THE NMR NEWSLETTER

No. 462

March 1997

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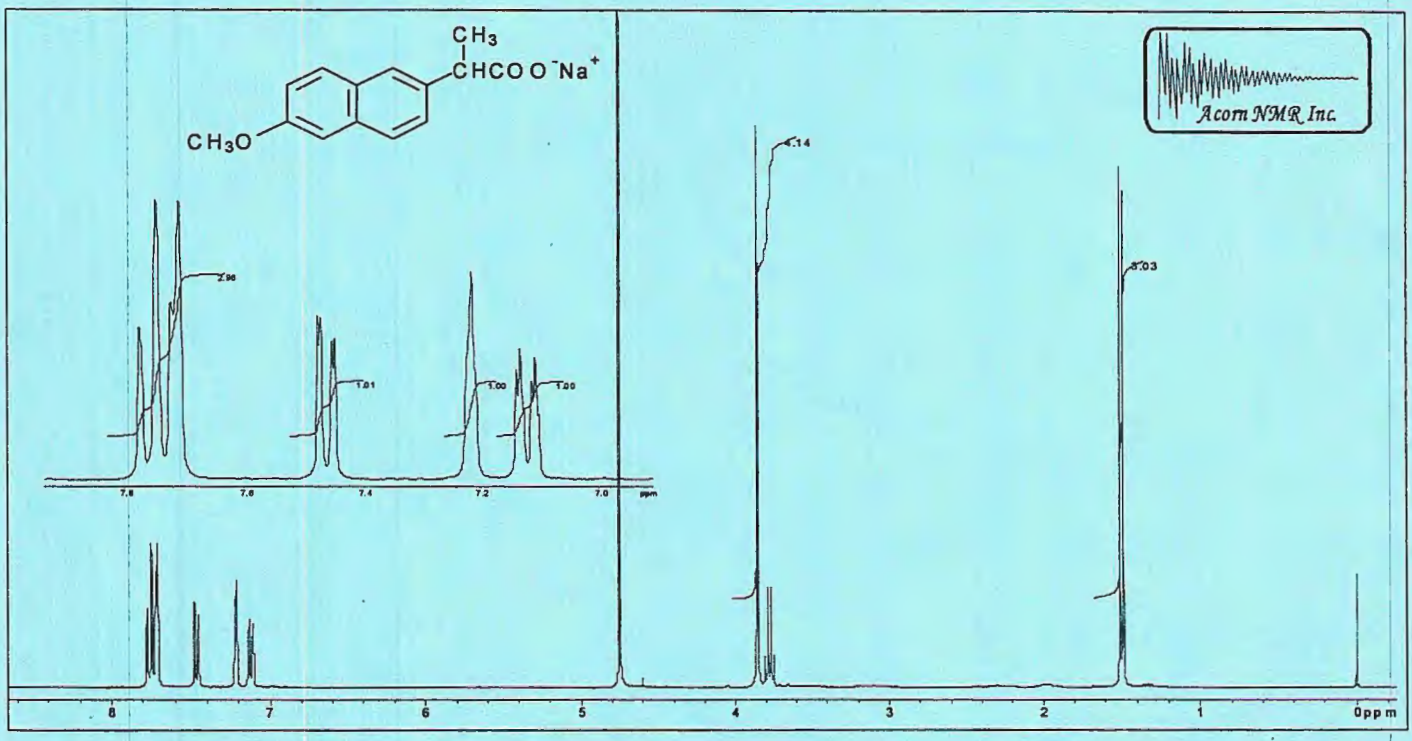

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FORTHCOMING NMR MEETINGS

5th Annual "Advances in NMR Applications" Symposium, Orlando, FL, **March 23, 1997**; Contact: Ms. Chris Tierney, Nalorac, 841-A Arnold Drive, Martinez, CA 94553;)510) 229-3501; Fax: (510) 229-1651; Email: christierney@nalorac.com. See Newsletter 460, 42.

38th ENC (Experimental NMR Conference), Orlando, FL, **March 23 - 27, 1997**; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87505; (505) 989-4573; Fax: (505) 989-1073. See Newsletter 460, 41.

International Society for Magnetic Resonance in Medicine, Fifth Scientific Meeting and Exhibition, Vancouver, BC, Canada, **April 12-18, 1997**; Contact: ISMRM, 2118 Milvia St., Suite 201, Berkeley, CA 94704, USA; (510) 841-1899; Fax (510) 841-2340; Email: info@ismrm.org.

Symposium on NMR Spectroscopy of Synthetic Macromolcules, ACS National Meeting, San Francisco, **April 13-17,** 1997; Contact: H. N. Cheng or English, A. D. See Newsletter 456, 20.

International School of Structural Biology and Magnetic Resonance, 3rd Course: Protein Dynamics, Function and Design; Erice, Sicily, Italy; **April 18-28, 1997**; Contact: Ms. Robin Holbrook, Stanford Magnetic Resonance Laboratory, Stanford University, Stanford, CA 94305-5055; (415) 723-6270; Fax: (415) 723-2253; Email: holbrook@smi.stanford.edu. See Newsletter 462, 54.

Symposium and Training: ^{13}C in Metabolic Research, Dallas, TX, **May 8, 1997;** Contact: J. Cody: (214) 648-5886; fax: (214) 648-5881; email: jcody1@mednet.swmed.edu, or N. Bonsal: (214) 648-5887. See Newsletter 462, 22.

Continued on page 10

The University of Texas Medical Branch at Galveston

School of Medicine
Graduate School of Biomedical Sciences
School of Allied Health Sciences
School of Nursing

Marine Biomedical Institute
Institute for the Medical Humanities
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Marine Biomedical Institute

February 17, 1997
(received 2/19/97)

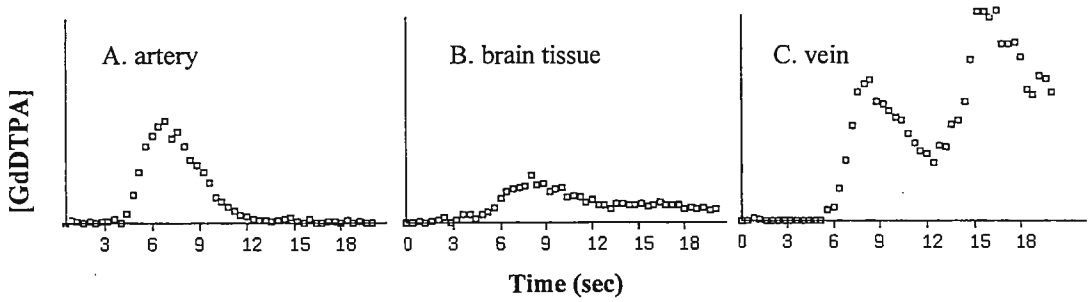
Dr. B.L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto CA 94303

BOLUS TRACKING WITH AN UPGRADED IMAGING CONSOLE

Dear Barry:

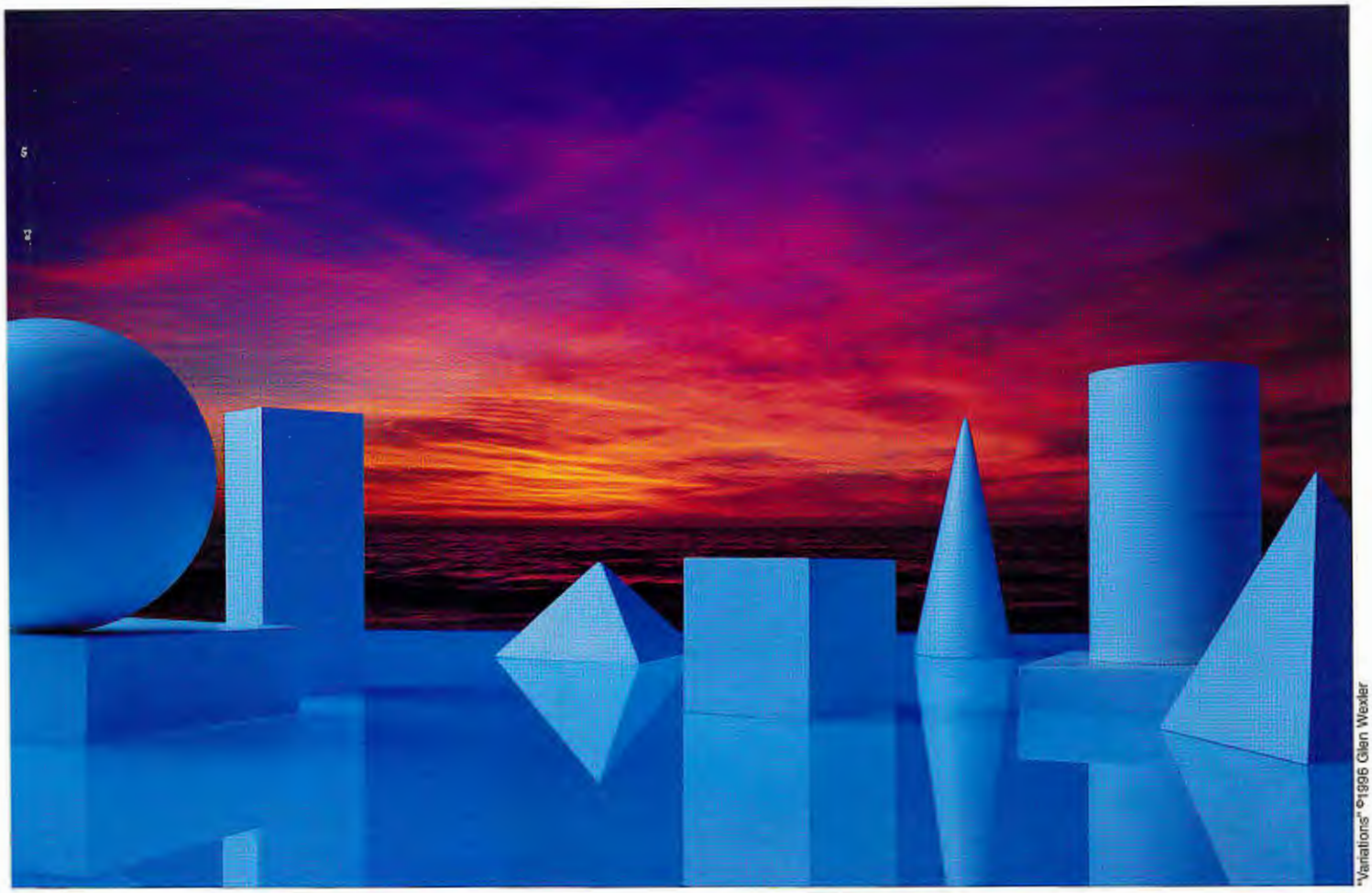
We recently upgraded our 4.7 T horizontal imaging system with the INOVA console and self-shielded gradients. One of the advantages of the INOVA is the elimination of the "host to acquisition link" or HAL – a sort of middleman computer shuttling data bits between the host and acquisition computers. As in the movie "2001 A Space Oddessy" HAL took control of our mission, at least our mission to perform dynamic bolus tracking experiments. In our experiments a bolus of paramagnetic tracer (GdDTPA) is injected into the tail vein or femoral vein of rats and its passage through a brain slice is recorded by sequential MRI scans. Under certain conditions the bolus passage can be complete within a couple of seconds, especially in fast areas such as arteries. Despite remaining well under the rf and gradient duty cycles, HAL demanded a sufficient repetition time (minimum 5 ms on our gradient echo scan to avoid the dreaded FIFO underflow message) and significant time between successive frames. Simply by eliminating the delay between frames we improved our frame repetition time from 0.7 s to 0.4 s. We suspect that we can also improve on the repetition time limitation. In the "out of the box" software (5.2 beta) the standard setup doesn't allow an acquisition time of less than 1 ms. We'll fix that later. For now we just enjoy hearing the sound of continuous gradients buzzing, rather than intermittent frames separated by 0.3 sec of dead silence.

In our preliminary tests using the new self-shielded gradient system we recorded excellent quality images of cerebral perfusion. We can read in the sequential images and analyze the hemodynamics in different regions of the brain using point-and-click graphics software that we wrote. Data from three such regions are shown below where time-concentration curves (same scale for all) were constructed based on the dynamic signal intensity reductions induced by GdDTPA. The bolus arrives earliest in the internal carotid artery feeding this region of the brain (A), then passes through the capillary beds in the brain tissue (B) and finally flows out through a draining vein (superior sagittal sinus, C). The measured concentrations are high in the artery and vein where the bolus is travelling as a plug compared to the brain tissue where the bolus is distributed throughout the capillary network. The appearance of a double bolus in C probably results from flow from two different regions of the brain that drain through a common vein. Using programmed curve fitting techniques we can estimate regional cerebral blood volume, transit time and blood flow, which can also be performed pixel-by- pixel in order to calculate the relevant parametric images. Now all we need is more RAM and disk space to handle all the extra images.



Best Regards,
Michael Quast, Jingna Wei, Nishanta Illangasekare, Jose Gonzalez and Ed Ezell

New Dimensions in NMR™



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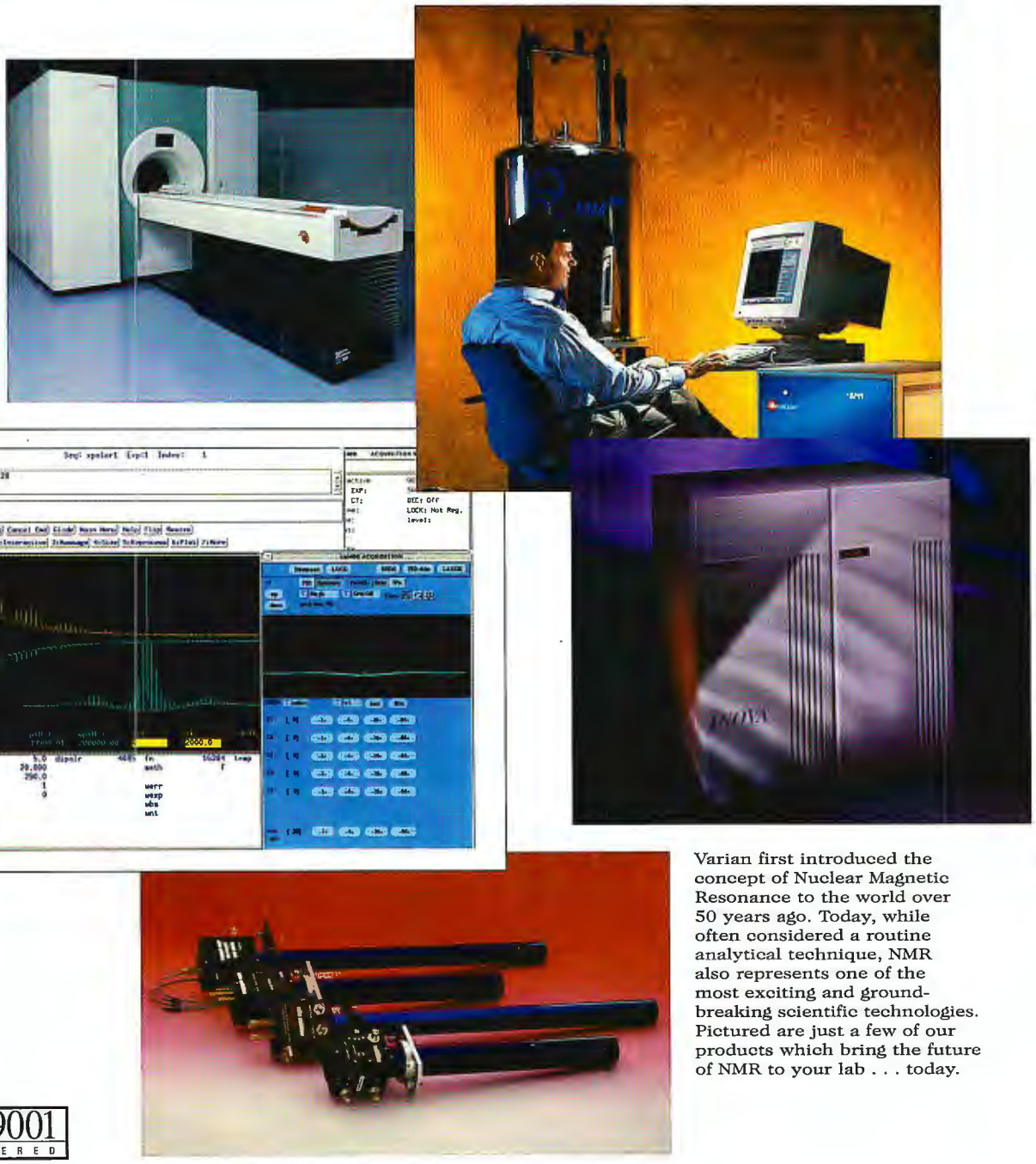

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Correlation of protein chemical shifts and dihedral angles

Tuesday, February 11, 1997
(received 2/14/97)

Barry Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Dear Barry:

The chemical shifts of proteins and other molecules have been used for quite some time to obtain qualitative structural information. The chemical shifts of the amide protons and amid nitrogens typically offer considerable hints about the amount of beta structure present. A quick glance at the HSQC data on a protein can usually allow a pretty reliable estimation of the amount of beta structure present and a little staring can often indicate quite a bit of information.

The conversion of the chemical shift information into quantifiable structural information has been coming along in bits and pieces. The groups of Sykes, Oldfield, Torchia, Bax, Kay, Wüthrich and others have developed a number of correlations between the chemical shifts of particular sites in proteins with structural features. We thought it would be interesting to pursue the matter along a slightly different path.

We first did the empirical correlations between the observed chemical shifts and dihedral angles for five backbone atoms. A typical correlation plot in shown on the next page. The map shows for example, as is well known, that downfield shifts correlate with beta character. However, the maps allow assigning a definite value to the probability that a particular chemical shift defines a particular dihedral angle. The data from about forty proteins was combined to obtain the map.

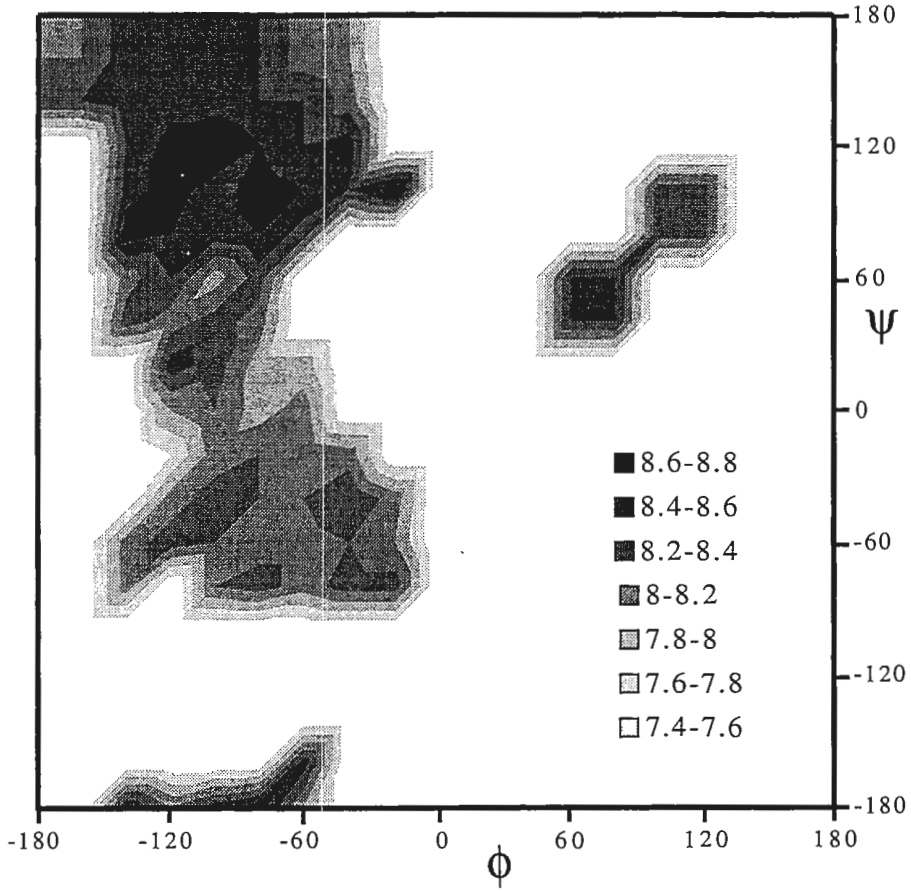
It was clear to us, as to others before us, that no one chemical shift correlation map was sufficient to tightly define a dihedral angle. However, the information in the chemical shifts of five atom sites allows a much better prediction of the actual dihedral angle. Simultaneous use of the five, independent empirical chemical shift to dihedral angle correlations based on the data from the forty or so proteins allows the actual experimental set of five chemical shifts to be used to generate a probability map for the dihedral angles of that amino acid. A typical plot is shown on the next page. This information can be used in protein structure refinement as will be described elsewhere.

Sincerely,

Richard Beger

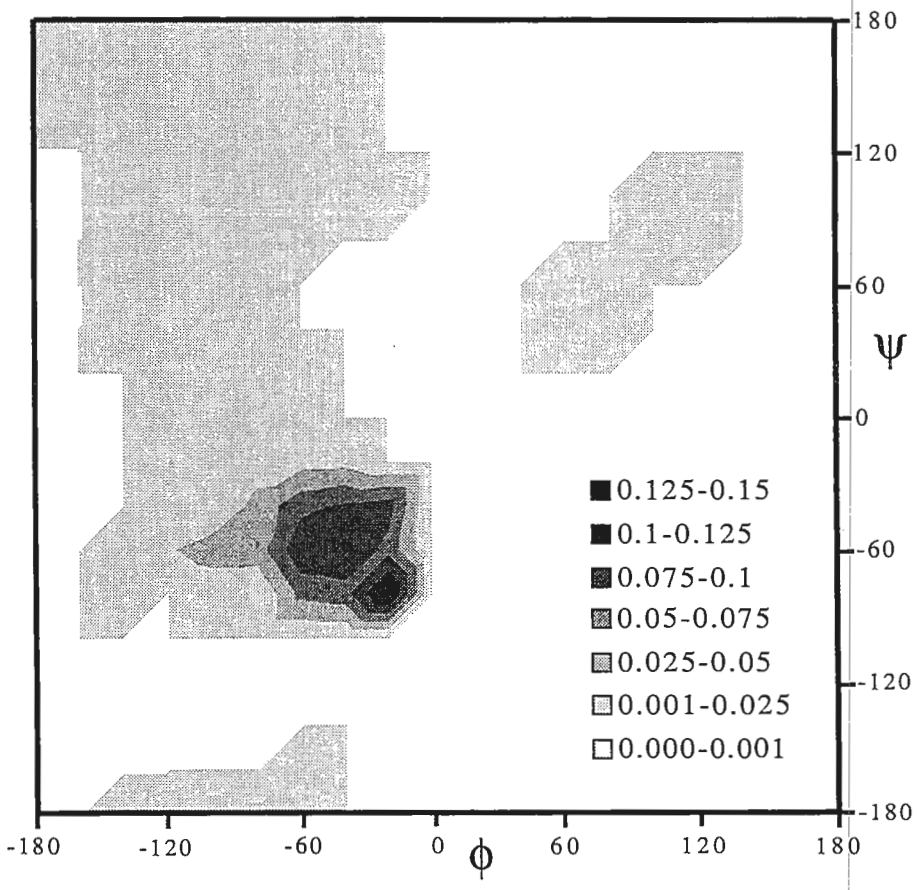
Philip Bolton

^1H Amide Chemical Shift



The plot on the left depicts the empirical correlation between the dihedral angles and the chemical shift of the amide proton. The correlation plot is based on the experimental data of about forty proteins. It is seen that some of the correlations are fairly high but there are typically several sets of dihedrals which correlate with any particular chemical shift. The plot below shows the predicted correlation between the dihedral angles and the experimental chemical shifts of five atoms of a single residue. The regions of highest probablity are those that agree best with all five experimental chemical shifts.

Normalized Z^5 for Val_{63} of Human Macrophage



The simultaneous correlation of five, independent chemical shifts generally narrows down the region of dihedral angle space consistent with the experimental data to a well defined, fairly small region. The results shown are for a typical residue.

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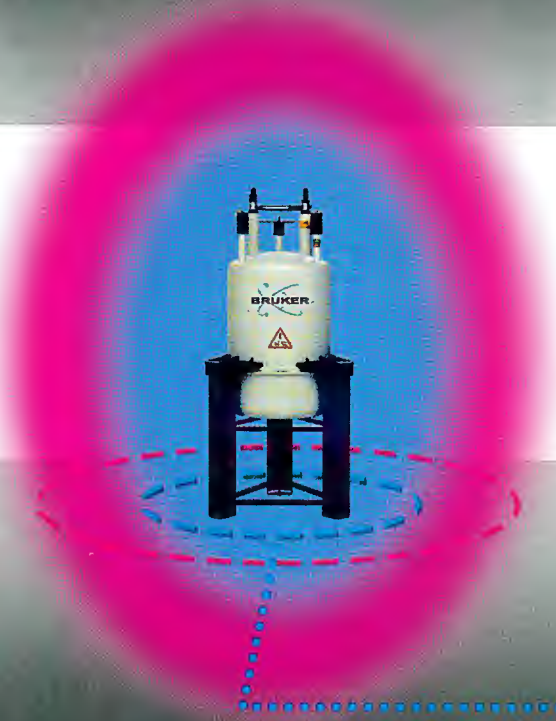

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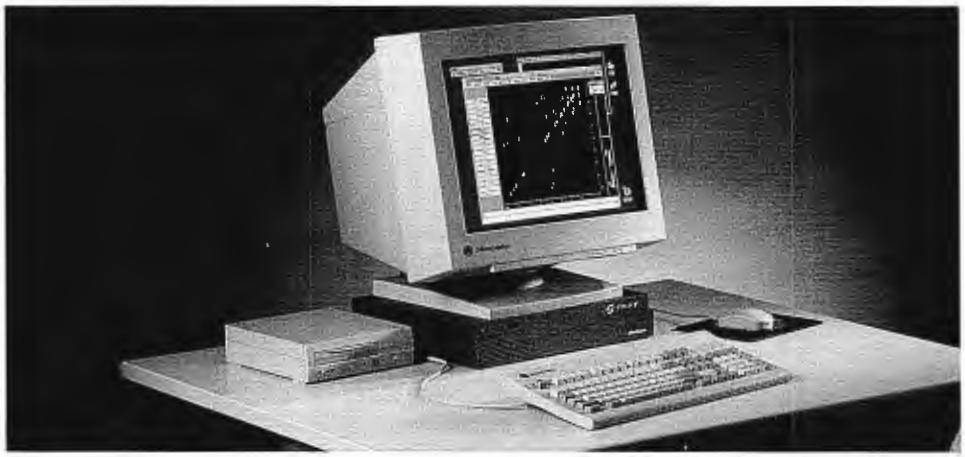

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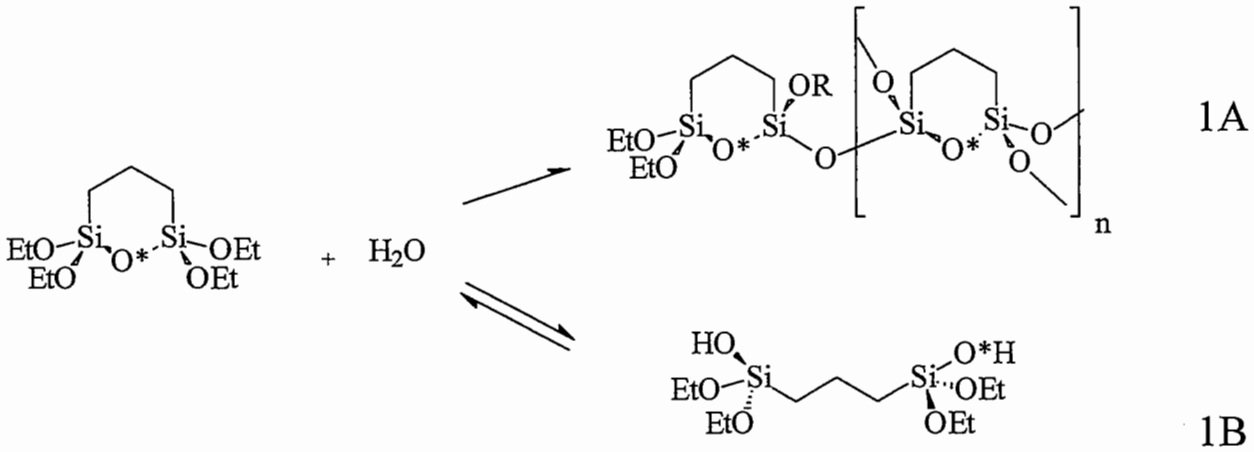
^{17}O NMR : The Role of Reversible Condensation in Cyclic Disilsesquioxanes[1]

Dear Barry,

(received 2/18/97)

The use of ^{17}O NMR to characterize materials is a growing area of interest here at Sandia National Labs. Recently the role of reversibility during the acid catalyzed condensation reactions of cyclic silsesquioxanes were probed using ^{17}O NMR.



The cyclic disilsesquioxanes containing a single ^{17}O label in the Si–O*–Si position was isolated and purified. In general, this cyclic precursor is very stable and requires elevated temperatures to induce further acid catalyzed condensation (1A) to produce sol-gel materials. Other observations had suggested that the cyclic was also involved in a reversible reaction with the acyclic propyl bridged silsesquioxane (1B). The ^{17}O NMR spectra for the labeled cyclic disilsesquioxane as a function of reaction time is shown in Figure 1. At the initiation of the acid condensation reaction (2 equivalents of 1N HCl) a single dominant ^{17}O resonance is visible, corresponding to the labeled cyclic ($\delta = 67.5$). Also visible are two weak resonances resulting from the natural abundance ^{17}O signal from the EtOH solvent ($\delta = 6.0$), plus a trace of SiO^*H ($\delta = 36.5$). The 2 equivalents of natural abundance H_2O are not visible. As time progresses a new resonance appears on the high frequency side of the dominant cyclic resonance ($\delta = 85.7$), and can be attributed to those labeled cyclic silsesquioxanes that have undergone further condensation reactions (1A). Note that for this reaction the ^{17}O label is retained within the ring. More interesting is the appearance and increase in intensity of the low frequency resonances corresponding to H_2O^* ($\delta = 0.0$ ppm) and $Si\text{-}O^*H$ ($\delta = 36.5$). The most probable mechanism for the appearance of a ^{17}O label in these different positions and reaction species is scrambling due to a reversible cyclization as shown in (1B). The reversibility is approximately the same time scale as the condensation reaction of the cyclic. Both the ^{29}Si and ^{17}O NMR signal for this propyl bridged alkoxide 1B, $\delta(^{17}O) = 25.0$, were not observed during the condensation reaction, suggesting that the acyclic species (1B) exist at a very low concentration with the equilibrium in (1B) lying strongly to the left.

These results show the utility of ^{17}O NMR to probe the reaction kinetics of during the formation of sol-gel materials, and allows information not easily obtained from ^{29}Si NMR to be realized.

---

[1] This work was supported by the United States Department of Energy under Contract DE-AC04-94AL85000. Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy.

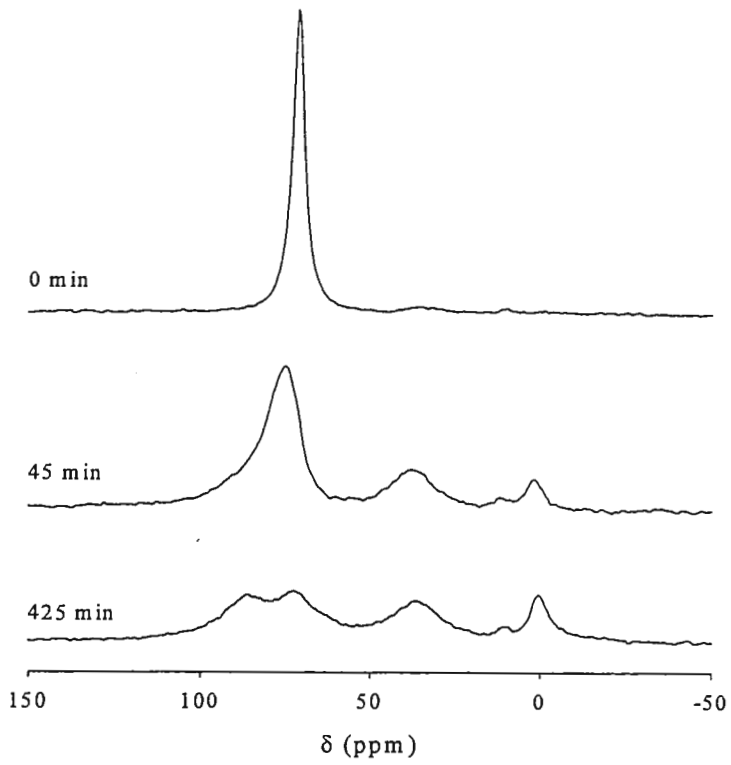


Figure 1. ^{17}O NMR at 54.24 MHz for the acid catalyzed condensation reaction of ^{17}O labeled cyclic disilsesquioxane as a function of time. Spectra were obtained using 64 scan averages, with a 500 ms recycle delay on a standard 5 mm broadband probe. All experiments were performed at 298K. The condensation reaction was initiated by adding 2.0 equivalents of 1N HCl (unlabelled). The ^{17}O label is clearly distributed through various reaction products, including H_2O which can only result from a reversible cyclization reaction.

Todd M. Alam Joseph Carpenter Douglas A. Loy

Forthcoming NMR Meetings, continued from page 1:

6th Meeting of AUREMN (NMR Users Association of Brazil), Rio de Janeiro, Brazil, **12 - 16 May, 1977**; Contact: Snia Maria C. de Menezes, Petrobás/Cenpes/Diquim/Radial 2, Quadra 07 - Ilha do Fundão, 21949-900 Rio de Janeiro, Brazil; Tel. +55 21 598-6171 and 598-6914; Fax. +55 21 598-6296; Email; sonia@cenpes.petrobas.gov.br.

39th Rocky Mountain Conference on Analytical Chemistry, Denver, Colorado; NMR Symposium, **August 4-7, 1997**: Contact: J. P. Yesinowski, Code 6120, Naval Research Laboratory, Washington, DC 20375-5342; 202-767-0415; fax 202-767-0594; email yesinowski@nrl.navy.mil. See Newsletter 458, 8.

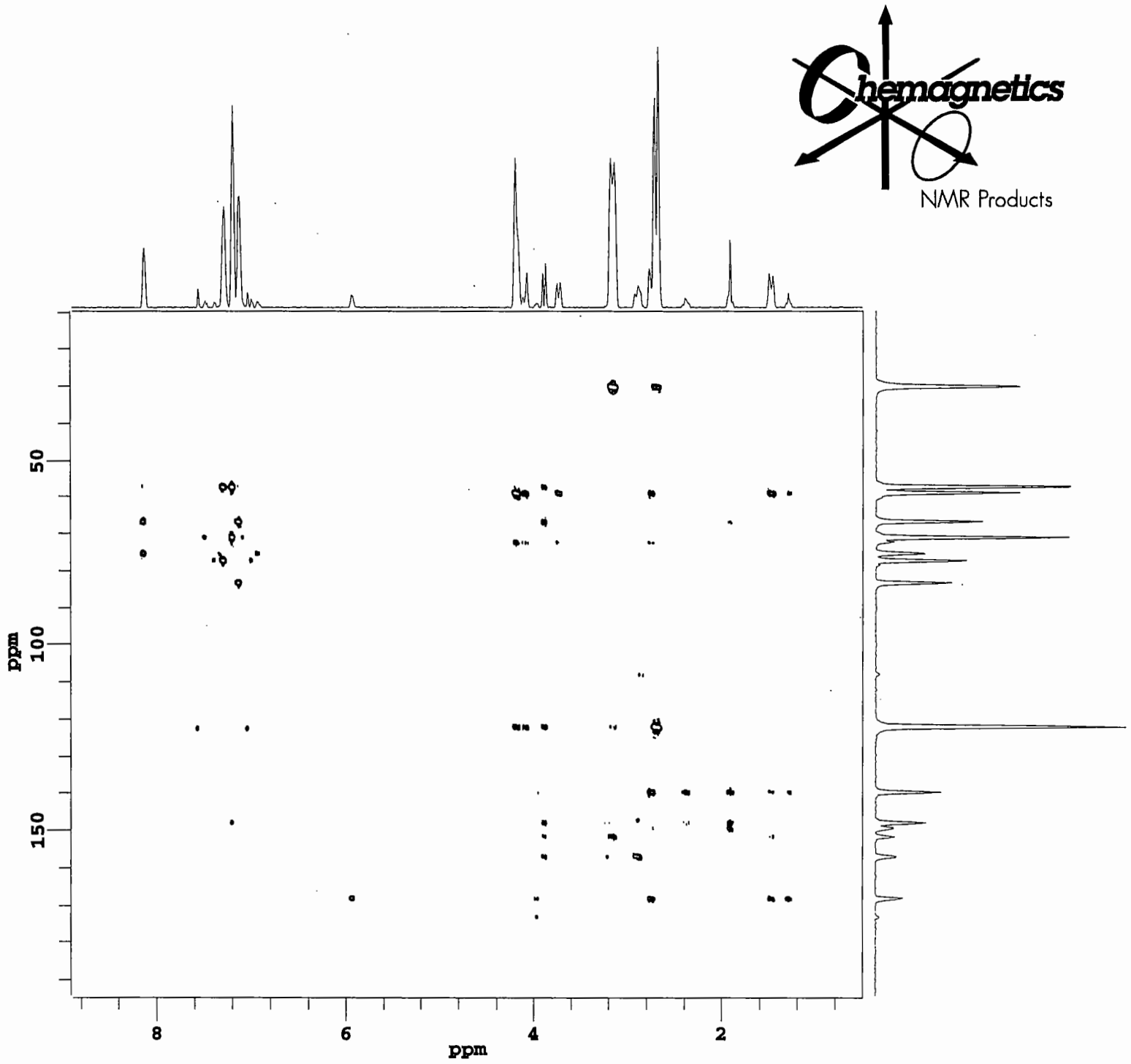
Fourth International Meeting on Recent Advances in Magnetic Resonance Applications to Porous Media, Trondheim, Norway, **Aug. 31 - Sep. 3, 1997**; Contact: John J. Attard, SINTEF Unimed MR-Center, N-7034 Trondheim, Norway. Tel: +47 73 59 89 25; Fax: +47 73 99 77 08; Email:john.attard@unimed.sintef.no;

4th International Conference on Magnetic Resonance Microscopy "Heidelberg Conference in Albuquerque", **Sept. 21-25, 1997**: Contact: E. Fukushima, The Lovelace Institutes, 2425 Ridgecrest Drive SE, Albuquerque, NM 87108-5127; (505) 262-7155; Fax: (505) 262-7043. See Newsletter 449, 37.

Missouri Magnetic Resonance Symposium (MMRS-VIII), Tan-Tar-A Lodge, Lake of the Ozarks, Osage Beach, MO, **October 31, 1997**. Contact: Frank D. Blum, Department of Chemistry, University of Missouri-Rolla, Rolla, MO 65409-0010; 573-341-4451, fblum@umr.edu, http://www.chem.umr.edu/midwest32.html

39th ENC (Experimental NMR Conference), Asilomar ***[sic]*** Conference Center, Pacific Grove, CA, **March 22 - 27, 1998**; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87505; (505) 989-4573; Fax: (505) 989-1073. See Newsletter 460, 41.

Additional listings of meetings, etc., are invited.



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Gradient HMBC of Strychnine

Because it measures long range couplings, HMBC typically exhibits low sensitivity compared to other indirect detection techniques. Even so, this data set of 10% strychnine in d-chloroform was collected in eleven minutes! Two scans per row achieved the signal to noise and lack of t_1 ridges shown here. This clearly demonstrates the huge time advantage of gradient spectroscopy.

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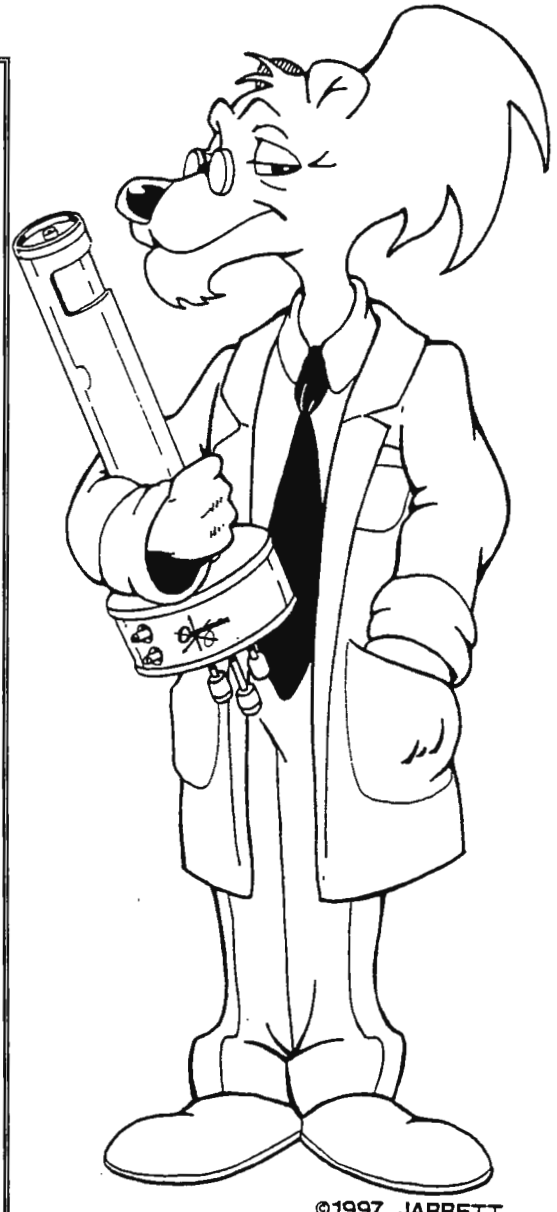

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The NMR Newsletter - Book Reviews

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"Encyclopedia of Nuclear Magnetic Resonance"

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D.M. Grant and R.K. Harris

John Wiley & Sons, Ltd., Baffins Lane, Chichester, West Sussex PO19 1UD, England. Fax: +44-(0)1243-775878. 1996. ISBN 0-471-938718-8, 5,323 pages. £2,250. Vol. 1 is available separately, at £125: ISBN 0-471-958395-5. Also available from John Wiley and Sons, Inc., 605 Third Ave., New York, NY 10158-0012. Tel. 1-800-225-5945. Fax: 212-850-6088. The complete set, US$3,600; Vol. 1, US$225.

It is entirely proper that upon the 50th anniversary of the discovery of nuclear magnetic resonance the publisher John Wiley & Sons should project, complete and publish an eight-volume encyclopedia which encompasses the whole of the field as it has developed over that period. The Wiley people, particularly those in the English branch of the firm, have had a long association with the field through the publication of numerous texts, reference volumes and the journal *Magnetic Resonance in Chemistry* (*née Organic Magnetic Resonance*).

Under the expert editorships of David Grant and Robin Harris the subject has been broken down into five subsections with their respective sub-editors as follows: 1. J.W. Emsley, Inorganic Applications; Polymer and Liquid Crystalline Solutions; Quadrupolar Nuclei; One- and Multi-Dimensional Spectroscopy of Solutions; 2. B.C. Gerstein, Physical Applications; Solid Methods; Solid-State Applications; 3. S.I. Chan, Biological Applications; 4. T.C. Farrar, Instrumentation; Organic Applications; Relaxation Topics; Theory; 5. I.R. Young, Biomedical Applications; Imaging Principles and Applications. The total number of pages, including a detailed index, is 5323. The binding, print style and size, and paper quality are all first class. The eight volumes comprise a handsome set.

Volume 1 (also available separately, *v.s.*) concerns itself with the history of magnetic resonance, starting with an interesting overview written by E.D. Becker, C.L. Fisk and C.L. Khetrapal. Since my introduction to the subject was a lecture by Felix Bloch in a seminar given to the Physics Department of Florida State University in 1954, this introduction was literally déjà vu all over again. As an organic chemist, I couldn't pretend to follow all the nuances of Bloch's lecture, but when the famous slide demonstrating three different types of protons in ethanol was shown, it was evident to a young me that NMR was going to play a very important role in my chosen subject field. Such has certainly proved to be the case.

Following this overview are a series of articles varying from one to several pages by a wide range of investigators, each of whom has made important contributions to the field. These reminiscences are a pure delight to read and offer important insights in how the subject developed over the years. Anyone chosen to make a contribution here may count himself a major player in the NMR field.

continued

Volumes 2 through 8 consist of a series of specialized articles falling within the five major areas noted above. The first article is entitled Abdominal MRA, while the last is Zinc Fingers. Some of these articles attack such specialized areas such as the shimming of high field magnets by V.W. Miner and W.W. Conover, while others give more general overviews such as Cranial Nerves Investigated by MRI by A.N. Hasso and P. Fritzsche. Each volume starts with a list of abbreviations and acronyms followed by a repeat of the initial foreword, a list of symbols and a detailed table of contents. The final volume contains an Imaging and Medical Glossary, a list of contributing authors (34 pages of names) and a detailed index (32 pages).

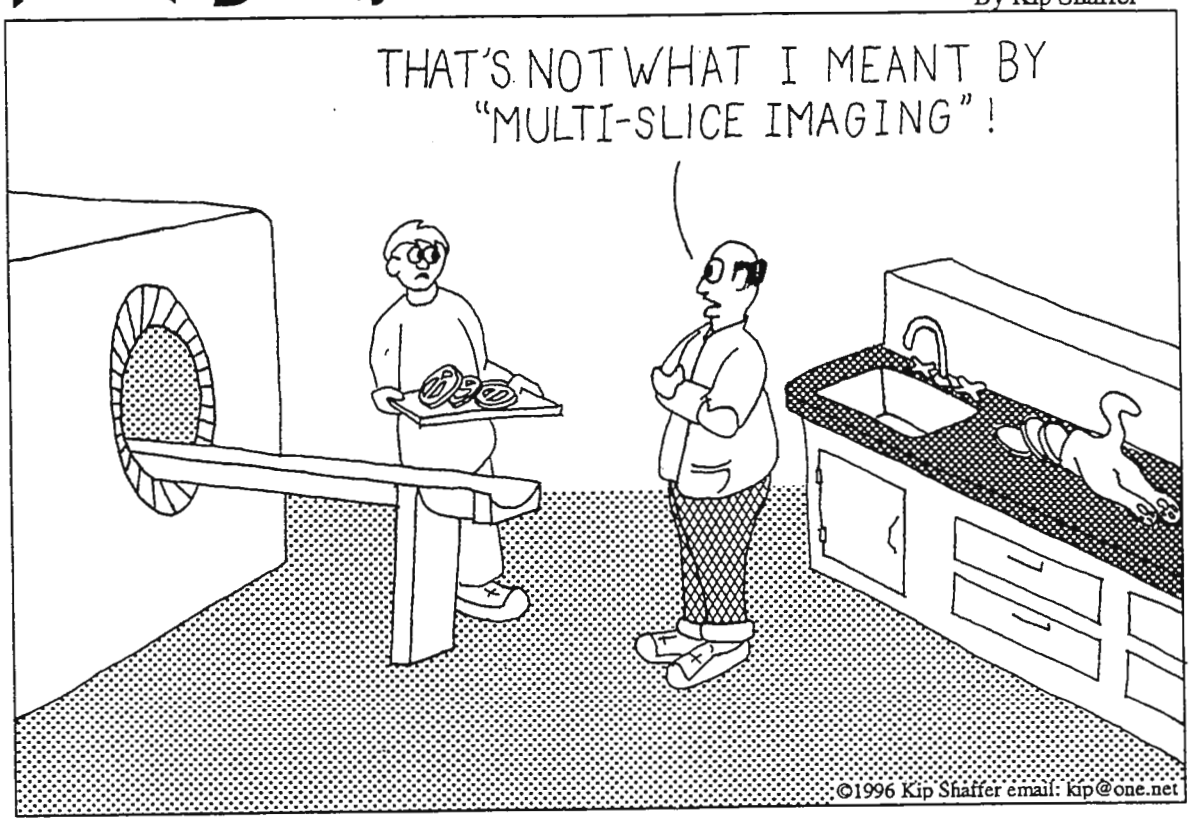
The Editors and Contributing Authors as well as the publishers all deserve our thanks for a job well done. The monumental task of the final copy editing was done by P.M.E. Lewis, the erstwhile and originating Editor-in-Chief of *Organic Magnetic Resonance* and *Magnetic Resonance in Chemistry*. If there are typos remaining, I did not find them.

As my colleague, Dave Minter, pointed out after browsing several volumes. Every school offering Ph.D.'s in science ought to have this set at hand. I would think this to be true of all research laboratories where magnetic resonance plays a role. Specialized reference texts are made passé by these volumes.

WBS

Field of Dreams

By Kip Shaffer



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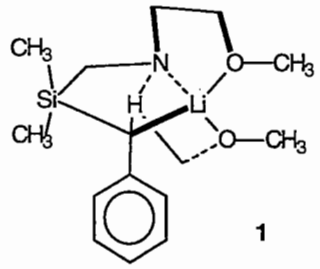
February 20, 1997 (received 2/21/97)

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

Diastereomerically Selected Benzylic Lithium Compound

Dear Barry:

As is well known NMR has not been a good technique for investigating ion-pairing since fast exchange of ions among ion-pairs averages shifts among the different species present. Lately, in experiments to slow down this process we prepared different allylic and benzylic lithium compounds with pendant ligands in the hope that encapsulation of lithium would slow down its exchange rate and thus reveal NMR of the ion-pairs unperturbed by dynamic effects, for example **1** and **2**. Needless to say such compounds have always been regarded as conjugated lithium carbanide salts.



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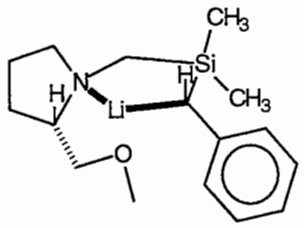

2

Reality is often more surprising than what one imagines. Several of these compounds display at low temperature one bond ^{13}C, ^{6}Li coupling of 2 to 4 Hz (for the first time), implying small detectable C, Li covalence with associated "s" character, so, these are not ion-pairs at all. That ^{13}C, ^{6}Li coupling is observed in the first place is because encapsulation of lithium slows down its interspecie exchange rate.

The small value of monomeric $^{1}J(^{13}C, ^{6}Li)$ is another anomaly. For reasons which have never been properly explained a wide variety of RLi species (R = aryl, vinyl, alkyl, alkynyl) display $^{1}J(^{13}C, ^{6}Li)$ values of 16 Hz - quite independent of the nature of the organic moiety. Accepting the approximations of Karplus, Grant, Lichtman theory one is forced to conclude that the "s" character associated with these C,Li bonds in these compounds is inversely related to the bond order or covalence. What a coincidence! Something for the theoreticians. Details: All carbons in compound **1** are magnetically non-equivalent at 200 K, supporting the proposed structure. With increasing

temperature averaging of the two methoxy ^{13}C resonances as well as pairs due to $^{13}CH_2O$ and NCH_2CH_2 to single lines at their respective centers provided the dynamics of rotation of coordinated lithium around the Si-C(benzyl) bond i.e. between two sides of the benzyl plane. These two rotamers are enantiomeric.[1]

In the case of **2**, incorporating a 2S-methoxymethylpyrollidino group the two rotamers around the Si-e(benzyl) bond are diastereomeric. At 190 K, with slow rotation around this bond ^{13}C NMR displays just one set of shifts; a second rotamer is not detected by NMR. This explains why Chan (McGill) obtained ca 99% enantiomeric excess in products of reactions of **2** which generated new chiral centers.[2] Interestingly reagent **2** made from racemic 2-methoxymethylpyrollidine which could take the form of four stereoisomeric rotamers around the Si-C(benzyl) bond gives only one set of resonances, with the same shifts as 2(2s). Clearly these come from the enantiomeric pair one of which is 2(2s).

Best wishes for the New Year.
Yours sincerely,

Gideon Fraenkel
Professor of Chemistry

Jinhai Wang
Postdoctoral Researcher

GF/ds

1. Fraenkel, G.; Martin, K. *J. Am. Chem. Soc.*, **1995**, *117*, 10336-10344.

2. Chan, T.H., Pellon, P. *J. Am. Chem. Soc.*, **1989**, *111*, 8737-8739.

"We trained hard, but it seemed that every time we were beginning to form into teams, we would be reorganized. I was to learn later in life that we tend to meet any new situation by reorganizing, and a wonderful method it can be for creating the illusion of progress, while producing confusion, inefficiency and demoralization."

- Gaius Petronius AD 66

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750	51	15	60	3.8	29	45
600	51	10	150	3.4	28 or 40	40
500	51	10	150	3.1	28 or 40	40
400	54	8	365	2.9	23	45
300	54	3	365	2.9	23	45
270	54	2.7	365	2.9	23	45
200	54	2	365	2.9	23	45
100	54	1	365	2.9	23	45
600	89	12	90	3.4	18 or 26	73
500	89	15	120	3.4	18 or 26	73
400	89	10	180	2.9	18 or 26	73
300	89	3	365	2.9	18 or 26	73
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LABORATOIRE DE RESONANCE MAGNETIQUE NUCLEAIRE
METHODOLOGIE ET INSTRUMENTATION EN BIOPHYSIQUE
CNRS UPRESA 5012

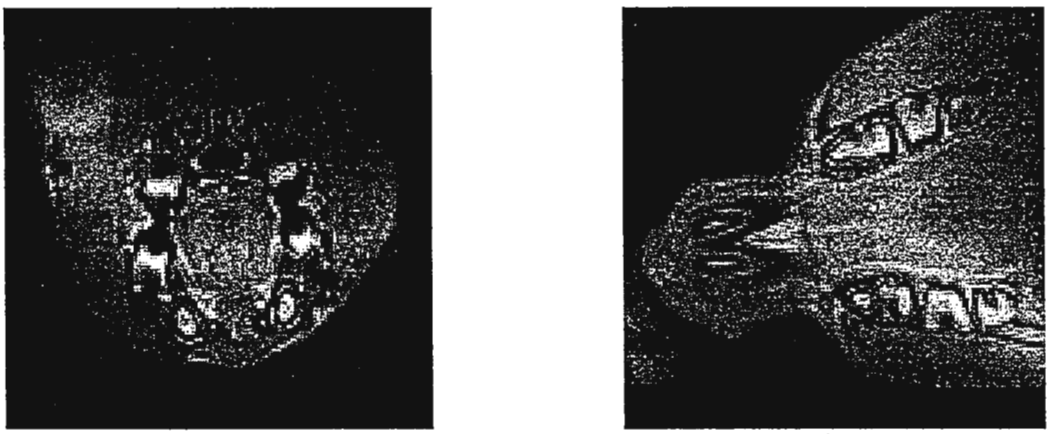
January 22th, 1997
(received 2/4/97)

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

***In vivo* dental imaging**

Dear Dr. Shapiro,

We have recently employed high spatial resolution MRI to observe the dento-maxillary structure of the rat. Images were performed at 2T using an Oxford 85/310 superconducting magnet with a 50 mT/m maximum capability shielded gradient and a S.M.I.S. Surrey II console. A three week old rat mandible placed above a half birdcage RF coil permitted us to obtain multi-orientation images using spin-echo imaging sequences. We could easily observed the pulp of all teeth. The periodontal ligament embedding the molars and incisors calcified tissues could be clearly seen.
The use of a well established imaging technique for the dental region is now used on animal models (rat and dog) and employed by people of our faculty for dentistry. High resolution MRI technique seems suitable to visualize the buccal area and it may represent a useful tool for diagnosis of dental diseases.



a **b**

Figure 1 : High resolution magnetic resonance image of the dental system in a young rat (FOV = 1.8 x 1.8 cm^2; in plane resolution 140 x 140 μm^2; slice thickness : 0.7 mm).
(a) Transverse view in the middle of the first molar. (b) Coronal view at the crown level.

Sincerely yours,

Olivier Beuf Michèle Lissac André Briguet

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Symposium and Training:

^{13}C in Metabolic Research

THE UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER AT DALLAS
Thursday, May 8, 1997

This program is aimed at faculty, fellows and students using or considering ^{13}C NMR or ^{13}C mass spectrometry for metabolic studies. The morning session is an introduction to ^{13}C NMR isotopomer analysis, metabolic questions which can be answered, factors in experimental design and interpretation, and analysis of ^{13}C NMR spectra. Software needed for both experimental analysis and simulation will be demonstrated. In the afternoon session, the guest faculty will review current applications of ^{13}C for metabolic research.

PROGRAM SCHEDULE

7:45 **On Site Registration**

TRAINING: INTRODUCTION TO ^{13}C NMR ISOTOPOMER ANALYSIS FOR METABOLIC STUDIES

8:15 **Designing the Question and the Experiment** *Craig R. Malloy, M.D.*

9:00 **Cardiac Metabolism by ^{13}C NMR: Kinetics and the Non-Steady State Experiment** *A. Dean Sherry, Ph.D.*

9:45 **Hepatic Metabolism and Complex Pathways by ^{13}C NMR: the Steady-State Experiment** *F. Mark Jeffrey, D.Phil.*

10:30 **Break**

10:45 **Participants' Presentations and Discussion**

12:00 **Adjourn**

SYMPOSIUM: ^{13}C NMR and ^{13}C MASS SPECTROMETRY IN METABOLIC RESEARCH

1:00 **Magnesium Regulation in Erythrocytes Studied by ^{13}C NMR** *Maren Laughlin, Ph.D.*

2:00 **^{13}C Mass Spectrometry for Metabolic Analysis *In Vivo*** *Robert Wolfe, Ph.D.*

3:00 **Break**

3:30 ***In Vivo* ^{13}C MRS in Clinical Research** *Rolf Gruetter, Ph.D.*

4:30 **Quantitative Analyses of High Resolution NMR Spectra** *Paul A. Keifer, Ph.D.*

5:30 **Wine and Cheese Reception at the A. W. Harris Faculty Club**

6:30 **Buffet Dinner at the A. W. Harris Faculty Club**

7:15 **The Human Radiation Experiments: the Future for Radioisotopes in Clinical Investigations** *Bernard Landau, M.D., Ph.D.*

TRAVEL AWARDS

Limited funds are available for students, fellows and young faculty with strong interest in biological ^{13}C NMR. Awardees must actively participate in the morning training session. For more information, please contact Navin Bansal, Ph.D., at (214) 648-5887.

REGISTRATION

The regular advance registration fee is $80. Advance registration for students, fellows and residents is $35. In order to facilitate planning, the last day for advance registration is May 1, 1997. Late and on-site registration fee is $95 ($50 for students and fellows). The coffee break, reception and buffet dinner are included in the registration fee. No money will be refunded if registration is canceled after May 5, 1997. For more information, please contact Ms. Jean Cody tel.: (214) 648-5886, fax: (214) 648-5881, email: jcody1@mednet.swmed.edu, or visit our WWW homepage: http://www.swmed.edu/home_pages/rogersmr or call Ms. Dolly Christensen at (214) 648-8013.

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Resolution at 50% 1% $CHCl_3$ 5 mm spinning	< 0.45 Hz
Lineshape 1% $CHCl_3$ 5 mm non-spinning	
at 0.55%	< 6 Hz *
at 0.11%	< 12 Hz *
Spinning Sidebands	< 1%
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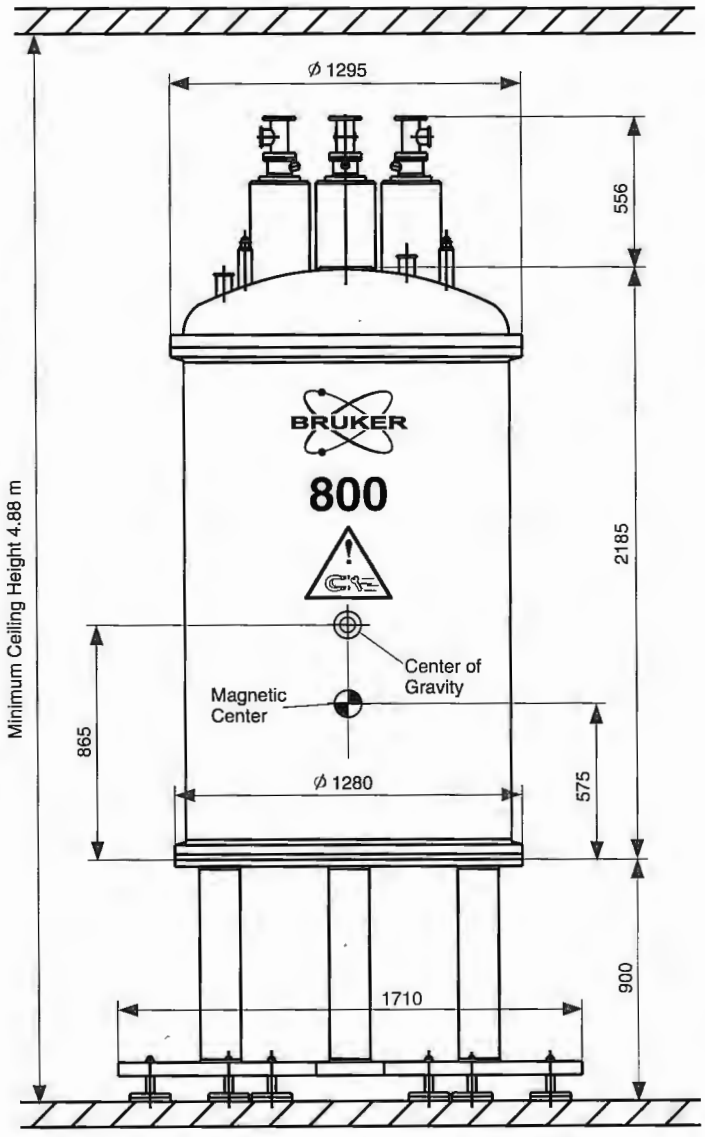

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29.01.1997
Marburg, den 285520

(received 2/10/97)

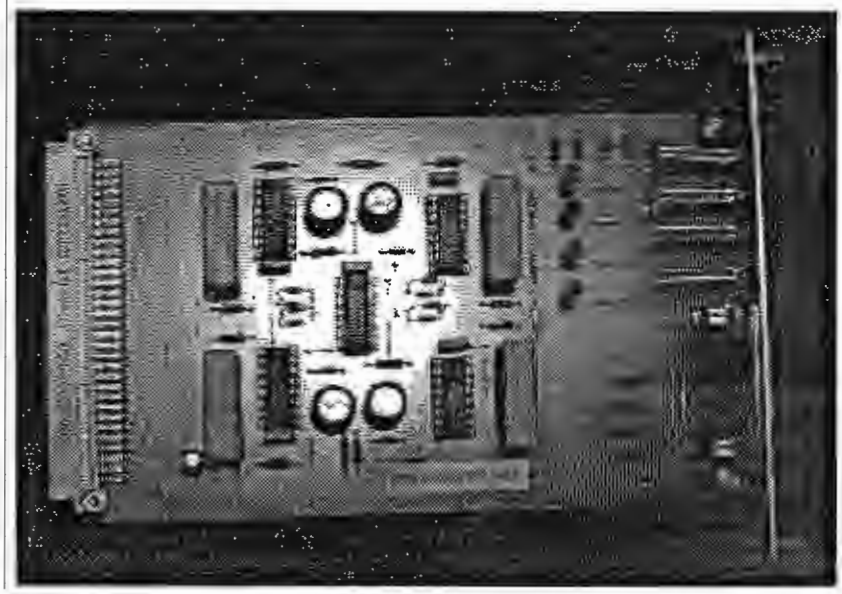
Prof. Dr. B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CAL. 94303
USA

The NMR Fan Project

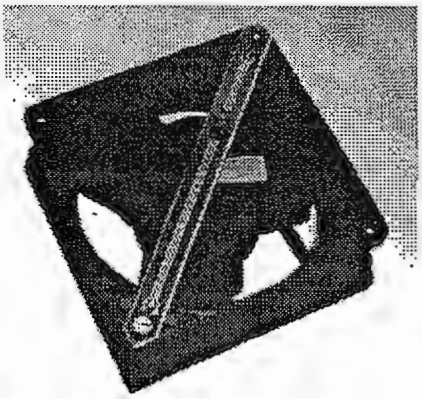
Dear Barry,

In 1987 F. H. Köhler communicated in this precious journal (349-16) an excellent idea, how to protect NMR instruments against the malfunction of fans. Indeed, it is our experience, that major costs in maintaining NMR spectrometers arise ultimately from fans which get stuck after about 4-5 years.
We have therefore decided to build controlling devices for all four of our instruments (Bruker ARX-200, AC-300, AM-400 and AMX-500) and have now finished in fitting all of the fans (approx. 100) of these instruments with optoelectronic devices which report failure of the turning rate to a control unit for each spectrometer. In general, our electronics people followed the outline published by Köhler; in detail, however, many changes and some more modern devices were used.
A typical board which controls four fans is shown in the photograph along with a modified fan and also a picture of the central control unit is given. The costs to refit one spectrometer completely with such a fan control amounts to about 1000 DM, not including development and labour.
A more detailed account, including schematics, can be reached via my home page (http://sg1508.chemie.uni-marburg.de/~stb/stb.html), or directly on the home page of our electronic shop (http://www.chemie.uni-marburg.de/~ewfb15/fan/fanpro.html). The device has already saved us twice from major trouble.

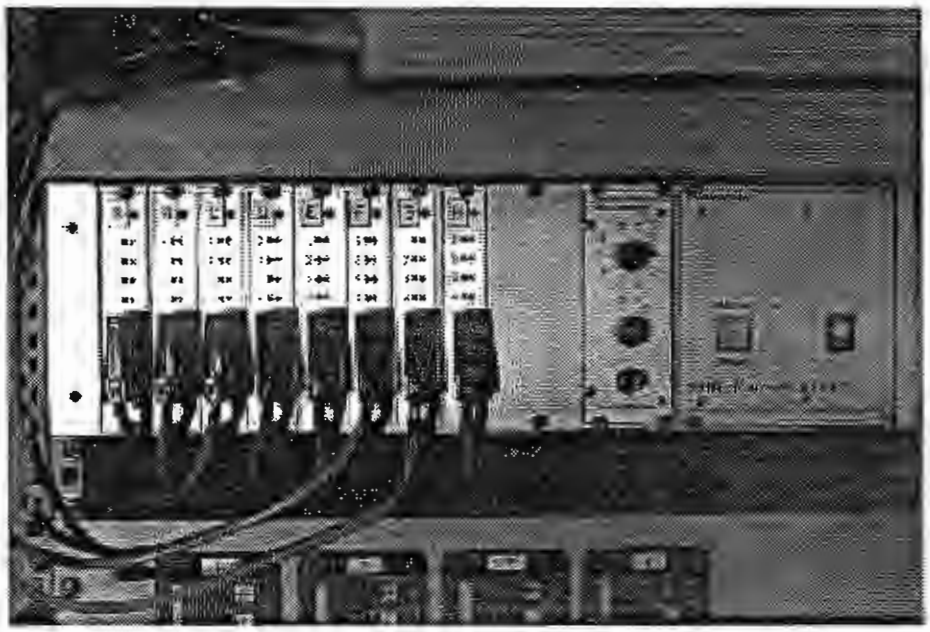
[S. Berger] [H. Ruhwedel] [M. Riehl]



Electronic board to control 4 fans



Spectrometer fan fitted with the turning rate detector



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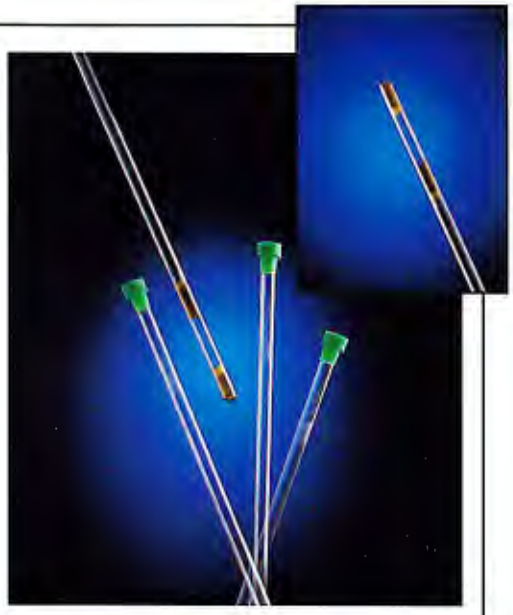

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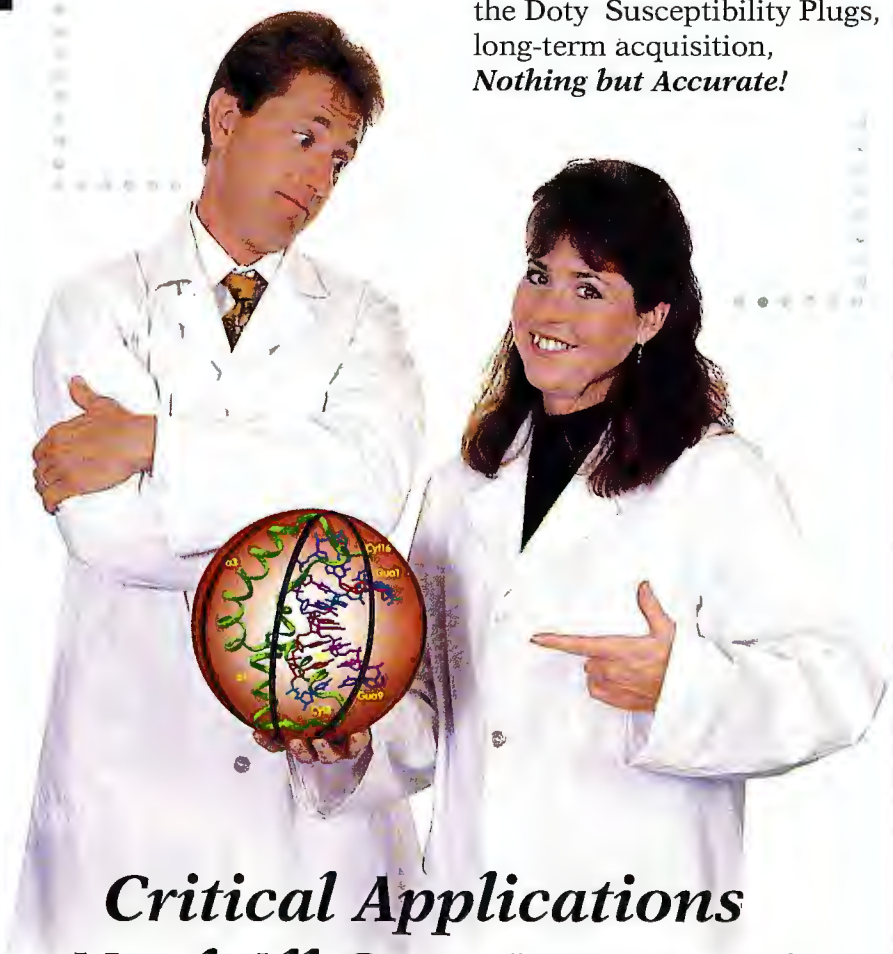

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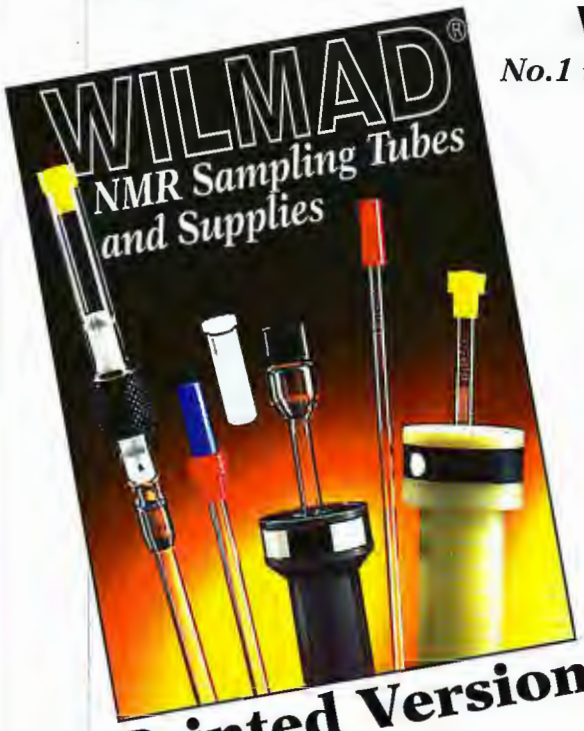

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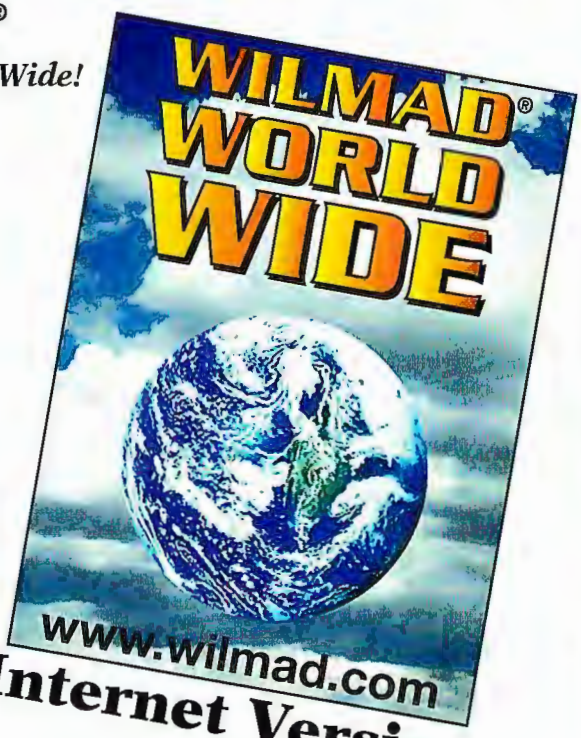

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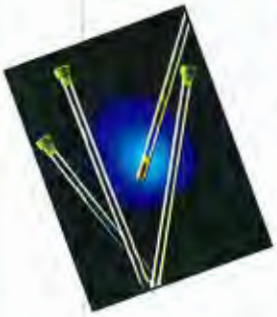

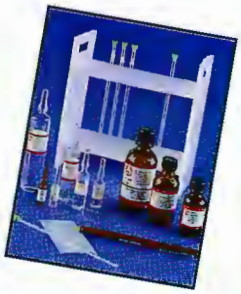

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February 12, 1997 (received 2/14/97)

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

Protein Dynamics Delineate Binding Interactions of Stromelysin Ligands

Dear Dr. Shapiro:

Matrix metalloproteinases, including stromelysin, are involved in tissue remodeling and connective tissue degradation associated with certain pathological conditions including cartilage degradation in arthritis and tumor progression and metastasis. Inhibitors of this class of enzyme may have therapeutic value in the treatment of these diseases. The catalytic domain of human stromelysin has been used as a target protein in the discovery of inhibitors to the enzymes. Stromelysin has an extended active site centered around the catalytic zinc atom. Ligands can potentially bind to stromelysin in the left or the right side of the active site. We have used NMR spectroscopy to study a variety of ligands, representative of both binding orientations.

We have studied the dynamics of stromelysin complexed with representative ligands of each group. The pulse sequences used to record ^{15}N R_1, R_2 and steady-state $^{15}N\{^1H\}$ NOE were modifications of those described previously [1] to include pulse field gradients for artifact elimination, coherence selection and solvent suppression. As an example, the relaxation rates of stromelysin/PNU-99533 (a right-side binding ligand) and stromelysin/PNU-107859 (a left-side binding ligand) were analyzed following the procedures developed by others [2] to extract order parameters for each backbone nitrogen atom. Differences in the order parameters obtained for the two complexes are plotted as a function of residue number in Figure 1.

Distinctly different dynamics profiles were observed for each complex. Since the two ligands had previously been found to bind to stromelysin in different sides of the active site cleft, this was not unexpected. In the stromelysin/PNU-107859 complex, backbone nitrogen atoms of residues that are located in the empty right side of the active site have significantly high mobility with low order parameters, including T108, T109, G110, A131, Y141, H142 and D146. In contrast, these same residues demonstrated highly restricted internal motion in the stromelysin/PNU-99533 complex, indicating that ligand binding causes the right side of the active site to become rigid. Interestingly, those residues that interact with PNU-107859 in the left side of the active site, including Y73, A83, H84, A87, N93, H119, E120, H123 and F128, had virtually identical order parameters in the presence or absence of ligand. Thus the left side of the active site is relatively well formed with less flexibility

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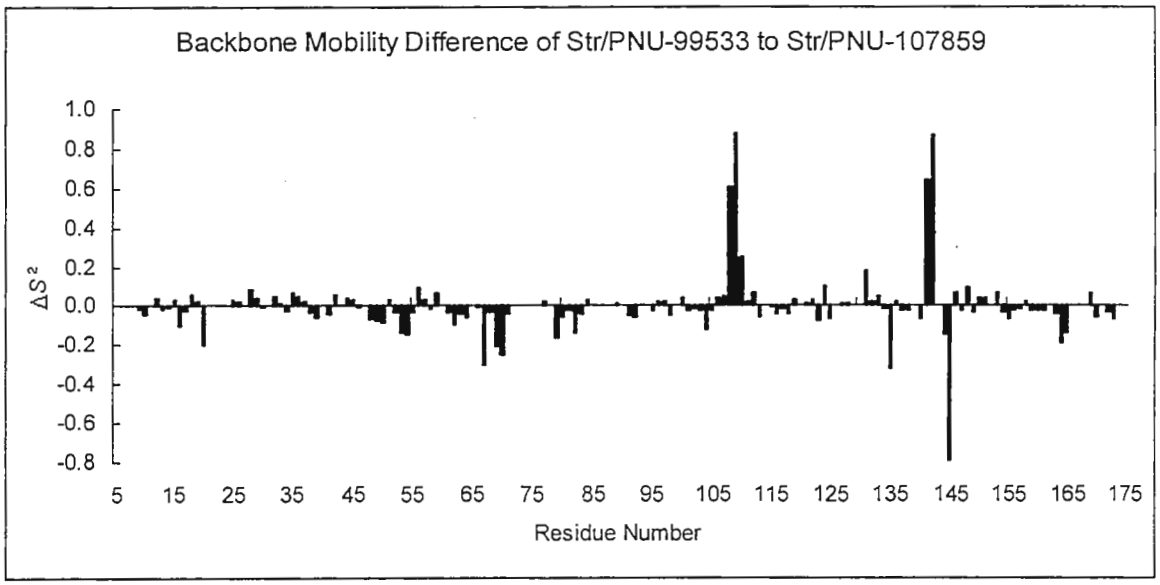
Figure 1



than the right side of the active site. These observations provide useful information to the structure-based drug design process.

1. Barbato, G., Ikura, M., Kay, L. E., Pastor, R. W. & Bax, A. (1992) *Biochemistry 31*, 5269-5278.

2. Mandel, A. M., Akke, M. & Palmer, A. G. III (1995) *J. Mol. Biol. 246*, 144-163.

Peng Yuan Brian Stockman

Please credit this contribution to the account of Dr. Paul Fagerness.

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

January 30, 1997
(received 2/7/97)

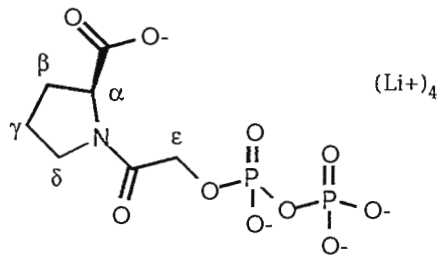
Effects of Magnesium on Cis-Trans Isomerization of a Proline phosphonate

Dear Professor Shapiro:

Conformational studies of compound 1, a potent inhibitor of mevalonic acid pyrophosphate decarboxylase, were performed. COSY, ROESY and HMQC spectra were acquired for the compound. From 1D ^{1}H and 2D COSY spectra, two sets of resonances were observed which indicated that the compound exists in conformational equilibrium in water solution. A ^{1}H-^{13}C HMQC experiment showed the existence of two sets of distinct carbon resonances which indicate a cis and trans isomerization of the glycolyl group about the proline ring.

The ROESY spectrum showed cross peaks between delta protons (δ) of the proline ring and methylene protons (ε) of the glycolyl group in both the cis and trans form (figure 1). Upon addition of $MgSO_4$ to compound 1, ROE cross peaks between the delta protons (δ) of the proline ring and the methylene protons of the glycolyl group (ε) were only observed for the trans form (figure 2).

These results suggest a rapid equilbrium between the cis and trans form where magnetization between δ protons and ε protons is transferred from the trans to cis conformer. Addition of magnesium sulfate however, slows the interconversion between the cis and trans isomers hence ROE buildup is only observed between δ and ε protons in the trans form.



1

Sincerely,

Xiaolu Zhang, Ph.D.

Nina C. Gonnella, Ph.D.

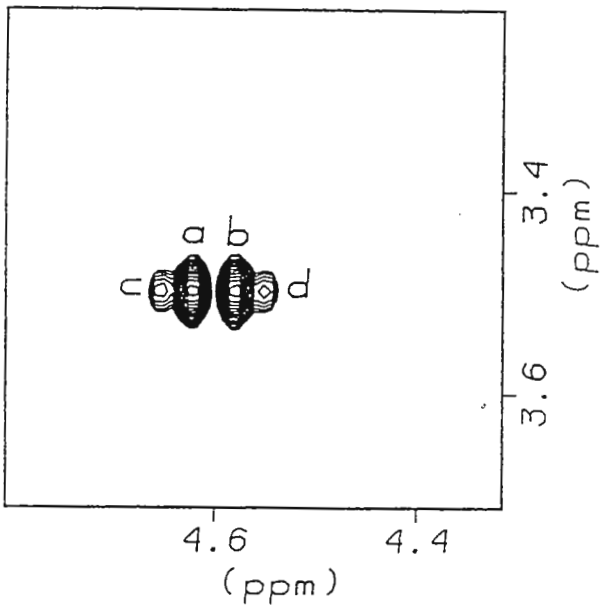


Figure 1. Expanded 500 MHz ^1H-^1H ROESY spectrum of compound 1 in D_2O solution at 30°C. A spin-locking mixing time was 200ms. The cross peaks a and b are between the glycolyl methylene group (4.62 and 4.58 ppm) and the proline $C^{\delta}H_2$ (3.50 ppm) in the *trans* form, and c and d are between the glycolyl methylene group (4.65 and 4.54 ppm) and the proline $C^{\delta}H_2$ (3.50 ppm) in the *cis* form.

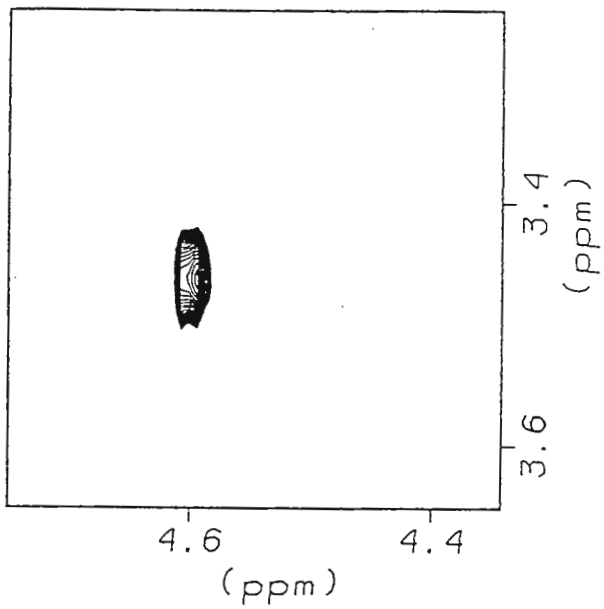


Figure 2. Expanded 500 MHz ^1H-^1H ROESY spectrum of compound 1 with $MgSO_4$ in D_2O solution at 30°C. A spin-locking mixing time was 200ms. The cross peak is between the glycolyl methylene group (4.59 ppm) and the proline $C^{\delta}H_2$ (3.46 ppm) in the *trans* form.

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- Thermal
- Blanking

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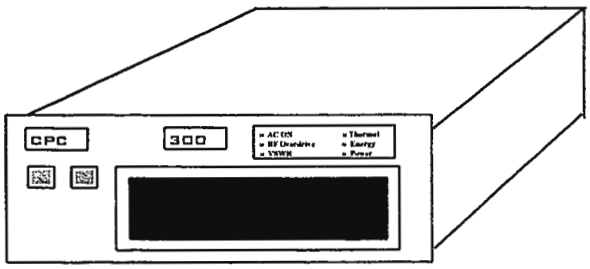

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Imaging of Velocities in Water Surface Waves

Dear Barry,

recently we were inspired by engineers to think about NMR imaging of flow in waves on the surface of a liquid. Such results will be very important for the design of cooling devices etc., especially if the liquid consists of two different chemical phases.

We came up with a design, that uses a little coil on top of a paddle made from a polymer film light enough to swim on the water surface of a half-filled tube (cf. Fig. 1a). If an AC (f = 1 - 10 Hz) current is fed into the coil it starts to swing like a loudspeaker membrane in the magnetic field of the NMR magnet. This vibration stimulates surface waves which are phase locked to the AC. Therefore, traveling water „hills" and „valleys" appear stationary if triggered by the AC and can be followed by variation of a mixing time prior to imaging (cf. Fig. 1b).

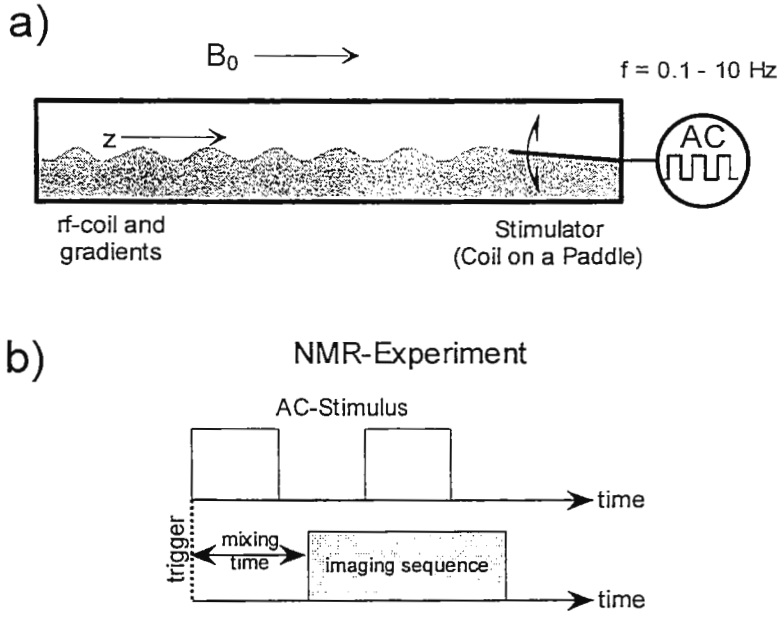

Fig. 1a) Experimental setup designed for a horizontal bore magnet. 1b) NMR imaging sequence triggered by the AC stimulation.

By incrementing the mixing time in a constant fashion a simple 1D NMR image along the tube axis (z-direction) or the moving direction of the waves displays the modulation of the water surface. This is shown in Fig. 2 where the periodicity of the waves can clearly be recognized. However, the simple „sine"-like modulation is overlayed by more complex features which are probably due to overtones induced by the paddle and to wall reflections.

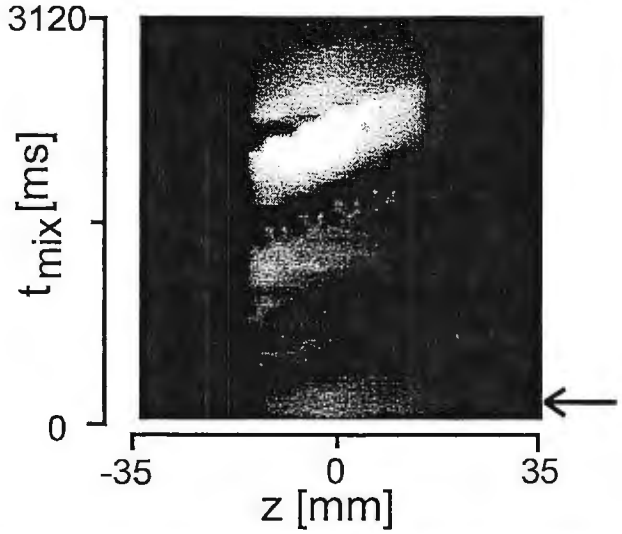

Fig. 2: 1D images along the z-axis for different mixing times. The AC-stimulation frequency was set to 1.5 Hz. The increase in intensity for long mixing times is a T_1 artifact due to a insufficiently short recovery delay.

This experimental setup allows to investigate different „snapshots" of a moving surface wave. For instance, a chemical-shift selective image could discriminate the motion of water and an oil layer on top.

The aim of this project is to measure flow velocities in different stages of such waves. Thus, a flow-compensated, flow-encoding sequence [1,2] was triggered, so that velocities in a „hill" of a wave were detected. The result is shown in Fig. 3. It can clearly be seen in the velocity vector plot, that the main movement of water is close to the surface and that its main direction is perpendicular to the surface. This is of course necessary, because the water has to move upwards to form a „hill". However, more complicated situations can be envisioned and will be investigated.

Sincerely,

B. Blümich

P. Blümler

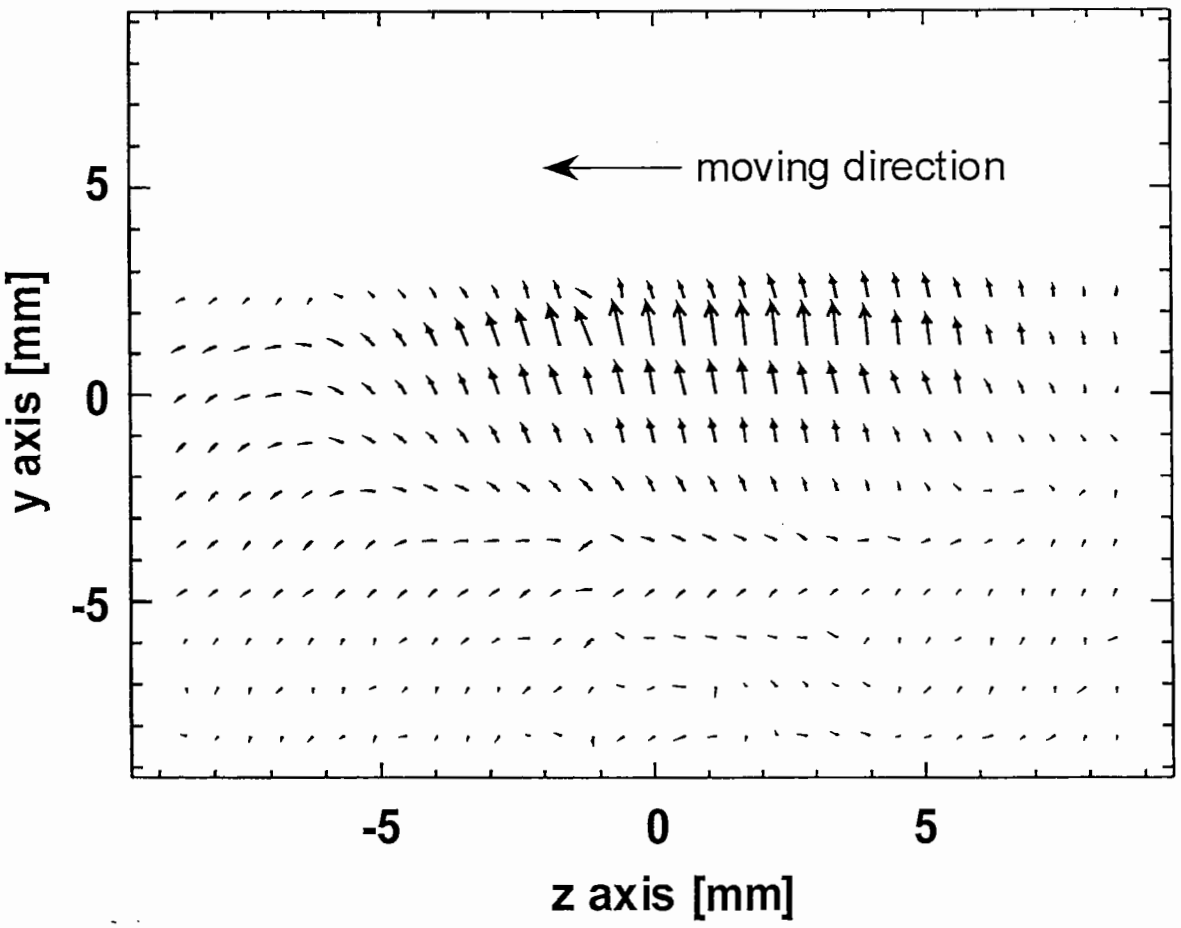

Fig. 3: Velocity vector plot measured in a wave „hill" by an NMR flow-encoding sequence [2]. The imaging sequence was triggered at the mixing time indicated by an arrow in Fig. 2. The artifact in the center is caused by a DC offset. Intensities (noise) from the image background have been removed for this representation (blank space above to water signal).

References:

[1] J. M. Pope and S. Yao, *Concepts Magn. Reson.* **5** (1993) 281-302.

[2] S. Laukemper-Ostendorf, K. Rombach, P. Blümler, and B. Blümich, *Bruker Application Note* (1997) in press.

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Agenda includes:

The Role of NMR in the Study of Drug Metabolism.
John Shockcor, John Lindon and Jeremy Nicholson, Glaxo Wellcome

Carbon 13, A Renaissance?
Andy Roberts, Duncan Farrant and Philip Sidebottom, Glaxo Wellcome

Liquid Phase Combinatorial Chemistry and Characterization of Intermediates by Routine Solution State NMR.
Ron Kim, Mahua Manna, Steve Hutchins and Kevin Chapman, Merck & Company

Experimental Aspects of Advanced Diffusion Measurements with PFG NMR.
Donghui Wu, Aidi Chem and Charles S. Johnson, Jr., University of North Carolina

Evaluation of Superconducting Probes and Preliminary Results for Biomacromolecular, Metabolite and Natural Product Compounds.
R. Andrew Byrd and Siddhartha Sarma, NCI-FCRDC
John Shockcor, Glaxo Wellcome
Gary Martin, Pharmacia & Upjohn, Inc.
Ernest W.-H. Wong, Conductus, Inc.
Ron Crouch and Toby Zens, Nalorac Corporation

Structure Determination of Proteins in the 30 kD Range and New Methods for Determining Long Range Order.
G. Marius Clore, National Institutes of Health

High Field Offers More Than High Resolution and Sensitivity.
Ad Bax, National Institutes of Health

Quadruple Resonance Probes - New Tools for Biological NMR.
Arthur Pardi, University of Colorado
Gershon Wolfe and Brian Marsden, Nalorac Corporation

Advances in Solution State NMR Probe Performance.
Toby Zens and Gershon Wolfe, Nalorac Corporation

Application of $^{1}H/^{31}P/X$ Triple Resonance Experiments in Organometallic Chemistry.
Emilio Bunel, E.I. DuPont

$^{1}H/^{13}C/^{29}Si$ Triple Resonance Heteronuclear 3D NMR of Organosilicon Compounds at Natural Abundance.
Peter Rinaldi, University of Akron

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Heart, Lung, and
Blood Institute
Bethesda, Maryland 20892

(received 2/21/97)

February 18, 1997
James A. Ferretti
Bldg. 3, Room 412
MSC-0380
NIH
Bethesda, MD 20892-0380

31-P CHEMICAL SHIFT ANISOTROPY IN ATP

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

Dear Barry,

Thanks for the yellow reminder as well as the phone call. Our primary (and almost only) interest these days is in protein-DNA recognition with specific application to homeodomain containing proteins. However, in collaboration with Terry Stadtman, also of NHLBI, we are carrying out studies on the stereospecific enzyme catalyzed incorporation of oxygen-18 into ATP. Needless to say, carrying out the necessary controls is never as straight forward as one hopes. In the process of setting up to carry out these experiments, I ran the spectrum of sodium adenosine triphosphate (ATP) just to determine the usual experimental parameters on our AMX600 using a broadband inverse detection probe. The sample was made up to 5 mM concentration in ATP and the pH was adjusted to 7.2 (no buffer). I added a five fold excess of EDTA (after running some spectra before adding the EDTA) until I reached constant linewidth. After spending the requisite amount of time shimming I ran an ordinary one-pulse experiment. I noticed immediately that the intensity of the resonances of the gamma-phosphorus was only one third the intensity of the corresponding resonances of the alpha and beta phosphates. To confirm that this was not a case of incomplete relaxation (even though I already confirmed that the integrals for the three phosphates were the same), I increased the delay time from 3s to 10s and repeated the experiment with the same result.

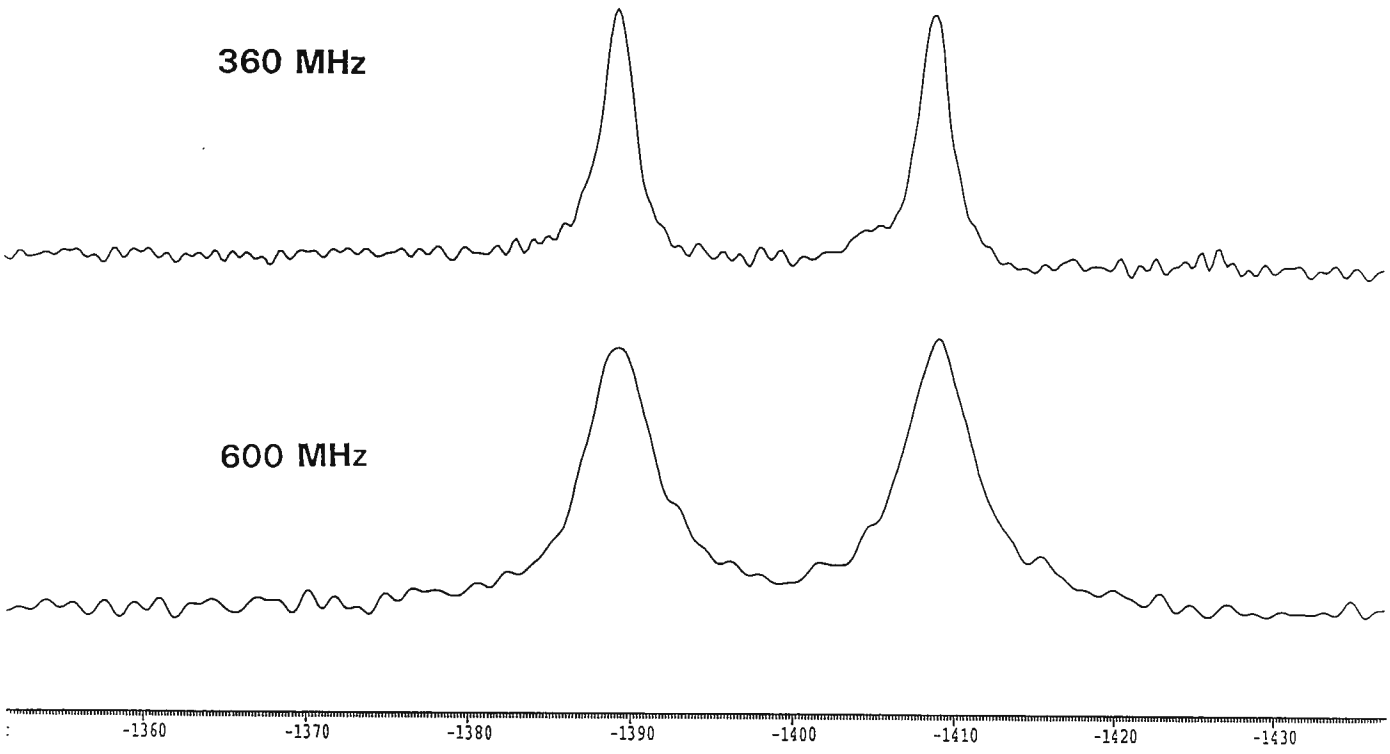
At that point I became somewhat curious and took the same sample tube and I ran the same experiment under the same conditions (T = 320 K) on our AMX360 again with a broadband inverse detection probe. At 360 MHz the intensity of the gamma resonances were much closer to those of the alpha and beta resonances. I then carefully measured the linewidths of the resonances at both 360 MHz and 600 MHz. They were 5.4 Hz and 1.6 Hz for the gamma and beta resonances, respectively at 600 MHz and 2.6 Hz and 1.4 Hz for the same resonances at 360 MHz (see figure). I did not use the alpha resonances since the protons were noise decoupled and I did not want to deal with any residual broadening. The digital

resolution in both cases is about 0.3 Hz/point.

The interpretation of this observation is not too difficult. The excess broadening of the gamma resonances over the beta resonances 3.8 Hz and 1.2 Hz at 600 MHz and 360 MHz, respectively. If this excess broadening represents a measure of the chemical shift anisotropy contribution to T_2, then one would expect an increase in the excess broadening to be about 2.8 (the ratio of the square of the field strength), and the observed ratio is 3.2, which is quite close given the various random and digital sources of error. The surprising point here is that Un and Klein in 1989 reported the components of the chemical shielding tensor in single crystals of salts of bis(2-pyridyl)-amine - ATP complexes and found that the chemical shift anisotropies were larger for the alpha and beta phosphorus atoms than for the gamma phosphorus atom. The results described here clearly demonstrate that in solution the shift anisotropy is larger for the gamma phosphorus of ATP. I do not know if this result will be of any consequence for people studying phosphate metabolism *in vivo*. However, it does point out that one might be in for some surprises as we move to higher magnetic field strengths.

Best regards,

James A. Ferretti



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at 8:15 PM

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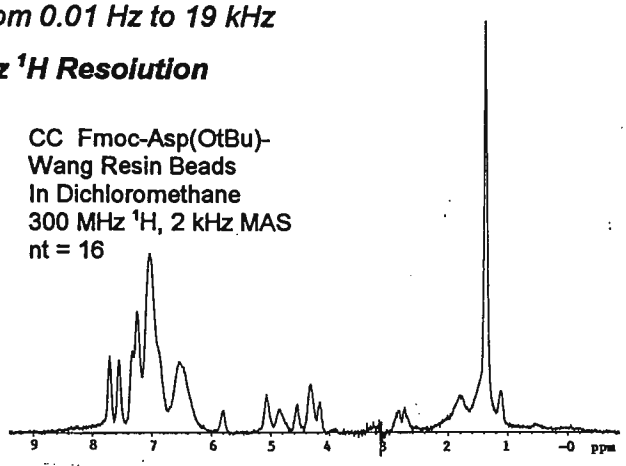
CC Fmoc-Asp(OtBu)-
Wang Resin Beads
In Dichloromethane
300 MHz ^{1}H, 2 kHz MAS
nt = 16



Low-Cost Upgrade Options (at time of probe purchase or later):

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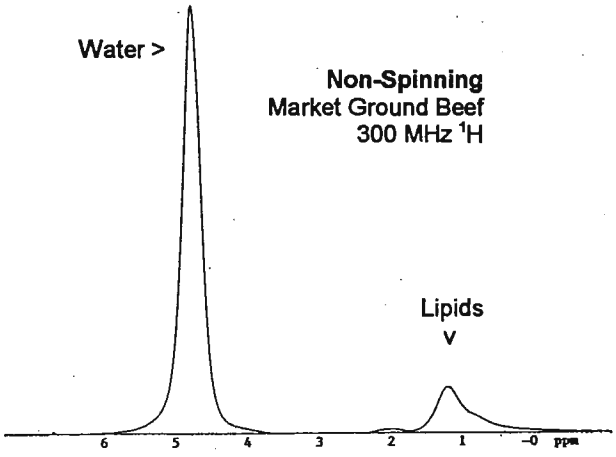
Water >

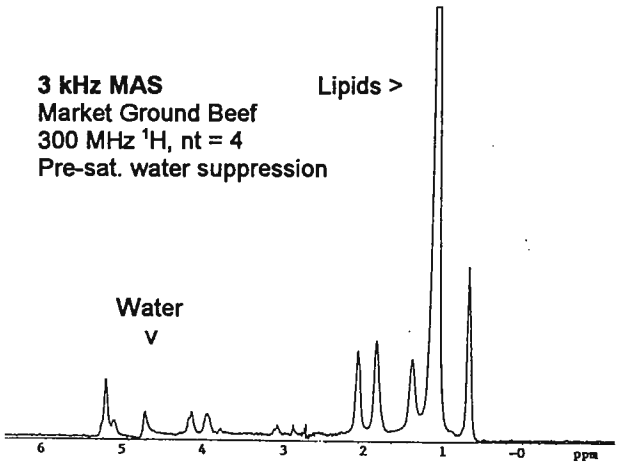
Non-Spinning
Market Ground Beef
300 MHz ^{1}H

Lipids
v



3 kHz MAS Lipids >
Market Ground Beef
300 MHz ^{1}H, nt = 4
Pre-sat. water suppression

Water
v



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SYDNEY N.S.W. 2006
AUSTRALIA

Prof P. W. Kuchel
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(received 1/27/97)

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

NMR 'Diffusion-Diffraction' of Water in Red Cell Suspensions

Dear Barry,

Last September I returned home after spending 5.5 months in Prof Peter Stilbs' superb Department at the KTH in Stockholm; and for 5 months prior to that, Prof Haggai Gilboa was my host for a most fascinating time at the Technion in Israel. While in Stockholm Peter Stilbs, Andrew Coy (a Post Doc, formerly in Paul Callaghan's lab in NZ) and I did some experiments that I had planned some time but I had had to wait to gain access to a spectrometer which could deliver strong magnetic field gradient pulses of the order of 0.2 - ~1.0 T m^{-1}. Peter's Bruker AMX 300 can achieve up to ~0.24 T m^{-1} with a Cryomagnet Systems Inc probe, and homebuilt current supply.

The reason we wanted to do the experiments in question is a follows: The structure of the pores in some composite materials can be inferred from the pulsed field-gradient spin-echo (PFGSE) NMR experiment on the water that diffuses in the interstices, or inside the cavities, that make up the material [1,2]. These data can be analysed by using a 'q-space' plot that may display the so called 'diffusion-diffraction' effect. The effect appears not to have been reported for biological systems, thus far, but it has been alluded to in a general review of diffusion in biological systems [3].

Our analysis was conducted on suspensions of oxygenated (and hence diamagnetic) human red cells and the data showed that [4]: (1) red cell suspensions displayed diffusion-diffraction of water (Fig. 1); (2) the shape of the q-space plots depended on the direction along which the diffusion was measured, *i.e.*, there was diffusion anisotropy which implied orientation of the cells in the homogeneous magnetic field; (3) the anisotropy was altered in a predictable way by converting the haemoglobin to a paramagnetic form with sodium nitrite; (4) the form of the q-space plots was altered in a predictable way by an inhibitor of erythrocyte water transport; (5) the pseudo-first-order rate constant characterising the covalent inhibition of water transport, by p-chloromercuribenzenesulfonate (p-CMBS), was measured; (6) and the cell diameter and

intercellular spacing were measured from the positions of the interference minima and maxima in the q-space plots (Fig. 1) [1,5]. The position (q) of the distinct diffraction minimum corresponds to water diffusing in an ensemble of cylinders (red cells with their disc-planes parallel to $\mathbf{B}_0$) of diameter 6.7 μm (= 1.22/q) which is close to the expected ~8 μm

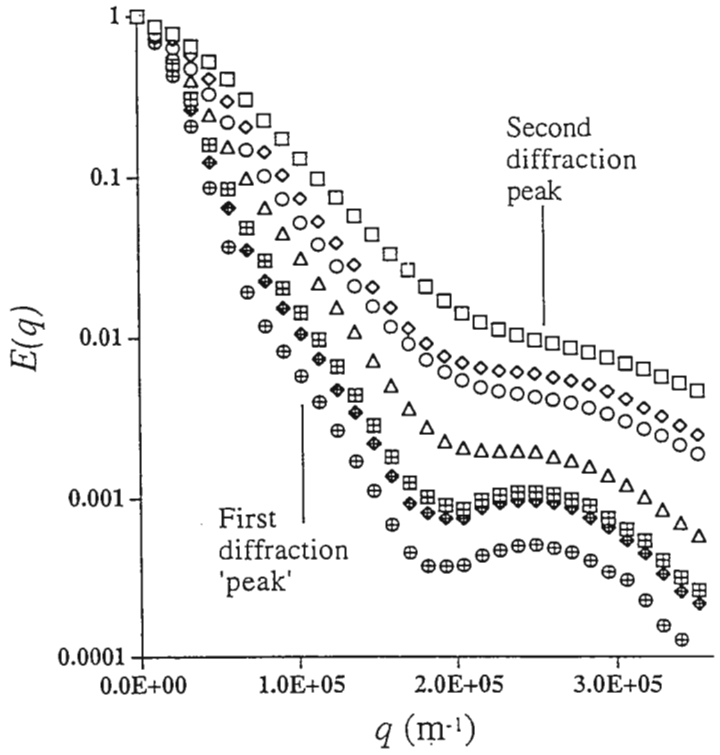

Fig. 1. Diffusion-diffraction of water in suspensions of human red cells.
Water ^{1}H NMR PFGSE signal intensity $E(q)$, as a function of q (g, was varied), and haematocrit of erythrocyte suspensions, at 25 °C. Data set accumulated in 25 min. Haematocrit values, from the top of the figure (%) 93, 83, 73, 63, 47, 42, and 25. NMR parameters: τ = 20 ms; δ = 4 ms; Δ = 20 ms; maximum field gradient, 2.05 T m^{-1}.

The ability to measure cell-size, as we have done *in vitro*, bodes well for doing similar experiments on solid tissues *in vivo* (using the NMR diffusion-diffraction experiment). This may be of considerable medical-diagnostic significance given that, in neoplasia, cell sizes can change systematically, as can the water content of the tissue.

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5. Callaghan, P. T., *J. Magn. Reson. A*, 117, 94, 1995.

Yours sincerely,

Philip Kuchel

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Chloroform-*d*, 99.8 atom % D
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References: (1) Dorn, H.C. *Anal. Chem.* **1984**, *56*, 747A. (2) For recent reviews, see: (a) Hofmann, M. et al: *LaborPraxis Med.* **1993**, *17*, 36. (b) Braumann, U. et al. *GIT Fachz. Lab.* **1994**, *38*, 77. (c) Spraul, M. et al. *Anal. Proc.* **1993**, *30*, 390. (d) Spraul, M. et al. *Bruker Rep.* **1990**, 12. (3)(a) Seddon, M.J. et al. *J. Pharm. Biomed. Anal.* **1994**, *12*, 419. (b) Spraul, M. et al. *Methodol. Surv. Bioanal. Drugs* **1994**, *23*, 21. (c) Spraul, M. et al. *Anal. Chem.* **1993**, *65*, 327. (d) Spraul, M. et al. *J. Pharm. Biomed. Anal.* **1993**, *11*, 1009. (e) Wilson, I.D. et al. *J. Chromat. A* **1993**, *617*, 324. (f) Spraul, M. et al. *J. Pharm. Biomed. Anal.* **1992**, *10*, 601. (4) Roberts, J.K.; Smith, R.J. *J. Chromat. A* **1994**, *677*, 385. (5) Johnson, S. et al. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1499. (6)(a) Albert, K. et al. *Anal. Chem.* **1989**, *61*, 772. (b) Also see references 2-12 from reference 2d.

Deuterated NMR Solvents

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15,180-7 — **5g $16.15; 10g $30.70; 25g $72.80; 50g $126.10; 10 x 10g $273.00**

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27,047-4 — **100mL $14.20; 1L $18.70; 2L $28.05; 6 x 1L $92.40; 4 x 2L $84.00; 4 x 4L $128.20; 18L $110.25**

Toluene, 99.8%, HPLC grade
27,037-7 — **100mL $14.10; 1L $18.40; 2L $27.65; 6 x 1L $93.00; 4 x 2L $82.80; 4 x 4L $147.80**

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

February 18, 1997
(received 2/19/97)

Measuring Spectrometer Use on Spectrometers Controlled by Macintosh Computers

Dear Dr. Shapiro:

Many teaching and research budgets have tightened over the past several years causing a higher priority to be placed on accurate accounting of scientific instrument usage. We, like many Chemistry departments at large universities, have several NMR spectrometers that support a wide range of projects. A few labs are involved in NMR-intensive projects and use continuous large blocks of spectrometer time. For example, a researcher working on the structure determination of a large biomolecule may typically use blocks of time that range in size between 12 hours and 1 week. We have found this type of use easy to moniter accurately due mainly to the small number of instrument users involved.

Another group of users are synthetic chemists. A typical spectrometer use session for these users consists of 3 to 15 minutes for collection of proton and/or carbon spectra. We have approximately 70 synthetic chemists who primarily use two 300 MHz spectrometers. Most days there are between 20 and 40 different spectrometer use sessions at each 300 MHz spectrometer. We found that accurate accounting of 300 MHz spectrometer use requires a mandatory login, logout procedure. The spectrometers, a General Electric QE-300 and a GN-300, are both equipped with Tecmag Acquisition Systems and Apple Power Mac 8100/80 computers. There are several commercial program packages that claim to provide both security and usage accounting. Many of these are reviewed in the November, 1996 issue of Macworld. The main features we were looking for included the following. 1. The need for a spectrometer user to enter a name and password in order to use the spectrometer. 2. The ability to record the amount of spectrometer time used during each session. 3. The ability to compile regular reports of spectrometer use that could be used for billing purposes. 4. Finally, we also wished to have control over folder and file access by spectrometer users. We began our search about a year ago and unfortunately we found substantial problems with the first two products we tried.

We obtained ultraSECURE 3.54 from usrEZ Software. It was easy to install and set up but after using it many days we noticed that there were several gaps in the log-in log-out record. We discussed our problem with usrEZ several times and no remedy was found so we decided to try something else. The next program we tried was Empower Pro 5.0 from Magna. We found this easy to install and set up on an older Mac running System 7.1. When we installed Empower Pro on a Power Mac 7200 running System 7.5.3, we found that the pull down menus at the top of the Mac screen did not function properly. Apparently, the Empower Pro version that we had was not compatible with newer Macs and/or MacOS versions. The apparent high sensitivity to MacOS version prompted us to abandon Empower Pro.

We then learned about a package produced by Hi Resolution Software (www.hi-resolution.com) named MacAdministrator. This package had more features than we needed but was recommended by a local Mac expert so we decided to try it (a free demo version is available). It takes a bit longer to become familiar with MacAdministrator than the previously mentioned products due to the larger size of MacAdministrator. MacAdministrator uses a client - server approach for administration. Users log in to a Mac which controls the spectrometer (the client) and a user authentication process contacts a server which has lists of valid users and access privileges. The server also records login and logout times. A potential disadvantage of this approach is that one needs a separate computer to act as a server. One may think that the expense of using a server for access control and usage recording for a small number of spectrometers is unjustifiable. We have found this not to be the case and will show that MacAdministrator has been financially beneficial for us below.

After installing a few MacAdministrator clients and a server, we had some trouble with occasional client crashes during log-in. We found that there was a conflict between the screensaver we were using (Darkside) and MacAdministrator. MacAdministrator can use it's own screensaver when no one is logged in but there is no MacAdministrator screensaver option when users are logged in and we thought it would be wise to use a screensaver during long acquisitions. However, this was not a good choice for two reasons. One was the conflict mentioned above and the other is that the Darkside screensaver interrupts the NMRscripts (Applescripts) one can use to collect and process spectra with Tecmag's MacNMR. Once Darkside was removed, the MacAdministrator package functioned flawlessly. Prior to installation of MacAdministrator we had used AfterDark screensaver successfully with MacNMR. However AfterDark and MacAdministrator don't work well together. Currently we have elected not to use a screensaver during times when users are logged in.

Once one has log-in, log-out data, MacAdministrator can create a Claris FilemakerPro database file that allows one to compile and present the data in a number of ways; FilemakerPro must be purchased separately. One can compile data over any period of time on a per user and per machine basis. At the present time we are compiling monthly NMR use on a per lab and per machine basis and then simply multiplying the hours used by the hourly usage rate to obtain our

bills for each lab. The software provided by MacAdministrator does not allow one to compile NMR use for different user-definable times during the day (ie. 9am-5pm, 5pm-12am) nor can one automatically compute bills. However, the preceeding could be done by appropriate modification of an existing FileMaker Pro database.

We use an ethernet-based AppleShare network for communication between MacAdministrator server and clients. When File Sharing on the spectrometer Macs was active, users could remotely access their data. However, a few spectrometer users reported variable temperature control instability when File Sharing on the spectrometer Mac was active. We decided that the risk of spectrometer instability was not worth the convenience of remote data access. We have a networked Mac that functions as a NMR data processing station and has active File Sharing. This Mac is remotely mounted by the spectrometer Macs and data can be readily transferred from the spectrometer Macs to the data processing station Mac or any other Mac that has active File Sharing. Thus, users at the spectrometers can readily transfer data to other locations but the spectrometer Macs cannot be accessed from remote locations.

The cost for MacAdministrator (5 clients and one server), FileMaker Pro, and a used Power Mac 6100/60 to function as a server was about $1400. Currently we are collecting about $1,200 a month in user fees for our two 300 MHz spectrometers. Before using MacAdministrator, spectrometer users were told to use a separate program to record their spectrometer usage. The usage recording program was very user friendly and could be accessed at an X-terminal adjacent to the spectrometers. The monthly 300 MHz spectrometer user fees averaged $750 during the last half year that the previous usage recording program was used. The difference in amount of user fees collected before and after installation of MacAdministrator is due to the fact that recording of spectrometer use is no longer voluntary. We have configured MacAdministrator so that it is not possible to use the spectrometers without logging in. If one considers the above MacAdministrator costs and the fees collected before and after installation of MacAdministrator, one can see that use of MacAdministrator makes good financial sense for us. Other MacAdministrator benefits include quick and easy compilation of spectrometer use, and ability to allow spectrometer users access to only those Files and Folders that are necessary for data acquisition and storage.

Feel free to contact me at jfe@virginia.edu or 804-924-3163 if you have questions about any of the above.

Sincerely,

Jeff Ellena
Senior Scientist

International School of Structural Biology and Magnetic Resonance
3rd Course: Protein Dynamics , Function and Design

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The basic principles of these methods of study of protein structure and dynamics - x-ray diffraction, NMR, molecular dynamics and molecular modeling - will first be given in a series of introductory lectures. Additional presentations will focus on specific examples of protein structure determination, experimental and theoretical studies of protein dynamics by different methods, protein-ligand interactions, structure-function relations in proteins, and protein and protein analog design.

GENERAL INFORMATION

Prospective participants should apply to either:

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stating: (1) date and place of birth, nationality, qualifications and present position; (2) address, fax and phone numbers and email address; and (3) list of publications.
Applicants interested in submitting unpublished results should send the title and an abstract of about 200 words. Selected papers will be presented and discussed in special sessions.

The total fee, including full board and lodging (arranged by the School) will be US $1,200. Limited financial aid available. Participants should arrive by 5 p.m. on the 16th.

THE CLOSING DATE FOR RECEIPT OF APPLICATIONS IS MARCH 15, 1997. NO APPLICATION FORM IS REQUIRED.

Information on the Course is available on the world wide web at
http://cmgm.stanford.edu/SMRL/Erice97.html

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Attendance will be limited to ~75 students, to be selected by the Co-Directors. Further details will be mailed with the acceptance letter.

Jean-François Lefèvre
Co-Director of the School

A. Zichichi
Director of the Centre

Oleg Jardetzky
Co-Director of the School

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

Deadline Dates

No. 463 (Apr.)	21 Mar. 1997
No. 464 (May)	25 Apr. 1997
No. 465 (June)	23 May 1997
No. 466 (July)	27 June 1997
No. 467 (Aug.)	25 July 1997

* Fax: (415) 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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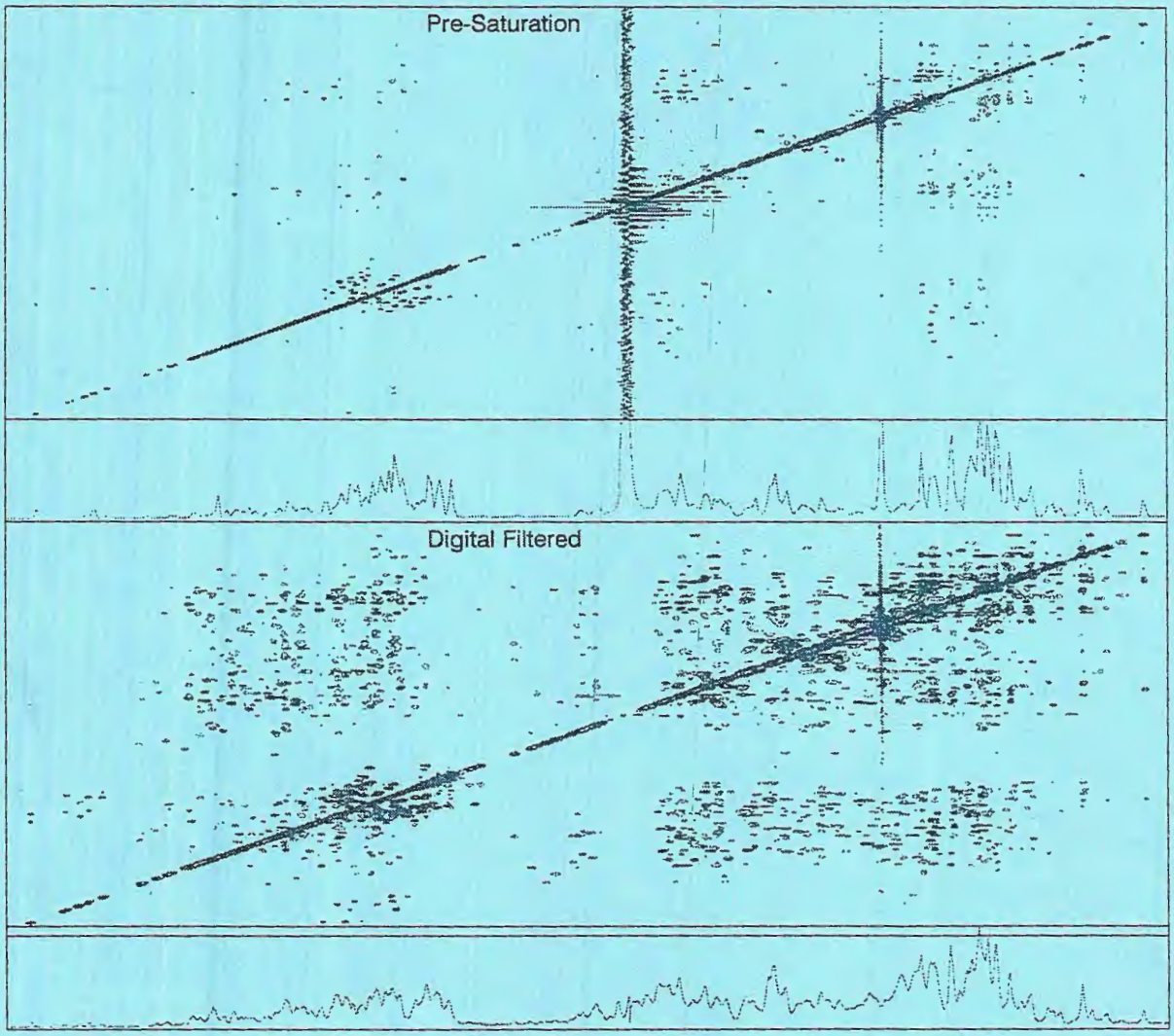

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This data shows the digital filtering capability of JEOL USA's ECLIPSE NMR workstation. Eclipse does digital filtering via software after the data is acquired, not via hardware during acquisition. This offers a significant advantage because with software digital filtering the acquisition is completed before you filter the data.

JEOL feels spectrometer time is best spent acquiring new data rather than repeating experiments because conditions were not optimized. It takes more time to write this kind of software, but JEOL took the time. Now you can use the ECLIPSE NMR Advantage to your advantage.

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