

**THE**  
***NMR***  
**NEWSLETTER**

**No. 480 !!**  
**September 1998**

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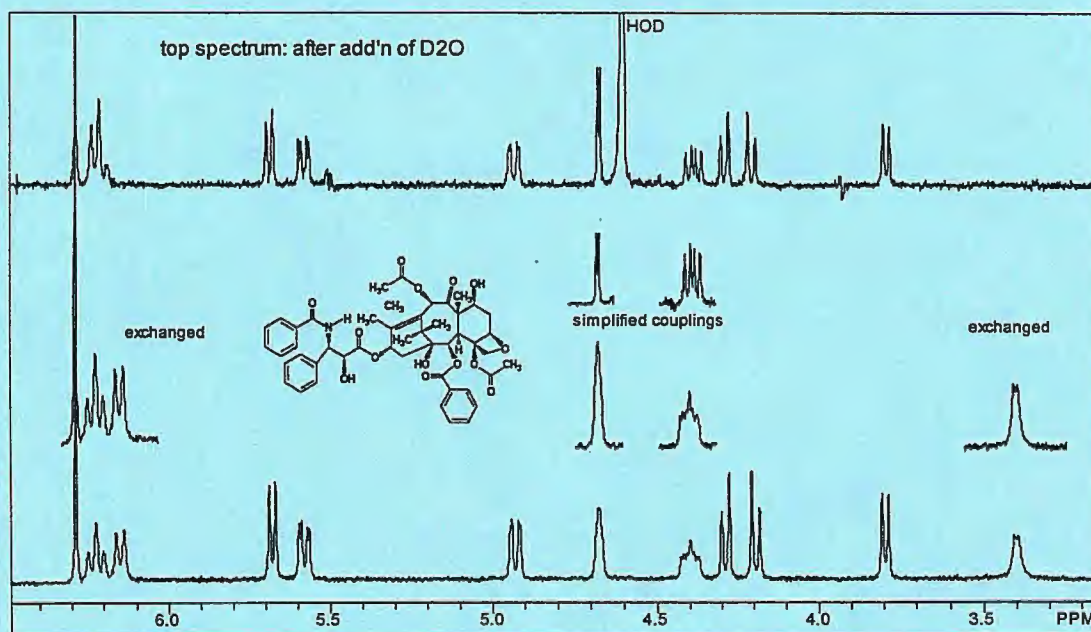
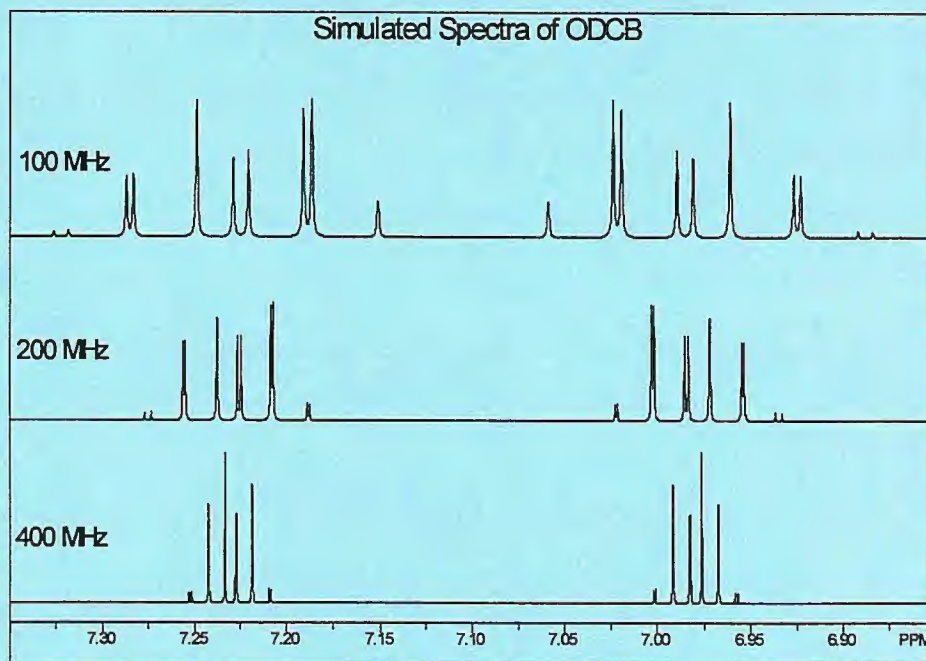
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**FORTHCOMING NMR MEETINGS**

**XVIIIth International Conference on Magnetic Resonance in Biological Systems**, Tokyo Metropolitan University, **August 23 - 28, 1998**. Contact: Professor M. Kainosho, Department of Chemistry, Tokyo Metropolitan University; +81-426-77-2544; Fax: +81-426-77-2525; e-mail: kainosho@raphael.chem.metro-u.ac.jp; <http://icmrbs98.chem.metro-u.ac.jp>

**NMR<sup>2</sup>-New Mexico Regional NMR**, Advanced Materials Laboratory, Sandia National Laboratories, Albuquerque, NM, **October 3, 1998**. Contact: T. M. Alam, Sandia National Laboratories, MS 1407, Albuquerque, NM 87008-1407; [tmalam@sandia.gov](mailto:tmalam@sandia.gov); 505-844-1225.

**NMR Technologies: Development and Applications for Drug Design and Characterizations**, Baltimore, MD, **October 29-30, 1998**; Contact: J. Laakso, Cambridge Healthtech Institute, 1037 Chestnut St. Newton Upper Falls, MA 02164; 617-630-1300; Fax: 617-630-1325; [chi@healthtech.com](mailto:chi@healthtech.com); <http://www.healthtech.com/conferences/>.

**NMR of Polymers and Biopolymers**, Symposium at the 54th SouthWest Regional ACS Meeting, Baton Rouge, LA, **November 1-2, 1998**, For Symposium schedule: [members.aol.com/ACKolbert/symposium.html](http://members.aol.com/ACKolbert/symposium.html); Contact: A. C. Kolbert <mailto:ackolbert@aol.com> or Xiaolian Gao, [xgao@uh.edu](mailto:xgao@uh.edu)

**NMR Spectroscopy of Polymers**, Breckenridge, Colorado, **January 24-27, 1999**; an International Symposium Sponsored by the Division of Polymer Chemistry, American Chemical Society; Organizers: P. T. Inglefield and A. D. English; Registration contact: Neta L. Byerly, Division of Polymer Chemistry, Inc., Virginia Tech, 201 Hancock Hall, M.C. 0257, Blacksburg, VA 24061; 540-231-3029; Fax: 540-231-9452; email: [nbyerly@vt.edu](mailto:nbyerly@vt.edu).

**40th ENC (Experimental NMR Conference)**, Clarion Plaza Hotel, Orlando, Florida, **February 28 - March 5, 1999**, immediately preceding Pittcon in Orlando; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87505; (505) 989-4573; Fax: (505) 989-1073; Email: [enc@enc-conference.org](mailto:enc@enc-conference.org).

**Pittcon '99**, Orlando, FL, **March 7-12, 1999** (50th year celebration of the Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy.) Contact: The Pittsburgh Conference, Dept. CFP, 300 Penn Center Blvd., Suite 332, Pittsburgh, PA 15235-5503; 412-825-3220; Fax: 412-825-3224; e-mail: [pittconinfo@pittcon.org](mailto:pittconinfo@pittcon.org)

continued on inside back cover

## *Many Thanks - Forty and Counting.*

*With the September 1988 issue, No. 480, The NMR Newsletter completes 40 years of continuous monthly publication. It has come a long way from its inception, but its mission remains the same - to provide a forum for the sharing of information in the NMR community.*

*The Newsletter began in Pittsburgh, Pa., in October 1958, as a collaboration with Aksel Bothner-By, and with the total financial support of Mellon Institute (now part of Carnegie-Mellon University). Along the way Illinois Institute of Technology and Texas A&M University also made contributions that enabled the Newsletter to continue.*

*The Newsletter would not have survived without the support of Sponsors and Advertisers, who make it possible to provide the Newsletter to subscribers at a modest fee. We owe all of them our gratitude and support.*

*However, it is you, the contributors of technical material, who have made the Newsletter the world-wide communications vehicle it is today. Your willingness (with just the occasional gentle nudge) to share your techniques, discoveries and thoughts with each other that have made the Newsletter the unique publication it is.*

*We've enjoyed the opportunity the Newsletter has given us to maintain longstanding friendships and develop new ones. It's been a truly rewarding experience.*

*Many thanks for a great 40 years. Please keep those contributions coming - year 41 begins next month!*

*Barry Shapiro  
Lee Shapiro*

*1 September 1998*



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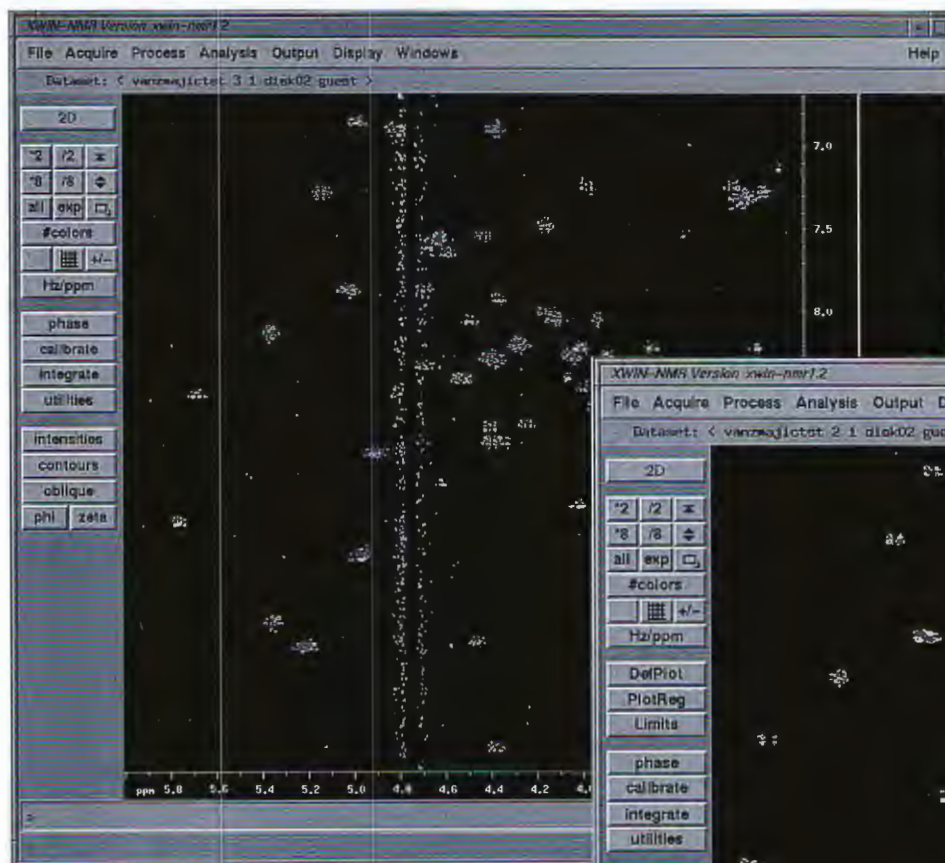
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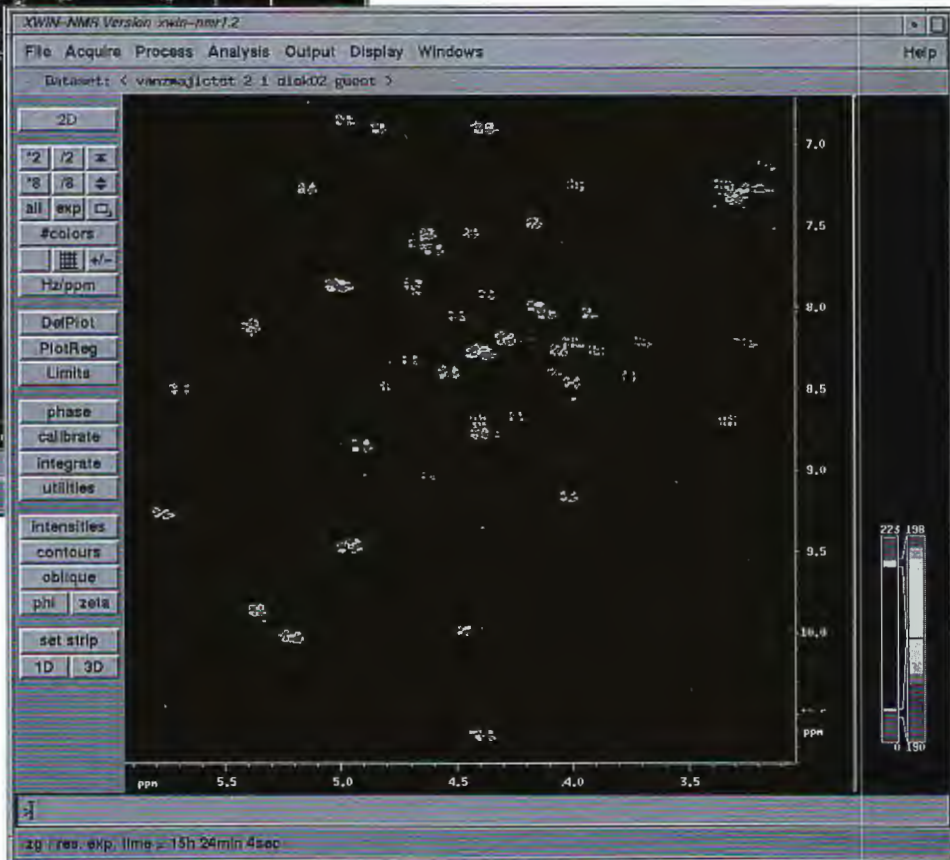
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National Institute of Diabetes and  
Digestive and Kidney Diseases  
Bethesda, Maryland 20892Dr. B.L. Shapiro  
NMR Newsletter  
966 Elsinore Court  
Palo Alto, CA 94303

August 10, 1998

(received 8/20/98)

Single crystal protein NMR in solution

Dear Barry:

For many years we've lived with the notion that the solid phase is needed to study all the interesting interactions, such as quadrupole couplings, dipolar couplings, and chemical shift anisotropy. In the liquid state, all these parameters average to zero, leaving us with a "featureless" spectrum, containing only the isotropic shifts and possibly some J couplings. As first demonstrated by Saupe and Englert over 35 years ago (1), if molecules are dissolved in a liquid crystalline medium the anisotropic parameters are simply scaled down from their static value. However, scaling factors are typically quite large ( $\geq 0.01$ ) and the spectrum of all but the smallest molecules become intractable as a result of the large number of still very large dipolar interactions. Much weaker alignment of the molecules can be obtained as a result of its own magnetic susceptibility anisotropy, but in this case the anisotropic interactions of interest are scaled down by a factor of  $10^{-4}$ - $10^{-6}$  (2-4) and can become difficult to measure accurately, particularly in macromolecules with inherently large natural line widths.

Last year, we discovered that proteins dissolved in a dilute nematic liquid crystalline phase of disk-shaped phospholipid particles, known as bicelles (5) and originally developed for a different purpose, retain a residual degree of order. In this medium, the dipolar couplings are scaled by just about the right amount ( $\sim 10^{-3}$ ) relative to the static case (6,7), and the one-bond dipolar couplings are sufficiently large for easy measuring. The degree of molecular alignment is sufficiently weak that multi-bond interactions are generally much smaller than the line widths. Thus, spectral complexity does not increase relative to the isotropic high resolution spectrum but one-bond (and several two-bond) dipolar interactions can be measured easily.

In contrast to common practice in liquid crystal NMR, for proteins we find it easiest to define the alignment in terms of a diagonalized traceless tensor,  $A$ , and to define the orientation of this matrix relative to the molecular frame by the Euler angles  $\alpha, \beta$ , and  $\gamma$ , rather than by the undiagonalized Saupe matrix,  $S$ . In the frame where  $A$  is diagonal, a dipolar coupling between two nuclei is given by  $D^{AB}(\theta, \phi) = D_a^{AB} \{ (3 \cos^2 \theta - 1) + 3/2 R (\sin^2 \theta \cos 2\phi) \}$  where  $R$  is the rhombicity defined by  $D_r^{AB}/D_a^{AB}$ ;  $D_a^{AB}$  and  $D_r^{AB}$  (in units of Hertz) are the axial and rhombic components of the traceless second rank diagonal tensor  $D$  given by  $1/3[D_{zz}^{AB} - (D_{xx}^{AB} + D_{yy}^{AB})/2]$  and  $1/3[D_{xx}^{AB} - D_{yy}^{AB}]$ , respectively, with  $|D_{zz}^{AB}| \geq |D_{yy}^{AB}| \geq |D_{xx}^{AB}|$ ;  $\theta$  the angle between the A-B interatomic vector and the z axis of the tensor; and  $\phi$  is the angle which describes the position of the projection of the A-B interatomic vector on the x-y plane, relative to the x axis.  $D_a^{AB}$  subsumes various constants, including the gyromagnetic ratios of the two nuclei  $\gamma_A$  and  $\gamma_B$ , the inverse cube of the distance between the two nuclei,  $\langle r_{AB}^{-3} \rangle$ , and the unitless axial component,  $A_a$ , of the molecular alignment tensor  $A$ :  $D_a^{AB} = -(\mu_0 h / 16\pi^3) \gamma_A \gamma_B \langle r_{AB}^{-3} \rangle A_a$ .

Clearly, for a given measured value of the dipolar coupling there are generally an infinite number of  $(\theta, \phi)$  combinations for which  $D^{AB}(\theta, \phi)$  equals the measured dipolar coupling. These  $\theta, \phi$  pairs map out a cone (for an axially symmetric alignment tensor), or a distorted, taco-shaped

cone for the general case of a rhombic alignment tensor.

If the preferred orientation of the molecule relative to the liquid crystal director could be changed, a second alignment tensor  $A'$  would apply (with different Euler angles relative to the molecular frame). A dipolar coupling measured in this second case maps out a different cone of allowed orientations in the molecular frame. Typically, the two cones will have two points where they intersect one another (one if they just touch one another; four if  $A$  and  $A'$  have the same orientation but different rhombicity). These numbers need to be doubled as the allowed orientations of the internuclear vector cannot be distinguished from the opposite orientations. So, there typically are four (or eight) possible solutions that are simultaneously compatible with the two dipolar couplings measured for a given interaction. Measurement of the dipolar coupling for a third, independent orientation of  $A$  can reduce this number to two.

If the orientation of  $A$  were solely determined by the shape of the protein, the only way to change the orientation of  $A$  would be to change the shape of the surface of the particles which make up the liquid crystalline phase, or the shape of the protein. Although this latter option appears to defeat the purpose when the aim is to study the structure of the protein, this is not necessarily so. For example, if a piece of polypeptide is added at either the N- or C-terminus of the protein, this generally has no effect on the structure of the folded domain but it does change the overall shape. Sometimes a so-called His-tag sequence is added to the native polypeptide sequence in order to facilitate its purification. The orientation of  $A$  is different with and without this His-tag sequence. Moreover, the net charge on this histidine-rich tail can easily be changed by dropping the pH from 7.5 to 5.5 and this changes not only the average conformation of the tail, but also can modulate very weak electrostatic interactions between the protein and the phospholipid liquid crystalline matrix. This weak electrostatic interaction can be amplified if a net charge is added to the phospholipid particles, which actually can also stabilize the liquid crystalline phase.<sup>8</sup> So there appear to be multiple ways for rotating the solute protein relative to its alignment tensor, all of which were found to work well when tested for the proteins ubiquitin and BPTI. Some more details hopefully will appear in JACS in the not-too-distant future.

As an example, Figure 1 maps the possible orientations of the N-H bond vector of residue Leu<sup>6</sup> in BPTI for two slightly different compositions of the liquid crystalline matrix. In one case pure bicelles ([DMPC]:[DHPC] = 3; 5% w/v) were used; in the second experiment the bicelles were "doped" with positively charged CTAB ([DMPC]:[DHPC]:[CTAB] = 15:5:1). As can be seen in Figure 1, the point where the two cones intersect falls very close to the orientation of the N-H bond vector observed in the crystalline state by a combination of X-ray and neutron diffraction. This turns out to apply for virtually all amides in this protein, confirming that this protein has a very similar structure in the crystalline state and in the aqueous solution separating the large (~600 Å diameter) bicelles.

In essence, the ability to rotate the molecule relative to the liquid crystal director provides a stereoview of the protein. It is also somewhat analogous to solid state single crystal NMR, except that the goniometer adjustment in our case is of the trial-and-error type, and not all orientations are accessible.

Kindest regards,



Benjamin E. Ramirez



Ad Bax



- (1) Saupe, A.; Englert, G. *Phys. Rev. Lett.* **1963**, *11*, 462-465.
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- (3) Tolman, J. R.; Flanagan, J. M.; Kennedy, M. A.; Prestegard, J. H. *Proc. Natl. Acad. Sci. USA* **1995**, *92*, 9279-9283.
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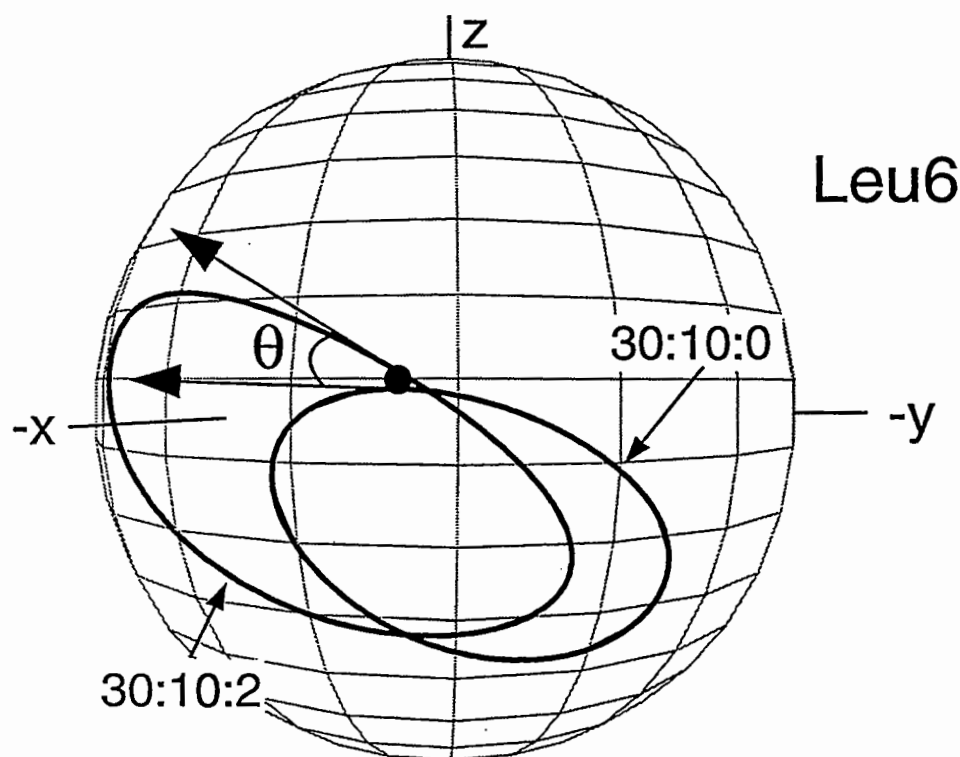


Figure 1. Cones of Leu<sup>6</sup> N-H vector orientations compatible with the measured dipolar couplings in undoped bicelles (30:10:0) and in positively charged bicelles (30:10:2). Orientations are given in the coordinate frame of the X-ray crystal structure. The angle  $\theta$  at which the two distorted cones intersect equals 35°. The average angle of intersection is 25°. The solid dot marks the orientation of the N-H vector in the crystal structure, with the hydrogen position model-built with the XPLOR program, assuming H<sup>N</sup> falls exactly in the C'-N-C<sup>α</sup> plane.

**Carlsberg Laboratory**  
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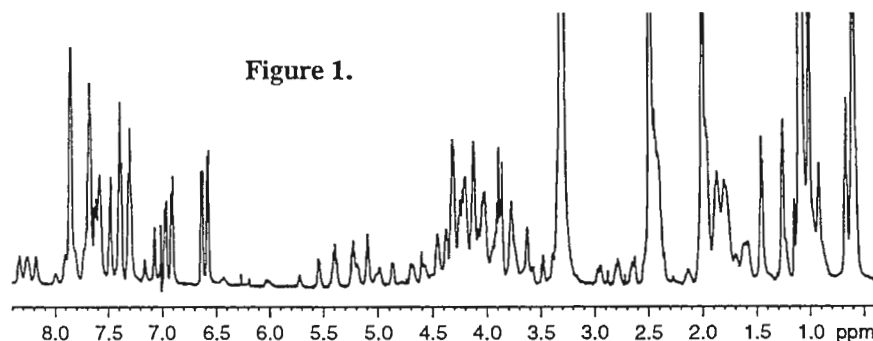
Professor B. L. Shapiro  
 The NMR Newsletter  
 966 Elsinore Court  
 Palo Alto CA 94303, USA

August 17, 1998  
 (received 8/24/98)

Title: Structural assignments using NMR nano-probe technology.

Dear Barry

The use of an NMR nano-probe for studying resin-bound compounds is a rapidly developing and reliable method of obtaining high-resolution spectra. Here at the Carlsberg Laboratory, we are currently exploring the use of a nano-probe in the characterization of resin-bound compounds and have obtained good 1D and 2D spectra that allow structural assignments to be made for small peptides and glycopeptides with a length of at least 6 amino acids. One advantage of using the nano-probe is that it offers the possibility of following chemical reactions on solid phase without cleaving them from the resin. Another objective of using the nano-probe is to work towards using only one bead for the characterization of a given compound or the product of a given synthesis. The quality of the spectra that we have obtained seems however to be significantly dependent on the solid support used for the synthesis. Here, we are mostly working with synthesis done on new solid supports engineered and synthesized in the laboratory of Prof. Morten Meldal<sup>1</sup> at the Carlsberg Laboratory. Among other structure related research we also focus on the possibility of using NMR and the nano-probe technology for the characterization of the different newly synthesized resins.



In our studies we have used a Varian 500 MHz selective <sup>1</sup>H nano-probe. The resolution of the spectra obtained on resin-bound materials is excellent considering the amount of sample available. Spectral quality and resolution like the one shown in Figure 1 can be obtained on a sample containing ~5 beads.

Yours Sincerely

*Charlotte H. Gotfredsen*  
 Charlotte H. Gotfredsen

*Jens Ø. Duus*  
 Jens Ø. Duus

<sup>1</sup> Renil, M., Meldal, M. (1996) *Tetrahedron Lett.* 37, 6185-6188.

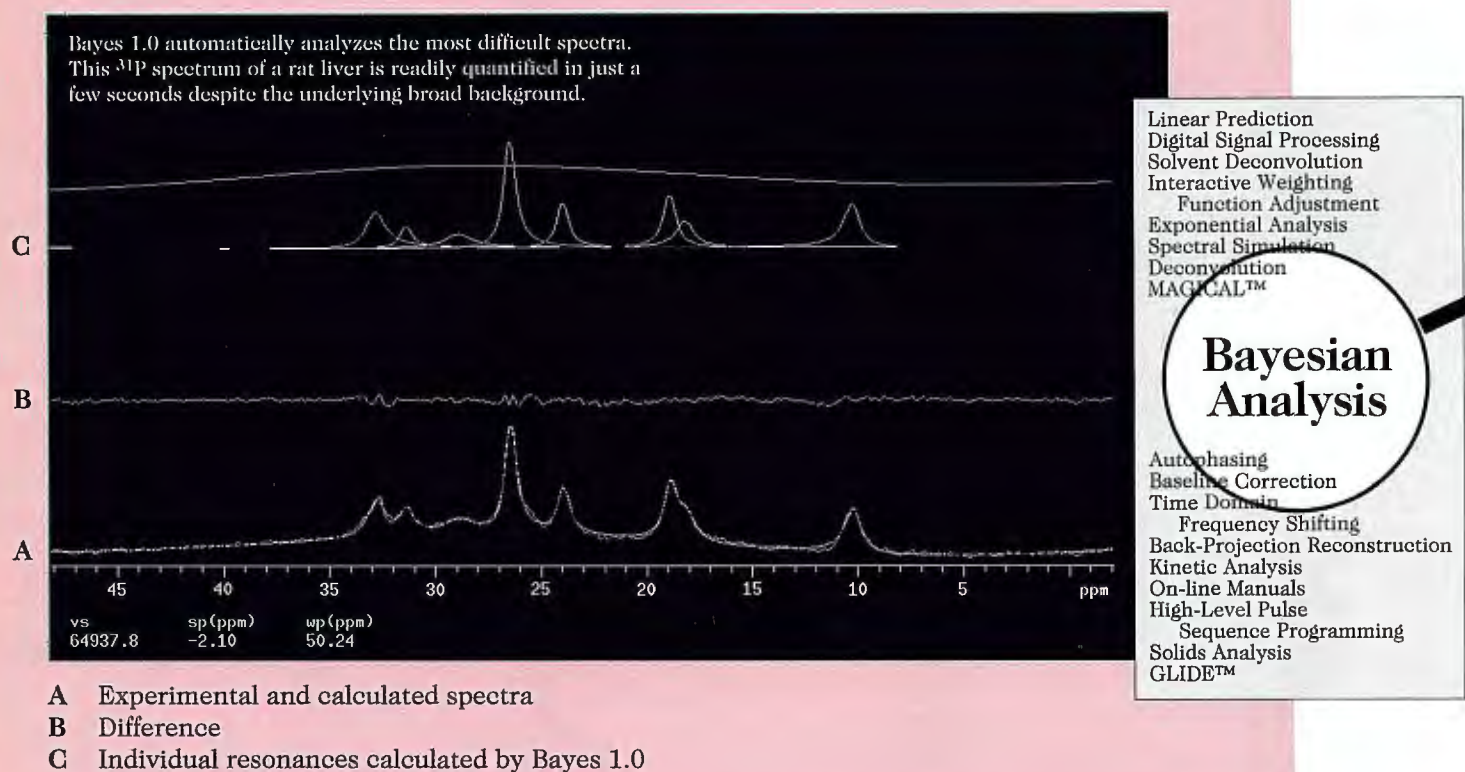
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# Results You Can Believe In



## New Bayes 1.0 Software Automates 1D Analysis

Bayes 1.0 software, the result of a collaborative effort between Washington University, Monsanto, and Varian, revolutionizes NMR spectral analysis. Bayes 1.0 is a unique tool which quantifies analysis of time domain data quickly and easily, ensuring reliable results. The first software to implement Bayesian analysis for 1D FIDs, Bayes 1.0 will take a postulated model, fit it to the experimental data, and show the correlation between observed and calculated results — all at the click of a mouse!

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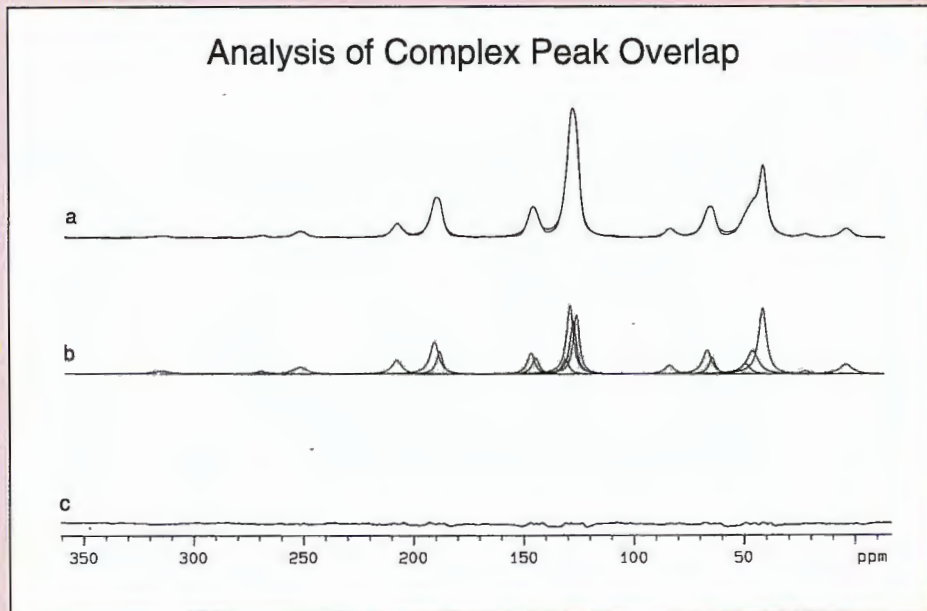
- Believable results
- Quantifies analysis of time domain data
- Enhances signal amplitude, frequency, and linewidth analysis
- Available as an add-in to VNMR software

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# Bayes 1.0 Applications

## I.

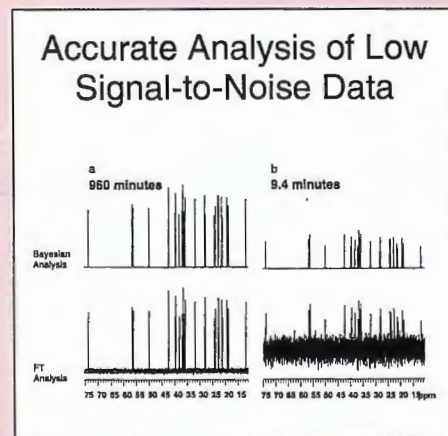
a. Overlay of Bayesian-modeled and experimental  $^{13}\text{C}$  CP/MAS spectra of polystyrene, b. Bayesian analysis of the FID of polystyrene, showing individual modeled resonances in the frequency domain, c. Difference spectrum from subtraction of FT spectrum from FT of Bayesian-modeled spectrum.



I

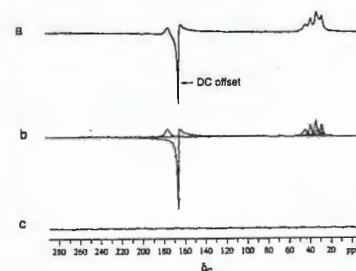
## II.

a.  $^{13}\text{C}$  FT spectrum of cholesterol, 8192 transients, total experiment time 960 minutes (bottom) and Bayesian-modeled spectrum (top), b.  $^{13}\text{C}$  FT spectrum of cholesterol, 80 transients, total experiment time 9.4 minutes (bottom) and Bayesian-modeled spectrum (top), demonstrating the accuracy of Bayesian analysis even under low signal-to-noise conditions.



II

## Resonance Analysis in the Presence of Spectral Distortion



III

## III.

a. Overlay of Bayesian-modeled and experimental 32 MHz  $^{13}\text{C}$  CP/MAS spectra of Nylon 6,6, b. Bayesian analysis of the FID of Nylon 6,6, showing individual modeled resonances in the frequency domain, and demonstrating accurate modeling of resonances in the presence of a strong DC offset, c. Difference spectrum from subtraction of FT spectrum from FT of Bayesian-modeled spectrum.

Spectra provided courtesy of Dr. W. C. Hutton, Monsanto, Co.

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**Lilly Research Laboratories**

A Division of Eli Lilly and Company

Lilly Corporate Center  
Indianapolis, Indiana 46285  
(317) 276-2000August 18, 1998  
(received 8/24/98)  
Dear Barry,**SMASH\***

This letter is an initial announcement of the convening of an NMR meeting, focused on applications to small molecules, which will provide a much needed augmentation to the ENC program.

For many years now the ENC has served as the premier meeting for NMR spectroscopists, showcasing the various disciplines of NMR spectroscopy. Most disciplines have also developed their own forum (i.e., Keystone for biomolecular, Rocky Mountain for solids, and ISMRM for imaging) to provide an opportunity for more in-depth discussion. The only group not possessing a separate forum are those NMR spectroscopists involved in the various aspects of small molecule structure determination. We believe this group comprises the largest number of NMR spectroscopists practicing today, and although many of the prominent scientific meetings such as the Eastern Analytical Symposium and the ACS meetings contain sessions devoted to small molecule NMR, none of these conferences (including the ENC) can adequately serve the needs of the small molecule NMR spectroscopists. Since the application of NMR is an extremely important tool in the pharmaceutical, chemical, and agricultural industries, it is not unexpected that there would be, at some point, a meeting devoted exclusively to the use of NMR in solving problems related to small molecules.

During the last ENC at Asilomar, a group of approximately twenty NMR spectroscopists met to discuss the possibility of organizing a meeting focusing on topics of interest to those of us involved in small molecule applications of NMR spectroscopy. After a spirited discussion it was agreed that there was definitely a need for a conference of this type and that late-summer of 1999 should be targeted for the first organized meeting. The following list of potential topics is not meant to be all inclusive, but to provide a starting point for developing a well-rounded, inclusive program.

- Structure elucidation and characterization
  - strategies for structure elucidation
  - drug metabolites
  - natural products and associated trace components
  - nuclei other than  $^1\text{H}$
  - strategies for post-acquisition data processing
- NMR for small samples
  - micro/sub-micro/nano/ $\mu$ coil approaches
  - Handling and preparing small and extremely small samples for NMR analysis
- NMR as a tool in combinatorial chemistry and high throughput screening
- Development and applications of LC-NMR, flow-NMR, LC-NMR-MS and related techniques
- Pulse sequence development
- Diffusion spectroscopy
- Advancements in NMR probes and magnets

In addition to the list of topics, the group at Asilomar also expressed a desire for the conference to be held in mid August near an airport servicing international flights. Other ideas were expressed including the desire not to have concurrent sessions, the desire to have a poster session, and the potential of having informal workshops. We are currently finalizing a location which will provide housing, meals, and conference accommodations, and we will communicate the final details as they become available.

I am contributing this letter on behalf of the organizing committee *pro tem* (whose names are listed below) and all of the small molecule NMR spectroscopists who attended the Asilomar organizational meeting. We welcome any and all comments on the program, potential session chairs, potential presenters, location. Please send comments to one of the people listed below until a more formal mechanism is in place.

A special thanks to Barry for providing access to the NMR Newsletter.



Steven R. Maple  
Eli Lilly and Company  
Lilly Corporate Center, DC3811  
Indianapolis, IN 46285  
(317) 276-1389  
maple\_steven\_r@lilly.com

Gary E. Martin  
Pharmacia & Upjohn  
MS 4821-259-277  
Kalamazoo, MI 49001-0199  
(616) 833-6283  
gary.e.martin@am.pnu.com

Alistair G. Swanson  
Pfizer Central Research  
Ramsgate Road, Sandwich  
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44 1304646637  
alistair\_swanson@sandwich.pfizer.com

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Field Strength (Tesla)	4.7			7.0			9.4		11.7	
Nominal Room Temperature Bore Access (mm)	54	89		54	89	150	54	89	51	89
Magnet Type (Standard or shielded)	Standard	Standard		Standard	Standard	Standard	Actively Shielded	Actively Shielded	Actively Shielded	Actively Shielded
Field Stability (Hz/hour <sup>1</sup> H)	<2	<2		<3	<3	<15	<8	<10	<10	<10
Axial 5 Gauss Stray Field Contour (Metres)	1.81	2.65		2.19	2.75	4.2	1.5	1.8	1.8	2.5
Radial 5 Gauss Stray Field Contour (Metres)	1.42	2.0		1.7	2.2	3.3	1.0	1.3	1.3	1.75
Cryostat Type	Compact	T3	T3	Compact	T3	T3	T5	T3	T4FB	T4FB
Minimum Helium Refill Interval (Days)	80	235	203	80	235	203	120	183	150	150
Helium Refill Volume (Litres)	26	79	68	26	79	68	101	62	83	83
Year Hold Cryostat Option Available	X	✓	✓	X	✓	✓	X	X	X	X
Nitrogen Refill Interval (Days)	14	14	14	14	14	14	22	14	15	15
Minimum Nitrogen Refill Volume (Litres)	32	61	61	32	61	61	135	61	81	81
* Minimum Operational Ceiling Height (Metres)	2.69	2.92	2.92	2.69	2.92	2.92	4.16	2.9	3.1	3.1
System Weight (kg) Including Cryogen's	120	315	391	133	325	399	1050	400	610	625

NMR Operating Frequency (MHz <sup>1</sup> H)	600		750		800		900	
Field Strength (Tesla)	14.0		17.6		18.8		21.1	
Nominal Room Temperature Bore Access (mm)	51	89	51		63		63	
Magnet Type (Standard or shielded)	Actively Shielded	Standard	Standard	Standard	(2.2K) Pumped		(2.2K) Pumped	With Iron Shield
Field Stability (Hz/hour <sup>1</sup> H)	<10	<12	<15	<15	<15		<15	<15
Axial 5 Gauss Stray Field Contour (Metres)	2.5	5.0	7.6	8.69	6.3		12.2	8.73
Radial 5 Gauss Stray Field Contour (Metres)	1.75	3.9	6.1	6.89	5.0		9.7	3.81
Cryostat Type	T5FB	T4FBL	T6	T6L	T7		T8	
Minimum Helium Refill Interval (Days)	120	90	60	60	60		60	
Cryostat Helium Refill Volume (Litres)	101	60	187	216	328		1200	
Minimum Nitrogen Refill Interval (Days)	15	15	14	14	14		15	
Nitrogen Refill Volume (Litres)	136	100	137	162	167		1800	
* Minimum Operational Ceiling Height (Metres)	3.16	3.4	3.78	3.97	3.97		8.75	
System Weight (kg) Including Cryogen's	1180	1200	3000	4000	4000		18000	

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		External Diameter (Cryostat Bore Size)	Internal Diameter (NMR Probe Diameter)
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18/89/73	18	89mm	73mm
26/89/73	26	89mm	73mm
28/51/40	28	51mm	40mm
40/51/40	40	51mm	40mm
29/51/45	29	51mm	45mm
36/63/51	36	63mm	51mm

### UK

Oxford Instruments  
NMR Instruments,  
Old Station Way  
Eynsham, Witney,  
Oxon, OX8 1TL  
England  
Tel: +44 (0)1865 884500  
Fax: +44 (0)1865 884501  
e-mail: info.nmr@oxinst.co.uk

### France

Oxford Instruments SA  
Parc Club-Orsay  
Universite,  
27, rue Jean Rostand,  
91893 - Orsay Cedex,  
France  
Tel: +33 1 6941 8990  
Fax: +33 1 6941 8680

### Germany

Oxford Instruments  
GmbH  
Kreuzberger Ring 38,  
Postfach 4509,  
D-6200 Wiesbaden,  
Germany  
Tel: +49 611 76471  
Fax: +49 611 764100

### Japan

Oxford Instruments K.K.  
Haseman Building,  
201106 Tomioka,  
Tokyo,  
Japan 135  
Tel: +8 3 5245 3261  
Fax: +8 3 5245 4472

### USA

Oxford Instruments  
NMR Instruments,  
3120 Hansen Way,  
M/S D177, Palo Alto,  
CA 94304-1030,  
USA  
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(received 8/3/98)

28th July 1998

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Professor G C K ROBERTS  
0116 252 5533  
(Direct line)

### FACSIMILE

0116 252 3013

### Dr L Y LIAN

0116 252 3055  
(Direct line)

0116 252 2522  
(Switchboard)

## Achieving Accurate Diffusion Coefficient Measurements of Proteins.

Dear Dr. Shapiro,

Recently, the use of NMR diffusion coefficient measurements to study proteins has increased dramatically. The majority of studies have been concerned with the aggregation of proteins. Some of these have attempted to relate the diffusion coefficient to the molecular weight of the protein, more precisely the diffusion coefficient can be related to the solvent accessible surface area. Though both methods have only been shown to be semi-quantitative. Other studies have used diffusion to investigate hydration and to detect conformational changes in proteins. For these types of study, errors can occur if changes in viscosity are not properly taken into account.

All NMR diffusion measurements demand accuracy and reproducibility. There are a number of factor which must be considered if accurate and reproducible diffusion coefficient measurements are to be achieved. These include: (1) eddy currents generated by magnetic field gradients (2) water suppression (3) restricted diffusion (4) thermal gradients within the sample (5) gradient linearity. All of these factors can lead to unreliable diffusion coefficient measurements<sup>1</sup>. The problems associated with eddy currents have long been recognised and pulses sequences proposed, such as the LED sequence, which overcome these. For diffusion coefficient measurements of proteins in aqueous solutions good water suppression is desirable, and can be achieved with presaturation and frequency selective pulses or with WATERGATE, allowing high receiver gains to be used without the fear of distorted signal intensities. The problems accompanying restricted diffusion can be easily circumvented by ensuring that no interfaces in the direction of the gradient are within the receiver coil. Thermal gradients will lead to an increase in the observed diffusion coefficient through convection. Adequate time for thermal equilibrium to be achieved should be allowed before data is collected. A pulse sequence has been proposed which will suppress convection<sup>2</sup>, and may be useful in some cases. The importance of obtaining a linear gradient does not seem to have been widely recognised until recently<sup>1</sup>; a non-linear gradient leads to the multi-exponential decay of diffusion data. The effects may not be apparent from a decay curve but will result in different values of the diffusion coefficient being obtained if different sections of the decay curve are fitted. Gradient non-linearity can also be detected by the use of diffusion weighted images or by repeating diffusion coefficient measurements with different diffusion attenuation parameters.

In summary, in order to make accurate and reproducible diffusion coefficient measurements the factors listed above should be considered.

Please credit this contribution to Gordon Roberts' subscription.

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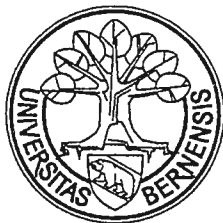
Yours sincerely,

Marcus L. Tillett

Lu-yun Lian

Timothy J. Norwood





## University of Berne

Department of  
Chemistry and Biochemistry  
NMR-Spectroscopy

Freiestrasse 3  
CH - 3012 Bern

*Prof. Dr. Peter Bigler*

Tel: +41 (31) 631 39 48  
Fax: +41 (31) 631 34 24  
E-mail: [bigler@ioc.unibe.ch](mailto:bigler@ioc.unibe.ch)

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

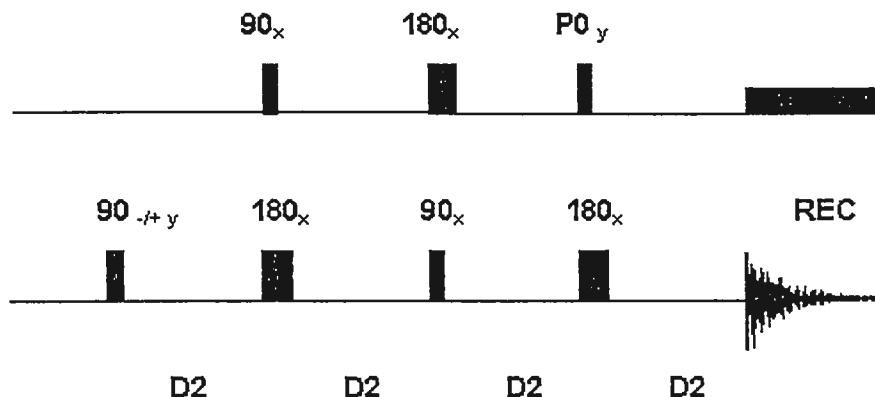
july 10<sup>th</sup> 1998  
(received 7/29/98)

### DEPTQ

Dear Dr. Shapiro

<sup>13</sup>C DEPT is certainly one of the most widely used routine NMR experiments. Due to its „inherent handicap“, i.e. the missing signals of quaternary carbons in the corresponding spectra, it is usually applied together with a one-pulse <sup>13</sup>C experiment. A closer inspection, however, reveals that with a simple extension (see below) the signals of quaternary carbons may be detected as well - even in a single scan - without sacrificing any of the well-known benefits of the basic DEPT experiment such as its suitability for full spectral editing. Compared to the one-pulse <sup>13</sup>C experiment with a maximum NOE decreased intensities for Cq's must be taken into account with DEPTQ. Nevertheless the overall efficiency is increased, since in most cases a DEPTQ experiment will suffice and the application of an additional <sup>13</sup>C one-pulse experiment will be restricted to a few critical cases.

For full spectral editing, i.e. the calculation of Cq-, CH-, CH<sub>2</sub>- and CH<sub>3</sub>-subspectra, the phase of the initial <sup>13</sup>C pulse must be set as y/-y in two subexperiments. Adding the corresponding data and subtracting it from each other yields the Cq and the CH<sub>n</sub> subspectra respectively. Whereas the Cq subspectra obtained with the three <sup>1</sup>H-selection pulses P0 (45, 90, 135) are simply coadded, the CH<sub>n</sub> subspectra may be further processed in the usual way.



Yours sincerely

Peter Bigler

UNIVERSITY OF CALIFORNIA, BERKELEY  
Department of Chemistry

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Thomas Meersmann, c/o Pines Group, University of California, Department of Chemistry, Berkeley CA 94720  
phone: 510 642 2094, Fax: 510 486 5744, email: meersman@dirac.cchem.berkeley.edu

Berkeley, 08/11/98

(received 8/13/98)

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

**Re: Breaking of Atomic Symmetry at High Magnetic Field Strengths**

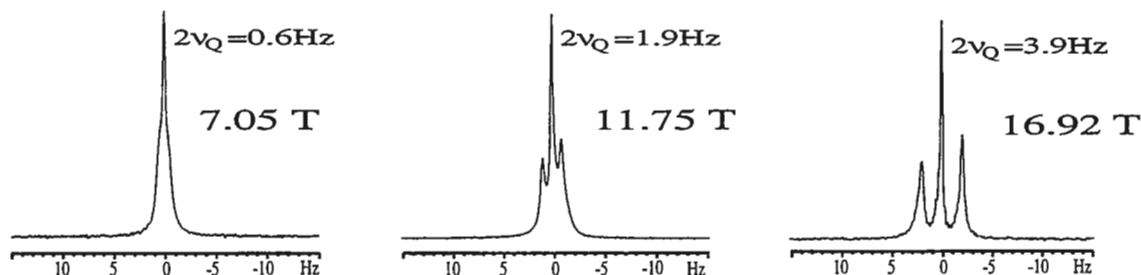
Dear Dr. Shapiro,

I would like to report about a rather peculiar phenomenon discovered about half a year ago using  $^{131}\text{Xe}$  NMR spectroscopy<sup>1</sup>. Meanwhile, theoreticians have worked on this subject<sup>2</sup> and we have continued with some more experiments on  $^{83}\text{Kr}$ <sup>3</sup> since I moved to California last April.

It is usually assumed that the strong magnetic fields used in NMR will not affect the molecular or atomic structure of our samples. However, in the light of the recent results on Xenon-131, there is some reason to believe that this assumption is wrong. Fortunately, the effect is very subtle and will not affect most NMR measurements. Indeed, it is so weak, that it can only be detected by one of the most sensitive detectors available for this purpose: Xenon-131 gas-phase NMR spectroscopy. The large electron cloud of a xenon atom is easily disturbed giving rise to a large chemical shift range which therefore serves as a sensitive detector for its environment. This has been extensively exploited over the past two decades for the study of porous materials<sup>4,5</sup> and more recently in combination with optical pumping for the investigation of smaller surface areas<sup>6</sup>. Usually, the xenon-129 ( $I=1/2$ ) isotope is used for this purpose due to its larger gyromagnetic ratio and more favorable relaxation times. However, the nuclear quadrupole moment of the other NMR active isotope, xenon-131, is even more susceptible to any distortion of the electron cloud. The nuclear quadrupole moment will interact with the electric field gradient (EFG) caused by any of such distortion thus leading to quadrupolar coupling. In the pure gas phase, the xenon atom assumes spherical symmetry (at least in the time average within the NMR time scale) and no coupling should occur in the gaseous xenon-131. However, interaction and exchange of xenon-131 atoms with the surrounding container walls are known to lead to a quadrupolar splitting observable in the gas phase<sup>7-9</sup>. The new results obtained from measurements at very high magnetic fields indicate that a field dependent quadrupolar splitting will occur in the gas phase even in the absence of any interactions with the container wall. Using multiple quantum filtered<sup>10,11</sup>  $^{131}\text{Xe}$  NMR, it was possible to separate the (known) surface effects from a 'bulk' (-i.e. gas phase) effect<sup>1</sup> (note, that it was also possible to exclude possible magnetic alignment effects of Van der Waals complexes). Fig. 1 shows the quadrupolar splitting of gas-phase xenon-131 at different field strengths. The clear field dependence of the splitting cannot be explained by surface interactions. Closer inspection shows a linear and quadratic dependence of the quadrupolar coupling upon the applied magnetic field.

The explanation for this effect may be the following: The external magnetic field induces an electric current in the electron orbitals which causes a magnetic moment. This is well known as the diamagnetic current responsible for magnetic susceptibility and the chemical shift in NMR

spectroscopy. The induced magnetic moment will however interact with the external magnetic field (by which it was caused) and may lead to a distortion of the atomic orbitals, hence causing a quadrupolar splitting with quadratic dependence upon the applied field. The induced magnetic moment may also interact with the magnetic moment of the nucleus, resulting into a coupling which depends linearly on the applied field. Salsbury and Harris estimated the size of the effect to be in agreement with observed splitting<sup>2</sup>. They also pointed out that the linear term is to be expected much weaker than the quadratic term, except for elements with very high atomic numbers  $Z$ .



**Figure 1.:** Gas-phase xenon-131 NMR Spectra at 7.05 T (i.e. 300 MHz proton frequency), 11.75 T (500 MHz) and 16.92 T (720 MHz). The gas was contained inside a 6 mm i.d. Pyrex tube at 400 kPa (4 atm) and  $\sim 300\text{K}$ .

Note again, that the effect is very weak. Even for xenon at 16.92 T the splitting is  $2\nu_Q = 3.9\text{ Hz}$ . Measurements on  $^{83}\text{Kr}$  ( $I=9/2$ ) at 16.92 T (720 MHz proton frequency) did not lead to an observable splitting within the 1.2 Hz linewidth (home build probe). A 10 kV DC electric field applied on xenon-131 at 16.92 T did not cause any appreciable change in the splitting. Similar effects in molecular systems in liquids or gas phase will be difficult to separate from magnetic alignment effects and any field induced splitting in solids<sup>12</sup> is most likely masked by short transverse relaxation times. Nevertheless, the availability of very high magnetic fields with high homogeneity may lead to related discoveries in other systems.

Please credit this contribution to the Pines Group.

with best regards,

Thomas Meersmann

- <sup>1</sup> T. Meersmann and M. Haake, Phys. Rev. Lett. **81**, 1211 (1998).
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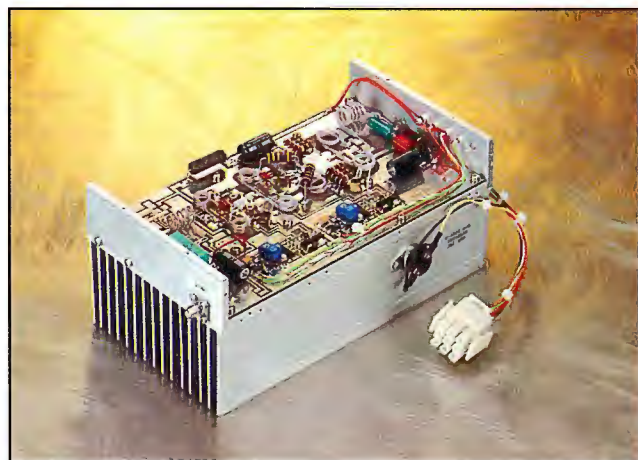
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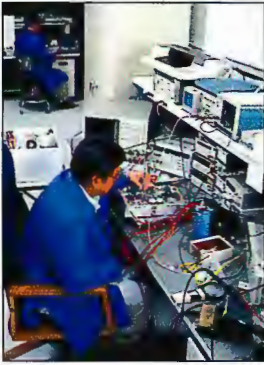
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Department of Chemistry  
**Professor Gideon Fraenkel**  
 Phone: 614-292-4210  
 e-mail: [fraenkel@mps.ohio-state.edu](mailto:fraenkel@mps.ohio-state.edu)

Newman and Wolfrom Laboratory  
 100 West 18th Avenue  
 Columbus, OH 43210-1185  
 Phone 614-292-2251  
 FAX 614-292-1685  
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July 27, 1998  
 (received 8/10/98)

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

# 1,3 Li Sigmatropic Shift in an Allylic Lithium Compound

Dear Barry,

To show how easily one is fooled: We reported recently how, due to restricted stereochemistry of solvation, some internally coordinated allylic lithium compounds assume folded, monomeric, partly delocalized structures with small detectable C,Li covalency, see **1**, below. These structures lie between the delocalized solvated ion-pairs, **2** and the localized unsolvated species **3** which from their NMR spectra, resemble alkenes.

Expecting to produce the unsubstituted compound, **1**  $R_1, R_2 = H$ , we deprotonated **4** ( $CH_3Li$ ) and were surprised that at room temperature the allyl  $C_1, C_3$  carbons gave a single sharp peak in  $^{13}C$  NMR at 59 $\delta$  (toluene solution) implying perhaps a delocalized allyl structure. Meanwhile, Roland Fleischer, in my group, did the crystal structure of expected **1**  $R_1, R_2 = H$  and found it indeed had the folded internally coordinated structure but as a lithium bridged dimer, **5**. Thinking perhaps we had missed something in the  $^{13}C$  NMR, we looked again and noticed that with decreasing temperature the  $C_1, C_3$  peak at 59 $\delta$ , broadened and disappeared into the baseline by 200 K.

Assuming now that our solution sample has the folded structure, monomer or dimer, then the above behavior is most likely the result of a fast 1,3 lithium sigmatropic shift. In the folded structure the minimum  $^{13}C$  NMR shift between  $C_1$  and  $C_3$  would be >23 ppm, at 75 MHz, >1725 Hz. Using such a shift the broadened line of >100 Hz at 230 K corresponds to a lithium shift rate of  $4.8 \times 10^4 s^{-1}$ . At 230 K the 1,3-Li sigmatropic shift observed for **1**  $R_1, R_2 = Si(CH_3)_3$  had a rate of  $15.6 s^{-1}$ . That the unsubstituted compound **1**  $R_1, R_2 = H$  should be so much faster need not be surprising since the disilyl compound must undergo several concerted sterically hindered motions to effect a degenerate sigmatropic shift. It is also amusing that the average of the  $C_1, C_3$  shifts for **1**  $R_1, R_2 = H$  is close to what is observed for allyl lithium.

The broadening observed for  $C_1, C_3$   $^{13}C$  resonances of **1**  $R_1, R_2 = H$  far exceeds what might be expected for a system with  $C_1, ^7Li$  spin coupling undergoing intermolecular C,Li exchange and  $^7Li$  quadrupole induced relaxation. With decreasing temperature the exchange rate would decrease while the  $^7Li$  quadrupole induced relaxation rate would increase. Both processes, when sufficiently fast, would have the effect of averaging the  $^{13}C$  splitting due to



-2-

$^1J(^{13}\text{C}, ^7\text{Li})$ . So in principle, with decreasing temperature, the  $^{13}\text{C}$  resonance would start off as a sharp singlet, broaden, possibly resolve into a multiplet (1:1:1:1 for a monomer), then broaden averaging the splitting and narrow into a single line at the lower temperature. The intermediate broadening would not exceed  $3 \times ^1J(^{13}\text{C}, ^7\text{Li})$  or ca 25 Hz. Such behavior is not observed. Our data support a folded structure undergoing a fast 1,3 Li sigmatropic shift.

All the best to you and your newsletter.

Yours sincerely,

*Gideon*

Gideon Fraenkel  
Professor

*Joseph Duncan*

Joseph Duncan  
Research Associate

*Roland*

Roland Fleischer  
DAAD Fellow\*

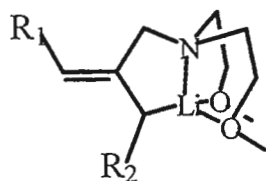
*Albert*

Albert Chow  
Research Associate

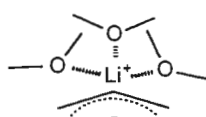
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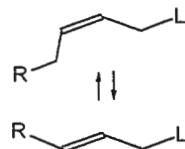
1. Fraenkel, G.; Qiu, F. *J. Am. Chem. Soc.* **1997**, 119, 3571-3579.



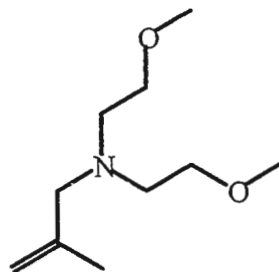
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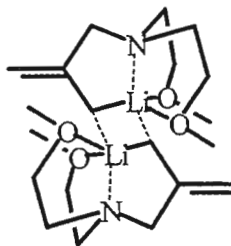
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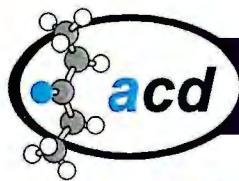
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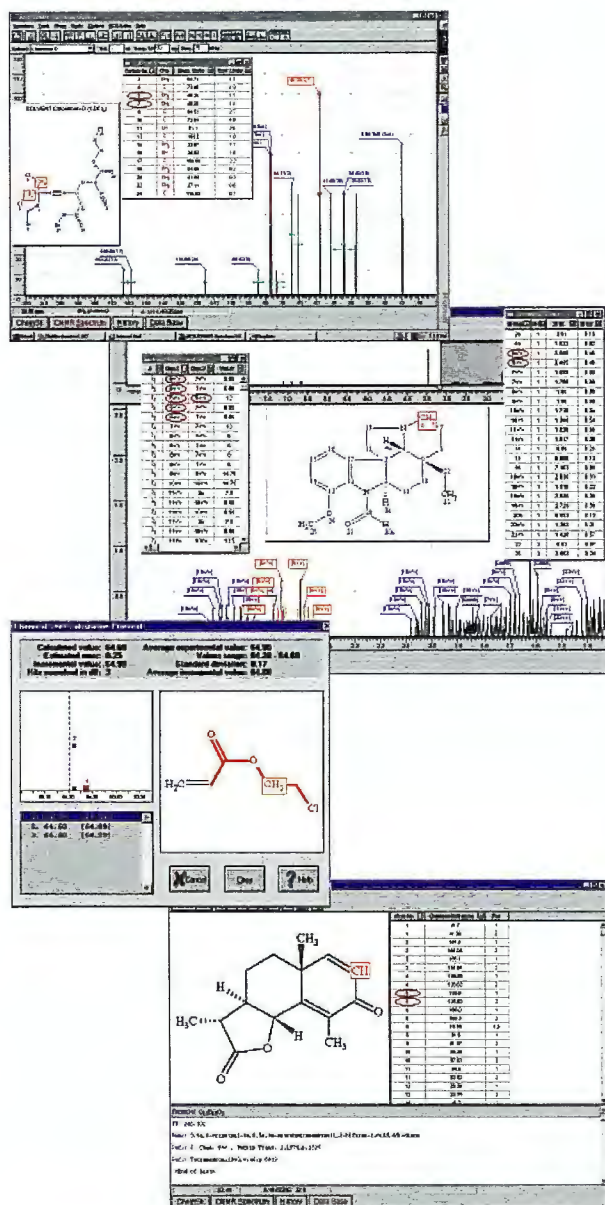
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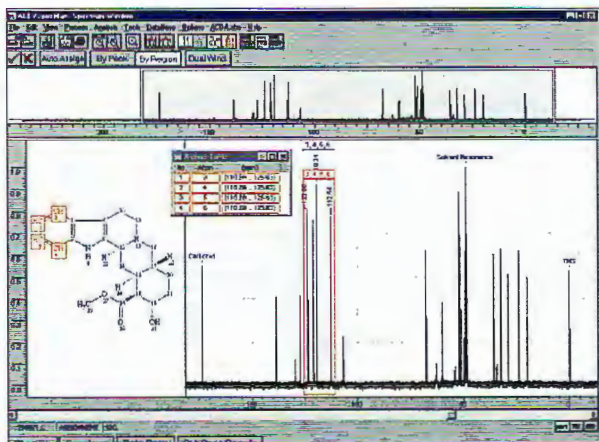
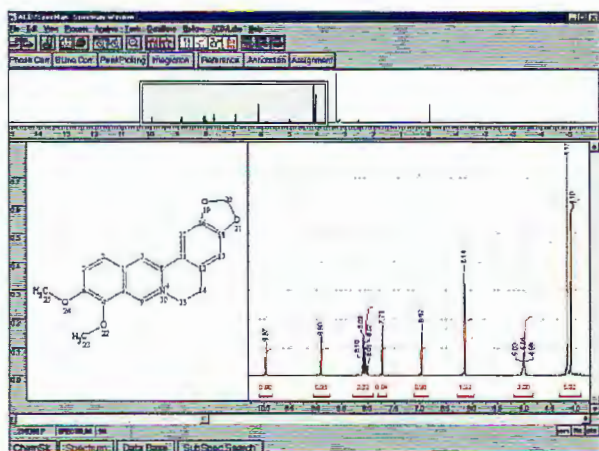
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Tsukuba  
Ibaraki 305-0047  
Japan  
Ph: (81-298) 58 6186  
FAX: (81-298) 58 6144  
e-mail: wprice@wri.co.jp

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

August 4, 1998  
(received 8/17/98)

## PGSE NMR Gradient Pulse Shapes Reproducibility

Dear Barry,

It is well known that the severity of eddy currents generated by gradient pulses is strongly influenced by the rise time of the gradient pulses. Accordingly shaped (e.g., sine or ramped) gradient pulses are commonly used to alleviate this problem. On the other hand, if the eddy current problem can be sufficiently well-addressed, square gradient pulses are the ideal shape since they maximize the degree of dephasing in a given time and thus increase the likelihood of achieving the conditions of the short gradient pulse approximation. However, there is another factor which has not been so much emphasized in the literature and that is the relationship between the shape of the gradient pulse and the amplifier behaviour. While it is easy to understand that a pulse will never be truly rectangular given that the current amplifier will not be able to provide an infinitely fast rise time. I think that it is worthwhile to consider the experimental aspects of the 'reverse' problem - what happens when you ask the gradient system for a shape that exceeds the amplifier's ability.

I first checked the eddy current settling time on our system, a Bruker DRX 300 standard bore equipped with a diff30 high gradient probe (see Fig.1) using a sample with an extremely small diffusion coefficient (~ 5% polystyrene Mw 20 000 000 in CCl<sub>4</sub>). It is clear that the eddy current effects have almost totally subsided by  $t_e = 3$  ms after a  $\delta = 2$  ms square pulse with a strength of 1050 G cm<sup>-1</sup>.

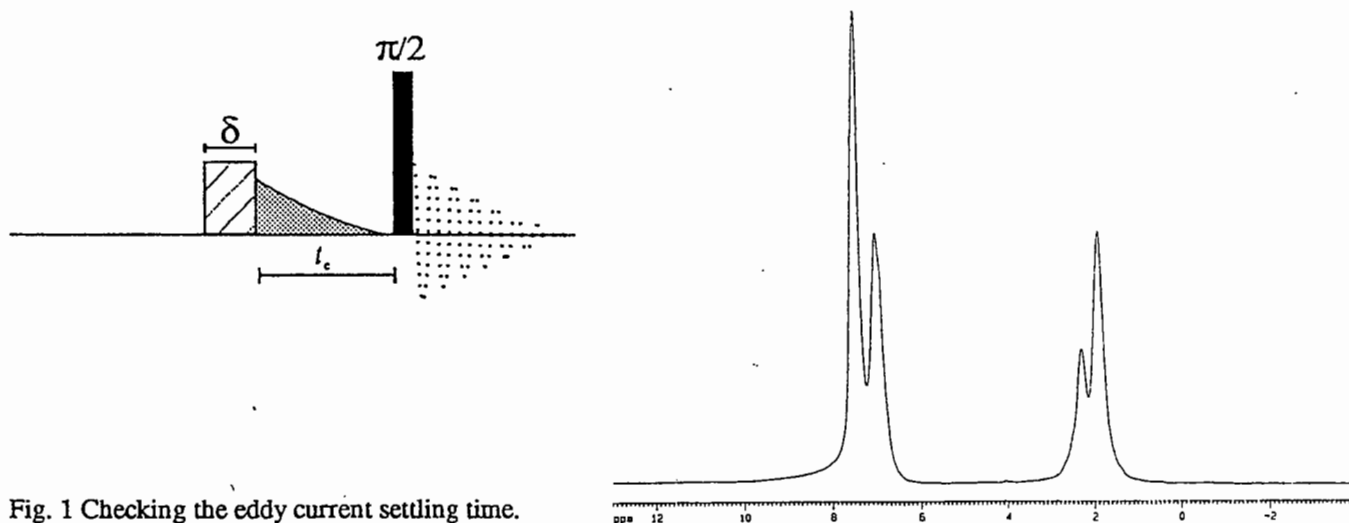
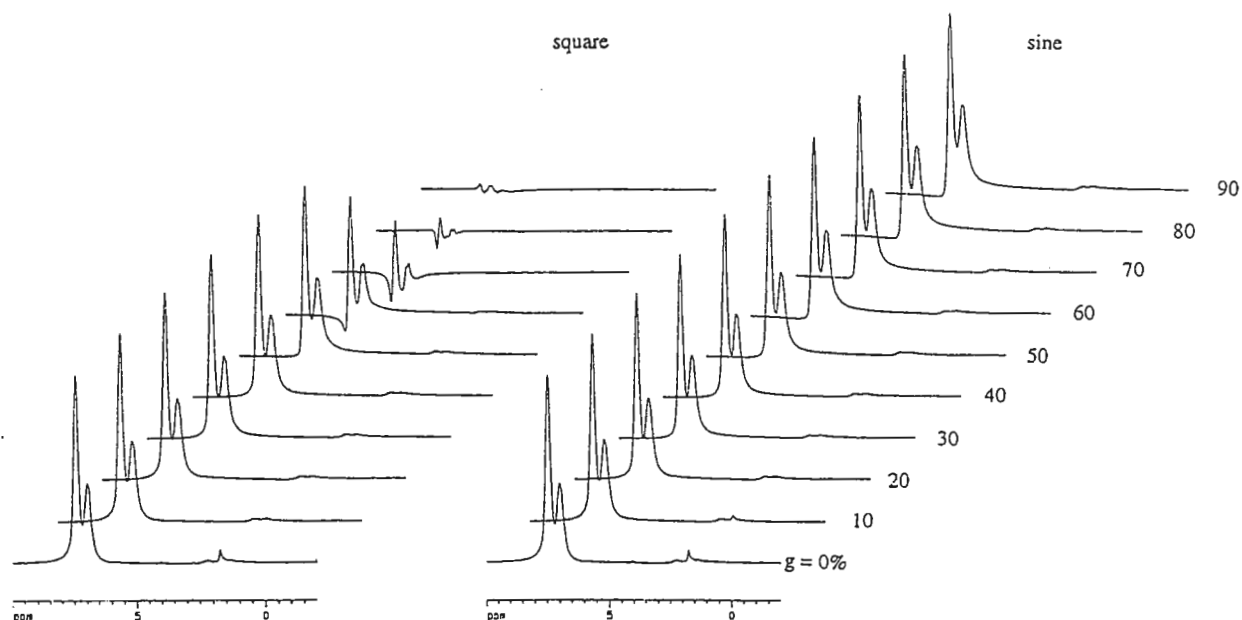


Fig. 1 Checking the eddy current settling time.



Needless to say, equally good results are obtained for a half sine shaped gradient pulse. What was more interesting though was to compare the two gradient pulse shapes in a Hahn-spin echo-based sequence (see Fig. 2). As can be seen, for small gradient strengths the pulse shape doesn't make too much difference (of course if we were trying to extract the diffusion coefficient it would !). In both cases we have left more than 4 ms between the gradients and the  $\pi$  pulse or acquisition so the vast difference between the two is not due to eddy currents. Instead it seems that the difference is due to the fact that the amplifier cannot (sufficiently) reproducibly handle the fast rise time. Consequently, due to pulse mismatch there is a residual phase shift. As this phase shift increases the signal is rapidly attenuated. Clearly it would be all too easy to confuse this artifactual attenuation with diffusion !



## References

- 1) Price, W.S. 1997. Pulsed Field Gradient NMR as a Tool for Studying Translational Diffusion, Part 1. Basic Theory. *Concepts Magn.Reson.* 9:299-336.
- 2) Price, W.S. 1998. Pulsed Field Gradient NMR as a Tool for Studying Translational Diffusion, Part 2. Experimental Aspects. *Concepts Magn.Reson.* 10:197-237.

Please credit this to the account of Prof. Y. Arata.

Yours sincerely

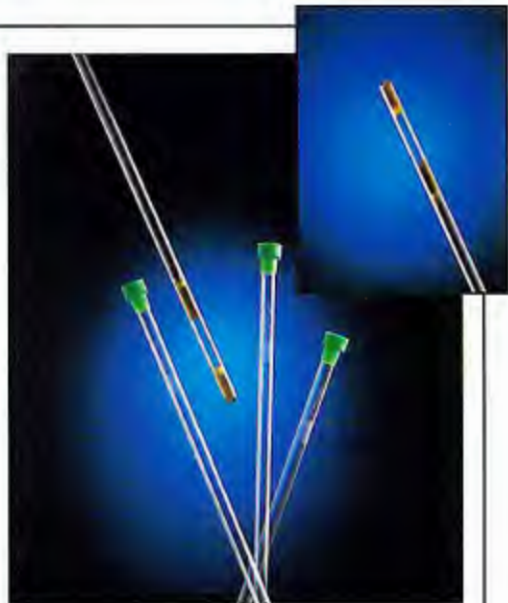
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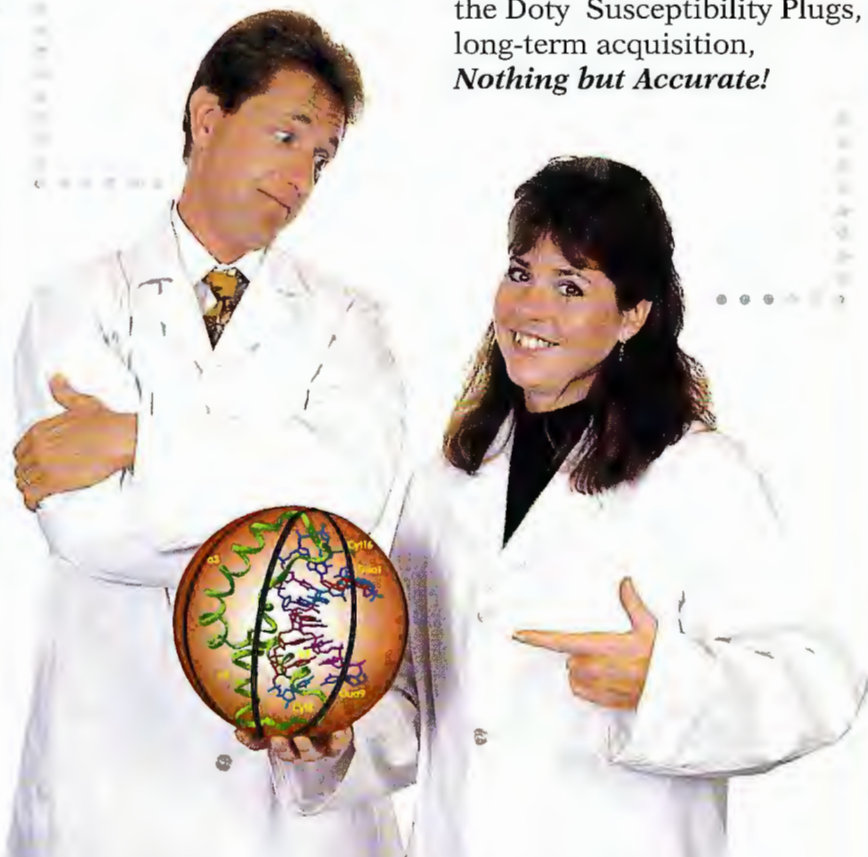
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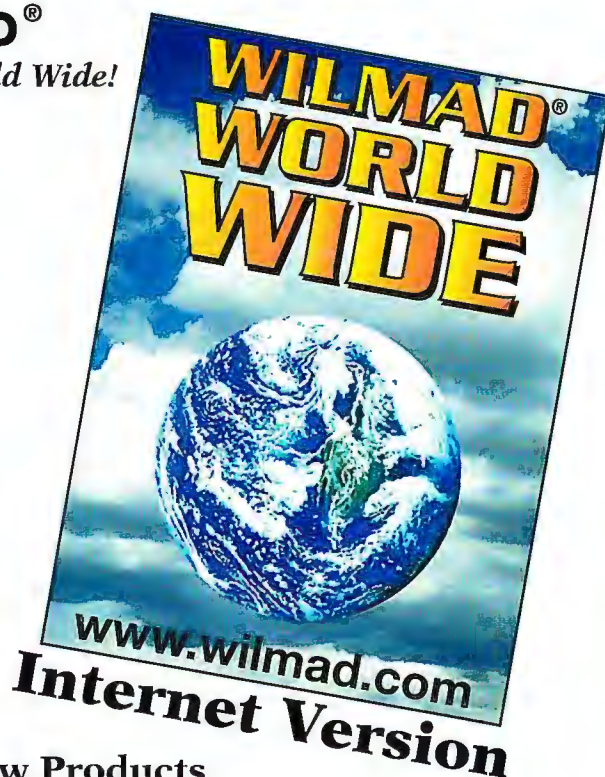
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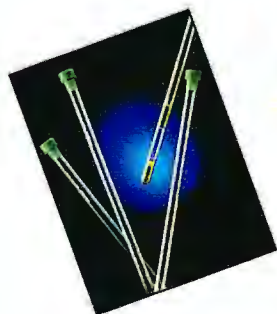
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August 21, 1998  
(received 8/24/98)

**Computerized determination of  $^2\text{H}$  NMR order parameters**

Dear Dr. Shapiro,

One of our routine tasks in membrane research is to measure  $^2\text{H}$  NMR order parameters of lipid hydrocarbon chains. Since the pioneering studies by Seelig and coworkers [1], it is known that lipid order parameters are very sensitive to the smallest changes in lipid area per molecule and membrane hydrophobic thickness. There is considerable interest in measuring these small changes because they are relevant to the function of membrane proteins.

Our standards of  $^2\text{H}$  NMR data acquisition and processing were adapted from publications by the laboratories of Jim Davis [2] and Myer Bloom [3]. We have combined the recommended procedures into a user-friendly computer program written in Mathcad (MathSoft, Inc., Cambridge, MA). The program runs on any IBM-compatible PC and handles all processing tasks after the raw data have been acquired.

Here is a brief description of the procedures: the carrier frequency of the instrument is placed at the center of the spectrum, and the  $^2\text{H}$  NMR complex free induction decays (FID) are acquired with a phase-cycled quadrupolar echo pulse sequence [4]. The raw FID are then transferred to the PC. The program corrects baselines and phases the FID to zero the signal in the imaginary channel. The time of the echo maximum in the real signal channel is determined with a resolution of one tenth of a dwell time unit by fitting a spline function to the data points. Spline interpolation is also used to calculate free induction decay signals in real and imaginary channels that are time base corrected to start data processing exactly at the echo maximum. If desired, the program contracts the spectral width by a procedure of digital filtering that was described in a paper by Prosser et al. [5]. DePaked spectra [6] are calculated using the algorithm of McCabe and Wassall [7]. The program calculates spectral moments, assigns order parameters for every methylene group and the terminal methyl group of saturated hydrocarbon chains, and calculates parameters like lipid area per molecule and membrane hydrophobic thickness. Processing takes just a few minutes per spectrum.

At several points in the program, the intermediate result of processing is displayed, and the operator must confirm parameters that the program determined in automation. These safeguards alert to mistakes in setting of spectrometer parameters, malfunction of instrumentation, and errors in sample preparation. For example, we see immediately if the carrier frequency was not perfectly centered, we easily identify problems

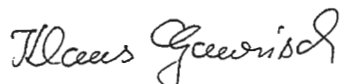


with rf-phase or amplification in one of the two quadrature detection channels, and we detect spectral asymmetry caused by magnetic field inhomogeneity.

This program has been in use at my lab for the last four years. During this period, we have had no problems comparing order parameter measurements by different operators, since data acquisition and processing are conducted strictly by the same standards. We observed very good agreement even when data were recorded on different spectrometers. However, processing of data that are acquired on older instruments may suffer from problems with stability of receiver phases and amplitudes as well as from poor digitizer performance. Mathcad's programming language is very user-friendly. It is easy to alter or extend the program, add graphs, export or import data at any point of processing.

We offer this program for use by other investigators.

Sincerely yours,



Klaus Gawrisch

Laboratory of Membrane Biochemistry and Biophysics  
12420 Parklawn Dr., Rm. 158

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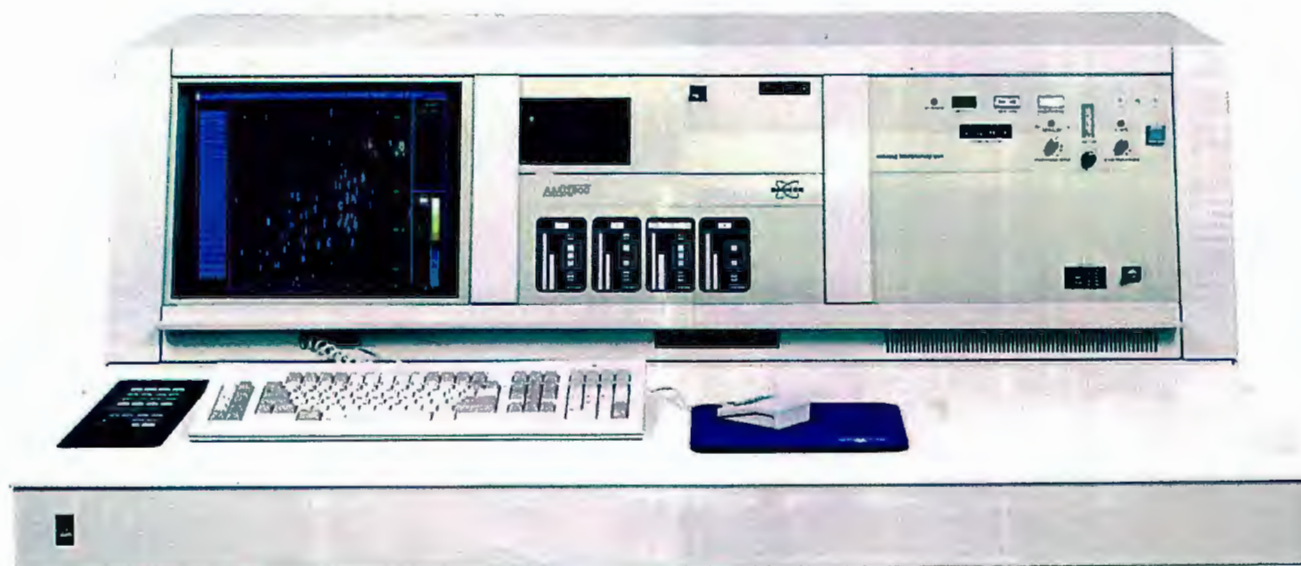
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7. McCabe, M.A., Wassall, S.R. (1995) *J. Magn. Reson. B106*, 80-82

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29 July 1998

(received 8/11/98)

B. L. Shapiro, Publisher  
NMR Newsletter

### Exposing the H in an H-Free Coil

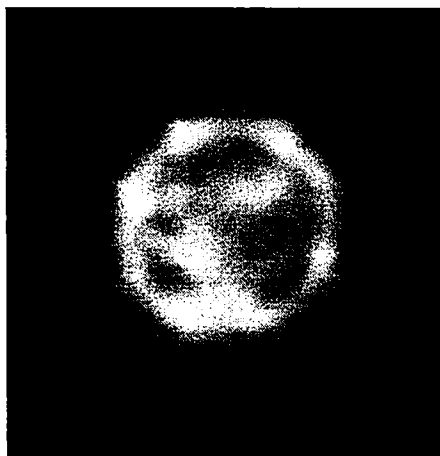
Dear Dr. Shapiro and readers:

We have been imaging a number of things with nastily short  $T_2$ s lately; most successfully, inert fluorinated gases in lungs (Magnetic Resonance in Medicine **39**(1):85-88). Projection imaging, Lauterbur-style, with FIDs, whilst taking into account the data missing from the center of  $k$ -space works so well that we've taken to imaging empty NMR coils.

In keeping with the current trend of grocery store fare that proudly proclaims the absence of typical ingredients, we had Paul Morris (Morris Instruments, Gloucester, Ontario) make for us a Fluorine-Free birdcage coil for imaging  $^{19}\text{F}$  and a similar Hydrogen-Free variety for  $^1\text{H}$ . In my naiveté, I (DOK) assumed the former would be the greater challenge, because my previous efforts involved replacing F-rich variable capacitors with inferior tasting F-Free ones. But Paul's use of inductive coupling for both tuning and matching made Fluorine exorcism a snap. The greater challenge turned out to be hydrogen exclusion.

I would have assumed that using a 6 cm diameter birdcage to image an 11 cm diameter object would be tricky, but a slightly modified version (the gradient coils get a rest during the longer recovery time, which accommodates a longer  $T_1$ ) of the lung-imaging pulse sequence produced an excellent  $^1\text{H}$  image of tape on the outside of the  $^1\text{H}$ -Free coil's rf shield. After the appropriate Teflon® for tape exchange, the bigger surprise was the image of " $^1\text{H}$ -Free" coil, version 2, which vilified the Pyrex® coil form. After confirming my suspicion that Pyrex® glass contains no hydrogen, by obtaining the H-Free list of ingredients from Corning, I made another image, including broken pieces of a Pyrex® custard dish inside

One of 52  $x$ - $y$  planes of a 3D  $^1\text{H}$  image, showing broken pieces of a Pyrex® custard dish inside the Pyrex® coil form (bright circle in image) of the " $^1\text{H}$ -Free" coil, version 2. The 8 blips outside the form are, as yet, unidentified, but probably associated with the tuning and matching coils. The 12 faint segments forming the outermost ring are associated with the shield form. It appears non-circular in section because the imaging magnetic field gradients are not linear out there.



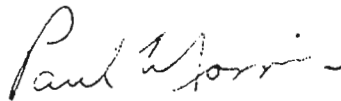
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the Pyrex® coil form. The  $^1\text{H}$  signal that came from the regions of space occupied by Pyrex® had a  $T_2$  of a couple hundred  $\mu\text{s}$ , comfortably long for imaging. Paul did some calling around and discovered that the way to avoid OH groups in glass is to order a special variety of H-Free fused silica, such as GE type 214A.

These stories usually have a twist that helps one put one's ignorance into perspective. I was talking to the brother of one of my rock climbing friends a couple of weeks later at a party, who, to my surprise, nodded knowingly when I mentioned that Pyrex® contains hydrogen. "Oh yes," he said, "Most glasses will contain a substantial amount of OH. In particular, the additives that make Pyrex® less brittle, by putting it under compression after it cools, will contain OH groups. You will be better off with pure fused silica."



Dean O. Kuethe  
LRRI,  
honorary NMR

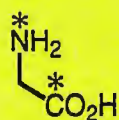


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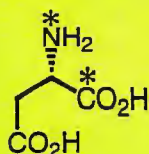
### **Equipment Wanted.**

A used quadrature receiver, as found in an older Bruker SXP or similar spectrometer (up to 200 MHz, input attenuator, and bandwidth control). Please contact Dr. Norbert Buettgen at: [n.buettgen@physik.uni-augsburg.de](mailto:n.buettgen@physik.uni-augsburg.de).



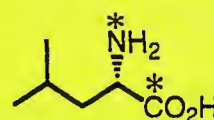
**Glycine-1-<sup>13</sup>C, <sup>15</sup>N**

>99 atom % <sup>13</sup>C  
>99 atom % <sup>15</sup>N



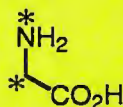
**L-Aspartic Acid-1-<sup>13</sup>C, <sup>15</sup>N**

>99 atom % <sup>13</sup>C  
>99 atom % <sup>15</sup>N



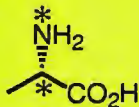
**L-Leucine-1-<sup>13</sup>C, <sup>15</sup>N**

>99 atom % <sup>13</sup>C  
>99 atom % <sup>15</sup>N



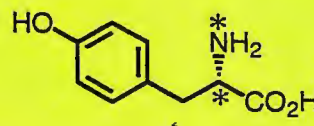
**Glycine-2-<sup>13</sup>C, <sup>15</sup>N**

>99 atom % <sup>13</sup>C  
>99 atom % <sup>15</sup>N



**L-Alanine-2-<sup>13</sup>C, <sup>15</sup>N**

>99 atom % <sup>13</sup>C  
>99 atom % <sup>15</sup>N



**L-4-Hydroxyphenylalanine-2-<sup>13</sup>C, <sup>15</sup>N**

>99 atom % <sup>13</sup>C  
>99 atom % <sup>15</sup>N

*The above Amino Acids are a representative sample of double labelled compounds currently available from Isotec. Our chemists regularly synthesize a variety of Carbon-13, Nitrogen-15 double-labelled compounds as well as many other isotopically labelled compounds.*

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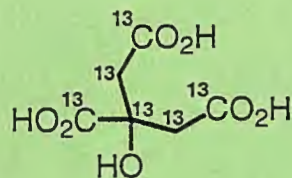
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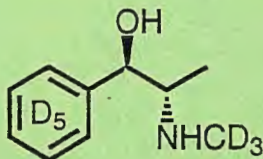
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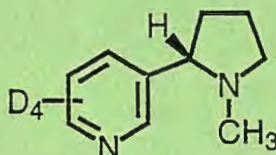




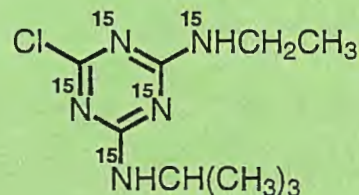
Citric Acid-<sup>13</sup>C<sub>6</sub>



(1R, 2S)-(-)-Ephedrin-d<sub>8</sub>



S-(-)-Nicotine-2,4,5,6-d<sub>4</sub>



Atrazine-<sup>15</sup>N<sub>5</sub>

The compounds shown above are a few examples of custom synthesis compounds that Isotec offers.

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Isotec does not depend on any outside sources to supply our starting material. Today, Isotec is the only commercial producer that separates and enriches over 30 different stable isotopes, including <sup>13</sup>C, <sup>17</sup>O, <sup>18</sup>O, <sup>15</sup>N and Deuterium. This independence gives us a tremendous cost savings and delivery time advantage in custom synthesis. Our on-site production capabilities and ready supply of

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Department of Chemistry and Biochemistry  
Newark, Delaware 19716-2522

Cecil Dybowski  
Professor

(302) 831-2726  
FAX: (302) 831-6335  
Internet: dybowski@udel.edu

August 13, 1998  
(received 8/17/98)

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

### Lead NMR Relaxation in the Solid State

Dear Barry,

There are only a few reports of the NMR spectroscopy of inorganic lead compounds in the solid state. A perusal of the literature shows that the quintessential material for study is  $\text{Pb}(\text{NO}_3)_2$ . We have found it is orders of magnitude easier to obtain a spectrum of  $\text{Pb}(\text{NO}_3)_2$  than any other solid inorganic compound. The question is why should it be so?

One reason is that the shift anisotropy is quite a bit smaller and the spectrum is spread over a narrow range for  $\text{Pb}(\text{NO}_3)_2$ . Although we have not done extensive measurements of others, it is obvious from the conditions we must use to obtain spectra that the  $T_1$  of  $\text{Pb}(\text{NO}_3)_2$  must be shorter than that in other compounds. [Precise measurements of the  $T_1$ s of these other compounds will obviously be quite difficult because of the time it takes to get a quantitative signal.]

Peter Beckmann, who has spent the year on sabbatical from Bryn Mawr College, and I have been investigating the  $T_1$  behavior of lead nitrate in the solid state to specify its relaxation behavior. The preliminary results (using a Bruker MSL 300) are interesting. At all temperatures, all parts of the anisotropic resonance relax with the same time constant, *i.e.* there is not a noticeable anisotropy to  $T_1$ . The relaxation time varies from about 8 seconds at 298 K to about 6 seconds at 370 K, with an activation energy of about 4 kJ/mole. (This relaxation behavior clearly allows efficient signal averaging in a reasonable time to obtain high-quality spectra.) We are currently investigating the field dependence to determine the contributions from chemical-shift anisotropy. It might be interesting to speculate what other mechanisms may influence  $T_1$  in lead nitrate that are not active in other materials, but it is far too early to discuss them here.

Yours truly,

*Cecil*

Cecil Dybowski  
Professor



## **The NMR Newsletter - Book Reviews**

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

### **"NMR Data Processing"**

by

**Jeffrey C. Hoch and Alan S. Stern**

Wiley - Liss (John Wiley & Sons, Inc.), New York, 1996; ISBN 0-471-03900-4;  
\$67.50 (hardcover); available through John Wiley & Sons, Inc. (<http://www.wiley.com>)

Data processing in NMR is an essential part in the process of extracting relevant information from the time domain function – considering now the vastly dominant area of pulsed-FT NMR as pioneered by Richard Ernst. Most users don't have to bother with details of this process, especially not with the particular algorithms and their implementation in software. As a result, however, data processing has become a "black box" to many, and automated routines have taken over in most commercial software packages. This practice makes the user's life more convenient, no question, but many times at the price of less than optimal information enhancement and quality of presentation. Hoch and Stern's book is one of the rare, highly professional publications focusing on data processing in high resolution (FT) NMR.

This book consists of a Preface, seven chapters on 186 pages, followed by three pages of thoroughly filtered references and six pages of index. The Preface is a clear assessment of the scope of the book, *viz.*, not "to achieve a comprehensive treatment of the subject", but "to provide an exposition of some fundamental principles and a set of tools to apply those fundamentals", and also to facilitate new developments.

The first chapter presents a brief historical summary of FT NMR and related data processing, then introduces some basic definitions, such as spectrum, resolution, sensitivity, noise, FID, and the basic relation between time and frequency domain information. Chapter 2 is a compressed, yet exhaustive summary of fundamentals of the discrete Fourier transformation (DFT). DFT of some special functions (delta, step, exponential and gaussian functions) closes this chapter, which leads to the next subject; application to NMR (Chapter 3).

This chapter is perhaps closest to the interests of most users who do routine applications. It pays considerable attention to apodization, data acquisition schemes, discusses oversampling, and phase correction. The authors take a close look at various artifacts, such as quad-images, zero-spike, baseline curvature, unwanted (solvent) signal, and some ways to avoid/remove them by data processing. Multidimensional data processing and few special characteristics of such data constitute an important part of this chapter.

In Chapter 4 we find an excellent summary of various linear prediction methods, their thorough and comparative analysis, as well as practical considerations on their use. The following chapter discusses maximum entropy (MaxEnt) reconstruction, as an alternative to DFT with example applications both in 1D and nD. Prospects and limitations of nonlinear sampling, which requires MaxEnt reconstruction, and which can reduce the overall time needed for acquisition of a multidimensional experiment dramatically, are also presented here.

*continued*

It was a really good idea to insert a chapter about emerging methods, even the case that it is not clear at this time which of these will become widely used in future software implementations. The methods introduced here are: iterated soft thresholding, smoothing by wavelets, Bayesian techniques, and multi-taper spectrum analysis. The last chapter in the book (a "light dessert"...) takes a brief look at visualization, quantification, and error analysis.

If I want to characterize this book with one word, I would say it is elegant. Its style is highly professional and yet entertaining, and although most methods are described with the help of plenty of mathematical formulas, readers with less interest in those will also find their way in understanding the message. The references are well selected, and there is a short "read further" summary at the end of each chapter. I can strongly recommend this book to all who want to peek in the "black box" of data processing, either with the purpose of software implementation or just to understand more about this essential toolkit.

**István Pelczer**

Department of Chemistry  
Princeton University  
Princeton, NJ 08544

ipelczer@princeton.edu

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### **The NMR Newsletter: Notice re E-mail**

The *Law of Unintended Consequences* strikes again! One unsought result of our recent changing from one ISP to another has been a thorough messing up of our ability to receive and send e-mail. This has been inflicted on us since about August 20. We think that the problem has been solved, but I wouldn't bet more than 17¢ that this will prove to be a permanent solution.

Allow us to suggest that any recent failing attempts to send e-mail to us or receive e-mail from us be repeated, or try a phone call (650-493-5971) or fax (650-493-1348). Our e-mail address remains **shapiro@nmrnewsletter.com**.

**Barry and Lee Shapiro**  
29 August 1998.

**Address all Newsletter  
correspondence to:**

Dr. B. L. Shapiro  
The NMR Newsletter  
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Palo Alto, CA 94303.  
650-493-5971\* - Please call  
only between 8:00 am and  
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**Deadline Dates**

No. 481 (Oct.) 25 Sept. 1998  
No. 482 (Nov.) 23 Oct. 1998  
No. 483 (Dec.) 27 Nov. 1998  
No. 484 (Jan.) 24 Dec. 1998  
No. 485 (Feb.) 22 Jan. 1999

\* Fax: 650-493-1348, at any hour. Do not use fax for technical contributions to the Newsletter, for the received fax quality is very inadequate.

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**Forthcoming NMR Meetings**, continued from page 1:

Spin Choreography - a symposium in appreciation of Ray Freeman, Cambridge, England, **April 8-11, 1999**;  
web site: <http://mchsg4.ch.man.ac.uk/mcmr/RF.html>; fax: c/o M.H.Levitt +46-8-15 2187; email: mhl@physc.su.se.

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

Additional listings of meetings, etc., are invited.



# How To Run JEOL's Eclipse<sup>+</sup> Spectrometer



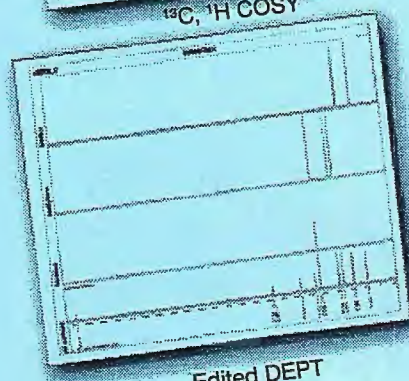
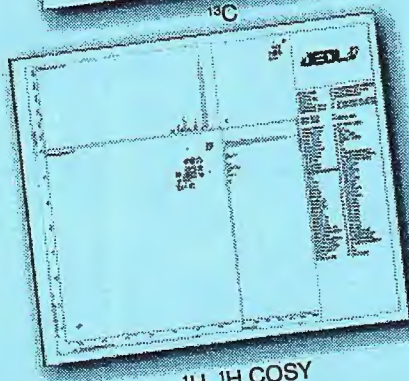
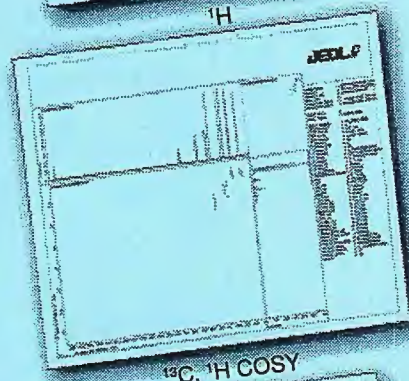
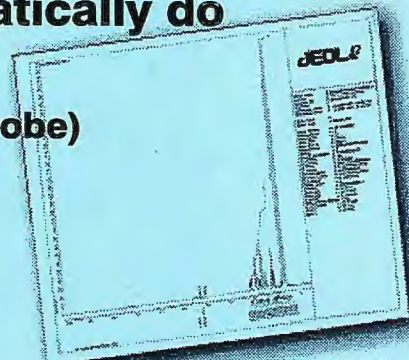
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