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D-129	Acetone-d <sub>6</sub> + 1% TMS	CD <sub>3</sub> COCD <sub>3</sub>	99.8%	0.8	-17	56	0.460 (20)
D-14	Chloroform-d	CDCl <sub>3</sub>	99.8%	1.50	-64	62	0.740 (20)
D-21	Chloroform-d	CDCl <sub>3</sub>	99.8%	1.50	-64	62	0.740 (20)
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D-130	Chloroform-d	CDCl <sub>3</sub>	99.8%	1.50	-64	62	0.740 (20)
D-28	Chloroform-d	CDCl <sub>3</sub>	99.8%	1.50	-64	62	0.740 (20)
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## FORTHCOMING NMR MEETINGS

- In Vivo Magnetic Resonance Spectroscopy Tutorial and Participatory Workshop, St. Louis, Missouri, **April 4 - 7, 1991**; See Newsletter 385, 58.
- 32nd ENC (Experimental NMR Spectroscopy Conference), St. Louis, Missouri, **April 7 - 11, 1991**; Contact: ENC, 750 Audubon, East Lansing, MI 48823; (517) 332-3667.
- 1991 Keystone Symposia on Molecular & Cellular Biology, Keystone, Colorado: **April 8-14, 1991**, *Frontiers of NMR in Molecular Biology; Proteolysis in Regulation and Disease; Protein Folding, Structure and Function*; See Newsletter 384, 46.
- Contrast-Enhanced Magnetic Resonance, a workshop of the Society of Magnetic Resonance in Medicine, Napa, California, **May 23-25, 1991**; Contact: S.M.R.M., 1918 University Ave., Suite 3C, Berkeley, CA 94704; (415) 841-1899, FAX: (415) 841-2340.
- Tenth International Meeting on NMR Spectroscopy, St. Andrews, Scotland, **July 8-12, 1991**; Contact: Dr. John F. Gibson, Secretary (Scientific), The Royal Society of Chemistry, Burlington House, London W1V 0BN, England.
- International Conference on NMR Microscopy, Heidelberg, Germany, **September 16 - 19, 1991**; See Newsletter 385, 28.

Additional listings of meetings, etc., are invited.

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**DEADLINE DATES**

No. 389 (February) ----- 18 January 1991  
No. 390 (March) ----- 15 February 1991  
No. 391 (April) ----- 15 March 1991  
No. 392 (May) ----- 19 April 1991

\* \* \* \* \*



## University of Turku

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Professor, Dr.  
Physical Chemistry

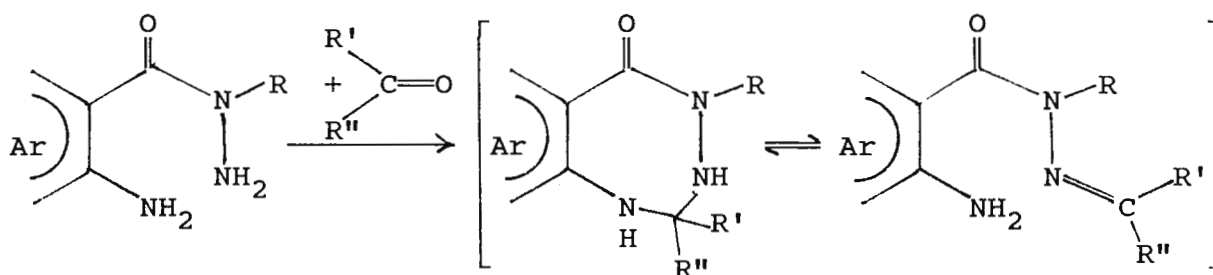
Dr. Bernard L. Shapiro  
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October 12, 1990  
(received 10/24/90)

## 2DNMR STUDIES OF RING-CHAIN EQUILIBRIA IN HYDRAZONES

Dear Dr. Shapiro,

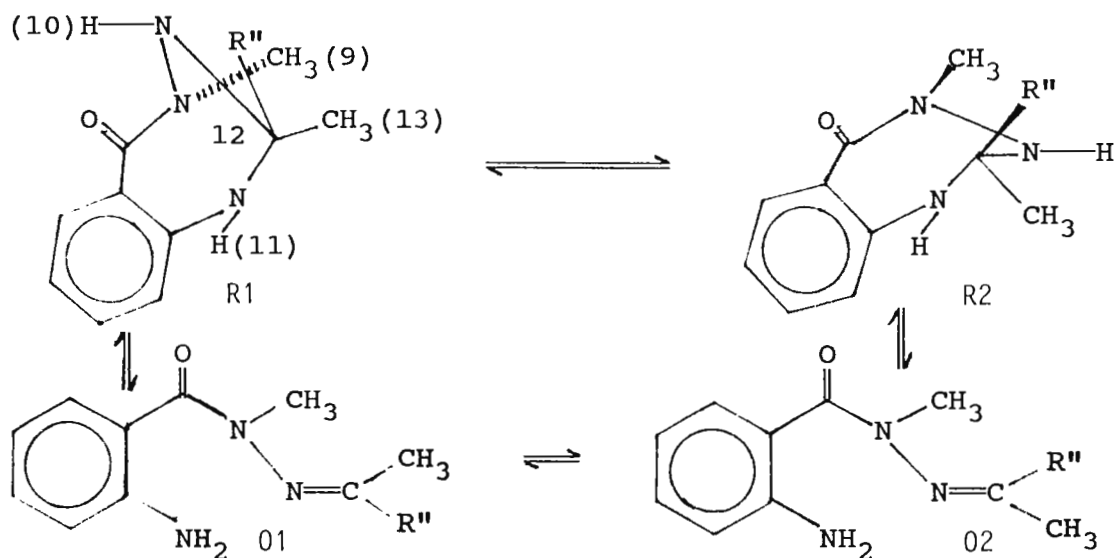
The reactions of ortho-aromatic carbonylic acid hydrazides with simple ketones give condensed triazepinones and/or open-chain hydrazones:



I R' = Me, X = H; II R' = Me, X = Cl; III R', R'' = cyclohexyl, X = H; IV R' = iPr, X = H; V R' = tBu, X = H; VI R' = tBu, X = Cl; VII R' = Ph, X = H. I, II, IV-VII R'' = Me.

The tautomerization in  $\text{CDCl}_3$  solution<sup>1</sup> has been stated to depend on N-substitution and on the consequent conjugation, steric hindrance, ring closure and so forth.

Complete variable temperature  $^1\text{H}$  and  $^{13}\text{C}$  NMR chemical shift assignments of compounds (I-VII) enable us to draw a combined map for the conformers and tautomers, which are present up to four components in the equilibrium mixtures:



A combined use of standard one-bond and long-range  $^1\text{H}$ - $^{13}\text{C}$  chemical shift correlation 2D experiments (in  $\text{CDCl}_3$  on a Jeol GX-400 instrument) was crucial for the above purpose. The above experiments were optimized to 12.5 Hz response (40 ms and 20 ms compromised values for  $T_1$  and  $T_2$  delays) to help us to see three-bond C,H-trans-correlations with a satisfactory removal of the direct C,H-correlations.

At room temperature I and III adopt the R1 ring form with a quasi-axial H-10 in agreement with the crystal structure determined for I. The stabilization of this single ring form was indicated by the presence of a cross peak (c.p.) for C-7/H-9 and its absence for C-7/H-10 in 2D long-range  $^1\text{H}$ - $^{13}\text{C}$  correlation spectrum, as well as by the sharp H-8 and broad H-11 signals.

The behaviour of IV-VI at room temperature provides an example of the importance of the relative sizes of the R'' substituents in determining the conformational preference in the seven-membered heterocyclic system. Thus, IV exists in a two-component equilibrium (R1+O1) whereas V and VI represent a more complex three-component equilibrium (R1+O1+O2) due to the enhanced steric crowding even in R1.

A completely opposite trend was found for VII (R''=Ph) where the effective volume of the Ph substituent is even smaller than that of a methyl group thus changing the conformational energy difference between the two ring forms in favour of R2. Two sets of signals were observed (except for C-methyl) at room temperature corresponding to the complete four-component equilibrium shown above with a predominance of R2 and O1. This enabled us to find an extremely strong shielding of  $^1\text{H}$  and  $^{13}\text{C}$  signals of the N-methyl (2.23 and 16.9 ppm vs 3.40 and 39.0 ppm, respectively) due to the anisotropy of the Ph ring, the "deshielded shifts" being almost equal to those for the ring forms of the other compounds studied. The three-bond C,H-correlation mentioned above as well as C-6/H-2 and C-1/H-11 correlations were again necessary for spectral assignments. The latter c.p. and the shift of H-2 signals to 7.6-7.8 ppm caused by an anisotropy effect of the carbonyl group also speak for the hindered rotation of the aryl group and its coplanarity with the carbonyl group due to intramolecular hydrogen bonding.

The first process to freeze out in the case of VII was the E,Z isomerization around the C=N bond at about  $-20^\circ\text{C}$  and three sets of signals were appeared in  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra. At ca  $-40^\circ\text{C}$  the signals of both ring forms could also be observed and the presence of a four-component equilibrium was confirmed. Further 1D and 2D experiments are in progress in order to clarify better the influence of different substituents on the phenyl ring and other factors on the above equilibria.

1. Gál, M., Tihanyi, E. and Dvortsák, P. Acta Chim. Hung. 123, 55-61 (1986).

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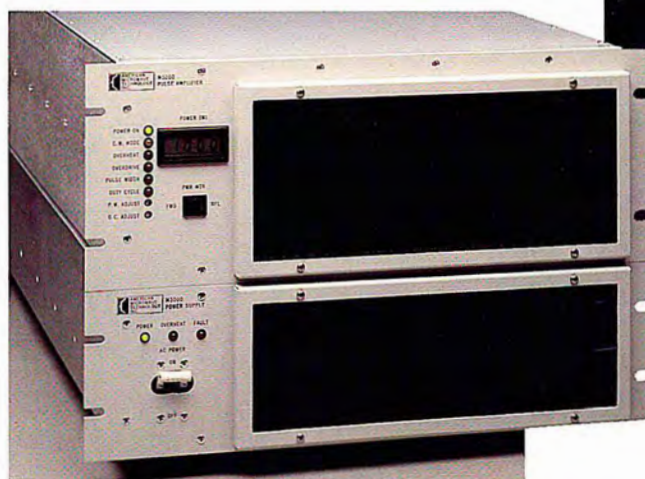
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**Dr. Bernard L. Shapiro**  
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**Palo Alto, CA 94303, U.S.A.**

(received 10/15/90)  
 Oct. 1 1990

## **MAS-Spinning of Rubber to average homonuclear dipolar Interactions**

Dear Dr. Shapiro,

Rubber and some other elastomers are somewhat on the fascinating borderline between liquids and solids (from the viewpoint of the nuclear spins). It is well established to perform  $^{13}\text{C}$  CP/MAS studies to obtain highly resolved carbon spectra for chemical analytical purpose and to study the cross polarization dynamics (consult your tyre manufacturer) to learn about the physical structure (1). However we have done very simple  $^1\text{H}$  1D and 2D experiments which are able to do a similar job. With emphasis on the techniques but not on the sample (a typical commercial rubber product) we like to highlight some features of these experiments done on a Varian 400 MHz Unity spectrometer.

Fig. 1) Fast sample spinning is essential to obtain  $^1\text{H}$  spectra which show resolution with respect to different chemical shifts. The experiments clearly show that dipolar coupling among the protons is averaged out to a large extent when spinning around 10 kHz. For these experiments a 5mm probe based on the Jakobsen design (2) was used and there were no problems to spin the granular rubber stuff (particle size approx. 1mm). We were not able to see J coupling. Additional multiple pulse line narrowing schemes did not improve the resolution. The results can be interpreted in terms of chemical structure similar to the  $^{13}\text{C}$  data.

Fig. 2) Once resolution on the chemical shift scale is obtained one can play with  $^1\text{H}$  2D exchange experiments of the NOESY type. The experiments show that there are different characteristic times for the buildup of cross peak intensity for the different connections. These data contain information about molecular structures and distances in these rubber phases.

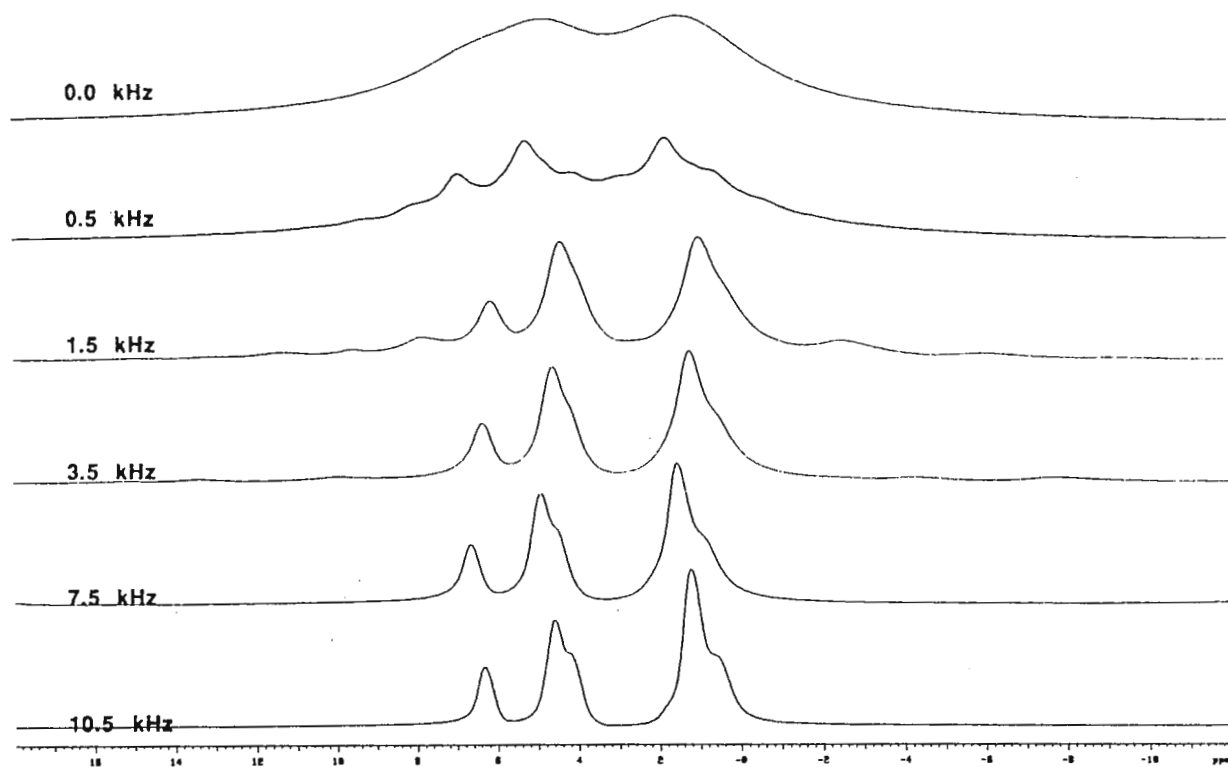
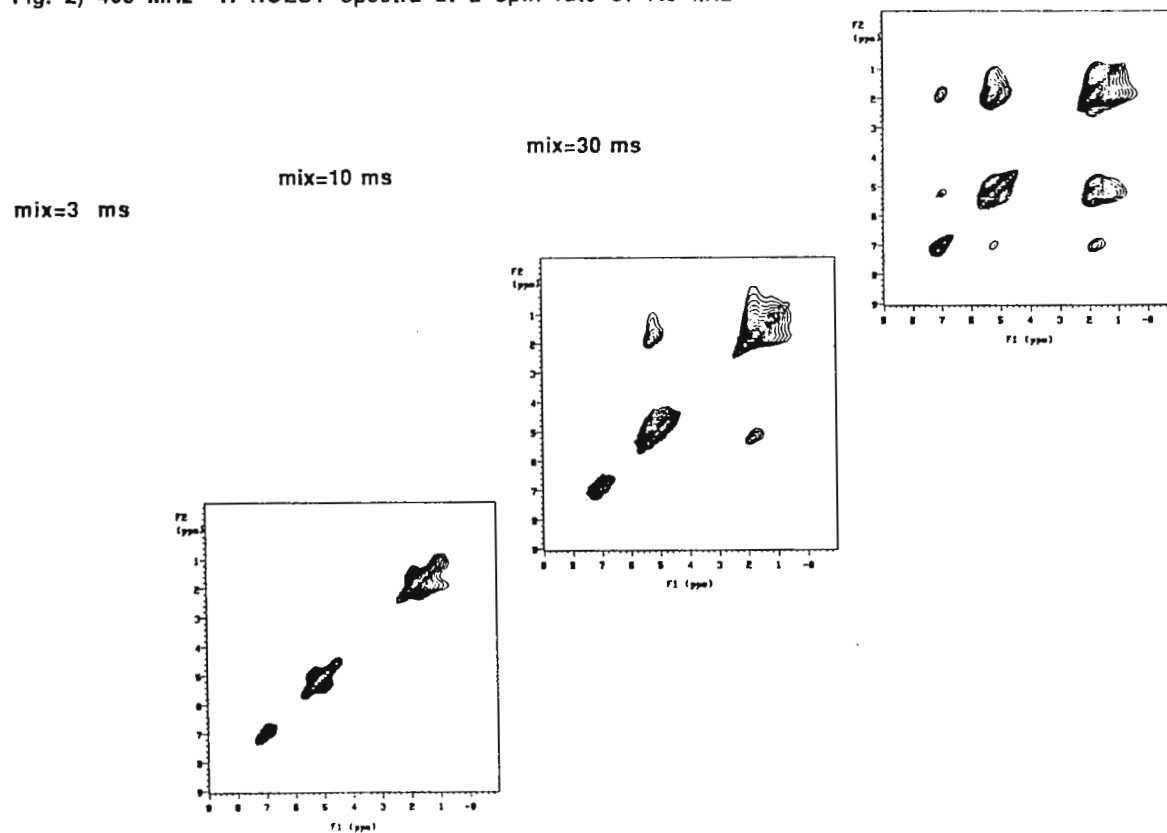
Note that due to the high sensitivity only basic phase cycling is necessary and the experimental times both for 1D and 2D are quite short since the  $T_1$ s are not too bad.

(1) R. A. Komoroski (Ed.), High Resolution NMR Spectroscopy of Synthetic Polymers in Bulk, VCH Publishers, Inc. Deerfield Beach, Florida (1986)

(2) H. J. Jakobsen et. al., Poster WP 19, 31<sup>st</sup> ENC Asilomar April 1990

Sincerely Yours

Peter Meier  
 NMR Applications Laboratory

Fig. 1) 400 MHz  $^1\text{H}$  spectra of a synthetic rubber at different spin rates (5mm MASS rotor)Fig. 2) 400 MHz  $^1\text{H}$  NOESY spectra at a spin rate of 7.5 kHz

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

October 1, 1990  
(received 10/18/90)

"Non-invasive  $^{31}\text{P}$  NMR Spectra of Rat Liver *in vivo*; Standardization of Gradient Current and Animal Weight"

Dear Professor Shapiro:

A gradient controller system (based on a design reported by J.J.H. Ackerman, private communication) was constructed in our laboratory for use with our Varian XL-400 NMR spectrometer. This gradient system was used in conjunction with a home built surface coil probe [Gonnella and Silverman, J. Mag. Res. ,24 (1989)] to destroy surface signals allowing detection from deeper lying sample. Our *in vivo* studies on rats successfully demonstrated that  $^{31}\text{P}$  NMR spectra could be obtained from rat liver without contamination from surrounding muscle and without surgery (figure 1). However several factors needed to be considered before this technology could be used in an actual therapeutic study.

The first item which had to be considered was the size of the rat, which must be limited by the physical dimensions of the coil. The radius of the surface coil determines the depth of the sample from which signal can be obtained. The thickness of the abdominal muscle varies in the animals depending on their size. Thus in very large animals, the gradient coil is not capable of randomizing the signal from the entire thickness of the muscle. Furthermore, the surface coil used in these experiments cannot receive signal from liver of large rats because the distance between the coil and liver is too large. On the other hand, very small animals were also not suited to these experiments. This was due to problems obtaining the ideal adjustment of the surface coil size and gradient current which would allow observation of  $^{31}\text{P}$  NMR signals from the liver.

In order to establish an appropriate weight range needed to obtain *in vivo*  $^{31}\text{P}$  NMR spectra of rat liver without surgery, animals weighing 150g to 400g were tested. Use of the gradient coil on rats smaller than 200g produced very weak signal from the liver, while for rats larger than 275g, it was difficult to completely randomize the signal from the abdominal muscle. We found that weights of 220g to 275g were the best for the non invasive examination of rat liver and required gradient current from 1.0 to 1.5 amps with a pulse duration of .001s. With this weight and current range, no contamination from abdominal muscle was observed (absence of phosphocreatine) and no compromise in signal area occurred.

The pulse sequence, which was written for the Varian XL-400 and used in these experiments, is given in figure 2.

Hence we have determined standard conditions for conducting non-invasive  $^{31}\text{P}$  NMR evaluation of rat liver using a gradient controller system fitted to a conventional vertical bore spectrometer. This technology can now be applied to a therapeutic study.

NO SURGERY  
GRADIENT OFF

NO SURGERY  
GRADIENT = 1.4 AMP

SURGICALLY EXPOSED  
RAT LIVER

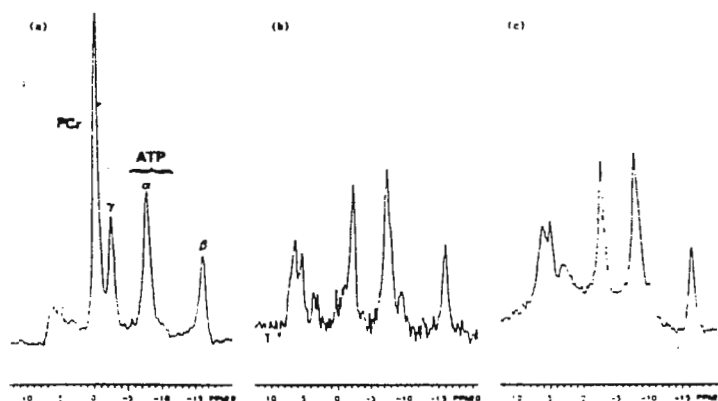


figure 1

P-31 NMR Spectra obtained from a rat in vivo:

- (a) rat abdominal muscle
- (b) Rat liver from intact animal
- (c) Rat liver surgically exposed

"PULSE SEQUENCE FOR Hahn SPIN ECHO COMBINED WITH PULSED SURFACE GRADIENT."

2992 NINA GONNELLA 6-21-87

2993

2994 PROCEDURE PULSESEQUENCE;

2995

2996 VAR TAUREAL;

2997

2998 BEGIN

2999

3000 GETVAL(TAU, 'TAU', 'P1');

3001 P1:=2.0\*P1; PUTVAL(P1, 'P1');

3002

3003 "PHASE CYCLING"

3004

3005 HLV(CT,V1); HLV(V1,V1); "V1=0000111122223333"

3006 MOD4(CT,V2); ADD(V2,V1,V2); "V2=0123123023013012"

3007 DBL(CT,V3); ADD(V3,V1,OPH); "OPH=020213132023131"

3008

3009 "PREPARATION PERIOD"

3010

3011 STATUS A;

3012 HSELA('D1');

3013

3014 "PULSES"

3015

3016 STATUS B;

3017 RGPULSE(PW,V1,ROF1,ROF1);

"FIRST RF PULSE"

3018 SPION;

"TURN POSITIVE GRADIENT PULSE"

3019 DELAY(TAU);

3020 SP1OFF;

3021 RGPULSE(P1,V2,ROF1,ROF2);

"SECOND RF PULSE"

3022 SPION;

"TURN ON NEGATIVE GRADIENT PULSE"

3023 DELAY(TAU);

3024 SP1OFF;

3025

3026 "DETECTION"

3027

3028 STATUS C;

3029

3030 END;

3031 N-L

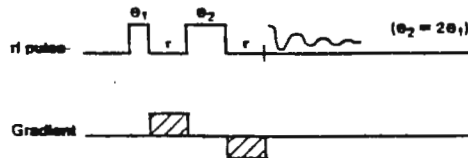


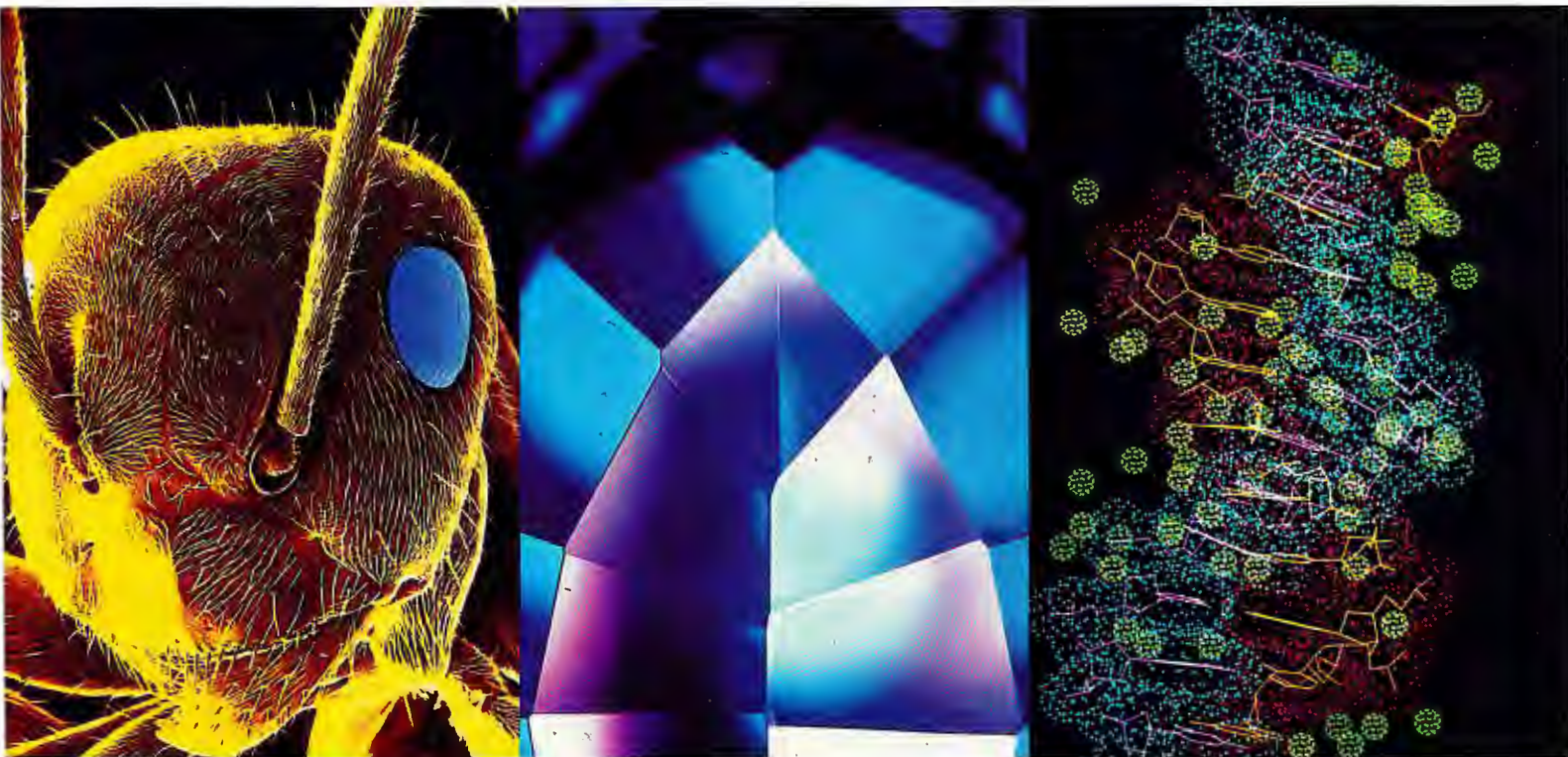
figure 2

Sincerely,

*Nina C. Gonnella*

Nina C. Gonnella, Ph.D.  
NMR Laboratory

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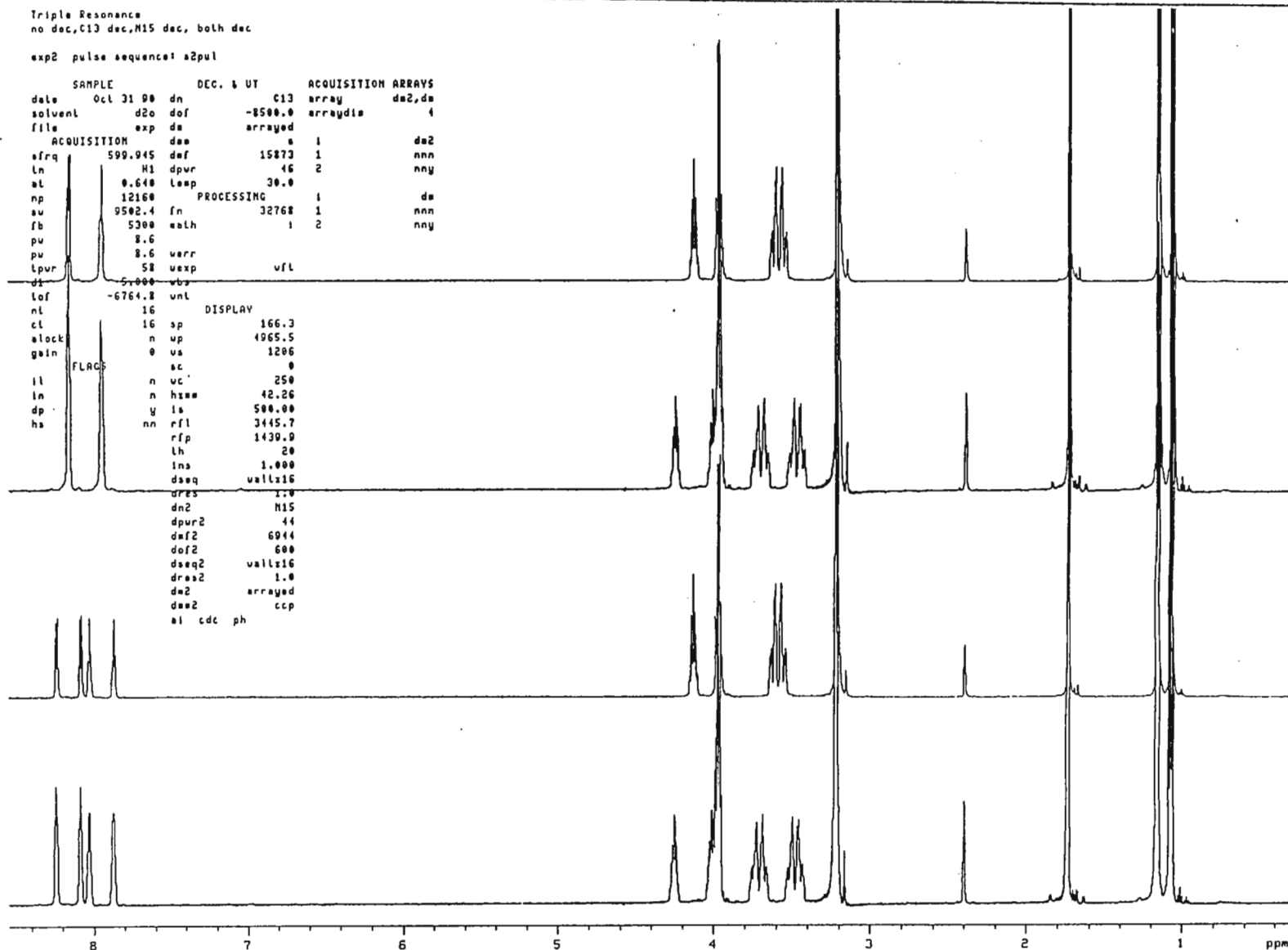
## NMR WITH A FUTURE

**varian** 

# TRIPLE RESONANCE: 1H-{13C}, 1H-{15N} AND 1H-{13C,15N}

Advances in genetic engineering have led to the facile incorporation of stable isotopes in biochemically significant materials. Double-labelling permits very specific NMR studies and often these require the ability to pulse and/or decouple nuclei such as  $^{13}\text{C}$  and  $^{15}\text{N}$  simultaneously within a pulse sequence. Here, UNITY-600 MHz proton spectra illustrate this capability on a doubly-labelled compound. The middle two spectra show separate  $^{13}\text{C}$  and  $^{15}\text{N}$  decoupling, while the top spectrum shows simultaneous  $^{13}\text{C}$  and  $^{15}\text{N}$  decoupling.

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## MERCK SHARP &amp; DOHME RESEARCH LABORATORIES

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BYRON H. ARISON, Ph.D.  
SENIOR INVESTIGATOR  
ANIMAL & EXPLORATORY DRUG METABOLISM

(201) 594-5394  
FAX: (201) 594-6645

September 20, 1990  
(received 10/29/90)

Prof. Barry Shapiro  
966 Elsinore Court  
Palo Alto, California 94303

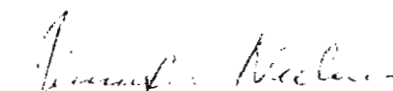
**On the Occasional Virtue of Carrying Out a Poorly Thought-Out Experiment**

Dear Barry,

Recently we were involved in biosynthetic studies on efrotomycin using doubly labeled [1,2- $^{13}\text{C}$ ]acetate together with unlabeled glucose in the fermentation medium. Even though the assigned C-13 spectrum had been published [R. Dewey *et al.*, J. Antibiotics, Vol. 38, No. 12, 1691-1698 (1985)] it was nevertheless felt that an APT experiment could prove helpful in sorting out the congested HC-O and vinylic regions which would be further cluttered by  $^{13}\text{C}$ - $^{13}\text{C}$  couplings. The resulting spectrum, part of which is shown in the accompanying figure, suggested a gross missetting of the phases when initially viewed on the screen. A more sober appraisal, however, indicated that the typical evolution time of 7 ms fortuitously results in the  $^{13}\text{C}$ - $^{13}\text{C}$  doublets being almost exactly  $180^\circ$  out of phase with the unenriched peaks. This can be seen in the seven methine signals between 70-92 ppm where the unenriched peaks are inverted and the flanking doublets associated with the enriched signals are upright. Note that with the quaternary C-28 near 101 ppm the reverse situation obtains. Thus, the APT experiment did indeed simplify the analysis but not in the manner we had anticipated.

A planned series of APT experiments varying the delay period to define the oscillatory behavior of the doublets could not be carried out because of sample degradation.

  
Byron Arison

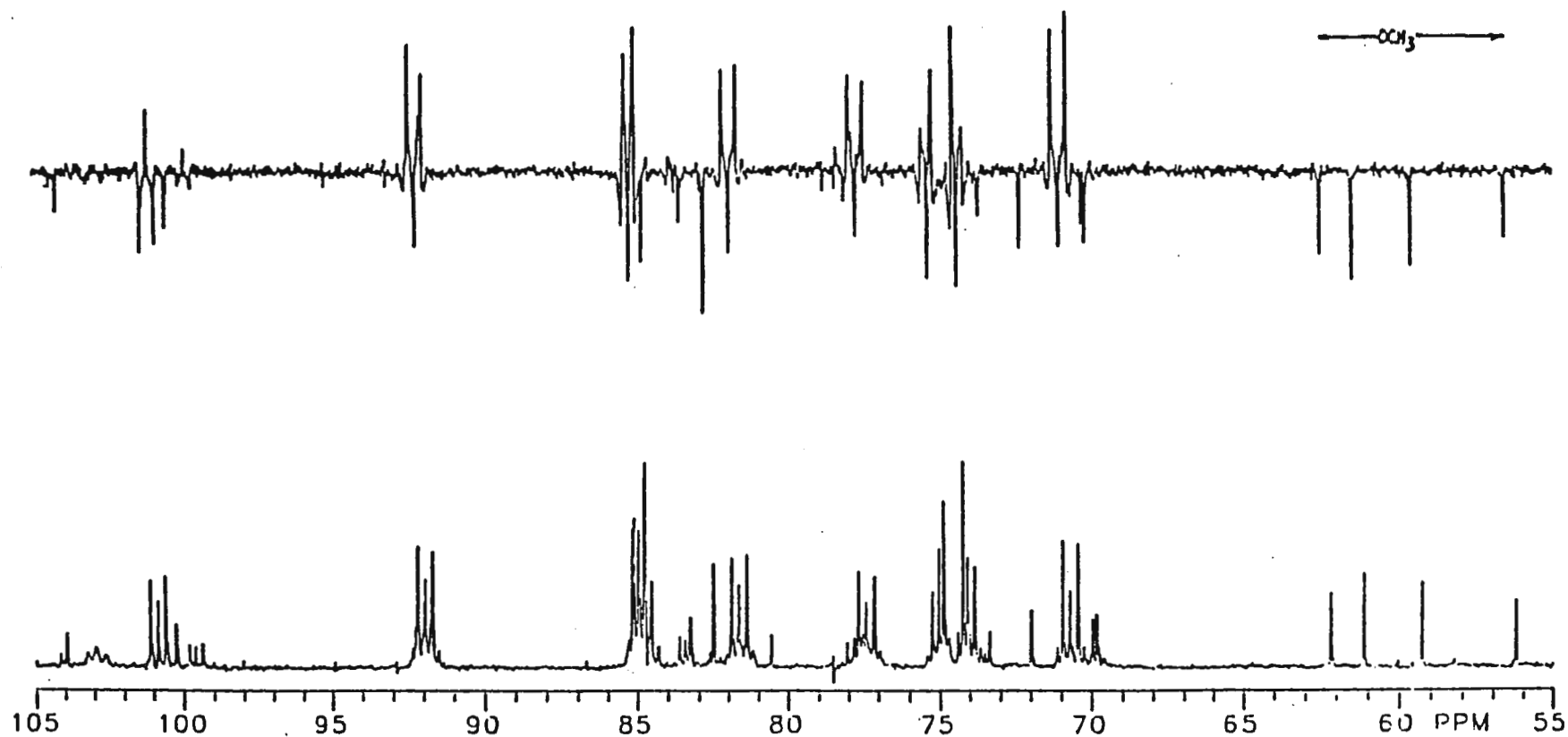
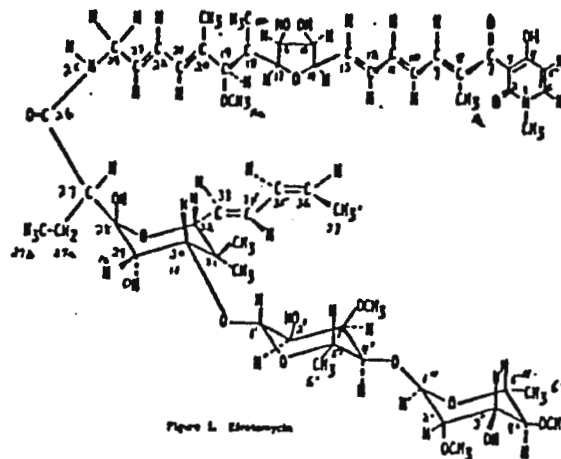
  
Jennifer Nielsen

attachment

Derived from?  
 EFROTOMYCIN<sup>13</sup>C-1,2 ACETATE  
 PLUS UNLABELLED GLUCOSE

UPPER TRACE:APT

LOWER TRACE:NORMAL SPECTRUM





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

(received 10/15/90)

### $^1\text{H}$ - $^{15}\text{N}$ HMQC's and Proteins

Dear Dr. Shapiro,

Barry

For the better part of the past year we have been using the  $^1\text{H}$ - $^{15}\text{N}$  HMQC experiment to help in the assignment of an increasingly larger number of peptides and small proteins currently under study in our lab. The robustness of the experiment, the ease with which it can be conducted and the high quality of data that it produces have made this particular heteronuclear technique a local lab favorite.

Unfortunately the heavy use of the special power amplifiers and associated paraphernalia on our Varian VXR 500 has taken its inevitable toll. During one recent experiment conducted on a rather dilute 0.8 mM sample of *E. coli* thioredoxin (labelled to about 70%  $^{15}\text{N}$  enrichment) our ENI amplifier sadly "expired" and the experiment was terminated after just 70 of the 256 increments were collected. With a fair bit of trepidation and a healthy dose of skepticism the data was, nevertheless, processed and to our great surprise produced the rather striking spectrum shown below (figure 1). As a comparison we include the same region of a spectrum (albeit done at a lower temperature and a higher pH) collected some days earlier wherein all 256 increments were successfully acquired (figure 2). There is little to distinguish the two and, in fact, it might be argued that the spectrum depicted in figure 1 is superior in quality to that of figure 2! Indeed the high quality from this 1/4 complete experiment proved to be so good that it, alone, permitted a nearly complete assignment of the  $^{15}\text{N}$  spectrum of *E. coli* thioredoxin to be made.

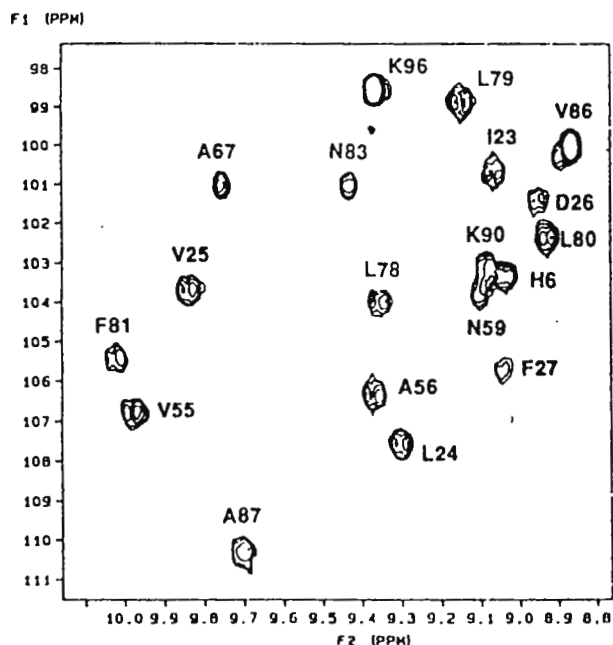


Figure 1.  $^1\text{H}$ - $^{15}\text{N}$  HMQC of 0.8 mM *E. coli* thioredoxin, pH 5.5, 35 °C. Total of 96 scans and 70 increments, collection time: 10 hrs.

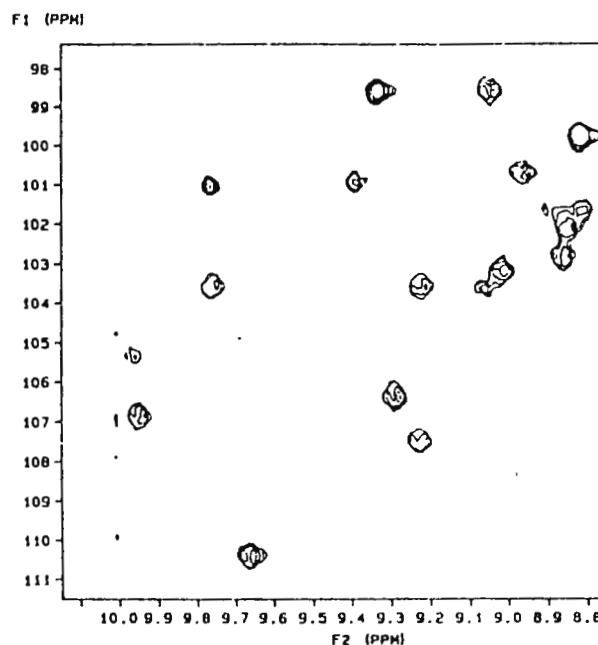


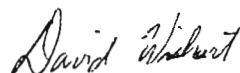
Figure 2.  $^1\text{H}$ - $^{15}\text{N}$  HMQC of 0.8 mM *E. coli* thioredoxin, pH 7.5, 25 °C. Total of 96 scans and 256 increments, collection time: 36 hrs.


It is also rather interesting to note some of the "fine structure" features evident in both figures 1 and 2. In particular, a number of very obvious doublets are prominently featured in these two spectra. We believe these doublets are a manifestation of the large  $^3J_{\text{HN}\alpha}$  coupling in peptide bonds which are so characteristic of residues in  $\beta$  pleated sheets and other extended conformations commonly found in proteins. In fact, the correspondence of doublets in the HMQC spectra with residues later identified to belong to  $\beta$  strands proved to be almost 90%. This would strongly suggest that the identification of doublets in  $^1\text{H}$ - $^{15}\text{N}$  HMQC spectra allows the quick and easy identification as well the simple enumeration of residues involved in  $\beta$  strand configurations -- a kind of NMR equivalent of CD or Raman spectroscopy.

So to conclude, it seems that our little brush with misfortune in the form of a temperamental amplifier and an unexpectedly dilute protein sample has provided us with some unexpected benefits a few rather useful insights. These might be summarized as follows:

- 1) The  $^1\text{H}$ - $^{15}\text{N}$  HMQC experiment can be successfully conducted in about 1/4 time usually allotted without using any special processing requirements.
- 2) The appearance of strong doublets in an  $^1\text{H}$ - $^{15}\text{N}$  spectrum permits the easy identification of amino acid residues involved in  $\beta$  strand configurations.
- 3) The  $^1\text{H}$ - $^{15}\text{N}$  HMQC experiment can be routinely conducted on  $^{15}\text{N}$  enriched protein samples of much less than 1mM.
- 4) The level of  $^{15}\text{N}$  enrichment for protein samples need not exceed 60-70% (compare the cost of 70% enriched  $\text{NH}_4\text{Cl}$  feedstock to 99.9% enriched -- the savings are not inconsequential!)

All the best,

  
David S. Wishart

  
Brian D. Sykes



## Felix / PC

### NMR Data Processing Software

FMR cooperates with Hare Research in providing the NMR community with Felix/PC (tm) NMR data processing software and software utilities for IBM compatible PCs. The software is available in either a 1D or Multi-D package. Felix/PC is a "toolbox" of NMR data processing routines which allow the operator to perform all common and many unusual processing functions. It is an extremely powerful processing package rivaling many packages on "more powerful" computers.

#### 1D Package:

- Full range of apodization routines.
- Forward and reverse transforms.
- On screen "real time" phasing, expansion and difference routines.
- Several types of baseline correction routines.
- Automatic and manual peak picking and labeling.
- Total spectrum and "broken" integration routines.
- 1D data table sizes up to 64K words.
- Complete macro functions.
- "Locate" menuing system.
- Graphics support for HPGL and Postscript.

#### 1D / 2D Package:

- Process up to 4 dimensional without transposition.
- 1D data table sizes up to 32K words.
- 2D data table sizes up to 2K x 2K.
- Color coded contour displays and plots.

Felix/PC requires a 100% compatible IBM PC computer (8088, 8086, 80286 or 80386) with an with 640 K of memory, a 80x87 coprocessor, a hard disk and an IBM compatible CGA, EGA or VGA graphics adapter.

If Felix/PC is to be used with data from NMR spectrometers, data format translation is required. Data format translation is the responsibility of the buyer. Data format translation software is available as a separate purchase.

Felix software is also available for other computers such as SUN and IRIS systems. Felix/PC and Felix is available from Hare Research for only a small handling charge (\$150.00) to all academic and government institutions. Demo software packages are available.

### Data Translation Software.

Both Nicolet/GE and Bruker provide Kermit and X-Modem data transfer software for their spectrometers. This software can easily communicate with a PC running any one of the many software communication packages using Kermit or X-Modem transfer protocol at transfer speeds up to 38K Baud.

Once the data is transferred using X-Modem or Kermit protocols, with FMR's GOSSIP or by any other means, data translation software packages are available to convert the Nicolet/GE 1280 20 bit word or the Bruker Aspect 24 bit word into floating point Felix/PC words. Key parameters are also converted from the Nicolet/GE and Bruker integer and floating point header parameters into the respective file headers for Felix/PC:

- Spectrometer Frequency.
- Sweep Width.
- Data Table Size.
- Non-Quadrature / Quadrature Data.

Some Varian conversions are available from other vendors. The capability to process several manufacturers' data with a single software package can make life in a mixed instrument laboratory easier for many users.

Parallel port 1280 to PC transfers are in development.

### BXR Data Transfer & Translation Software

BXR is a set of programs that transfers data files from the Bruker Aspect computers to PC computers. BXR stores the data in translated files that Felix/PC can read. Parameters related to data processing are transferred for use by Felix. Transfer rates of up to 19200 baud are usually routine (> 100 KBytes per minute). In normal operation the PC and the Aspect are connected with a communication cable and the BXR transfer program started on the PC. The unattended PC then waits for files to be transferred by the Aspect. There is no need to halt the PC program. You can start and stop the transfer program on the Aspect without stopping and restarting BXR on the PC. Under this condition, the PC waits for additional files from the Aspect until you halt it. This is for convenient data transfers to an unattended PC.



# GOSSIP

**GOSSIP** is a new two-way data transfer program written by FMR for data transfer between IBM compatible PC computers and the Nicolet/GE 1280. Data transfers can be done at rates up to 38.4K baud (about 700 Nicolet Words per second with overhead). This function gives the 1280 user a new spectrum of capabilities:

**Inexpensive mass data storage.** Once the data is on the PC, large capacity, inexpensive and reliable magnetic and optical disks and tape backups are abundant. 330 MByte disks sell for as little as \$2000. This makes long term data backups and personal spectral archives practical.

**Many alternate NMR data processing packages** are available for the PC. When GOSSIP is combined with data translation software and one of these data processing packages, convenient and inexpensive desktop NMR processing becomes possible.

**The processed data is immediately available** for direct incorporation into many popular **word processing and desktop publishing** packages.

## TMON

With the TMON operating system for the 1280, transfers to the PC can be done in two ways.

**FILTRN** - RS-232 transfers can be done using the Nicolet/GE FILTRN program from the TMON operating system to GOSSIP on the PC. This can be done at rates up to 38.4K baud (about 700 Nicolet Words per second with overhead).

**NMR Programs (QE, GN and NT)** - Transfers can be done from inside the NMR programs. These programs support foreground and background RS-232 transfers at rates up to 38.4K baud (about 700 Nicolet Words per second with overhead). These transfers can be automated under MACRO control of the 1280 so that when the experiment is finished the data is automatically transferred. Overnight and/or sample changer operations can automatically store copies of the data on a waiting PC.

## DEXTER

With the DEXTER operating system for the 1280, transfers to the PC can be done in two ways.

**FILTRN** - RS-232 transfers can be done using the Nicolet/GE FILTRN program from the DEXTER operating system to GOSSIP on the PC. This can be done at rates up to 38.4K baud (about 700 Nicolet Words per second with overhead).

**NMR Programs (NT)** - FMR provides a package of software which includes an *overlay for the 1280 NMR program* and the GOSSIP PC program. With this package transfers can be done from inside the NMR program **IN BACKGROUND** and at rates up to 38.4K baud (about 700 Nicolet Words per second with overhead).



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Ottawa, Canada  
K1A 0R6

October 12, 1990  
(received 10/19/90)

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

$^{67}\text{Zn}$  resonances at variable pH

Dear Barry:

It is possible to concentrate acidic ( $\text{pH} = 1 \rightarrow 4$ ) process streams containing  $\text{ZnSO}_4$  by hyperfiltration so that they may be more economically recycled to a refining process. The selectivity of the filtration increases with increasing pH. Is this due to aggregation of  $\text{Zn}^{2+}$  to larger species?

It has been reported that there is no change in  $^{67}\text{Zn}$  chemical shift with concentration for  $\text{ZnSO}_4$  solutions although there are changes for the chloride, bromide and iodide.<sup>(1)</sup> I have looked at the chemical shifts and line widths of  $^{67}\text{Zn}$  as a function of concentration and pH. There is no significant change in chemical shift. The line widths are listed below.

Conc. (Molar)	pH	Line Width	pH	Line Width	pH	Line Width
1.86	5.47	51.2	4.16	63.4	1.20	66.0
0.93	5.80	31.8	4.37	31.8	1.24	31.8
0.46	6.04	36.6	4.55	22.0	1.29	23.2
0.23	6.15	22.0	4.74	24.4		

The conclusion is that there is no NMR evidence for aggregation of zinc sulphate at higher pH.

Yours truly,

S. Brownstein

SB/la

- (1) B.W. Epperlein, H. Cramer, O. Lutz and A. Schwenk Z. Naturforsch. 29A, 1553 (1974).



## McMASTER UNIVERSITY

Department of Chemistry

1280 Main Street West, Hamilton, Ontario L8S 4M1

Telephone: (416) 525-9140

FAXMAIL (416) 522-2509

October 10, 1990  
(received 10/24/90)

## OFFLINE DATA PROCESSING ON A BUDGET

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

Dear Barry,

We are now up and running on our offline data processing system here at McMaster. Money is tight, as usual, so we have gone with a transfer over the parallel port from our three ASPECT 3000's and an old ASPECT 2000 to a bunch of IBM PS/2's, which were donated to us under an IBM Canada/ McMaster joint project. Joe Laughlin in the software department at Bruker in Boston was very helpful in getting the FASTRAN software running, so we can ship data back and forth very reliably now. For one-dimensional processing on the PS/2's we are using a package called NMR286 from SoftPulse Software (Box 504, Guelph, Ontario Canada N1H 6K9). This is an excellent program, with all we need for 1D work, and it flies along pretty quickly on the FT's. On a standard 8MHz AT, an 8K FT takes about 16 seconds, but on a new 33 MHz 386/387 system this drops to less than a second. We are hoping (!) that this offline capability will free up more spectrometer time, since people don't have to clutter up consoles while they work up their data. Next year we'll let you know if this was successful. All the best.

Yours truly,

Alex D. Bain  
Associate Professor of  
Chemistry

**University of  
Arkansas  
for Medical  
Sciences**

4301 W. Markham  
Little Rock, Arkansas  
72205-7199  
501-686-6105

October 23, 1990 (received 10/27/90)

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

### **$^{31}\text{P}$ NMR Analysis of Phospholipids in Human Amniotic Fluid**

Dear Barry,

Quantitative analysis of phospholipids in amniotic fluid has proven clinically useful in the assessment of fetal lung status. The ratio of phosphatidylcholine (PC) to sphingomyelin (SM) in amniotic fluid, the "L/S ratio", forms the basis of a well-established index of fetal pulmonary maturity. Clinical assays of the primary amniotic fluid phospholipids are typically obtained from TLC-densitometry of extracts, but inadequacies in reproducibility and predictivity associated with this method provide an incentive to investigate the applicability of  $^{31}\text{P}$  NMR. Although sensitivity and resolution problems hamper analysis of whole fluid, a two-phase solvent-reagent system developed by Meneses and Glonek (1) substantially reduces  $^{31}\text{P}$  line widths for extracted phospholipids. In collaboration with Drs. Mark Shifman and Alex Pappas in the department of Pathology at UAMS, we have recently used  $^{31}\text{P}$  NMR of extracts to profile phospholipids in amniotic fluid from a variety of patients.

Spectra were obtained at 121.65 MHz on a General Electric GN-300 FTNMR spectrometer using a dedicated 5 mm  $^{31}\text{P}$  probe (Cryomagnet Systems, Inc.). WALTZ proton decoupling, temperature stabilization, longer phase settling time, and locking on the deuterium resonance of  $\text{CDCl}_3$  were utilized (2) to reduce linewidths below 1 Hz. Extracts were initially run in  $\text{CDCl}_3$ -MeOH- $\text{D}_2\text{O}$  (10:4:1), using  $\text{Cs}_4\text{EDTA}$  to remove polyvalent metal cations from the organic phase (1). This system did not adequately resolve SM from phosphatidylserine (PS), but adjustment of the solvent composition to a ratio of 63:14:4 afforded sufficient resolution for our purposes.

The spectra in Figs. A-C, obtained from three different patients, represent an approximate gestational progression of phospholipid profile. They range from an "immature" spectrum with a low PC/SM ratio of 1.1 (Fig. A), through a transitional spectrum with increasing PC/SM (7.9) and minor phospholipids (Fig. B), to the unambiguously "mature" lung profile of Fig. C (PC/SM=21).

High PC/SM ratios with detection of phosphatidylglycerol (PG) indicate fully functional fetal lung status.

We find that the  $^{31}\text{P}$  NMR-derived PC/SM ratios reflect the gestational rise in total PC, including the more surface-active (and clinically relevant) saturated fraction ignored by the commonly-used cupric acetate TLC visualization method. Sample preparation time is comparable to that for TLC-densitometry, and data acquisition by  $^{31}\text{P}$  NMR is more rapid in some cases. To date, we have examined 33 patients and found better correlation with gestational age for  $^{31}\text{P}$  NMR than for TLC-densitometry. The predictive capacity of this method remains to be established by studies where clinical status is more rigorously defined.

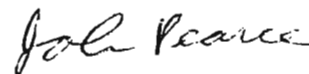
1. P. Meneses and T. Glonek, *J. Lipid Res.* 29, 679 (1988).
2. H. T. Edzes, T. Teerlink, and J. Valk, *Abstracts, 8th Annual Meeting, Society of Magnetic Resonance in Medicine*, Aug., 387 (1989).

Sincerely,



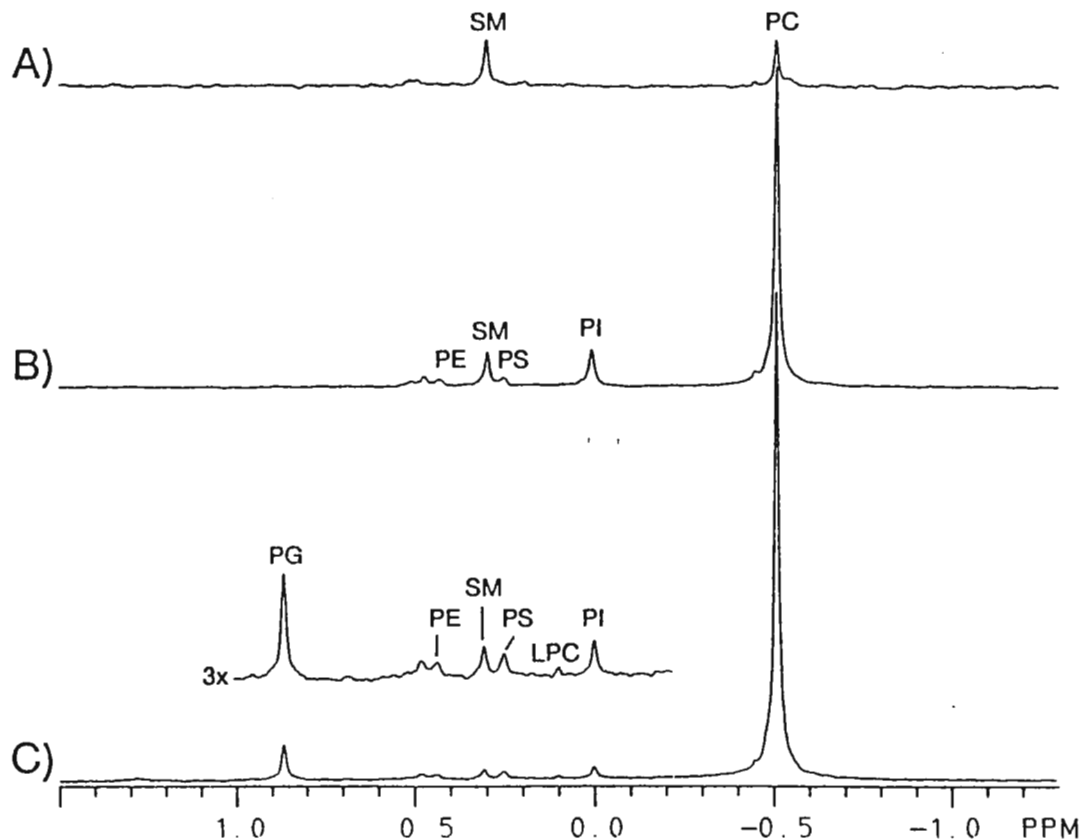
Richard A. Komoroski

Associate Professor of Radiology and Pathology



John M. Pearce

Research Assistant



# Not even a coffee break.



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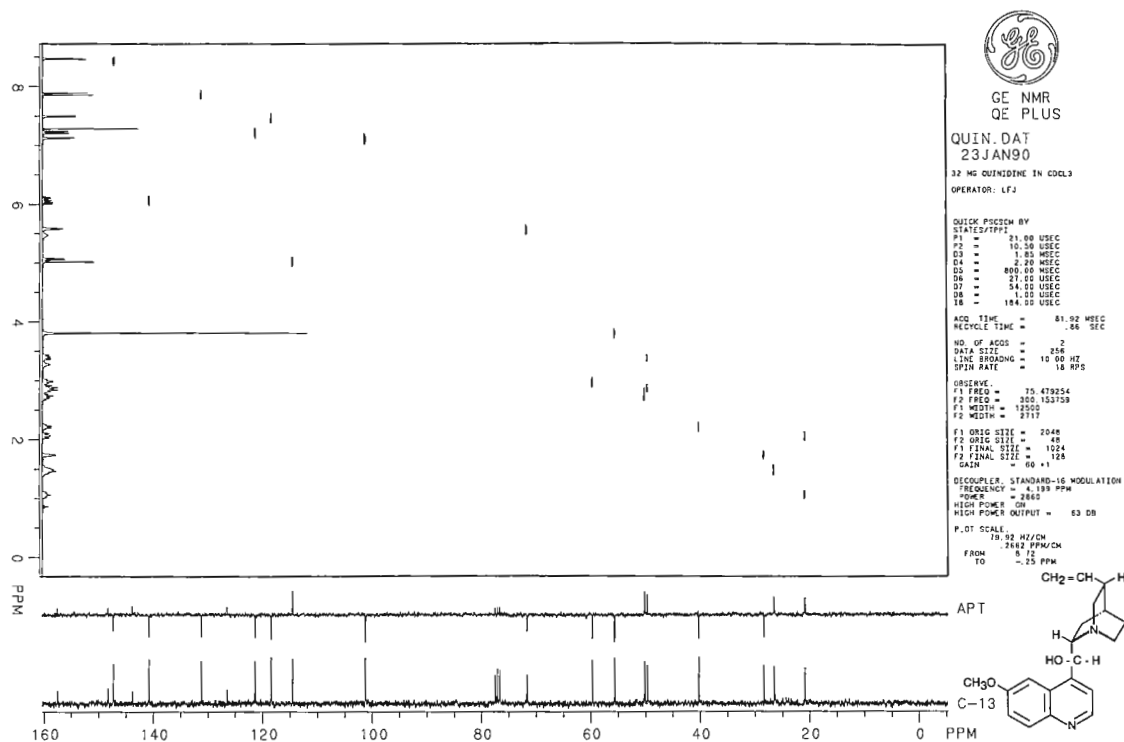
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An automated run using MACRO mode operation on a sample of 32 mg of quinidine in 0.5 ml chloroform-d (0.20M). Data were obtained using the 5 mm broadband probe. <sup>1</sup>H, <sup>13</sup>C, APT and phase sensitive 2D data were collected, processed and plotted—including the 2D contour—in only 8.2 min.

## UNIVERSITY OF CALIFORNIA, DAVIS

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UCD NMR FACILITY

DAVIS, CALIFORNIA 95616

November 7, 1990  
(received 11/9/90)Dr. Bernard L. Shapiro  
TAMU Newsletter  
966 Elsinore Court  
Palo Alto, CA 94303**RE: Successful Installation of Omega Spectrometers;  
Alert to Omega Users of Repetition Rate Problems**

Dear Dr. Shapiro:

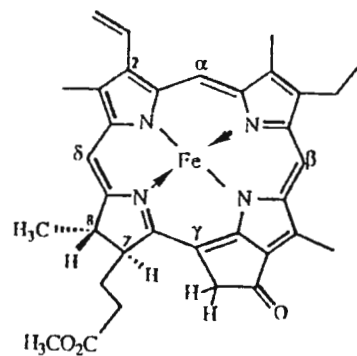
Within the last year we have had two new GE-NMR Omega high resolution spectrometers, an  $\Omega$ -300 and an  $\Omega$ -500, successfully installed here at the UCD NMR Facility. They are currently being used for a wide variety of multinuclear and 2D experiments such as COSY, NOESY, TOCSY, ROESY, and HMQC. Systems studied to date include paramagnetic heme proteins, diamagnetic proteins, carbohydrates, nucleic acids, and natural products. Overall, we are quite satisfied with the performance of both the  $\Omega$ -300 and  $\Omega$ -500.

Recently we have been working to optimize the simple absolute mode COSY experiment on model paramagnetic porphyrin and chlorin systems, for the purpose of applying what we learn about data collection and processing to our paramagnetic protein systems. Figure 1 is a COSY spectrum collected on the  $\Omega$ -300 of a model chlorin, Fe-pyropheophorbide  $a$  (CN)<sub>2</sub>, with  $T_1$  values from 10 to 150 msec. All expected spin connectivities are seen. Although this data is processed with a magnitude calculation, other datasets collected in phase-sensitive mode have shown exceptionally flat baselines over large bandwidths, a great asset for our studies of paramagnetic systems.

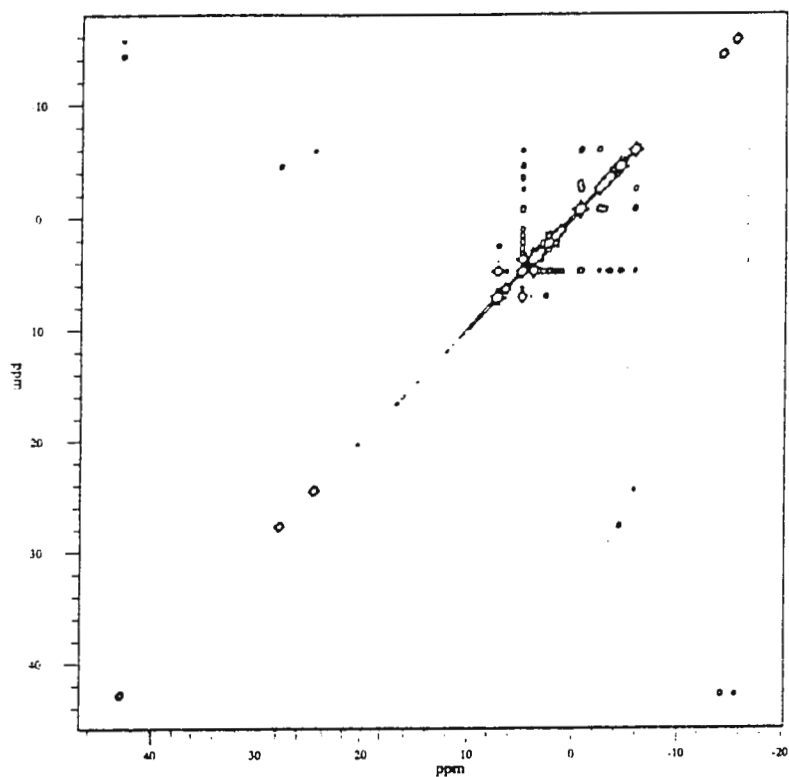
However, experiments just completed to study signal-to-noise as a function of rapid repetition rates for the model system have revealed a serious limitation of the Omega systems: the pulse sequence recycle time is actually longer than the value set by the user. For example, we set up a series of COSY experiments with repetition rates of 8 to 110 times per second, but manual timing of  $t_1$  blocks clearly showed us that the actual rates were only 7 to 32 times per second, with an average 21 msec of 'extra' recycle time added on by the computer (the pulse train itself is accurate as determined on an oscilloscope). Further, we found that additional recycle time was added for all pulse sequences examined (one-pulse, COSY, TOCSY, etc.), although the amount of added time varied with the particular experiment, reaching 160 msec for TOCSY. GE-NMR has been notified and we understand they are actively working to achieve a solution of the problem for the Omega-PSG spectrometers.

Sincerely,

  
Kelly A. Keating  
Jeffrey S. de Ropp  
Gerd N. La Mar  
Director



(a)



(b)

**Fig. 1** (a) Structure of Fe-pyropheophorbide  $\alpha$  (CN)<sub>2</sub>. (b) Absolute mode COSY of (a) in DMSO-d<sub>6</sub>/D<sub>2</sub>O, collected on the  $\Omega$ 300 at a repetition rate of 12 scans/second. The data was processed with a sinebell squared window (phase shifted 0), a magnitude calculation applied to  $t_1$ , and symmetrized. The streaks at ~5 ppm are from the solvent. Note the cross peaks detected from resonances with large hyperfine shift: 2-H $\alpha$  (42.5 ppm) and 2-H $\beta$  trans and cis (-14 and -15.8 ppm); 8-H (28 ppm) and the 8-CH<sub>3</sub> (-4.5 ppm); and between the 7-H (24.5 ppm) and 7-C $\alpha$ H (-6 ppm).



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

October 17, 1990.  
(received 11/1/90)

<sup>133</sup>Cs NMR: First metal ion to show sub-cellular compartmentation by  
"in vivo" NMR.

Dear Barry,

In connection with our ongoing "in vivo" NMR studies of ion transport in root tissue, we developed a need to understand the exact nature of ion compartmentation within functioning cells.

Whereas  $K^+$  is hindered by its high degree of magnetic resonance invisibility due to a strong quadrupolar lattice interactions observed "in vivo" [1]; <sup>133</sup>Cs has a small quadrupolar lattice interaction (spin 7/2, natural linewidth 0.75 Hz) and is close to 100% NMR visible. The relative receptivity of  $Cs^+$  is 2 orders of magnitude higher than  $K^+$ . Previous studies by London and co-workers [2] suggest that  $Cs^+$  may be substituted for  $K^+$  in transport studies of red blood cells. In addition since the  $Cs^+$  chemical shift is highly dependent on anionic environment no shift reagents were necessary to simultaneously examine the internal and external  $Cs^+$  in the spectra of red blood cells.

In our studies, we describe the first direct NMR observation and assignment of both cytoplasmic and vacuolar resonances representing subcellular compartmented  $Cs^+$  in living plant tissue (Fig. 1). Following relaxation time and morphological studies, we assigned the low field resonance (I) to cytoplasmic  $Cs^+$  and mid field resonance (II) to vacuolar  $Cs^+$ . The high field signal (III) corresponds to the  $Cs^+$  in the perfusion medium. These initial results, confirm that the anionic strength of the cytoplasmic compartment of plant root tissue is higher than that of the vacuolar compartment. In addition we note that movement of  $Cs^+$  in the root cells goes sequentially from the cytoplasm to the vacuole (Fig. 1), but only after a critical concentration is established in the cytoplasm.

We anticipate that in vivo <sup>133</sup>Cs NMR will be exploited, as is <sup>31</sup>P NMR, to evaluate intracellular changes in response to environmental stress.

A full account of this work will be reported in BBA (1990) 1054:169-175.

Sincerely,

Philip Pfeffer

Dominique Rolin

1. Springer, C.S. (1987) Ann. Rev. Biophys. Chem. 16, 375-399.
2. Davis, D.G., Murphy, E. and London, R.E. (1988) Biochem. 27, 3547-3551.

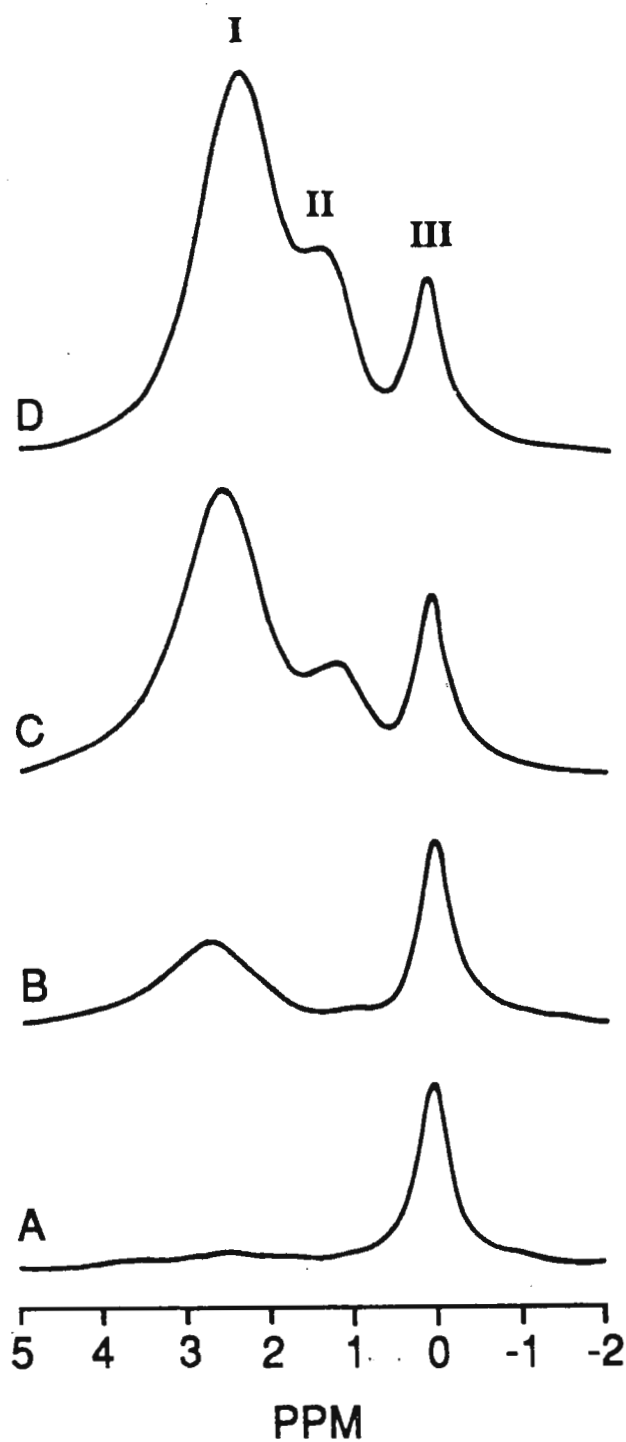


FIGURE 1. 52.3 MHz  $^{133}\text{Cs}$  NMR spectra of approximately 600-900 excised (3-5mm) maize (*Zea mays* BF-43) root tips from 3 day old seedlings perfused with 50mM glucose, 10mM CsCl, 0.1mM  $\text{CaSO}_4$  buffered with MES and Bis-Tris Propane to pH 6.0. Acquisition parameters; 4K data points, spectral width = 1000 Hz,  $90^\circ$  pulse = 7.4  $\mu\text{sec}$ , pulse delay 30 sec, 32 transients per spectrum, exponential line broadening 10 Hz. (A) 19 min after adding the 10mM CsCl to the perfusion medium (B) 1h, 30min after perfusion with the medium containing 10mM CsCl; (C) 7h, 45min of perfusion and (D) 15h, 15min of perfusion.

# When faced with a tough analytical problem . . .

## QUESTION

*How do you find all the thiophenol derivatives matching YOUR CARBON SPECTRUM?*

## ANSWER

**Sadtler Structure Assignment Library**

### STEP:1

Search For  
Thiophenol Derivatives.

Structure Search Version 1.0

File Draw Search View Print Library Utility

CAS Registry Search  
Exact Match Search  
Substructure Search

Source Structure: c1ccccc1S  
Number of Hits: 128

Index	HQ1	Lib	Entry	Name
1	1	13C1	70	PHENYL DISULFIDE
2	1	13C1	90	BENZENESULFONYL CHLORIDE
3	1	13C1	287	BENZENESULFONYL FLUORIDE
4	1	13C1	290	BENZENESULFONYL FLUORIDE, SODIUM SALT
5	1	13C1	227	P-TOLUENESULFONIC ACID, METHYL ESTER
6	1	13C1	355	P-TOLYL DISULFIDE
7	1	13C1	732	METHANOL, P-TOLYLSULFONYL-
8	1	13C1	982	BENZENESULFONIC ACID, HYDRATE
9	1	13C1	983	BENZENESULFONIC ACID, SODIUM SALT
10	1	13C1	987	P-TOLUENESULFONIC ACID, BUTYL ESTER
11	1	13C1	988	BENZENESULFONAMIDE
12	1	13C1	910	P-TOLUENESULFONAMIDE, N-BUTYL-
13	1	13C1	974	ACETIC ACID, PHENYLTHIO-
14	1	13C1	997	P-TOLUENESULFONYL CHLORIDE
15	1	13C1	1837	P-TOLUENESULFONAMIDE, N-METHYL-
16	1	13C1	1129	ANILINE, O-METHYLTHIO-
17	1	13C1	1170	SULFIDE, PHENYL 2-PHENYLPROPYL
18	1	13C1	1296	SULFIDE, P-BROMOPHENYL METHYL
19	1	13C1	1383	SULFIDE, METHYL N-NITROPHENYL

### STEP 2:

Match Those Derivatives  
With Your Spectrum.

NMR Search 2.12

File Search View Library Print Utility Import Page

Unknown Entry

PEAK SEARCH PARAMETERS

Peak Tolerance: 0.3 ppm (value between 0.1 and 2.0)

Minimum No. of Peak Match: 4

Algorithm

☐ Forward Search

☒ Reverse Search

Cancel

OK

## YOUR SEARCH IS OVER!

NMR Search 2.12

File Search View Library Print Utility Import Page

LIB PEAK LOCATION

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Sadtler ID: ST71

First Peak Table ==  
(Total of peaks: 5)

No.	Location	Intensity
1	15.60	4
2	124.90	5
3	126.70	9
4	128.70	9
5	138.60	1

Source Library: 13C1 - C-13 NMR STANDARDS  
<<Unknown Buffer>>  
File Name: THIDEMO.NPF  
Chem. Name: ODIFEROUS SPECIES  
CAS Registry Number: unknown  
Comment: process shutdown 12/9/89, green

READY

STRUCTURE

Print View

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# Sadtler $^{13}\text{C}$ NMR Structure Assignment Library

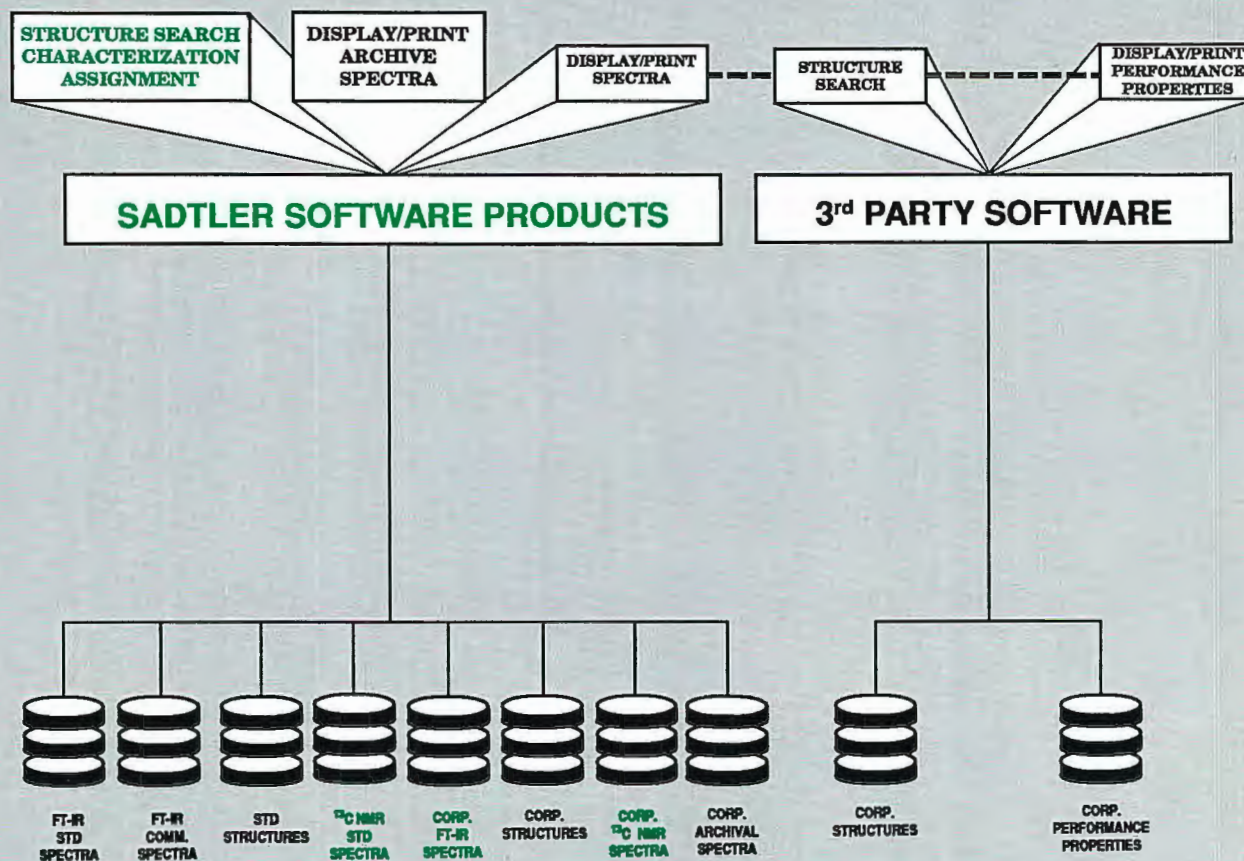
## *The Sadtler $^{13}\text{C}$ NMR Structure Assignment Library consists of:*

The Sadtler Standard  $^{13}\text{C}$  NMR Spectra Library  
containing entries for 30,000 pure compounds

Sadtler  $^{13}\text{C}$  NMR Search Software

Sadtler  $^{13}\text{C}$  NMR Molecular Structure Library  
(the corresponding 30,000 chemical structures)

Sadtler Molecular Substructure Search Software



The assignment library provides a unique access to Sadtler's  $^{13}\text{C}$  NMR spectra that correlates molecular properties with chemical shifts. Structure elucidation is facilitated by searching anticipated structural features and measured chemical shifts.

# ARGONNE NATIONAL LABORATORY

9700 SOUTH CASS AVENUE, ARGONNE, ILLINOIS 60439

October 22, 1990  
(received 10/25/90)

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

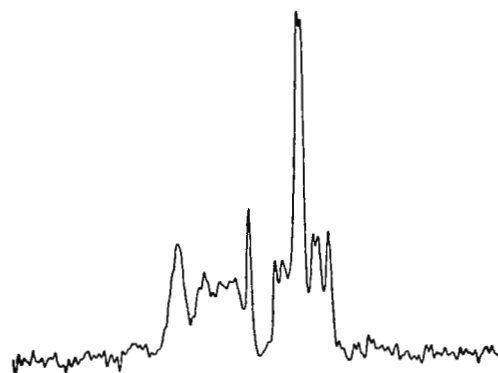
## Solid $^{13}\text{C}$ NMR of Rotted Deck

Dear Barry:

Earlier this spring, I entered onto my 23-year old deck from the kitchen with trepidation, knowing that its very foundation was wavering under my feet. Having slowly traversed the width, I carefully began to test the outside hand railing, whereupon the railing plunged to the ground six feet below. Horrified, I clutched the corner post as the deck flooring began to sag beneath me. I quickly leaped to the ground just in time to see the deck crash before me. Obviously, the harsh Chicago winter and the torrential rains of spring took their final toll on my deck, which the summer before appeared to be in reasonably good shape. As I peered up at the rotted rubble, I began to wonder why the wood had decayed away in a relatively short period of time. Alas, this seemed to be a task for solid  $^{13}\text{C}$  NMR, so I gathered specimens of the rotted deck for analysis.

ROTTED WOOD

The figure at the right shows  $^{13}\text{C}$  CP/MAS spectra (at 25 MHz, contact time = 3 ms,  $\nu_r = 4$  kHz) of the two specimens: a rotted wood (top) specimen dark red in color that could easily be hand pulverized into a coarse powder, and a specimen of partially rotted wood (bottom) that was sampled a few centimeters from the previous one. The latter specimen was slightly discolored but retained the physical integrity of normal wood along with most of its strength. Aromatic resonances from  $\delta$  110–160 ppm and the sharp resonance at  $\delta$  55 ppm can be assigned to carbons of lignin, while the sharp resonances at  $\delta$  64, 73, 85, and 106 ppm are carbons in cellulose structures. The appearance of less intense resonances at about  $\delta$  170 ppm indicates oxidation of the samples. The most salient trend observed with degree of specimen decay is the progressive loss of cellulose: the partially rotted wood and rotted wood samples analyze for 55% and 50% cellulose by weight, respectively. For comparison, fresh pine wood is about 70 weight % cellulose.

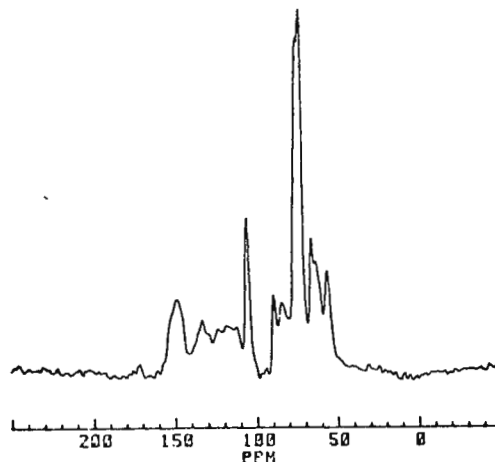


PARTIALLY ROTTED WOOD

Of course, the lesson to be learned is that the deck was decaying long before it collapsed. However, loss of structural integrity of wood occurs over an extremely narrow range in cellulose content, somewhere between 50–55 weight %.

Sincerely,

Robert E. Botto  
Chemistry Division



**KARL-FRANZENS-UNIVERSITÄT GRAZ**  
**Institut für Organische Chemie**

24. Okt. 1990

A-8010 Graz,

Heinrichstraße 28

Tel. (0316) 380 —

(received 10/31/90)

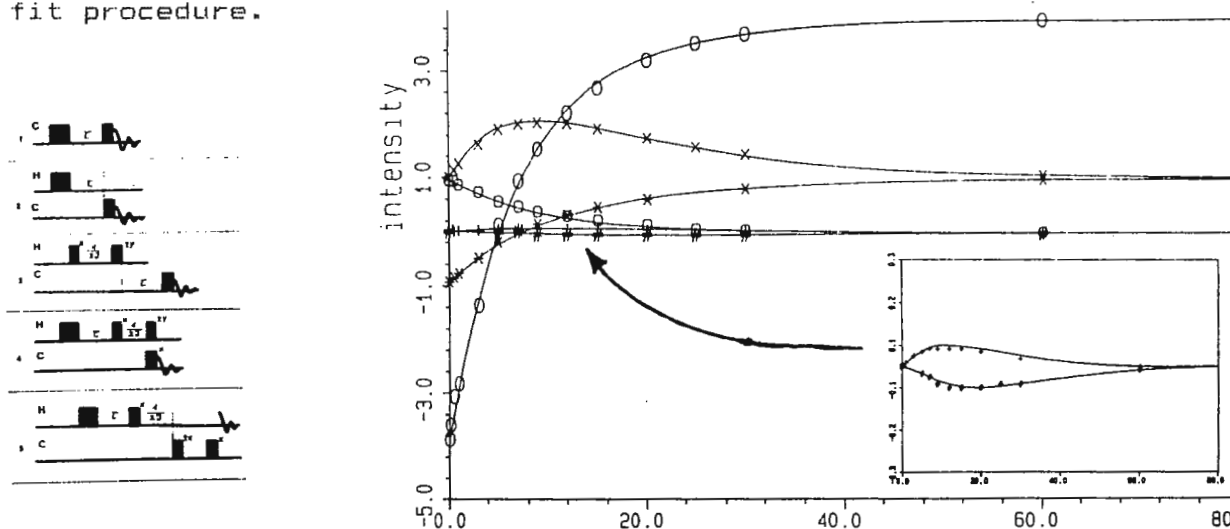
Unser Zeichen:

Prof. Dr. B. Shapiro  
 TAMU NMR Newsletters  
 Elsinor Court  
 Palo Alto, California 94303 USA

Dear Dr. Shapiro !

The more data the better the fit !

The "normal modes" formalism, which was proposed by the group of Grant, depends - with respect to it's results - to an enormous degree on the outcome of an iterative multi parameter fit procedure. The correlation thereby connects parameters like the rotation diffusion behavior, random field contributions and chemical shift anisotropy to the time evolution of different kinds of magnetization. In addition to the well known inversion recovery pulse sequences 1 and 2 we adopted the sequence 3 to get information about the behavior of the so called zz-order of magnetization, whereas especially sequence 5 turns out to be of benefit in detecting the relaxation of the protons in  $^{13}\text{C}$  isotopomers. The wealth of additional significance obtained by making use of sequences 3, and 5 thereby increases the reliability of the fit procedure.



The figure shows the normal modes of formic acid measured at 200 MHz. \*  $^a v_1$  after A inversion, x  $^a v_1$  after X inversion, o  $^s v_3$ , +  $^s v_3$  after A inversion, #  $^s v_3$  after X inversion, o  $^a v_2$  after X inversion.

Yours sincerely

*H. Sterk*  
 H. Sterk

*G. Kontaxis*  
 G. Kontaxis



October 17, 1990 (received 10/18/90)

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

## NMR INVESTIGATION OF CROSSLINKING IN MELAMINE-FORMALDEHYDE AEROGELS

Dear Barry:

We have prepared organic aerogels that are both colorless and transparent from the aqueous, sol-gel polymerization of melamine with formaldehyde. The optical clarity of the aerogels has been correlated with the pH of the polymerization. Transparent aerogels are only obtained at pH ~ 1.5-1.8. We have used N-15 and C-13 NMR to compare the crosslinking chemistry, composition, and relaxation times of a transparent and opaque melamine-formaldehyde (MF) aerogel.

Melamine is a hexafunctional monomer capable of reaction at each of the amine hydrogens. Under alkaline conditions, formaldehyde adds to the above positions to form hydroxymethyl (-CH<sub>2</sub>OH) groups. In the second part of the polymerization, the solution is acidified to promote condensation of these intermediates, leading to gel formation. The principal crosslinking reactions include the formation of (1) diamino methylene (-NHCH<sub>2</sub>NH-) and (2) diamino methylene ether (-NHCH<sub>2</sub>OCH<sub>2</sub>NH-) bridges.

Differences in the number and type of chemical crosslinks were thought to be responsible for differences in the optical properties of MF aerogels. Based upon this hypothesis, C-13 and N-15 NMR were used to determine the chemical shifts and relaxation parameters of an opaque (pH~0.7) and transparent (pH~1.5) aerogel. Attempts to follow the reaction *in situ* were hindered by line-broadening from MF "clusters" generated in solution. This same effect was observed in previous NMR studies on the sol-gel polymerization of resorcinol with formaldehyde.

We have measured T<sub>1</sub>, T<sub>1</sub>rho, T<sub>CH</sub> or T<sub>NH</sub>, and T<sub>1</sub>rho(H) on two preparations of N-15 labeled melamine formaldehyde (MF) aerogels using N-15 CPMAS and two nonlabeled preparations using C-13 CPMAS (see below). These two N-15 labeled preparations differ only in the pH of the acid catalyzed condensation reaction, pH 0.7 and 1.5. The two samples differ substantially in their optical clarity, the pH 0.7 sample being much more opaque. The relaxation times appear in Table 1. The close agreement of the relaxation times indicate that the two preparations are essentially identical. The pH of the reaction appears to affect only the aggregation process, and thus the pore size of the aerogel, not the structure of the polymer network.

Similarly, two samples of MF aerogels, CA1218H (clear) and CA0104N (opaque), were studied using C-13 CPMAS. The relaxation times for these two samples appear in Table 2. Here, again there is close agreement in the values except for the T<sub>1</sub>rho(H) values where one of the samples requires a two component fit. If this difference is maintained, after further study, a difference in local proton environments for the two preparations would be indicated.

Best Regards,

*Ray*

Raymond L. Ward

Richard W. Pekala

Table 1. MF aerogels; N-15 NMR

	MFA (pH=0.7)		MFA (pH=1.5)	
T <sub>1</sub> (N)	174 ppm	45.6 s	T <sub>1</sub> (N)	---
	96 ppm	43.6 s		---
T <sub>1</sub> rho(N)	174 ppm	12.9 ms	T <sub>1</sub> rho(N)	174 ppm 15.5 ms
	96 ppm	3.6 ms		96 ppm 4.3 ms
T <sub>NH</sub>	174 ppm	2.95 ms	T <sub>NH</sub>	174 ppm 2.84 ms
	96 ppm	0.08 ms		96 ppm 0.09 ms
		(62.3%)		(95%)
		0.83 ms		0.9 ms
		(37.7%)		(5%)
T <sub>1</sub> rho(H)	174 ppm	10.5 ms	T <sub>1</sub> rho(H)	174 ppm 11.7 ms
	96 ppm	7.2 ms		96 ppm 8.1 ms

Table 2. MF aerogels; C-13 NMR

	CA 1218H			CA 0104N	
T <sub>1</sub> (c)	168 ppm	21.6 s	T <sub>1</sub> (c)	168 ppm	22.1 s
	52 ppm	25.35 s		52 ppm	24.1 s
T <sub>1</sub> rho(c)	168 ppm	41.6 ms	T <sub>1</sub> rho(c)	168 ppm	40.4 ms
	52 ppm	8.3 ms		52 ppm	7.0 ms
T <sub>CH</sub>	168 ppm	0.48 ms	T <sub>CH</sub>	168 ppm	0.46 ms
	52 ppm	0.15 ms		52 ppm	0.01 ms
		(68%)			(67.5%)
		0.27 ms			0.15 ms
		(32%)			(32.5%)
T <sub>1</sub> rho(H)	168 ppm	7.49 ms	T <sub>1</sub> rho(H)	168 ppm	5.94 ms
	52 ppm	16.5 ms		52 ppm	5.66 ms
		(30%)			
		4.4 ms			
		(70%)			



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

october 17th 1990  
(received 10/23/90)

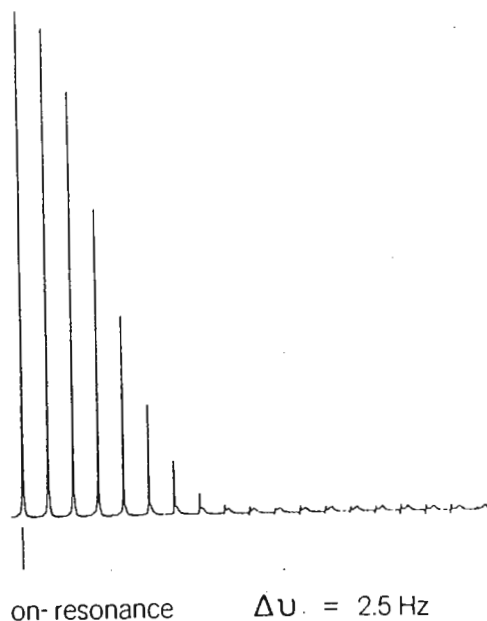
## DETERMINATION OF EXCITATION PROFILES

Dear Dr. Shapiro

recently the application of shaped weak pulses or DANTE pulsetrains which excite essentially pure absorption signals with a desired profile in frequency domain has become most popular. To experimentally determine and to prove the expected frequency profiles in z-, x- and y-direction for a given shaped pulse, the transmitter (or decoupler) frequency has to be stepped in small increments through the resonance frequency of a given signal.

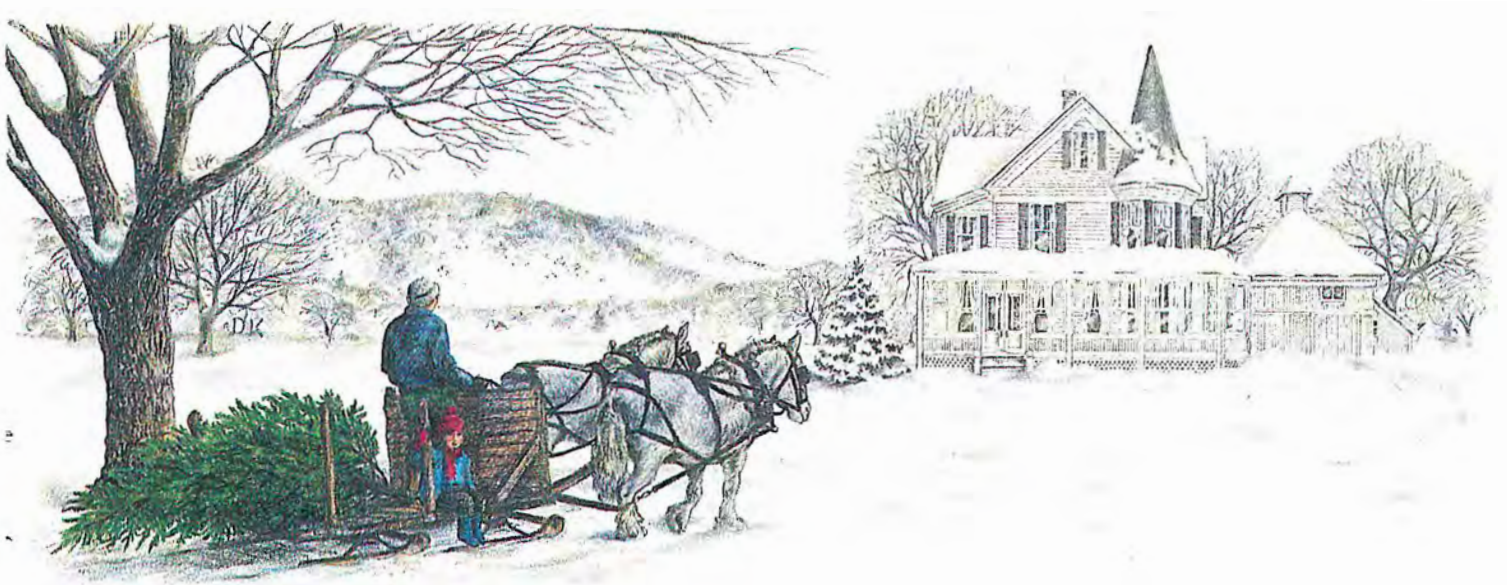
We have developed two simple **PASCAL routines to generate the necessary frequency lists** (FQLIST) used in our BRUKER microprograms either for normal or reverse mode of detection. The programs are available on request (please enclose a floppy).

Figure 1 shows the correspondingly determined z-excitation profile of a 80 ms gaussian  $1024\ 180^\circ$  pulse as applied on our BRUKER AM 400 spectrometer equipped with a selective excitation unit SEU.



Yours sincerely

Dr. P. Bigler



Dear Colleagues:

Each year during the holiday season we pause to reflect on the year gone by and the year to come. We are grateful to you, the NMR community, for your continued support and confidence in Doty Scientific and our products.

During this season of "Peace and goodwill toward men" we would like to stop and say "Thank you". We look forward to continuing to serve you in the coming year.

We wish you a holiday season filled with joy and peace.

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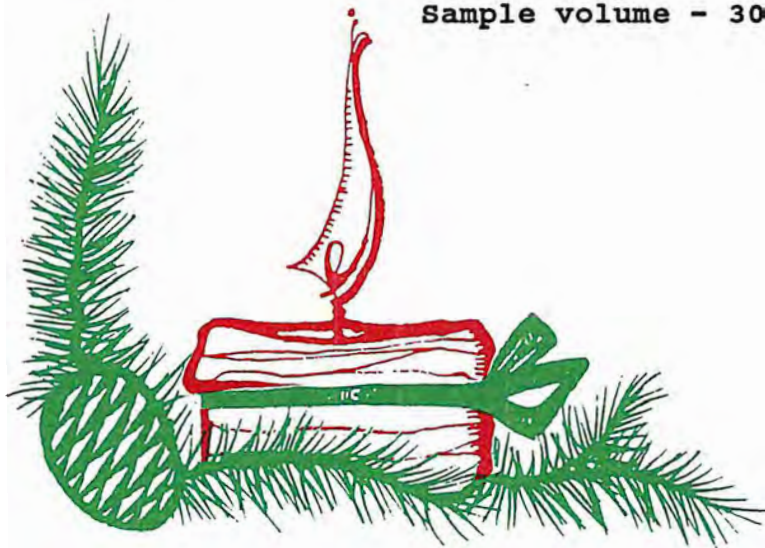
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## INSTITUTE OF CHEMICAL PHYSICS Academy of Science USSR

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

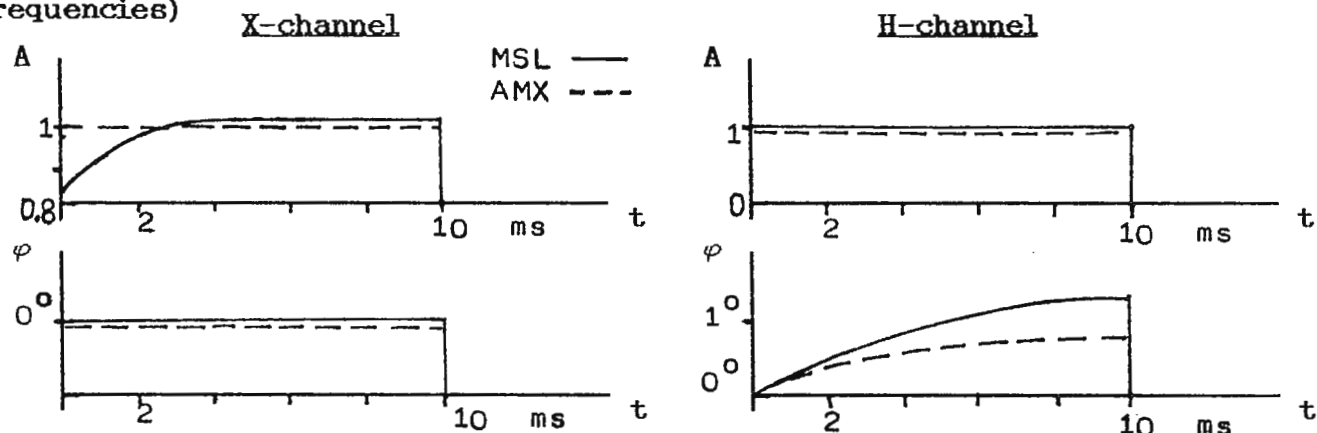
117344 Moscow  
ul. Kosygina - 4  
USSR  
(received 11/6/90)  
October 30, 1990

Something about performance of transmitter systems

Dear Professor Shapiro,

Cross-polarisation is a promising technique for magnetization transfer in liquids (1). It is well known that this method requires simultaneous irradiation of both I and X spin systems with sufficiently strong RF-fields during a period of about 10 ms length. Hence, the question of the amplitude and phase stability becomes of a great importance. It is especially true in the case of composite-pulsed cross polarisation period (2).

During this year our interest lied in the field of the cross-polarisation, so we had tested two NMR spectrometers AMX-400 and MSL-300. The typical examples of the amplitude and the phase dependences on time are shown on the pictures bellow. Output power was 25 W for X-channel and about 30 W for decoupler ( $^{13}\text{C}$  and  $^1\text{H}$  frequencies)



The curves for the phases were measured by means of the receiver of the NMR spectrometers. Performances of decouplers are about the same for both instruments. The "rise time" of the phases is about 7 ms, after that the stability is excellent. The difference is much more significant for X-channel: the linear amplifier of AMX-400 shows very good amplitude and phase stability (better than 1%); C-class transistor transmitter of MSL can't generate flat RF-pulse, though of course it is possible to use high power booster of MSL instrument, which gives much better results.

We believe that for effective cross-polarisation based coherence transfer in liquids the linear transmitters are really needed.

Sincerely  
Dmitriy Yu. Artemov

1. L.Muller, R.R.Ernst, Molecular Physics. 38, 963 (1979).
2. D.Yu.Artemov, J. Magn. Reson. (1990) In Press.

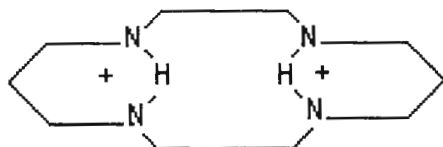
# Intramolecular Hydrogen Bonding in 1,4,8,11-tetraazacyclotetradecane (Cyclam)

Michael J. Minch  
Department of Chemistry  
University of the Pacific, Stockton, CA 95211

Sir:

(received 11/7/90)

Sometimes even a simple experiment tells a great deal. The title compound is a cyclic polyamine with four basic nitrogens. In the course of determining  $^{13}\text{C}$  spectra of cyclam as a function of pH, we found that the chemical shifts of the methylene carbon resonances are pH dependent over the range 13.5 to 11 as the first and second nitrogen protonations occur. However the spectrum is pH independent from 11 to 2.5 and only below pH 2.5 do the carbon lines again move as the third and fourth protonations occur. The exceptional stability of the dication has been observed by conventional titration studies but our NMR spectra give direct evidence of the reason for this unusual stability. In principle there are three different pairs of nitrogens that could be protonated in the dication of cyclam and, in each of these structures, there are five or six chemically different carbons if protons were localized on individual nitrogens. The isomers and the numbers of different carbons are 1,4- $\text{H}_2$  (six carbons); 1,8- $\text{H}_2$  (five carbons); and 1,11- $\text{H}_2$  (five carbons). However we observe only three carbon lines at any pH, which implies that protons are not localized on individual nitrogens. A symmetrical intramolecular hydrogen bonded structure with only three chemically different carbons agrees most closely with the published crystal structure of the *Bis*-perchlorate salt of cyclam.



We are currently investigating the proton spectra of cyclam and related cyclic polyamines in 60%  $\text{H}_2\text{O}$ .

Respectfully  
*Mike*  
Mike Minch

10/12/90 (received 10/16/90)

Professor Bernard L. Shapiro  
Texas A&M NMR Newsletter  
966 Elsinor Ct.  
Palo Alto, CA 94303

Using a LIBRA/Macintosh-II computer system on an NT-300

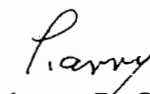
Dear Dr. Shapiro,

Due to the aging of the computer system on our Nicolet/GE NT-300, we thought it necessary to try and revive our ancient spectrometer with a new computer system. Limited funds compounded the problem of whining disk drives and we decided to go with the LIBRA system (tecmag, Inc.). Since this upgrade, it has been quite easy to implement pulse sequences via the graphically based pulse sequence design, typical of most Macintosh applications. Along with the ease of use we have substantially increased our computing and storage power with a 80 Mbyte Hard disk, 12 MFlop Array Processor (MacDSP from Spectral Innovations, Inc.) and 2D processing with FTNMR (Hare Research, Inc.) via EtherTalk to the University's VAX cluster.

We have found, however, that it was necessary to modify (invert) the 0/180 phase line in the Spin Decoupler. It seems that the direction of the phase may vary from spectrometer to spectrometer but may be determined with a simple one pulse experiment through the  $^1\text{H}$  decoupler coil. The phasing may be corrected in either the Hardware or the Software and most likely will be taken care of in the Software in the near future by tecmag.

We have been able run a number of interesting experiments with this new computer system including HOHAHA<sup>1</sup>, TPPI<sup>2</sup> and hypercomplex<sup>3</sup> Phase-Sensitive COSY, and Phase-Sensitive NOE<sup>3</sup> experiments to name a few. Another interesting note is that the MLEV type decoupling is written in a text file that is compiled and sent to the pulse programmer, since it is written in this manner it needs only to be written once and the user can click on its icon at whatever event in the pulse sequence whenever he wishes to implement it. The MacNMR application along with the Lock and Variable Temperature programs run under MultiFinder (a multi-tasking-like operating system) so that other applications may be run as well, such as word processing. In fact, this letter was written while running an experiment.

  
Kenneth D. Hope

  
Larry D. Sims

---

## REFERENCES

1. A. Bax and D. G. Davis, *J. Magn. Reson.*, **65**, 355 (1985).
2. D. Marion and K. Wuthrich, *Biochem. Biophys. Res. Commun.*, **113**, 967 (1983).
3. D. J. States, R. A. Haberkorn, and D. J. Ruben, *J. Magn. Reson.* **48**, 286 (1982).



Department of Chemistry

Professor Gideon Fraenkel

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BITNET TS6191@OHSTVMA120 West 18th Avenue  
Columbus, OH 43210-1173Phone 614-292-2251  
FAX 614-292-1685  
TELEX 332911

Answer Back Code: OSU CHEM UD

October 31, 1990 (received 11/8/90)

Dr. B. L. Shapiro  
TAMU NMR Newsletter  
966 Elsinore Court  
Palo Alto, CA 94303Correction: Relative  
Motions of Ions  
Within Ion-Pairs

Dear Barry:

The two sentences starting on line 8 parag. 2 of our recent letter 385-51 should have read:

mixture, 88/10. "Of particular interest is the non-equivalence of all carbons on the pendant ligand, at low temperature, 160 K. Line-shape analysis of the  $^{13}\text{C}$  signal averaging which takes place with increasing temperature,  $\Delta$  with  $\blacktriangle$ ,  $\circ$  with  $\bullet$ ,  $\square$  with  $\blacksquare$  and the two methoxy carbons, reveals that the exchange rates responsible for these line-shape changes are all the same with  $\Delta H^\ddagger = 7.6$  kcal and  $\Delta S^\ddagger = -15$  eu." These effects must be the result of rotation of

With apologies and best regards.

Yours sincerely,

Gideon Fraenkel  
Professor of Chemistry

To: TAMU Newsletter Readers

We are in need of a Varian cavity, either TE<sub>102</sub> or TM<sub>011</sub> preferred, to fit a E-line or Century series EPR spectrometer. We are aware that many Varians have been sent to the ironmonger, but people usually keep their cavity for "sentimental" reasons. We want to buy an old cavity - we will have it reconditioned, if necessary - as these are no longer sold by Varian.

Please contact Professor Lawrence J. Berliner at the addresses noted above if you can help us out.

Sincerely yours,

Lawrence J. Berliner  
Professor of Chemistry



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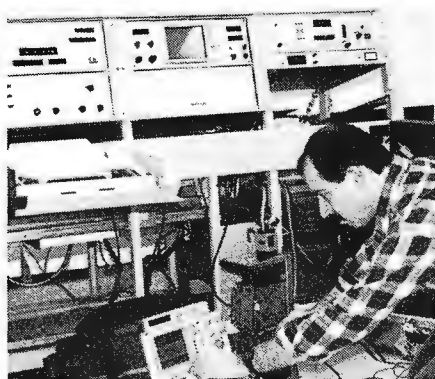
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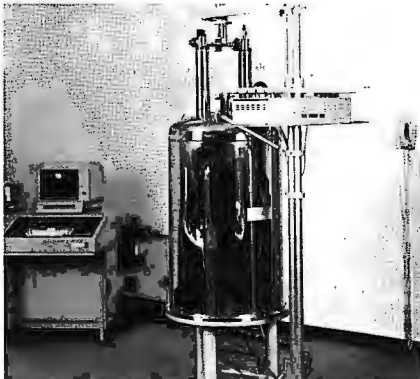
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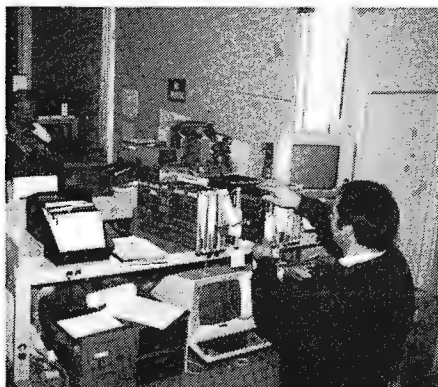
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**A Tutorial and Workshop Devoted to Nonmedical,  
Industrial and Solid State Biomedical Applications of  
Nuclear Magnetic Resonance Imaging**

---

**Massachusetts General Hospital  
MGH NMR Center  
Charlestown (Boston), Massachusetts  
May 13 - 14, 1991**

---

Nuclear Magnetic Resonance Imaging (NMRI or MRI) is a mature and well-proven noninvasive technique which has brought a revolution in medical diagnostic radiology. Quite recently, there has been a surge in the development of nonmedical applications of MRI covering a multitude of areas ranging from materials science to chemistry, physics, engineering, fluid flow and botany. Materials that have been studied include ceramics, polymers, elastomers, composites, geological materials, oil cores, wood, porous media, soils, biomaterials and medical prostheses.

The purpose of this tutorial and workshop is to acquaint industrial and academic scientists and engineers with the principles and practice of magnetic resonance imaging, especially as applied to problems in materials science, industrial R & D, quality control and nondestructive testing. The presentation will consist of lectures by several internationally known researchers, and will include a tour of the MGH NMR Center. This workshop should provide an excellent forum for the discussion of novel ideas for adapting MRI technology in many areas.

The expanded two day format will allow for a number of contributed papers. Please submit a camera-ready 15 cm wide by 10 cm high abstract on plain white paper, showing title, authors, affiliation and abstract text to the address shown below by April 1. Mark the envelope "Materials Workshop." If there is sufficient demand, the proceedings of the workshop will be published.

For more information contact:

Phone:

Internet:

Jerome L. Ackerman

617-726-3083

jerry@nmr-r.mgh.harvard.edu

Leoncio Garrido

617-726-5820

garrido@nmr-r.mgh.harvard.edu

Massachusetts General Hospital

NMR Center

149 13th Street

Charlestown, MA 02129

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617-726-5819



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Your responsibilities will entail applications research and development, customer demonstrations, assisting in product development and technical sales support activities.

Requirements include a BS in Chemistry, preferably a Master's or PhD, with a minimum of 4 years' experience in NMR techniques and instrumentation. Your skills and experience should encompass liquid state, solid state or microimaging NMR with demonstrated familiarity in current techniques along with computer and NMR pulse sequence programming. Hardware experience is desirable. Some travel will be required. Respond to Dept. AC.

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**varian**



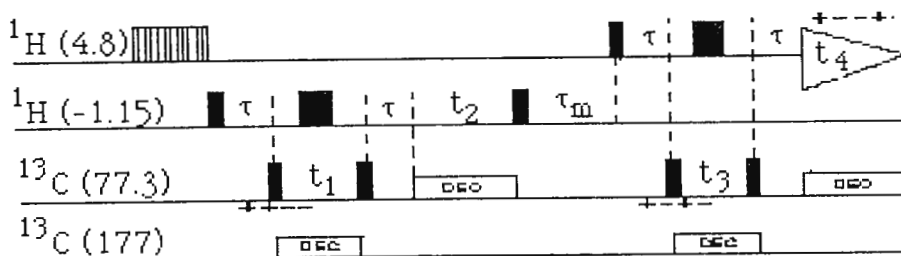
October 27, 1990  
(received 10/29/90)

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

Re: [ $^{13}\text{C}$ ,  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^1\text{H}$ ] 4D NMR

Dear Dr. Shapiro:

We report here on our first experiences with 4D NMR spectroscopy (1), which is part of our continuing effort to develop NMR methods for the study of larger proteins and macromolecular complexes in solution. The sequence used is:



The 4D spectrum can be most easily understood as an editing of a 2D NOESY spectrum, where protons resonating in  $f_2$  are edited by the frequency of their attached heteronuclei ( $f_1$ ) and protons in  $f_1$  by the frequency of their attached heteronuclei ( $f_3$ ). At first sight, it may appear that when this experiment is not performed with two different heteronuclear species (2), that no additional information is obtained as compared to the 3D variants of the experiment. However, as shown in the figure, a remarkable improvement in resolution is achieved by going from 3 to 4 dimensions using the  $^{13}\text{C}$  nucleus twice. The figure is composed of a projection of all data in the aliphatic region on a single plane, the "2D" experiment. This "2D" experiment is edited in  $f_2$  to yield a 64 plane "3D" data-set, from which 2 planes are shown in the figure (actually obtained as projections of the 4D data). These "3D" data are further edited in  $f_1$  to yield 64 planes per 3D data set. Two of these planes out of the 4D experiment are shown for each of the "3D" planes. It is clear that a large resolution enhancement is obtained as compared to the 3D data, allowing many more NOEs to be unambiguously identified for more accurate 3D structure determinations. Note that almost no diagonal signals are observed in the planes of the 4D data; diagonals occur only in those planes where  $f_1 = f_3$ . This means, that cross peaks between protons that have absolutely degenerate resonance frequencies can be resolved, provided that the frequencies of the attached  $^{13}\text{C}$  nuclei are different, and that the identification of NOE peaks close to the diagonal is facilitated, as indicated by arrows in a 4D plane in the figure.

The experiment was carried out with 3.8 mM  $^{13}\text{C}$  labeled T4-lysozyme (19.7 kDa), prepared by Drs. L.P. McIntosh and F.W. Dahlquist at the University of Oregon, in 9 days using a modified Bruker AM500 spectrometer. The data was collected as  $36 \times 128 \times 32 \times 2048$  ( $t_1 \times t_2 \times t_3 \times t_4$ ) real points and was  $64 \times 256 \times 64 \times 384$  ( $f_1 \times f_2 \times f_3 \times f_4$ )

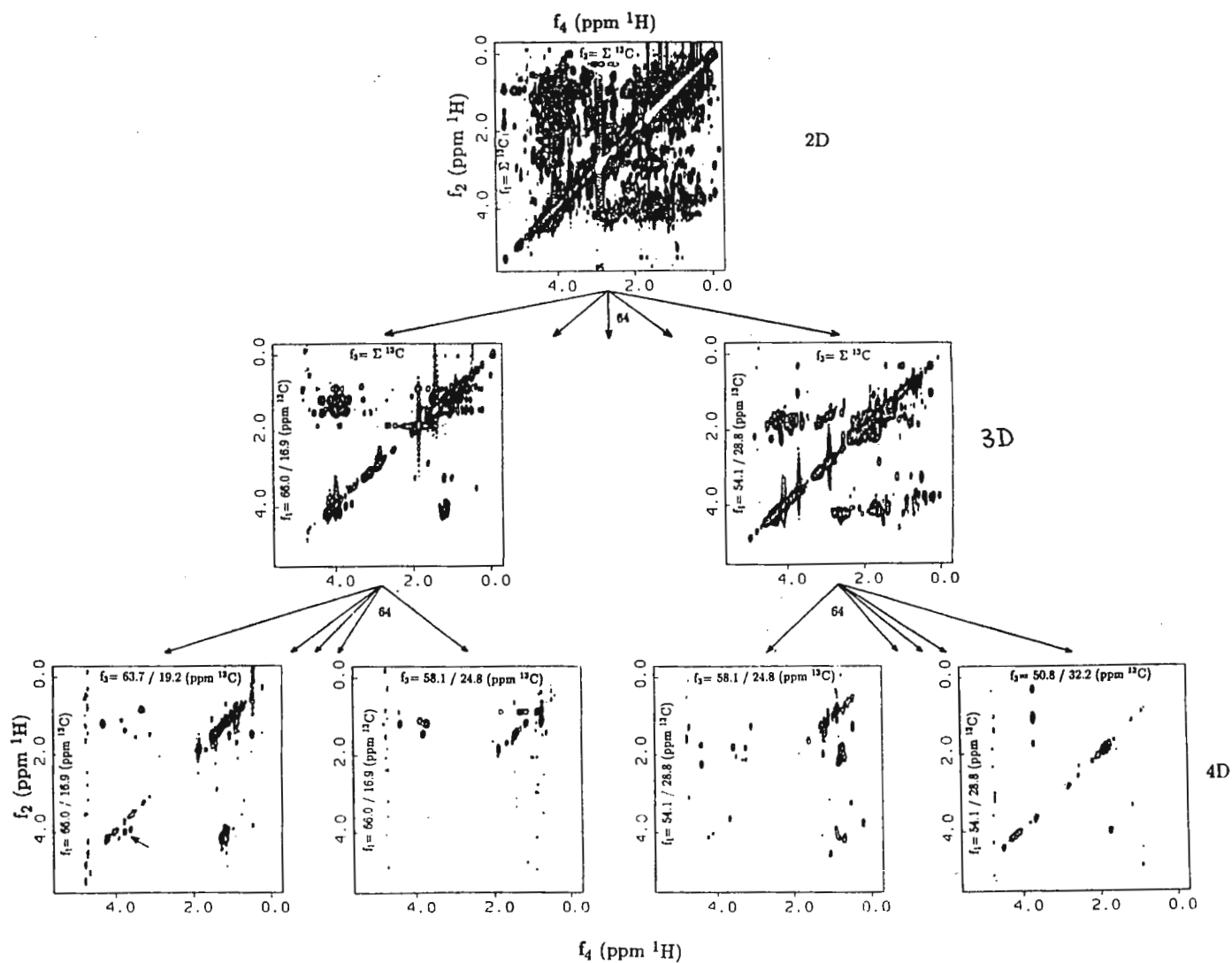
points (4096 NOESY planes) after transformation. The sensitivity of the experiment was found to be as that of an overnight 2D NOESY.

Sincerely Yours,

Hugh Eaton	Stephen Fesik	Robert Gampe	Gerd Gemmecker
<i>Hugh</i>	<i>Steve</i>	<i>Robert Gampe</i>	<i>Gerd</i>
Placido Neri	Edward Olejniczak	Andrew Petros	Erik Zuiderweg
<i>Placido</i>	<i>Ed</i>	<i>Andrew</i>	<i>Erik</i>

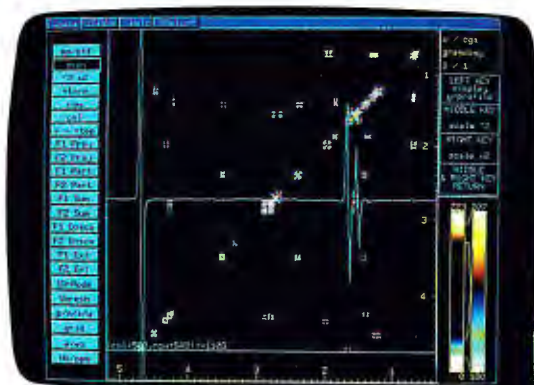
1) Presented at the XIV International Conference Magnetic Resonance in Biological Systems, Warwick, Sept. 1990

2) L.E. Kay, G.M. Clore, A. Bax, A.M. Gronenborn, Science 249, 411 (1990)



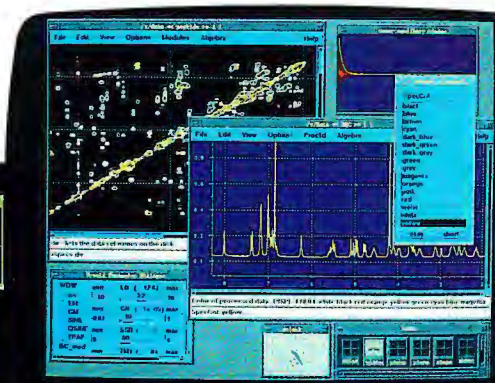
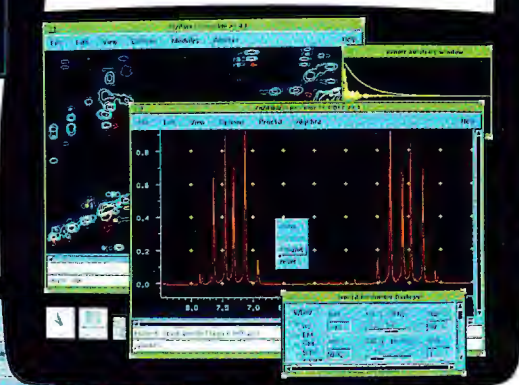
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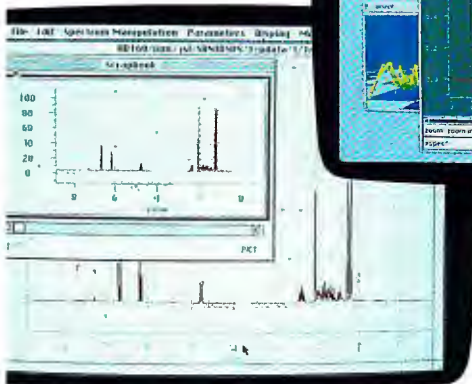
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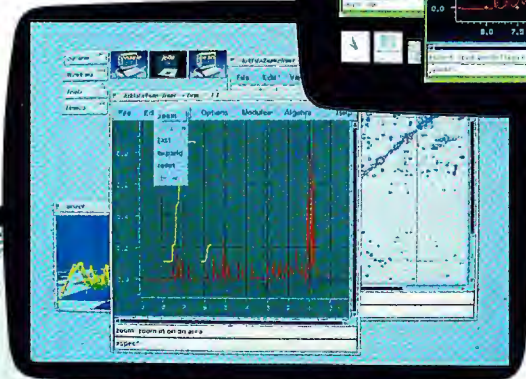


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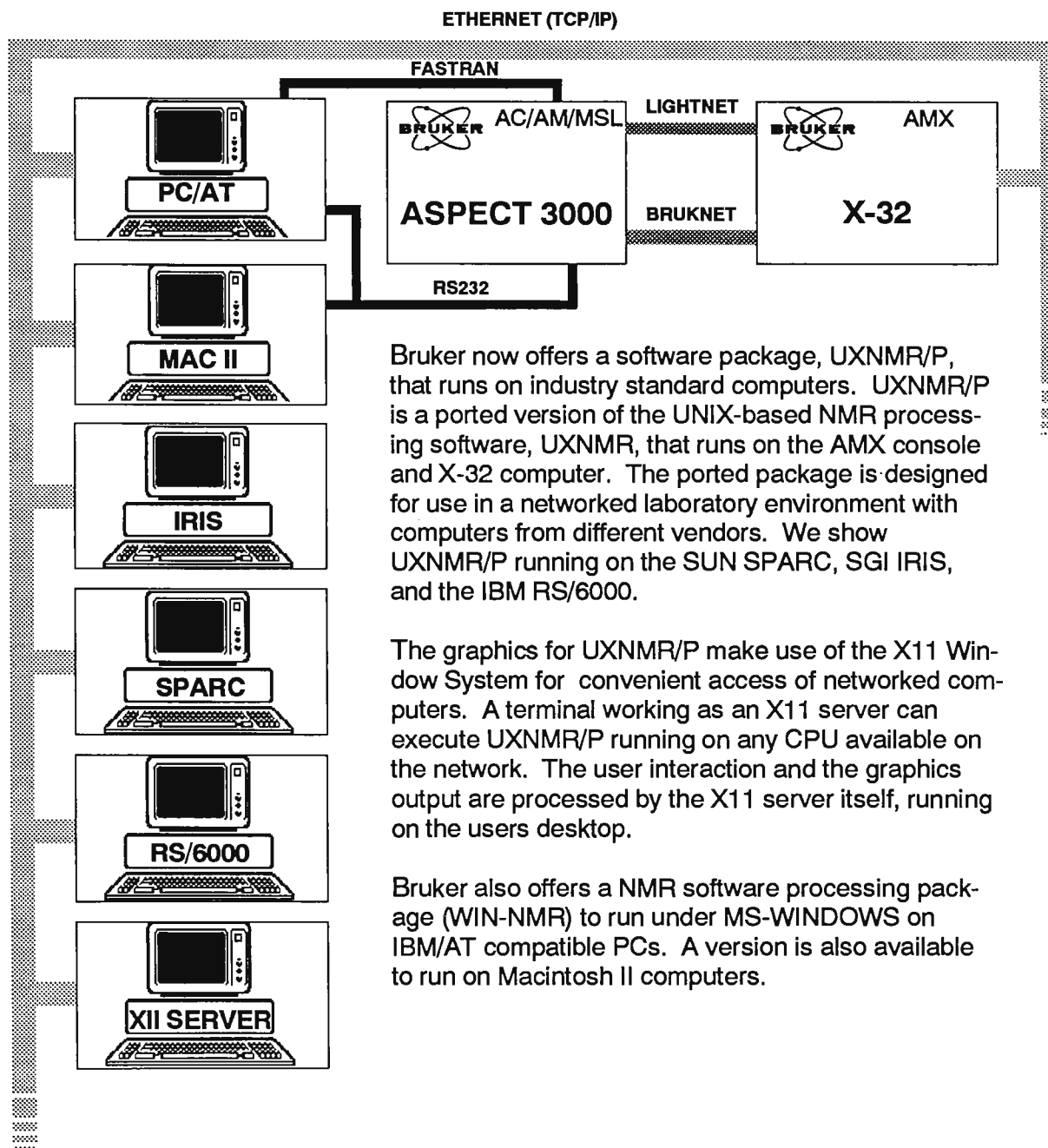


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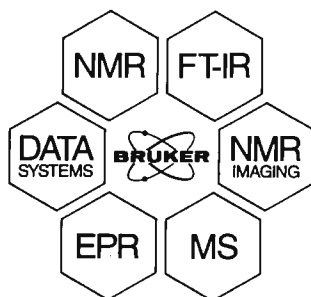
# BRUKER SOFTWARE AND NMR NETWORKING



Bruker now offers a software package, UXNMR/P, that runs on industry standard computers. UXNMR/P is a ported version of the UNIX-based NMR processing software, UXNMR, that runs on the AMX console and X-32 computer. The ported package is designed for use in a networked laboratory environment with computers from different vendors. We show UXNMR/P running on the SUN SPARC, SGI IRIS, and the IBM RS/6000.

The graphics for UXNMR/P make use of the X11 Window System for convenient access of networked computers. A terminal working as an X11 server can execute UXNMR/P running on any CPU available on the network. The user interaction and the graphics output are processed by the X11 server itself, running on the users desktop.

Bruker also offers a NMR software processing package (WIN-NMR) to run under MS-WINDOWS on IBM/AT compatible PCs. A version is also available to run on Macintosh II computers.



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# The University of Georgia

Complex Carbohydrate Research Center

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

(received 10/26/90)

October 24, 1990  
HvH 90-A-153

## *A new application of the Overbodenhausen experiment*

Dear Dr. Shapiro:

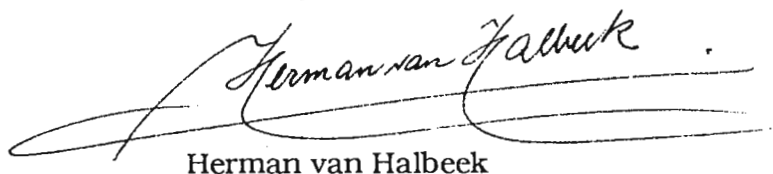
While searching for long-range C,H coupling constants in oligosaccharides, we found that a slightly modified version of the so-called Overbodenhausen experiment [1] allowed us to accurately measure such long-range heteronuclear couplings, along with homonuclear H,H couplings. The original Overbodenhausen experiment [1] was designed for tracing one-bond C,H correlations. The essential modification we implemented in the pulse sequence [1] is a short spin-lock pulse (SL) at the end of the preparation period (cf. [2]):

$$\begin{array}{l}
 {}^1\text{H:} \quad (\pi/2)_x \quad \tau \quad \pi^* \quad \tau \quad \text{SL}_x \quad (\pi/2)_y \quad \Delta \quad \pi \quad \Delta \quad (\pi/2)_x \quad \text{acquisition} \\
 {}^{13}\text{C:} \quad \quad \quad \pi \quad \quad \quad (\pi/2)_\phi \quad \quad \quad (\pi/2)_\psi
 \end{array}$$

This spin-lock pulse purges not only the  ${}^1\text{H}$  magnetization that is not coupled to  ${}^{13}\text{C}$  [2] but also all antiphase terms in the density matrix that evolved during  $2\tau$  due to homonuclear couplings. If the preparation time  $2\tau$  is chosen long enough for terms to evolve due to heteronuclear couplings, one detects pure-phase  ${}^1\text{H}$  multiplets which are *in-phase* with respect to *homo*-nuclear and *anti-phase* with respect to *hetero*-nuclear couplings. The sensitivity of the experiment is critically dependent on how much magnetization is being purged by the spin-lock pulse. For optimum sensitivity, either a judicious choice of the duration of the preparation delay is necessary, or the  ${}^1\text{H}$  inversion pulse  $\pi^*$  in the middle of the preparation period is made selective such that all pertinent homonuclear couplings are refocused.

We have applied this version of the Overbodenhausen experiment to a trisaccharide, namely, sialyl- $\alpha$ (2 $\rightarrow$ 6)-lactose. Fig. 1 shows the structure of the trisaccharide and on trace (A) its  $^1\text{H}$  spectrum in  $\text{D}_2\text{O}$ . Fig. 1(B) shows the multiplets of protons coupled to the anomeric carbon (C2) of the NeuAc residue. Figs. 1(C) and 1(D) show the multiplets of NeuAc H9<sup>R</sup>, H9<sup>S</sup>, and H8, obtained with the same pulse sequence but with the delay  $\tau$  adjusted to  $(2^1J_{\text{CH}})^{-1}$ . The magnitudes of the heteronuclear couplings can readily be obtained from the antiphase patterns. It is also evident from Fig. 1, however, that  $^1\text{H}$  multiplets that heavily overlap in spectrum 1(A) and are usually inaccessible by any homonuclear technique, are now unmasked. The patterns, which are in-phase with respect to the homonuclear couplings, are well separated, thus allowing the measurement of chemical shift and  $^2J_{\text{HH}}$  and  $^3J_{\text{HH}}$  coupling constants. The strength of our experiment lies in the fact that authentically strongly coupled  $^1\text{H}$  spin systems are turned into weakly coupled spin systems, a feature of special importance for editing  $^1\text{H}$  spectra of oligosaccharides.

Sincerely,



Herman van Halbeek

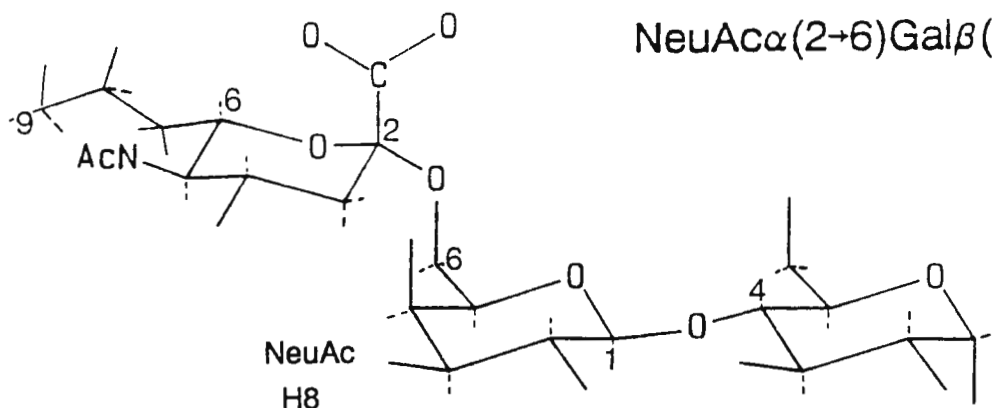


Leszek Poppe

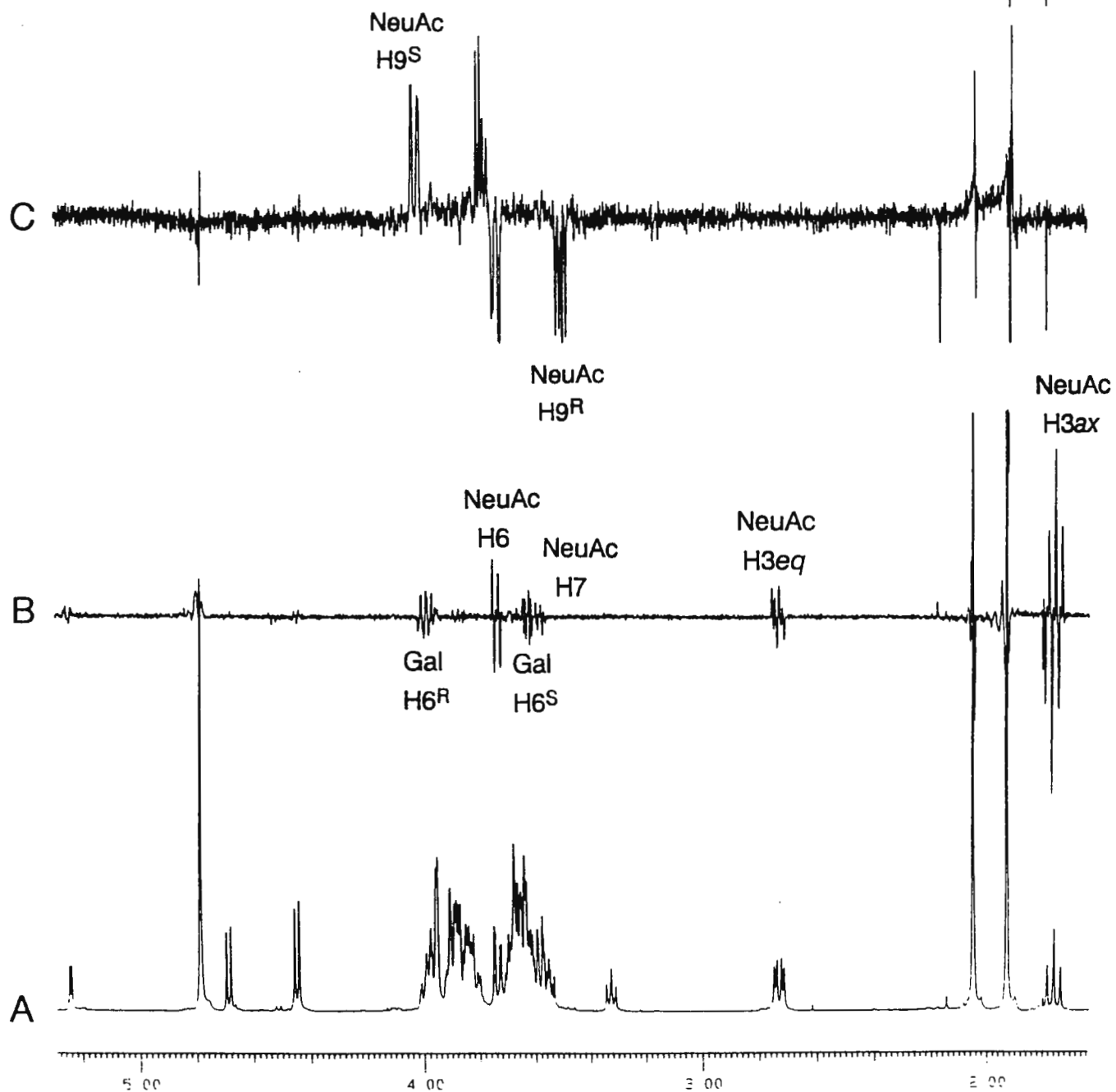
- [1] G. Bodenhausen and D. Ruben, *Chem. Phys. Lett.* **69**, 185 (1980).  
 [2] G. Otting and K. Wüthrich, *J. Magn. Reson.* **76**, 569 (1988).

---

Fig. 1. (A) 1-D  $^1\text{H}$ -NMR spectrum of sialyl- $\alpha$ (2 $\rightarrow$ 6)-lactose at 500 MHz recorded on a Bruker AM-500 spectrometer.  
 (B) 1-D Overbodenhausen spectrum with a preparation delay of 82 ms and a 5-ms spin-lock pulse. The selectivity was obtained by placing the  $^{13}\text{C}$  carrier frequency at the NeuAc C2 resonance and by randomly jittering the  $\Delta$  interval. The phase cycling of the pulses and receiver was the same as in Ref. 2. 3200 scans were accumulated with acquisition time 1.4 s and relaxation delay 0.5 s.  
 (C) and (D) 1-D Overbodenhausen spectra obtained with a preparation delay of 3 ms. The selectivity was obtained in an analogous way to (B), that is, by placing the  $^{13}\text{C}$  carrier frequency at the NeuAc C9 and C8 resonances, respectively, and by randomly jittering the  $\Delta$  interval.

NeuAc $\alpha$ (2 $\rightarrow$ 6)Gal $\beta$ (1 $\rightarrow$ 4)Glc

D





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MR Research Center  
Div. of Radiology, Desk L-10

November 12, 1990  
(received 11/19/90)

## Determination of tissue pH from the $^{19}\text{F}$ MR spectra of 5-fluorouracil (5FU) and its metabolites

Dear Barry,

For standard solutions, Keniry et al. demonstrated that the chemical shift difference between the  $^{19}\text{F}$  resonances of the drug 5-fluorouracil (5FU) and its cytotoxic form fluoronucleotide,  $\delta(5\text{FU-Fnuc})$ , can be used as a measure of pH (1). To assess whether  $\delta(5\text{FU-Fnuc})$  can be used for determination of tissue pH, C3H mice with subcutaneous RIF-1 tumors were treated with 5FU and examined by both  $^{31}\text{P}$  and  $^{19}\text{F}$  MRS. For  $^{31}\text{P}$  MRS (400  $^\circ\text{C}$ -pulses with  $\text{TR}=3$  s; 81 MHz) and  $^{19}\text{F}$  MRS (2400  $^\circ\text{C}$ -pulses with  $\text{TR}=0.5$  s; 188 MHz) of the tumors a 20 mm  $\phi$  solenoidal coil was used.

Linear regression analysis of  $^{31}\text{P}$  MRS determined tumor pH vs. the chemical shift difference between 5FU and Fnuc peaks in the  $^{19}\text{F}$  MR spectrum, yielded the expression  $\text{pH} = 6.11 + 0.22 * \delta(5\text{FU-Fnuc})$  with  $r=0.76$  and  $P=0.018$  (2). This indicates that it is feasible to use  $^{19}\text{F}$  MRS of 5FU and its metabolites for assessment of tissue pH.

A single-tuned 17 mm  $\phi$  surface coil was used for  $^{19}\text{F}$  MRS monitoring (2400 pulses of  $90^\circ$  in the center of the plane of the coil with  $\text{TR}=0.5$  s; 188 MHz) of the catabolism of 5FU in the liver region of tumor bearing mice and controls. After a 5FU dose of 130 or 260 mg/kg i.p., all liver spectra showed well resolved Fnuc, 5FU,  $\alpha$ -fluoro- $\beta$ -ureidopropanoic acid (FUPA) and  $\alpha$ -fluoro- $\beta$ -alanine (FBAL) peaks. During the two hours of  $^{19}\text{F}$  monitoring  $\delta(5\text{FU-Fnuc})$  decreased steadily, from  $4.85 \pm 0.02$  SEM) to  $4.68 \pm 0.05$  (260 mg/kg, tumor bearing mice;  $n=13$ ),  $4.64 \pm 0.08$  (260 mg/kg, controls;  $n=7$ ) and  $4.50 \pm 0.09$  SEM (130 mg/kg, tumor bearing mice;  $n=14$ ). Using the above expression, this translates into a slight, though highly significant ( $P<0.0001$ ), acidification of the liver from  $\text{pH } 7.18 \pm 0.01$  SEM to  $7.14 \pm 0.01$ ,  $7.13 \pm 0.02$  and  $7.10 \pm 0.02$  SEM.

Decreases in liver pH observed after administration of fructose and induction of hypoxia have been associated with anaerobic glycolysis and the formation of lactic acid. To our knowledge this is the first report of chemotherapy induced decreases in liver pH (3).

1. M. Keniry, C. Bentz, R.H. Shafer, T.L. James. Cancer Res. **46**: 1754-1758, 1986.

2. P.E. Sijens, N.J. Baldwin, T.C. Ng. Magn. Reson. Med. (in Press).

3. P.E. Sijens, Y. Huang, N.J. Baldwin, T.C. Ng. Cancer Res. (Subm.).

Please credit this contribution to Thian C. Ng's account.

Sincerely,

Paul E. Sijens

## HARVARD MEDICAL SCHOOL

DEPARTMENT OF BIOLOGICAL CHEMISTRY  
AND MOLECULAR PHARMACOLOGYOctober 24, 1990  
(received 10/29/90)

Tel. (617) 432-

Bernhard Shapiro  
Editor  
TAMU NMR Newsletter  
966 Elsinor Court  
Palo Alto, CA 94303250 Longwood Avenue  
Boston, Massachusetts 02115**Dispersive Baseline Correction in 2D and 3D Spectra of Samples Containing Water**

Dear Barry:

We made the experience that off-the-shelf-base plane correction routines did not perform well for 2D NMR spectra of samples in H<sub>2</sub>O. Usually, these routines did not correct well for streaks along  $\omega_2$  reaching out from the  $t_1$  noise band of the water. These routines correct by assuming that the base line can be approximated by a polynomial, and the best fit of the base line with this approximation is subtracted from the spectrum. To our experience, spectra recorded in H<sub>2</sub>O with presaturation of the water result in large dispersive distortions with the center of the dispersive signal at the water. This is the case, for example in NOESY and TOCSY spectra.

We wrote a routine that subtracts a dispersive component, in addition to the polynomial correction<sup>1</sup>. This was achieved in the following way. The dispersive line centered at the water signal can be approximated by a  $1/f$  line shape at a few line widths apart from the center. We take a number of sample points, usually at the ends of the spectra and in empty spectral regions around 6 ppm. These are then fitted to the base plane function  $b(f)$ :

$$b(f) = a_{-1} f^{-1} + a_0 + a_1 f^1 + a_2 f^2 \dots$$

This function is only used to obtain the weights  $a_{-1}$ ,  $a_0$ ,  $a_1$ ,  $a_2$ , ... So far we have only used up to 1<sup>st</sup> order terms. In the actual correction, the  $f^{-1}$  dependence is then replaced with a dispersive line shape where the line width is estimated from the width of the water signal. This choice of the line width is not crucial.

This dispersive fit was applied to 2D and 3D spectra and gave results to our satisfaction. Fig. 1 shows a row from a NOESY spectrum of the protein kistrin in H<sub>2</sub>O solution. We have incorporated the routine in Dennis Hare's 2D and 3D software FTNMR and FELIX<sup>1</sup>.

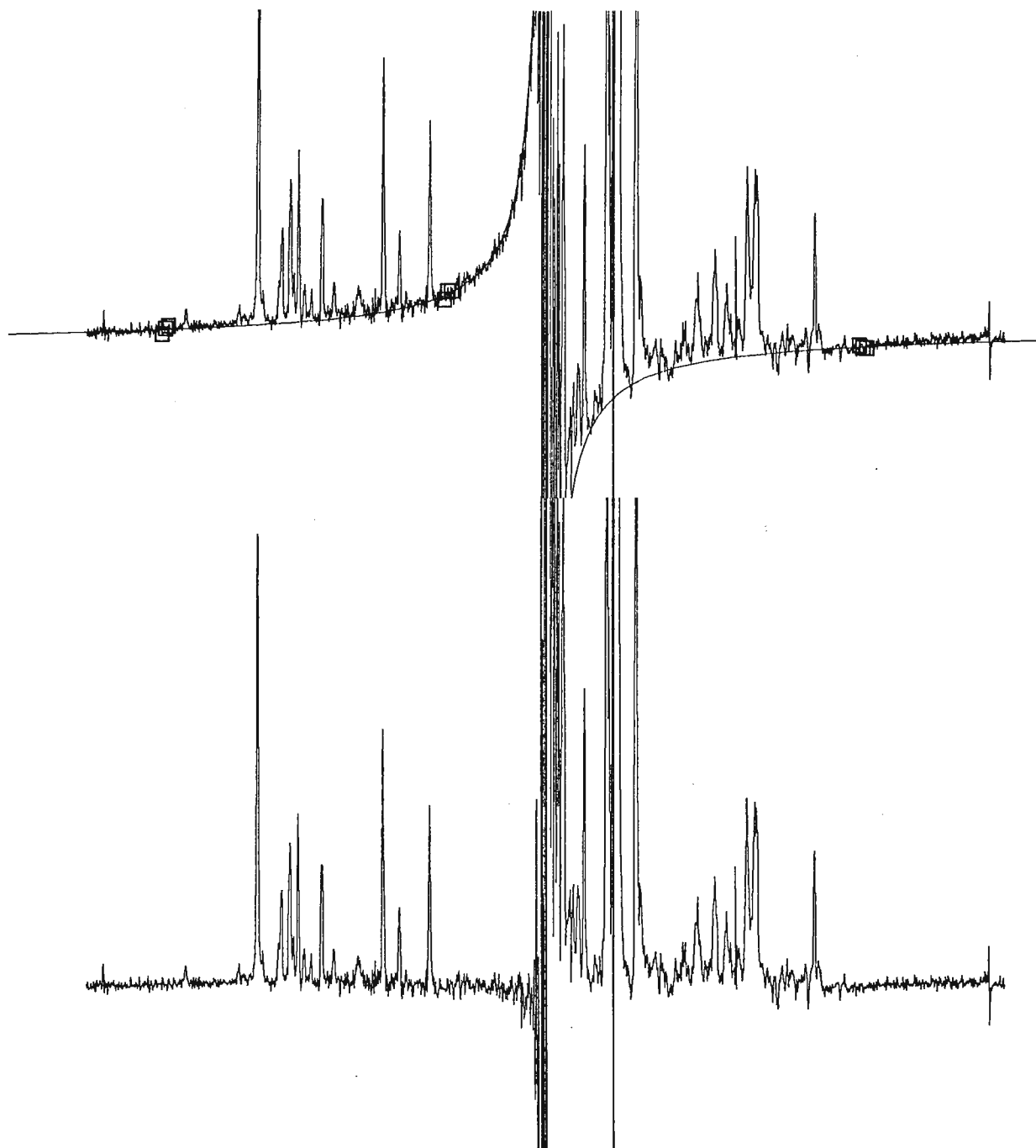
1. M. Adler & G. Wagner, J. Magn. Reson. (1991), in press.

Sincerely

Marc Adler

Gerhard Wagner

1



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October 24, 1990  
(received 11/2/90)

Dr. Bernard L. Shapiro  
 Editor/Publisher  
 TAMU NMR Newsletter  
 966 Elsinore Ct.  
 Palo Alto, CA 94303 USA

The APT curve for Methane.

Dear Professor Shapiro:

The afternoon when your salmon fish-mamey apple colored reminder disrupted my concentration from reading what some giants of nmr wrote about THE NMR GIANT James N. Shoolery in the TAMU NMR Newsletter published in September 1990, I was also deeply involved in remembering my early interactions with nmr and with Jim. This is a period of time placed in the sixties which I will not detail here. I simply want to say to Jim: Thank you for all you did for nmr; thank you for being a so nice friend over more than 25 years.

On reading Jim's APT paper<sup>1</sup> I felt motivated, just for a theoretical exercise, to extend the equations to methane. It is obvious that such a situation might only arise in natural gas mixtures, but in any event here is the deduction:

Jim established<sup>1</sup> that for C, CH, CH<sub>2</sub> and CH<sub>3</sub> the APT mathematical expressions are:

$$C : S/S_o = 1$$

$$CH : S/S_o = \cos \pi J \tau$$

$$CH_2 : S/S_o = \frac{1}{2} (1 + \cos 2\pi J \tau)$$

$$CH_3 : S/S_o = \frac{1}{4} (3 \cos \pi J \tau + \cos 3\pi J \tau)$$

from where it follows that:

$$CH_n : S/S_o = \cos^n \pi J \tau$$

since:

$$\cos^{2n} \alpha = \frac{1}{2^{2n}} \begin{Bmatrix} 2n \\ n \end{Bmatrix} + \frac{1}{2^{2n-1}} [\cos 2n\alpha + \begin{Bmatrix} 2n \\ 1 \end{Bmatrix} \cos (2n-2)\alpha + \dots + \begin{Bmatrix} 2n \\ n-1 \end{Bmatrix} \cos 2\alpha]$$

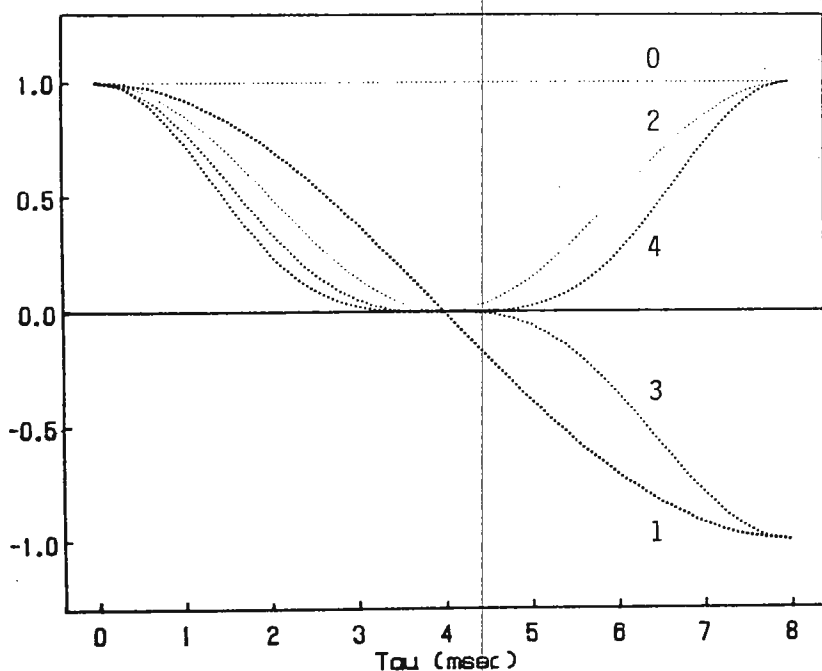
and therefore:

$$CH_4 : S/S_o = \frac{1}{8} (3 + 4 \cos 2\pi J \tau + \cos 4\pi J \tau)$$

One can numerically solve the five equations in the range from  $0^\circ$  to  $180^\circ$  or from 0 to  $\pi$  as shown in the table:

	0	45	60	90	120	135	180	$^\circ$
	0	$1/4$	$1/3$	$1/2$	$2/3$	$3/4$	1	$\pi$
C	1	1	1	1	1	1	1	
CH	1	$1/\sqrt{2}$	$1/2$	0	$-1/2$	$-1/\sqrt{2}$	-1	
CH <sub>2</sub>	1	$1/2$	$1/4$	0	$1/4$	$1/2$	1	
CH <sub>3</sub>	1	$1/2\sqrt{2}$	$1/8$	0	$-1/8$	$-1/2\sqrt{2}$	-1	
CH <sub>4</sub>	1	$1/4$	$1/16$	0	$1/16$	$1/4$	1	

or one can plot the five functions on a PC as shown in the figure:



APT for CH<sub>n</sub>

n = 0, 1, 2, 3, 4.

Perhaps some reader might be motivated to test this experimentally and even to do something similar for DEPT. But what seems clear, is that many readers would like to see again one of those company cards that Jim used a quarter of a century ago and which is reproduced below.



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*Pedro Joseph Nathan*  
Pedro Joseph Nathan

1.- S.L. Patt and J.N. Shoolery, J. Magn. Reson., 46, 535 (1982).

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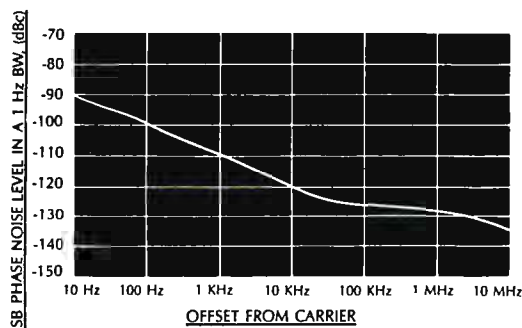
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<b>Spurious Outputs</b>	Discrete: Harmonics: Phase Noise: $\mathcal{L}(1 \text{ Hz})$ : Noise Floor:	– 70 dB (– 55 dB, 1/2 & 3/2 $f_{\text{out}}$ above 310 MHz) – 30 dB at full output (– 40 dB at lower level) – 63 dBc (0.5 Hz to 15 KHz) including effects of internal standard 100 Hz/100 dBc, 1 KHz/110 dBc, 10 KHz/120 dBc, 100 KHz/125 dBc – 130 dBc/Hz
<b>Frequency Standard</b>	Internal:  External Drive: Aux. Output:	OCXO or TCXO $3 \times 10^{-9}$ /day or $1 \times 10^{-9}$ /day $\pm 1 \times 10^{-8}/0-50^{\circ}\text{C}$ or $\pm 1 \times 10^{-8}/0-50^{\circ}\text{C}$ $1 \times 10^{-8}$ /year or $2 \times 10^{-8}$ /year 10 MHz, 0.4Vrms into 300 $\Omega$ ; 5 MHz, 0.5Vrms into 300 $\Omega$ 10.000 MHz, 0.4Vrms into 50 $\Omega$ (Note: internal or external standard required for operation)
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October 25, 1990 (received 10/29/90)

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

### JOVE: An Alternative to the UNIX vi Editor

It is increasingly apparent that most NMR spectroscopists will be unable to avoid computers with UNIX-based operating systems in their workplaces for much longer. Although many of the powerful features of UNIX are certainly welcome they come with some associated unpleasanties. One of the more annoying features of UNIX is the vi text editor that accompanies it. Although experienced UNIX users can expound at length on the power of this editor, it is very difficult for a novice to even keep from hopelessly butchering a document with vi. Also, vi has some untraditional "features" such as requiring the user to change modes to delete characters after inserting them (no, you can't just hit the delete key), and many common actions such as cutting and pasting require much dexterity to accomplish with any speed. As an added insult, even the quick reference cards supplied by the computer manufacturers are virtually incomprehensible to anyone not already intimately familiar with the vi editor.

Many institutions have also recognized the difficulties associated with the vi editor and have installed other text editors on their UNIX-based machines. One of the most popular alternatives is EMACS, an easy to learn, customizable text editor that is probably also the most powerful UNIX text editor available. The EMACS editor code is published by the GNU free software institute, and is available by anonymous FTP from various sources. Unfortunately, EMACS is somewhat difficult to install and requires a large amount of memory to run so it can slow down multiple user machines significantly. Also, it is written mostly in LISP instead of the more familiar C.

In the past year I have installed JOVE (Jonathan's Own Version of EMACS) on a Sun-4, Sun-3, and a MicroVAX running ULTRIX, and I found the installations to uncomplicated. I have recently found that quite a few academic institutions have installed JOVE for the same reasons I did: it offers much of the power and ease of use of EMACS but takes up less memory and is much easier to install. Also, the program is written in brief and concise C code, so it is easy to edit if you have the urge to do so. The NMR spectroscopists here have been very happy with JOVE and we find that such features as cut and paste, split windows, interactive shells in windows, a nice C development environment, and macro generation are very convenient with this editor. In addition, JOVE comes fully, but not overly, documented, and includes a nice manual and tutorial.

Although vi users will still have the advantage of working with a standard that is available on most other UNIX machines, JOVE is certainly a more friendly alternative. It should also be noted that JOVE users will feel right at home with EMACS, and versions of all three editors are available for non-UNIX Macintoshes and IBM PC compatibles.

Here are some brief instructions on where to get JOVE and how to install it. I will supply my own jove.rc (startup initialization) file and a quick reference page for anyone who wants it.



-JOVE (page 2)

- 1) Download jove.tar.4.14.Z from cayuga.cs.rochester.edu by anonymous FTP. Don't forget to set file type as binary. This file will consume about 4 Mbytes and is the latest version that I know of; other versions are available elsewhere.
- 2) Put this file in its own directory and uncompress it with '> uncompress jove.tar.4.14.Z' to give jove.tar.4.14.
- 3) Unarchive jove.tar.4.14 with '> tar xvf jove.tar.4.14 '.
- 4) Optionally edit wind.c so ScrollStep = 1 instead of 0. This gives you normal scrolling.
- 5) Make directories bin, lib, and man in the JOVE directory.
- 6) Edit Makefile to tell it where these directories are, these are the statements BINDIR=, LIBDIR=, and MANDIR= near the top.
- 7) Do a '>make', this will take a while.
- 8) Do a '>make install', this will take a lot less time.
- 9) The executable is now "xjove".
- 10) In the /doc directory are files to print out the manual.  
In the /bin directory is a copy of xjove as jove.  
In the /lib directory is the startup file jove.rc.  
In the /man directory are the man pages for JOVE.
- 11) Rename "xjove" to "jove" and running teachjove will start a tutorial.
- 12) All files and directories except jove and lib/jove.rc can be deleted.
- 13) Optionally edit jove.rc to set up any defaults and key assignments you want.
- 14) Optionally alias "jove" in .login file to something like "j".
- 15) For more information read all the README's.

I of course do not guarantee that any of this will work, but I do guarantee that it worked for me, and the version I have is virus free.

Sincerely,

Douglas E. Brown



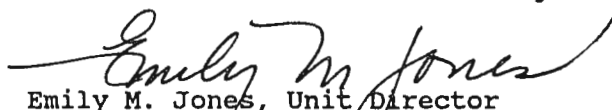
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Emily M. Jones, Unit Director

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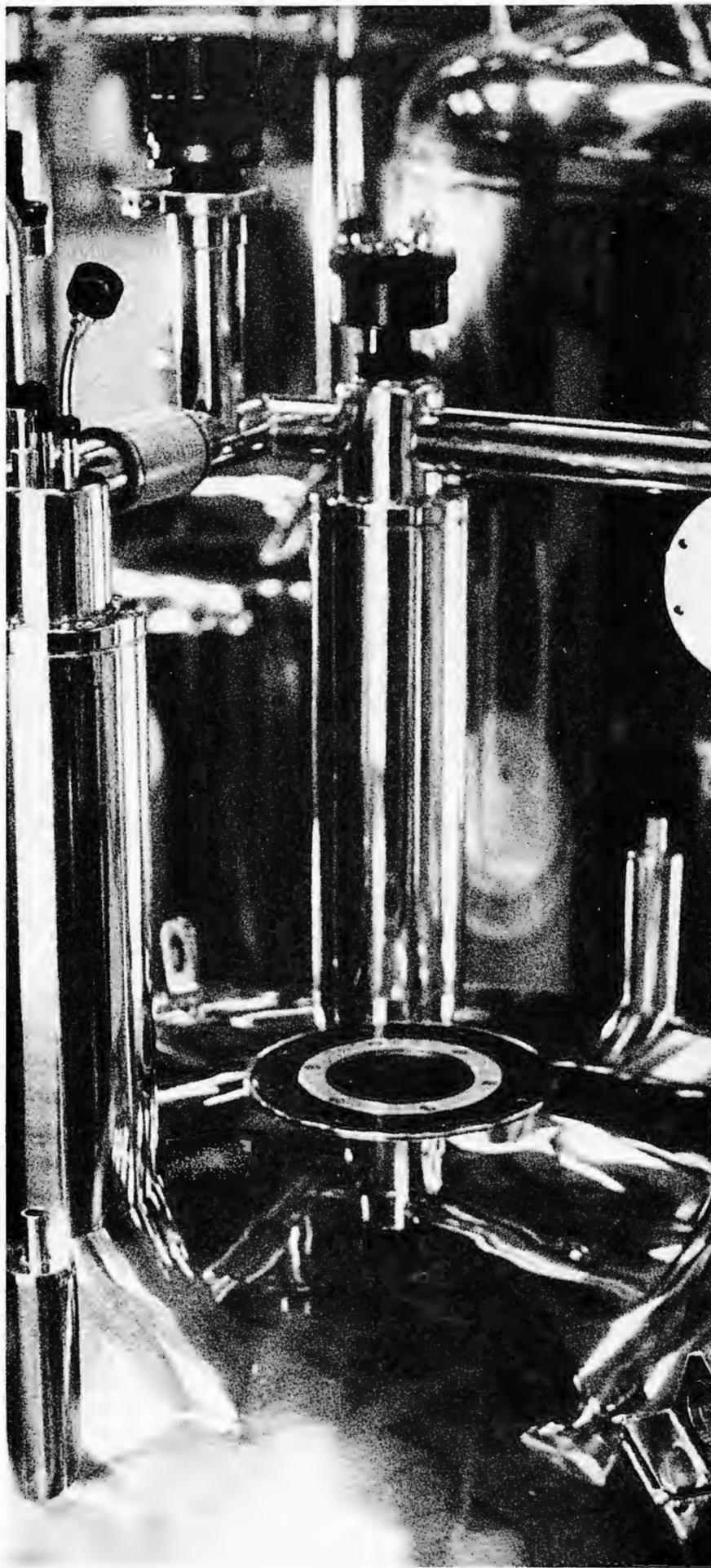
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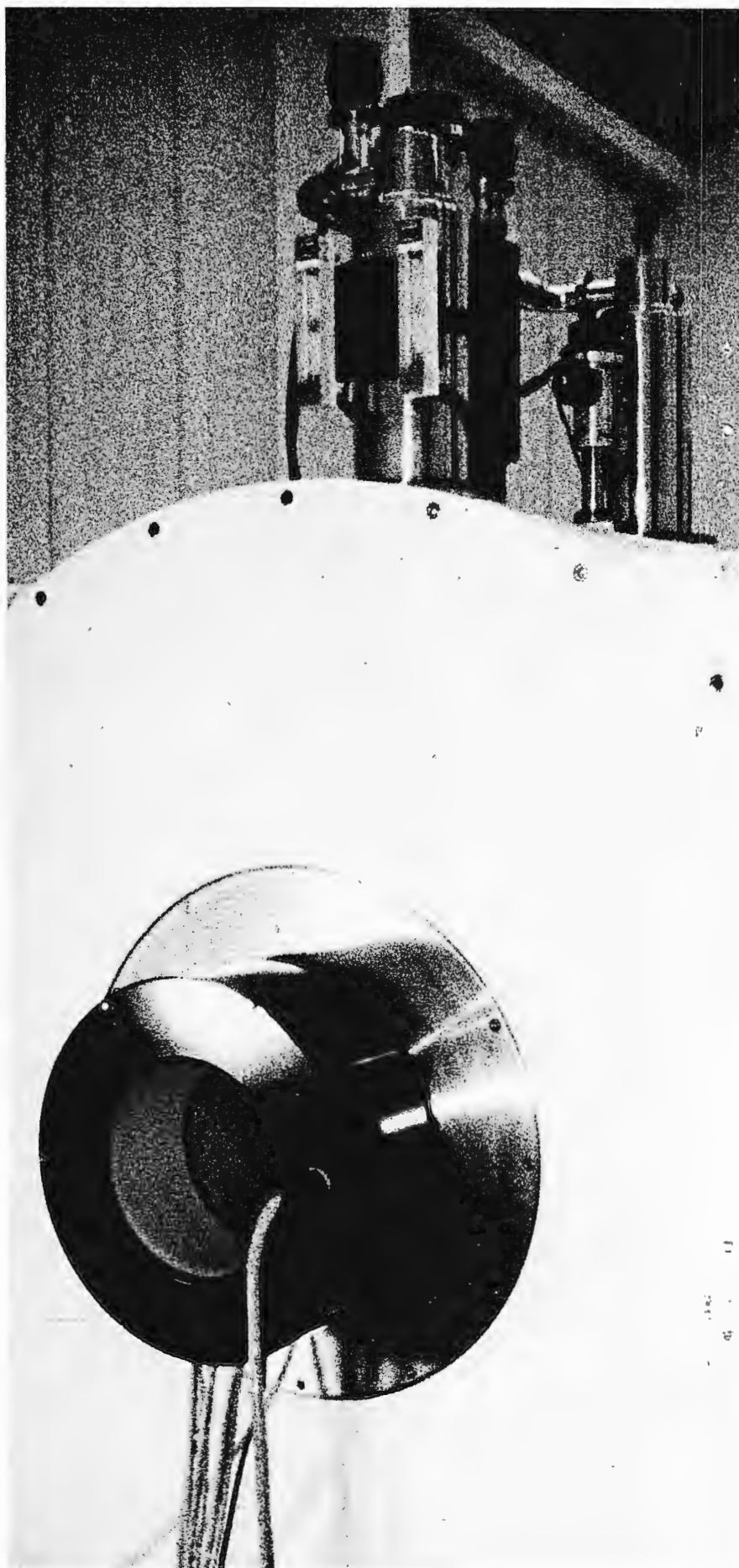
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National Institute of  
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November 1, 1990 (received 11/5/90)

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

Title: Intraocular oxygen kinetics in real time in vivo

Dear Barry,

It has been well established that the spin-lattice relaxation rate  $(T_1)^{-1}$  of both fluorine and carbon nuclei in perfluorocarbons (PFC) is linearly related to the partial oxygen pressure ( $PO_2$ ) under conditions of no flow and constant temperature (1,2). To investigate the usefulness of this property *in vivo* we used the vitrectomized rabbit eye model in which the vitreous of one eye is first gas-compressed and two days later the gas is exchanged for non-emulsified perfluorotributylamine (FTBA) (usually about 1.3 ml) (3). After waiting at least six hours for the oxygen to reach steady-state, inversion recovery experiments are done using a surface coil positioned over the eye and hyperbolic secant full and half-passage pulses were applied for inversion and sampling. Typically, we measure a 1400:1 signal-to-noise ratio on the  $CF_3$  resonance with this setup. Using a calibration curve obtained with a phantom of FTBA at 37°C, these relaxation rates are converted into an oxygen partial pressure. This procedure was validated against oxygen microelectrode results in the literature and good agreement was found.

To investigate how sensitive our setup is to oxygen transients, we performed the following experiment: a spectrum is obtained at a tau value in which the  $CF_3$  resonance has just past through the null point (usually around 900 ms). The fractional intensity change near the null point is very sensitive to small changes in the  $T_1$  value. Thus, these condition were used to obtain a spectrum every 8 sec. After establishing an intensity baseline for the  $CF_3$  resonance while the animal was ventilated, via a tracheotomy, with room air, the ventilation gas was changed to 100%  $O_2$  for 1 min. The result from a typical experiment is shown in Figure 1. Clearly, the oxygen influx into the FTBA is well defined by this method. After returning the animal to room air, an apparent lag in response is observed presumably due to the oxygen reservoir of the long ventilation lines going into the magnet. To verify that our response was due to oxygen flux in the eye, we raised the intraocular pressure above the systemic pressure via a plastic catheter positioned in the aqueous humor. This catheter is attached to a water reservoir 180 cm above the animal. Since the pressure in the eye was above the systemic pressure it effectively cut off circulation to the eye. Under this condition, we repeated the above experiment of ventilating the animal for 1 min with oxygen. As seen in Figure 2, no intensity increase is observed. Please credit this to Bob London's account.

Sincerely,

Bruce A. Berkowitz

Charles Wilson

Diane Hatchell

- 1) M'H.A. Hamza, G. Serratrice, M.-J. Stebe, J.-J. Delpuech, *J. Am. Chem. Soc.* **103**, 3733 (1981).
- 2) P. Parhami and B.M. Fung, *J. Phys. Chem.* **87**, 1928 (1983).
- 3) B.A.Berkowitz, C.A.Wilson, D.Hatchell, and R.London, *Magn. Reson. Med.*, in press.

Figure 1

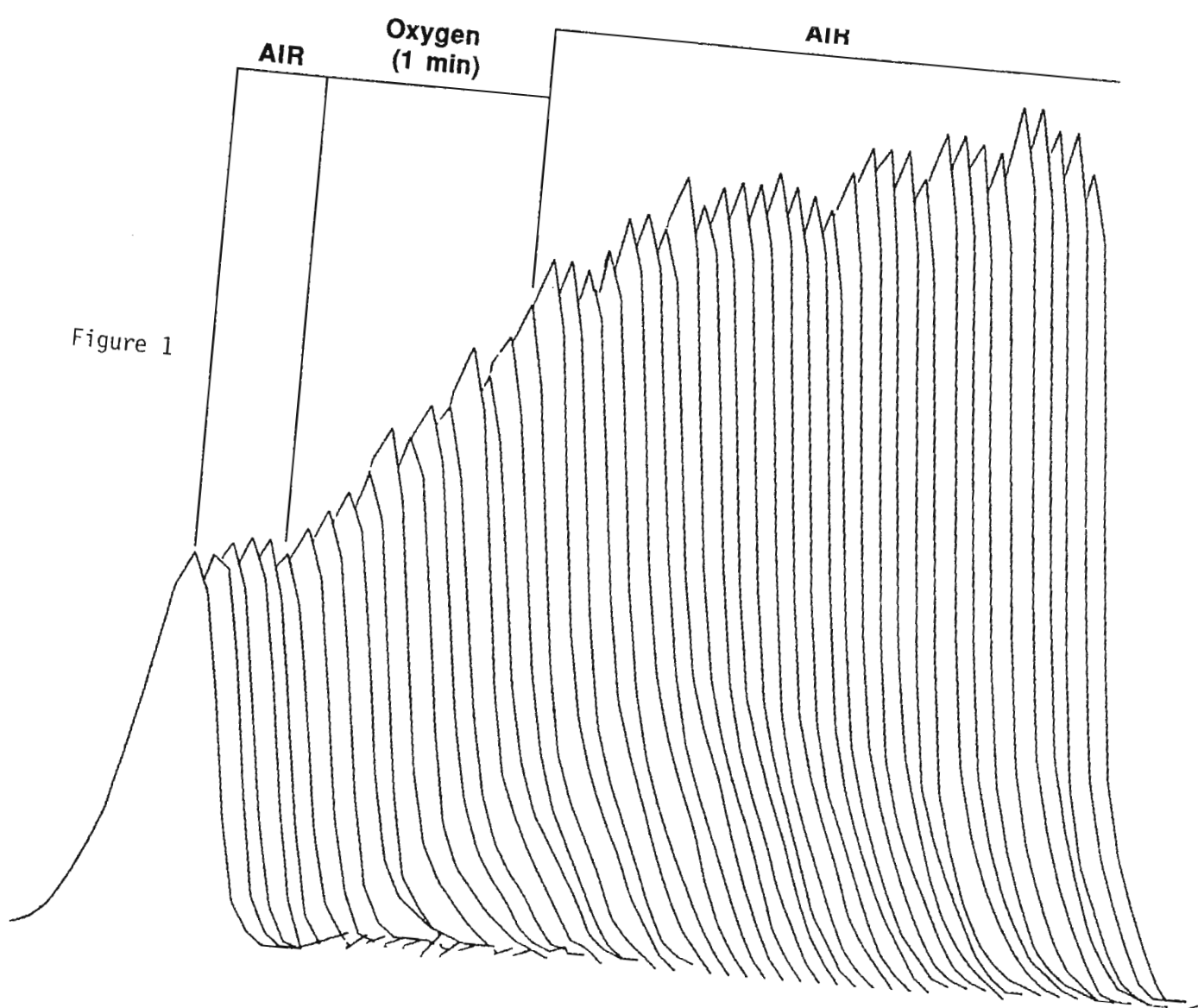
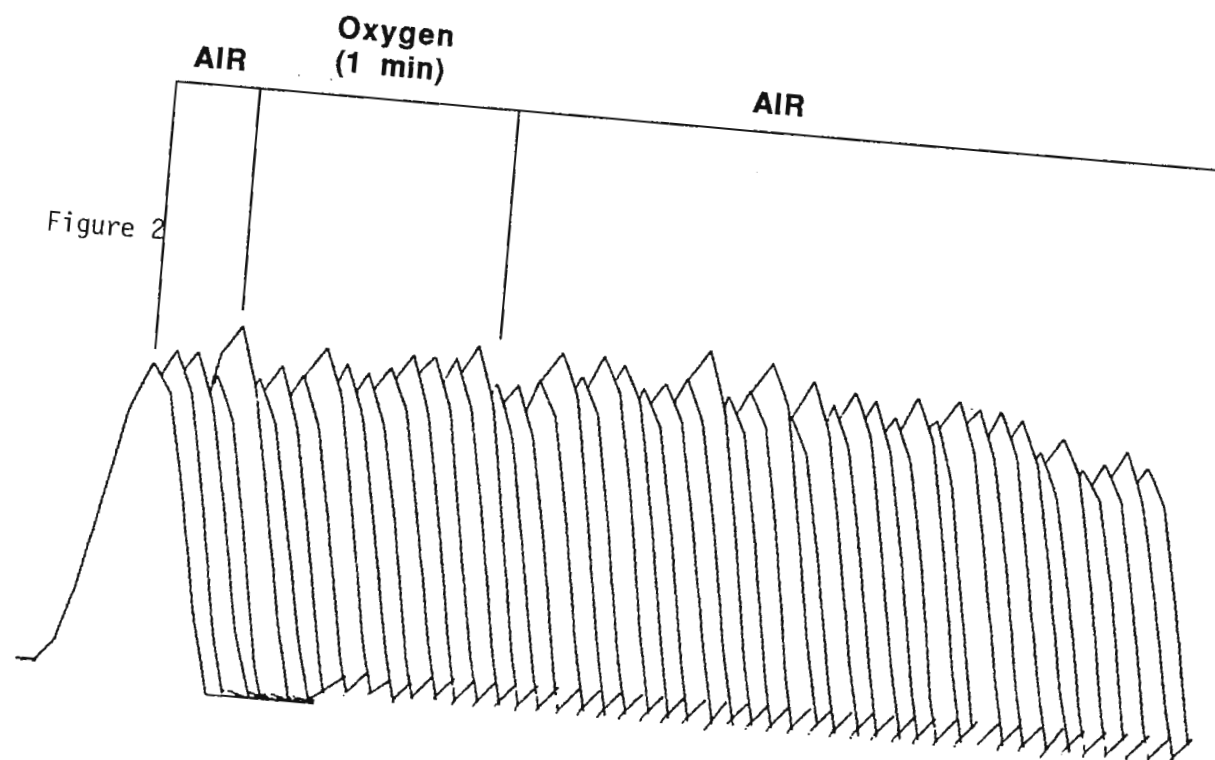


Figure 2



Tenth International Meeting on

# NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

University of St Andrews, Scotland

8–12 July 1991

## Introduction

The Tenth international meeting on NMR Spectroscopy will take place at the University of St Andrews, Scotland from Monday 8 July to Friday 12 July 1991, with participants foregathering on the afternoon and evening of Sunday 7 July 1991.

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

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

1969	Birmingham	1983	Edinburgh
1972	Guildford	1985	Cambridge
1975	St Andrews	1987	Canterbury
1978	York	1989	Warwick
1981	Exeter		

## Scientific Programme

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

### 1 Experimental Techniques

Chairman: R Freeman

Invited Lecturers: A Pines and J Keeler

### 2 Structure and Dynamics I (Multinuclear)

Chairman: K G Orrell

Invited Lecturers: R Benn and G Hägele

### 3 Structure and Dynamics II (Smaller Biomolecules)

Chairman: D Turner

Invited Lecturers: C Dobson and H Kessler

### 4 Non-medical Imaging (For Non-specialists)

Chairman: L D Hall

Invited Lecturers: P Callaghan, R Gordon and T A Carpenter

### 5 In-Vivo Spectroscopy

Chairman: I D Gadian

Invited Lecturers: P Luyten and J Ackermann

### 6 Solid-state NMR

Chairman: K J Packer

Invited Lecturers: R G Griffin and A T Bell

### 7 Biological Macromolecules

Chairman: G C K Roberts

Invited Lecturers: J L Markley and J Feeney

### 8 Aspects of Computation (Modelling, automation, databases)

Chairman: A E Derome

Invited Lecturers: R Ernst and D Hare

## Poster Sessions and Contributed Papers

Two poster sessions are planned for the programme, together with two early evening sessions restricted to short papers presented by graduate students. There will also be an opportunity for a strictly limited number of short contributions to be presented orally in the symposia. Anyone wishing to contribute an oral paper or a poster, should submit **NOT LATER THAN 25 JANUARY 1991** a title and brief abstract (according to the proforma described in the accompanying documentation) to Dr John F Gibson, The Royal Society of Chemistry, Burlington House, London W1V 0BN, indicating the appropriate symposium topic. The brief abstracts of those accepted will be issued as a book to all who attend the meeting.

## Displays

There will be displays of NMR equipment, books, programmes etc. Visitors will be welcomed at the four display suites organised by the manufacturers of NMR Spectrometers.

## Social Programme

A full programme of evening social events is planned.

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: A visit to a distillery, a visit to Blair Castle, a mountain walk up Schiehallion and others to be announced.

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, excluding VAT), and the accommodation for the full five day period will be around £140 full board.

## Bursaries

Partial student bursaries will be available to any EEC student whose attendance cannot be covered by their funding body.

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

Please send me further details of the tenth international meeting on **NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY**, to be held at the University of St Andrews, Scotland, 8-12 July 1991. (Available in February/early March 1991).

**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

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

- ☐ I am interested in attending the 10th NMR meeting and would like to receive the Second Circular
- ☐ Please send me a bursary application form
- ☐ I intend to offer a paper for presentation at the Meeting
- ☐ POSTER presentation preferred
- ☐ ORAL presentation preferred
- ☐ ORAL presentation (by graduate students only)
- for Symposium \_\_\_\_\_

*Please indicate type of presentation preferred and the number of the particular symposium.*

**Further Information**

Further information, including details of the programme, confirmation of the fees and other charges, together with the application form, will be sent to all who have notified their interest in the conference by returning the attached tear-off slip, as instructed to:

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

Tel: 071 437 8656

Telex 268001

Fax: 071 437 8883

It is expected that this further information will be circulated late February/early March 1991.

All correspondence and enquiries concerning the conference should be addressed to either Dr John F Gibson at the above address or to Dr O W Howarth, Department of Chemistry, University of Warwick, Coventry, CV4 7AL

Tel: 0203 523187

**Organising Committee**

Dr P Beynon, Dr D B Davies, Dr A E Derome, Professor R Freeman, Professor I D Gadian, Professor L D Hall, Dr O W Howarth (Chairman), Dr I Jones, Dr R K Mackie (Local Arrangements Co-ordinator), Mr P Meadows, Dr K G Orrell, Professor K J Packer, Dr P Regan, Professor G C K Roberts, Professor L Sutcliffe, Dr D Turner.

**XI Symposium on NQR**

The attention of potentially interested participants is also drawn to the 'XI Symposium on NQR', to be held at King's College, London, from 15 to 19 July 1991. Further information on this meeting can be obtained from: Professor J A S Smith, Department of Chemistry, King's College, Strand, London WC2R 2LS, UK.

**Supported Reagent Chemistry**

The Royal Society of Chemistry is organising an International symposium on 'Supported Reagent Chemistry' at the University of York from 2 to 5 July 1991, the week before the NMR meeting. Further information about this meeting may be obtained from Dr John F Gibson, Secretary (Scientific), The Royal Society of Chemistry, Burlington House, London W1V 0BN, UK.

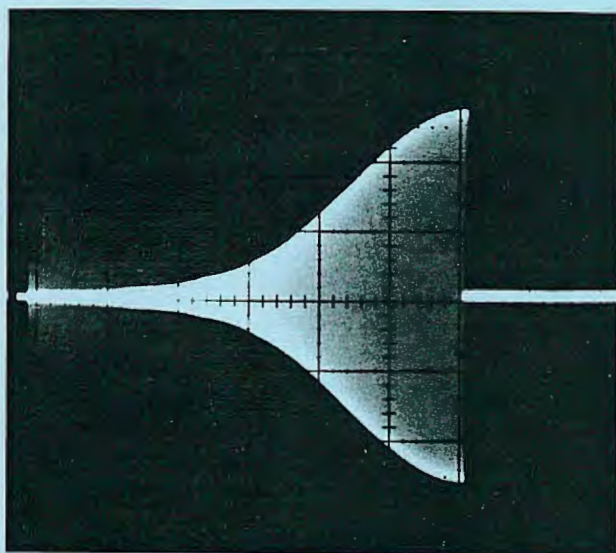
# Omega

## Pulse Shaping Made Simple

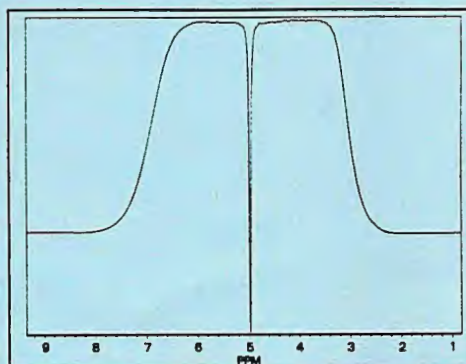
Omega PSG (Pulse Sequence Generator) boards provide very flexible control of both amplitude and phase on each transmitter channel. Through a unique combination of instruction and waveform memory, waveform libraries can be

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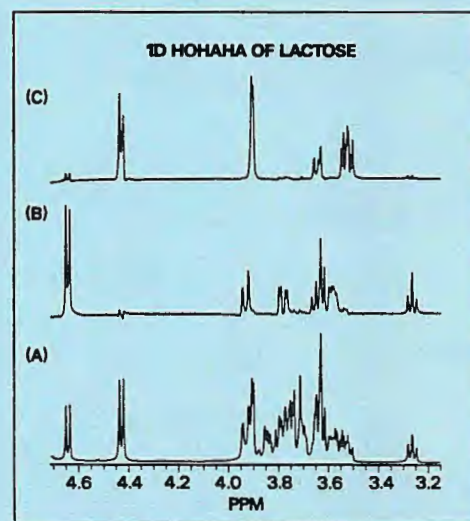
### Wave Shaping on the Omega 500 PSG



An oscilloscope trace of a half-Gaussian pulse. The pulse is defined by 250 points and the duration is 10 ms.



The result of applying a  $180^\circ$  half-Gaussian pulse to a sample of doped water. The water resonance has been broadened by introducing a large Z1 current in the room temperature shims. The half-Gaussian pulse width is 200 ms and the width of the "burned hole" is 12 Hz.



TOCSY of Lactose (10mM in  $D_2O$ ).

Bottom spectrum (A) is a simple one pulse spectrum. Middle spectrum (B) is a 1D-TOCSY spectrum, where anomeric proton at 4.43 ppm has been selectively irradiated with a half-Gaussian pulse. Top spectrum (C) is a 1D-TOCSY spectrum when the anomeric proton at 4.65 ppm has been selectively irradiated with a half-Gaussian pulse.

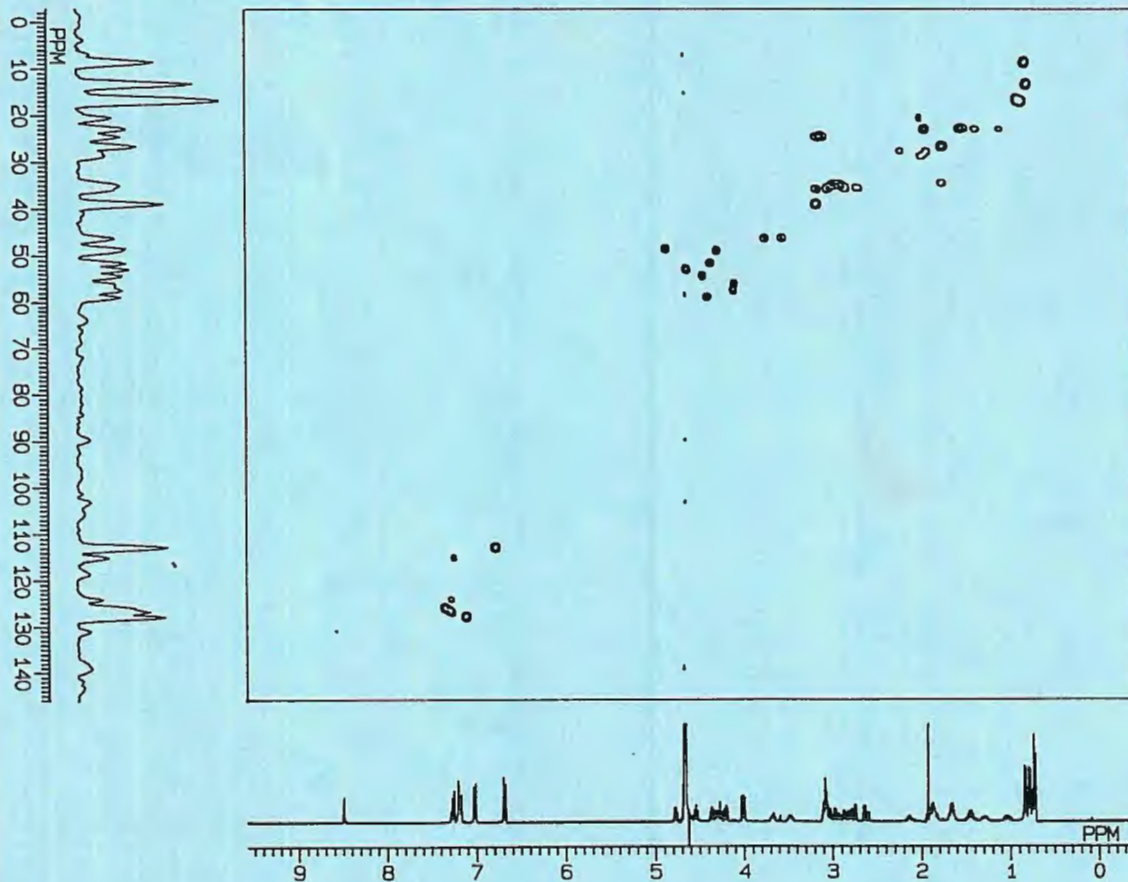


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