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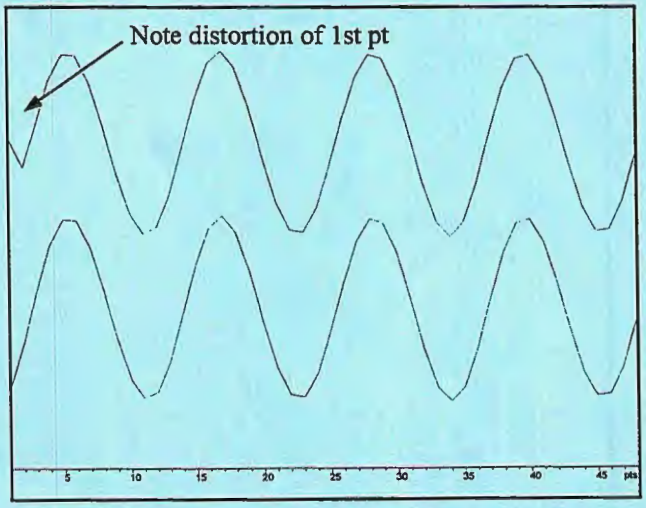
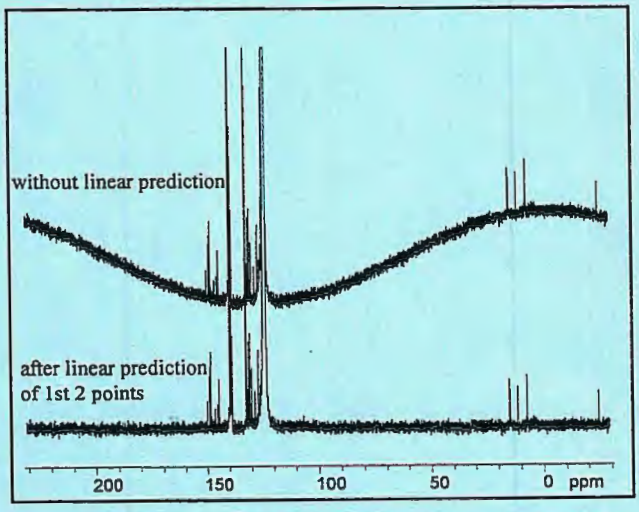


The first 48 points of a ^{31}P FID. Unprocessed (top) and after linear prediction to correct first 2 points.



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FORTHCOMING NMR MEETINGS

37th ENC (Experimental NMR Conference) "Farewell to Asilomar", Asilomar Conference Center, Pacific Grove, CA, **March 17 - 22, 1996**; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87501; (505) 989-4573; Fax: (505) 989-1073. See Newsletter 448, 23.

Society of Magnetic Resonance, Fourth Scientific Meeting and Exhibition, New York, NY, **April 27 - May 3, 1996**; Contact: SMR Office, 2118 Milvia St., Suite 201, Berkeley, CA 94704; (510) 841-1899; Fax: (541) 841-2340. E-mail: info@smr.org . Future meetings: 1997, April 12-18, Vancouver, BC, Canada; 1998, April 18-24, Sydney, Australia; 1999, Philadelphia, PA; 2000, Denver, CO.

NMR Symposium at the 38th Rocky Mountain Conference on Analytical Chemistry, Denver, Colorado, **July 22-25, 1996**; Contact: Dr. Joel R. Garbow, Monsanto Company, 700 Chesterfield Parkway North, St. Louis, MO 63198; (314) 537-6004; Fax: (314) 537-6806; e-mail: jrgarb@snc.monsanto.com; See Newsletter 445, 48.

XVIIth International Conference on Magnetic Resonance in Biological Systems, Keystone, Colorado, **August 18 - 23, 1996**; Contact: ICMRBS, 1201 Don Diego Avenue, Santa Fe, NM 87501; (505) 989-4735; Fax: (505) 989-1073. See Newsletter 448, 36

38th ENC (Experimental NMR Conference), Orlando, FL, **March 23 - 27, 1997**; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87501; (505) 989-4573; Fax: (505) 989-1073.

Additional listings of meetings, etc., are invited.

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December 13, 1995
(received 12/20/95)

Dr. B.L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
PALO ALTO, California
U.S.A. 94393

Re: Gradient Instability Revisited

Dear Barry;

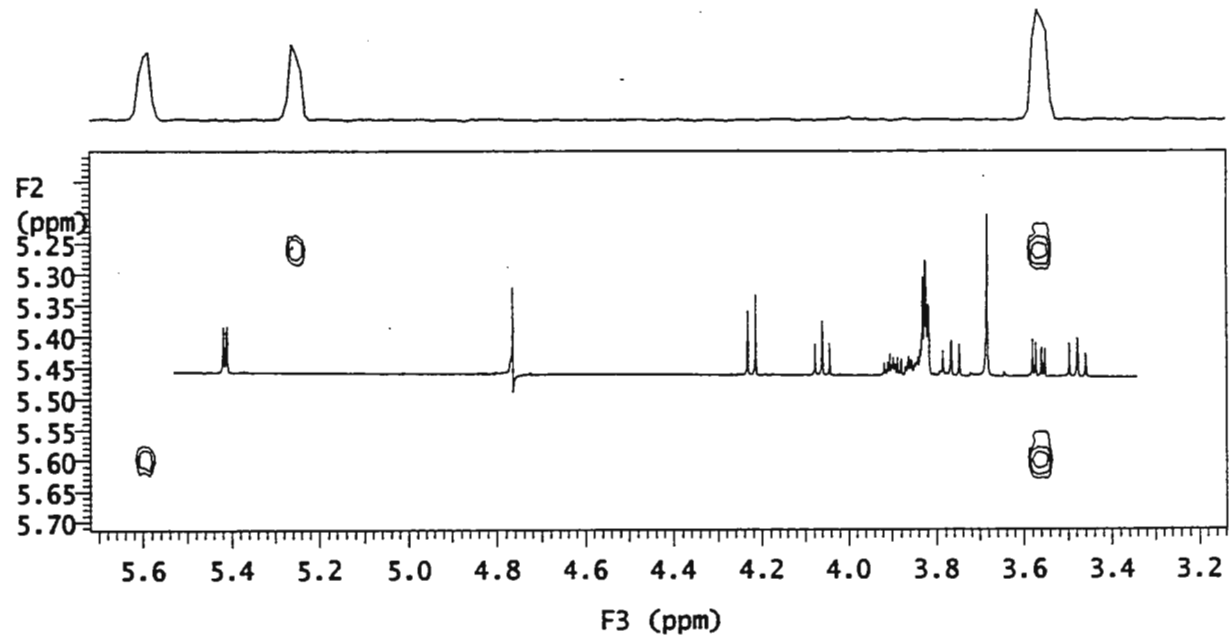
Thanks for your beautiful but most dreaded of all ultimatum letter. — In February of this year I reported on how to detect gradient instability. The source of the instability was traced to very slow sample rotation. With the source of the instability removed, the grep-hmqc-cosy experiment reported by Ralph and Boban (1) was set up on our Unity 500 Spectrometer and the results from sucrose in D_2O are shown below. A data matrix of 512x128x128 was collected defining sweep widths of 1300 (F3), 1300 (F2) and 9000 (F1, for ^{13}C), respectively. A one second relaxation delay was used with one acquisition per t1, t2 incrementation. Shown in the Figure is the contour plot of the F2-F3 plane at the G-1 ^{13}C resonance frequency (F1 slice at about 93 ppm) which shows the direct ^1H response at ~5.40 ppm split both in F2 and F3 by directly bonded proton coupling and the G-1, G-2 proton connectivity at ~3.56. The inset shows the normal ^1H spectrum.

Sincerely,

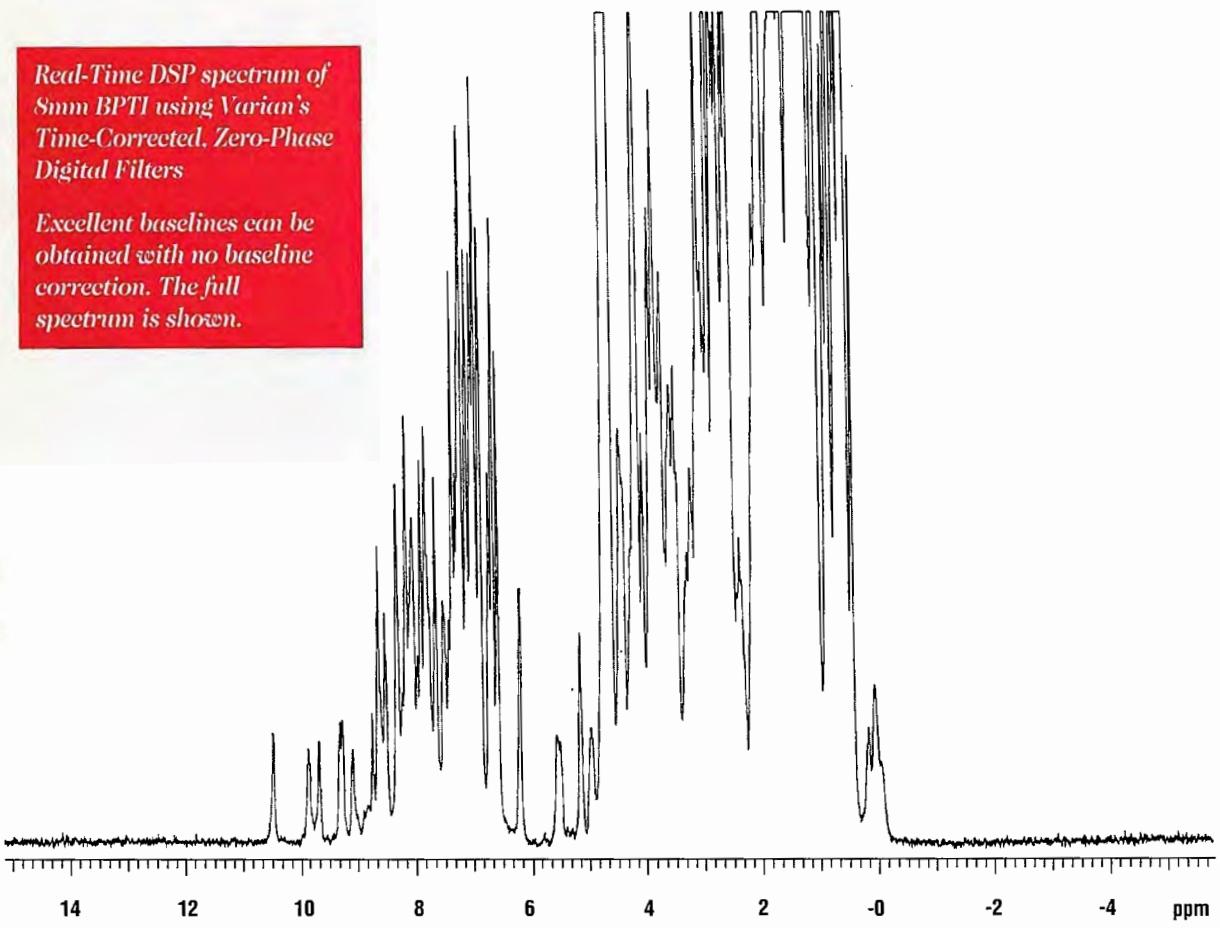
Tom

Tom Nakashima

(1) R.E. Hurd and B.K. John, *J. Magn. Reson.*, **92**, 658 (1991).
TTN:lf



The Last Word in DSP From the First Name in NMR



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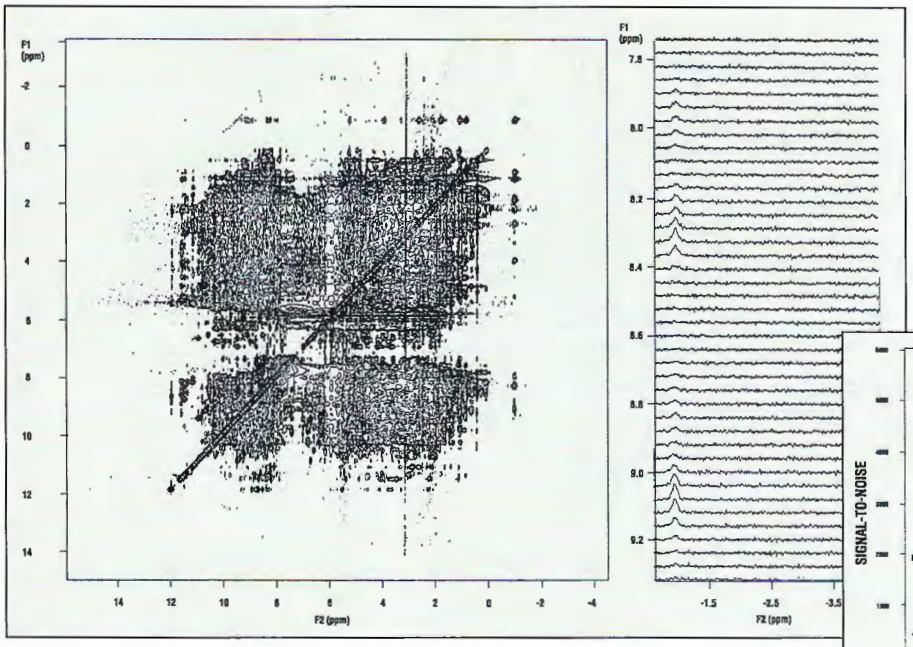
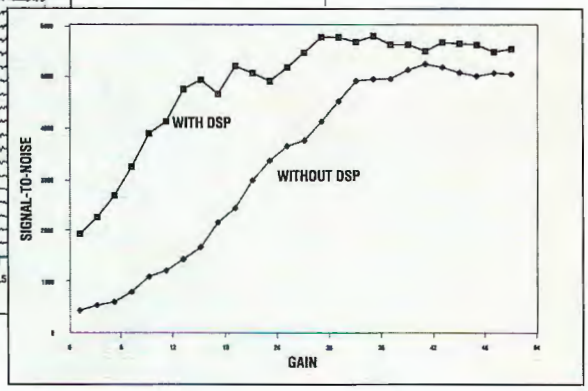


2D NOESY of 10mm lysozyme using DSP with absolutely no baseline correction or linear prediction. The expanded stacked plot on the right shows some of the weakest cross-peaks with no hint of "wandering baseline".

Plot of S/N vs receiver gain with and without DSP, showing the large improvements possible with Varian's DSP.



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Dr B.L.SHAPIRO
NMR Newsletter
996 Elsinore Court
Palo Alto, CA 94303

AN UNUSUAL LONG-RANGE DEUTERIUM ISOTOPE EFFECT ON ^{1}H CHEMICAL SHIFT

Dear Barry,

we have recently studied the keto-enol tautomerism of the dihydroxyperylenequinone sistem of a number of natural compounds[1]. As the equilibrium shown below is fast, the populations of each tautomer were obtained from the value of the coupling constants between the proton of the hydrogen-bonded OH groups and the adjacent carbon atoms, i.e. $J(C_3,OH)$ and $J(C_4,OH)$ (see Figure 1).

The parent compound **1** is planar, whereas the natural substances studied (**2** and **3** for example) assume a helical shape, owing to the steric strain of the substituents on the polycyclic ring.

One of the most important factors governing this tautomeric equilibrium is the strength of the intramolecular phenol-quinone hydrogen bonds, which is related to the distortion from planarity. Thus the strength of the hydrogen bond was evaluated from the proton shift of the OH groups and the primary deuterium isotope effect. δ_{OH} and $\Delta\delta(^1H,^2H)$ are linearly correlated, while the positive sign found for the latter is an indication[2] of a double-minimum in the hydrogen bond potential.

Although the deviation from planarity is significant for all the natural substances studied (**2** and **3** can be thermally transformed into atropoisomers with opposite helicity), the intramolecular hydrogen bonds are in general strong. δ_{OH} range from 14.8 to 16.2 ppm and $\Delta\delta(^1H,^2H)$ from 0.300 to 0.500 ppm.

In the case of tautomeric systems, secondary deuterium isotope effects on ^{13}C shift have also been studied[3,4].

We performed deuteration experiments at the hydroxy groups and observed extensive effects on the hydrogen and carbon atoms of the whole perylenequinone system. A surprisingly large effect (+0.025 and +0.055 ppm for **2** and **3** respectively), over 11 bonds was found at the phenolic OH protons.

Similar positive isotopic effects, but smaller is magnitude, were found in naphthazarine and in other naphthoquinones and anthraquinones ($^7\Delta\delta$ = +0.009 and +0.007 ppm respectively)[8], (see Figure 2). The observation of a negative isotope effect, $^8\Delta\delta$, on the OH shift in 1,8-dihydroxyanthraquinones was explained by Hansen[3] with a steric strain associated with a lengthening of the intramolecular hydrogen bonding.

We are now studying the isotope effect on ^{13}C shifts and looking for a possible correlation with the hydrogen bond strength and the deviation from planarity in our compounds.

A ⇌ B

Fig.1 Principal tautomers of dihydroxyanthraquinone **1**. Other tautomers can be considered, but they are much less stable.

	2	**3**	
$^2J(C_3,OH)$	≤ 0.3	2.7	Hz
$^2J(C_4,OH)$	5.2	3.2	
A%	100%	50%	

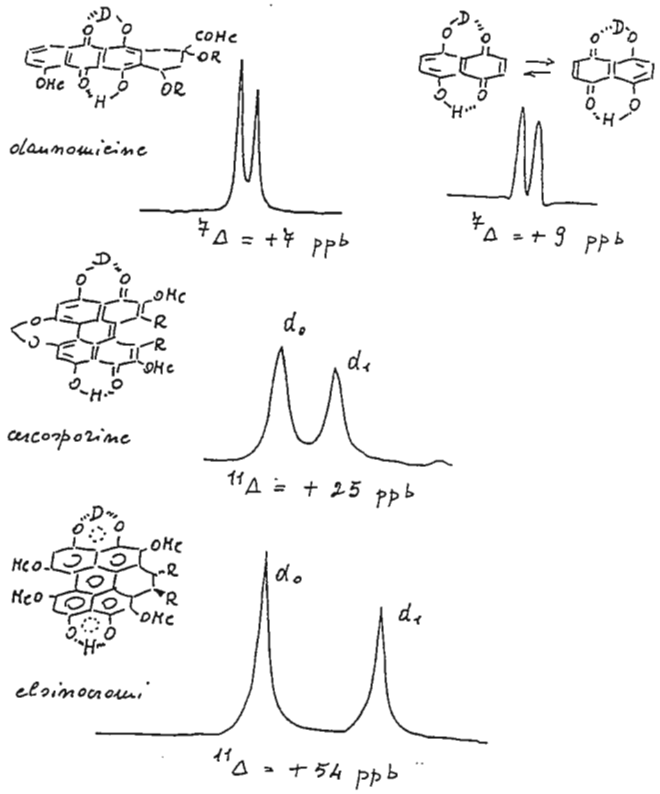

Fig.2 Long range isotope effect at the phenolic OH protons.

With sincere best wishes,

R. Mondelli

L. Scaglioni

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   J. Chem. Soc. Perkin Trans., **2**, 1447 (1993)

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4. C. Engdahl, A. Gogoll, U. Edlund
   Magnetic Resonance in Chemistry, **29**, 54 (1991)

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

December 7, 1995

Dear Barry:

How good are J couplings?

Organic chemists have long been concerned with the question how quantitative the relation between three-bond J couplings and the dihedral angle really is. The J coupling presumably can be influenced by a large number of factors other than the dihedral angle. For example, it is well established that the electronegativity of substituents has a significant effect. Other variables, such as hydrogen bonding, bond strain, electric field gradients and solvent effects have also been implicated. Nevertheless, Altona and co-workers (1) showed for a large series of model compounds that ^{1}H-^{1}H J couplings can be predicted with an rms of 0.36 Hz by an extended Karplus relation which takes electronegativity effects into account.

For J couplings related to the backbone angle ϕ in proteins, substituent effects are the same for all residues (excluding glycine), and the standard Karplus relation is anticipated to be sufficient. Pardi et al. (2) were able to fit measured J couplings in BPTI to a Karplus curve to within about 0.8 Hz. Bartik et al. (3) convincingly demonstrated that uncertainty in the X-ray ϕ angles used for predicting the $J(H^{N}\text{-}H^{\alpha})$ couplings has a significant effect on the agreement between measured J couplings and those predicted by the X-ray structure ϕ angles, using Pardi's Karplus curve. Rms agreement between measured J couplings and those predicted by the X-ray structure ϕ angles improved from 1.6 Hz for a 2.5 Å structure of lysozyme to 0.8 Hz for a structure solved at 1.5 Å resolution.

Using some ultra-reproducible method (4) for measuring $J(H^{N}H^{\alpha})$, we found that the agreement between measured values and those predicted by the 1.8-Å X-ray structure of ubiquitin is 0.54 Hz. The question then was to what extent is this value of 0.54 Hz determined by uncertainties in the X-ray, and how much it was influenced by any of the other factors, particularly thermal ϕ angle fluctuations and hydrogen bonding of the backbone amide proton.

Figure 1 plots the difference between the $J(H^{N}H^{\alpha})$ predicted on the basis of the X-ray ϕ angle and the values actually measured as a function of ϕ. Clearly, for ϕ angles near -120°, where the ϕ-angle dependence of the Karplus curve is near zero, the agreement is much better than for ϕ angles in the region where the derivative of the Karplus curve is large. Brüschweiler and Case have pointed out that if the magnitudes of the random ϕ angle fluctuations are different for different residues, this will result in an error in the J value predicted from the Karplus curve which is largest in the region where the second derivative is at a maximum, i.e., near ϕ = -120°. The fact that our J values fit best to the curve near ϕ = -120° and worst near ϕ = -75°, where the second derivative is zero, indicates that the thermal ϕ angle fluctuations are quite uniform in human ubiquitin.

An explanation compatible with Figure 1 is that the uncertainty in the ϕ angle is responsible for the difference between measured and predicted J values as this difference would increase with the derivative of the Karplus curve. More convincing evidence that this really is the case is obtained by comparing the difference in predicted and measured J values for $^{3}J(H^{N}H^{\alpha})$ and $^{3}J(H^{N}C^{\beta})$. For -100° < ϕ < -80°, the two Karplus curves have opposite and nearly constant slopes. If the true ϕ angle for a given residue were slightly larger than that of the X-ray, it would result in a measured $^{3}J(H^{N}H^{\alpha})$ value smaller than predicted, and larger than predicted for $^{3}J(H^{N}C^{\beta})$. Indeed, figure 2 indicates that there is a strong correlation between these deviations. The same type of

correlation is observed when comparing $^3J(H^NH^\alpha)_{meas} - {}^3J(H^NH^\alpha)_{pred}$ with the deviations between measured and predicted $^3J(H^NC')$ and $^3J(H^\alpha C')$ couplings. Altogether, our data suggest that one may be able to determine the time-average ϕ angle in small proteins with an uncertainty of as little as $\pm 2^\circ$, better than what can be obtained with even the very best X-ray studies. This allows us to study very subtle structural changes in proteins that result from, for example, mutations, intermolecular interactions or a range of other sources. A rather detailed account of this work will, hopefully, appear in JACS in the foreseeable future.

Kindest regards,

Andy Wang Ad Bax

(1) Altona, C.; Franke, R.; de Haan, R.; Ippel, J. H.; Daalmans, G. J.; Hoekzema, W. A. J. A.; van Wijk, J. *Magn. Reson. Chem.* **1994**, *32*, 670-678.
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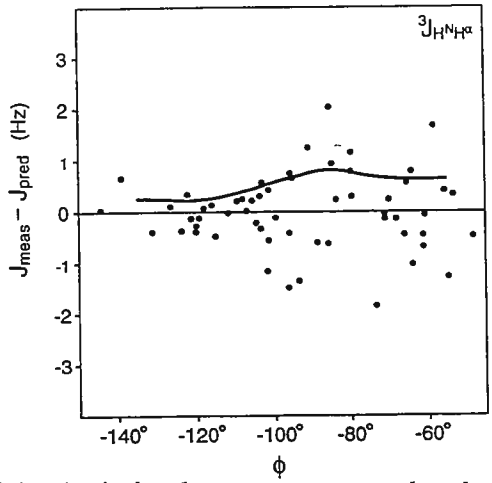

Figure 1. Plot of the deviation between measured and predicted J values for $^3J_{H^NH^\alpha}$.

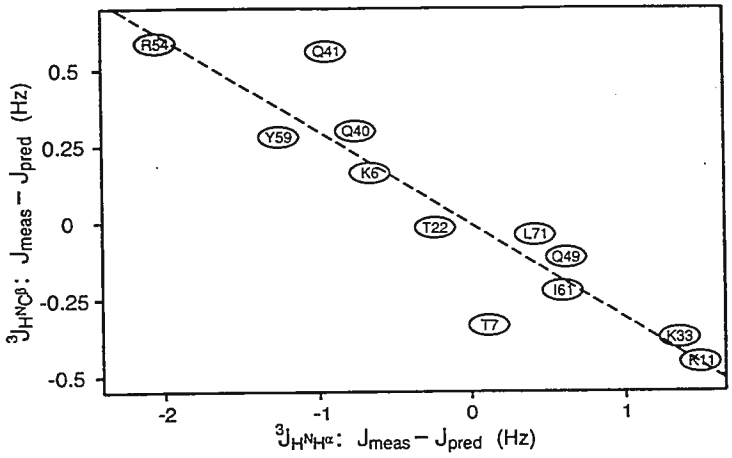

Figure 2. Correlation plot of $\delta_J = J_{meas} - J_{pred}$, derived using ϕ_{XRAY} angles, between $^3J_{H^NH^\alpha}$ and $^3J_{H^NC\beta}$ for all residues in the range $-100^\circ \leq \phi_{XRAY} \leq -80^\circ$.

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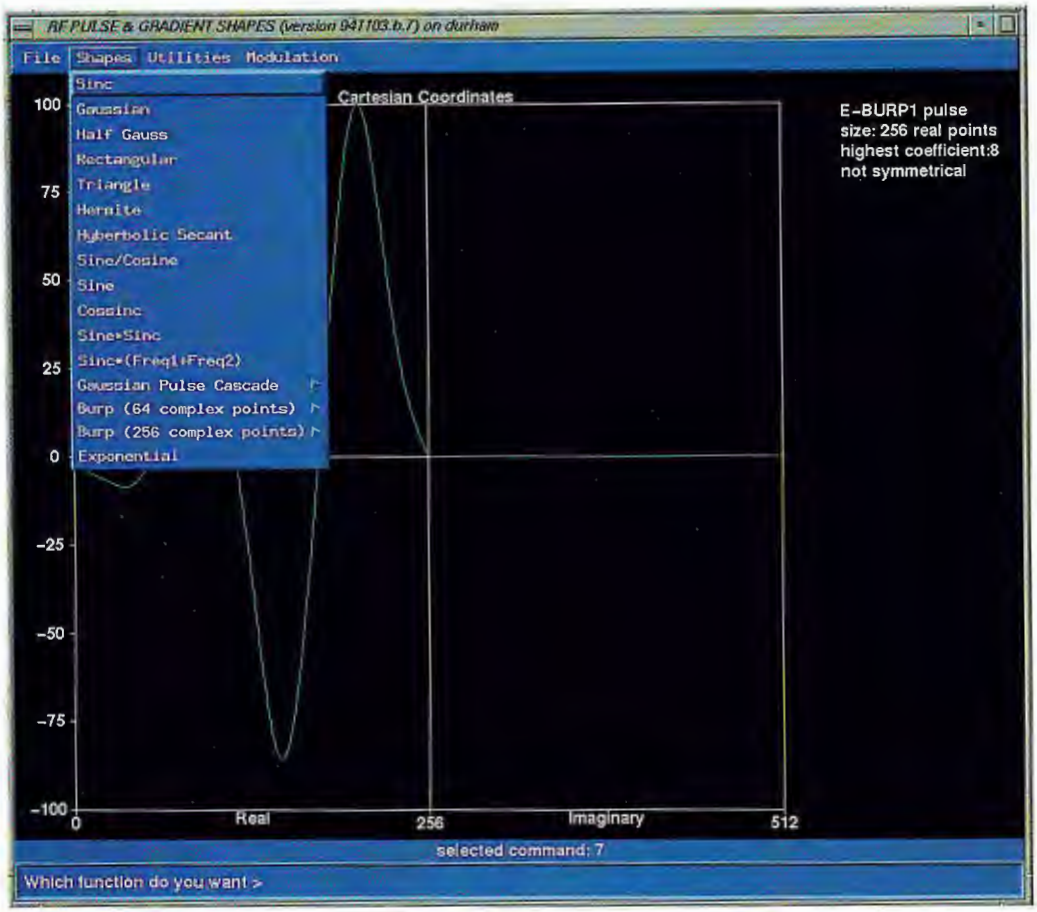

Figure 1: Select a shape and specify the parameters

Bruker's new NMR software package, *XWIN-NMR*™, offers a windows-based utility for creating RF pulse shapes, called *xShape*.

- Enter *xShape* and select a shape from a list of predefined options.
- The program prompts you to enter appropriate parameters to completely define the shape.
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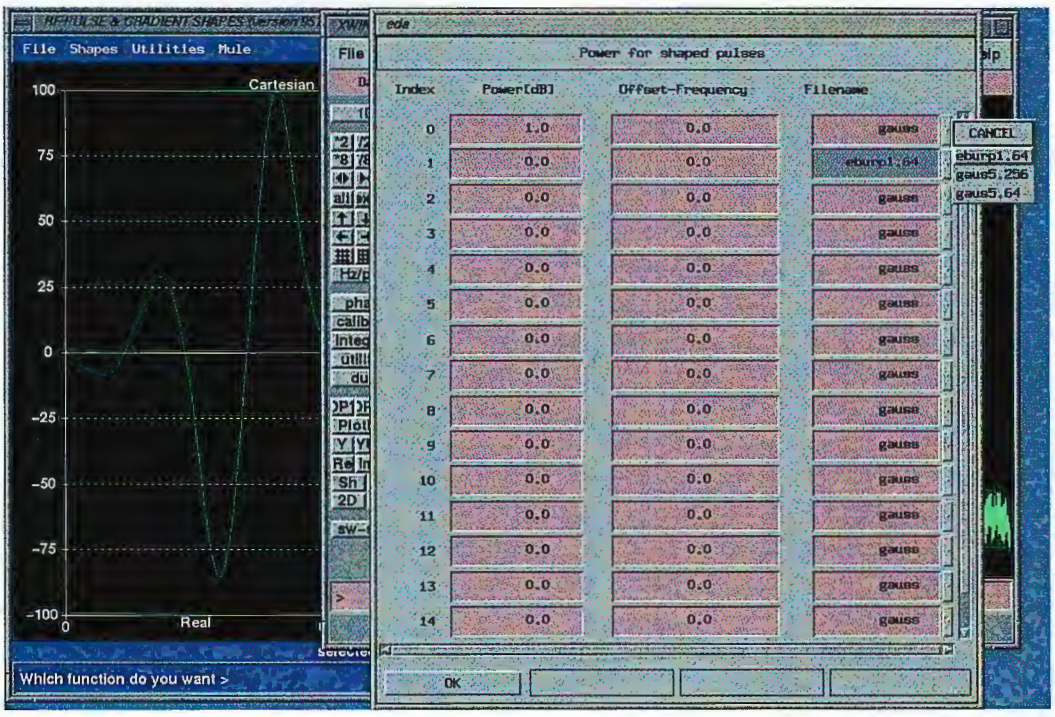

Figure 2: Enter the optimized shape into pulse sequence

The *xShape* routine can also read ASCII text files for shapes created in other software programs, and save them in the *XWIN-NMR*^{TM} format. This makes any pulse shape available for pulse sequences. Pulse shapes are only limited by your imagination, not by the software!

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The NMR Newsletter
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RE: Fractional deuteration for studying protein/ligand complexes

Dear Barry:

We have recently determined the three-dimensional structure of the phosphotyrosine binding (PTB) domain of the Shc protein (residues 17-207) complexed with a twelve residue tyrosine-phosphorylated peptide derived from the nerve growth factor receptor (TrkA).[1] The structure of this newly discovered domain consists of a β-sandwich and three α-helices and differs from the well-characterized SH2 domains that also bind to tyrosine-phosphorylated peptides and proteins. These structural differences between the PTB and SH2 domains impart markedly different binding specificities for tyrosine-phosphorylated proteins which is critical for the selection of particular signalling pathways.

In order to determine the structure of this relatively large complex, we relied on the use of random fractional deuteration. The advantages of fractional deuteration for reducing spin diffusion and obtaining narrower signals with higher sensitivity in homonuclear NMR spectra have been described.[2] More recently, the utility of fractional deuteration for assigning the backbone resonances of proteins when combined with ^{13}C- and ^{15}N-labeling has been demonstrated.[3,4] In our studies of the PTB domain/phosphopeptide complex, we found fractional deuteration to be useful in at least three areas. Similar to the findings of others, fractional deuteration dramatically improved our ability to assign the backbone resonances of the protein. This is due to the favorable ^{1}H, ^{13}C, and ^{15}N relaxation rates caused by the partial deuterium labeling which allowed constant time spectra with higher

digital resolution to be recorded. Fig. 1a depicts a projection of a constant time HNCA spectrum of uniformly $^{15}N,^{13}C$-labeled protein that was fractionally (75%) deuterated. The sensitivity and resolution are markedly improved compared to an HNCA spectrum of the fully protonated protein (Fig. 1b). The second application of fractional deuteration was to facilitate the side chain assignments. This was accomplished using a HC(CO)NH-TOCSY experiment that correlates the side chain signals to the backbone amides of the adjacent residue. Much better sensitivity was obtained using the fractionally deuterated versus the fully protonated sample. Finally, many more intermolecular NOEs used in defining the structure of the complex were detected in ^{13}C-edited (F_1), ^{13}C-,^{15}N-filtered (F_3) 3D NOE experiments employing the fractionally deuterated protein, especially intermolecular NOEs involving β-CH_2 protons which rapidly relax in proteins of this size (manuscript in preparation).

The fractionally deuterated and ^{13}C-/^{15}N-labeled protein can be easily prepared by growing bacteria that overexpress the protein on a medium of ^{13}C-labeled glucose, ^{15}N-ammonium chloride, and 75% D_2O. Due to the ease of sample preparation and great utility of fractional deuteration, we are currently using this approach in all of our NMR studies of large protein and protein/ligand complexes.

1. Zhou et al., Nature, 378, 584-592 (1995).
2. LeMaster and Richards, Biochemistry, 27, 142-150 (1988).
3. Grzesiek et al., J. Am. Chem. Soc., 115, 4369-4370 (1993).
4. Yamazaki et al., J. Am. Chem. Soc., 116, 11655-11666 (1994).

Sincerely,

Michael Sattler Ed Olejniczak Ming-Ming Zhou

Andrew Petros John Harlan Steve Fesik

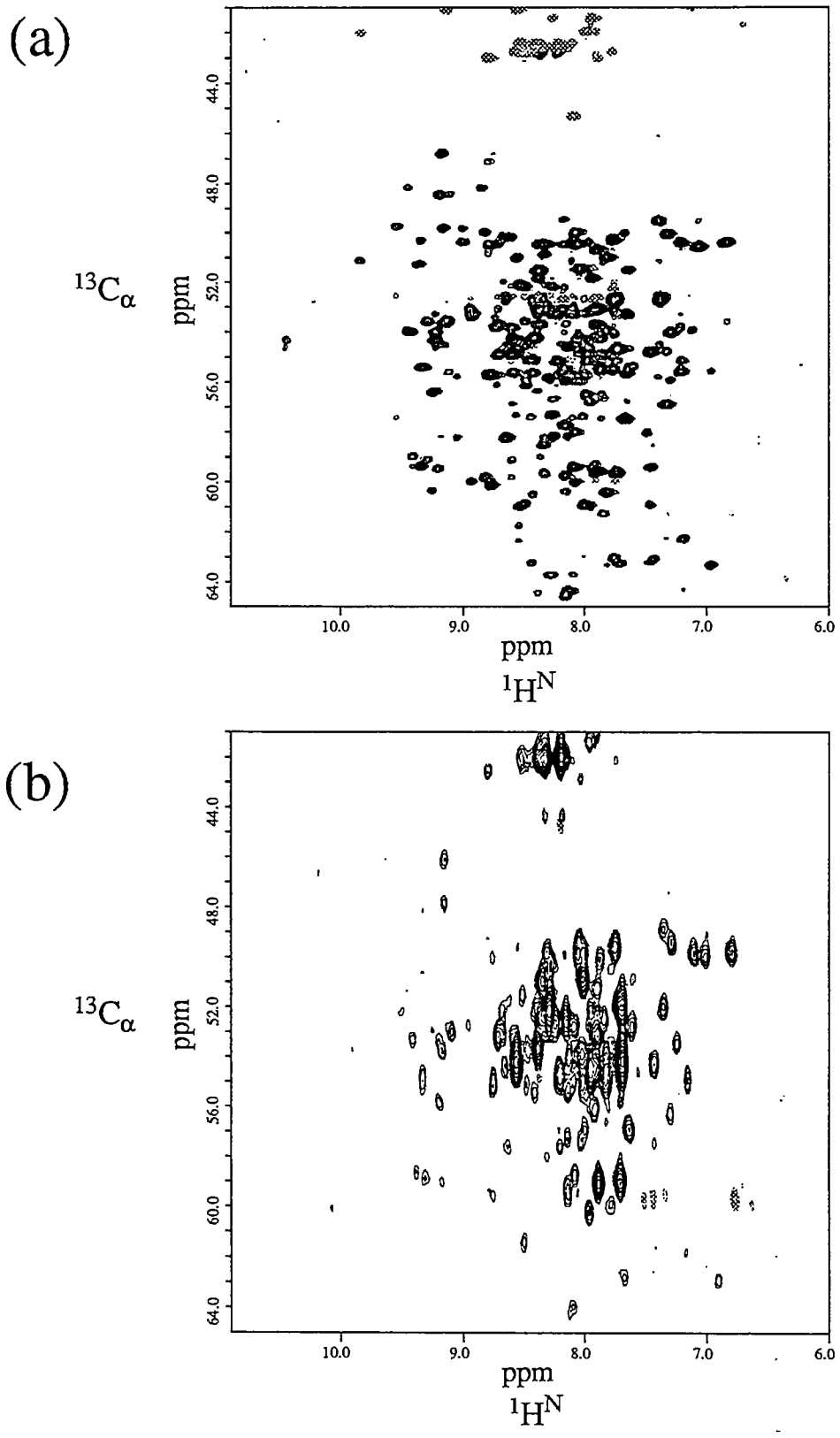

Fig. 1. Projections of two 3D HNCA spectra recorded on the Shc PTB domain complexed with a TrkA phosphopeptide in which the protein was uniformly ^{13}C- and ^{15}N- labeled and (a) fractionally (75%) deuterated or (b) fully protonated.

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Prof. Dr. Bernhard L. Shapiro
Editor TAMU NMR Newsletter
966 Elsinore Court

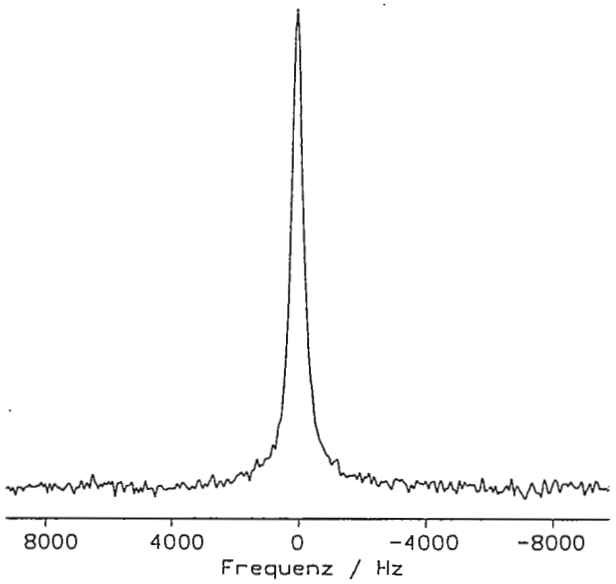
Palo Alto
California 94303, U.S.A

Tübingen, den 30.11.1995
Lu/Al

Large Volume Spectroscopy with Heteronuclei

Dear Barry,

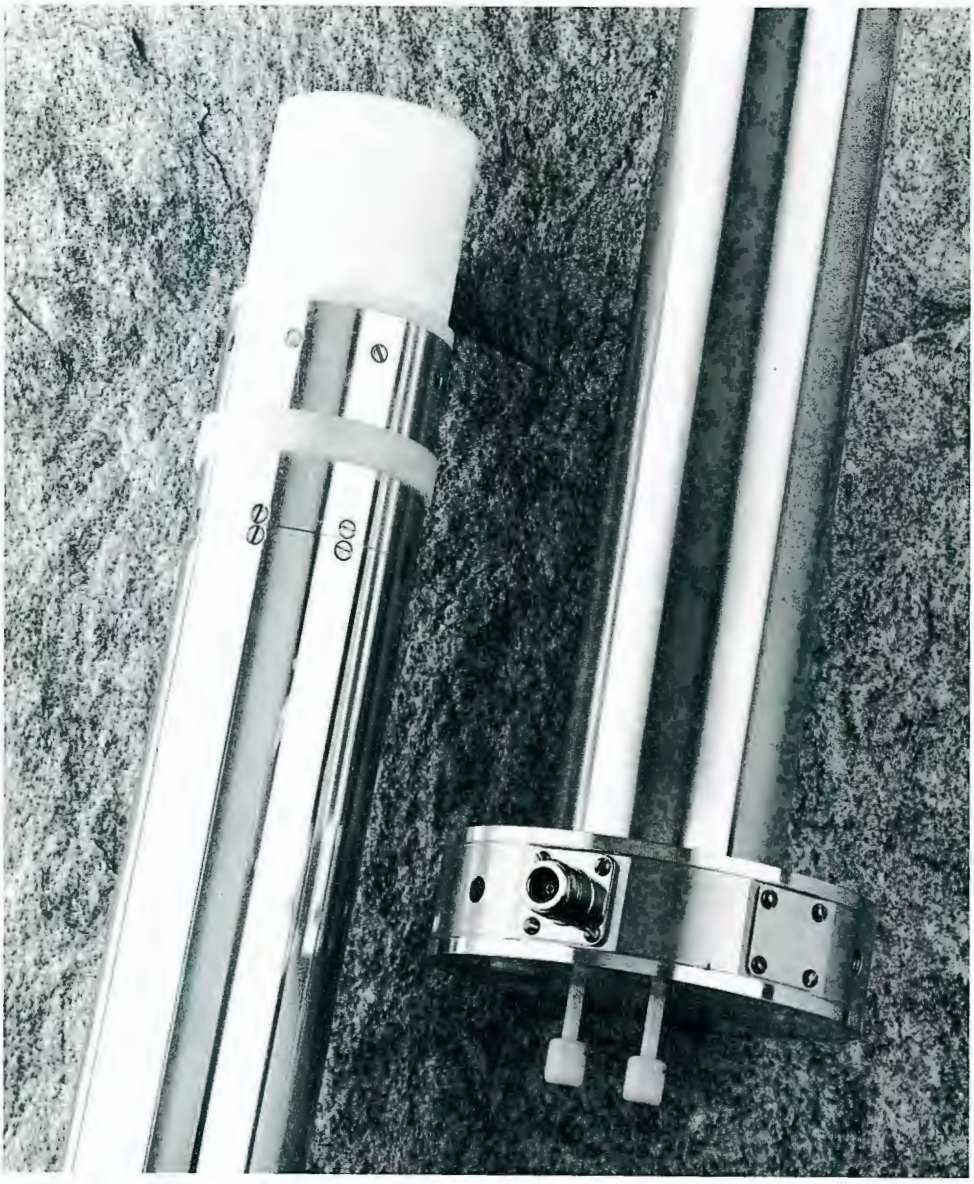
here I am again!
In the last years we worked mainly in the area of methology and application of human in vivo NMR imaging and spectroscopy. We used 1.5 T whole body imagers and found that homogeneity and stability are high enough also to perform large volume spectroscopy with heteronuclei, e.g. ^{11}B , ^{23}Na, ^{27}Al, ^{51}V, etc.
So we were able to detect in a 500 ml sample the ^{51}V NMR signal of a 1 micromolal aqueous solution of $NaVO_3$ within 2 hours with a S/N = 20. Another example is the ^{129}Xe resonance in pure xenon gas at atmospheric pressure showing a longitudinal relaxation time of nearly 4 hours. But also short T_1 can be measured with imagers using some tricks: The signal given below is a ^{81}Br NMR signal from an inversion-recovery measurement of a 5 millimolal aqueous solution of LiBr in a 500 ml sphere (Scans: 512, repetition time: 50 ms, inversion time: 4.8 ms). The $T_1 = 857 \times 10^{-6}$ s.



Merry Christmas and a Happy New Year
Sincerely yours

Otto

Wideline Stationary Probe



The wideline probes from Chemagnetics provide the high performance required to achieve high quality spectroscopic data.

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Recent advances in plug-in design have reduced the level of ringing which can cause spectral artifacts to inhibit spectral interpretation.

The probe takes advantage of the Chemagnetics variable temperature system, allowing easy sample loading without affecting the variable temperature hardware.

Features	Benefits
Full Multinuclear Range	The highband wideline probe provides observation of either proton or fluorine spectra and the low band probe provides observation of frequencies as low as 20 MHz.
Background minimized	The high band probe can be made to reduce either proton or fluorine background signals.
Easy to use plug-ins	5 mm and 10 mm plug-ins are provided for specified nuclei to cover almost all experimental samples.
Efficient RF design	Allows minimal delay times to be used to obtain the highest quality spectra.
Exclusive VT Stack Design	Permits full temperature range to be exploited without compromise of the probe performance.

Typical Specifications

Probe Outer Diameter	70 mm
Sample Diameter	5.0 or 10.0 mm
Sample Volume (5.0 mm)	0.1 mL
Sample Volume (10.0 mm)	0.5 mL
"X" Channel Frequency Range	20 MHz-^{31}P
"H" Channel Frequency Range	^{1}H-^{19}F
Temperature Range	−150°C to +200°C
1H/19F 90° Pulse Width (5.0 mm)	≥2.0 µs
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December 7, 1995 (received 12/16/95)

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

The American "Research Bubble"

I was very interested in Richard Ernst's commentary in the November issue of **The NMR Newsletter** and your invitation to others to contribute likewise. Instead of a technical contribution, here are some of my ruminations that are tangentially related to Ernst's letter. These comments relate to science, basic research, and technology in the United States. To preface, I believe that a not inconsiderable part of the motivation for ***basic*** research is curiosity about how the universe operates.

In recent years, the media, news and scientific trade magazines, and newspapers featured various 'authorities' who blamed the state of the U.S. economy, the lack of American competitiveness, U.S. budget deficit, earlier poor management practices, budget overruns etc., for such events as the SSC scenario, the continuing downsizing and elimination of basic research in industry, the cutbacks of basic research in government laboratories, etc. I believe that the makers of such statements are perspectively challenged. We need to look beyond such facile, fashionable rationalizations and examine a fundamental American characteristic, the general public attitude towards scientific research in the U. S.

The U.S. public is anti-intellectual and, at best, topically tolerant of basic science and basic research. In the 19th century, there was much public interest in science, as expressed in the interest in the science lectures in the Chatauqua Lectures. But this interest was in science as a minor ***form of entertainment***; such "gee whiz" lectures with magical demonstrations struck the public's imagination, just as some modern space engineering exploits did in recent decades. Many things, that the public thinks is science, catch the public's imagination even while there is a deep-seated antagonism to science. Recall all the movies and TV and radio programs that depict the practitioners of basic research as "mad scientists" even while people enjoy the many things that came about because of basic research. This dichotomy reflects the traditional eagerness of the U.S. public to use new technology. New technology has traditionally been readily available to, and embraced by, the U.S. public. For example, within a couple of years after the first telephone message to Dr. Watson, local telephone systems were put into operation in small-town areas in Illinois. Also, recall Thomas Edison and the eager acceptance of his practical inventions. Characteristics of the public attitude and social/political/economic conditions in the U.S. led to rapid development of technology from scientific developments that were mainly made elsewhere. This technology was made readily available and affordable to the general

public. This set of conditions has been in marked contrast to that in other Western cultures. In contrast to widespread interest in technology, only a few people were deeply interested in science and funded the great scientific projects, such as the Mt. Palomar telescope. This represents the climate in America. For a while, however, the situation was changed.

For several decades, we "enjoyed" a research bubble. The unintentional blower of this bubble was the late German dictator Adolph Hitler. His actions resulted in many great scientists leaving continental Europe. Many of them came to the U.S. and worked to defeat him; without them, the Manhattan Project would not have been undertaken. The success of that project created in the U.S. public mind a sense that science was actually *useful* for something, because it contributed to national security. This feeling was not universal, because of the reaction, in some political circles in the U.S., against the atomic bomb and the ambivalence towards continuing the development of nuclear weapons. Nevertheless, the Cold War, and especially Sputnik, did result in a great boost in research funding. Parenthetically, Sputnik happened just after I completed my Ph.D. and I could see the great increase in research funding. It became fashionable to do research. Many companies set up research whether they really needed it or not; if the CEO's lacked the insight to do so, management consultant firms were available to provide guidance. There was a great amount of blind faith that desirable (i.e., useful, profitable) results somehow would ensue from research. The Federal government created and then expanded the national laboratories. All of this led to jobs for more scientists and engineers; the colleges and universities were only too glad to oblige by expanding their science departments, using the free-flowing Federal dollars, and training ever increasing numbers of Ph.D.'s. Consequently, many went into science because of the perception of well-paying, secure jobs in government, industry, and academia.

Significantly, while the Cold War was being fought, important civilian technologies resulted from the national security-inspired research and the U.S. public gladly embraced them. For example, hand calculators were developed by Hewlett-Packard for the Apollo program. This miniaturization of electronics led to the rapid development of computer technology and some, like the PC, became socially important (incidentally, because of a bad decision by IBM management). Of course, there are the down-sides. This very same technology has made the World of 1984 possible with 'Big Brother' monitoring and controlling all of us - which was the world that we, of my generation, had hoped to avoid by fighting the Cold War in the first place.

Many people had thought that continuance of high-level basic research is irreversible, that the benefits are irrefutably self-evident. But what are the benefits that the public sees? Profits can be readily made without basic research in the U.S. And the public does not miss that of which it is ignorant. As before the research bubble, technology may continue to advance because of basic science done elsewhere in the world. Anyway, the bubble did cause several 'normal' centuries of scientific/technological advances to occur in just several decades. In those decades, science done in the U.S. was coupled to technological advances in a fairly synergistic process.

Before the bubble, those who entered science did so mainly because of a love of science; they knew that 'practicing' science was its own reward. With the end of the Cold War and the consequent perception that national security considerations are no longer relevant, the research bubble has burst and the level of basic research interest in the U.S. has returned to that of the days before Hitler. The current obsession with the "bottom line" by both industry and academia

reflects this. While the bubble dissipates, it is fashionable to eliminate basic research, whether elimination is fundamentally justified.

I had hoped that a good, sustainable level of genuine basic research could continue, and that we would not revert all the way back to 'normal.' But we must realize that the process of Federal funding inevitably applies a corruptive political/social filter to the research that does get funded. This filter includes the motivations of the decision makers, not all of whom are in the government. Much of decision making is forged by fashion, like the vagaries of the stock market. To illustrate my contention, several months ago, a young NMR scientist sent me the following e-mail message that I reproduce *verbatim*: "Just remember my prediction. Sometime shortly after the year 2000, McKinsey will be back telling the oil (and other) companies how vital research is to their long term vitality, and how important it is to keep a work force with a long-time commitment to the company business. And the sheep-like herd of highly paid managers will listen and obey. Mark my words." I hope he is right. But if he is, it is disturbing that such important decisions should be made in this way. Maybe that is the way it always was!

Sincerely,

Don

Donald E. Woessner

Continued from page 20

10. Liquid-like Molecules in Rigid Matrices and in Soft Matter.
    A. Swollen Polymers and Gels; J. P. Cohen-Addad.
    B. Fluids in and on Inorganic Materials; F. P. Fraissard.
    C. Magnetic Resonance in Food Science; B. P. Hills.

The quality of each contribution is uniformly good. Each chapter contains many references. There is a 7-page index.This is a book that deserves to become part of the science library holdings of major research institutions.

John G. Albright
Department of Chemistry
Texas Christian University

The NMR Newsletter - Book Reviews

Book Review Editor: **William B. Smith**, Texas Christian University, Fort Worth, TX 76129

" Dynamics of Solutions and Fluid Mixtures by NMR "

Edited by

Jean-Jacques Delpuech

John Wiley & Sons, Chichester, England; 1995
ISBN 0-471-95411-X. 580 pages + index. $79.95

This book gives a current description of the use of modern NMR methods for the measurement of a wide range of dynamic properties of molecules, ions, and atoms in liquids, quasi-liquids, and at liquid-solid interfaces. There are 10 chapters in which the chapters 9 and 10 are divided into 2 and 3 sections respectively each written by different contributors. The authors of each chapter give detailed discussions of theory and experimental technique pertaining to particular applications along with descriptions and discussions of recent experimental work. The bibliographies are extensive and current. Not surprisingly, there is a strong French/European connection in the choice of contributors.

The contents of the book are accurately indicated by the chapter headings:

1. Introduction: Dynamic Phenomena in NMR; J.-J. Delpuech.

2. Time scales in NMR: Relaxation Phenomena in Relation with Molecular Reorientation; D. Canet and J. B. Robert.

3. Time scales in NMR: Nuclear Site Exchange and Dynamic NMR; J.-J. Delpuech.

4. Nuclear Paramagnetic Spin Relaxation Theory. Paramagnetic Spin Probes in Homogeneous and Microheterogeneous Solutions; P. O. Westlund.

5. Quadrupolar Probes in Solution; J. Grandjean and P. Laszlo.

6. Solvent Exchange on Metal Ions: A Variable Pressure NMR Approach; U. Frey, A. E. Merbach and D. H. Powell.

7. Applications of Field Gradients in NMR; D. Canet and M. Decorps.

8. Surfactant Solutions: Aggregation Phenomena and Microheterogeneity; B. Lindman, U. Olsson and O. Söderman.

9. Polymers and Biopolymers in the Liquid state.
   A. Local Dynamics of Large Molecules: Synthetic Polymers in Solution and Melts; M. A. Krajewski-Bertrand, F. Lauprêtre and L. Monnerie.
   B. NMR and Dynamics of Biopolymers; L. Y. Lian and I. L. Barsukov.

continued on page 19

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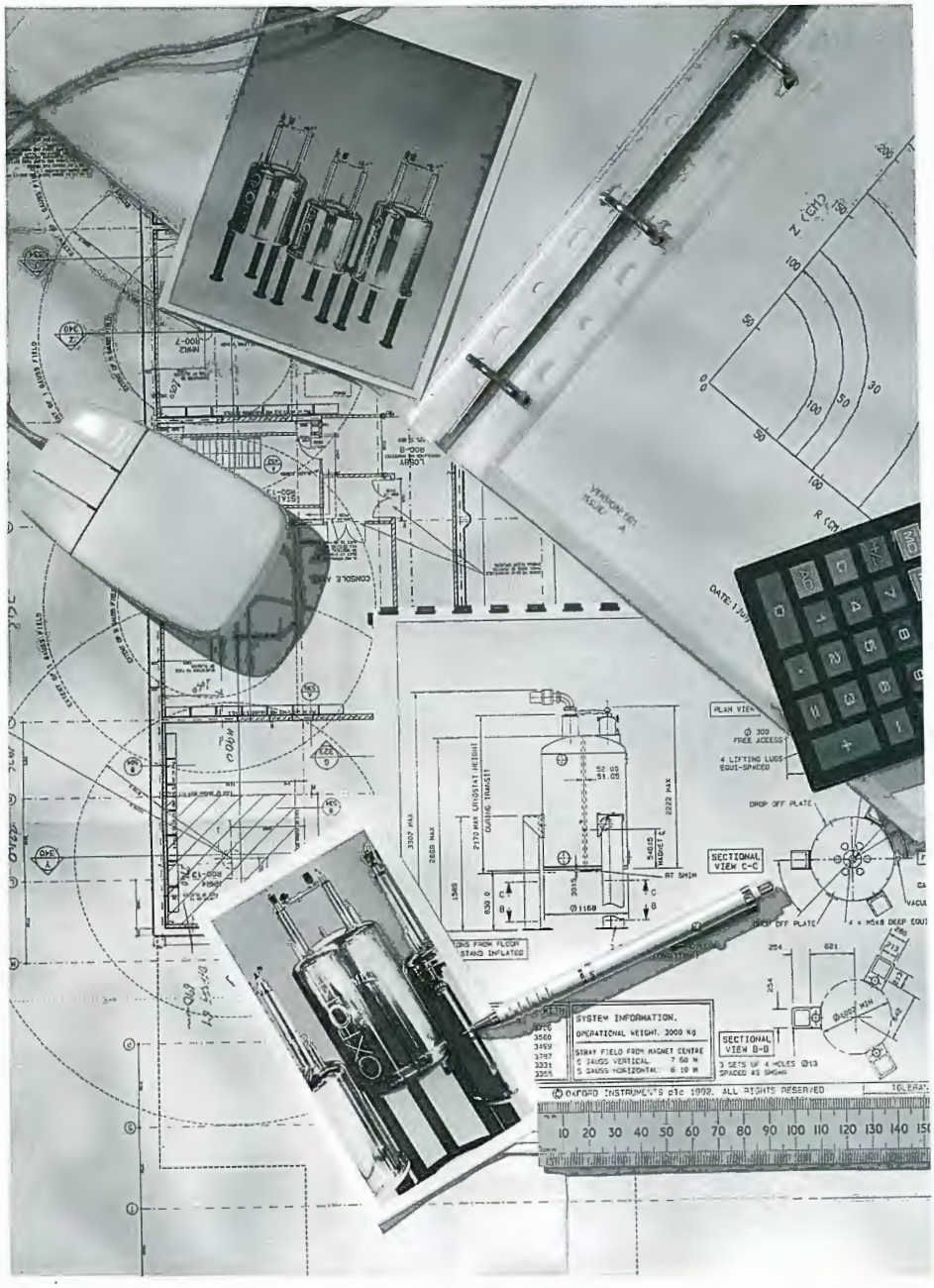

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750	51	15	60	3.8
600	51	10	120	3.4
500	51	10	150	3.2
400	54	8	365	2.8
360	54	8	365	2.8
300	54	3	365	2.8
270	54	2.7	365	2.8
200	54	2	365	2.8
100	54	1	365	2.8
500	89	15	120	3.4
400	89	10	180	2.8
360	89	10	365	2.8
300	89	3	365	2.8
270	89	2.7	365	2.8
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The 37th ENC, March 17 - 22, 1996
The Asilomar Conference Center, Pacific Grove, California

Asilomar has been the traditional location of ENC for decades, and has helped to shape the characteristic spirit of ENC, particularly the unique coexistence of academic presentations with exhibitions of instruments and products. In spite of the many attractive features of Asilomar, the 37th ENC is likely to be our last meeting at this site. Because of the ever-increasing attendance and ceaseless growth of interest of vendors, the Executive Committee has decided to move ENC to locations that are better equipped to meet the technical challenges. There will be other reminiscences, of a less sentimental nature, with an after-dinner address by Alfred Overhauser. The remainder of the 37th ENC will be marked by a strong commitment to look forward to many promising developments, new methods, novel applications and exciting technology.

Geoffrey Bodenhausen, Chair, 37th ENC

CONFERENCE LOCATION. All technical sessions, vendor hospitality suites, and exhibits will be at the Asilomar Conference Center, 800 Asilomar Boulevard, Pacific Grove, California 93950. Phone: (408) 372-8016.

Asilomar, "the refuge by the sea," is located at the tip of the Monterey Peninsula overlooking the Pacific Ocean. It occupies 105 acres of secluded forest and dunes which are preserved by the California State Park System as a nature center and historic site.

AIR TRAVEL. The San Francisco International Airport is approximately 120 miles from Asilomar and the San Jose Airport is about 65 miles. If you fly into either of these, you will need a rental car for transport to Asilomar. It is recommended that you use the Monterey airport, where shuttle van service will provide transportation to Asilomar at a cost of $12 per person. If you rent a car and are staying on-site at Asilomar, please be aware that parking is very limited. You may be required to find parking on the street.

DRIVING. If you drive from either San Francisco or San Jose, make your way to California Highway 1 and go South. After you pass the Monterey exits take the second Pacific Grove exit (Route 68 West). Travel West on Route 68 for approximately 10 minutes (watch for where Route 68 West turns left). Near the bottom of the hill, turn right on Asilomar Boulevard. The main entrance to Asilomar is at the intersection of Asilomar Blvd. and Sinex Street.

REGISTRATION. Registration is $150. Contact ENC, (505) 989-4573, to obtain a registration form.

POSTERS. Posters must be submitted on the form provided by ENC. Please call (505) 989 4573 to obtain the form. Posters with commercial content or flavor should be displayed in the vendor suites. Posters should include experimental aspects of NMR and/or novel or original applications or techniques. Poster presenters must be registered for the conference. **DEADLINE for receipt of abstracts is December 22, 1995.**

SPECIAL EVENTS.

Sunday, 6-8 pm	**St. Patty's Day Welcome, Crocker Hall.** Your wearin' o' the green will bring ya green beer 'n Irish stew. For all conference registrants. *Note: There will be no regular dinner service at Asilomar on Sunday evening.*
Thursday, 7-9 pm	**Banquet at Asilomar.** A choice of Beef Wellington or vegetarian will be accompanied by California wines. Tickets required: $25 per person. *Note: There will be no regular dinner service at Asilomar on the evening of the banquet.*
Thursday, 9-9:45 pm	**After Dinner Address: Alfred Overhauser,** "Dynamic Nuclear Polarization: A Reminiscence." *Merrill Hall.*

EMPLOYMENT CENTER. There will be bulletin boards set aside for employment notices. If you post an employment notice, do not exceed U.S. letter size or European A4 format. If you will be seeking employment, please bring at least five copies of your resumé to the conference.

FOR ADDITIONAL INFORMATION: Contact ENC, 1201 Don Diego Avenue, Santa Fe, NM 87505 (USA). Phone: (505) 989-4573. Fax: (505) 989-1073. E-mail: 70404.2407@compuserve.com

The 37th ENC Program Highlights
March 17 - 22, 1995

SUN

3-9 pm **Registration**
6-8 pm **St. Patrick's Day Reception**
8-midnight **Vendor suites open (optional)**

MON

8 am **Opening Remarks:** *Geoffrey Bodenhausen, Chair, 37th ENC*
8:05-9:50 am **Applications of Solid-State NMR,** *Hellmut Eckert, Session Chair*
8:05-8:30 am **James Haw**, Texas A&M University, College Station, *Solid State NMR and Theoretical Studies of Reactive Intermediates*
8:30-8:55 am **Angelika Sebald**, Universität Bayreuth, *CPMAS and Molecular Dynamics in Inorganic and Organometallic Compounds*
8:55-9:20 am **Ferdinando Borsa,** Iowa State University, Ames, *Ionic Dynamics in Superionic Glassy Conductors from Li and B NMR and Relaxation*
9:20-9:50 am Promoted poster talks
9:50-10:15 am **Break**
10:15-12 noon **Neither Liquid nor Solid,** *Anthony Bielecki, Session Chair*
10:15-10:40 am **Claudia Schmidt,** Universität Freiburg, *Liquid Crystals Under Shear in Different Geometries*
10:40-11:05 am **Robert Tycko**, NIH, Bethesda, *Structural Studies in Ambiguous Phases*
11:05-11:30 am **Michael Shapiro**, Sandoz Research Institute, East Hanover, *Something Old, Something New, Something Borrowed, Something Blue; MAS NMR Studies of Solvent-Swollen Resin*
11:30-12 noon Promoted poster talks
12-2 pm **Lunch Break**
2-3:30 pm **New Methods for NMR in Liquids,** *Gaetano Montelione, Session Chair*
2-2:15 pm **Susanta Sarker**, Smith-Kline Beecham, King of Prussia, *Non-Destructive Identification of Materials Bound to a Single Resin Bead by NMR: Implications for Combinatorial Chemistry*
2:15-2:30 pm **Raphael Brüschweiler,** ETH, Zürich, *Quantitative Molecular Dynamics by NMR Relaxation*
2:30-3:30 pm Promoted poster talks
3:30-4 pm **Break**
4-6 pm **Posters Session A,** *James Roberts, Chair*
6-12 pm **Vendor suites open**

TUES

7-8 am **Chair's Breakfast for Students,** *Crocker Dining Hall*
8-9:45 am **Methods for Solid State NMR 1,** *Ruth Stark, Session Chair*
8-8:25 am **Robert Griffin**, Massachusetts Institute of Technology, Cambridge, *Recoupling, Decoupling, and Dynamic Polarization in Rotating Solids*
8:25-8:50 am **Ann McDermott**, Columbia University, New York, *Studies of Enzyme Active Sites and Enzyme Mechanism by Solid State NMR*
8:50-9:15 am **Jacob Schaefer**, Washington University, St. Louis, *REDOR of Clusters of Spins*
9:15-9:45 am Promoted poster talks
9:45-10:15 am Break
10:15-12 noon Methods for *in-vivo* NMR & Imaging, *Jerome Ackerman, Session Chair*
10:15-10:40 am **Peter van Zijl**, Johns Hopkins University Medical School, Balitmore, *Diffusion Tensor Spectroscopy and Imaging*
10:40-11:05 am **Joanne Ingwall**, Brigham & Women's Hospital, Boston, *NMR Spectroscopy of the Heart*
11:05-11:30 am **Axel Haase**, Universität Würzburg, *Multidimensional NMR Microscopy of the Heart*
11:30-12 noon Promoted poster talks
12-2 pm **Lunch Break**
2-3:35 pm **Computer Simulations & NMR Measurements: A Fruitful Relationship,** *Christian Griesinger, Session Chair*
2-2:25 pm **Wilfried van Gunsteren,** ETH Zürich, *Comparison of Simulated Structural and Dynamical Molecular Properties with Experimental Data: What We Can Learn*
2:25-2:50 pm **Axel Brünger**, Yale University, New Haven, *Title to be announced*
2:50-3:35 pm Promoted poster talks
3:35-4 pm **Break**
4-6 pm **Poster Session B,** *James Roberts, Chair*

WED

8-9:45 am **Exotica I,** *Karen Gleason, Session Chair*
8-8:25 am **Paul Callaghan**, Massey University, New Zealand, *NMR in Antarctica*
8:25-8:50 am **Michael Mehring**, Universität Stuttgart, *Ultra High Resolution NMR of Optically Polarized Atoms*
8:50-9:15 am **Heinz Jänsch,** Universität Marburg, *Highly Polarized Atoms on Single Crystal Surfaces*
9:15-9:45 am Promoted poster talks
9:45-10:15 am **Break**

WED con't

10:15-12 noon **Automated Spectral Assignment,** *Shaw Huang, Session Chair*
10:15-10:40 am **John Markley**, University of Wisconsin, Madison, *Software Tools for Processing, Analyzing, and Archiving Biomolecular NMR Data*
10:40-11:05 am **Gaetano Montelione**, Rutgers University, Piscataway, *Automated Analysis of Protein Resonance Assignments from Triple Resonance NMR Data*
11:05-11:30 am **Michael Wittekind**, Bristol-Myers Squibb, Princeton, *Automated Strategies for the Assignment of NMR Resonances of Large Proteins*
11:30-12 noon Promoted poster talks
12-2 pm **Lunch Break**
2-3:35 pm **Instrumentation,** *John Delayre, Session Chair*
2-2:25 pm **Howard Hill**, Varian Associates, Palo Alto, *Superconductive High Resolution NMR Probes*
2:25-2:50 pm **Frank Laukien**, Bruker Instruments, Billerica, *Development and Performance of Cryogenic High-Resolution Probes*
2:50-3:35 pm Promoted poster talks
3:35-4 pm **Break**
4-6 pm **Poster Session C,** *James Roberts, Session Chair*
6-12 pm **Vendor Suites open**

THUR

8-9:40 am **Biomolecular NMR,** *Angela Gronenborn, Session Chair*
8-8:25 am **Mitsuhiko Ikura**, Ontario Cancer Institute, Toronto, *Structure and Dynamics of Calcium Binding Proteins and Basal Transcription Factors*
8:25-8:50 am **A. J. Shaka**, University of California, Irvine, *Spectra You Can Trust: Excitation Sculpting in High Resolution NMR Experiments*
8:50-9:15 am **James Keeler**, Cambridge University, *Sensitivity Enhancement by Random Fractional Deuteration*
9:15-9:40 am **Cees Hilbers**, University of Nijmegen, *NMR of Single-Stranded DNA Binding Proteins Encoded by Filamentous Phages*
9:40-10:15 am **Break**
10:15-12 noon **Slow Motion & Conformational Heterogeneity,** *Laura Lerner, Session Chair*
10:15-10:40 am **Bertil Halle**, University of Lund, *Nuclear Magnetic Relaxation Dispersion Studies of Internal Water in Proteins*
10:40-11:05 am **James Prestegard**, Yale University, New Haven, *Protein Structure from Residual Dipolar Splittings in Very High Field Solution Spectra*
11:05-11:30 am **Catherine Zwahlen**, National High Magnetic Field Laboratory, Tallahassee, *NOESY Studies of Macromolecules with Suppression of Spin Diffusion*
11:30-11:55 am **Gottfried Otting**, Karolinska Institute, Stockholm, *Protein Solvation in Aqueous Solution*
12-2 pm **Lunch Break**
2-3:30 pm **Exotica II,** *Alexander Pines, Session Chair*
2-2:25 pm **A. N. Garroway**, Naval Research Laboratory, Washington, DC, *Pure NQR of Large Specimens*
2:25-2:50 pm **Gil Navon**, Tel Aviv University, *Proton MRI Detection of Solute Nuclei Through Relaxation Coupling*
2:50-3:15 pm **Jan Schmidt**, University of Leiden, *Magnetic Resonance of Single Molecules*
3:15-3:30 pm Promoted poster talk
3:30-4 pm **Break**
4-6 pm **Poster Session D,** *James Roberts, Session Chair*
7-9 pm **Banquet,** *Crocker Dining Hall*
9-9:45 pm **After Dinner Address: Alfred Overhauser,** "Dynamic Nuclear Polarization: A Reminiscence." *Merrill Hall*
6-12 pm **Vendor suites open (optional)**

FRI

8-9:40 am **New Methods for Solid State NMR II,** *Joel Garbow, Session Chair*
8-8:25 am **Terry Gullion**, Florida State University, Tallahassee, *Detecting Dipolar Interactions between Spin-1/2 and Quadrupolar Nuclei by Rotational Echo Adiabatic Passage Double Resonance (REAPDOR)*
8:25-8:50 am **Lucio Frydman**,University of Illinois, Chicago, *High-resolution NMR of Half-Integer Quadrupoles at the Magic Angle*
8:50-9:15 am **Gary Drobny**, University of Washington, Seattle, *Solid State NMR Studies of Nucleic Acids*
9:15-9:40 am **Hans Jakobsen**, Aarhus University, *Anisotropic Shielding and Quadrupole Coupling Interactions in Solid State NMR of Half-Integer Quadrupolar Nuclei: MAS, Static and Single Crystal NMR*
9:40-10:15 am **Break**
10:15-11:55 **New Methods for Liquid State NMR II,** *Gerhard Wagner, Session Chair*
10:15-10:40 am **Ray Freeman**, Cambridge University, *Another Chapter in the Broadband Decoupling Saga*
10:40-11:05 am **Lewis Kay**, University of Toronto, *Methods for Studying Protein Dynamics and Dynamical Proteins*
11:05-11:30 am **Ad Bax**, NIH, Bethesda, *Recent Developments in Protein NMR*
11:30-11:55 am **Richard Ernst**, ETH Zürich, *Farewell to Asilomar*
11:55 am **Closing Remarks:** *James Roberts, Chair, 38th ENC*

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Oct. 26, 1995
(received 11/24/95)

From: Glaxo Wellcome
5 Moore Drive
Bioanalytical & Structural Chemistry
Venture Center
RTP, N.C. 27709

Dear Barry,

We have entitled our submission: **"Getting to Know a New Devil"**. Several months have passed since Unity Plus consoles were installed on the existing 500 and 600MHz magnets in the lab. A couple of personality quirks in the **"New Devil"** that we have encountered are described below.

Initially, the 600 system (4 transmitters (Xmtr), 4 amplifiers (amp), configured with our convention as tn(H/F), dn(N15); dn2(C13); and dn3(X), respectively, was brought to life with SunOS and VNMR 4.3b. Sandy Farmer pointed out that if frequency dn2=dn3 (e.g.. C13 on both channels) then the frequency from Xmtr 4 is automatically combined with that from Xmtr 3 at low power then routed to the dn2 power amp. The good in this is that one can get two different C13 frequencies from two Xmtrs through one amp/transmission line to the probe. The bad part is if you want to employ the dn3 power amp, you'll need a fifth Xmtr board. As an alternative, one may get around the combining issue through the use of shifted laminar pulses to generate the 2 desired frequencies from one Xmtr/amp. This preserves Xmtr4/dn3 amp for additional application.

A few weeks later we got the new version of the operating system, Solaris, and VNMR 5.1a. Once installed, we found that the condition dn2=dn3 no longer auto combined. John Kilpatrick and Frits Vosman of Varian produced the following software patch for four channel systems that tames the unruly demon. Log in as user VNMR1 do the following:

vnmr1>psggen (script to create the necessary directories and files)
vnmr1>cd ~/vnmrsys/psg (go to VNMR1 psg directory)
vnmr1>cp /vnmr/psg/initfunc.c . (copy initfunc.c to the VNMR1 psg)
vnmr1>vi initfunc.c (edit the file)
Search for the declaration: double diff_basefrq; which appears shortly after the second appearance of set_ampbits. Insert the two new following lines

```
extern double rfchan_getbasefreq();
extern int rfchan_getampband();
```

directly after the double diff_basefrq; declaration and then save the file.
vnmr1>mv /vnmr/psg/initfunc.c orig_initfunc.c (save original just in case)
vnmr1>psggen (regenerates directories and files with change)
vnmr1>cp /vnmr/psglib/s2pul.c ~/vnmrsys/psglib/s2pul.c (copy s2pul.c)
vnmr1>seqgen s2pul (compile a sequence which provides rf from dn2 and dn3)

Set dn2='C13' and dn3='N15' and cable the lowpower rf 'out3' and 'out4' to a scope. Set dm2 and dm3='y' and do a setup. You should see rf from both dn2 and dn3 (125 and 50 @500MHz, respectively). Set dn3='C13' and check the scope and you should rf only from out3 and nothing from out4.

To enable this patch for others than vnmr1, one needs to move up the library file from the /vnmr1/vnmrsys/psg directory to each users /username/vnmrsys/psg directory. Do this:

vnmr1>cd /username/vnmrsys/psg
vnmr1>mv libpsglib.so.1.0 libpsglib.so.1.0_nopatch (save existing lib file)
vnmr1>cp ~/vnmrsys/psg/libpsglib.so.1.0 libpsglib.so.1.0

Now if you recompile the username's s2pul.c or other pulse sequences the low power channel combining patch should function when dn2=dn3.

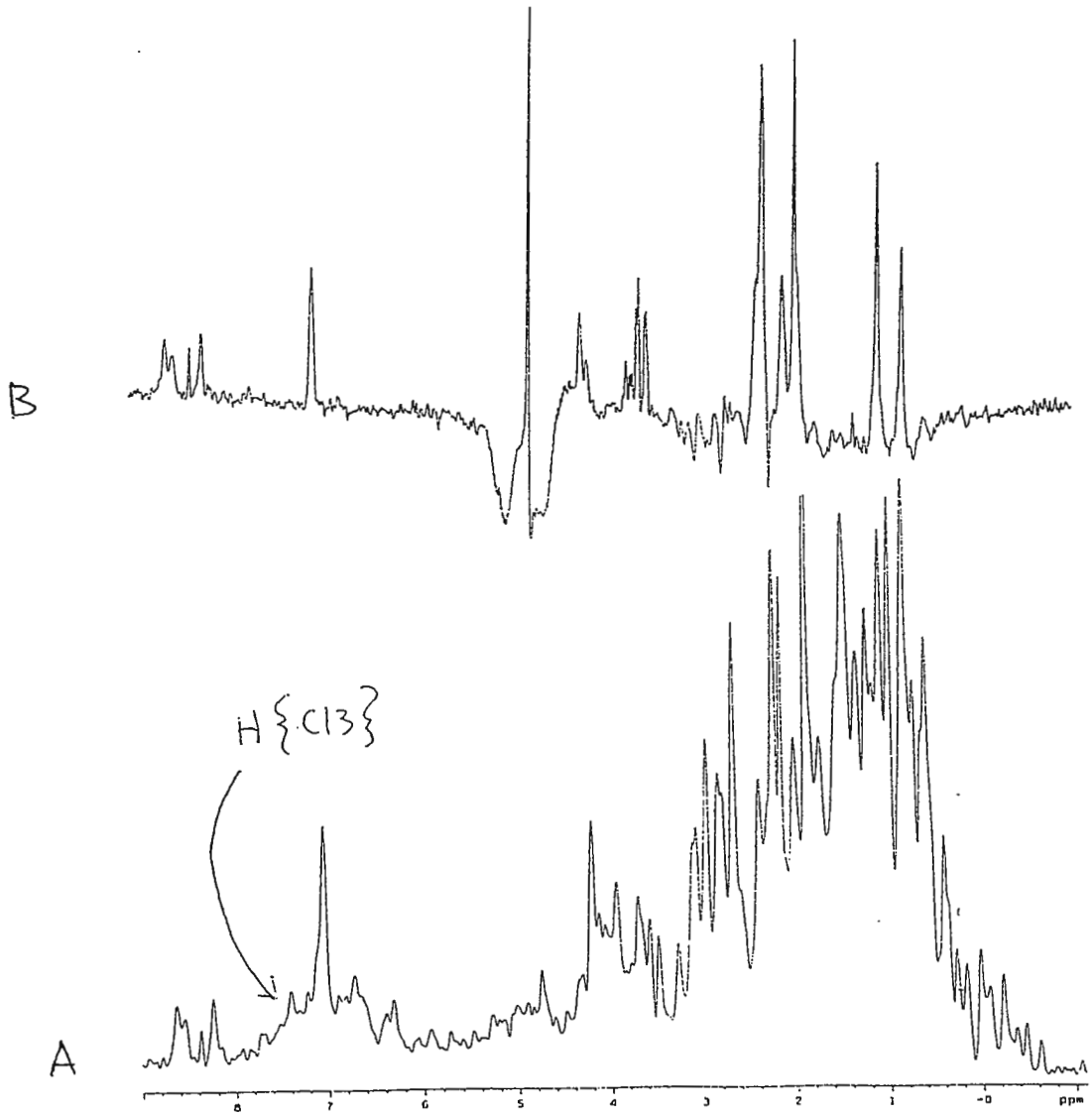
A second gremlin we encountered was detected on the 500Mhz system (4 Xmtrs, 5 amps configured with our convention as tn(H/F), dn(N15); dn2(C13 or H/F with required MANUAL rf

cable swap from out3 (and db25 RS232 control line to the appropriate amp); and dn3(X), respectively. While implementing an isotope filtered noesy sequence, we noticed the 'H{C13}' suppression was poor as demonstrated in figure 1A. Eventually, the problem was traced to the nucleus argument for dn3 not being defined (e.g. dn3="). Despite the fact that dn3 was not used in the pulse sequence it still introduced a problem as manifest in the NMR spectrum. Once defined as dn3='N15', the resulting spectrum had better 'H{C13}' suppression (1B). The final word from Varian was to set all channels to some frequency whether they are in use or not.

Regards,

Robert Gampe Don Davis Robert Xu Steve Brown Tai He Xia

Figure 1:First row from 2D Isotope Filtered Noesy (Ikura & Bax, JACS, 114, 1992) sequences of 1.3mM SH2{C13,N15 labeled} with a bound, unlabeled ligand wherein (a) the channel configuration was tn('H1',510MHz), dn('N15',61MHz), dn2('C13',136MHz) and dn3('',34.5MHz). (b) channel configuration was tn('H1',510MHz), dn('N15',61MHz), dn2('C13',136MHz) and dn3('N15',61MHz) . The reported frequencies (with 10.5MHz IF) were measured with a counter directly from each PTS main output.



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November 26, 1995
(received 12/5/95)

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

Dear Barry,

The absolute sign of $^1J_{13_{C-19_F}}$ in solid fluorobullvalene

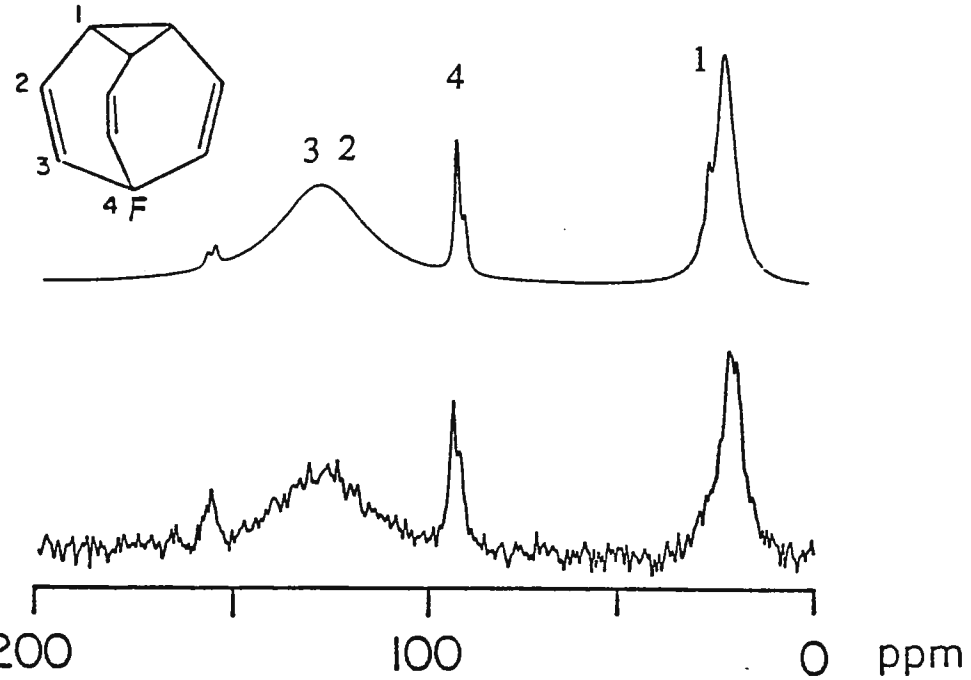
The absolute sign of scalar couplings can normally not be obtained from the structure of NMR spectra. It can however be determined if it is correlated with other interactions whose signs are known. The carbon-13 MAS spectrum of solid fluorobullvalene provides an example for the latter situation. Fluorobullvalene crystallizes entirely as isomer 4, i.e. with the fluorine bound to the bridgehead carbon in the molecule (see insert in figure). The molecules in the solid undergo fast three-fold jumps about their C_3-symmetry axes, resulting in line broadening of the MAS signals of carbons 1,2 and 3, while that due to carbon 4 remains sharp. An example of such a spectrum, recorded at 85°C, is shown in the figure (K. Müller, H. Zimmermann, C. Krieger, R. Poupko and Z. Luz (submitted)). The MAS signals of carbon 4 exhibit a splitting (160 Hz) which is ascribed to the scalar coupling $^1J_{13_{C(4)-19_F}}$. The doublet is however not symmetric with the high field component of the center band weaker than the low field one and reversely so for the first low field spinning side band (the corresponding high field one is obscured by the strong signal of carbon 1). This behaviour reflects the combined effect of the chemical shift anisotropy of carbon 4 and the direct C(4)-F dipolar coupling. The explanation is similar to that given by H. Miura, T. Terao and A. Saika (J.Chem.Phys. 85,2458 (1986)) fo the $^{13}C-^1H$ spectrum of calcium formate. The situation in fluorobullvalene is similar to that for CH_3F (K.W. Zilm and D.M. Grant. J.Am.Chem.Soc.103, 113 (1981)) and particularly simple because both tensors are uniaxial with colinear principal direction (parallel to the molecular C_3 axis).

The two sets of spinning side bands of carbon 4 correspond to molecules with fluorine spins in the $m_F = \mp 1/2$ states. They are centered around $(\nu_o\sigma^4_{iso} + m_F{}^1J_{13_{C(4)-19_F}})$. The intensity of the spinning side bands can be calculated from the Herzfeld-Berger theory (J.Chem.Phys.73,6021 (1980)) using effective axially symmetric chemical shift tensors with $\nu_o(\sigma^{eff}_{\parallel} - \sigma^{eff}_{\perp}) = \nu_o(\sigma^4_{\parallel} - \sigma^4_{\perp}) - \frac{3}{2}m_F D$, where $D = 2h\gamma_{:F}\gamma_C/r^3 = 19.98$ kHz is the

$^{13}C(4)$ $-^{19}F$ dipolar coupling and $\sigma_{\parallel}^4 - \sigma_{\perp}^4 = -90$ ppm is the anisotropy of the carbon 4 chemical shift tensor. From the fact that the high field component in the center band is weaker than the low field one, it follows immediately that $^1J_{13_{C(4)}-19_F}$ is negative, as also found by Zilm and Grant for CH_3F and is apparently common for aliphatic C-F bonds.

With best regards,

K. Müller R. Poupko Z. Luz



Bottom: Experimental carbon-13 CPMAS spectrum (at 75.46 MHz) of fluorobullvalene at 85^oC and a spinning rate of 4.86 kHz. Top: Calculated dynamic MAS spectrum for a three-fold jump rate of $3.5 \times 10^4 s^{-1}$. The spectrum of carbon 4 was calculated as a superposition of two subspectra centered at $(\nu_o \sigma_{iso}^4 \pm 80)$Hz with effective chemical shift anisotropies of (6790 ∓ 14990) Hz.

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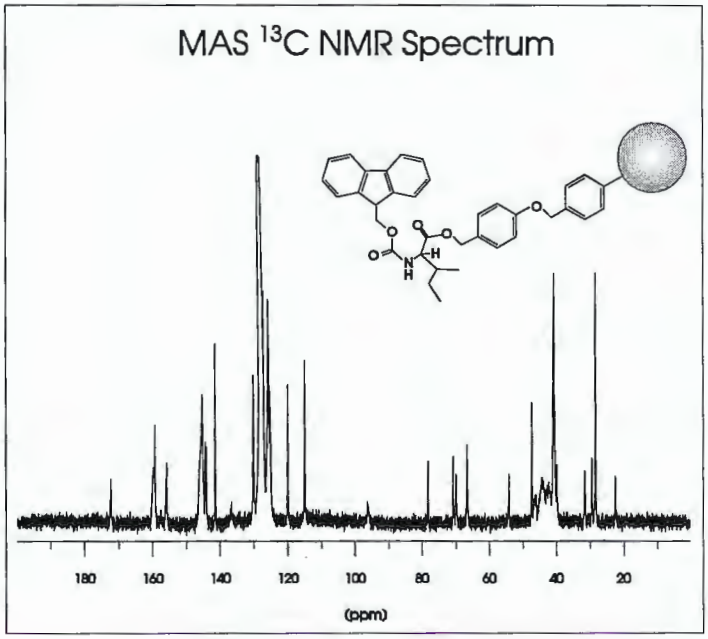

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Figure 1: ^{13}C MAS spectrum of a typical compound [3].

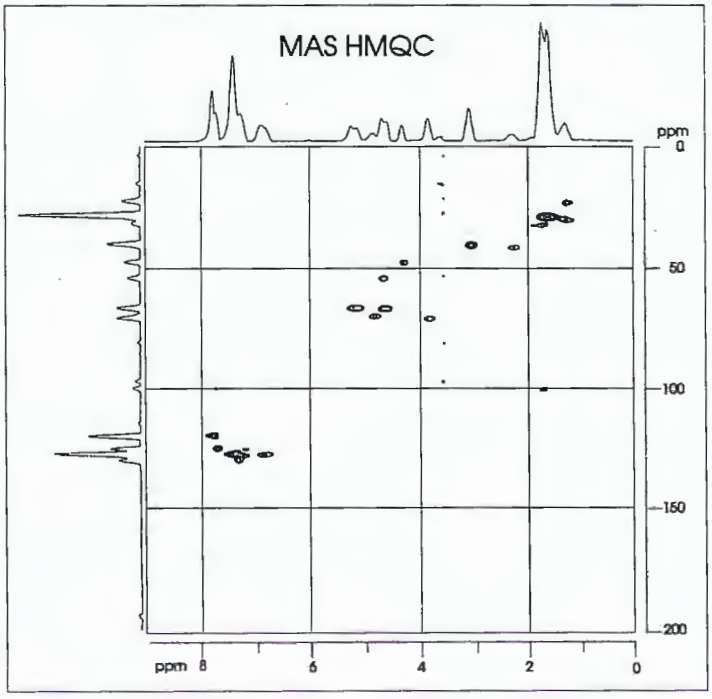

Figure 2: A two dimensional HMQC spectrum of the compound shown in Figure 1.

[1] C.C. Leznoff, Acc. Chem. Res. **11**, 327 (1978)
[2] J.M.J. Frechet, Tetrahedron **37**, 663 (1981)
[3] R.C. Anderson, M.A. Jarema, M.J. Shapiro, J.P. Stokes and M. Ziliox, Bruker Report **142/96**

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December 12, 1995
(received 12/14/95)

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

Variation of Polyethylene Phase Morphology Due to Sample Milling as Revealed by ^{13}C CPMAS NMR[1]

Dr. Shapiro,

Degradation of organic polymers and materials continues to be an area of active research at Sandia National Labs. There have been numerous investigations reported in literature of the phase morphology in polyethylene (PE) using solid-state ^{13}C CPMAS NMR. From these previous investigations it is clear that the production and thermal history of the polymer plays a major role in the observed phase morphology. We recently received a reminder that the sample preparation history can also play an important role in the observed polymer morphology. Figure 1 shows ^{13}C CPMAS spectrum for the same polyethylene sample prepared for NMR analysis in two different ways. In Fig.1A is the spectrum for a PE sample that was manually cut prior to packing in the rotor, while Fig.1B is the spectrum for the same sample impact milled at liquid N_2 temperature. The original justification for sample milling was to produce a more uniform particle size to aid in sample packing, both for increased signal to noise and rotor stability. The spectra in Figure 1 clearly show distinct differences between the two samples. In Fig.1A only two major resonances are observed, corresponding to the crystalline orthorhombic ($\delta = 33.0$) and the amorphous ($\delta = 31.5$) phase for PE. In Fig. 1B the relative ratios of these phases changes, plus an additional resonance (*) at $\delta = 34.3$ is evident. This downfield resonance has been attributed to a monoclinic crystalline phase,[2] characteristic of deformation or strain in PE samples. Evidently the impact process during sample milling created the new phase. In addition, the relaxation time $T_{1\rho}$ for the different phases in these PE samples are also changed with milling. It is clear that close attention must be given to the sample preparation history of polymer samples in which phase morphology are being investigated.

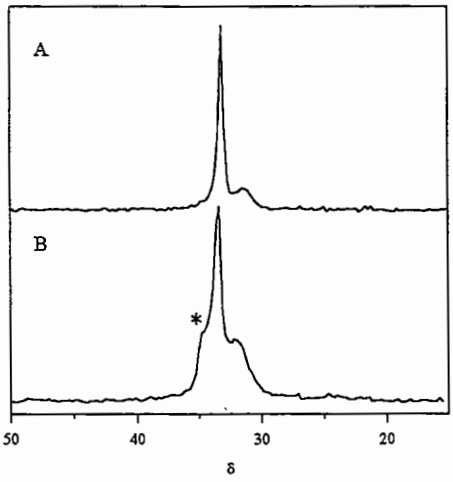
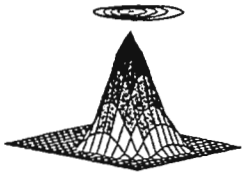


Figure 1. ^{13}C CPMAS spectrum of PE for different sample preparation techniques: (A) PE sample cut into small pieces, (B) PE sample impact milled at liquid N_2 temperatures for 60 seconds. All spectra were obtained under identical conditions using a 4 mm rotor on a AMX400, with 32 scan average and 1 ms contact time.

Sincerely,

Todd M. Alam Roger A. Assink Mathew Celina Ken T. Gillen Roger L. Clough

[1] This work supported by the US Department of Energy under Contract DE-AC04-94AL85000.
[2] VanderHart, D. L. and Khoury, F. *Polymer* **1984**, 25, 1589.



XVIIth International Conference on Magnetic Resonance in Biological Systems August 18-23, 1996 - Keystone, Colorado, USA

Conference Office

1201 Don Diego Avenue
Santa Fe, NM 87505, USA

Phone: (505) 989-4735
Fax: (505) 989-1073

The 17th in the series of biennial International Conferences on Magnetic Resonance in Biological Systems will be held at the Conference Center in Keystone, Colorado, August 18 - 23, 1996. This is the first meeting in this series to be held in North America since 1988.

Conference Program. A broadly based program has been planned, covering new magnetic resonance methods, applications of high resolution NMR to structural biology, application of solid state NMR techniques, use of EPR in studying a variety of paramagnetic systems, *in vivo* spectroscopy and imaging, and a minisymposium on Biomolecular NMR and Drug Discovery.

Sessions are currently being planned in the following areas:

Membrane proteins and lipids	Gradients and coils	Electron transfer
Protein-nucleic acid interactions	Water-macromolecule interactions	Dynamics
Cellular inorganic ions	Paramagnetic proteins	Nucleic acid structure
Oligosaccharides	Protein folding and stability	Protein structure
Cellular metabolism kinetics	Enzymes and catalysis	Diffusion and perfusion
Magnetic resonance microscopy	New instrumental methods	

Biomolecular NMR and Drug Discovery (Minisymposium):

Signal transduction and cellular receptors	
Enzyme inhibitors	Viral proteins

The conference will feature 12 plenary lectures, along with about 80 invited lectures and 25 short talks in three parallel sessions. Three poster sessions, each accommodating up to 200 posters, will permit participation by a large number of workers active in many aspects of biological magnetic resonance.

Conference locale. The meeting will be held at the Keystone Conference Center. Keystone is a planned resort community in the Rocky Mountains, about 75 miles west of Denver. Most air travelers will fly to the new Denver International Airport, which has good domestic and international connections. Rental cars and shuttle buses are available from the Denver Airport to Keystone. The Conference Center, opened in 1989, will be the site of all lecture and poster sessions, with coffee breaks and display of vendor materials in the foyers and terraces. The Keystone Resort includes two hotels, as well as condominium units, many restaurants in all price ranges and full recreational facilities for swimming, boating, golf, tennis, hiking and trail riding. August weather at Keystone is usually very pleasant, with daytime high temperatures running 20°-30° C.

Further information. A second circular, providing details of the scientific program, along with registration and accommodation forms, will be sent out in February. This announcement will include a call for contributed papers. Please contact the conference office to obtain the second circular.
Telephone: (505) 989-4735. Fax: (505) 989-1073. E-mail: 70404.2407compuserve.com

A page has been established on the World Wide Web [http://nmrsgi1.ncifcrf.gov/icmrbsxvii] to provide updated information on the program as it is developed.

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PROF. RAY DUPREE

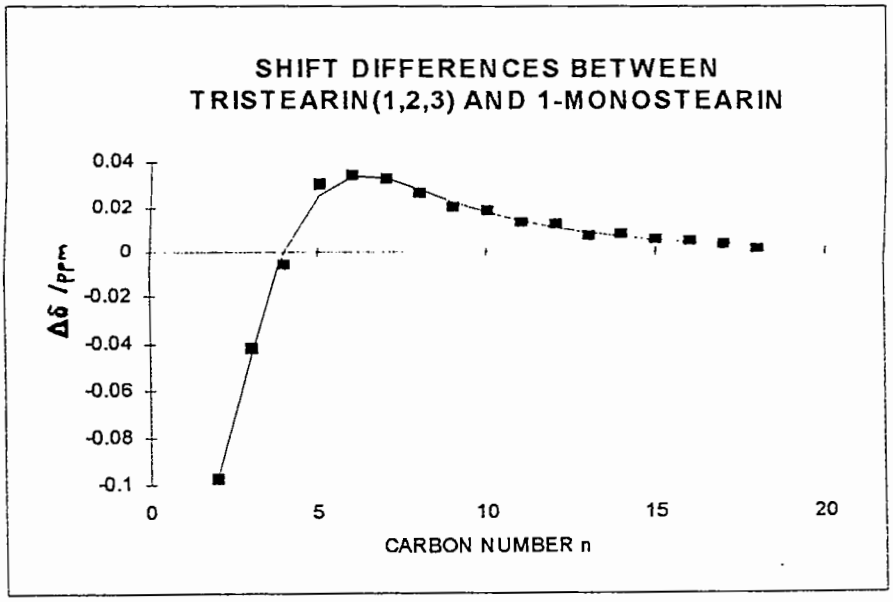
30th November 1995
(received 12/5/95)

Dear Barry,

New Insights from Small Shifts

We NMR spectroscopists tend to ignore small variations in shift as being artefacts of solvent or temperature change. But these are unlikely explanations when very similar molecules are being compared, in the same solvent and at the same temperature. They are even less likely when one has, for example, two equal alkyl chains placed differently within one molecule, such as the outer and inner chains in a simple triglyceride. In a speculative project, we are investigating such differences, using all the care we can summon, including generous digitisation and additional spectra from mixtures, in order to find if these shift differences tell a story.

The graph below shows one of our sets of results. It plots the shift differences between the outer (1,3) stearate chains in tristearin (basically, sheep fat at its worst) and the single, outer chain in 1-monostearin. Although these differences are certainly small, they vary in a fairly smooth way with the chain position n, suggesting that they are monitoring genuine electronic interactions. The line represents a fit to an arbitrary function consisting of two opposed exponentials, one decaying rapidly with exponent an^2, and the other decaying more slowly with exponent bn, where a, b and the relative weighting of the two decays are all determined by curve-fitting to the data points.



At this exploratory stage, I suspect that the 'rapid decay' approximates some sort of through-bond interaction, whose magnitude reflects the removal of the other two chains. In support of this, our preliminary results for the removal of different chains, relative again to tristearin, correlate sensibly with the remoteness of the chain loss from the start of the chain under observation. The 'slow decay' is more problematic, but I guess that it represents the average physical closeness of the chains, regardless of how they are attached to the glyceryl backbone. Thus it may relate to the vexed question of the solution conformation of triglycerides. Interestingly, a small but definite 'slow decay' is observed at one outer chain when the other one is removed. This would be unlikely if the chains always splayed out, well away from each other, in chloroform solution.

We plan to study other types of chain, such as oleate, and then to assess whether we can move to the more challenging problem of micelles.

Best wishes Oliver Howarth

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Richard A. Komoroski, Ph.D.
Professor

UAMS MEDICAL CENTER

November 28, 1995
(received12/2/95)

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

Title: *In Vitro* NMR Spectroscopy of Schizophrenic Brain

Dear Barry:

In collaboration with Dr. M. Omori of Fukui Medical School in Japan, as well as Drs. C.N. Karson, W.S.T. Griffin, R.E. Mrak, and M.M. Husain at UAMS and the Little Rock VA Hospital, we have been using high resolution ^{1}H NMR to follow changes in metabolite levels postmortem in the brains of individuals who suffered from schizophrenia. Localized *in vivo* ^{1}H NMR is being pursued in several laboratories, including our own, as a tool for elucidating several facets of this devastating disorder. We will describe our *in vivo* work in a later letter. It is important to confirm changes seen *in vivo* by isolation of the tissue and examination of the extracts *in vitro*, where possible. For a disease like schizophrenia, where an accepted animal model is lacking, this means postmortem studies on human brain.

Schizophrenia is a disorder characterized by multiple types of symptoms. Dysfunctions in several brain regions have been proposed. We studied extracts of 8 DSM-III-R schizophrenic and 10 age-matched control brain samples from five regions (frontal and temporal cortex, thalamus, amygdala, and cerebellum) removed at autopsy by 300 MHz ^{1}H NMR on a GE GN-300 spectrometer. TSP was employed as an internal quantitation reference. Concentrations were determined for acetate, alanine, aspartate, N-acetyl-aspartate (NAA), N-acetyl-aspartyl-glutamate (NAAG), choline (Cho), creatine, γ-aminobutyric acid, glutamate (Glu), glutamine, glycine, inositol (Inos), lactate, succinate, taurine, and valine.

Somewhat surprisingly, we found no statistically significant difference ($p<0.05$, Mann-Whitney U test) for any metabolite for any brain region. However, if NAA is corrected for hydrolysis by adding the acetate value, we see a reduction ($p=0.041$) in NAA (a putative neuronal marker) in the thalamus. Differences in Glu in temporal cortex and thalamus approached significance ($p=0.062$). We saw no differences for Cho or Inos, for which differences have been seen *in vivo*. These results only partially support *in vivo* work, where NAA reductions have been seen by some workers for some brain regions in schizophrenia. Our results suggest that any changes in metabolite concentrations between schizophrenics and normal individuals will be small, and difficult to observe *in vivo*. The small differences we may be observing in thalamus are consistent with recent work where intensity differences were seen for thalamus between the summed MRI scans of schizophrenics and controls.

Sincerely,

Richard A. Komoroski

John Pearce

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

December 20, 1995
(received 12/22/95)

NMR Imaging of Crumb Rubber in Asphalt

Dear Barry,

Most people are probably not aware that the road system in the U.S. is the largest, continuous, manmade structure ever built, comprising about 2 million miles of paved roads, ~ 95% of which are asphalt concrete. Most people are also probably not aware that maintaining and improving these roads costs more than $10 billion a year, so that preventing moisture damage, rutting, low temperature cracking and other failures can represent a considerable savings in tax dollars. Some people probably know that there are a lot of scrap tires causing problems in landfills, breeding mosquitos, etc. For some reason, when there is a surplus of this nature, one solution seems to be- "Use it For Paving". Witness sulfur in asphalt, polymers in asphalt, even glass is asphalt. Now it's scrap tires in asphalt because of the Intermodal Surface Transportation Act of 1991, which federally mandated States to mix a certain amount of crumb rubber (scrap tires) with asphalt for paving (up to 20% by 1997). Now, federal law makes the use of crumb rubber voluntary, but its use has attracted much attention as a way to construct improved roadways. However, studies have not been done to determine whether the two materials are compatible. Do components in the asphalt dissolve the rubber, do they swell the rubber at mix temperatures (~150 °C), etc.?

One of the problems is that tires are black, so is asphalt, and when the two are mixed, they are really black! So how does one know what happens in such a mixture? Well, it appears that magnetic resonance imaging might have applications to this problem and we have just started performing some experiments using a Chemagnetics microimaging probe.

As it turns out, tire rubber can be imaged, but asphalt cannot because of favorable and unfavorable relaxation times of the two components. The top left image shows 3 pieces of natural rubber dispersed in 40 mesh crumb rubber particles that filled a 23 mm vial to a height of about 8 mm. In this case, both materials are imaged, but because of the particle size of the crumb rubber, all one sees is a band. The top right image shows a different sample of the two materials mixed in asphalt. The natural rubber is visible; the crumb rubber is barely visible, but this is because not enough was mixed into the asphalt. The bottom left image shows that natural rubber still gives an image after having been heated to 200 °C; however, the crumb rubber did not give an image. The bottom right image shows that neither the natural nor the crumb rubber was imaged in asphalt after the mixture was heated to 200 °C. Are these relaxation time effects, or did the asphalt interact with the rubber components, rendering them invisible? We don't know, but hope that by the time we receive your next missive, we will.

Best regards

Fran Miknis Dan Netzel

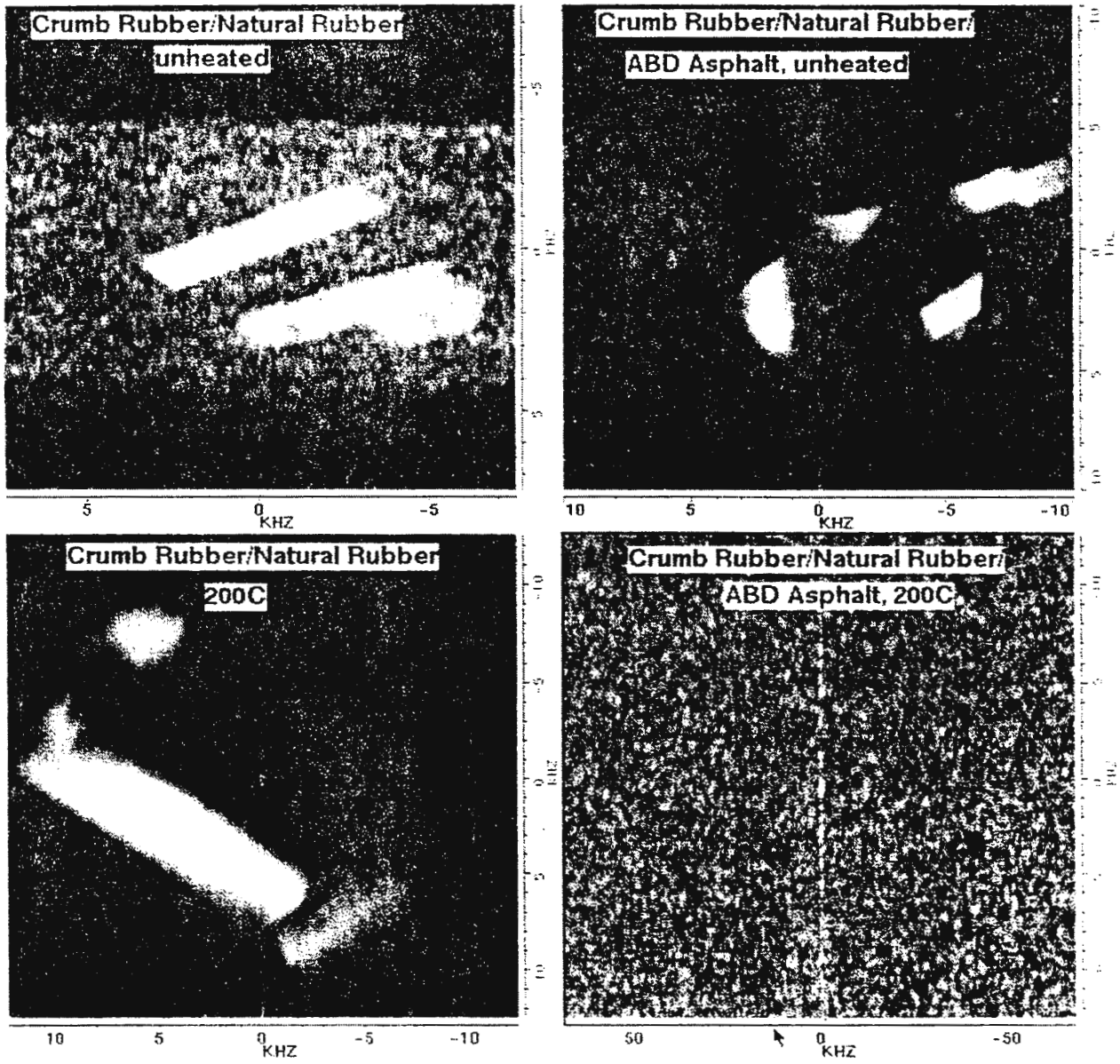

Figure 1. Images of heated and unheated natural and crumb rubber with and without asphalt. Images on left are of crumb and natural rubber in absence of asphalt. Images on right are in presence of asphalt. (scale: 1 kHz = 1 mm)

Address all Newsletter correspondence to:

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

(415) 493-5971* - *Please call only between 8:00 am and 10:00 pm, Pacific Coast time.*

Deadline Dates

No. 450 (Mar.)	23 Feb. 1996
No. 451 (April)	22 Mar. 1996
No. 452 (May)	26 April 1996
No. 453 (June)	24 May 1996
No. 454 (July)	28 June 1996

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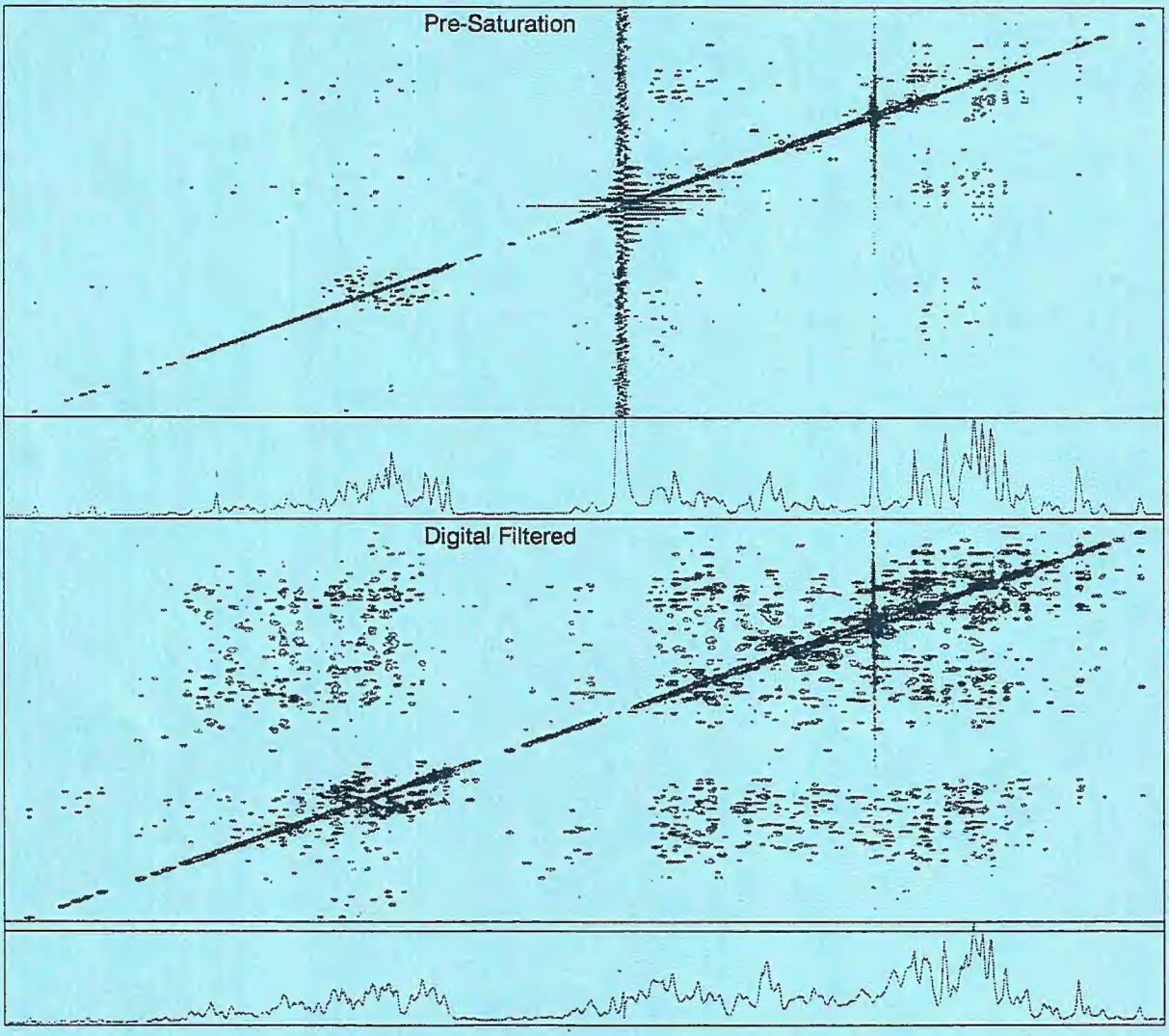

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