105** 6191 (1983)). The two spectra shown in the figure are those of KF-silica and KF-alumina, both at a loading of 3.3 mmol KF/g support and both air dried at  $400^\circ\text{C}$ . The main peak occurs at -129 ppm in KF-silica and -156 ppm in KF-alumina. These positions suggest that the species forming are  $\text{SiF}_6^{2-}$  on silica (literature value, -129 ppm) and  $\text{AlF}_6^{3-}$  on alumina. A mixed sample of  $\text{KAlF}_4$  and  $\text{K}_3\text{AlF}_6$ , diluted with either KBr or alumina to reduce dipolar interactions, gives a peak at -155 ppm; i.r. evidence indicates that  $\text{AlF}_6^{3-}$  is forming rather than  $\text{AlF}_4^-$ .

The spectra were obtained on a Bruker AC200 using our home-built  $^{19}\text{F}$  m.a.s. probe, and the samples were spun at about 3300 Hz. Because of the high chemical shift anisotropy of fluorine (323 ppm for KF, equivalent to 65 kHz on our instrument), spinning side bands can be seen on either side of each peak.

Yours Sincerely,

 Jack M. Miller,  
Professor of Chemistry.

Figure:

(a) KF-alumina, 3.3 mmol  $\text{g}^{-1}$ (b) KF-silica, 3.3 mmol  $\text{g}^{-1}$ 





The Squibb Institute  
for Medical Research

November 29, 1988  
(received 12/2/88)

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

**Characterization and Quantification of the Pseudopolymorphs  
of Aztreonam by  $^{13}\text{C}$  CP/MAS**

Dear Dr. Shapiro,

Aztreonam is a synthetic, monocyclic beta-lactam antimicrobial agent which is active against gram-negative organisms. Four distinct crystalline forms of aztreonam ( $\alpha$ ,  $\beta$ ,  $\delta$ , and  $\epsilon$ ) have been observed through the utilization of powder x-ray diffraction (XRD) techniques. The  $\delta$  and  $\epsilon$  forms may only be generated by specific recrystallization techniques utilizing dichloromethane/ $\text{H}_2\text{O}$  and dimethylacetamide, respectively. These two forms are not usually encountered. The  $\beta$  form of aztreonam is the active antimicrobial agent and is obtained through recrystallization of the  $\alpha$  form from ethanol solutions. XRD techniques could be used to determine the amount of  $\alpha$  aztreonam present in production lots of the  $\beta$  pseudopolymorph, but differential scanning calorimetry has proven to be more sensitive. Solid state carbon-13 NMR is now being investigated as a possible quantitative technique.

The solid state  $^{13}\text{C}$  NMR spectra of  $\alpha$  and  $\beta$  aztreonam are shown below (Figure 1). These spectra were acquired on a Bruker AM-250 spectrometer under magic angle spinning conditions (4.5 kHz) utilizing the cross polarization technique (2 msec. contact time, 10 sec. recycle time, 5.50  $\mu\text{sec}$ . pulse width,  $90^\circ$ ). A total of 256 transients were co-added (4K data set, spectral width 15500 Hz), and a 10 Hz line broadening factor used to improve the signal-to-noise ratio. It is readily apparent that these experimental conditions were sufficient to acquire excellent spectra.

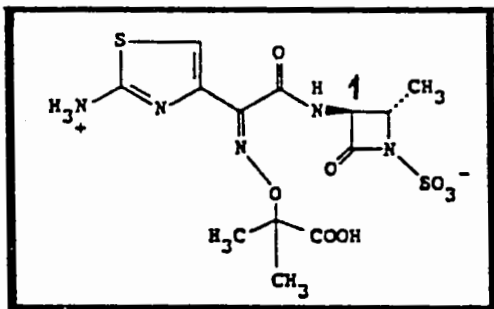
It is interesting to note that the  $\alpha$  form of aztreonam displays three distinct carbonyl resonances at 174.5, 165.7, and 160.3 ppm (externally referenced to TMS). In contrast, the  $\beta$  form displays two resonances (170.8 and 162.3 ppm) with the possibility of a third resonance appearing as a shoulder at approximately 160 ppm. A slight shift in frequency also exists for the amine carbon (C1) in each compound ( $\alpha$  60.5 ppm,  $\beta$  64.3 ppm). These differences in resonances for equivalent carbons clearly show the distinct spatial orientation of each pseudopolymorph and allow one to develop a quantitative solid state NMR assay.

Quantitative analysis by NMR necessitates that a number of precautions are taken as outlined recently by J.K. Gard *et al.* (TAMU, 359, p. 50). Saturation was prevented by measuring the spin-lattice relaxation time in the rotating frame ( $T_{1\rho} = 1.5$  sec.) and incorporating the appropriate  $5 * T_1$  recycle time into the pulse sequence. The outlined experimental parameters previously



discussed have also addressed any possible problems with adequate S/N, and digitization errors. The contact time was also optimized by measuring the absolute intensity of the specific resonance as a function of the contact time,  $T_{cp}$ . At the present time, approximately twenty reference samples are being prepared within the concentration range of 0 - 20 %  $\alpha$  content within  $\beta$  (wt. % basis). Quantitative spectra will be acquired under two different experimental conditions. One set of spectra will utilize the contact time of 1.0 msec. which is optimized for quantitation of the amine resonances. The other data set will employ the average optimal contact time for the carbonyl resonances, 2.0 msec. Peak area measurements will be performed by integration and by spectral curve fitting. The results will be compared and the appropriate method used to validate the assay. From the present spectra, it is apparent that the resonances which will be used for quantitation will overlap with each other, spectral deconvolution techniques (MEM, LP) may then be utilized.

From the preliminary results obtained, solid state NMR appears to be a very promising technique to assay pharmaceutical samples. One of the main advantages is that this technique is non-destructive and experiences no preferential orientation effects which may be encountered in XRD and diffuse reflectance infrared Fourier transform spectroscopy (DRIFTS) methods.



Sincerely,

*David E. Bugay*  
David E. Bugay

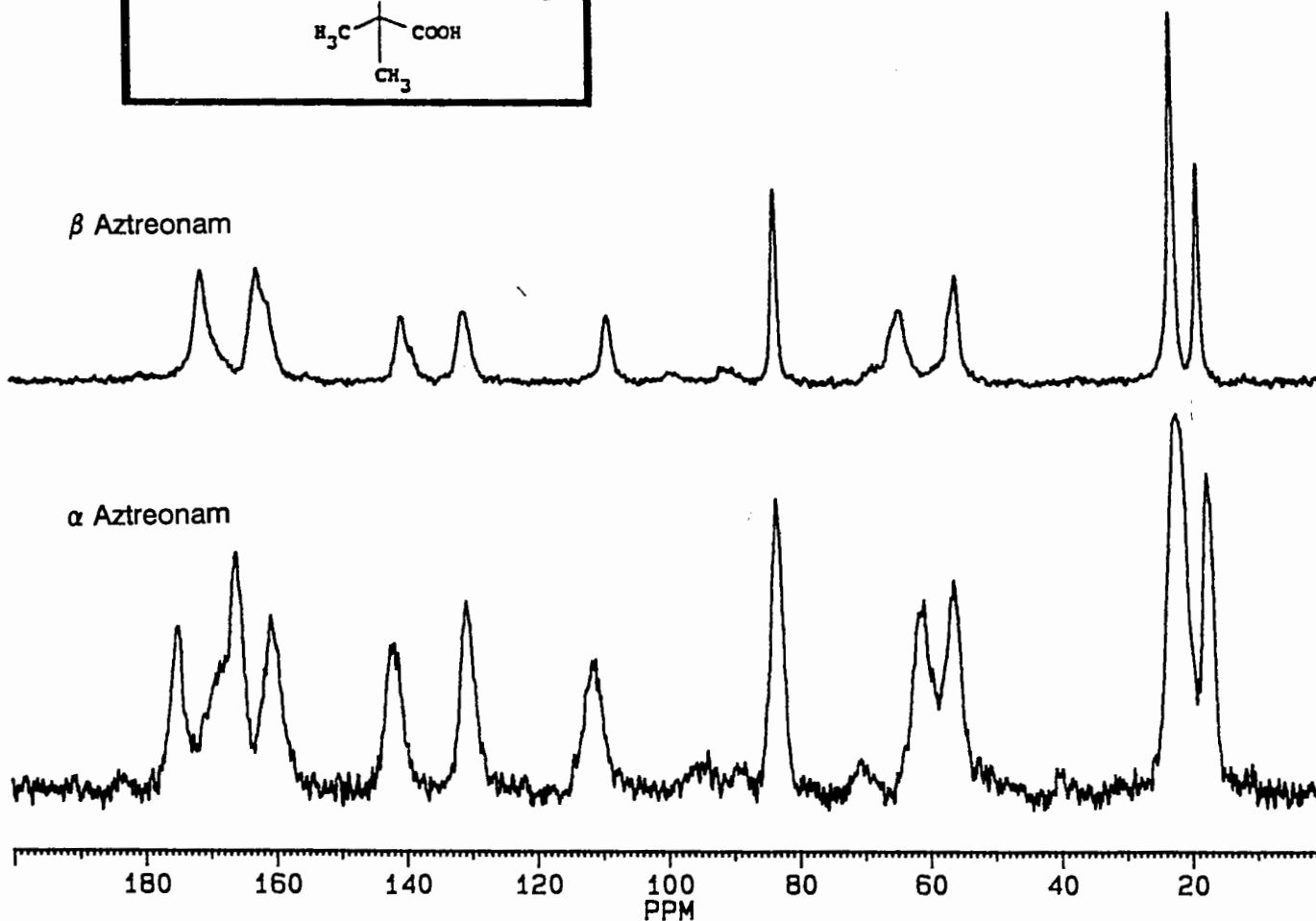


Figure 1.  $^{13}\text{C}$  CP/MAS NMR spectrum of  $\alpha$  and  $\beta$  Aztreonam.

**THE JOHNS HOPKINS UNIVERSITY**  
**SCHOOL OF MEDICINE**  
*and*  
**THE JOHNS HOPKINS HOSPITAL**

DEPARTMENT OF RADIOLOGY  
 AND  
 RADIOLOGICAL SCIENCE

Mailing Address:  
 THE JOHNS HOPKINS HOSPITAL  
 Baltimore, Md. 21205

November 23, 1988

Dr. Bernard L. Shapiro  
 Editor/Publisher  
 TAMU NMR Newsletter  
 966 Elsinore Court  
 Palo Alto, California 94303

"Evaluation of  $^{31}\text{P}$  Sensitivity on Wide-Bore Magnets"

Dear Barry:

Many of us have assumed that in order to obtain higher sensitivity on biological samples where metabolite concentrations are limited, the larger the sample volume within the coils, the greater the sensitivity. In theory this is true, but in practice gains in sensitivity due to an increase in sample volume are often negated by the increase in linewidth due to the poorer field homogeneity obtainable in the larger bore probes. We have been conducting  $^{31}\text{P}$  sensitivity tests of our Bruker AM 360 WB in our 10 mm broad-banded probe and our 20 mm  $^{31}\text{P}/^{13}\text{C}$  pneumatically switchable probe. Under the conditions of our experiment (0.1 M phosphate, pH 7; SW = 2000 Hz; AQ = 2.048 s) we obtain a S/N of 150 and 130 in the 10 and 20 mm probes, respectively. Most of the differences can be attributed to the better field homogeneity in the 10 mm sample. The linewidth obtained on the 10 mm probe was 2.5 Hz and 5.2 Hz for the 20 mm probe. Even in biological samples we see slightly higher sensitivity with the 10 mm probe. We have obtained quite satisfactory  $^{31}\text{P}$  NMR spectra of

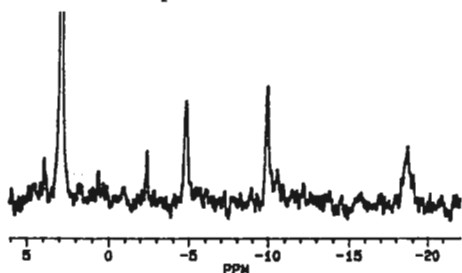


Figure 1

perfused murine RIF-1 cells embedded in an alginate gel in our 10 mm probes (Figure 1). This spectrum was obtained in 8 minutes from  $10^8$  RIF-1 cells embedded in alginate gel. The savings in the numbers of cells, culture media, and perfusate realized by using the smaller volume of the 10 mm probe has made this our system of choice for perfused cell studies.

We would be interested in hearing from other readers about the relative sensitivity of their 10 and 20 mm probes. Until the next ultimatum...

Sincerely yours,

*Michael P. Gamcsik*

Michael P. Gamcsik

*Jerry D. Glickson*

Jerry D. Glickson

*Janna P. Wehrle*

Janna P. Wehrle

*Kathy A. McGovern*

Kathy A. McGovern

## Non-magnetic Capacitors for NMR Applications



*An array of Polyflon non-magnetic capacitors, many of which are used in NMR/MRI applications.*



*Polyflon's rugged trimmer and variable capacitors meet rigid NMR/MRI specifications.*

Polyflon's variable, trimmer and fixed capacitors meet critical non-magnetic, high voltage, high power, high Q NMR specifications.

A test report was recently submitted to Polyflon by a University deeply involved in NMR research. Polyflon trimmers were subjected to various tests in order to gather essential data (Q, DF, L, ESR, EPR) for use in the design of NMR RF equipment. Tests were conducted at 10, 100, 200, 400, 500, and 600 MHz. These trimmers were first exposed to a 4.7 Tesla magnetic field for detection of the presence of any magnetic particles in the trimmers. These tests conclusively showed there were no magnetic particles present.

Maximum dissipation displayed by the trimmers was 0.000125 with a minimum less than 0.0001, resulting in Q measurements from 8,000 to more than 10,000, at 600 MHz. (NOTE: Customers, who have tested Polyflon trimmers in their own laboratories, have measured Q's greater than 20,000 at 500 MHz.) The inductance of the trimmers was less than one nHy and maximum ESR at 160 milliohms with minimum EPR at 100 megohms.

Polyflon trimmers and variable capacitors provide linear tuning with no reversal in capacitance during capacitor adjustment. They are used in NMR pulsed applications

with operating voltages up to 15 Kv peak and duty cycles ranging up to 10 %. Standard range of variable capacitor designs are available with a minimum capacitance of less than 1 pF to a maximum capacitance of 125 pF.

Fixed capacitors, used for 6 Kv peak pulsed applications, are available with capacitance values from 50 pF to 250 pF. For 10 Kv peak voltage applications, fixed capacitors are available with capacitance values ranging from 25 pF to 150 pF.

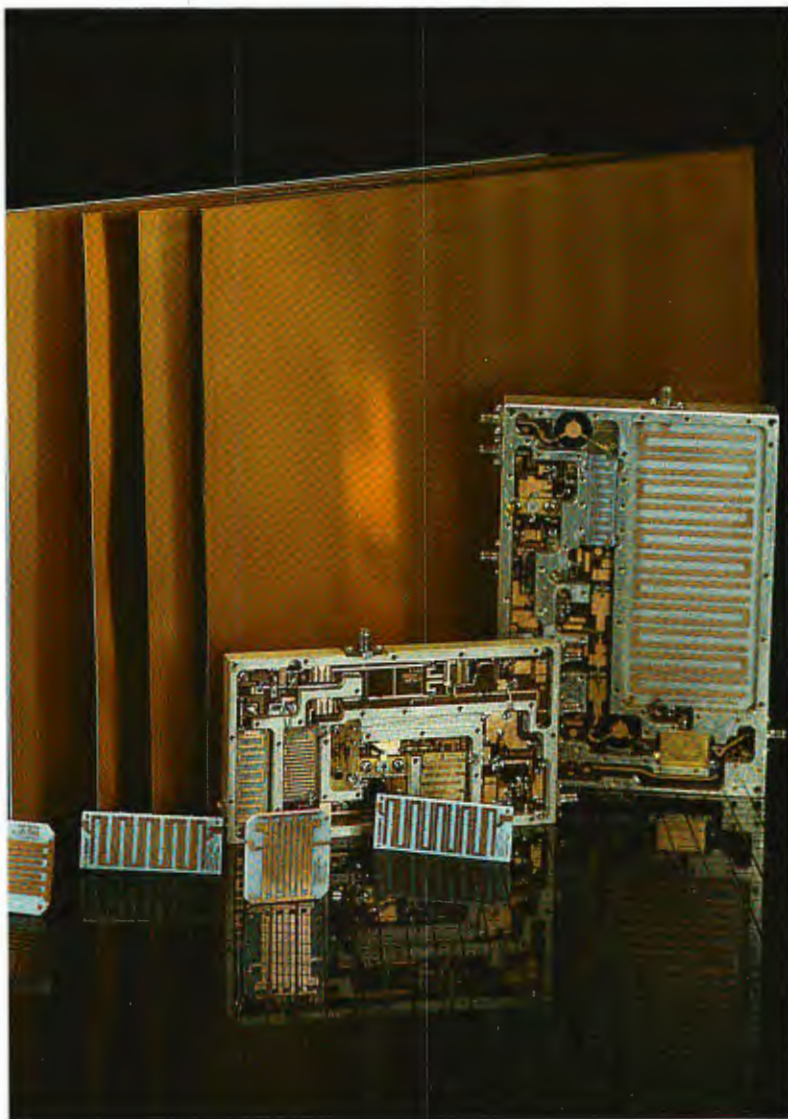
Polyflon also designs and manufactures variable, trimmer and fixed capacitors to customer specifications.

### Polyflon Capacitor Advantages:

- Non-magnetic
- Low dissipation factor (low loss)
- Extremely High Q
- Low ESR
- High EPR
- Linear tuning (no capacitance reversal)
- High voltage capability
- Rugged design
- Long operating life



## Material Technology for NMR Product Applications



*Pure PTFE dielectric is used in all Polyflon CuFlon® microwave substrates, assuring low loss.*

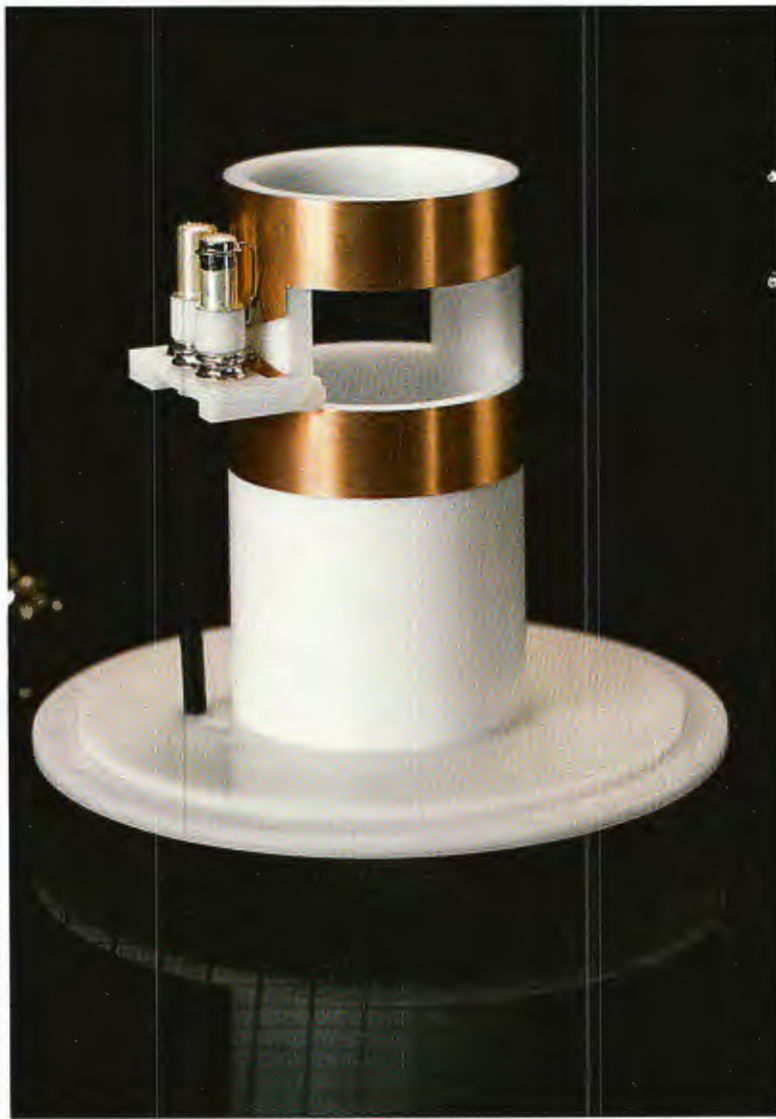
Polyflon uses only pure PTFE dielectric in its CuFlon® microwave substrates which provides one of the best low loss dielectrics in the industry.

Since nothing is added to the PTFE, the dielectric constant of 2.1 remains consistent over an extremely wide range of frequencies.

The unique, proprietary electroplating technology for PTFE, developed by Polyflon, permits design and fabrication of superior RF components.

An intimate bond is produced between the metal surfaces and the PTFE, with no other element or media between them. The dissipation factor and Q is then that of the PTFE substrate itself.

Very low loss components are produced with this technol-



*80 MHz copper plated PTFE saddle coil assembly.*

ogy that can be used with excellent results at very high microwave frequencies.

Polyflon's CuFlon substrate materials, found in many NMR/MRI applications, are used in various coil designs such as surface, solenoid and saddle configurations. CuFlon is also used as a substrate in pulsed RF amplifiers, wide-band RF transformers, and chip capacitors for tuning and matching elements.

Polyflon's expertise in the PTFE plating technology can and does provide customers with rugged and reliable products for critical NMR/MRI applications.

*Call or write for information.*

# CRANE

®

# POLYFLON

Polyflon Company • 35 River Street, New Rochelle, NY 10801  
Tel: (914) 226-7000 • FAX: (914) 226-2004



國立清華大學  
NATIONAL TSING HUA UNIVERSITY

HSINCHU, TAIWAN 30043, REPUBLIC OF CHINA

DEPARTMENT OF CHEMISTRY

CHEMISTRY BUILDING

Professor Bernard L. Shapiro  
966 Elsinore Court  
Palo Alto, CA 94303  
U. S. A.

Dec. 5, 1988  
(received 12/12/88)

" $^1\text{H}$  NMR Resonance Assignments in Methyl Group Region of Cobrotoxin"

Dear Professor Shapiro:

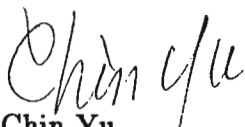
Cobrotoxin is a neurotoxic protein isolated from the venom of Taiwan cobra (naja naja atra). This protein, which blocks the neuromuscular transmission at the post-synaptic membrane by the specific binding to the acetylcholine receptors, contains 62 amino acid residue (Mr 6949) with 4 disulfide bond bridges.

Shown in Figure is a DQF-COSY spectrum of methyl group region for a 20 mM cobrotoxin in  $\text{D}_2\text{O}$  (pH=3.6). There are two isolusine (Ile 50, Ile 52) and a valine (Val 34) residues in this plot. The assignment of  $\delta$  and  $\gamma$  methyl groups in isolusine residue were confirmed by cross peaks in corresponding position in NOESY spectrum (not shown).

The DQF-COSY experiment were recorded on our Bruker AM-400 spectrometer equipped with an Aspect 3000 computer. The 2D data was processed on a micro Vax III computer, using a version of the Fourier transform software of Dr. Dennis Hare.

Sincerely,

Chang-Shin Lee  
Research Assistant

  
Chin Yu  
Associate Professor of Chemistry

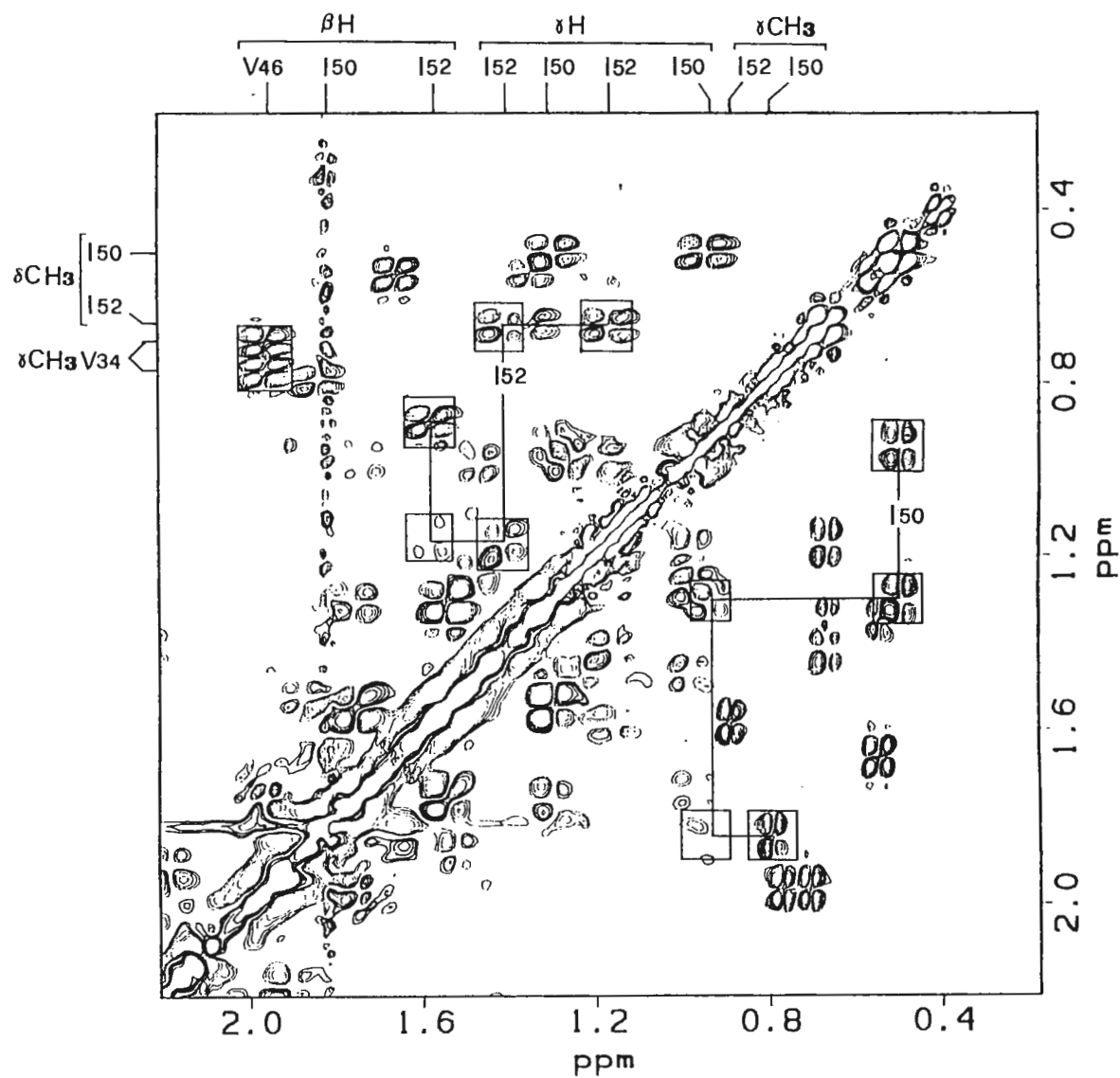


Figure 2QF-COSY spectrum of cobrotoxin of methyl group region



THEIX  
63122 CEYRAT  
FRANCE

Professor B.L. Shapiro  
966 Elsinore court  
Palo Alto  
California 94303  
ETATS UNIS

### FOIE GRAS and NMR

Theix, 1988 December 6  
(received 12/17/88)

Dear Professor Shapiro,

For Christmas we are very glad to send you some spectra of FOIE GRAS. NMR is a suitable method to check the quality of this famous French food. Moreover as every one knows, NMR is a non destructive method, so there were some advantages in carrying out these studies! Professors G.J. and M.L. Martin in Nantes could give you some information as to the best drink.

Lipid content was determined by proton spectroscopy (Fig.1) with a magnet of 0.47 T and a 10 cm wide bore. Using  $^{13}\text{C}$  spectroscopy, different data could be obtained. The unsaturation index was easily evaluated by comparison of olefinic carbons. The position of different fatty acids on  $\text{C}_{1,3}$ ,  $\text{C}_2$  glycerol was determined by selective observation of carbonyl carbons of triglycerides (Fig. 2). The lipolysis was evaluated by difference in chemical shift between carbonyl of free fatty acids and triglycerides.

**Merry Christmas and Happy New Year !**

A handwritten signature in black ink, appearing to read "Bonnet", with a long horizontal flourish extending to the right.

MADELEINE BONNET

A handwritten signature in black ink, appearing to read "Renou", with a long horizontal flourish extending to the right.

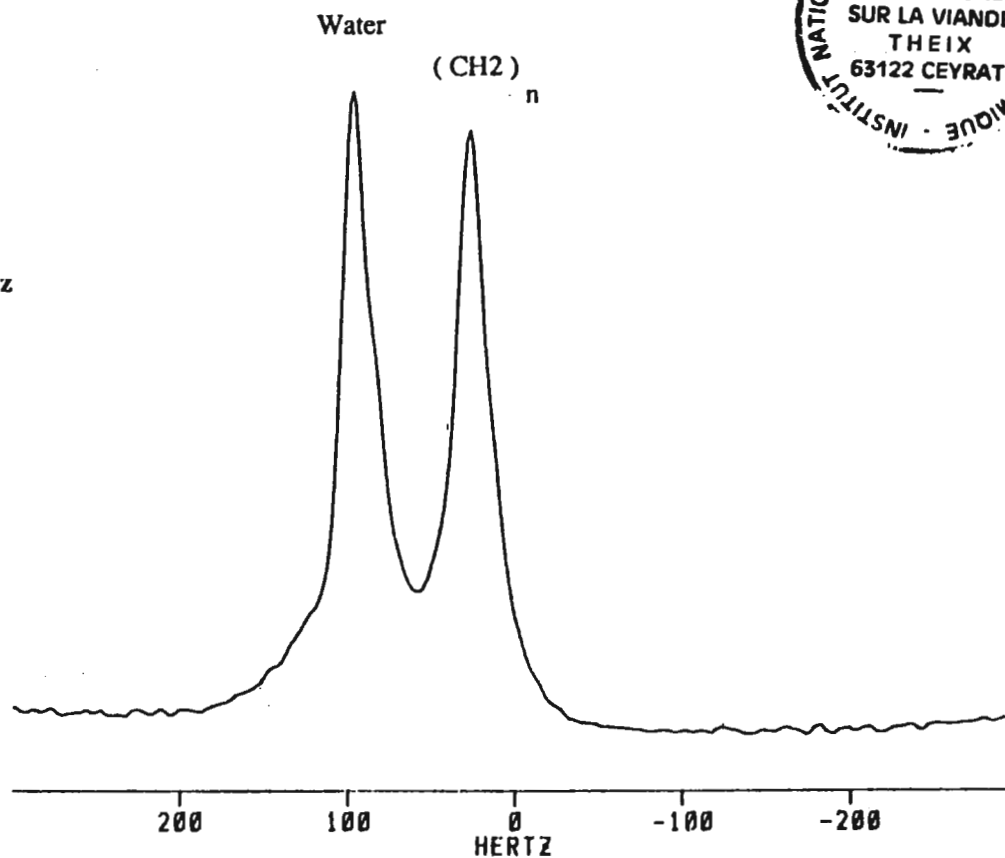
J.P.RENOU

## FOIE GRAS



II-1 20 MHz  
(10 cm)

Figure 1

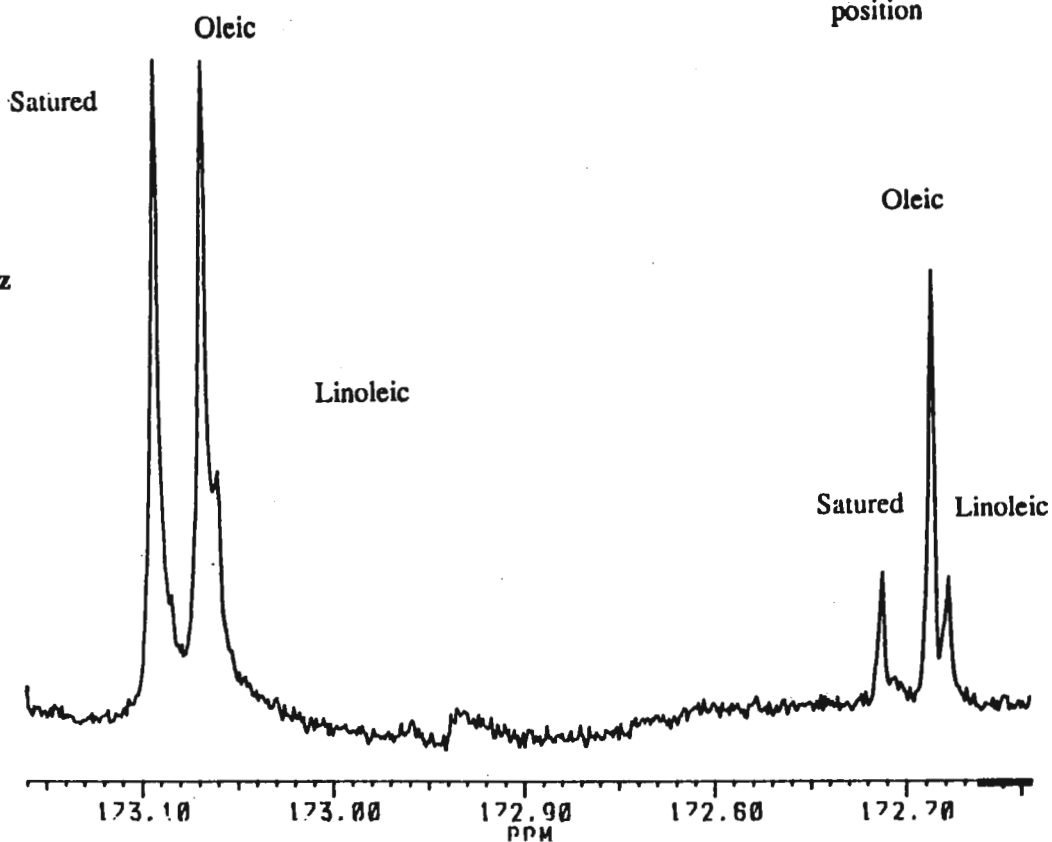


1-3  
position

2  
position

C-13 100MHz  
(10 mm)

Figure 2.





# NMR Sample Tubes

For evidence of Norell's high performance quality, we reproduce **CERTIFICATES** submitted by individuals who actually tested and compared our tubes vs those of our competition. SEE OTHER SIDE.

## Don't let them fool you!

Claims of infinitely better bargains are worthless! In general, such claims are made only by those who do not have credible data or perhaps do not comprehend the meaning of finite values.

If you want to be "THRIFTY", we recommend our economical No. 502 NMR Sample Tube, which is of higher quality with closer tolerances than competitor's "Thrift Tube" and yet sells for \$0.75 each in lots of 100 tubes, and \$0.70 each in lots of 300 tubes.

For **HIGH PRECISION** and **ULTRAPRECISION** work, we recommend our No. 507-HP and No. 508-UP NMR Sample Tubes.

### 5mm o.d. THIN WALL NMR SAMPLE TUBES

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

Standard tube length: 178mm (7 inches);  
o.d.  $4.97 \pm 0.013$ mm (0.0005 in.);  
i.d.  $4.20 \pm 0.025$ mm (0.001 in.);  
camber  $\pm 0.013$ mm (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. 507-HP HIGH PRECISION for high resolution NMR

Standard tube length: 178mm (7 inches);  
o.d.  $4.97 \pm 0.013$ mm (0.0005 in.);  
i.d.  $4.20 \pm 0.025$ mm (0.001 in.);  
camber  $\pm 0.025$ mm (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. 506-P PRECISION for medium and high resin. NMR

Standard tube length: 178mm (7 inches);  
o.d.  $4.97 \pm 0.025$ mm (0.001 in.);  
i.d.  $4.20 \pm 0.025$ mm (0.001 in.);  
camber  $\pm 0.025$ mm (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. XR-55 PRECISION FOR medium and high resin. NMR

Standard tube length: 178mm (7 inches);  
o.d.  $4.97 \pm 0.025$ mm (0.001 in.);  
i.d.  $4.20 \pm 0.025$ mm (0.001 in.);  
camber  $\pm 0.03$ mm (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. 505-P PRECISION for medium and high resin. NMR

Standard tube length: 178mm (7 inches);  
o.d.  $4.97 \pm 0.03$ mm (0.001 in.);  
i.d.  $4.20 \pm 0.03$ mm (0.001 in.);  
camber  $\pm 0.04$ mm (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. 502 THROWAWAY TYPE

Standard tube length: 178mm (7 inches)  
o.d.  $4.97 \pm 0.05$ mm (0.002 in.);  
i.d.  $4.20 \pm 0.05$ mm (0.002 in.);  
camber  $\pm 0.07$ mm (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.

### 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.  $10.00 \pm 0.013$ mm (0.0005 in.);  
i.d.  $8.76 \pm 0.025$ mm (0.001 in.);  
camber  $\pm 0.007$ mm (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 resin. NMR

Standard length: 178mm (7 inches);  
o.d.  $10.00 \pm 0.013$ mm (0.0005 in.);  
i.d.  $8.76 \pm 0.025$ mm (0.001 in.);  
camber  $\pm 0.013$ mm (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 resin. NMR

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

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

**NOTE:** Other tube sizes  
available, please inquire.

#### PTFE VORTEX PLUGS

All sizes - specify tube size...\$40/lot of 5  
Rods for all Vortex Plugs.....\$10 each.

#### PTFE Machined Tube Caps

5mm ... \$25/25 caps; \$45/50 caps  
10mm ... \$28/25 caps; \$50/50 caps



**PRECISION THIN WALL<sup>®</sup>**  
**XR-55 NMR<sup>®</sup>** SAMPLE TUBES

**A new dimension in performance!**  
**... only \$2.00 each, in lots of 100 tubes.**

**Over 1,000,000 in use in USA and over 1,000,000 outside USA.**

Norell, Inc., 314 Arbor Ave, Landisville, NJ 08326 Tel. 609-697-0020, toll-free 1-800-222-0036





21

I have evaluated Norell's XR-55 Precision NMR Sample Tubes and found them to be:

☐ Excellent ☒ Very Good ☐ Satisfactory ☐ Unsatisfactory

Norell's XR-55 NMR Sample Tube was compared with the following competitive tube or tubes:

WILMAD CAT. No. 528 PP

(give cat. number and name of manufacturer)

Type of NMR equipment used in the above evaluation: Varian EM-300

Name: Peter Balocco Title: Phys. Teach.

Address: 1000 E. 1st St., Dayton, OH 45424

Date: July 22, 1982

Phone: 937-272-7311

We expect your findings from the supplied batch of 100 tubes to be unbiased and we reserve the right to share your findings with others inquiring about our NMR sample tubes. Norell, Inc. 314 Arbor Ave., Landsville, NJ 08326 USA.

CERTIFICATE 107

6

I have evaluated Norell's XR-55 Precision NMR Sample Tubes and found them to be:

☒ Excellent ☐ Very Good ☐ Satisfactory ☐ Unsatisfactory

Norell's XR-55 NMR Sample Tube was compared with the following competitive tube or tubes:

EM 300 Varian NMR

(give cat. number and name of manufacturer)

Type of NMR equipment used in the above evaluation: The SRA Instrument

Name: L. WANKS

Address: 3231 20th Street, S.E., Atlanta, GA 30316

Date: July 1982

Phone: 404-525-9999

We expect your findings from the supplied batch of 100 tubes to be unbiased and we reserve the right to share your findings with others inquiring about our NMR sample tubes. Norell, Inc. 314 Arbor Ave., Landsville, NJ 08326 USA.

CERTIFICATE 167

I have evaluated Norell's XR-55 Precision NMR Sample Tubes and found them to be:

☐ Excellent ☒ Very Good ☐ Satisfactory ☐ Unsatisfactory

Norell's XR-55 NMR Sample Tube was compared with the following competitive tube or tubes:

WILMAD 507 PP

(give cat. number and name of manufacturer)

Type of NMR equipment used in the above evaluation: Varian EM-300

Name: J. C. Edwards Title: ASST. Prof

Address: Box 40 MTSY

Date: July 1982

Phone: 605-948-2954

We expect your findings from the supplied batch of 100 tubes to be unbiased and we reserve the right to share your findings with others inquiring about our NMR sample tubes. Norell, Inc. 314 Arbor Ave., Landsville, NJ 08326 USA.

CERTIFICATE 125

I have evaluated Norell's XR-55 Precision NMR Sample Tubes and found them to be:

☐ Excellent ☐ Very Good ☐ Satisfactory ☐ Unsatisfactory

Norell's XR-55 NMR Sample Tube was compared with the following competitive tube or tubes:

WILMAD 507 PP

(give cat. number and name of manufacturer)

Type of NMR equipment used in the above evaluation: Varian EM 300

Name: STEVEN WASSER Title: Staff Chemist

Address: 2100 S.E. Main St.

Date: 4/7/82

Phone: 714-957-7350

We expect your findings from the supplied batch of 100 tubes to be unbiased and we reserve the right to share your findings with others inquiring about our NMR sample tubes. Norell, Inc. 314 Arbor Ave., Landsville, NJ 08326 USA.

CERTIFICATE 111

I have evaluated Norell's XR-55 Precision NMR Sample Tubes and found them to be:

☐ Excellent ☒ Very Good ☐ Satisfactory ☐ Unsatisfactory

Norell's XR-55 NMR Sample Tube was compared with the following competitive tube or tubes:

528-PP

(give cat. number and name of manufacturer)

Type of NMR equipment used in the above evaluation: WH-250 Bruker

Name: L. Overman Title: Professor

Address: Department of Chemistry

Date: 7-8-82

Phone: 714-933-7156

We expect your findings from the supplied batch of 100 tubes to be unbiased and we reserve the right to share your findings with others inquiring about our NMR sample tubes. Norell, Inc. 314 Arbor Ave., Landsville, NJ 08326 USA.

CERTIFICATE 105

I have evaluated Norell's XR-55 Precision NMR Sample Tubes and found them to be:

☐ Excellent ☒ Very Good ☐ Satisfactory ☐ Unsatisfactory

Norell's XR-55 NMR Sample Tube was compared with the following competitive tube or tubes:

WILMAD 507 PP

(give cat. number and name of manufacturer)

Type of NMR equipment used in the above evaluation: Varian EM 300

Name: John H. H. H. Title: Asst. Prof

Address: University of California

Date: 7/1/82

Phone: 916-484-4458

We expect your findings from the supplied batch of 100 tubes to be unbiased and we reserve the right to share your findings with others inquiring about our NMR sample tubes. Norell, Inc. 314 Arbor Ave., Landsville, NJ 08326 USA.

CERTIFICATE 126



# PERFORMANCE



While our competition makes many empty claims ..... we give you instead actual performance test results carried out by NMR Spectroscopists who signed their name to authenticate them. Norell, Inc. 314 Arbor Ave., Landsville, NJ 08326 USA



**Amoco Corporation**

Amoco Research Center  
Post Office Box 400  
Naperville, Illinois 60566  
312-420-5111

December 6, 1988 (received 12/9/88)

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

Dear Barry:

Rotor Tachometer for a Chemagnetics Solids Probe

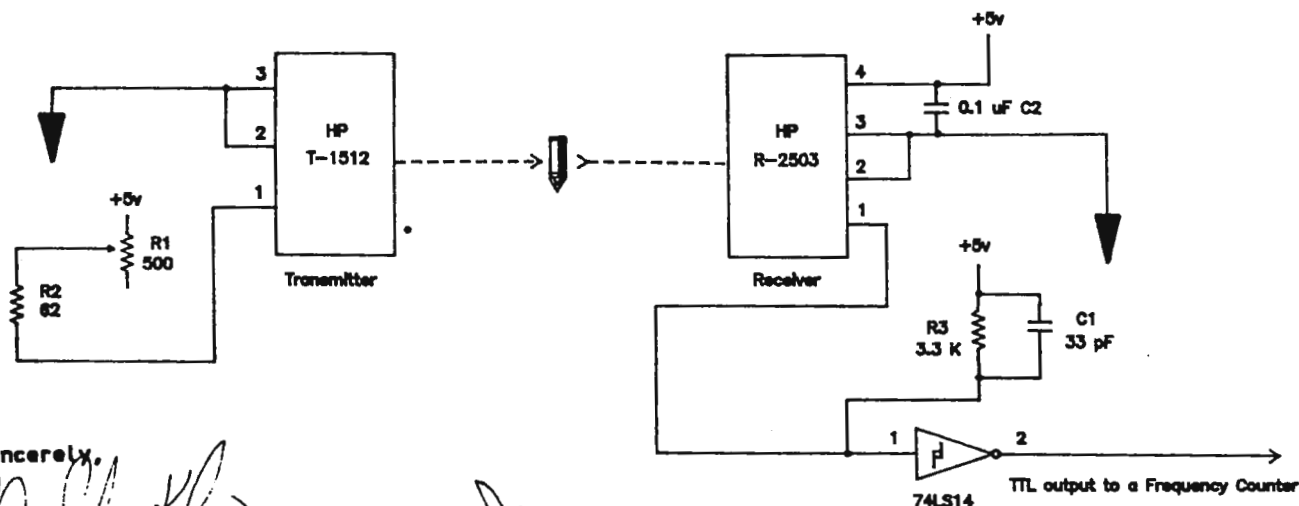
Several of our spectrometers (M-100, CMX-200, NTC-300 and VXR-400) are equipped with Chemagnetic probes used to study a variety of nuclei in the solid state. It should be obvious from the range of spectrometers interfaced to Chemagnetic probes that we are quite pleased with their performance. However, we have found the absence of a tachometer to be an annoyance that we have recently corrected.

The main components of the tachometer circuit (Figure 1) are a Hewlett Packard fiber optic transmitter (HP T1512) and receiver (HP R2503). The transmitter provides a constant light source to illuminate the rotor, while the light reflecting from the rotor is sent to the receiver. A black stripe painted down the side of a white rotor will interrupt the reflected light and cause the receiver to turn on and off. This generates a signal out of the receiver that corresponds to the frequency of the revolutions of the rotor.

To implement the design, a duplex fiber optic cable (HP HFBR3610) was inserted into a hole, perpendicular to the rotor, in the side of the probe spinning module. The cable was then routed through the top of the probe head and, to avoid sharp bends, out through the top of the magnet bore. Half of the cable carries light emitted by the transmitter. The intensity of this light can be varied with potentiometer R1 (in series with current limiting resistor R2) in order to achieve optimum signal on the receiver output. Too much light reflecting off of the rotor gives an unstable signal, while not enough light causes the receiver to malfunction. The receiver (containing a photodetector and a DC amplifier) transforms the reflected light provided by the other half of the fiber optic cable into a TTL signal. The signal is then fed through a Schmitt trigger inverter to sharpen its edges. The output of the inverter is tied to a front panel BNC jack for connection to an external frequency counter to display the rotor speed.

The tachometer has been in use on two Chemagnetics solids probes for over one month (on a Varian VXR 400). Rotor frequency calculations, using spinning side bands on an NMR spectrum, have proven the tachometer to be extremely accurate.

Figure 1: Rotor Tachometer Circuit



Sincerely,

*J. J. Klein*  
J. J. Klein

*G. J. Ray*  
G. J. Ray

## Ninth International Meeting on

## NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

**University of Warwick at Coventry**  
**10-14 July 1989**

### **Introduction**

The ninth international meeting on NMR Spectroscopy will take place at the University of Warwick at Coventry from Monday 10 July to Friday 14 July 1989, with participants foregathering on the afternoon and evening of Sunday 9 July 1989.

The meeting is being organised jointly by the Royal Society of Chemistry, and the Society's NMR Discussion Group.

The meeting is the ninth in the series (now biennial), previous meetings having taken place as follows:

|                 |                |                 |                 |
|-----------------|----------------|-----------------|-----------------|
| 1969 Birmingham | 1972 Guildford | 1975 St Andrews | 1978 York       |
| 1981 Exeter     | 1983 Edinburgh | 1985 Cambridge  | 1987 Canterbury |

### **Scientific Programme**

The meeting will deal with selected topics in NMR Spectroscopy and will comprise the following eight symposia, with the Chairmen and Invited Lecturers as indicated:

#### **1. Structural Elucidation in the Liquid State**

Chairman: J Feeney  
Invited Lecturer: D Turner

#### **2. Solid State**

Chairman: C J Groombridge  
Invited Lecturers: To be announced

#### **3. Non-Medical Imaging NMR Spectroscopy**

Chairman: E W Randall  
Invited Lecturers: L D Hall  
To be announced

#### **4. Biological Applications**

Chairman: J R Everett  
Invited Lecturers: J Griffiths  
W E Hull

#### **5. New Experimental Techniques**

Chairman: G A Morris  
Invited Lecturers: A Bax  
R Freeman

#### **6. Polysaccharides and Glycoproteins**

Chairman: C Brown  
Invited Lecturers: R A Dwek  
D Williams

#### **7. Data Analysis and Artificial Intelligence**

Chairman: R A Heammon  
Invited Lecturers: U Edlund  
M E Munk

#### **8. Less Common Nuclei**

Chairman: D G Gillies  
Invited Lecturers: C J Jameson  
J Jonas

### **Poster Sessions and Contributed Papers**

Two poster sessions are planned for the programme. There will also be an opportunity for a limited number of short contributions to be presented orally in the symposia. Anyone wishing to contribute a paper to one of the poster sessions, or to one of the symposia, should submit, **NOT LATER THAN 23 JANUARY 1989** a title and synopsis (up to 250 words) to Dr John F Gibson, the Royal Society of Chemistry, Burlington House, London W1V 0BN, indicating the appropriate symposium topic.

ICI is offering a student poster prize for the best poster presented solely by a student. The Organisers request that an indication is included on the synopsis as to whether the poster is eligible for consideration for the ICI student poster prize.

### **Social Programme**

A full programme of evening social events is planned, to include:

University Reception (Sunday)  
Civic Reception (Motor Museum) or Cathedral Tour (Tuesday)  
Conference Dinner (Thursday)

As has been the practice with all previous NMR meetings, the scientific sessions on Wednesday will terminate at lunchtime, so as to enable persons to participate in organised excursions on Wednesday afternoon and evening. Excursions proposed include: the Cotswolds (walking or touring), Stratford and other places of historic interest and scenic beauty in the area.

In addition, an accompanying persons programme will be arranged.

### **Fees**

The fees for attendance at the meeting have not been finalised, but it seems likely that the conference fee will be around £100 (students £50), and the accommodation for the full five day period will be around £100.



TO: Dr John F Gibson  
Secretary (Scientific)  
The Royal Society of Chemistry  
Burlington House  
London W1V 0BN

Please send me further details of the ninth international meeting on **NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY**, to be held at the University of Warwick at Coventry, 10-14 July 1989. (Available in February/early March 1989).

**PLEASE WRITE NAME AND ADDRESS CLEARLY ON THIS LABEL**

Name .....  
Address .....  
.....  
.....  
.....

*If undelivered, please return to:*

*The Royal Society of Chemistry,  
Burlington House, London W1V 0BN, UK.*

Please insert an 'X' in the appropriate box(es):

☐ I am interested in attending the 9th NMR meeting and  
would like to receive the Second Circular.

☐ I intend to offer a paper, for POSTER/ORAL  
presentation in Symposium. (Synopsis due 23 January 1989.)

.....  
Please indicate whether POSTER or ORAL contribution preferred, and also the particular symposium.

**NMR SPECTROSCOPY IN VIVO**  
(clinical applications)

"ICR 89" Satellite Congress  
LYON - July 10-11-12, 1989

The program will include invited lectures and posters (deadline for abstracts  
1st March 1989).

• **INVITED SPEAKERS:**

A.L. BENABID, J.F. BUDINGER, Ch. BOESH, B. CHANCE, P. COZZONE,  
J. FRAHM, D. GADIAN, J.D. GLIKSON, J.R. GRIFFITHS, C.B. HIGGINS,  
D. HOULT, J.M. LHOSTE, P.R. LUYTEN, R.L. NUNNALLY, B. ROSS, J.  
SEELIG, C.M. SEGEARTH, E.A. SHOUBRIDGE, R.G. SHULMAN, A.  
SYROTA, F. TERRIER, M.W. WEINER.

• **PRESIDENTS OF THE CONGRESS:** M. AMIEL, P. SERVOZ-GAVIN

Official languages : English, French  
Simultaneous translation.

• **SCIENTIFIC PROGRAM**

Thursday 11th July

Session 1 : Methods in NMR Spectroscopy-Potential hazards  
Session 2 : From Animal to human applications.

Wednesday 12th July

Session 3 : Clinical applications : Brain, oncology, pharmacology.  
Session 4 : Posters  
Session 5 : Clinical applications : liver, kidney, heart, muscle.

• **FOR FURTHER DETAILS**

Mailing Address, Conference Secretariat :

Pr. AMIEL  
Hôpital Cardiologique B.P. LYON-MONTCHAT  
69394 LYON Cedex 03, France  
Telephone Number 78542881.

# NMR

## NEWSLETTER

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LIFE IN THE ROTATING FRAME

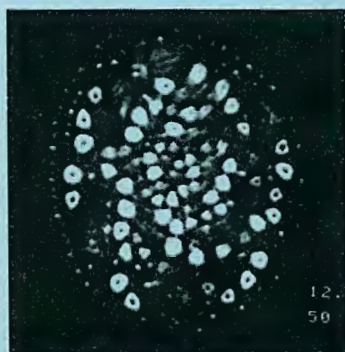
# CSI 2T Applications

## Shielded Gradients and NMR Microscopy

In spin warp imaging, there is a trade-off between minimum TE and maximum resolution. Even if rise and fall times were zero and phase encoding occurred during the entire echo delay, a  $\pm 2$  Gauss/cm gradient range and a TE of 2 msec would provide best case resolution of 0.32 mm. This translates to a 7 cm field of view in a  $256 \times 256$  matrix. To improve resolution by a factor of 10, TE may be increased by a factor of 10 (which is not acceptable in a sample with short T2 values) or gradient strength may be increased by a factor of 10. The long echo times required for T2 weighted images create an undesired loss of signal in many non-T2 weighted image experiments. These effects, however, are tolerable at 2 Gauss/cm for resolution at the 100-200 micron level.

Clearly, added signal that would be available with a shorter TE would be useful. The current practical limits of high signal-to-noise NMR micro imaging are greatly reduced by high strength shielded gradients. A 50 micron resolution image of an Agapanthus bud is shown in Figure 1. Unlike very high field ( $> 7$  Tesla) micro NMR imaging, magnetic susceptibility effects at 2T do not compromise the 50 micron digital resolution obtained during these gradient strengths.

In a second example, (Figs. 2 and 3), 25 micron resolution is achieved in a small phantom by using a moderate access (5 cm) rf coil. The phantom consists of seven small capillary pipets in a 5 mm NMR tube. Data was collected as a  $32 \times 256 \times 256$  DEFT data set.



**Fig. 1**—Agapanthus bud  
Matrix  $256 \times 256$ , TR 200  
Slice 2 mm, TE 30  
FOV 12.8 mm, NEX 4,  
45° Tip Angle DEFT  
Sequence



**Fig. 2**—16 contiguous 1 mm  
slices  
FOV 6.4 mm, NEX 4.  
TR 150 msec, Field Strength  
2T, TE 14 msec



**Fig. 3**—Expanded view of  
four of the 16 slices shown  
in Fig. 2.



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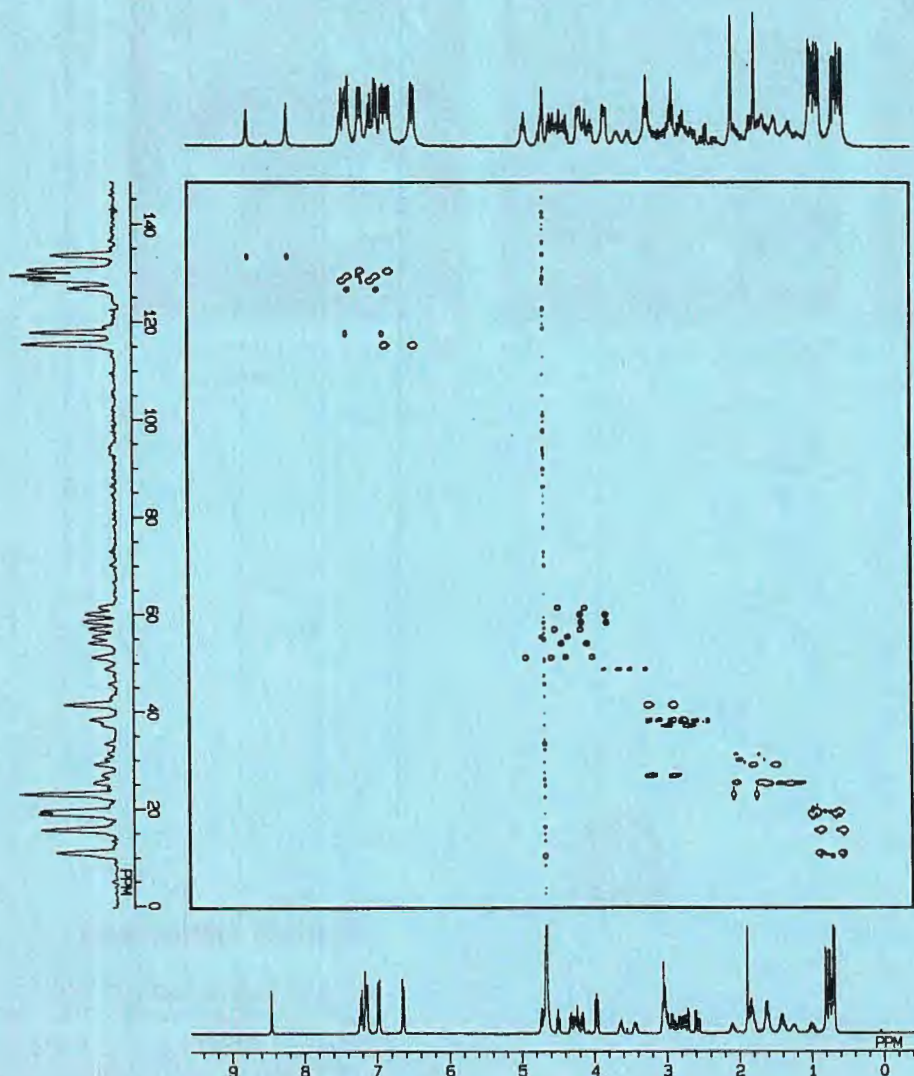
# JEOL GSX-FT NMR Systems

## Subject: Rf STABILITY

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