

Special Section: **On the Occasion of Jim Shoolery's Retirement**

Introduction	Shapiro, B. L.	3
Jim Shoolery - Career Highlights	Varian Associates	4
Jim Shoolery Patents	Anderson, W. A.	5
Shoolery Vignettes (<i>Including Tau-Delta Redux!</i>)	Anet, F. A. L.	7
Jim Shoolery: Some Reminiscences of Early NMR	Becker, E. D.	9
Dr. James N. Shoolery, an NMR Constant	Bible, R. H., Jr.	12
Knox Vobiscum	Bothner-By, A. A.	13
The "Golden Age" of NMR	Ernst, R. R.	14
Marathon Man	Freeman, R.	15
Jim Shoolery, the Johnny Appleseed of NMR	Grant, D. M.	17
Jim Shoolery Selected as Varian Fellow	Varian Associates	18
Jim Shoolery - His Impact in Defining NMR as It is Today	Gray, G. A.	19
On the Retirement of James N. Shoolery	Johnson, L. F.	21
[Scientific] Remains	Lauterbur, P. C.	23
In Appreciation of Jim Shoolery	Roberts, J. D.	25
High Resolution NMR - 1952 to 1990	Shoolery, J. N.	27

Simple 3D Graphics Display; A Recall of ^{15}N Peptide Shift Values	Cowburn, D.	29
Single Scan F_1 "Quadrature Detection" in 2D NMR	Brereton, I., Crozier, S., and Doddrell, D. M.	33
Cross-Relaxation Studies	Lee, T.-S., and Hwang, L.-P.	35
NMR Analysis of Polymer Mixtures	Cheng, H. N.	39

Continued on page 2

A monthly collection of informal private letters from Laboratories of NMR. Information contained herein is solely for the use of the reader. Quotation is *not* permitted, except by direct arrangement with the author of the letter, and the material quoted *must* be referred to as a "Private Communication". Reference to the TAMU NMR Newsletter by name in the open literature is strictly forbidden.

These restrictions apply equally to both the actual Newsletter participant-recipients and to all others who are allowed open access to the Newsletter issues. Strict adherence to this policy is considered essential to the successful continuation of the Newsletter as an informal medium of exchange of NMR information.

TABLE 1 DEUTERATED SOLVENTS

Cat. No.	Description	Formula	Min. Purity (%)	Density (g/ml)	MP (°C)	BP (°C)	$-X_v \times 10^6$ @ (°C)
D-11	Acetone- d_6	CD_3COCD_3	99.8%	1.1	17	58	0.551 (32)
D-120	Acetone- d_6 + 1% TMS	CD_3COCD_3	99.8%	1.1	17	58	0.551 (32)
D-13	Acetone- d_6	CD_3COCD_3	99.8%	0.87	34	57	0.460 (20)
D-121	Acetone- d_6 + 1% TMS	CD_3COCD_3	99.8%				
D-129	Need Deuterated Solvents? WILMAD HAS YOUR SOLUTION! Cost-conscious quality NMR solvents offered by Wilmad, such as $CDCl_3$, are frequently priced lower than more traditional sources. Included in this offering are the most common solvents, like Acetone- d_6 , Benzene- d_6 , D_2O , and DMSO- d_6 , as well as some of the most unusual solvents for specialty applications, like 1,1,2,2-Tetrachloroethane- d_2 , Octane- d_8 , and Trifluoroacetic Acid- d .						
D-14	Chloroform- d	$CDCl_3$	99.8%	1.50	-64	62	0.740 (20)
D-21	Chloroform- d + 1% TMS	$CDCl_3$	99.8%				
D-122							
D-130							
D-28							
D-31							

VARIAN
BOX/500 SHEETS

Cat. No.	Size	Instrument Model	Type
WCV-100 (S-100A)	11" X 26"	HA-100, HA-100B, HA-100D	Gridded-Two Color
WCV-60 (S-60C)	11" X 26"	HA-60, HA-60B, HA-60D	Gridded-Two Color
WCV-XL (S-XL)	11" X 26"	XL-100, XL-100B, XL-100D	Gridded-Two Color
WCV-XLFT-100	11" X 26"	XL-100 (CFT and FT)	Gridded-Two Color
WCV-XL-200	11" X 26"	XL-200, XL-300, XL-400	Gridded-Two Color
Use Plotter Paper and Pens? WILMAD HAS YOUR CHART! We provide the largest variety of paper and pens for NMR recorders or plotters available anywhere. Included in these listing are the newest spectrometers from Varian, Bruker, (and IBM), General Electric and JEOL, as well as the latest models, such as the Hewlett Packard 7475A, 7550A, and Thinkjet 2225A, Zeta 8 or 8A, and Western Graphtec 4730 plotters and printers.			
WCV-20 (CFT-20)	11" X 16 3/4"	CFT-20, FT-80, FT-80A	Gridded-Two Color
WCV-11 (CFT-11)	11" X 17"	All Models	Blank

Searching for the Unusual Requirement?
WILMAD HAS YOUR ANSWER!

The most comprehensive offering of "widgets, gadgets and specials" for NMR spectroscopy, including:

Spatula for 5mm NMR Tubes
Three types of Valve NMR Tubes
 (including the new J. Young Valve Tube)
Solvent Jet NMR Tube Cleaners
pH Electrode for 5mm NMR Tubes

Taperlok® NMR Tubes
A multitude of Coaxial Inserts
Alumina NMR Tube for Si-29 Studies
Ultra-thin wall NMR Tubes
Throwaway "THRIFT" and "ECONOMY" NMR Tubes

Serving the Spectroscopic Aftermarket



WILMAD GLASS COMPANY

Route 40 and Oak Road • Buena, NJ 08310 U.S.A.
 609-697-3000 • TWX 510-687-8911
 FAX 609-697-0536

TEXAS A&M NMR NEWSLETTER

NO. 384, SEPTEMBER 1990

AUTHOR INDEX

Allman, J. 53	Cowburn, D. 29	Griffey, R. H. 69	Mountford, C. 64
Anderson, D. E. 57	Crozier, S. 33	van Halbeek, H. 64	Narasimhan, P. T. 53
Anderson, S. E. 65	Dahlquist, F. W. 57	Hansen, P. E. 51	Ni, F. 83
Anderson, W. A. 5	Dalleska, N. F. 73	Helms, R. 52	Oldfield, O. 47
Anet, F. A. L. 7	Dickinson, C. Z. 65	Hwang, L.-P. 35	Palmer III, A. G. 81
Beal, R. B. 45	Doddrell, D. M. 33	Jelinski, L. W. 74	Pollak, K. 74
Becker, E. D. 9	Edwards, C. M. 77	Johnson, L. F. 21	Rajanayagam, V. 53
Bible, R. H., Jr. 12	Eichhorn, G. L. 45	Juneau, G. 41	Roberts, J. D. 25
Bothner-By, A. A. 13	Ernst, R. R. 14	Kispert, L. D. 48	Robinson, J. 77
Brereton, I. 33	Ezel, E. L. 59	Klein, R. F. X. 52	Ross, B. 53
Cala, P. M. 65	Fox, C. F. 46	Lauterbur, P. C. 23	Shapiro, B. L. 3, 84
Cavanagh, J. 81	Freeman, R. 15	Lee, T.-S. 35	Sheppard, D. W. 74
Chang, C.-T. 77	Fukushima, E. 52	Live, D. 63	Shoolery, J. N. 27
Cheng, H. N. 39	Grant, D. M. 17, 73	McIntosh, L. P. 57	Smith, L. L. 59
Chuknyisky, P. P. 45	Gray, G. A. 19	Mora, B. 53	Varian Associates 4, 18

TEXAS A&M NMR NEWSLETTER

NO. 384, SEPTEMBER 1990

ADVERTISER INDEX

American Microwave Technology, Inc. 49	International Equipment Trading, Ltd. 79
Bio-Rad, Sadtler Division 67	JEOL outside back cover
Bruker Instruments, Inc. 43	Norell, Inc. 71
Doty Scientific, Inc. 37	Polyflon Company 75
Fremont Magnetic Resonance 55	Varian 61
GE NMR Instruments 31, inside back cover	Wilmad Glass Company, Inc. inside front cover

SPONSORS OF THE TAMU NMR NEWSLETTER

Abbott Laboratories	The Monsanto Company
Analogic Corporation	New Methods Research, Inc.
The British Petroleum Co., Ltd. (England)	NMR Technologies Inc.
Bruker Instruments, Inc.	Norell, Inc.
Burroughs Wellcome Co.	The Procter & Gamble Company, Miami Valley Labs
Cryomagnet Systems, Inc.	Programmed Test Sources, Inc.
The Dow Chemical Company	Shell Development Company
Eastman Kodak Company	Siemens Medical Systems, Inc.
E. I. du Pont de Nemours & Company	Spectroscopy Imaging Systems Corporation
GE NMR Instruments	Spectral Data Services, Inc.
JEOL (U.S.A.) Inc., Analytical Instruments Division	Tecmag
The Lilly Research Laboratories, Eli Lilly & Company	Unilever Research
Merck Sharp & Dohme/Isotopes	Union Carbide Corporation
Millipore Corporation, Waters Chromatography Division	Varian, Analytical Instrument Division

The Newsletter's fiscal viability depends very heavily on the funds provided by our Advertisers and Sponsors. Please do whatever you can to let them know that their support is noted and appreciated.

FORTHCOMING NMR MEETINGS

- 22nd Annual Southeastern Magnetic Resonance Conference, October 11-13, 1990, Tuscaloosa, AL; Contact: L. D. Kispert (205) 348-7134; See Newsletter 384, 48.
- Bat-Sheva Workshop on New Developments and Applications in NMR and ESR Spectroscopy, October 14-24, 1990, Israel; Contact: Dr. D. Goldfarb, The Weizmann Institute of Science, Rehovot, Israel. See Newsletter 377, 10.
- 1990 Pacific Conference on Chemistry and Spectroscopy, October 31 - November 2, 1990, San Francisco; NMR symposia Thursday and Friday, Nov. 1, 2; Contact: Registration Chairman, Pacific Conference, P. O. Box 561, Palo Alto, CA 94302.
- Eastern Analytical Symposium, Garden State Convention Center, Somerset, NJ; NMR Symposia and Poster Sessions on Nov. 13 and 14, 1990; Contact D. C. Dalgarno or C. A. Evans, Schering-Plough Research, 60 Orange St., Bloomfield, NJ 07003; (201) 429-3957; FAX: (201) 429-3916.
- Recent Advances in NMR Applications to Porous Media (First International Meeting), November 14 - 16, 1990, Bologna, Italy; Contact: SERCOOP CONGRESSI, Via Massarenti 190, 40138 - Bologna, Italy; Tel. (51) 300811; Fax (51) 309477.
- Fourth Annual Missouri Magnetic Resonance Symposium, November 19, 1990, University of Missouri - Rolla; Contact: Frank D. Blum, Univ. of Missouri - Rolla, Dept. of Chemistry, 142 Schrenk Hall, Rolla, MO 65401; Internet: C2828@UMRVMB; Bitnet: C2828@UMRVMB.UMR.EDU.
- Advanced Tomographic Imaging Methods for the Analysis of Materials, Symposium at the Fall Meeting of the Materials Research Society, Boston, Mass., Nov. 26 - Dec. 1, 1990; See Newsletter 378, 57.
- 1991 Keystone Symposia on Molecular & Cellular Biology, Keystone, Colorado: April 8-14, 1991, *Frontiers of NMR in Molecular Biology; Proteolysis in Regulation and Disease; Protein Folding, Structure and Function*; See Newsletter 384, 46.

Additional listings of meetings, etc., are invited.

Table of Contents, cont'd.

Computer Simulation of the DANTE Pulse Sequence	Juneau, G.	41
Distance Measurements by Combined NMR-EPR	Eichhorn, G. L., Chuknyisky, P. P. and Beal, R. B.	45
Keystone Symposia - 1991 Conferences	Fox, C. F.	46
Progress with Proteins	Oldfield, O.	47
22nd Annual Southeastern Magnetic Resonance Conference, Oct. 11-13, 1990	Kispert, L. D.	48
$^1\Delta\text{N(D)}$ vs. $^2\Delta\text{CO(ND)}$	Hansen, P. E.	51
Position Available	Helms, R.	52
Free Acetic Acid- d_4	Klein, R. F. X.	52
Position Available	Fukushima, E.	52
New PCr Imaging vs. Primate Brain Metabolism	Mora, B., Narasimhan, P. T., Allman, J., Rajanayagam, V., and Ross, B.	53
Side Chain Carboxyl Group Assignment in Proteins	Anderson, D. E., McIntosh, L. P., and Dahlquist, F. W.	57
Carbon Spectrum of Camptothecin	Ezel, E. L., and Smith, L. L.	59
^{15}N NMR of DNA-Drug Complexes	Live, D.	63
Position Available	van Halbeek, H.	64
Position Available	Mountford, C.	64
Bumetanide Inhibits Sodium Efflux in Reperfused Myocardium	Dickinson, C. Z., Anderson, S. E., and Cala, P. M.	65
More Musings on Water Suppression <i>In Vivo</i>	Griffey, R. H.	69
Long Range Scalar Couplings Between Chemically Equivalent Nuclei	Dalleska, N. F., and Grant, D. M.	73
Position Available	Pollak, K.	74
Equipment Wanted	Sheppard, D.W.	74
Position Available	Jelinski, L. W.	74
Chemical Shift Reagents and Porous Media	Edwards, C. M., Chang, C.-T., and Robinson, J.	77
Sensitivity Improvement in 2D Heteronuclear Correlation Spectra	Cavanagh, J., and Palmer III, A. G.	81
Position Available	Ni, F.	83
TAMU NMR Newsletter: Sundry Notices	Shapiro, B. L.	84

* * * * *

Editor/Publisher: Bernard L. Shapiro
966 Elsinore Court, Palo Alto, California 94303, U.S.A. (415) 493-5971

Special Section

On the Occasion of Jim Shoolery's Retirement.

On September 28, Jim Shoolery of Varian Associates retires from full-time activity in the profession of NMR spectroscopy. This is surely a noteworthy, although somewhat unsettling, event, for as long as there has been NMR spectroscopy applied to chemical problems, Jim has been there.

The bare bones of Jim's vita are, if you will, deceptively simple. Born in Worland, Wyoming in 1925, Jim has called the San Francisco Bay Area home for all but the first few months of his life. A Bachelor of Science degree at Berkeley in 1948 was followed by graduate studies at Cal Tech, where he received his Ph.D. degree in 1952. During his graduate studies in the field of microwave spectroscopy, he became interested in NMR through contacts with John Waugh, a fellow student in the research group of Professor Donald Yost. Waugh was working in the then infant field of NMR, and immediately infected Jim with enthusiasm for this new discipline. Jim saw the immense potential of this exciting gift from the physicists, contacted Varian Associates in Palo Alto about exploiting this new tool, and the rest is, as they say, history.

To mark the occasion of Jim's retirement, several of his friends/colleagues/admirers/co-workers have provided the contributions which follow this brief introduction. My charge to these authors was to write whatever they wished, in whatever form they pleased, about Jim, his work, and the amazing longevity and diversity of his technical contributions. I am pleased that so many different perspectives on Jim's career could be gathered (on short notice) in one place, and that the man as well as his work is spoken to, especially by Dave Grant and Jack Roberts, whose words I especially endorse. (I would probably endorse Achibald McLauterbur's words, too, if I understood them.)

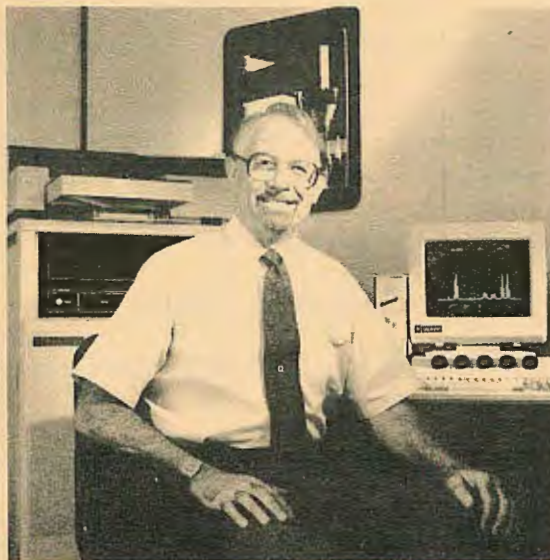
Also presented, for the record and the delectation of those whose acquaintance with NMR history is less than perfect, are a brief summary of some of the highlights of Jim's career, some photos, and finally, some comments by Jim himself. It is especially gratifying to have Jim's unique perspective, and I thank him for his willingness to share his thoughts with us.

During retirement, Jim hopes to do some consulting for Varian, and will surely phase his travels and lecturing on their behalf with visits to his rapidly expanding group of grandchildren. He may well resurrect an old, serious interest in photography, and has even threatened to take up golf (*Mirabile dictu!*).

As you read the letters which follow, try to imagine what state NMR spectroscopy would be in today if Jim has elected to stay in the microwave game. In scientific creativity and productivity he has excelled. He has graced his profession with an extraordinary blend of candor, civility, and cordiality. He has been the very model of a modern major scientist.

It is a pleasure to acknowledge the considerable assistance of Helen Gillespie of Varian Associates in putting together this special section of the Newsletter.

Barry Shapiro
28 August 1990



With a Gemini spectrometer, 1990.

Jim Shoolery - Career Highlights

- 1952** Jim joins Varian
 - Designed and constructed radio frequency unit for Varian's first high resolution NMR system. System installed at Humble Oil (now Exxon)
 - Proposed the concept of the Applications Laboratory
- 1953 -** Collaborated with scientists worldwide on:
- 1958**
 - Increased field strength: 10K, 14K, 21K gauss
 - Spinning samples
 - Variable temperature
 - Magnetic flux stabilization
 - Field gradient shimming with electric currents
 - Spin decoupling (Co-author with Arnold Bloom of first paper on this subject)
 Progressed hardware development from 30MHz to 100MHz
- 1958** Patent No. 2,864,995: "Apparatus for controlling the operation temperatures in gyromagnetic resonance spectroscopy"
- 1958 -** Established design criteria and introduced to market the user-friendly
- 1961** A-60, the first spectrometer priced to fit the average organic laboratory budget
- 1962** Patent No. 3,068,398: "Gyromagnetic resonance method and apparatus" with Sigurd Varian
 Patent No. 3,068,399: "Gyromagnetic resonance method and apparatus" (spin decoupling) with Felix Bloch and Martin Packard
- 1963** Patent No. 3,091,732: "Gyromagnetic resonance method and apparatus" (composite materials with modified magnetic susceptibility) with Wes Anderson
- 1961 -**
 - Rolled out Varian Applications Labs worldwide
- 1966**
 - Introduced the T-60 permanent magnet spectrometer
 - Introduced the HA-100 research NMR spectrometer
 - Introduced the HR-220 supercon NMR spectrometer
- 1965** Received Sargeant Award in Chemical Instrumentation
- 1968** Patent No. 3,394,300: "Gyromagnetic resonance method and apparatus" (use of integrator for quantitative analysis) with Martin Packard
- 1976** Developed microprobes for the XL-100, CFT-20 and FT-80 spectrometers
- 1981** Participated in the development of the APT experiment for determining the number of hydrogen atoms attached to carbon atoms in complex organic molecules and applied APT experiments to more powerful techniques, including 2D NMR
- 1982** Received Anachem Award in Analytical Chemistry
- 1983** Named Scientist of the Year by *Industrial R&D* Magazine
- 1986** Designed and implemented the menu system for NMR ease of operation in the GEMINI 200 and 300 supercon NMR systems
- 1989** Named Varian Fellow (ninth recipient of award in history of company)
- 1990** Jim retires from Varian



August 20, 1990

TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Re: Jim Shoolery Patents

Dear Barry:

In honor of Jim Shoolery's retirement from Varian, I would like to say a few words about Jim's contribution to the world of NMR by his patents. I know others will comment about his many publications, lectures and workshop contributions. One normally hears little about the patent literature and the contributions there. To do this I will list each patent, the co-inventors and say a few words about each patent.

U.S. Patent 2,864,994, issued Dec. 16, 1958
Apparatus for Controlling the Temperatures of Operation
in Gyromagnetic Resonance Spectroscopy.

This patent describes various NMR probe structures that provide means for controlling the temperature of the sample. Jim recognized very early the importance of being able to vary the temperature of the sample while observing its NMR spectrum as a means of gaining more information about a sample.

U.S. Patent 3,039,048, issued June 12, 1962
Gyromagnetic Resonance Detection Method and Apparatus

This patent is the NMR analogy of a dual beam optical spectrophotometer. Here the signal from the probe containing the sample is compared to a reference signal that is not perturbed by the sample. It is similar to various balancing systems except it is done in the time domain.

U.S. Patent 3,068,398, issued Dec. 11, 1962 with Sigurd Varian
Gyromagnetic Resonance Method and Apparatus

The idea expressed in this patent is that by changing conditions of the sample, such as the temperature, one may be able to determine the ratio of two or more components of a mixture within a sample. This could be done even if their

NMR signal components completely overlap. An example might be to determine the relative amounts of oil and water in a geological core sample.

U.S. Patent 3,394,300, issued July 23, 1968 with Martin Packard

Gyromagnetic Resonance Method and Apparatus

This is a continuation of the above patent. It extends the idea there to include an integrator to measure the area under the two signals and a balancing circuit to indicate the ratio of areas of the two or more signal components.

U.S. Patent 3,068,399, issued Dec. 11, 1962 with Felix Bloch & Martin Packard

Gyromagnetic Resonance Method and Apparatus

This patent is possibly the most important one of the group. It describes the spin decoupling method and apparatus. By applying a strong radio frequency field on the resonances of a first group of nuclei one can change the plurality and positions of the lines in the spectrum of a second group of nuclei that are coupled to the first group. This idea formed the basis for all double resonance and multi-resonance NMR techniques.


U.S. Patent 3,091,732, issued May 28, 1963 with Weston Anderson

Gyromagnetic Resonance Method and Apparatus

This patent describes the use of two or more materials of dissimilar magnetic susceptibility to construct NMR probes with materials that have an apparent uniform magnetic susceptibility as seen by the sample. The technique prevents undesired magnetic gradients to appear within the sample region thereby permitting one to observe very narrow NMR lines. These concepts have been used in essentially all of Varian's high resolution NMR probes since this invention.

I have greatly enjoyed working with Jim and have learned a great deal through our interaction.

Sincerely,



Weston Anderson
Principal Scientist



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

DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY
 405 HILGARD AVENUE
 LOS ANGELES, CALIFORNIA 90024-1569

August 30, 1990

Dear Barry:

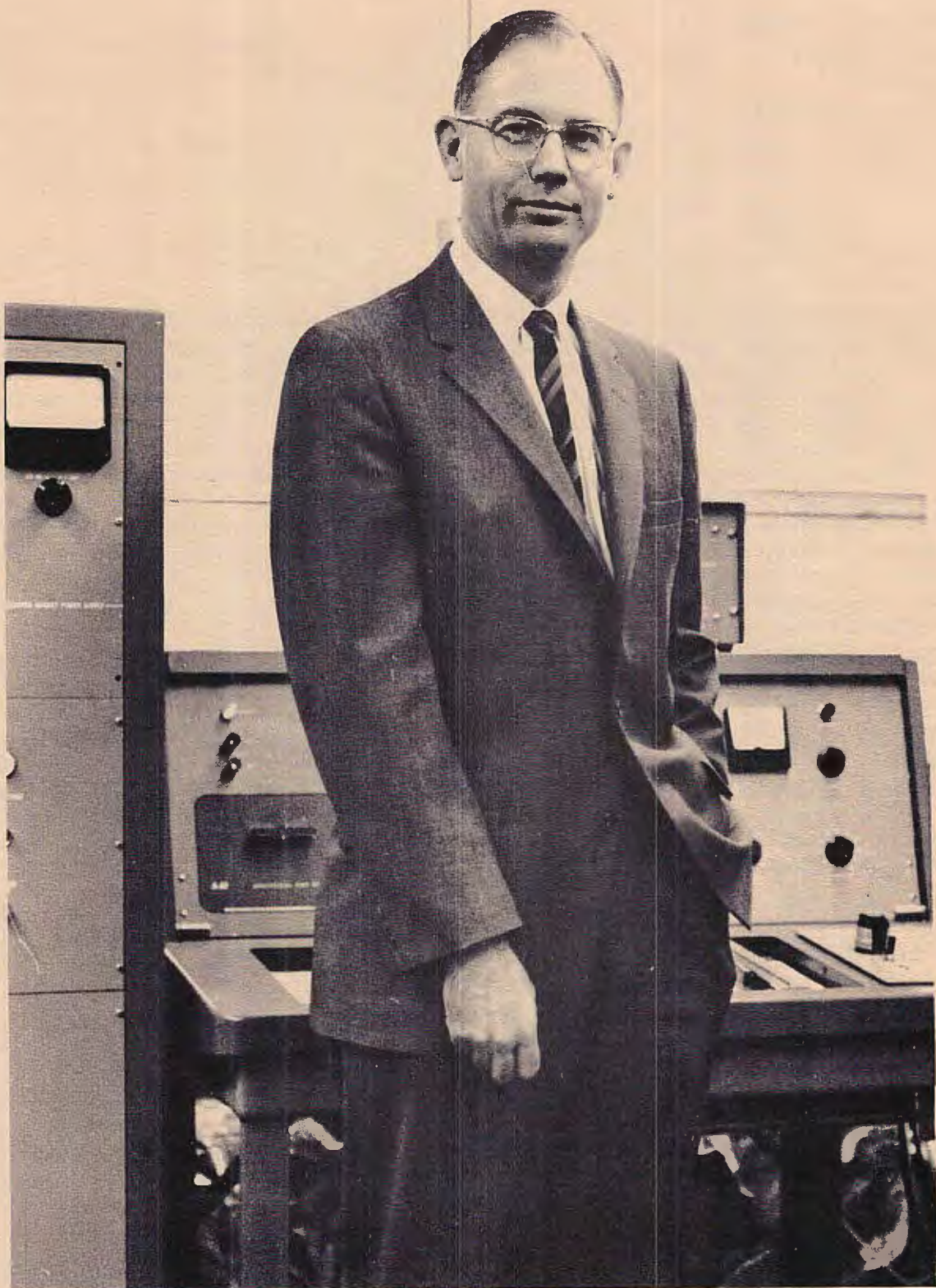
I am delighted to take part in a tribute to Jim Shoolery. Jim played a vital role in the development of NMR in its early commercial stages (1950's) in large part, I think, because he was at the interface between users (and potential users) and the then sole manufacturer (Varian Associates) of NMR spectrometers. His tremendous abilities as a teacher was just what was needed to introduce a revolutionary new technique that was emerging out of physics and chemical physics into physical, inorganic and organic chemistry. I was a spectator to this development in its earliest phase, being concerned mainly with natural product organic chemistry and then with physical organic and some organometallic chemistry. It became clear in the second half of that decade that NMR was going to be a powerful and, indeed, an essential tool in chemistry. I well remember the alacrity with which I scanned the back cover of JACS because every second issue or so had a fascinating advertisement from Varian in the long running series of "This is NMR at Work". I suspect that Jim Shoolery had much to do with the quality and chemical content of that series. A very important paper concerning the *practical usefulness* of NMR in structure determination in organic chemistry was published by Jim (with M. A. T. Rogers of Michigan State University as a co-author) in the October 1958 issue of JACS. This paper had figures of numerous steroid spectra and a quick glance at them was sufficient to show that they revealed many important structural features. If such complex molecules were routinely amenable to NMR, which is the critical point that the authors made, then essentially all organic and organometallic compounds should be grist to this technique. It should be noted that the steroid spectra were obtained at 40 MHz with phase detection by the difficult leakage method, and that useful information could be obtained even from a few milligrams of compound (of course, this was before the days of shim coils or lock signals, when tubes rather than transistors reigned supreme, and well before computers and FT methods were used in data processing from spectrometers). Actually, a couple of issues before the one containing the above landmark paper, the back cover of JACS displayed 60 MHz spectra of some steroids from which the tremendous advantage of higher field NMR was obvious!

Jim Shoolery has of course continued to be an outstanding teacher of NMR. His work (some with A. L. Bloom) on decoupling was pioneering and of great use in some of my early NMR investigations. His analysis of the factors involved in obtaining quantitative ^{13}C NMR integrals is of great importance and has been much quoted.

Are there any flaws in such a giant? Having lived through the tau-delta scale discussions of former years, which most people have happily forgotten, would it not have been nice if the delta scale, developed by Jim Shoolery (and others) and made into a *de facto* standard by Varian with the A-60 spectrometer had the scale with zero on the left rather than the right? At the time it seemed that having the magnetic field increasing from right to left was of paramount importance, but of course time has played a trick because most spectrometers now work at constant field and thus we are left with frequency (as well as the scale) increasing from right to left. The measurement of the chemical shift of a peak in a spectrum from its printed delta scale is thereby unnecessarily prone to error, in my experience. Of course, hindsight is 20-20 vision!

Sincerely yours

Frank A. L. Anet



Pre-beard, in 1961. In the background, the new A-60 spectrometer.

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

August 21, 1990

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

Jim Shoolery: Some Reminiscences of Early NMR

Dear Barry:

If it were not for Jim Shoolery, I might never have started doing NMR. It was 1954, and I was a graduate student at Berkeley. The seminar speaker -- one Dr. James N. Shoolery -- presented a spirited talk on a new spectroscopic method called NMR that had promise for elucidating the structures of certain molecules. The examples were interesting but were clearly well selected from among simple molecules. The resolution was not very good, and the sensitivity was poor. I thought that something useful might indeed come from NMR, but in spite of Jim Shoolery's enthusiasm I must say that I did not become wildly excited about it at that time. However, I did learn a little about the theory and about some of the potential uses of NMR.

Two years later, when I had obtained my Ph.D., moved to NIH and was doing research on hydrogen bonding in alcohols by infrared spectroscopy, I had occasion to recall Jim Shoolery's work on NMR. There was interest at NIH in the possible use of NMR for studying hydrogen bonding and for looking at small molecules of biological importance, but no one here knew much about NMR. As a result of my limited knowledge of the field and slight acquaintance with Jim, I was able to spend a week in his lab in order to evaluate NMR for our purposes. It was a fruitful period. Work done over about two days permitted me to develop information that was complementary to our IR data and to publish my first NMR paper [Becker, Liddel and Shoolery, *J. Mol. Spectroscopy* 2, 1 (1958)]. A figure from that paper illustrates the

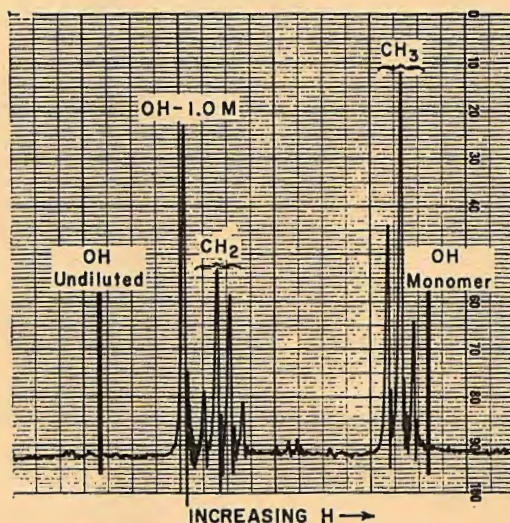


FIG. 1. NMR spectrum of ethanol in CCl_4 . The spectrum shown is for a mole fraction of alcohol $X = 0.01$. The positions of the OH resonance for $X = 1.0$ and $X \sim 0.003$ are indicated by vertical bars.

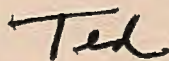
spectrum of ethanol at a concentration of 1.0 M in CCl_4 , together with an indication of the concentration dependence of the OH chemical shift. This was, of course, at 40 Mc/sec (Hz hadn't been invented), and data were referred to the methyl peak of the ethanol (TMS had not yet been proposed as an NMR reference). My report to NIH on the potential value of NMR led to our purchasing our first instrument, and I became de facto the local expert -- since I had had a whole week to learn NMR by looking over Jim Shoolery's shoulder!

That week in Jim's lab was the beginning of a long and pleasant friendship. I became aware of Jim's innovative and insightful approach to problems, his congenial and cooperative demeanor, and his scientific honesty and integrity. Among our accomplishments during that week in 1956 were probably the first ^{31}P NMR spectra of adenosine triphosphate and adenosine monophosphate. At 16 MHz, ^{31}P sensitivity was awful. Since coherent time averaging of NMR signals was still years in the future, we needed a 1 molar solution in a 15 mm test tube to get enough signal. Of course, the spinner worked only for 5 mm tubes, and the non-spinning linewidth in the 15 mm tube was large. I recall that Jim fabricated a spinner from a cork stopper and actually got it to spin rapidly with a strong compressed air jet. Of course, the wobble was awful, but the liquid continued to spin after the tube had stopped, just as Jim had hoped. It really did improve the resolution! Not enough to persuade us to publish, however.

Through the years Jim Shoolery has continued to pioneer new approaches to NMR. His early work on the spectra of alkaloids and steroids, for example, really opened up the use of NMR in studying natural products. His contributions to the development of the A-60 were critical in establishing NMR as a routine technique. And over the years as new methods were developed, Jim has continued to be in the forefront in showing us all how to get the most information from this little spinning nucleus.

All of us in NMR owe a great debt to Jim Shoolery. As he begins his retirement, I'd like to use this forum to thank him publicly for inspiring me personally and for the leadership he has provided to our field.

Sincerely,



Edwin D. Becker
Laboratory of Chemical Physics



Cover of the October 1983 issue of Industrial Research & Development -
Shoolery selected 1983 Scientist of the Year.

Searle Research and Development
Division of G.D. Searle & Co.
4901 Searle Parkway
Skokie, Illinois 60077
Telephone 312 982 7000
Telex 282475 (Domestic)
6871432 (International)

DR. JAMES N. SHOOLERY, AN NMR CONSTANT

On behalf of myself and all other NMR users, I would like to thank Jim Shoolery for helping us along the bumpy road of ever changing NMR. He has guided us from 30 MHz, one-dimensional, continuous wave, proton NMR to the magic of the two-dimensional carbon-carbon double-quantum experiment.

Always a teacher, Jim Shoolery has probably been NMR's strongest advocate. Jim's excitement over the possibilities offered by NMR to the chemist has been contagious. During his entire career, Jim has used NMR to push and pull and squeeze molecules until they gave up even their most intimate secrets.

Jim has constantly worked towards simplifying and reducing NMR instruments and data to the most practical level. His contributions include his early evolution of additive constants, his attention to ways of reducing sample requirements, his participation in evolving the APT sequence, and his work in many programs designed to help correlate all of the NMR data.

He has been enthusiastic in sharing his knowledge, and has always been available to discuss even the smallest problem.

His reputation was established early. I remember being asked by a colleague why I had made a particular chemical shift assignment. I replied that Jim Shoolery had made a similar assignment, to which my colleague responded, "Oh, that's okay then".

Jim has, indeed, been a five-star "product champion". Jim himself admits "I have glued things together in a few places. Perhaps there is some significance in that".

It is my hope that Jim is not really retiring, but only starting a new stage in his career. Even if he does truly retire, however, his spirit will still be in the laboratory, enthusiastically pushing and pulling and squeezing more chemical structure information from NMR.

Jim is more than a good scientist. He is gracious, he is kind, and he is a good friend.

In an NMR world which has seen constant changes, Jim Shoolery himself has always been a "constant".

Roy H. Bible, Jr.

Roy H. Bible, Jr.
Senior Fellow and Director
of Physical Methodology

SEARLE



Carnegie
Mellon

Department of Chemistry
Carnegie Mellon University
4400 Fifth Avenue
Pittsburgh, Pennsylvania 15213-3890

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

Dear Barry,

I was delighted to receive your phone call concerning the dedication of the upcoming issue of TAMU NMR to Jim Shoolery, and am tickled to be able to participate. Jim was my first contact with a real live high-resolution NMR-ist. He came to Boston in 1956 and installed our 40 MHz instrument in the basement of Mallinckrodt. He also instructed us in the arcane arts of obtaining spectra at that time: using a very long-handled wrench to tighten the bolts holding the pole pieces for shimming, tweaking the "paddles" to adjust the phase, and sweeping through the spectrum fast enough to make sure it did not escape completely.

NMR has changed a bit since then, and Jim has consistently been among the changers. I've always been amazed at the way he can sort out the phenomena of NMR and their possible applications so clearly and precisely; everything from complex double irradiation behavior to designing a micro cell.

I also feel kinship with Jim on one problem which I share with him, and that is the great frequency with which his name is misspelled. Why does that pesky "c" always slip in?

Speaking of micro cells, we have recently developed a design which might interest Jim (and others). To prepare our micro sample we use an ordinary 5mm sample tube and add one cc of hot heavy jello, made by dissolving 1-2% Knox unflavored gelatin in hot D₂O. Before the jello sets, we then introduce the non-polar sample, (for example cholesterol in deuteriochloroform) by means of a long-stemmed Pasteur pipette. It helps if the solvent is approximately matched in density to the D₂O. The droplet (1-20 μ l) assumes a beautiful spherical form, and is immobilized by the jello. The D₂O in the jello serves as a lock signal. The resolution obtainable is excellent. The most interesting factor from our point of view is that the droplet may be centered precisely in the r.f. coil, and excellent r.f. field homogeneity is obtained, meaning that evolution in the rotating frame may be followed. We can apply a 18,090 degree pulse, and still get a fid from a single line which is 50% as large as that produced by a 90 degree pulse.

Well- best wishes to Jim, and many years of enjoyment to come.

Sincerely,



Aksel A. Bothner-By

Laboratorium für Physikalische Chemie
Prof. Dr. R.R. Ernst

Zürich, August 22, 1990

0430

Universitätsstrasse 22

Durchwahl-Nr. 01/256 43 68

Telefonzentrale 01/256 22 11

Postadresse:

Laboratorium für Physikalische Chemie

ETH-Zentrum

8092 Zürich

Switzerland

Dr. Jim Shoolery
c/o Prof. Barry Shapiro
TAMU NMR Newsletter
966 Elsinore Court
PALO ALTO, CA 94303
U S A

Dear Jim,

It is a real pleasure for me to recall to my mind the "golden age" of NMR while writing this letter on the occasion of your retirement. When I arrived 1963 at Varian in Palo Alto, as a freshman in NMR with some basic knowledge but with very little practical experience, I already admired you as a great sourcerer who had not only developed all these marvellous practical applications, demonstrating that NMR could even be used, but also written enormously important papers such as "Effects of Perturbing Radiofrequency Fields on Nuclear Spin Coupling" Phys. Rev. 97, 1261 (1955) together with Arnold L. Bloom. I still consider this paper as a true marvel standing out from the sand of so many average quality papers by other authors. You developed, based on a very intriguing model, true understanding for the difficult phenomena of double resonance, a technique which at that time was of great importance providing real insight into the inner workings of spin systems. During my studies, being concerned with related problems, this has been one of the most influential papers for me.

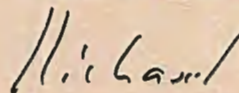
In 1963, it appeared to me that cw NMR has become a mature technique, like UV and IR spectroscopy. To find novel applications seemed more important than developing new variants of already well working techniques. Correspondingly, I felt that the application lab across the hall at 611 Hansen Way with masters like you and Roy Johnson was of much greater importance than the esoteric research efforts going on on the other side of the hall. And indeed many new achievements came out from the application lab, perhaps small improvements but of great and immediate practical importance. Finally, it turned out that basic research was nevertheless a good investment for Varian, but without the constant support and critics by the application lab, we in research would not have survived.

I admired your brilliant lectures on so many occasions, internal seminars, workshops, and conferences. You always fascinate the audience by some novel ingenious twists that make NMR even more practical. The long lasting series "NMR at Work" also was a true milestone in the history of NMR. It would be inconceivable without your contributions.

Whatever your plans are for the future, your image as one of the most influential contributors to NMR will not fade away and will remain as a perfect example how to successfully combine academic and practical interests. I wish you a prosperous and gratifying future full of activity and thoughtfulness.

Best regards.

Sincerely yours,



Richard R. Ernst



UNIVERSITY OF CAMBRIDGE
DEPARTMENT OF CHEMISTRY
Lensfield Road
Cambridge CB2 1EP

Professor Barry Shapiro,
Editor-in-Chief, TAMU NMR,
966 Elsinore Court,
Palo Alto,
CA 94303.

13 August 90

Marathon Man

Dear Barry,

You asked me to write a little vignette on the occasion of Jim Shoolery's retirement. Jim was one of the first to appreciate the seminal importance of NMR for chemistry, so his career has exactly matched the growth of high resolution NMR from the early 1950's to the present day. One of the true long-distance athletes in this field. I first came across Jim's work in 1958 when I was a post-doc in Paris, and it made an enormous impression at the time. It came in the form of a remarkable document (1) put out by Varian on "NMR World's Records" and was printed on green paper to mimic the sporting pages of American newspapers. There was a cute cartoon on the front page (Figure 1). It also showed the very best spectrum of the acetaldehyde quartet obtained at that time (Figure 2) run with a very slow magnetic field sweep so that the transient "wiggles" were fairly inconspicuous, and showing a full line width of 0.19 Hz (cps). The accompanying text was written in a lighthearted, throwaway style, but managed to imply that it was nevertheless pretty difficult to achieve this kind of result in practice. We certainly regarded this spectrum as an implicit challenge to the rest of the world.

One has to realize that in those days there was virtually no competition from other instrument manufacturers; if you wanted a high resolution NMR spectrometer, you almost had to be vetted by Varian to decide whether you were worthy of the honour, rather like being allowed to purchase a Rolls Royce. I guess deep down I knew I wouldn't have made the grade, so I was struggling to build my own high resolution machine from scratch -- the oscillators, amplifiers, probes, spinners . . . everything but the actual magnet itself. Consequently the Shoolery-Rogers pamphlet took on a very special status for my research and, working in France, there was no question of visiting Palo Alto to check on the experimental details. Here in Jim Shoolery's report was the indisputable evidence that it *could* be done if only one really tried. As all the usual things went wrong with my home-made spectrometer, I soon came to detest the smug character leaping over that damned magnet, and it was another two year's hard work before I could show an acetaldehyde quartet with comparable resolution (2) to Jim Shoolery's world record.

The Varian spectrum was run at 40 MHz whereas my spectrometer was still at 30 MHz. (Actually they were Mc/s in those days). Another unpleasant shock came when Jim Shoolery visited Paris to give a lecture and announced that they had now moved up to 60 MHz. They were now at twice the field strength! How can you compete with these people? By that time my post-doctoral stint had run its course and I left the French research group. They mercifully put my spectrometer in a basement *oubliette*. After all, they were all physicists and were beginning to realize that this new-fangled high resolution stuff could be the downfall of serious magnetic resonance research.

Kindest regards,

Ray

Ray Freeman

(1) Technical Information Bulletin Vol II by James N. Shoolery and Emery Rogers. I am indebted to Dr Shiro Satoh of Varian, Tokyo, for a copy of this historical document.

(2) R. Freeman and R. V. Pound, Rev. Sci. Instr. **31**, 103 (1960)

NMR WORLD'S RECORDS . . .

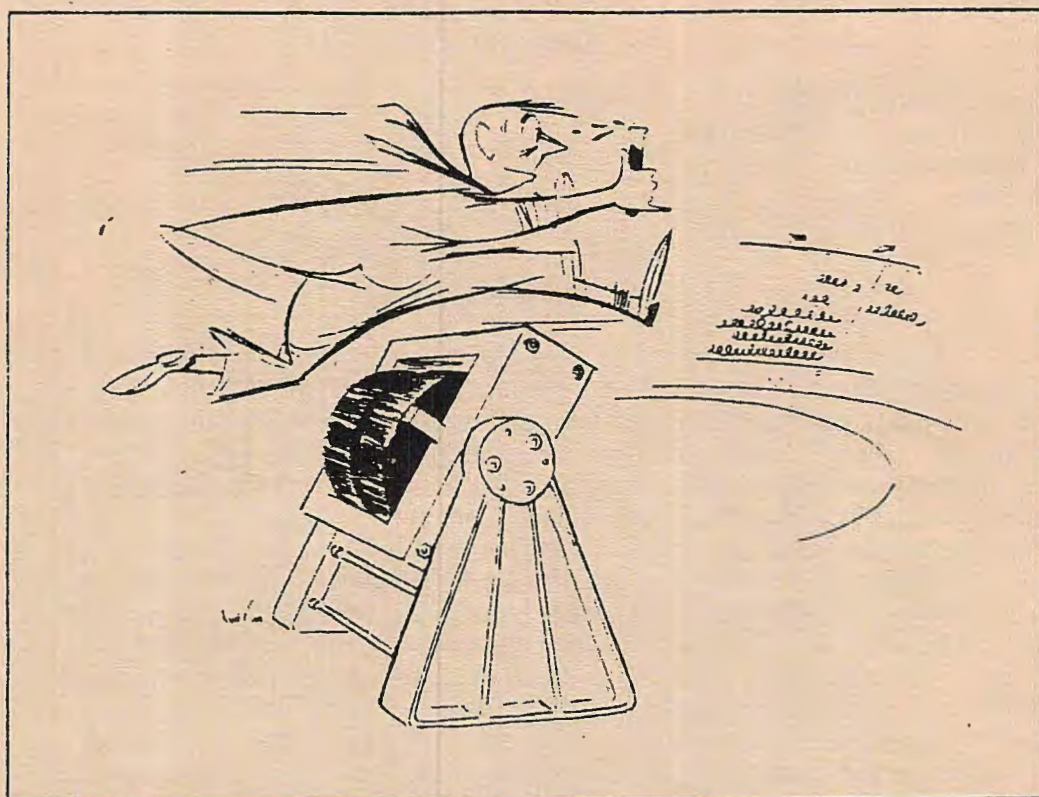


Figure 1

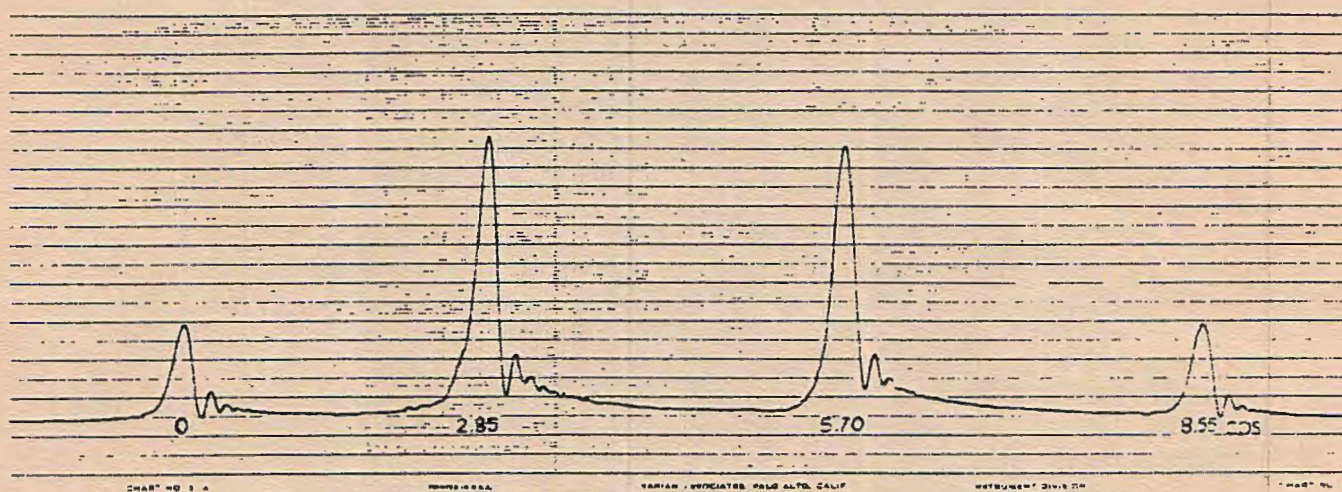


Figure 2 Acetaldehyde quartet at 40 MHz (1958)



David M. Grant
Distinguished Professor

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

Title: Jim Shoolery, the Johnny Appleseed of NMR

Dear Barry,

It is a singular honor to provide you with a letter of recognition for Jim Shoolery. Jim's enthusiasm for and persistent advocacy of NMR launched an era in which high resolution liquid NMR became the pre-eminent structural analytical tool of the practicing chemist. Thirty to thirty-five years ago it was Jim Shoolery who crisscrossed the nation, venturing also into the international scene, to plant the seeds of this ubiquitous methodology. Today the seedlings have literally blossomed into a forest of trees. Perhaps the forest now obscures the work of the Johnny Appleseed of magnetic resonance, and many of the young resonators likely have only minimal awareness of the seminal contributions of Jim Shoolery.

Jim did it all in the early days of NMR. He produced some of the very best early scientific work in the field and always, as you well know, was one of the favorites at the yearly ENC conferences of earlier decades. To this pillar of scientific work one must add the additional commendation earned for guiding the efforts of the dominant vendor which greatly benefitted the chemical community. His judgement of where the field was going and how to best optimize its impact on the majority of workers was uncanny. This type of scientific and commercial leadership is rare, and Jim stood out as the finest example of the industrial scientist who was admired and respected for his fundamental contributions to the spectroscopic science itself.

The early and perhaps still unpublished work of Jim on the proton-coupled ^{13}C natural abundance spectrum of acetic acid stands out in my memory as a specific case to illustrate the creative and innovative science which characterized Jim's prolific output. We at Utah had been struggling with the development of carbon-13 NMR methods, and Jim's work re-emphasized the importance of this isotope and that one should not shy away from the low natural abundance of this critically important nucleus. Without NOE and multiplet collapse enhancement he had shown the feasibility of obtaining a natural abundance spectrum. The work also did not use either FT methods or computer time averaging devices. Properly encouraged by his results, we trudged on with more than adequate rewards for our efforts.

As a man retires from the professional world, perhaps an even greater measure of his success lies in his ability to be a superb human while doing good professional work and providing outstanding leadership to a large and rapidly emerging field. Jim is such a person. Always fair minded. Never greedy for credit. Concerned more for the emerging science than for short term personal benefits and accolades. He even seemed to understand that 'good business' embodies a commitment to integrity, dignity and objectivity in his commercial responsibilities. Yes, we all owe a debt of gratitude to Jim. My personal best wishes go with him wherever he finds himself. He truly is one of the great!

Sincerely,

David M. Grant

Department of Chemistry

Henry Eyring Building
Salt Lake City, Utah 84112
(801) 581-8854

Jim Shoolery selected as Varian Fellow

Dr. James (Jim) Shoolery, senior applications chemist for Varian's NMR Instruments, was named their ninth and newest Fellow on November 14, 1989. This comes as little surprise to those who know and work with Jim. According to Howard Hill, a colleague and also a Varian Fellow, Jim has a worldwide reputation with the NMR community.

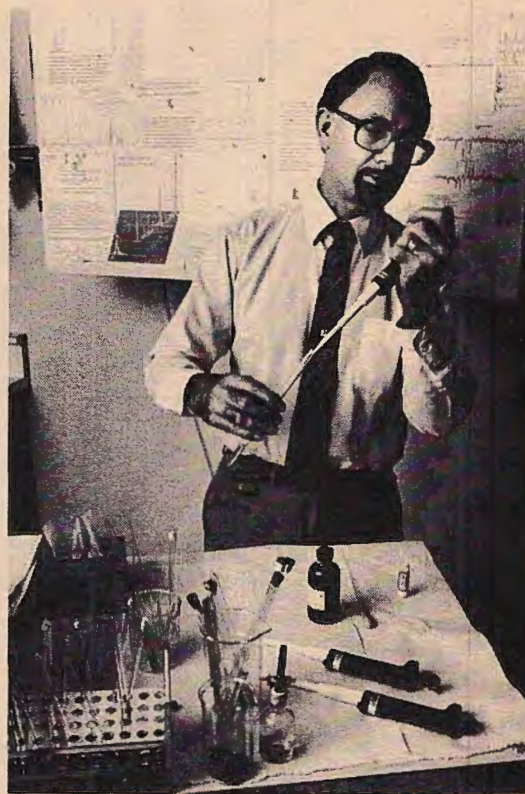
"He was instrumental in establishing the applications of high-resolution NMR at Varian in 1952 and has been actively involved in developments for most of the subsequent years," Howard notes.

Jim's selection was based on his numerous contributions to the development and application of NMR as an indispensable tool for chemists. Over the years, he has played key roles in the conception, development, and launching of several highly successful instruments and applications. From 1958 to 1961, for example, Jim established the design criteria and introduced to market the reliable, user-friendly Varian A-60 -- the first NMR spectrometer priced to fit the average organic laboratory budget. Of particular significance was a patent he developed with Felix Bloch and Martin Packard in 1962 which formed the basis for all double resonance NMR techniques. Most recently, he has been involved in the development of a user-friendly menu system for the low-cost Gemini research spectrometers.

With more than 160 scientific papers, innumerable lecture presentations, and five patents to his credits, Jim has helped Varian earn its reputation as a world leader in high-resolution NMR. He has received numerous awards, including the Sargeant Award in Chemical Instrumentation and the Anachem Award in Analytical Chemistry. In 1983, Jim was named Scientist of the Year by *Industrial Research & Development* magazine.

"During my scientific career, NMR has brought about more far-reaching changes in the way that organic chemistry is conducted than any other innovation, and has increased the productivity of organic chemistry immeasurably," Jim says. "It is a matter of considerable satisfaction to me that I have been so intimately associated with such a major scientific trend."

The Varian Fellows Program was introduced in 1988 to recognize significant individual technical achievement. Nominees are judged on their continuing sustained contributions to the company's products and technological base.



varian associates / 611 hansen way, box d-298 / palo alto, ca 94303
NMR Applications Laboratory

August 9, 1990

Dr. Barry Shapiro
966 Elsinor Court
Palo Alto, CA 94303

Jim Shoolery- His Impact in Defining NMR as it is Today

Dear Barry,

On the occasion of Jim's retirement from Varian, it is a personal pleasure to take this opportunity to highlight Jim's enormous impact on the field of NMR over the course of his career. Because of the tremendous growth in NMR, most practitioners in the field were not even born when Jim began at Varian. For them, and also for the rest of us, I think it is important to acknowledge how Jim has influenced how we work and the tools we have at our command.

Jim sold his talents to Varian with the idea that a chemist is vital to make and sell instruments to chemists for experiments that are interesting to chemists. At that time in 1952 Varian was a small company (only four years old) microwave amplifier tubes and experimenting with this new novelty called NMR. Jim saw the potential when he was a postdoc at Caltech and read the J. Chem. Phys. 1951 paper in which the three resolved peaks from ethyl alcohol were described. He contacted Varian and got himself a job. He immediately was put to work assembling a spectrometer and began the process of helping define the technique with the chemist in mind. During the fifties, Varian progressed with hardware development that resulted in electromagnets and rf systems for 30 MHz up to 100 MHz. Jim participated as first an Applications Chemist, then as the head of the NMR Applications Laboratory, and subsequently as Marketing Manager. He was central in the growth of Varian as a worldwide organization. He brought a chemist's perspective into the process of defining, testing and marketing NMR.

Although difficult to visualize today, NMR was a difficult "sell" to a skeptical audience during the fifties. The instruments were expensive, difficult to use and mostly oriented toward small molecules. Nevertheless, Jim recognized the vast fundamental potential and pushed the development of useful capabilities such as higher fields, variable temperature operation, spin decoupling, spinning samples, flux stabilizers, field/frequency locking, time-averaging, pulsed NMR, micro-cells, integration techniques for quantitative analysis, supercon magnets, heteronuclei, wideline NMR, and EPR. He guided the definition of the first "mass market" and "user-friendly" instrument, the A-60. This instrument brought NMR to the organic chemist as a hands-on spectrometer with high reproducibility and pre-calibrated chart paper - a revolutionary development!

At the same time Jim recognized that just having an instrument, even in a non-competitive environment, was not enough. People had to be shown that NMR was good for them. To accomplish this, Jim set up the first NMR Applications Laboratories, both in Palo Alto, at the Pittsburgh airport(!), and in other countries. These were instituted in the spirit of scientific inquiry, where scientists could come and do experiments to verify the utility and power of the technique for their problems. To educate the community, Jim instituted the "NMR At Work" series, which some of us can remember running on the back cover of JACS, to show solved problems using NMR. Under Jim's direction, the Applications Laboratories produced an NMR Spectral Catalog with a functional group index for applying NMR to a wide variety of organic compounds. Jim estimates that he has talked to as many as 20,000 people in the many years of seminars and workshops used to spread the message of NMR.

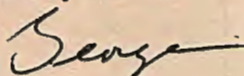
During the sixties, Jim was central to the explosive growth phase of NMR as its potential was fully recognized and exploited. He helped define the most popular permanent magnet system, the T-60, and consistently pushed the development of higher fields through the use of supercon magnets, resulting in the introduction of the HR220 and 300.

Jim returned to the Applications Lab in the seventies to resume his primary interest of developing and exploiting techniques that can solve chemical problems. He was central in pushing the development of micro-probes, first with a 1 mm insert for the XL-100 and then with the popular 1.7 mm capillary inserts for the CFT-20 and FT-80. He pursued his interest in quantitation by exploring the utility of ^{13}C NMR for analysis of fats and oils, including analysis of whole seeds. Jim spent a great deal of time promoting the benefits of FT NMR for the organic chemist and developed, with Steve Patt of Varian, the APT (Attached Proton Test) experiment. Jim also took advantage of the growing capability of multinuclear NMR to exploit ^2H NMR in natural abundance in organic molecules.

The last few years have been a period in which Jim has been further focused on making NMR available to the widest possible audience of users, principally in the development and evolution of the Gemini 200 and 300 FT spectrometers. Jim has used his experience in solving chemical problems to optimize the user interface and experiment array for these popular instruments. He continued to pursue his interests in using NMR to determine the structures of natural products using a variety of one- and two-dimensional techniques. He has collaborated with dozens of scientists around the world in joint research and publication.

Jim has been extremely productive throughout his career at Varian. He has published over 160 papers and has five patents. These patents cover inventions that include variable temperature NMR, spin decoupling, and compensated magnetic materials. He has received the Sargeant Award in Chemical Instrumentation in 1965, The Anachem Award in Analytical Chemistry in 1982, and was named Scientist of the Year by Industrial R&D magazine in 1983. He has been a strong voice within Varian for the NMR user, consistently reminding all of us of our customer's needs and expectations. We will miss Jim and wish him well in the future.

Sincerely Yours,



✓ George A. Gray
Senior NMR Applications Chemist



General Electric Company
P. O. Box 4905, Fremont, CA 94539

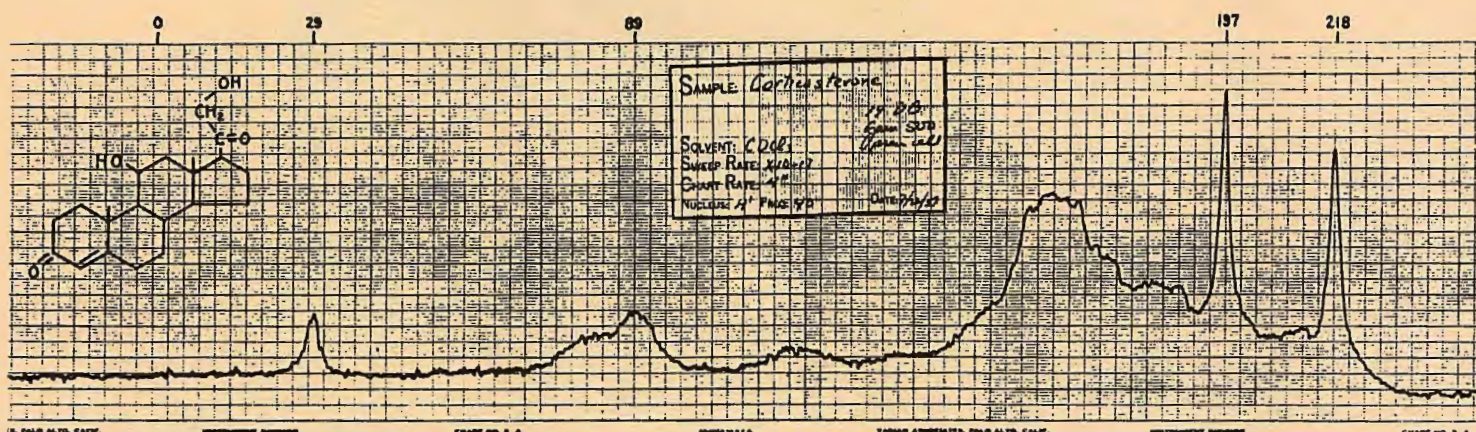
Dr. B. L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

August 20, 1990

On the Retirement of James N. Shoolery

Dear Barry,

It was a bright and calm day. Suddenly a shout rang out! It was a shout of exclamation by me, at the witness of generation of a high resolution proton NMR spectrum by Jim Shoolery as he introduced me to NMR instrumentation. I still have an original G-10 strip chart recording taken during my first day at Varian on July 22, 1957. Shown below is a reduction of that spectrum taken at 40 Mc and referenced in cps from external benzene.



For the next dozen years, or so, I worked for Jim in the applications lab developing applications, making demos, and ultimately managing the applications lab when Jim moved to Marketing Manager. I have fond memories of those years and my association with Jim. His guidance during that time laid the foundation for my career in NMR.

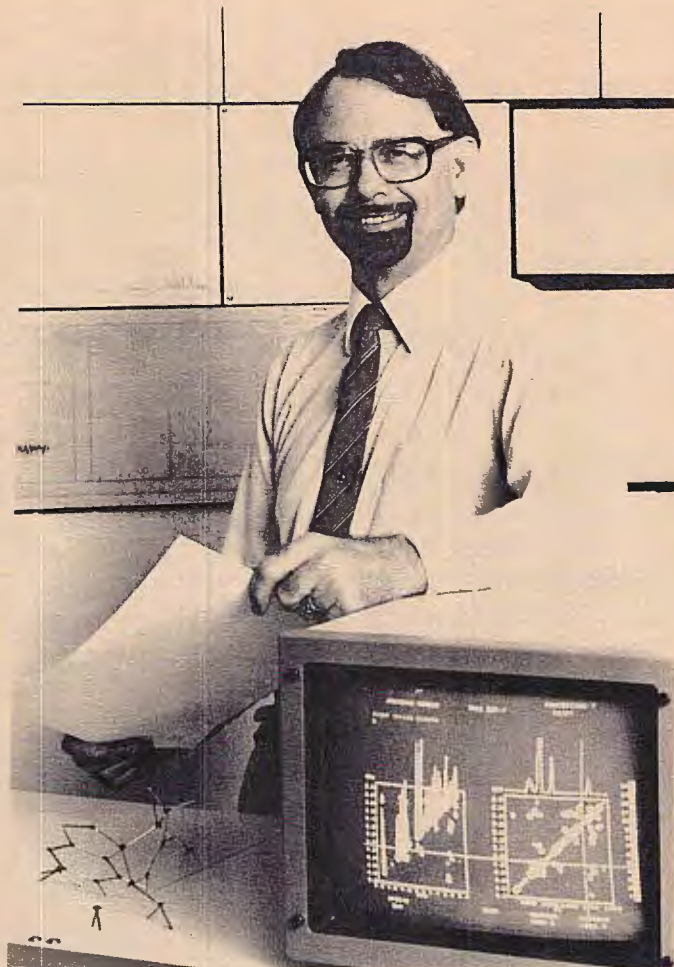
Jim's contributions to the field are outstanding. Over the years he has contributed greatly to the development of NMR spectroscopy and he has taught us all about the wonderful world of NMR. Here's wishing Jim a well-deserved and most pleasant retirement period.

Sincerely,

Roy

LeRoy F. Johnson

Jim in his element -
solving structural
problems, in 1983
on a VXR-400.



University of Illinois

College of Medicine at Urbana-Champaign

Department of Medical Information Sciences
 BIOMEDICAL MAGNETIC RESONANCE LABORATORY
 1307 West Park Street
 Urbana, Illinois 61801
 Phone: (217) 244-0600
 Fax: (217) 244-1330
 Email: bmrl@bmrl.med.uiuc.edu

August 16, 1990

Dr. James N. Shoolery
 Varian Associates

Dear Jim,

Archibald MacLeish had a blind spot. For him, science was dead dry birds in dusty cases, theories that proved beauty false. He never knew how close it is to poetry. Nevertheless, with apologies to him, and with bracketed substitutions, let me appropriate his "Poetical Remains" as

[SCIENTIFICAL] REMAINS


What will our reputations be?
 Whole things? Constructions
 Resisting time (that sea!)
 With the rock's persistent luck?

I doubt it. We leave behind
 An anthological rubble:
 Mind mingled with mind,
 Odd and even coupled.

But [science] thrives that way.
 Out of the tumbled coral
 One exquisite spray,
 Ivory, tipped with ore.

All of us who have lived through the classical, medieval and modern ages of NMR can look back and recognize the skillful poets among us, those whose styles and imaginations transcended categories and doubts and wove distinctive voices and meters into our communal epic. Others will, on this occasion, recall almost forgotten rhymes and schemes, or lost drafts and crossings-out, or serendipitous alliterations. Let me just celebrate the skill with which you helped to blend the lines of those who wrote for money, those who wrote for fame, and those who wrote for truth. Like all of the best ones, you loved it for the beauty in it.

Nostalgically,



Paul Lauterbur



With Virginia Royden, searching for the signal of some nucleus, at 0.94 T. 1953.
Note the sinister I/O device. In another context, Jim once referred to "the fine
line filter of the human hand."

CALIFORNIA INSTITUTE OF TECHNOLOGY

Pasadena, California 91125

Division of Chemistry and Chemical Engineering
Gates and Crellin Laboratories of Chemistry

John D. Roberts
Institute Professor of Chemistry, Emeritus

August 14, 1990

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

Dear Barry:

In Appreciation of Jim Shoolery

Jim Shoolery's impending retirement from Varian Associates marks the end of a definitive era for NMR spectroscopy and spectroscopists. As a catalyst, as a role model, Jim has a very special place in the field of chemical applications. He was in on the very start of the production, sale and installation of NMR spectrometers and has been a real benefit to all chemists using the technique. It is not surprising that this should be so, because Jim, with a PhD from Caltech (with Don Yost, 1952), came to Varian with a chemical, rather than NMR, background. That he had to learn NMR late was probably a good thing, because in the early days he appreciated better than most of its practitioners the problems chemists had in learning how NMR machines operated, how splitting occurred, the factors important to the chemical shift and so on.

Jim installed our first NMR machine, the HR-40, at Caltech in early 1956 and immediately demonstrated that one of our proudest preparations in that era was actually 3-methylmethylenecyclobutene, rather than 1,3-dimethylenecyclobutane. He was a great representative of Varian along with the wonderfully helpful engineer, Forrest Nelson. Jim and I collaborated on the design of a temperature-controlled probe insert and had many interactions as Varian led the field through introduction of new instrumentation.

I don't know whether or not Varian actually invented the concept of applications laboratories for helping customers getting acquainted with how instrumentation could be used for their research programs, as well as developing new techniques that benefited all workers in the field. Whatever the truth of that, Varian Associates, with Jim Shoolery playing a decisive role, certainly elevated the applications laboratory idea to a high degree of importance and the Varian

laboratory really was very significant in helping bring NMR to many institutions that might not have otherwise recognized its utility.

Varian Associates had a most important role in popularizing NMR by simplifying it. And in this, Jim Shoolery played a large part in defining what the capabilities of the A-60 spectrometer should be, which surely helped immensely in making this instrument a real blockbuster workhorse for chemistry. To be sure its vacuum tubes, mostly 12AX7's and 12AU7's, seemed to be operating near their limits, so that frequent tube changes were necessary, but the resolution was superb and operations marvelously simple. These instruments brought about an era of global NMR expansion.

Of course, NMR users are always a relatively unhappy bunch. The generally low sensitivity of detection of even proton signals in the early days (initially we used 1 M solutions!) made for push, push, push for higher and higher sensitivity. Finally, signal averaging came along and Varian came through with the marvelous DFS-60 for ^{13}C , which was a pathbreaker, especially in the hands of Frank Weigert, 16 papers from 2 years and 9 months of thesis work at Caltech. With the push for greater sensitivity, NMR instrumentation began to get more complex. The advent of off-resonance, noise and single-frequency decoupling, as well as spin-tickling provided powerful techniques, but at the cost of more complexity. Then, Fourier transform opened a new box of goodies by both enhancing sensitivity and by letting the smart cookies manipulate the FID in evermore complex ways.

Varian enhanced their research with great NMR practitioners such as Richard Ernst, Ray Freeman, Leroy Johnson and others who played pivotal roles in the development of modern NMR spectroscopy, and imaging as well. I do not know what Jim Shoolery's role was in bringing people of this caliber to Varian, but whether or not he selected the people, he surely helped immensely by the way he burnished Varian's tradition of excellent work on chemical applications.

Jim is a man of intellectual depth, personal warmth and integrity, as well as social consciousness. We will miss his work in this everchanging field, but his personal contributions will remain as highly significant underpinnings of the applications of NMR to chemistry.

With best wishes and thanks to Jim and his family.

Very truly yours,

Jack

P.S. More detail about my interactions with Jim and Varian is in my autobiography, *At the Right Place at the Right Time*, ACS Books, Washington D.C., 1990.

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

Dear Barry,

HIGH RESOLUTION NMR--1952 TO 1990

In 1952 Varian Associates, a relative newcomer to the infant electronics industry, brashly introduced a product looking for a market. The 30 MHz High Resolution NMR spectrometer could reproduce the experiments that had been reported in the literature, but it was not clear to very many chemists that practical applications existed. Since scientists and their bosses rarely spend money without at least some idea of getting something worthwhile for it, it seemed to me that Varian would need to create the market for NMR by demonstrating the kinds of problems that could be solved with this new product. I wrote a letter to the company in which I suggested that idea and expressed a willingness to be hired to do the job. (Varian didn't have a monopoly on brashness!) The ensuing positive response from Varian engaged me in a thirty-eight year love affair with NMR which will go on until one of us dies. (NMR is looking healthier and healthier as the years go by.) My retirement from full-time participation in the ongoing development and promotion of NMR on September 28, 1990, seems a fitting occasion to reflect briefly on the past, present, and future of this industry.

The 1950's saw NMR progress from a laboratory curiosity to a powerful problem-solving tool for those chemists brave enough to wrestle with it. Varian dominated the commercial market, largely through pursuing an aggressive research program and rapidly incorporating improvements in the product. Magnetic field strength was increased from the initial 0.7 T to 1.0 T, and then to 1.4 T. The introduction of the spinning sample, flux stabilization, variable temperature, and spin decoupling steadily increased the applicability of NMR to chemical problems, especially those in organic chemistry. But the engineering for an instrument that would meet the diverse needs of the rapidly evolving market was still missing.

The early 1960's marked the turning point for NMR with the introduction of the A-60. That product met the need for an easy-to-operate, stable, and reproducible spectrometer. Priced to fit the average organic laboratory budget, the A-60 started chemists down the path to an addiction from which they will never escape nor ever want to do so. The commitment to relatively large scale production required freezing the design to some degree, which opened the door to competition. The 1960's saw the growth of more companies in the NMR field, and there is no doubt that the chemist benefitted by the product improvements that resulted from free enterprise in action. Varian continued to lead the way with the development of superconducting magnets and pulsed Fourier transform techniques, but the market had to be shared with others.

The 1970's saw a degree of maturity achieved in the NMR industry. Field strengths continued to soar from 300MHz (7.1 T) to 500MHz, and data systems evolved from primitive computers of limited capacity and speed to integrated systems with greatly improved speed, memory, data storage, and software. Better engineering led to more reliable products that were easier to operate, and offered more problem-solving ability for the dollar.

The 1980's brought the payoff of all the earlier effort invested in applying computers to instrument control and data processing. An explosion of ingenious NMR experiments, based on a greatly improved understanding of what the nuclear spins are doing and what they can be made to do, provided the chemist with selective techniques with problem-solving powers beyond his wildest dreams.

Where is it all leading? It is hard to detect a significant slowdown in the evolution of NMR as

a more and more selective and powerful probe of molecular structure. Moreover, an explosive expansion of applications from primarily organic chemistry to biochemistry, medicine, inorganic chemistry, and materials science appears to be at hand. Consequently, it seems appropriate to predict, if one is given to this dangerous practice, a continuing healthy growth in the NMR industry, both in the number of instruments sold each year, and in the worldwide total dollar volume.

Continued magnet development, both in improving presently used magnetic materials and in construction techniques, could lead to a superconducting spectrometer operating in the range of 750 MHz to one GHz. Such improvements will probably come more gradually, and the price is likely to increase exponentially. Nevertheless, the requirements of leading research groups and regional research facilities indicate that a limited market exists for such a product. On the other hand, a breakthrough in the use of high temperature superconductors for high-field laboratory magnets could change the entire picture with regard to costs and field strengths, bringing about a dramatic increase in the size of the market. I would not delay purchase of a current model instrument for fear of impending obsolescence of the magnet, but I expect that the obstacles to incorporating the new superconductors in practical magnets will eventually be overcome and lead to an affordable high field instrument which will be easier to maintain.

Medicine and materials research will benefit from further improvements in imaging equipment and techniques and surely will represent a growing share of the NMR market. High performance NMR spectrometers, utilizing improved solid-state devices for amplifiers, switching, and data processing, seem poised to make an impact on applications of NMR to studying a variety of solid samples.

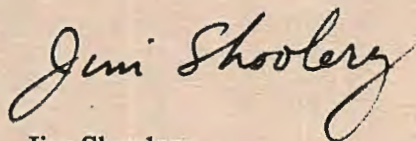
Leadership in the NMR industry will depend not only on the performance, reliability, and servicability of the hardware, but also upon the development and support of sophisticated software to take much of the decision-making and work out of obtaining the desired data. The fertile brains of NMR specialists can be depended upon to continue to churn out ingenious pulse sequences for selectively extracting information from complex chemical systems. These improvements should lead to a generation of instruments that will greatly increase the productivity of chemists and thus easily justify the investment required to make these powerful tools available.

Having been a party to getting this amazing phenomenon launched, and having toiled for most of thirty-eight years to add momentum to its growth, I confess to taking considerable satisfaction in the current results and future prospects. Just as many parents hope to raise their children to become valued members of society, so my early labors in NMR had the goal of contributing to a technique that would be useful to chemists. In that I feel I have achieved success and fulfillment beyond my wildest dreams. It has truly been a satisfying career.

I'll just end this with the thought that "Old NMR spectroscopists never die-- they just lose their coherence". I can certainly see this coming, and I just hope I have written this letter in time.

In appreciation of all your contributions to NMR through this newsletter, I salute you.

Sincerely,



Jim Shoolery
Varian NMR Applications Lab
Palo Alto, California

THE ROCKEFELLER UNIVERSITY

pro bono humani generis

1230 YORK AVENUE, NEW YORK, NEW YORK 10021-6399
212/570-8000, 212/570-7974(FAX)

August 13, 1990
(received 8/17/90)

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

Dear Dr. Shapiro:

Simple 3D Graphics Display; A Recall of ^{15}N Peptide Shift Values

There seems to be general agreement that the analysis of 3D NMR spectra is best done by detailed examination of 2D sections. Looking at the processed data in three dimensions using dynamic rotatable and translatable displays, may, however, be useful on occasions for rapid surveying of the data, finding the right contour levels, or impressing your colleagues, Deans, etc. As usual, I was reluctant to reinvent the wheel, and stumbled across a display program called AVS, which runs on the Stellar(Stardent) GS1000 here. The figures attached are black and white prints of fancy color displays at the graphics terminal. The spectra (see legend) were obtained and processed by Dr. John Glushka, and Dr. Carlos Rios. The sample of adenylate kinase from *E. coli* was provided by Dr. Octavian Barzu, Institut Pasteur. Processing was done with some extensions of our 'runmr' program. The 3D final output file for AVS is restricted to 255x255x255 at 256 levels, but this is not a big problem. The output section and the AVS program run very rapidly. The program details are trivial; I shall be happy to send a model subroutine for creating such a file to anyone requesting it. (E-mail is probably easiest for me, to cowburn@rockvax.rockefeller.edu).

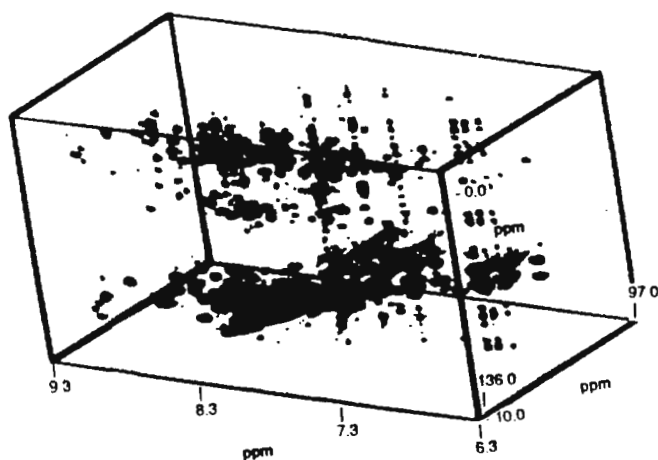
On another matter, I regret to announce the recall of a table of nominal ^{15}N shifts for random coil peptides, which appeared in *J. Am. Chem. Soc.* 1989, **111**, 7716-7722 (Table III). Since this table was put in specifically to help by providing a first approximation to expected values, this is naturally disappointing and embarrassing. To avoid any more calls on how to use the table ("cut it out of the Journal and toss in the waste basket"), please be assured that a corrected version has been put into *JACS* (1990, **112**, 2843). The errors were nearly all around or below the 3 ppm value which we had identified as the lower limit of interpretability of such shifts, at least currently. The conclusions of the article were unmodified.

Mea culpa,

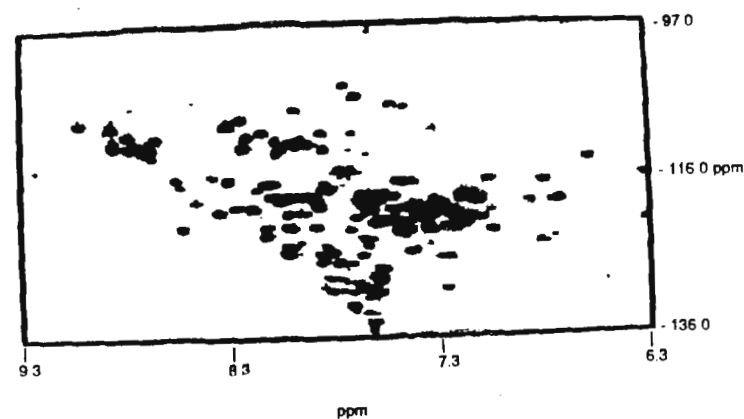


David Cowburn

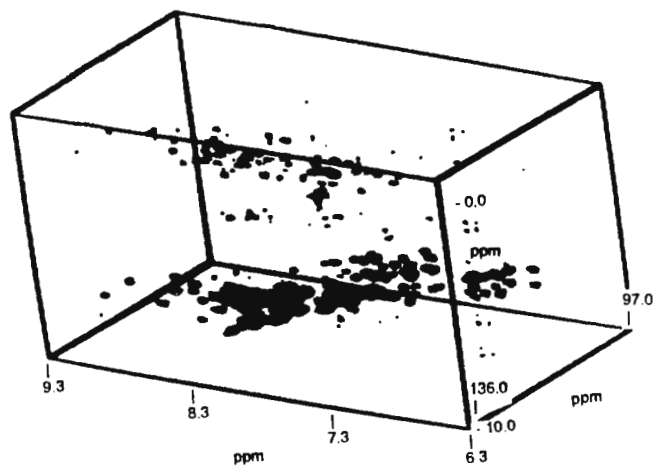
3D NOESY-HMQC spectrum of 2.5 mM ^{15}N -labeled adenylate kinase in 10% $\text{D}_2\text{O}/\text{H}_2\text{O}$ at pH 7.5, 25 ° C. The experiment was acquired on a GE GN-500 NMR spectrometer. The data were collected as a series of HMQC planes. A 1 s presaturation time and a mixing time of 80 ms was used. The t₁, t₂, and t₃ dimensions consisted of 64 x 64 x 2048 data points. A linear baseline correction and gaussian multiplication with a line broadening of -2 Hz and gb of 0.05 in the F3 dimension keeping the amide region and a 60 shifted sine bell and zero filling to 128 points was applied to the F1 and F2 dimensions yielding a final absorptive spectrum of the amide region consisting of 512 x 128 x 128 data points in the F3, F2, and F1 dimensions. (A,B) 3D-NOESY- ^{15}N -HMQC spectra with 256 x 128 x 128 data points in F3, F2, and F1 displayed. (c) F3-F2 plane projection corresponding to the HMQC, and (d) F3-F1 plane projection corresponding to the NOESY.



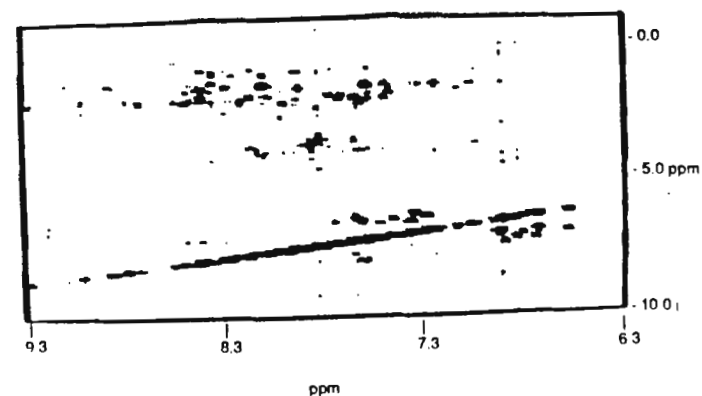
a.



c.



b.



d.

Not even a coffee break.



Seven days a week, twenty-four hours a day. For over three years, a QE automated NMR analytical spectroscopy system ran experiments at Searle Labs in Chicago with only a few hours of downtime.

This sterling work record helped Searle gather high quality data from both fully automated macro and manual routine experiments. Today, two QE automated systems:

- ▶ Accommodate the experiments of over 30 chemists
- ▶ Operate 24 hours a day, seven days a week
- ▶ Perform both manual and fully automatic macro experiments during the day
- ▶ Perform fully automatic macro programs at night and on weekends
- ▶ Adapt to a demanding user schedule of 15 and 30 minute time slots

Work smarter with the new QE Plus

With more speed and efficiency, the new QE Plus does the job even better—to meet your needs for automated performance day after day, year after year.

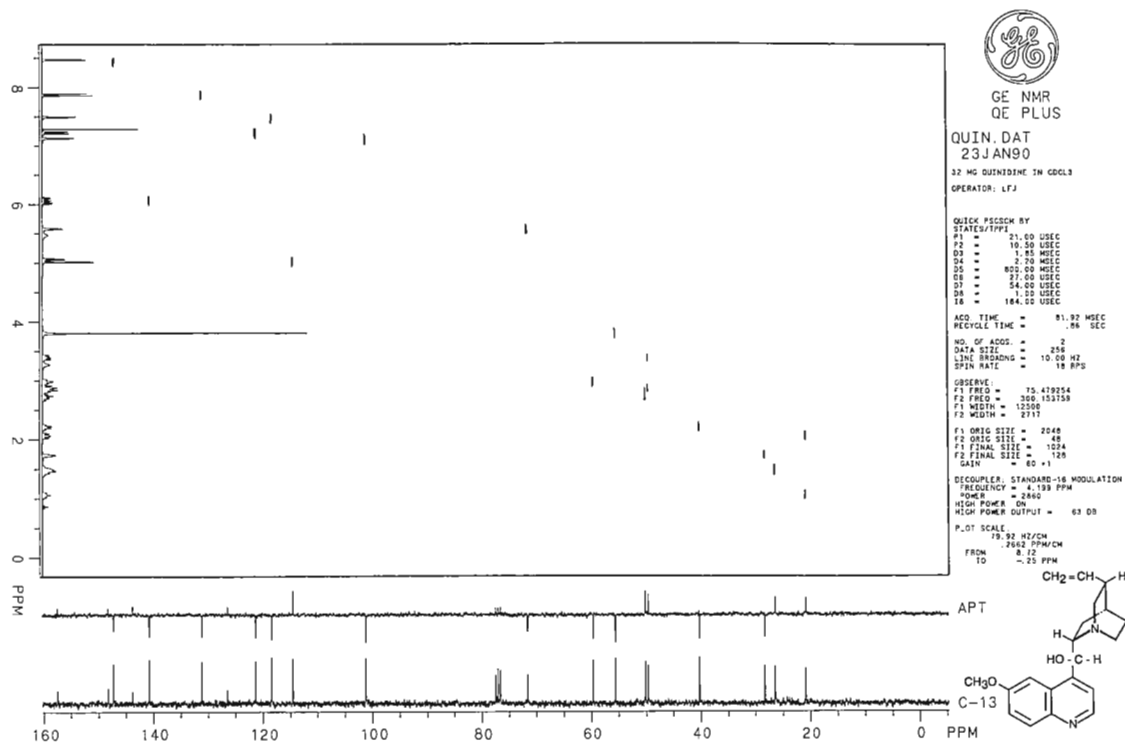
For more information on the new QE Plus, write 255 Fourier Ave., Fremont, CA 94539 for a full color QE Plus brochure. Or call 800-543-5934.

And get to work.



GE NMR Instruments
Put us to the test.

*The new QE Plus—for increased throughput
and greater automated capabilities.*



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



THE UNIVERSITY OF QUEENSLAND

CENTRE FOR MAGNETIC RESONANCE

c/o Mater Hospital
South Brisbane, Queensland, 4101 Australia

Tel (07) 846 2277
Fax (07) 844 8010

8th August, 1990 (received 8/15/90)

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

Dear Barry,

Single Scan F_1 "Quadrature Detection" in 2D NMR

Pulsed field gradients are finding ever increasing applications in high resolution NMR spectroscopy and we believe it will not be long before gradient accessories will be standard issue on most NMR systems. One interesting feature of gradient use in 2D spectroscopy is the possibility of producing quadrature detection in the F_1 dimension (N- or P- type selection) in a single acquisition, such as beautifully illustrated recently by Ralph Hurd in 'gradient enhanced' DQF-COSY and TOCSY experiments (1). We noticed a similar effect in the 2D double quantum experiment and have since applied the ideas to the standard COSY sequence. The time-saving benefits of not having to perform extensive phase cycling to obtain phase-sensitive 2D spectra are obvious, and in the case of multiple quantum filtering, excellent levels of solvent suppression can be achieved.

In the case of the COSY sequence, a pair of gradient pulses are applied, either side of the mixing pulse as shown in the sequence below. We rationalize the effect of the gradients as follows:

For a simple AX spin system the observable coherences for the X spin following the mixing pulse are of the form (2):

$$US_X \sin(\omega_S t_1) \cos(\pi J t_1) - I_Y S_Z \sin(\omega_S t_1) \sin(\pi J t_1) \quad [1]$$

where I and S represent the spin angular momentum operators for the A and X spins respectively. The first term of [1] represents the diagonal multiplet at $\omega_1 = \omega_2 = \omega_S$, and the second term, the antiphase cross peak at $\omega_1 = \omega_S$, $\omega_2 = \omega_I$. Because there is a sine-only dependence on t_1 , signals are observed at +ve and -ve frequencies in ω_1 and these are usually separated by phase cycling. If a short gradient pulse is applied for τ_D during the τ_1 evolution period, the first term of [1] becomes:

$$US_X \cos(\pi J t_1) \sin(\omega_S t_1 + \Delta \omega \tau_D) \\ = \frac{1}{2i} US_X \cos(\pi J t_1) [\exp(-i(\omega_S t_1 + \Delta \omega \tau_D)) - \exp(-i(\omega_S t_1 + \Delta \omega \tau_D))] \quad [2]$$

where $\Delta \omega$ is the frequency offset induced by the gradient.

Application of a second equal gradient pulse having the same time integral as the first immediately following the mixing pulse yields evolution as

$$\frac{1}{4i} U \cos(\pi J t_1) [S_+ \exp(i \Delta \omega \tau_D) + S_- \exp(-i \Delta \omega \tau_D)] \times \\ [\exp(i(\omega_S t_1 + \Delta \omega \tau_D)) - \exp(-i(\omega_S t_1 + \Delta \omega \tau_D))] \quad [3]$$

The terms in which $\Delta\omega$, the gradient induced offset remains represents dephased magnetization. Thus, the detected signal is given by

$$\frac{1}{4i} \cos(\pi J t_1) [-S_+ \exp(-i\omega_S t_1) + S_- \exp(i\omega_S t_1)] \quad [4]$$

which reduces to

$$-\frac{1}{2} U S_y \cos(\pi J t_1) \exp(i\omega_S t_1) \quad [5]$$

This represents quadrature detection of S_y with respect to t_1 and corresponds to N-type selection. Inverting the sign of the second gradient allows P-type selection as shown in the figure. This approach can also be applied to other 2D sequences incorporating gradient pulses.

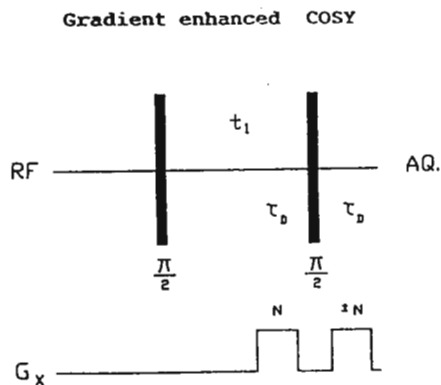
Best wishes,
Yours sincerely,

Ian Brereton

Stuart Crozier

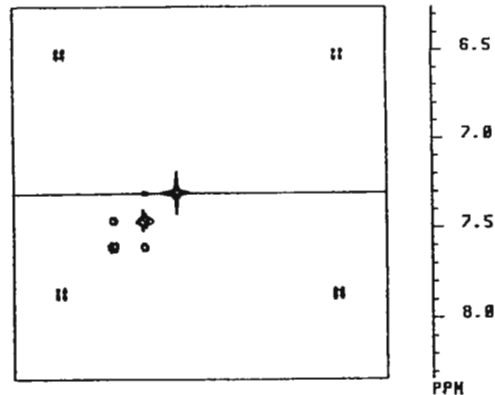
David Doddrell

1. R.E. Hurd, J. Magn. Reson. 87, 422 (1990).
2. O.W. Sorensen, G.W. Eich, M.H. Levitt, G. Bodenhausen and R.R. Ernst, Prog. NMR Spectrosc. 16, 163 (1983).

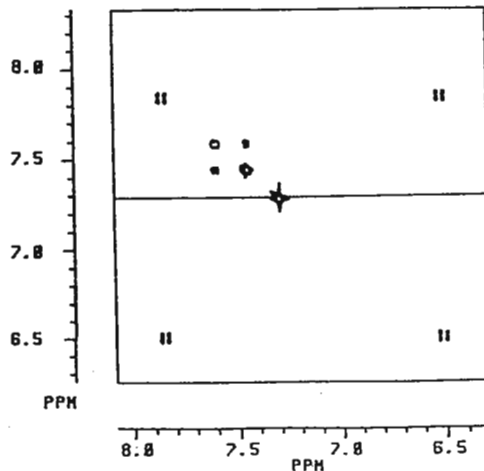


Cinnamic acid
20mM in $CDCl_3$
1 acquisition

Gradients +/-
N - type



Gradients +/-
P - type





NATIONAL TAIWAN UNIVERSITY

DEPARTMENT OF CHEMISTRY

ROOSEVELT ROAD SECTION 4

TAIPEI, TAIWAN, REPUBLIC OF CHINA

PHONE: 3635357 • 3636359

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

July 28, 1990
 (received 8/4/90)

Dear Dr. Shapiro:

Studies of Cross-Relaxation of Dipole-Dipole and Chemical Shift Anisotropy Interactions:
 Differential Recovery of Methyl ^{13}C Spectral Lines.

As part of our ongoing research effort into the study of cross relaxation in liquids, we have been studying spin recovery rate of proton coupled ^{13}C spectral lines of $(\text{CH}_3\text{O})_4\text{Si}$ in CDCl_3 solution at 210 K.

The pulse sequence utilized is basically an inversion recovery pulse sequence. The T_1 values for ^{13}C quartet are found to be 4.35 s, 8.26 s, 7.10 s, and 3.69 s. The independent-internal-rotation model¹ has been utilized and the correlation times 0.15 ps, 8.5 ps and 350 ps have been obtained for methyl rotation, rotation of methoxy group, and overall reorientation, respectively. The CSA parameter $\sigma_{\parallel} - \sigma_{\perp} = 67 \text{ ppm}^2$ is invoked to calculate T_1 values which give 4.03 s, 8.18 s, 7.26 s and 3.54 s. The agreement shows that the importance of cross correlation of DD and CSA interactions. The differential recovery rate is sensitive even for small difference in CSA parameters.

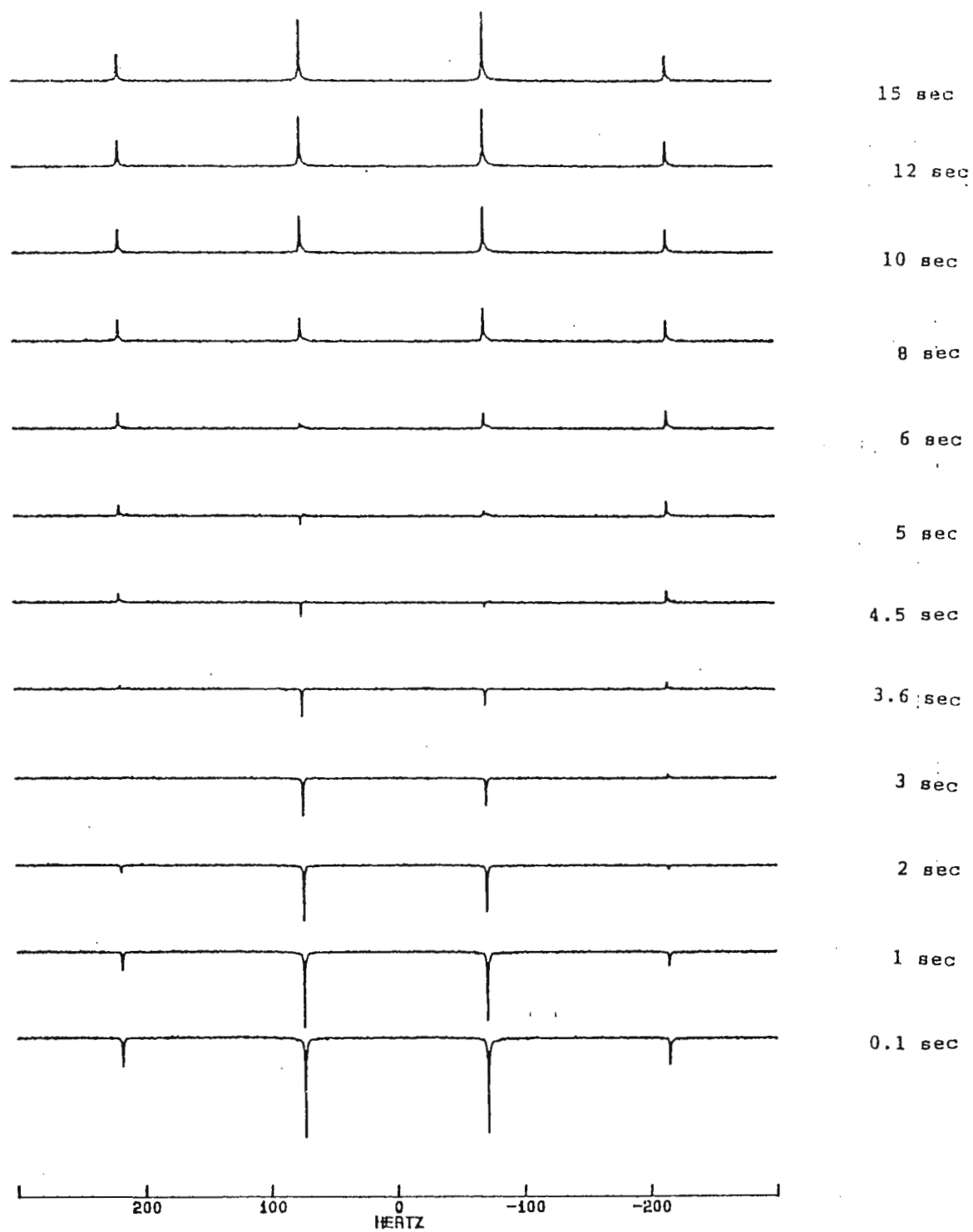
Truly yours,

Tai-Sung Lee

Lian-Pin Hwang

References:

- 1) Wittebort and A. Szabo, J. Chem. Phys. **69**, 1722 (1978)
- 2) M. Mehring "High Resolution NMR Spectroscopy in Solid" Spring Verlag, Heidelberg, 1978.

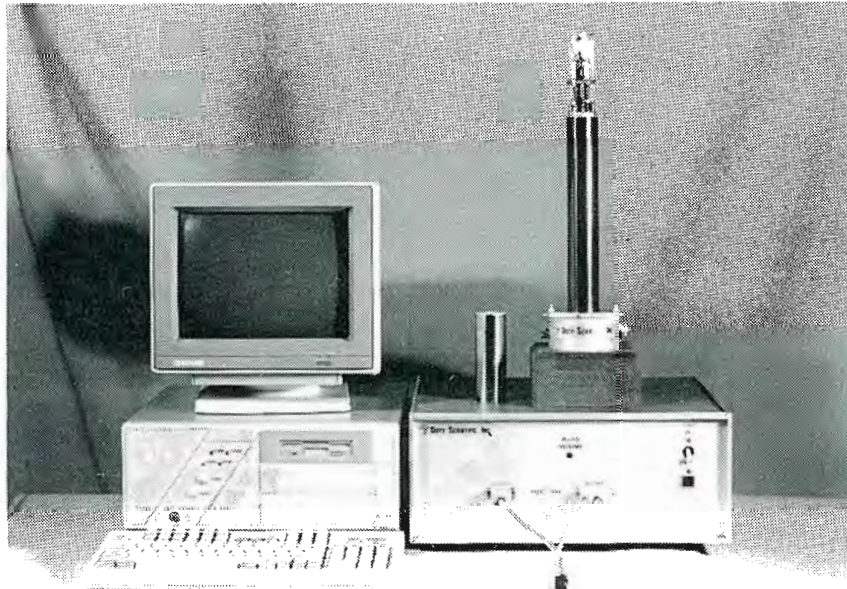


^{13}C Differential Recovery Spectra of $(\text{CH}_3\text{O})_4\text{Si}$ in CDCl_3



Doty Scientific, Inc.

TEMPERATURE CONTROLLER



DOTY SCIENTIFIC TEMPERATURE CONTROLLER

\$ 9,000.

AT Computer-Based, Five Channel, High Power, Fast Response

PID parameters and load parameters are automatically adjusted to provide wide range temperature control. Low noise, linear gain, 0-45 V 400 W total heater output, with 2 ms response time. Can be configured for all standard thermocouples and 100 Ω RTDs. Stability depends on conditions but can be better than 0.1°C. Sensor modules are available for low temp 3 K to 400 K, standard -180° to +400°C, high speed -180° to +250°C, or high temp -100° to +650°C. These plug in modules are easily exchanged to provide temperature control from 3 K to 650°C. One sensor module comes with the controller. When ordering, please specify which module is to be included. Additional modules can be ordered at anytime. Specify 120 VAC or 230 VAC.

ADDITIONAL TEMPERATURE CONTROLLER SENSOR MODULES (each) \$ 500.

(Sensor Module specifications follow on the back of this page.)

Sensor Module 1: Standard Variable Temperature.

(For high-resolution, high-temperature high-resolution, and standard MAS).

Accepts copper-constantan sample gas thermocouple and 100 Ω RTD cold junction compensation inputs. Single overheat-protected heater output.

Accuracy: $\pm 0.5^{\circ}\text{C}$ from -180°C to $+400^{\circ}\text{C}$ with user calibration.

Sensor Module 2: MAS High Speed Variable Temperature.

DSI high speed probes have two heater channels for dual air supply and require this sensor module with dual copper-constantan sample air thermocouple and 100 Ω RTD cold junction compensation inputs for accurate VT control. Supports an additional electronics region copper-constantan thermocouple. Dual, independent, overheat-protected heater outputs.

Accuracy: $\pm 0.5^{\circ}\text{C}$ from -180°C to $+250^{\circ}\text{C}$ with user calibration.

Sensor Module 3: Extreme High Temperature.

Accepts chromel-alumel spinner air sensor, with 100 Ω RTD cold junction, electronics region and dewar region copper-constantan thermocouples. Single, overheat-protected heater output.

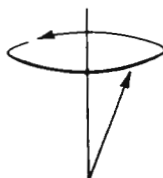
Accuracy: $\pm 1^{\circ}\text{C}$ from -100°C to $+650^{\circ}\text{C}$ with user calibration.

Sensor Module 4: Extreme Low Temperature.

Accepts sample gas RTD and carbon resistor sensors, dewar jacket, valve temperature, and exhaust gas 100 Ω RTDs, and a cryogen level resistive sensor. Dual, independent, overheat-protected, high power outputs for sample gas and exhaust gas heaters, with low power pulsed outputs for valve and dewar jacket exhaust heaters.

Accuracy: $\pm 0.2^{\circ}\text{C}$ from 3 K to 20 K, $\pm 0.5^{\circ}\text{C}$ from 20 K to 400 K.

Temperatures given are for the controller modules. Please do not exceed your probe specifications.



Doty Scientific, Inc.

600 Clemson Road
Columbia, S.C. 29223
USA

Office: (803) 788-6497

Fax: (803) 736-5495

Sales: (803) 699-3806

Service: (803) 699-3807



Hercules Incorporated
Research Center
Wilmington, DE 19894
(302) 995-3000
Telex: 83-5479

July 24, 1990
(received 7/30/90)

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

Dear Dr. Shapiro:

NMR Analysis of Polymer Mixtures

Many commercial polymers consist of mixtures of two or more components that differ from each other in composition or in microstructure. The mixture may be the result of blending of different polymer batches, polymer synthetic procedure (e.g., programmed comonomer feed rates), or the presence of multiple catalytic sites. The NMR spectra of such polymers contain contributions from all the components, and as such are difficult to analyze.

Recently, a general approach was developed to characterize the NMR spectral data of such polymers.¹⁻² The technique involves the use of reaction probability models and computer-assisted analytical approach³. Several computer programs have been written:

For whole polymers:

MIXCO.C3 Two-state E/B for polypropylene
MIXCO.C4 Two-state E/B for poly(1-butene)
MIXCO.TRIAD Two-state B/B and M1/M1 for copolymer
 triad sequence analysis

For polymer fractions:

MIXCO.C3X Three-state E/E/B for polypropylene
MIXCO.C4X Three-state E/E/B for poly(1-butene)
MIXCO.TRIAD/X Two-state B/B and M1/M1 for copolymer
 triad sequence analysis
MIXCO.TRIADX Three-state B/B/B for copolymer triad
 sequence analysis

As an illustration of the utility of this approach, an analysis of the published triad sequence data of Kuroda, et al.⁴ is shown here. In their careful characterization of an ethylene/1-butene copolymer, they separated it into five fractions by successive extraction with diisopropyl ether at 20°C (Fraction 1), n-hexane at 20°C (Fraction 2), n-hexane at its boiling point (Fraction 3), and cyclohexane at its boiling point (Fraction 4). The residual polymer (cyclohexane insolubles) was designated Fraction 5. Their result⁴ is duplicated in the following table.

Frac	Wt%	(BBB)	(BBE)	(EBE)	(BEB)	(BEE)	(EEE)
1	18.4	0.047	0.090	0.163	0.075	0.267	0.358
2	7.0	0.014	0.043	0.141	0.040	0.245	0.517
3	13.6	0.003	0.020	0.103	0.019	0.188	0.667
4	32.0	0.000	0.005	0.058	0.004	0.113	0.820
5	29.0	0.000	0.002	0.030	0.002	0.059	0.907

In the above table, E and B refer to ethylene and 1-butene, respectively.

The analysis of the combined NMR/fractionation data was carried out through the program MIXCO.TRIADX. The triad intensities were analyzed two fractions at a time, and different reaction probability models were tested. The data given in the above table turned out to fit a three-site model, two active sites being Bernoullian and one active site being first-order Markovian.

<u>Site #</u>	<u>Model</u>	<u>Reaction Probabilities</u>	<u>Fraction(s)</u>
1	1st order Markovian	$P_{be} = 0.712$ $P_{eb} = 0.597$	1 - - - -
2	Bernoullian	$P_b = 0.22$	1 2 3 4 -
3	Bernoullian	$P_b = 0.03$	- 2 3 4 5

Using the information on the weights of the fractions, one can determine the relative contribution of each active site to polymer generation. Site 3 (with $P_b = 0.03$) produces the most polymer (62%), followed by site 2 (34%). Site 1 (obeying first-order Markovian statistics) only contributes about 4% to the copolymerization.

This work (on the ethylene/1-butene copolymer) has just appeared⁵ in Polymer Bulletin, where the computational details are given.

Yours very truly,


H. N. Cheng

References:

1. H. N. Cheng, J. Appl. Polym. Sci., **35**, 1639 (1988).
2. H. N. Cheng, ACS Symp. Ser., **404**, 174 (1989).
3. H. N. Cheng, J. Appl. Polym. Sci. : Appl. Polym. Symp., **43**, 129 (1989).
4. N. Kuroda, Y. Nishikitani, K. Matsuura, and M. Miyoshi, Makromol. Chem., **188**, 1897 (1987).
5. H. N. Cheng, Polym. Bull.(Berlin), **23**, 589 (1990).



A.E. STALEY MANUFACTURING COMPANY 2200 E. ELDORADO STREET DECATUR, ILLINOIS 62525 TELEPHONE 217/423-4411

July 13, 1990
(received 7/21/90)

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

Computer Simulation of the DANTE Pulse Sequence

Dear Dr. Shapiro:

Selective pulses are finding many new applications, such as water suppression, and various 1-D versions of 2-D techniques. Unfortunately, special equipment is required to generate the pulse envelopes, which most NMR laboratories do not possess. However, selective pulse techniques have been with us for quite some time, one of which can very easily be performed on most instruments, DANTE¹. DANTE generates selective pulses by using a long chain of equal pulses separated by the reciprocal of the desired excitation frequency, i.e., **Pulse..Delay..Pulse..Delay..Pulse..etc.**

The problem with the Classical DANTE sequence is that it generates very poor excitation patterns. To demonstrate this, I have written a program in TURBO BASIC which simulates the effect of the pulses and delays on magnetization in the rotating frame. The program sets up a rotating frame using Cartesian coordinates with the magnetization initially along the z-axis. A pulse rotates the vector around the x-axis and during the delay time the chemical shift causes rotation around the z-axis to a new position. Another pulse rotates the vector again about the x-axis and another delay causes further precession around the z-axis. This is repeated until the pulse train is complete, i.e., a 90° pulse is achieved. The effect of the pulse train is calculated for a range of chemical shifts, e.g. 400 Hz., and plotted on the screen. A classical DANTE sequence of 18 pulses of equal intensity with delays of 1 msec. yields the miserable pattern shown in Figure 1.

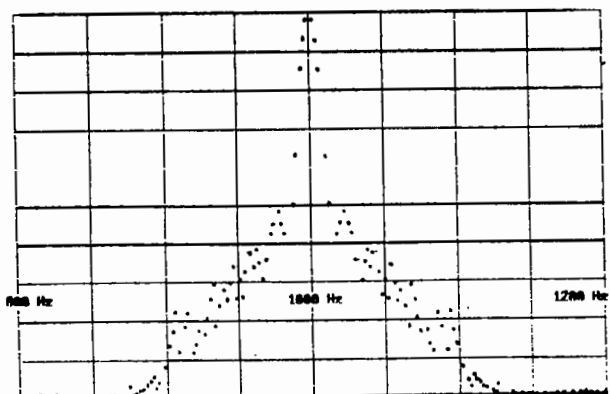


Fig. 1 Linear

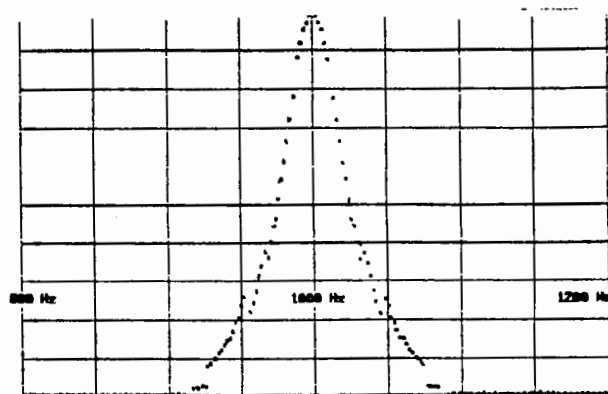


Fig. 2 Gaussian

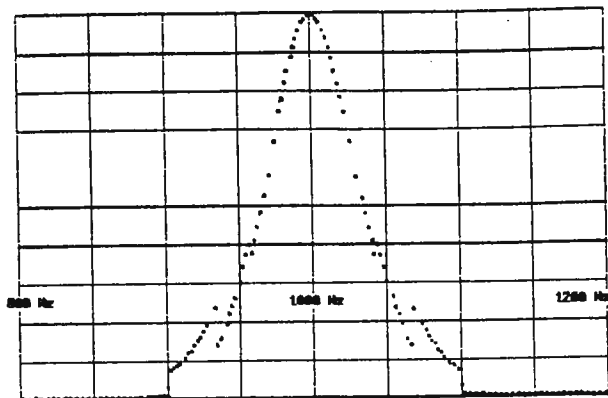


Fig. 3 Binomial

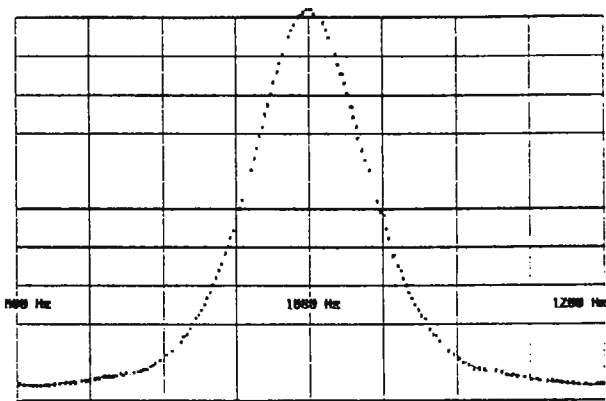


Fig. 4 Half-Binomial

A much better approach is to vary the intensity of the pulses in a binomial or Gaussian pattern. Figure 2 shows the excitation pattern for an 16 pulse Gaussian envelope and Figure 3 that of an 16 pulse binomial distribution. It has also been stated that half pulses are also supposed to be effective - Figure 4 shows the results of a 18 pulse half-binomial DANTE. However, the excitation pattern for the demi-pulse is broader and never reaches zero intensity.

Besides using more pulses, the excitation bands can be made much sharper by simply using higher integral multiples of the delay times, e.g. using four times the delay will result in a pattern similar to Figure 2 with 10% excitation only 20 Hz away from the center frequency. However, this generates additional excitation bands. The excitation frequency can also be set at the point of interest and the excitation pattern can be controlled by changing the delay time, being careful not to excite other signals at $1/n \cdot \text{delay}$.

The above findings can readily be implemented on most instruments for many applications.

Sincerely,

Gary Juneau

1. Gareth A. Morris, Ray Freeman, J. Magn. Reson. 29, 433-462 (1978)

Now, Bruker makes research routine.



Here are two systems to prove it.

The Bruker AC-E and AC-P NMR spectrometers are high performance, easy-to-use, systems. At the touch of a button, automation takes control of everything from lowering the sample and shimming to plotting, integrating and picking the peaks.

Research software gives you routine simplicity.

In the pushbutton mode, function keys across the top of the keyboard allow you to perform both basic and highly advanced measurements by pressing only one or two buttons. We back this up with our powerful and highly flexible research level software, which

includes a comprehensive library of preconfigured experiments ranging from routine proton/carbon to state-of-the-art 2D NMR spectroscopy.

Two models to choose from.

Both systems offer outstanding performance and both are available right now. The AC-E is an economical system ideal for routine use, with full pushbutton automation.



The AC-P is a research-grade system with advanced features such as a process controller for one-degree phase increments as needed for multiple quantum spectroscopy. As your interests grow, additional features such as the QNP accessory, automatic sample changer, bar code reader, CPMAS solids accessory and much more can be added to both systems.

For more information or to see the AC in action, please write:

*Bruker Instruments, Inc.
Manning Park, Billerica, MA 01821*

*In Europe: Bruker Analytische
Messtechnik GmbH, Silberstreifen,
D-7512 Rheinstetten 4, W. Germany*



Analytical Systems Worldwide

Spectrometer Performance – AC Series

Summary of Specifications for Basic System Configurations AC Series 100, 200, 250, 300 MHz

Probehead (5 mm)	Nucleus	Test	90° pulse (μs)	S/N			
				100	200	250	300
¹ H	¹ H	0.1% EB	< 10	35	85	120	175
¹ H/ ¹³ C	¹ H	0.1% EB	< 15	20	45	70	90
	¹³ C	ASTM	< 15	20	50	70	100
		10% EB		15	40	50	70
QNP	¹ H	0.1% EB	< 15	20	45	70	90
	¹⁹ F	0.05% TFT	< 20	20	45	70	100
	³¹ P	48.5 mM TPP	< 20	25	50	60	70
	¹³ C	ASTM	< 15	20	50	70	100
VSP multinuc. ³¹ P- ¹⁵ N		10% EB		15	40	50	70
	¹ H	0.1% EB	< 15	20	40	60	80
	³¹ P	48.5 mM TPP	< 15	15	30	35	40
	¹³ C	ASTM	< 15	20	50	70	100
		10% EB		15	40	50	70
	¹⁵ N	90% Form.	< 25		5	8	10
			SSB %	Lineshape (Hz)			
All Probes (5 mm)	¹ H	CHCl ₃	< 1	7/15	7/15	7/15	7/15
	¹³ C	C ₆ H ₆	< 0.5	3/7	3/7	3/7	3/7
				Resolution (Hz)			
	¹ H	ODCB		0.2	0.2	0.2	0.2
All Probes (5 mm)	¹³ C	C ₆ H ₆		0.2	0.2	0.2	0.2

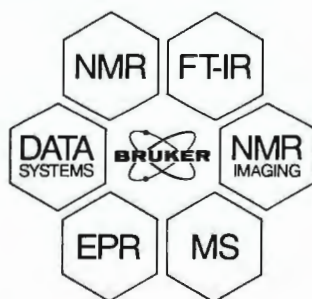
Magnet:	Helium refill interval (days)			
Standard	120	120	120	120
Long hold time	200	200	190	180
Ultra-long hold time	365	365	350	340

EB = ethylbenzene (for ¹³C with ¹H-dec.); ASTM=60% C₆D₆ in dioxane;
TFT=trifluorotoluene; TPP=triphenylphosphate; Form.=formamide (¹H-dec. without NOE);
SSB=spinning sidebands;
Lineshape: ¹H=CHCl₃ linewidth at ht. of ¹³C-satellites/at 20% this level
¹³C=C₆H₆ linewidth at 0.55%/0.11% level (¹H-dec.).
Dimensions and weights are approximate; voltage+10/-5% max. variation, otherwise
power stabilizer required; other line freq. or voltage upon request.

	Standard	Options
Transmitter		
Freq. range	¹ H/ ¹³ C ± 100 kHz	full multinuc. ²
Offset steps	100 Hz	0.01 Hz ^{1,2}
Phase shift steps	90°	< 0.5° ^{1,2}
¹H-decoupler		
Freq. range	150 kHz	
Offset steps	0.01 Hz	
Phase shift steps	90°	< 0.5° ^{1,2}
Max. power	5 W	40W ²
Attenuator range	60 dB	80 dB ²
Quad. receiver		
Spectral width	100 Hz – 100 kHz (cont.)	125 kHz ² , 50 kHz
Filter width (100 Hz Steps)	100 Hz – 100 kHz	100 Hz – 100 kHz; 150 kHz ²
ADC	12-bit	16-bit
Computer		
Memory	256 K / 24-bit	up to 1280 K / 24-bit
Max. FT size	128 K words	512 K words
Multi-pulse timing resol.	0.1 μsec	0.025 μsec ²
FT time (software)	1 K / 1.5 sec	
Co-processor		8 K / 1.5 sec ²
Array processor		64 K / 1.2 sec
Graphic display: colors	8	8
Pixel matrix	256 x 512	256 x 512
Plotter	A3 flat bed 8 colors	drum ² ; HP with auto-feed
Printer	dot-matrix	
Storage	160 MByte disk, floppy	tape
Communication	RS 232	KERMET/ETHERNET® Fiber optic LAN

1. Standard with the AC 300E 2. Standard for AC-P version

Nitrogen refill interval (days)	Minimal room height (cm)	Weight approx. (kg)
9	276	250
10	263	220
14	297	250
Console	w 126 x d 85 x h 91 cm	
Height with display	123 cm	
Weight approx.	300 kg	
Power consumption	220 V/50 Hz/3 kW	



Australia: BRUKER (Australia) Pty. LTD., Earlwood, New South Wales, Tel. 02-5589747
Belgium: BRUKER SPECTROSPIN S.A./N.V., Brussels, Tel. (02) 648 53 99
Canada: BRUKER SPECTROSPIN LTD., Milton, Ontario, Tel. (416) 876-4641
England: BRUKER SPECTROSPIN LTD., Coventry, Tel. (0203) 463770
France: SADIS BRUKER SPECTROSPIN SA, Wissembourg, Tel. (088) 94 98 77
India: BRUKER INDIA SCIENTIFIC Pvt. LTD., Andheri (West), Bombay, Tel. 22 62 72 32
Italy: BRUKER SPECTROSPIN SRL, Milano, Tel. (02) 23 50 09, 2 36 40 69
Japan: BRUKER JAPAN CO. LTD., Ibaraki, Tel. 0298-52-1234
Netherlands: BRUKER SPECTROSPIN NV, Wormer, Tel. (75) 28 52 51
Scandinavia: BRUKER SPECTROSPIN AB, Åkersberga, Sweden, Tel. (07 64) 6 80 60
Spain: BRUKER ESPANOLA S.A., Madrid, Tel. 341-259-20-71
Switzerland: SPECTROSPIN AG, Fällanden, Tel. 1-82 59 111
W. Germany: BRUKER ANALYTISCHE MESSTECHNIK GMBH, Rheinstetten, Tel. 0721-5161-0
 BRUKER ANALYTISCHE MESSTECHNIK GMBH, Karlsruhe, Tel. 0721-5967-0
 BRUKER-FRANZEN ANALYTIK GMBH, Bremen, Tel. 0421-8700-80
USA: BRUKER INSTRUMENTS, INC., Billerica, MA 01821, (617) 667-9580
 Regional Offices in Chicago / IL, Wilmington / DE, Houston / TX, San Jose / CA



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute on Aging
Gerontology Research Center
4940 Eastern Avenue
Baltimore, Maryland 21224

July 24, 1990
(received 8/15/90)

Professor Bernard L. Shapiro
Department of Chemistry
Texas A & M University
College Station, Texas 77843-3255

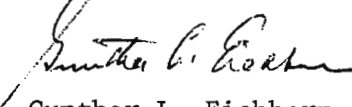
Dear Barry:

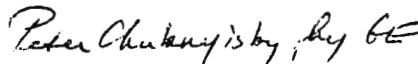
It is well known that a variety of NMR techniques are available for determining distances within and between molecules. Nuclear Overhauser effects and the paramagnetic effect on nuclear relaxation have been extensively used for this purpose. The latter is particularly suitable for distance measurements when metal ions are present and these can be substituted by paramagnets. There are also a variety of techniques for determining distances between metals; one of these is an EPR method developed by Leigh (J. Chem. Phys. 52, 2608) and extended in the laboratory of Villafranca (Adv. Inorg. Biochem. 4, 289).

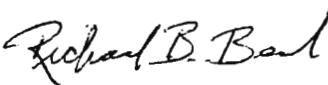
We have been engaged in a series of studies in which we have combined NMR and EPR techniques for distance measurements. E. Coli RNA polymerase contains two metals, Zn(II) and Mg(II), at the active site, and they can both be substituted by a paramagnet, e.g. Mn(II). By combining the well-known NMR methods for distance measurements from the metals to points on the substrates with EPR methods for the determination of metal-metal distances we have been able to clarify the spatial relationships between the two metals and two substrates. Some of the results of this work have been published (Biochemistry 29, 5987, 5994).

Further studies on similar systems are underway to use combined NMR-EPR methodology to monitor changes at the active site of the enzyme that would elucidate various aspects of the mechanism of RNA synthesis. Thus, we have compared systems in which template and substrate bases are or are not complementary and found differences between them.

Sincerely,


Gunther L. Eichhorn


Peter P. Chuknyisky


Richard B. Beal

Keystone Symposia

1991 Conferences

CG FRONTIERS OF NMR IN MOLECULAR BIOLOGY-II

Organizers: Peter Wright, John Markley and Masatsune Kainosho

April 8-14, 1991; Keystone, Colorado

Sponsored by: SmithKline Beecham Pharmaceuticals and
The Directors Sponsor Fund

Abstract Deadline: December 12, 1990

Mon 4/8—Registration (joint with Protein Folding meeting)

Keynote Address: R. Ernst, ETH Zentrum

Tue 4/9—STRUCTURAL ANALYSIS OF PROTEINS AND FOLDING INTERMEDIATES (joint with Protein Folding meeting): K. Wuthrich, ETH-Honggerberg; B. Matthews, Univ Oregon; H. Roder, Univ Pennsylvania; C. Dobson, Oxford Univ-UK

NMR METHODS: A. Bax, NIH; S. Fesik, Abbott Labs; R. Griffin, MIT

Wed 4/10—THREE-DIMENSIONAL STRUCTURE DETERMINATION: T. James, UC San Francisco; D. Case, Scripps Clinic

Discussion: DATA REDUCTION

PROTEIN STRUCTURE: I. Campbell, Oxford Univ; G. Clore, NIH; P. Wright, Scripps Clinic

Thur 4/11—NUCLEIC ACID STRUCTURE: B. Reid, Univ Washington; J. Feigon, UC Los Angeles; V. Fazakarty, Service Biochim Saclay-France

INTERACTIONS OF PROTEIN AND DRUGS WITH DNA: R. Kaptein, Univ Utrecht; D. Patel, Columbia Univ; C. Hilbers, Univ Nijmegen

Fri 4/12—PEPTIDES AND OLIGOSACCHARIDES: D. Wemmer, UC Berkeley; P. Kim, Whitehead Inst; R. Dwek, Oxford Univ

Banquet (joint)

Sat 4/13—LARGE PROTEINS/ISOTOPE LABELING: J. Markley, Univ Wisconsin; M. Kainosho, Tokyo Metropolitan Univ; R. Dahlquist, Univ Oregon; S. Opella, Univ Pennsylvania

PROTEIN DYNAMICS: G. Wagner, Harvard Medical School; G. Roberts, Univ Leicester; D. Torchia, NIH; C. Woodward, Univ Minnesota

Sun 4/14—Departure

PROGRAM—RELATED POSTER SESSIONS

1 Tuesday 4/9

2 Thursday 4/11

3 Friday 4/12

4 Saturday 4/13

CH PROTEOLYSIS IN REGULATION AND DISEASE

Organizers: Dennis Cunningham and Ralph Bradshaw

April 8-14, 1991; Keystone, Colorado

Abstract Deadline: December 12, 1990

Mon 4/8—Registration

Keynote Address: D. Steiner, Howard Hughes Med Inst

Tue 4/9—STRUCTURE, FUNCTION AND EVOLUTION OF PROTEASES AND PROTEASE INHIBITORS: T. Blundell, London Univ; R. Mac Donald, Univ Texas SW Med Ctr; R. Carrell, MRC Lab, Cambridge; M. Laskowski, Purdue Univ

PROTEASE PROCESSING: R. Bradshaw, UC Irvine; R. Schekman, UC Berkeley

Wed 4/10—PROTEASES IN INTRACELLULAR DEGRADATION AND PROTEIN TURNOVER: J. Smith, Massachusetts Gen Hosp; M. Rechsteiner, Univ Utah; A. Goldberg, Harvard Med Sch

PROTEOLYTIC PROCESSING DURING INFECTION BY HIV AND OTHER VIRUSES: B. Semler, UC Irvine; R. Swanstrom, Univ North Carolina; A. Wlodawer, NC/NIH; J. Strauss, California Inst Technol

Thur 4/11—PROTEOLYSIS IN CELL MIGRATION, DEVELOPMENT AND CANCER-I: F. Blasi, Univ Copenhagen; K. Dano, Rigs Hosp-Denmark; S. Strickland, SUNY-Stony Brook; J. Quigley, SUNY-Stony Brook

PROTEOLYSIS IN CELL MIGRATION, DEVELOPMENT AND CANCER-II: D. Rifkin, New York Univ Med Ctr; L. Liotta, NIH; N. Seeds, Univ Colorado; R. Pittman, Univ Pennsylvania Med Sch

Fri 4/12—PROTEOLYSIS IN HEMOSTASIS, INFLAMMATION AND WOUND HEALING: D. Loskutoff, Scripps Clinic & Rsch Fndn; C. Esmon, Oklahoma Med Rsch Fndn; G. Caughey, UC San Francisco; T. Hugli, Scripps Clinic & Rsch Fndn

Banquet

Sat 4/13—PROTEOLYSIS IN DISEASE/THERAPY-I: D. Cunningham, UC Irvine; C. Abraham, Boston Univ Med Sch; H. Fritz, Univ Munich; Z. Werb, UC San Francisco

PROTEOLYSIS IN DISEASE/THERAPY-II: J. Travis, Univ Georgia; R. Crystal, NIH; E. Haber, Squibb Inst Med Rsch; J. Mc Karrow, UC San Francisco

Sun 4/14—Departure

POSTER SESSIONS

1 PROTEASES: STRUCTURE, FUNCTION AND EVOLUTION

2 PROTEOLYTIC PROCESSING AND PROTEIN DEGRADATION

3 PROTEASES IN CELL MIGRATION, DEVELOPMENT AND CANCER

4 PROTEASES IN DISEASE/THERAPY

R PROTEIN FOLDING, STRUCTURE AND FUNCTION

Organizers: William DeGrado, Stephen Brenner and Dale Oxender

April 8-14, 1991; Keystone, Colorado

Sponsored by: Genentech, Inc and SmithKline Beecham Pharm

Abstract Deadline: December 12, 1990

Mon 4/8—Registration (joint with NMR meeting)

Tue 4/9—STRUCTURAL ANALYSIS OF PROTEINS AND FOLDING INTERMEDIATES (joint with NMR meeting): K. Wuthrich, ETH-Honggerberg; B. Matthews, Univ Oregon; H. Roder, Univ Pennsylvania; C. Dobson, Oxford Univ

PROTEIN FOLDING INTERMEDIATES: A. Fink, UC Santa Cruz; K. Kuwajima, Okkaido Univ; J. Baum, Rutgers Univ

Wed 4/10—PROTEIN FOLDING IN VIVO IN PROCARYOTES: J. King, MIT; C. Branden, Uppsala Biomed Ctr; G. Lorimer, E I DuPont & Co; L. Randall, Washington State Univ

PROTEIN FOLDING IN VIVO IN EUKARYOTES: M. Gething, Univ Texas SW Med Ctr; J. Rothman, Princeton Univ

Thur 4/11—MEMBRANE PROTEINS: D. Papazian, UC San Francisco; C. Brouillette, Univ Alabama;

Discussion: PEPTIDE AND PROTEIN MIMICS: D. Kemp*, MIT

ANTIBODIES: D. Davies, NIH; D. Hilvert, Scripps Clinic

Fri 4/12—PROTEIN ENGINEERING: J. Thornton, Univ London; J. Martia, Univ Liege; D. Agard, UC San Francisco; M. Herold, Hewlett-Packard

ENZYMES: J. Villafranca, Pennsylvania State Univ; C. Walsh, Harvard Med Sch; A. Mildvan, Johns Hopkins Univ Med Sch

Banquet

Banquet Address: A. Mc Lachlan, MRC Lab Molec Biol

Sat 4/13—THEORETICAL CONSIDERATIONS: D. Eisenberg, UC Los Angeles; Z. Wasserman, E I DuPont & Co; J. Novotny, Squibb Inst Med Rsch

DNA RECOGNITION: M. Green, Univ Massachusetts Med Ctr; R. Klevit, Univ Washington

Sun 4/14—Departure

POSTER SESSIONS

1 PROTEIN FOLDING (PROCARYOTES)

2 PROTEIN FOLDING (EUKARYOTES)

3 PROTEIN ENGINEERING

* Session Chairperson

Speakers listed above have been invited; program is subject to change.

(Please Detach and Return)

Keystone Symposia on Molecular & Cellular Biology

CG,CH,R

INFORMATION REQUEST FORM

Please send me Program and Application Information

Name (Last, First, Middle Initial): _____

Department: _____ Institution: _____

Address (Street/P.O. Box): _____

City: _____ State: _____ Zip Code: _____ Country: _____

Previous Address: _____

Business Telephone: _____ Telefax: _____

Please mail to: Keystone Symposia, 2032 Armacost Avenue, Los Angeles, CA 90025

Telephone: (213) 207-5042 Telefax: (213) 207-2397 Telex: 495012 attn. Keystone Symposia

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

August 9, 1990
(received 8/13/90)

Dear Barry:

Progress with Proteins

We have obtained the ^{57}Fe NMR spectra and spin-lattice relaxation times of ethyl isocyanide (EtNC), isopropyl isocyanide (iPrNC), and n-butyl isocyanide (nBuNC) ligated ferrous myoglobins (~ 12 mM, pH 7.1, 22°C) at 8.45 Tesla (corresponding to a ^{57}Fe Larmor frequency of 11.7 MHz). The isotropic chemical shifts are 9223, 9257 and 9238 ppm downfield from $\text{Fe}(\text{CO})_5$, which yields chemical shift anisotropies, $|\delta_\perp - \delta_\parallel|$, of 1288, 1260 and 1205 ppm, for the EtNC, iPrNC and nBuNC species, respectively. The T_1 values are very much longer than those found previously for carbonmonoxymyoglobin (~ 17 msec, H. C. Lee, J. K. Gard, T. L. Brown and E. Oldfield, J. Am. Chem. Soc. (1985) **107**, 4087) and are consistent with a change in sign of the chemical shift tensor upon moving from carbonmonoxymyoglobin to ferrocycytochrome c , as previously postulated by Baltzer (L. Baltzer, J. Am. Chem. Soc. (1987) **109**, 3479) and support his idea that δ_\perp in each of the ferrous heme proteins is at ~ 9000 ppm, and that it is principally a change in δ_\parallel that causes the large range of isotropic chemical shifts observed (from 8227 ppm in MbCO to 11197 in ferrocycytochrome c , corresponding to a δ_\parallel change from 5827 to 16282 ppm).

In addition, we have also obtained the oxygen-17 nuclear magnetic resonance (NMR) spectra of a variety of $[\text{C}^{17}\text{O}]$ -labelled heme proteins, including sperm whale (*Physeter catodon*) myoglobin, two synthetic sperm whale myoglobin mutants (His E7 \rightarrow Val; His E7 \rightarrow Phe), adult human hemoglobin, rabbit (*Oryctolagus cuniculus*) hemoglobin, horseradish (*Cochlearia armoracia*) peroxidase (EC 1.11.1.7) isoenzymes A and C, and *Caldariomyces fumago* chloroperoxidase (EC 1.11.1.10), in some cases as a function of pH, and have determined their isotropic ^{17}O NMR chemical shifts δ_i , and spin-lattice relaxation times, T_1 . We have also obtained similar results on a picket fence porphyrin: (5, 10, 15, 20-tetrakis-($\alpha, \alpha, \alpha, \alpha$ -pivalamidophenyl)porphyrinato) iron (II) (1-MeIm)CO, both in solution and in the solid-state. Our results show an excellent correlation between the infra-red C-O vibrational frequencies, $\nu(\text{C-O})$, and δ_i , between $\nu(\text{C-O})$ and the ^{17}O nuclear quadrupole coupling constant (e^2qQ/h , derived from T_1), and as expected between e^2qQ/h and δ_i . Taken together with the work of others on ^{13}C NMR of $[\text{C}^{13}\text{CO}]$ -labelled proteins, where we find an excellent correlation between $\delta_i(^{13}\text{C})$ and $\nu(\text{Fe-C})$, our results suggest the IR and NMR measurements reflect the same fluctuation, which is thought to be primarily the degree of π -backbonding from Fe-d to CO π^* orbitals, as outlined previously by Li and Spiro (Li, X.-Y. and Spiro, T.G. (1988) J. Am. Chem. Soc. **110**, 6024). The modulation of this interaction by the local charge field is supported by *ab initio* calculations (Cliff Dykstra and Joe Augspurger) that demonstrate an essentially linear correlation between the vibrational frequency of free carbon monoxide, and its carbon-13 and oxygen-17 chemical shifts, under a variety of external electrical influences. The correlations for carbon-13 and oxygen-17 shifts turn out to be in opposite directions, and the electronic structure calculations reveal that it is polarization of the electron charge density along the intermolecular axis that changes the chemical shielding oppositely for the carbon and oxygen nuclei. The experimentally determined correlation of the vibrational frequency with oxygen-17 quadrupole coupling constants is also seen in the calculations. Thus, backbonding is likely modulated by the distal interaction, between a uniform electric field and the shielding polarizability. Some of these ideas may help us understand the origins of chemical shift non-equivalencies in proteins.

Yours sincerely,

Epi

Eric Oldfield
Professor of Chemistry



First Announcement

Twenty-Second Annual Southeastern Magnetic Resonance Conference

October 11-13, 1990

University of Alabama
Tuscaloosa, AL 35487

Chairman: L. D. Kispert, Chemistry

Committee: J. W. Harrell and C. Alexander, Physics
A. Morrobel-Sosa, J. Peterson, and R. Timkovich, Chemistry

Department of Chemistry (205) 348-5954
Department of Physics (205) 348-5050
Fax (205) 348-9104

The 22nd Annual Southeastern Magnetic Resonance Conference will be held in Tuscaloosa on Friday, October 12 and Saturday, October 13, 1990, with registration on Thursday evening and a banquet on Friday night. The conference is sponsored by the Department of Chemistry and Physics at the University of Alabama with the assistance of industrial benefactors. All sessions will be held in the auditorium of the recently completed Tom Bevill Energy, Mineral, and Materials Science Research Building located on the campus of the University of Alabama. There will be invited lecturers in 2D and 3D NMR, gradient enhanced NMR spectroscopy, imaging, multi-quantum EPR spectroscopy, FTEPR and high field EPR plus contributed papers and posters. We hope you and your colleagues will be able to attend and to present a paper on your recent work. There will be a registration fee. Please note that the date of the conference has been changed from that announced last year due to some scheduling problems.

Additional information will be forthcoming. Please advise us of your interest by writing to:

Lowell D. Kispert
Department of Chemistry
University of Alabama
Tuscaloosa, AL 35487
Phone: (205) 348-7134

Instant Upgrade of RF Amplifier Performance in Your NMR/MRI System

Install an AMT Series 3000 solid-state pulse power amplifier—6–500 MHz at up to 1000 W—into your system. Instant upgrade!

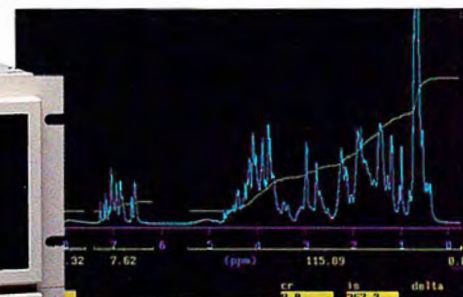
Here's just one example: AMT's RF power envelope detection system guarantees full protection. That means you can operate at low-level CW with full-power peaks on demand.

Pre-saturation water suppression? Cross polarization in solids? No problem—*now!*

Additional Key Features:

- Broadband Frequency Ranges—6–220 MHz, 200–500 MHz
- Key Power for Liquids & Solids—50, 150, 300, 1000 Watts
- Excellent Linearity—(± 1.0 dB)
- Low Pulse Droop—typically less than 5%
- Fast Low Noise Blanking—within 20 dB of KTB in 2μ s

For full information call your NMR/MRI system manufacturer or call Lowell Beezley at AMT: (714) 680-4936.



Models Available:

3205	6–220 MHz	300W
3200	6–220 MHz	1000W
3137	200–500 MHz	50W
3135	200–500 MHz	150W
3134	200–500 MHz	300W



an MMD company

1127 S. Placentia Avenue, Fullerton, CA 92631 (714) 680-4936 FAX: 714-871-2453

Model 3200 Series
6 - 220 MHz, Pulsed,
SOLID STATE, RF Power
Amplifier Systems

<u>Electrical Specifications:</u>	<u>Models:</u>	<u>3200</u>	<u>3205</u>
Frequency Range		6 - 220 MHz	
Pulse Power (min.) into 50 ohms		1000W	300W
CW Power (max.) into 50 ohms		100W	30W
Linearity (± 1 dB to 200MHz)		0-800W	0-250W
(To 220MHz)		0-600W	0-200W
Gain (typ.)		65dB	60dB
Gain Flatness		± 4 dB	± 3 dB
Input/Output Impedance		50 ohms	
Input VSWR		< 2:1	
Pulse Width		20mS	
Duty Cycle		Up to 10%	
Amplitude Rise/Fall Time		200nS typ.	150nS typ.
Amplitude Droop		5% to 10mS typ; 7% max	
Phase Change/Power Output		10 $^{\circ}$ to rated power typ.	
Phase Error Overpulse		4 $^{\circ}$ to 10mS duration typ.	
Noise Figure		11dB typ.	8dB typ.
Output Noise (blanked)		< 20dB over thermal	
Blanking Delay		< 5uS on, 2uS off, TTL signal	
Protection		1. VSWR- will withstand infinite VSWR at rated power 2. Input overdrive- up to +10dBm 3. Over duty cycle/pulse width 4. Over temperature	
<u>Supplemental Characteristics:</u>			
Connectors (on rear panel)		1. Input- BNC (F) 2. Output- Type N (F) 3. Blanking- BNC (F) 4. Interface- 25pin D(F), EMI filtered	
Indicators, Front Panel		1. Peak power meter 5. CW Mode 2. Over temperature 6. Overdrive 3. Over duty cycle 4. Over pulse width	
System Monitors		1. Thermal 2. DC power supply fault 3. Over duty cycle 4. Over pulse width	
Front Panel Controls		1. A.C. power 3. Duty cycle 2. Pulse width	
Cooling		Internal forced air	
Operating Temperature		+10 to 40 $^{\circ}$ C	
A.C. Line Voltage		120/240 VAC, $\pm 10\%$, 50-60Hz	
		(3200, 220/240V only)	
A.C. Power Requirements		2000 watts	700 watts
Package		Rack Mount	
Size (HWD, inches)		12.25x19x24	5.25x19x24

Prof. B. L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court

Palo Alto, CA 94303
USA

DATE 19900711/kt

OUR REFERENCE

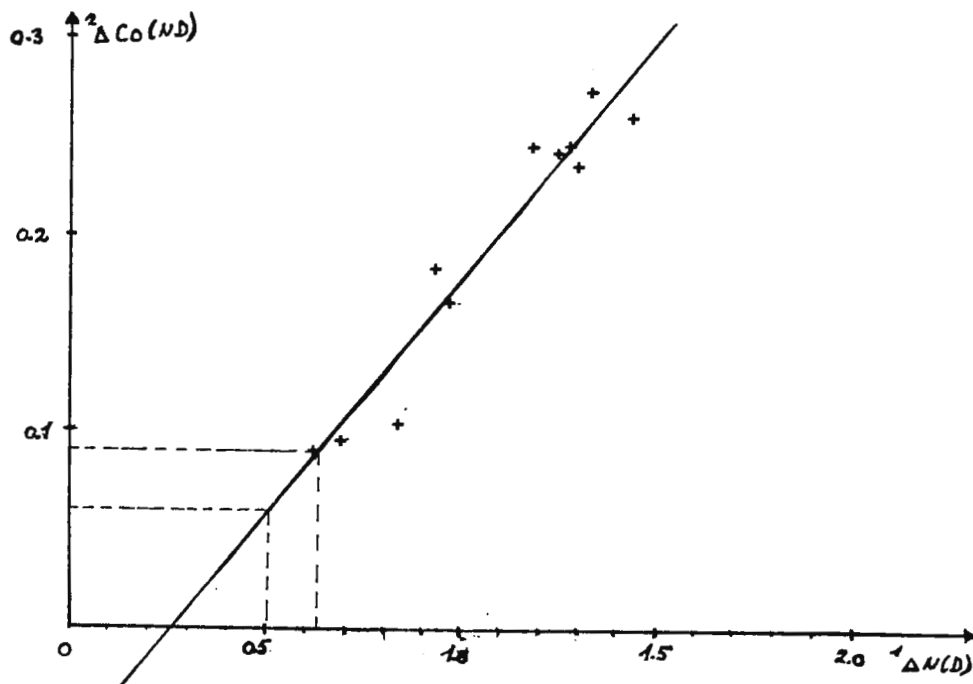
YOUR REFERENCE
(received 7/30/90)

$^1\Delta N(D)$ vs. $^2\Delta CO(ND)$

Dear Prof. Shapiro,

Isotope effects on ^{15}N chemical shifts have become increasingly important with the use of ^{15}N enrichment in proteins.

We have recently measured $^1\Delta N(D)$ in a number of enamines¹. A plot also including amides is shown below. A reasonable correlation is found between these two parameters. As $^2\Delta CO(ND)$ for proteins range between 0.06 and 0.09 (0.10) ppm it can be expected that $^1\Delta N(D)$ varies between 0.5 and 0.73 (0.78) ppm in proteins.



1. P. E. Hansen, R. Kawecki, A. Krowczynski, and L. Kozerski, Acta Chem. Scand. In press.
2. P. E. Hansen and Erik Tüchsen, Acta Chem. Scand. 43, 710 (1989).

Yours sincerely,

Poul Erik Hansen
Poul Erik Hansen

Position Available

NMR Instrumentation Scientist/ General Manager: A highly rewarding opportunity in instrumentation development management for solids NMR is now available in the company with the best eight-year growth record in the industry. Minimum requirements: Ph.D. in chemical physics, chemical engineering, physics, or electrical engineering, including research in NMR of solid samples and instrumentation development. Postdoc instrumentation development experience and management experience desirable. Minimum starting salary: \$65K, plus benefits. Send copy of transcripts and CV, including list of publications, to: Ms. Roseann Helms, Doty Scientific, Inc., 600 Clemson Rd., Columbia, SC 29223. EEO. M/V/H/F.

Free Acetic Acid- d_4 - I have 95 factory sealed bottles containing 80 - 85 g each of 99.5 % acetic acid- d_4 (MSD, Lot # D-269). I have no use for this solvent, but do not wish to needlessly throw it away. I will be happy to give it (for shipping costs only) to any interested legitimate researcher; note, however, that this is an "all or nothing" offer - please do not request "two or three bottles." If interested, please write to Dr. Robert F.X. Klein, Dept. Chem., Georgetown University, Wash., DC 20057-0001. Earliest postmark/first served. *Please include daytime phone number.*

LOVELACE MEDICAL FOUNDATION



POSTDOCTORAL FELLOW IN NMR STUDIES OF FLOW

We are seeking a postdoctoral fellow with interest in NMR studies of flowing systems. Knowledge of NMR physics, hardware, software, and/or hydrodynamics and rheology would be helpful. The fellow will do research in the development and application of NMR to velocity, density, and other hydrodynamic parameter determinations in single and multiphase flows in various geometries, mostly but not exclusively non-biological. Appointments are for one year, renewable for a second year by mutual agreement. Lovelace Medical Foundation is a small, private, research laboratory in a city of 600K at 1,600 meters above sea level. Interested candidates should send informative biographies including references with addresses and phone numbers to Eiichi Fukushima, Lovelace Medical Foundation, 2425 Ridgecrest Dr., SE, Albuquerque, NM 87108.

HMRI

HUNTINGTON MEDICAL RESEARCH INSTITUTES

WRITER'S TELEPHONE NUMBER:

(818) 397-3217

July 23, 1990 (received 7/28/90)

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

Dear Dr. Shapiro:

A New Method for PCr Imaging Reveals an Unexpected Facet of Primate Brain Metabolism

There is a great interest in the borderland between MR imaging and high-resolution MR spectroscopy *in vivo*. These two techniques share many features of hardware, software and conception. A case in point is the acquisition of chemical-shift resolved data with spatial localization in 2 or 3 planes (so called "chemical-shift imaging") and then to reconstruct pseudo-images of the individual resonance intensities. When overlaid upon the more highly resolved water-proton images, metabolic maps of clinical relevance have been obtained. The limitations of this approach are clear, and lie principally in the poor spatial resolution of the original data (usually 2-3 cm), and the low signal-to-noise in biological samples of some metabolites resulting in inordinately long imaging time.

We have been attracted by the technique of 'true-phosphorus imaging', first implemented for the PCr of skeletal muscle by Hsieh and Balaban [1]. PCr is also present in high concentrations in the mammalian brain, and its anatomical distribution as well as its turnover rate, via the key enzyme creatine kinase, is of great interest to physiologists. However, the simple spin-echo technique proposed for skeletal muscle does not work in the brain, where ATP and PCr have T₂ relaxation times that are too similar. Significant modifications to the technique are required. These have now been successfully developed by Bassem Mora and P.T. Narasimhan, working in the Huntington Medical Research Institutes' Magnetic Resonance Spectroscopy Laboratory.

Figure 1A shows the PCr image obtained from the monkey brain and Figure 1B shows the same image superimposed on the proton image. The results in phantoms and monkey brain are very encouraging, and PCr images with a spatial resolution of as little as 3 mm have been obtained in 30 minutes. And unlike PET, the procedure can be repeated at will. One potentially useful observation of repeated PCr images over the course of

HMRI

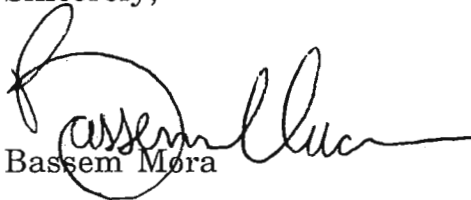
several hours in the same animal is that PCr is not uniformly distributed across the brain, and concentration of PCr varies with time. We conclude that the metabolism of the primate cerebral cortex is not static; fluctuations may occur with a time resolution of minutes.

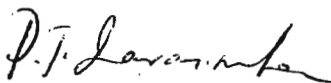
Figure 1





If correct, these findings imply that studies at a single time point, or in response to single functional stimuli, for example, visual stimulation, may be incomplete if they do not take account of an apparently "oscillating" biochemical baseline. From the technical point of view, we are encouraged to develop much faster PCr imaging methods to acquire this biological information. As far as we can judge, the "true" imaging methods will provide the necessary technical entrée.

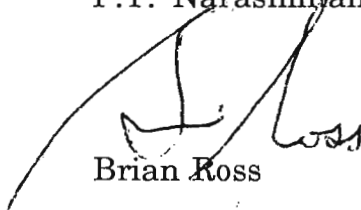
Sincerely,


Bassem Mora


P.T. Narasimhan


John Allman

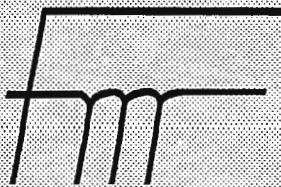

V. Rajanayagam


Brian Ross

Reference

1. Hsieh PS BR: ^{31}P imaging of *in vivo* creatine reaction rates. *J Magn Reson* 1987; 74:547-579.

Please credit this contribution to the subscription of
J. D. Roberts, Division of Chemistry and Chemical Engineering,
California Institute of Technology, Pasadena CA 91125



Fremont Magnetic Resonance

3315 Seldon Court
Fremont CA 94539
(415) 623-0722
(415) 623-0851 FAX

GOSSIP

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

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

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

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

TMON

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

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

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

DEXTER

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

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

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



Fremont Magnetic Resonance

3315 Seldon Court
Fremont CA 94539
(415)623-0722
(415)623-0851 FAX

Felix / PC

NMR Data Processing Software

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

1D Package:

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

1D / 2D Package:

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

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

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

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

Data Translation Software.

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

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

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

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

Parallel port 1280 to PC transfers are in development.

BXR Data Transfer & Translation Software

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



UNIVERSITY OF OREGON

August 1, 1990
(received 8/3/90)

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

Side Chain Carboxyl Group Assignment in Proteins

Dear Barry:

We have been studying the ionization behavior of carboxyl groups in T4 lysozyme. The ^{13}C resonances of the sidechain carboxyl groups of aspartic acid and glutamic acid provide a sensitive probe of the ionization state of these residues (1). Assignment of the ^{13}C carboxyl resonances and the pKa values to particular residues can be difficult. We have found the heteronuclear multiple bond correlation (HMBC) experiment (2) to be especially useful to connect the ^{13}C carboxyl resonances to our nearly complete assignment of the backbone ^1H and ^{15}N resonances (3).

Figure 1 shows the HMBC spectrum of T4 lysozyme in which the aspartic acid but not the asparagine residues have been labeled with 99% enriched ^{13}C γ aspartic acid (4). The crosspeaks result from the long range interaction of the C_α and C_β protons with the sidechain carboxyl ^{13}C of the 10 aspartic acid residues in the protein. There are several interesting features to the spectrum. First not all C_β protons give crosspeaks despite the orientation independent two bond coupling between the C_β protons and the carboxyl. This is most likely due to the mutual broadening of the C_β protons when the sidechains are rigidly held. The relatively long time required to generate coherence between the C_β protons and the carboxyl group makes T_2 relaxation and a serious competitor to crosspeak production. The second interesting feature is that crosspeaks involving C_α protons are observed for nearly all the aspartic acid residues. The three bond coupling of proton and ^{13}C is dependent on the sidechain conformation but can be about as strong as the two bond interaction (5). The C_α and C_β proton chemical shifts provide the basis for the assignments shown in the Figure.

References

1. Anderson, D.E., Becktel, W.J. and Dahlquist, F.W. (1990) *Biochemistry* **29**, 2403.
2. Bax, A. and Summers, M.F. (1986) *J. Am. Chem. Soc.* **108**, 1093.
Bax, A., Sparks, S.W. and Torchia, D.A. (1988) *J. Am. Chem. Soc.* **110**, 7926.
3. McIntosh, L.P., Wand, A.J., Lowry, D.F., Redfield, A.G. and Dahlquist, F.W. (1990) *Biochemistry* **29**, 6341.
4. McIntosh, L.P. and Dahlquist, F.W. (1990) *Quart. Rev. Biophys.* **23**, 1.
5. Hansen, P.E., Feeney, J. and Roberts, G.C.K. (1975) *J. Mag. Res.* **17**, 249.
6. Bax, A. and Marian, D. (1988) *J. Mag. Res.* **78**, 186.

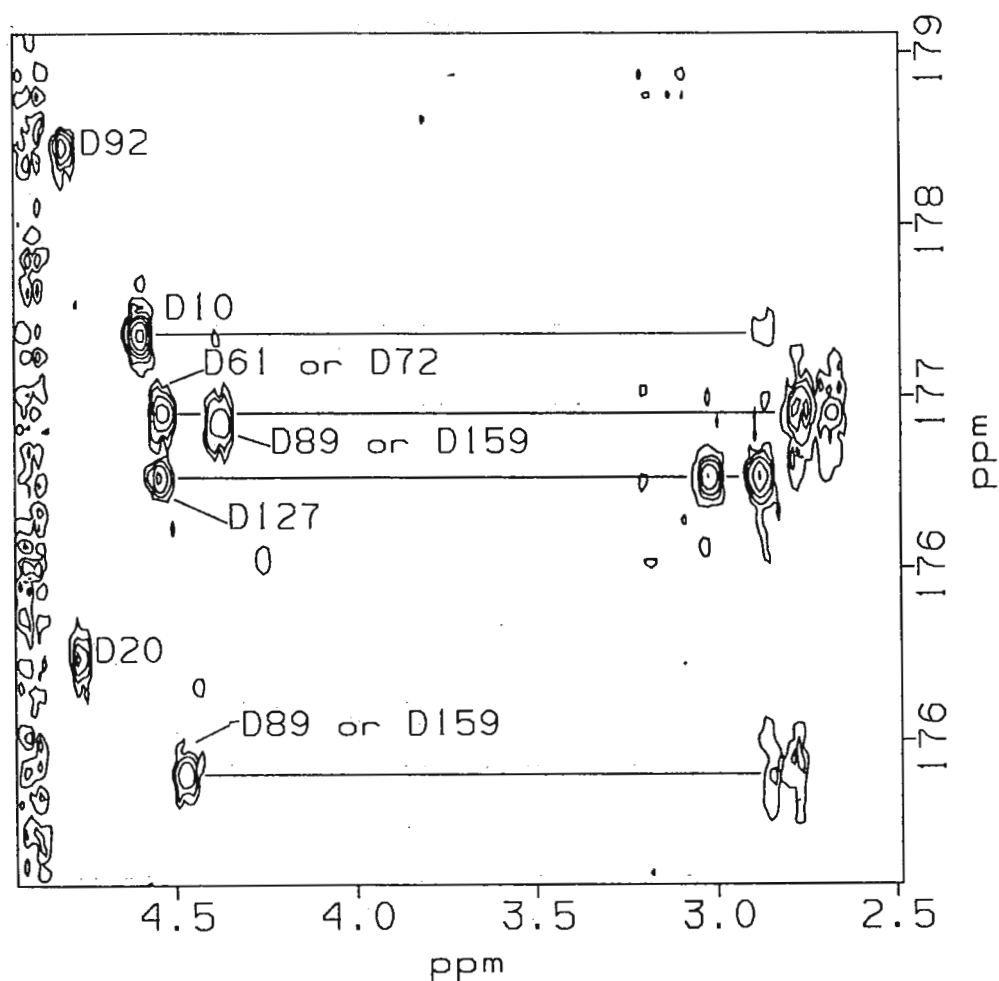


Figure 1: The ^1H - ^{13}C HMBC spectrum of $^{13}\text{C}_\gamma$ -aspartic acid enriched T4 lysozyme (2mM) in D_2O , pH* 5.6, 30 mM potassium phosphate, 100 mM KCl at 20°C . A delay of 50 msec was used to generate long range coherence. The spectrum was accumulated with 160 complex t_1 points (^{13}C SW = ± 3003 Hz) and 384 acquisitions per t_1 , and was processed in mixed mode format (6). The C_β proton resonances are between 2.5 and 3.5 ppm.

D. E. Anderson
Member, Institute
of Molecular Biology

L. P. McIntosh
Member, Institute
of Molecular Biology

Sincerely yours,

Frederick W. Dahlquist
Professor of Chemistry
Member, Institute
of Molecular Biology

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
UTMB Hospitals

DEPARTMENT OF HUMAN BIOLOGICAL CHEMISTRY & GENETICS
Division of Biochemistry

Area Code 409
761-2811

July 24, 1990
(received 7/27/90)

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

Carbon Spectra of Camptothecin

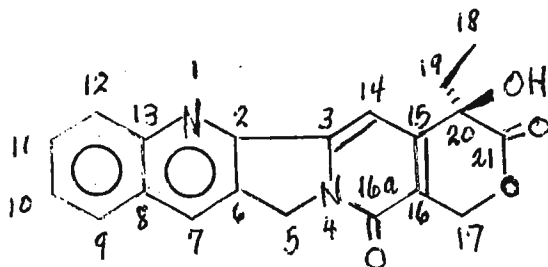
Dear Barry:

We have been occupied in assigning ^{13}C spectra of the promising antitumor agent camptothecin $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_4$ and its derivatives in support of a synthesis program of such derivatives at this University. Only an early assignment of Hutchinson *et al.*¹ was available at the inception of work. More recently ^{13}C assignments have been made from APT, COSY, selective INEPT, and 1D NOE and one-bond polarization transfer methods by Lin and Cordell,² but with the proviso that C-2, C-6, C-11, C-12, C-13, and C-15 data of Hutchinson *et al.* be reassigned.

Our assignments were made using APT, COSY, ^{13}C - ^1H HETCORR ($^3\text{J}_{\text{CH}}$ optimized at 7 Hz), and ^{13}C - ^1H HETCOSY (FUCOUP) sequences in straight-forward fashion with the JEOL GX270WB spectrometer. Camptothecin has ten quaternary carbons signals, seven of which lie close by one another, requiring care in assignment of crosspeaks in 2D spectra. Prior data and ours were obtained on $[\text{}^2\text{H}_6]$ -dimethylsulfoxide (DMSO) solutions, but by use of DMSO, $[\text{}^2\text{H}]$ -trifluoroacetic acid, and their admixtures adequate resolution of both ^{13}C (best resolved in trifluoroacetic acid) and ^1H (best resolved in DMSO) signals was achieved so that correlations and assignments could be made.

Our ^{13}C assignments for 13 carbon signals agree very acceptably with the 1974 assignments, but both sets of data (referenced against solvent DMSO δ_{C} -39.5 or -39.6¹) differ by about 1 ppm for most signals from those of Lin and Cordell referenced against internal tetramethylsilane (TMS). However, the Lin and Cordell published INEPT spectrum of camptothecin clearly shows carbon signals of DMSO at field lower than δ_{C} 40.

It appears that the data of Lin and Cordell suffer from misregister against the internal reference in some way. Thus, it be their ^{13}C data that need revision, along with a few assignments of the 1974 data. Data in the Table include our data, those of Hutchinson *et al.*, and those of Lin and Cordell. Because of increasing interest in camptothecin and derivatives as clinically useful antitumor agents and the need to have reliably assigned ^{13}C

Table. ^{13}C Spectra of Camptothecin

C	Our Data	Hutchinson et al.	Lin & Cordell
2	152.47	156.8 ^a	153.47
3	145.41	145.4	146.41
5	50.12	50.2	51.22
6	129.71	129.7	130.74
7	131.44	131.4	132.51
8	127.86	127.9	128.88
9	128.39	128.4	129.45
10	127.53	127.5	128.60
11	130.26	129.0 ^b	131.34
12	128.95	130.2 ^b	129.97
13	147.87	149.9 ^c	148.85
14	96.59	96.7	97.70
15	149.89	147.9 ^c	150.95
16	118.98	119.0	120.01
16a	156.73	- ^d	157.76
17	65.19	65.4	66.25
18	7.67	7.8	8.82
19	30.28	30.6	31.28
20	72.28	72.4	73.39
21	172.32	- ^d	173.45

a Value in disagreement with other data

b,c Original values requiring exchange

d Not recorded

spectra we feel this communication is necessary.

Yours truly,

Edward L. Ezel

Leland L. Smith

1. Hutchinson et al., J. Am. Chem. Soc. **96**, 5609 (1974).
2. Lin and Cordell, J. Natl. Products **53**, 186 (1990).

UNITY BRINGS NMR IMAGING DOWN TO SIZE



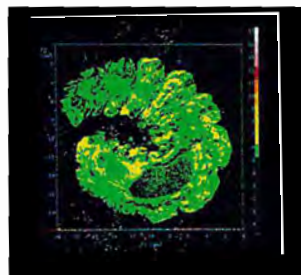
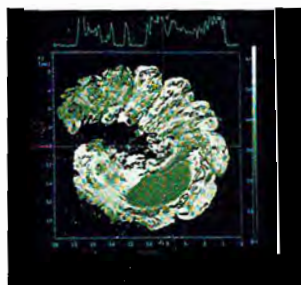
VARIAN COMBINES SPECTROSCOPY WITH MICROIMAGING

Built for the highest performance levels, the new UNITY™ NMR spectrometers combine high-field microimaging with high resolution spectroscopy. UNITY's state-of-the-art microimaging experiments for small samples address applications that range from biological and pharmaceutical to agricultural and material science.

Designed to bridge the operational gap between liquids, solids, and microimaging, this instrument can perform all three techniques and rapidly switch from one to the other with ease.

A wide variety of experiments can be accomplished at high performance levels due to the modular system architecture that's adaptable to a variety of configurations. Upgrading to additional capabilities can be accomplished at any time simply by adding the necessary system components.

Get the image of the future: invest in the most flexible technology of today to better progress toward the research of tomorrow. Invest in a UNITY NMR spectrometer. For additional information, please call the Varian office closest to you.



**Varian is your full-line
company for analytical
instrumentation**

NMR
UV-Visible-NIR
Atomic Absorption
Solid Phase Extraction
Liquid Chromatography
Gas Chromatography
GC/MS

Varian Associates
611 Hansen Way D-298
Palo Alto, CA 94303
U.S.A.
Tel: 1-800-356-4437

Varian AG
Steinhauserstrasse 6
CH-6300
Zug, Switzerland
Tel: (42) 44 88 44

Varian GmbH
Alsfelderstrasse 6
D-6100 Darmstadt
West Germany
Tel: (0 61 51) 70 30

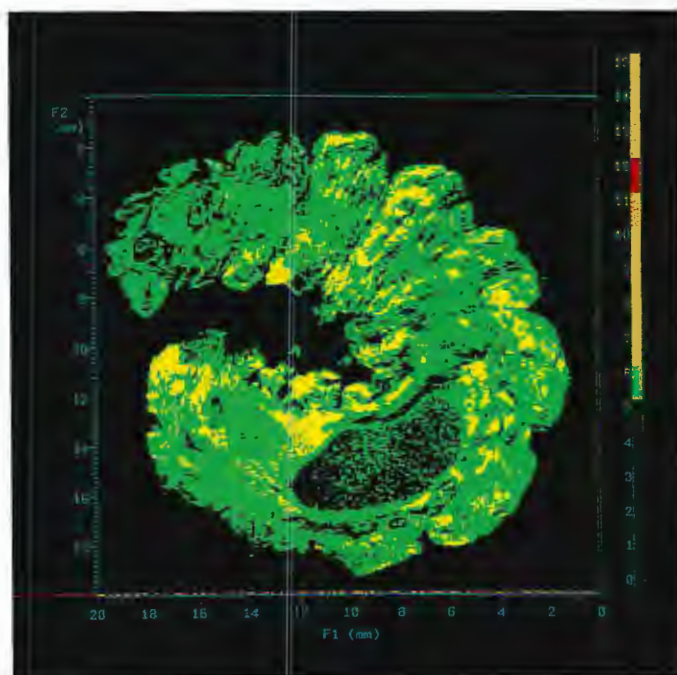
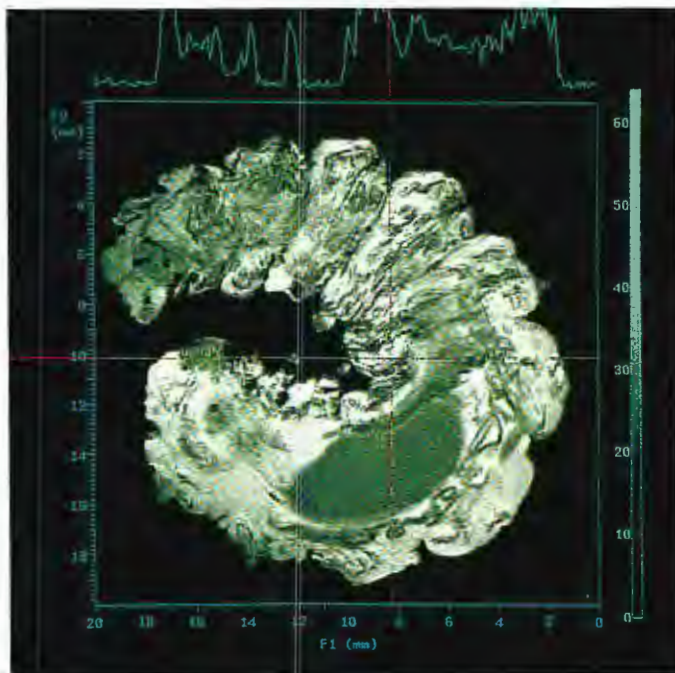
Varian Instruments Ltd.
3rd Matsuda Bldg
2-2-6 Ohkubo-Shinjuku
Tokyo, 169, Japan
Tel: (3) 204-1211

NMR WITH A FUTURE

varian

MULTI-SLICE MICROIMAGE OF A CATERPILLAR

Run on a Varian UNITY-300 NMR Spectrometer, this grayscale view of a caterpillar allows the spectroscopist to investigate his samples using non-invasive microimaging techniques. In addition, such samples can be studied over time to learn the physiological response to a stimulus. The UNITY-300 spectrometer utilized a gradient compensation (five time constants), a 60 gauss/cm air-cooled gradient set external to the probe, a 25 mm $^1\text{H}/^{19}\text{F}$ high resolution probe, and higher-order room temperature shims compensating the homogeneity of the bore to optimize the resolution of the image. Varian's ability to extend NMR imaging to small samples at high magnetic field strengths provides the user with state-of-the-art technology to answer questions.



EMORY UNIVERSITY

Department of Chemistry

1515 Pierce Drive
Atlanta, Georgia 30322
404/727-6585August 2, 1990
(received 8/6/90)Dr. Barry Shapiro
Texas A&M NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303¹⁵N NMR of DNA-drug
Complexes

Dear Barry:

HMQC heteronuclear methods have found wide application in the studies of proteins, facilitated by the ability to prepare labeled material biosynthetically. Studies involving ¹³C and ¹⁵N in oligonucleotides have been less practical since the logistics of enrichment are more formidable and one has to contend with samples at natural abundance. The prospect of using other nuclei as probes of sugar conformation and hydrogen bonding is nonetheless attractive, and with some patience can be accomplished at natural abundance. Although there are several reports of ¹³C studies, not much has been reported for ¹⁵N shifts in DNA oligomers. In an effort to test the value of using ¹⁵N as an NMR probe, we have examined two duplexes, d(GGTATACC)₂ (I) and d(GGAATTCC)₂ (II) in both the presence and absence of the drug netropsin. Using the simplest HMQC sequence in water with only one ¹H pulse, and using a Redfield 21412 composite pulse for that, we have been able to observe the ¹H - ¹⁵N correlations for the imino protons in these systems. Earlier ¹H NMR work by Patel's (1) group and X-ray studies from Dickerson's lab (2) indicated that the drug would hydrogen bond to the O2's of the T residues in the minor groove. This C2 carbonyl group is adjacent to the imino NH, reminiscent of a peptide linkage, and one would expect that as in a peptide hydrogen bonding interactions to the carbonyl oxygens would cause a downfield shift of the nitrogen. The table below shows the observed shifts for the imino nitrogens. Only the central nucleotides are affected by drug binding to the central regions of the duplexes. The constancy of the shifts for base pairs near the ends is consistent with earlier conclusions that there is no direct drug binding to them, and the basic B-DNA conformation is not distorted with possible changes in interstrand H-bonding. These results demonstrate the usefulness of investigating intermolecular interactions with DNA via ¹⁵N NMR. The samples were about 8 mM in duplex in 0.4 ml, and spectra were obtained in about 16 hrs. One of the contour maps with a projection of the multiquantum axis is shown below.

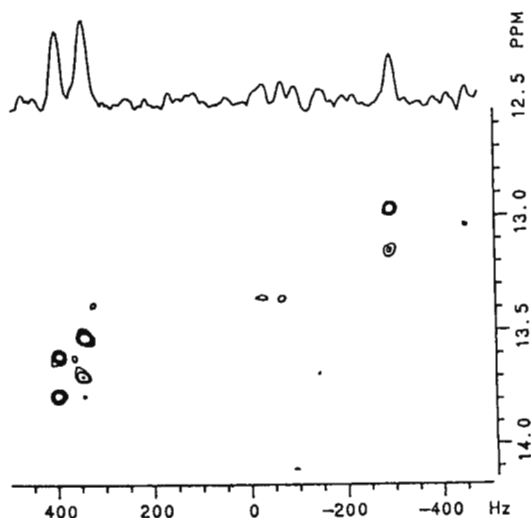
Nitrogen shifts from NH₃

Base Pair	I	I + netropsin
G2-C7	147.05	147.01
T3-A6	158.03	160.33
A4-T5	158.46	unobserved
	II	II + netropsin
G2-C7	147.20	147.47
A3-T6	155.93	160.03
A4-T5	155.50	158.66

Terminal base pairs were too broad for observation.

Sincerely,

David Live



1. D. Patel and L Shapiro; *Biopolymers*, 25, pp. 707-727 (1986).
2. M. L. Kopka et. al.; *PNAS USA*, 82 pp. 1376-1380 (1985).

POSITION AVAILABLE

The Complex Carbohydrate Research Center (CCRC) at the University of Georgia is seeking an **NMR technician** to begin November 1, 1990, or as soon as possible thereafter. The successful candidate will operate state-of-the-art NMR laboratory (including Bruker AMX-600, AM-500 and AM-250 spectrometers with Aspect-X-32 and Aspect-3000 computer systems) and collaborate with the Center's NMR spectroscopist, carbohydrate researchers, and instrumentation manager. B.S. or M.S. in chemistry and experience in operating NMR instrumentation required. Salary in the upper teens, depending on experience. Address inquiries or letter of application (including *curriculum vitae*) and arrange for two letters of reference to be sent to: Dr. Herman van Halbeek, Complex Carbohydrate Research Center, University of Georgia, 220 Riverbend Road, Athens, Georgia 30602 (telephone: 404-542-4438). Application deadline October 15, 1990. The University of Georgia is an Equal Opportunity/Affirmative Action institution.



The University of Sydney
AUSTRALIA

**RESEARCH FELLOW IN
NMR SPECTROSCOPY**

Department of Cancer Medicine
Reference No. 28/04

Applications are invited from enthusiastic scientists to join a multidisciplinary team utilising magnetic resonance spectroscopy to study the role of membrane lipids in tumour biology. This is part of an international program which includes scientists and clinicians from the EEC and other Commonwealth countries.

Applicants should be familiar with Bruker equipment. Preference will be given to applicants with expertise in organic chemistry since verification of NMR assignments by chemical methods is required.

Successful applicants will be offered a one year contract in the first instance with probable renewal.

The department is well equipped with: a wide bore 360 MHz NMR spectrometer with microimaging facility, ultracentrifuge, HPLC, GC, etc. Tumour and cell models to be studied are established in the laboratory with well qualified staff working in this aspect of the program.

For further information write to Dr Carolyn Mountford or phone (+612) 692 3675, fax (+612) 692 4105.

Salary: A\$33,163-\$A43,096 per annum.

Closing: 7 November, 1990.

Method of Application: Applications, quoting reference no., including curriculum vitae, list of publications and the names, addresses and FAX numbers of three referees, to the Registrar, Staff Office, University of Sydney, N.S.W. 2006, Australia by the above date.

Equal employment opportunity and no smoking in the workplace is University policy.



DEPARTMENT OF HUMAN PHYSIOLOGY

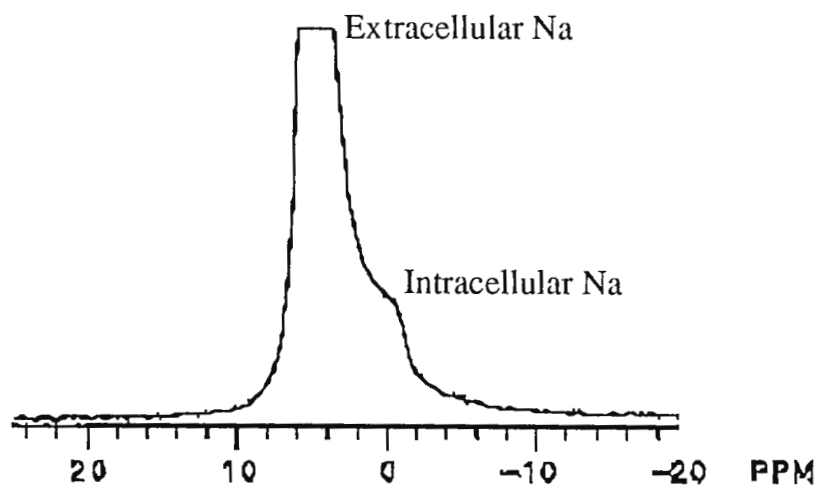
SCHOOL OF MEDICINE
DAVIS, CALIFORNIA 95616July 18, 1990
(received 7/21/90)Dr. B.L. Shapiro
TAMU Newsletter
966 Elsinore Court
Palo Alto, CA 94303Re: BUMETANIDE INHIBITS SODIUM EFFLUX IN REPERFUSED MYOCARDIUM

Dear Barry,

Our previous studies have shown that during hypoxia, the intracellular Na (ICNa) of rabbit hearts increases due to increased uptake via net Na/H exchange, not decreased extrusion by Na/K ATPase (Cala et al., Comp. Biochem. Physiol. 90A:551-555, 1988). Using Langendorf perfused rabbit hearts, shift reagents and ^{23}Na NMR spectroscopy, we are now investigating the roles of active (Na/K ATPase) and passive (Na/H, Na+K+2Cl) Na transport during ischemia and reperfusion.

Experiments were performed on isolated rabbit hearts obtained from New Zealand albino rabbits weighing 2-3 kg. A cannula attached to a pulsatile pump driven perfusion system was inserted and tied into the aorta. Perfusion pressure was monitored by means of a strain gauge transducer connected by a perfusate filled cannula to the aortic cannula. Heart mechanical function was monitored by pressure measurement from a second cannula tied securely into the left ventricle. After beginning perfusion, the hearts were inserted to hang freely from the perfusion cannula within a 30 mm OD NMR tube. The hearts, in the NMR tube, were lowered into the active volume of a ^{23}Na probe within the magnet of a Nicolet Magnetics NT-200 wide bore spectrometer operated in the Fourier transform mode. The hearts were bathed in perfusate exiting the pulmonary artery and removed by suction outside the probe's active volume. Data from "1-pulse" (constant excitation pulse length) experiments were collected over five minute intervals, signal averaging 1000 free induction decays. ICNa was measured using 15 mM Dysprosium triethylenetetraminehexaacetic acid (DyTTTHA) to separate intra- and extracellular signals. Calibrated integrals of peak areas were used to quantitate intra- and extracellular Na. The HEPES buffered perfusate was equilibrated with 100% O_2 and titrated to pH 7.4 ± 0.05 at 25°C .

FIGURE 1



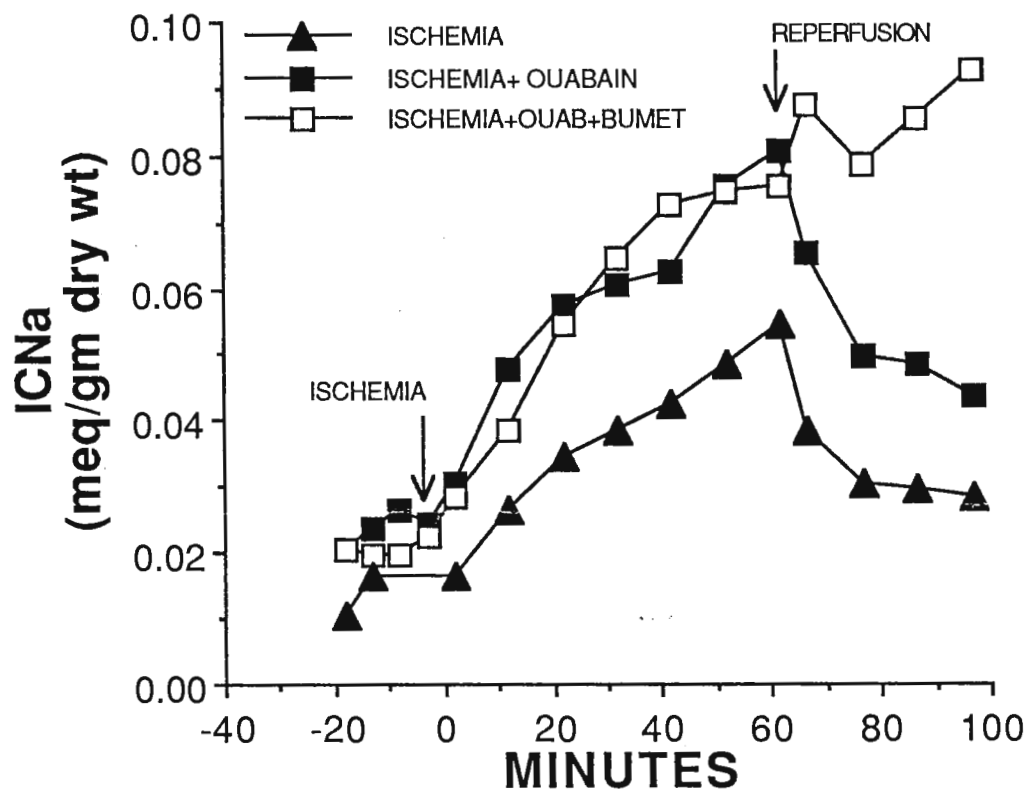
Dr. B.L. Shapiro (page 2)

July 18, 1990

Three protocols were employed. The first, (ISCHEMIA) in figure 2 required induction of total ischemia by clamping the perfusate line for one hour, after which, the heart was observed during 30 minutes of reperfusion. The second, (ISCHEMIA + OUABAIN) separated passive and active Na transport, by inhibition of the Na/K pump using K⁺ free modified Krebs-Henseleit solution plus 1 mM Ouabain, for 10 minutes prior to global ischemia and during reperfusion. The third (ISCHEMIA + OUAB + BUMET) added 20 μ M Bumetanide (a specific inhibitor of Na+K+2Cl transport) to the perfusate.

Figure 2 shows ICNa vs time for the three protocols (n=3 hearts in each). As observed during hypoxia, the data show that ICNa rises steeply during the 60 minute period of ischemia and that the increase in ICNa is due to increased uptake (Na/H exchange) as opposed to decreased extrusion (Na/K ATPase). Despite the fact that the Na/K pump is inhibited, ICNa decreased during post-ischemia reperfusion. Addition of Bumetanide to the K⁺ free perfusate prevented the decrease in ICNa. These data suggest that post-ischemic Na extrusion in myocardium is in part mediated by Na+K+2Cl cotransport.

FIGURE 2



Sincerely,

C.Z. Dickinson, S.E. Anderson, P.M. Cala

(Please credit the contribution to Tom Jue's account)

When faced with a tough analytical problem . . .

QUESTION

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

ANSWER

Sadtler Structure Assignment Library

STEP:1

Search For
Thiophenol Derivatives.

Structure Search Version 1.0
File Draw Search View Print Library Utility
CAS Registry Search
Exact Match Search
Source Structure Search
Number of Hits: 128

Index	Hit	Lib	Entry	Name
1	1	13C1	71	SULFIDE, METHYL PHENYL
2	1	13C1	73	PHENYL DISULFIDE
3	1	13C1	90	BENZENESULFONYL CHLORIDE
4	1	13C1	287	BENZENESULFONYL FLUORIDE
5	1	13C1	288	BENZENESULFONYL FLUORIDE, -
6	1	13C1	227	P-TOLUENESULFONIC ACID, METHYL ESTER
7	1	13C1	355	P-TOLYL DISULFIDE
8	1	13C1	732	METHANOL, P-TOLYLSULFONYL-
9	1	13C1	982	BENZENESULFONIC ACID, HYDRATE
10	1	13C1	983	BENZENESULFONIC ACID, SODIUM SALT
11	1	13C1	987	P-TOLUENESULFONIC ACID, BUTYL ESTER
12	1	13C1	988	BENZENESULFONAMIDE
13	1	13C1	918	P-TOLUENESULFONAMIDE, N-BUTYL-
14	1	13C1	974	ACETIC ACID, PHENYLTHIO-
15	1	13C1	987	P-TOLUENESULFONYL CHLORIDE
16	1	13C1	1897	P-TOLUENESULFONAMIDE, N-METHYL-
17	1	13C1	1129	ANILINE, O-METHYLTHIO-
18	1	13C1	1178	SULFIDE, PHENYL 2-PHENYLPROPYL
19	1	13C1	1296	SULFIDE, P-BROMOPHENYL METHYL
20	1	13C1	1293	SULFIDE, METHYL N-NITROPHENYL

STEP 2:

Match Those Derivatives
With Your Spectrum.

NMR Search 2.12
File Search View Library Print Utility Import Page
Unknown Entry
PEAK SEARCH PARAMETERS
Peak Tolerance: 0.3 ppm (value between 0.1 and 2.0)
Minimum No. of Peak Match: 4
Algorithm:
☐ Forward Search
☒ Reverse Search
Cancel
OK

YOUR SEARCH IS OVER!

NMR Search 2.12
File Search View Library Print Utility Import Page
LIB PEAK LOCATION
© 1987, 1988-1990 Bio-Rad, Division. All Rights Reserved.
Sadtler ID: ST71
=== First Peak Table ===
(Total of peaks: 5)
No. Location Intensity
1 15.60 4
2 124.90 5
3 126.70 9
4 128.70 9
5 138.60 1
Source Library: 13C1 - C-13 NMR STANDARDS
File Name: THIDEMO.NPF
Chem. Name: ODIFEROUS SPECIES
CAS Registry Number: unknown
Comment: process shutdown 12/9/89, green
READY

109.05 ppm
ad, Sadtler Division. All Rights Reserved.

STRUCTURE
Print View
4-methylthiophenol

... look to **SADTLER**
for the knowledge to end your search.

BIO-RAD

**Sadtler
Division**

3316 Spring Garden Street,
Philadelphia, Pennsylvania 19104.
Telephone: (215) 382-7800.
Telefax: (215) 662-0585. TWX: 710 670-1186.

**MICROSOFT
WINDOWS**
Version 3.0 Compatible Product

Sadtler ^{13}C NMR Structure Assignment Library

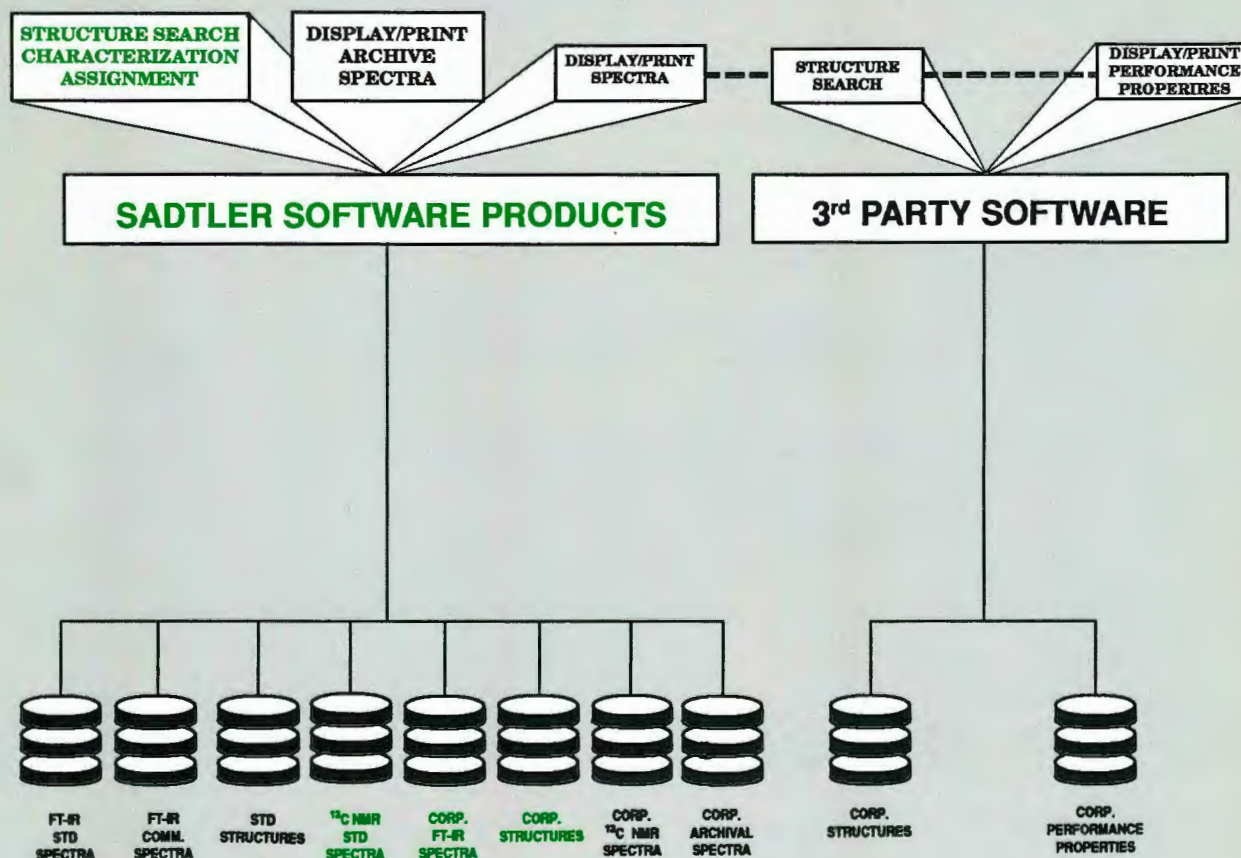
The Sadtler ^{13}C NMR Structure Assignment Library consists of:

The Sadtler Standard ^{13}C NMR Spectra Library
containing entries for 30,000 pure compounds or better

Sadtler ^{13}C NMR Search Software

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

Sadtler Molecular Substructure Search Software



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



 BAYLOR UNIVERSITY MEDICAL CENTER

3500 Gaston Avenue
 Dallas, Texas 75246
 (214) 820-0111
 Cable Address: BAYLORDAL

August 4, 1990
 (received 8/17/90)

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

More Musings on Water Suppression In Vivo

Dear Dr. Shapiro:

This note has been delayed by my move to the Department of Radiology at Baylor University Medical Center in Dallas, TX. The Baylor MRI facility is directed by Dr. Steve Harms, and has state-of-the-art research programs in MRI fast scan methods, signal processing, and in vivo proton spectroscopy.

It is amusing to reflect on how many man-hours have been invested in generating strategies for water bashing in proton spectroscopy. Many of the old ideas continue to resurface in localized human spectroscopy, like swamp monsters in a bad nightmare. However, most of these methods are not suited for localized proton spectroscopy in humans, where quantitation and low power deposition are important. This point has been lost in the rush to use 1331 hard pulses, which have a small flip angle and produce a flat baseline, but at the cost of amplitude distortion across the bandwidth. The use of hard pulses is a no-no in localized spectroscopy, where the degree of localization ($>10^5$) must be greater than the degree of water suppression (10^3).

The WEFT method has enjoyed a renaissance with the development of adiabatic pulses for frequency-selective inversion. Luyten and den Hollander have shown that WEFT works well in vivo, although the degree of suppression isn't as good as other methods might achieve. Part of this problem may be related to the fact that good water suppression is more difficult using PRESS localization than in STEAM-based methods.

Another promising strategy is based on the use of frequency-selective RF pulses and magnetic field gradient pulses. These "CHESS" or chemical shift selective pulses dephase the magnetization from water. The most effective combinations of CHESS pulses are based on

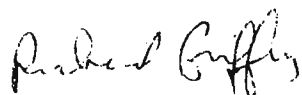
SUBMERGE, which Doddrell and coworkers first described in 1987.

Three CHES pulse pairs are used to excite and dephase the signal from water prior to localization. Suppression is optimized by varying the durations of the field gradient pulses, by interactively changing the amplitudes and phases of the RF pulses, or both.

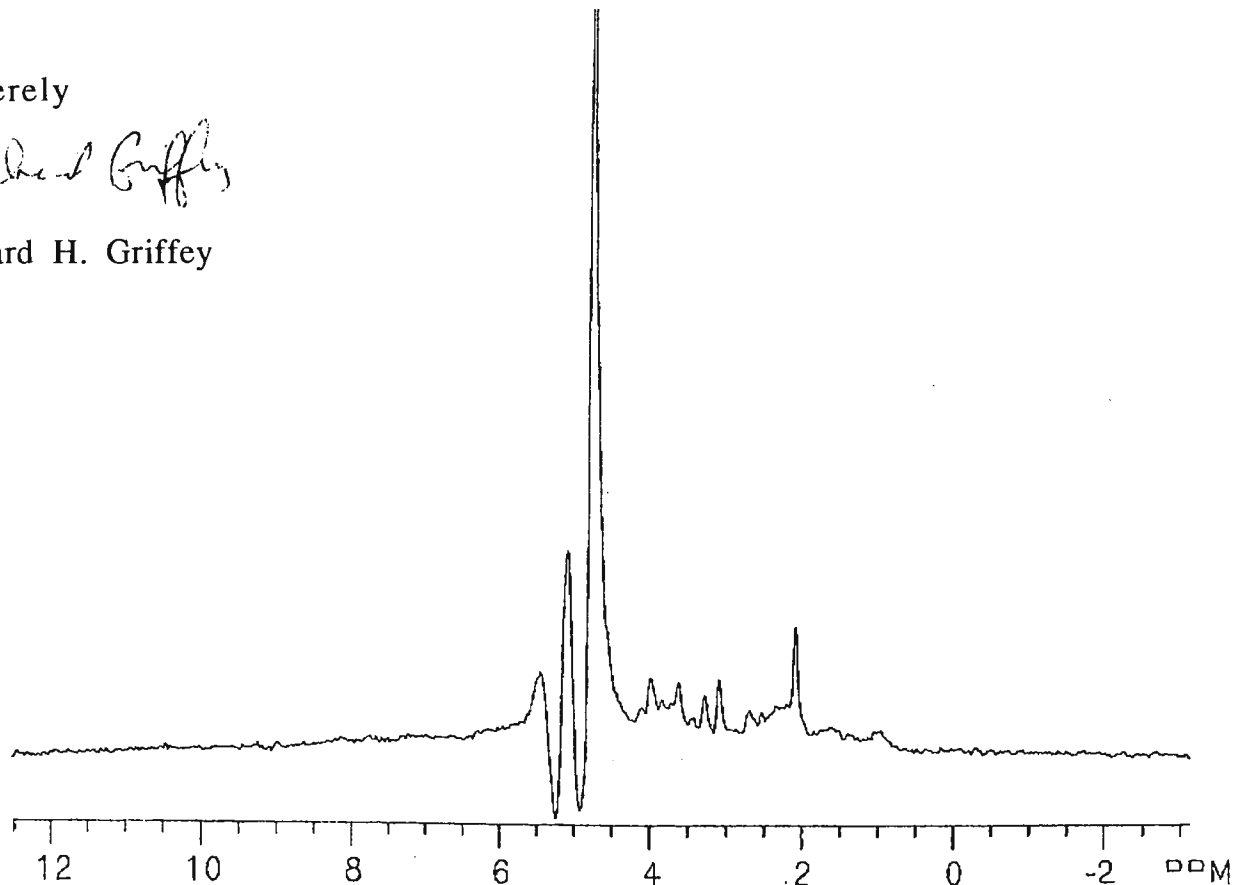
Initially, the amplitudes of the three selective RF pulses are set to approximately $\pi/2$ radians. I find that the amplitude of the first pulse should be increased to a point where the amplitude of the water signal just inverts. Next, the amplitude of the second RF pulse is increased to a point where the water magnetization is driven back to positive. Finally, the amplitude of the third pulse is increased to give the best null of the water signal. This may seem time-consuming, but the relative ratios of the RF pulses have been reasonably constant at 75:55:45 in the patients studied to date. A typical 3 minute spectrum from an 8 mL volume of human brain obtained at 63.87 MHz is shown below.

Most important, the baseline is flat, ie this isn't just a hole-burn-ing process. A major concern is what happens to the water magnetiza-tion. The dephasing by magnetic field gradients disperses the water signal randomly across a large frequency range. Within the spectral bandwidth, this water magnetization appears as added noise. So, it is critical to use enough field gradient pulse to disperse most of the water outside the bandwidth. These techniques work best on animal systems with >100 mT/M of field gradient, but are satisfactory on whole body scanners with 10 mT/M gradient sets.

Sincerely



Richard H. Griffey



NMR Sample Tubes


Performance Comparison

carried out at

HARVARD UNIVERSITY

is further proof of

NORELL'S SUPERIOR NMR Sample Tube Quality!



1990 PRICE LIST

5mm o.d. THIN WALL NMR SAMPLE TUBES

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

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.013 mm (0.0005 in.);
i.d. 4.20 ± 0.025 mm (0.001 in.);
camber ± 0.013 mm (0.0005 in.).
For additional length,
add \$0.24 per cm (\$0.60/in.).

1-99 tubes...\$4.50 ea.
100-299...\$4.25 ea.
300 +\$4.00 ea.

**Our
top
quality
tube!**

No. 507-HP HIGH PRECISION for high resolution NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.013 mm (0.0005 in.);
i.d. 4.20 ± 0.025 mm (0.001 in.);
camber ± 0.025 mm (0.001 in.).
For additional length,
add \$0.21 per cm (\$0.50/in.).

1-99 tubes...\$3.00 ea.
100-299...\$2.95 ea.
300 +\$2.90 ea.

No. 506-P PRECISION for medium and high resln. NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.025 mm (0.001 in.);
i.d. 4.20 ± 0.025 mm (0.001 in.);
camber ± 0.025 mm (0.001 in.).
For additional length,
add \$0.16 per cm (\$0.40/in.).

1-99 tubes...\$2.50 ea.
100-299...\$2.45 ea.
300 +\$2.40 ea.

No. XR-55 PRECISION FOR medium and high resln. NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.025 mm (0.001 in.);
i.d. 4.20 ± 0.025 mm (0.001 in.);
camber ± 0.03 mm (0.0015 in.);
For additional length,
add \$0.08 per cm (\$0.20/in.).

1-99 tubes...\$2.20 ea.
100-299...\$2.00 ea.
300 +\$1.90 ea.

No. 505-P PRECISION for medium and high resln. NMR

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.03 mm (0.001 in.);
i.d. 4.20 ± 0.03 mm (0.001 in.);
camber ± 0.04 mm (0.002 in.);
For additional length,
add \$0.08 per cm (\$0.20/in.).

1-99 tubes...\$1.80 ea.
100-299...\$1.75 ea.
300 +\$1.70 ea.

No. 502 THROWAWAY TYPE

Standard tube length: 178mm (7 inches);
o.d. 4.97 ± 0.05 mm (0.002 in.);
i.d. 4.20 ± 0.05 mm (0.002 in.);
camber ± 0.07 mm (0.003 in.);
For additional length,
add \$0.08 per cm (\$0.20/in.).

1-99 tubes...\$0.80 ea.
100-299...\$0.75 ea.
300 +\$0.70 ea.

LARGE VOLUME NMR SAMPLE TUBES

10mm o.d. THIN WALL NMR SAMPLE TUBES

No. 1008-UP ULTRA PRECISION for ultra high resolution NMR

Standard length: 178mm (7 inches);
o.d. 10.00 ± 0.013 mm (0.0005 in.);
i.d. 8.76 ± 0.025 mm (0.001 in.);
camber ± 0.007 mm (0.0003 in.).
For additional length,
add \$0.20 per cm (\$0.50/in.).

1-5 tubes...\$14.50 ea.
6-25...\$13.75 ea.
26 +\$12.95 ea.

No. 1005-P PRECISION for medium and high resln. NMR

Standard length: 178mm (7 inches);
o.d. 10.00 ± 0.013 mm (0.0005 in.);
i.d. 8.76 ± 0.025 mm (0.001 in.);
camber ± 0.013 mm (0.0005 in.).
For additional length,
add \$0.20 per cm (\$0.50/in.).

1-5 tubes...\$9.50 ea.
6-25...\$9.25 ea.
26 +\$9.00 ea.

20mm o.d. THIN WALL NMR SAMPLE TUBES

No. 2005-P PRECISION for medium and high resln. NMR

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

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

NOTE: Other tube sizes
available, please inquire.

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

PTFE Machined Tube Caps
5mm\$40/25 caps; \$75/50 caps
10mm\$43/25 caps; \$80/50 caps

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

SEE PERFORMANCE on REVERSE!

NORELL, INC. 22 Marlin Lane, Mays Landing, NJ 08330 USA
Tel: 609-625-2223; Fax: 609-625-0526; in USA call us toll-free at 1-800-222-0036

PLEASE NOTE: Our Sales Offices have MOVED to a larger and more spacious facility:
 NORELL, INC., 22 Marlin Lane, Mays Landing, NJ 08330 USA; Tel: 609-625-2223; 800-222-0036; Fax: 609-625-0526

Why compromise in quality and even pay higher prices?
 ... for NMR tubes specify Norell -- accept no substitutes
We have the lowest prices in the industry!



JAB132.001
 DATE 30-11-88

SF 500.135
 SY 83.0
 O1 7900.000
 SI 32768
 TD 32768
 SW 5000.000
 HZ/PT .305

PW 5.0
 RD 0.0
 AQ 3.277
 RG 32
 NS 72
 TE 297

FW 6300
 Q2 7925.000
 DP 10H P0

LB 0.0
 GB 0.0
 CX 36.00
 CY 0.0
 F1 2.700P
 F2 .401P
 HZ/CM 31.950
 PPM/CM .064
 SF 5426.67

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

☒ Excellent ☐ Very Good ☐ Satisfactory ☐ Unsatisfactory

Norell's XR-55 NMR Sample Tubes were compared with the following competitive tube or tubes: WILMAD 528-PP

(Give cat. no. and name of manufacturer)

Type of NMR equipment used in the above evaluation: BRUKER AM-500

Date: Nov 30, 1988 Name: SCOTT VIRGIL Title: GRADUATE STUDENT

Address: 12 OXFORD STREET #314
CAMBRIDGE, MA 02138
 Telephone: (617) 495-4039

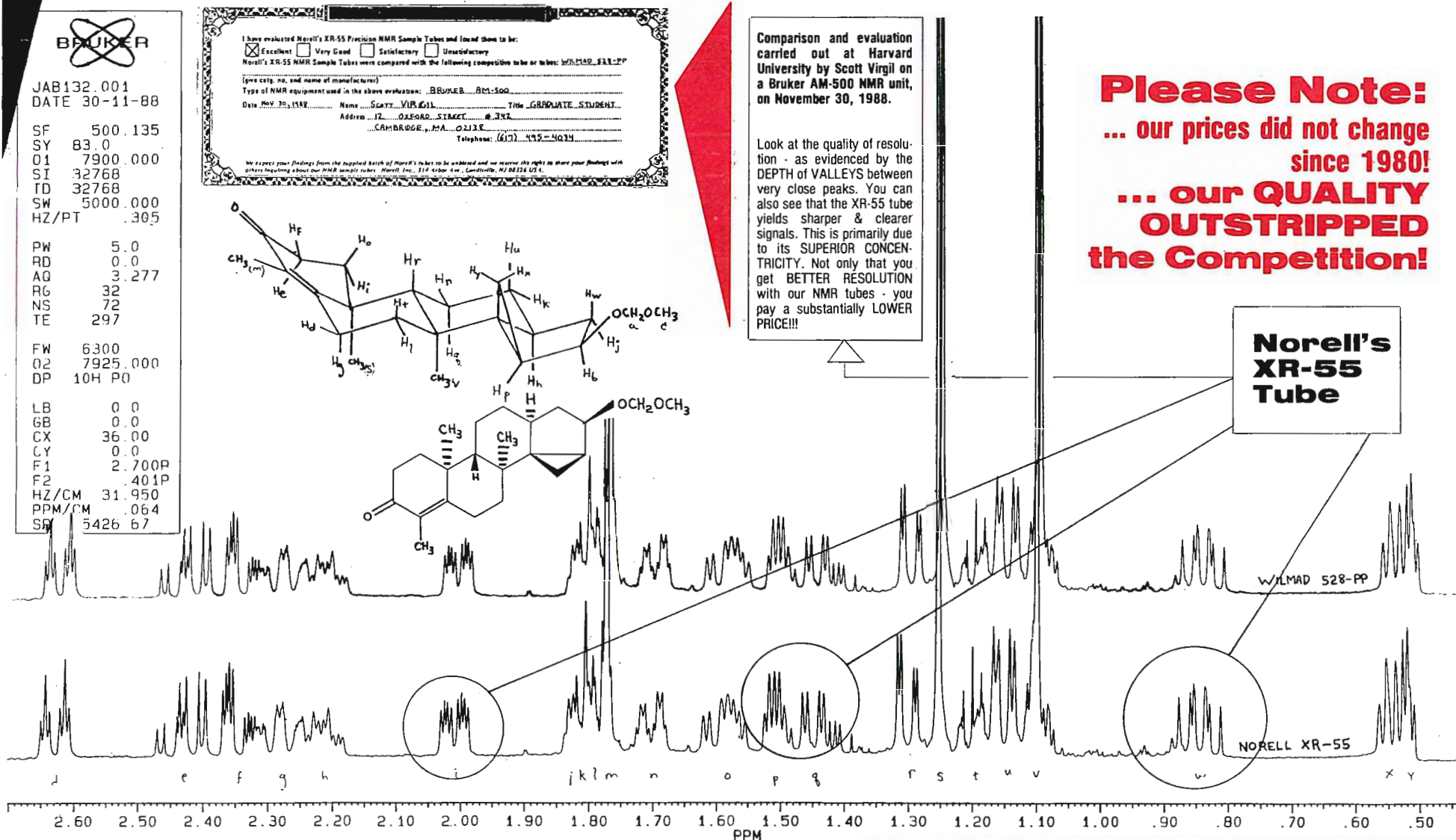
We expect your findings from the supplied batch of Norell's tubes to be unbiased and we reserve the right to share your findings with others inquiring about our NMR sample tubes. Norell, Inc., 22 Marlin Lane, Landville, NJ 08330 USA.

Comparison and evaluation
 carried out at Harvard
 University by Scott Virgil on
 a Bruker AM-500 NMR unit,
 on November 30, 1988.

Look at the quality of resolution - as evidenced by the DEPTH of VALLEYS between very close peaks. You can also see that the XR-55 tube yields sharper & clearer signals. This is primarily due to its SUPERIOR CONCENTRICITY. Not only that you get BETTER RESOLUTION with our NMR tubes - you pay a substantially LOWER PRICE!!!

Please Note:
 ... our prices did not change
 since 1980!
 ... our **QUALITY**
OUTSTRIPPED
 the Competition!

**Norell's
 XR-55
 Tube**



NORELL, INC., 22 Marlin Lane, Mays Landing, NJ 08330 USA Tel: (609)625-2223; (800)222-0036; Fax: (609)625-0526

PRECISION NMR SAMPLE TUBES



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

(received 8/4/90)

Dear Dr. Shapiro,

Long Range Scalar Couplings between Chemically Equivalent Nuclei

Prof. Josef Michl asked if we could apply NMR to provide an insight into the proton structure of Bicyclo[1.1.1]pentane-1,3-dicarbonitrile (Fig. 1) using liquid crystal solvents in NMR spectroscopy. The ^1H spectrum of over 60 lines was taken in the liquid crystal ZLI 2806 and interpreted using standard techniques. Starting values for the D_{ij} 's were obtained using geometrical considerations and immediately produced a spectrum that somewhat resembled that obtained experimentally, but refused to converge to a successful fit without careful variation of the J_{ij} 's over a broad range. This produced a fit (using PANIC on an Aspect 3000 computer) with 62 unique transitions assigned and RMS error of 0.24 Hz with values for the dipolar coupling of $D_{12} = 399.71 \pm 0.03$ Hz, $D_{13} = 54.62 \pm 0.03$ Hz; $D_{14} = 35.49 \pm 0.05$ Hz, $D_{16} = 208.83 \pm 0.05$ Hz. The scalar terms included a geminal (H_1, H_2) coupling of 2.24 ± 0.07 Hz and a 4J (H_1, H_4) coupling of -9.02 ± 0.09 Hz. We suspect that the existence of two possible mechanisms of 4J couplings, $H_1\text{-}C_2\text{-}C_1\text{-}C_4\text{-}H_4$ and $H_1\text{-}C_2\text{-}C_3\text{-}C_4\text{-}H_4$, is responsible for the large magnitude of this coupling.

Sincerely,

Nathan F. Dalleska

David M. Grant

P.S. One of us (NFD) enjoyed March in Paris working with Prof. Jacques Courtieu on the fit and his assistance and hospitality are greatly appreciated.

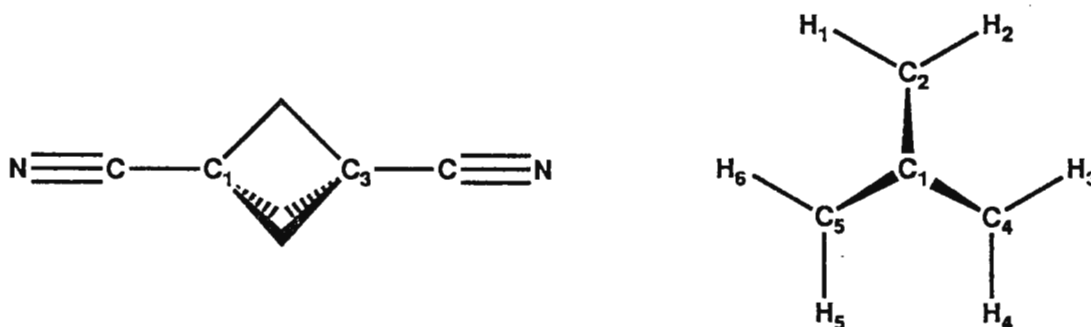


Figure 1. Structure of Bicyclo [1.1.1] pentane-1,3-dicarbonitrile.

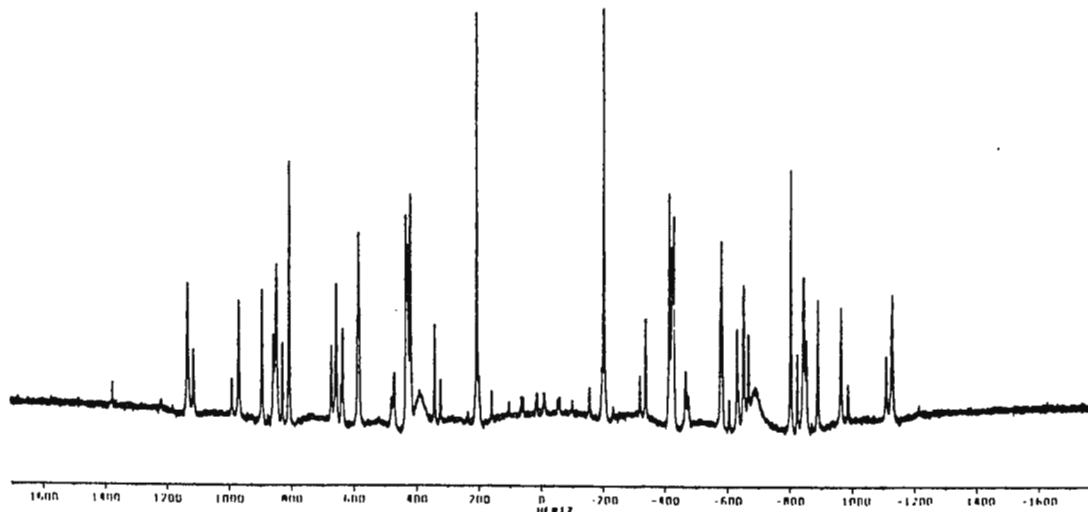


Figure 2. 250 MHz 290K ^1H NMR Spectrum of Bicyclo [1.1.1] pentane-1,3-dicarbonitrile 5% wt/wt in ZLI 2806.

Position Available

Union Carbide has an immediate opening for an NMR spectroscopist at our Bound Brook Technical center located in central New Jersey. The position is in the NMR laboratory of the R&D Analytical Section. This laboratory is currently equipped with a Bruker AM-360, an IBM WP-270/SY, and an IBM WP-200/SY with a C-13 CPMAS accessory. Two additional high field spectrometers are expected in January of 1991.

The successful applicant will have a Ph.D. degree in chemistry with experience in high resolution, high field multinuclear NMR. Experience in polymer analysis and 2-D, multipulse, and solid state NMR would also be valuable. The assignment involves coresponsibility for operation of the NMR laboratory and requires extensive interaction with other members of the technical staff. The focus of the NMR laboratory is on the structure elucidation of polymers and polymer-related materials.

Interested applicants should send their resume to DR. K. POLLAK - UNION CARBIDE CORPORATION, P.O. 670, BOUND BROOK, NJ 08805. Salary and benefits are competitive and commensurate with qualifications and experience. Union Carbide Corporation is an equal opportunity employer.

Equipment Wanted: We need a N.M.R. probe that can be used with a VARIAN spectrometer model HA-100D-15. The magnet is a 7700 lb. VARIAN electromagnet with 15 inch pole pieces, model V-3800-1. If you have such a probe that you are not using and can spare, we would appreciate having it. Also, a "lock-box" would be useful if you have one to spare. Call Dr. D. W. Sheppard at (304) 473-8023, or write him at West Virginia Wesleyan College, Box 68, Buckhannon, WV 26201.

Postdoctoral Position in NMR Microscopy

Available immediately, a postdoctoral position involving biophysical applications of MRI at microscopic dimensions. Bruker AM360 micro-imager and SISCO 7.0 T (300 MHz) horizontal bore systems available for research along the lines described in:

- (1) "Stroboscopic NMR Microscopy of the Carotid Artery," Behling, Tubbs, Cockman, and Jelinski, *Nature* **341**, 321-323 (1989).
- (2) "Stroboscopic NMR Microscopy of Arterial Blood Flow," Behling, Tubbs, Cockman, and Jelinski, *Biophys. J.* **58**, 267-271 (1990).
- (3) "Measurement of Slow Anisotropic Diffusion with Microscopic MRI," Hoatson, Cockman and Jelinski, *Soc. Mag. Res. in Med., Works in Progress*, 1287 (1990).

Send resume and three letters of recommendation to Lynn W. Jelinski, Head, Biophysics Research Department, AT&T Bell Laboratories, 600 Mountain Avenue, Room 1C-427, Murray Hill, NJ, 07974.



We can Electroplate PTFE

Any shape, any size - to your specs!

If you are looking for low loss tangent, low dielectric constant, very high volume resistivity, chemical inertness and insignificant water absorption, and you want it all at the same time, you can only find it in pure PTFE.

And if you are looking for electroplated PTFE you can only find it at Polyflon.

According to many authorities "nothing sticks to Teflon®"... it just can't be done. Actually, at Polyflon we've been doing it successfully for years. It has been proven in many diverse applications ranging from microwave communications to magnetic resonance imaging. The molecular bond between PTFE and the electrodeposited material is very strong, creating distinct advantages for products and components.

- Electroplated PTFE reduces corona: Without interfacial air entrapments, voids or inclusions, corona cannot easily be initiated.

- Electroplated PTFE reduces interfacial losses: especially at higher frequencies, because of the tight molecular bond and because the low loss tangent of PTFE at high frequencies is negligible.
- Electroplated PTFE improves mechanical connections: solder can be flowed directly onto the surfaces of electroplated PTFE to produce an integral, solderable surface.

There are many applications for electroplated PTFE, from the smallest capacitors to the largest imaging coils. It might be the solution to a problem that you are currently facing.

Call or write Polyflon to find out how our capabilities may solve a problem application and/or improve the performance of your product.

Teflon is a registered trademark of DuPont Company.

CRANE®

POLYFLON

Polyflon Company • 35 River Street • New Rochelle NY10801
Tel: (914) 636-7222 • FAX: (914) 633-3664

TAKING ADVANTAGE OF PURE PTFE'S QUALITIES IN RF & MICROWAVE APPLICATIONS

PTFE Provides High Performance

Electroplated PTFE meets the most demanding mechanical and electrical design requirements. Polyflon's unique electroplating process ensures a powerful molecular bond between the PTFE dielectric and conductive metal layer. Without voids or entrapments, this bond ensures products with no corona at the interface, for superb high-voltage performance.

Polyflon's CuFlon® Pure PTFE microwave substrates electroplated with copper, matches the peel strength of copper clad laminates at 8 lb/sq. in. (min.). Custom applications utilizing this process have typically exceeded peel strengths of 15 lb/sq. in.

Electroplated PTFE withstands continuous temperatures of 175°C and 225°C short term without damage to the plated material, dielectric, or the bond between them. This makes electroplated PTFE ideal for solder reflow and surface mount circuit processing, along with other high-temperature processing techniques.

Electroplated PTFE also performs well at low temperatures, even under cryogenic conditions. While most substrate materials become brittle below -196°C, PTFE remains ductile at -268°C — nearly the temperature of liquid helium. As a result, electroplated PTFE is suitable for many superconductive designs, as well as circuits and systems in harsh environments, including avionics and space-related systems.

Why Pure PTFE?

Pure PTFE exhibits extremely low loss, with a dielectric constant of 2.06. This value does not change with temperature or frequency, permitting the design of stable broadband circuits with high performance over wide temperature ranges.

Pure PTFE features high surface resistivity, more than 10^{16} ohms/sq, and high volume resistivity, greater than 10^{18} ohm-cm. Its dissipation factor is less than 0.00045 from 1 to 3 GHz and 0.0003 up to and beyond 18GHz. These characteristics account for pure PTFE's low leakage current and negligible power loss, even in high voltage applications.

The combination of pure PTFE and Polyflon's proprietary electroplating process produces materials that handle a wide range of applications, from specially shaped antennas and tiny, non-magnetic high voltage trimmer capacitors to medical imaging coils for NMR/MRI systems. Whatever the requirement, Polyflon's electroplated PTFE can fit your needs for today's applications and tomorrow's opportunities.



POLYFLON

Polyflon Company • 35 River Street • New Rochelle, N.Y. 10801 • Tel: (914) 636-7222 • FAX: (914) 633-3664

TEXAS A&M UNIVERSITY

ENGINEERING IMAGING LABORATORY

MAIL STOP 3116

COLLEGE STATION TEXAS 77843

409/845-4292

August 5, 1990

(received 8/16/90)

Dr. Barry Shapiro
Texas A&M NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Chemical Shift Reagents and Porous Media

At the Engineering Imaging Laboratory on the Texas A&M University campus we are concerned with developing MRI and other imaging methods for the purposes of investigating phenomena important to the engineering disciplines. Our major effort at the present time is the investigation of fluid flow in porous media. The fundamental understanding of this phenomena is vital to increased oil recovery from the existing reservoirs. To get an idea of just how important the understanding of this phenomena is, one needs to know that 60% of the oil in the ground is going to stay there using present oil recovery methods. MRI is one of the few ways to visualize and quantify, on a local scale, fluid flow phenomena in porous media. If the understanding of this phenomena is improved by our work and the amount of recoverable oil by is increased by 1% our research efforts will have been a great success.

One of the principle problems to solve is the development of a reliable way to distinguish oil and water in porous media samples. For example, they can be distinguished on the basis of differential relaxation times or chemical shift. For bulk fluids any of the many contrast enhancement methods will work. When the fluids are contained in a porous sample, however, the results are much different. Relaxation times are dominated by fluid/surface interactions and pore geometry, resulting in a decrease in the difference between oil and relaxation times. Secondly, in all but a few cases the resonance lines in reservoir rock samples broaden because of magnetic impurities and ion containing clays, obscuring any chemical shift between the fluids. What we report here is an attempt to enhance the chemical shift of the aqueous phase and therefore be able to use chemically selective imaging sequences to easily discriminate between aqueous and organic phases.

In figures 1 and 2 we show our results for two different shift reagents, MnCl_3 and PrCl_3 in unconsolidated porous media samples consisting of sand in two different sizes. The Pr^{+++} ion

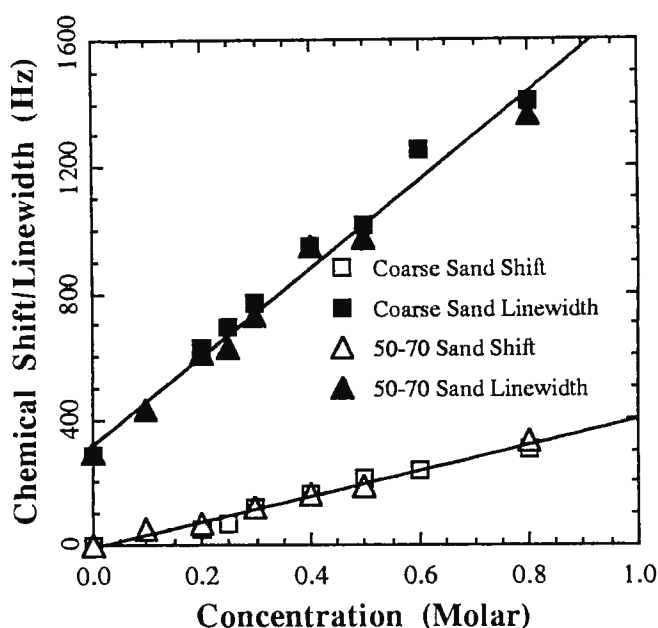


Figure 1: Chemical Shift and Linewidth for PrCl_3 solutions in two sand sizes. Lines are least squares fits of the sum of the linewidth or shift data.

shifts the water resonance because of an anisotropic interaction between the unpaired f electron and the water protons¹. In the case of Mn^{+++} , the shifts mechanism is a contact interaction between the protons and the unpaired d electron¹. In both cases the shift is seen to be linear as one might expect.

To our dismay the chemical shift reagents also caused the linewidth to increase. The cause of the line broadening is a mechanism known to affect the linewidth of powdered samples.^{2,3,4} The random size shape and orientation of the fluid filled pores create field inhomogeneities proportional to the difference in the static magnetic susceptibility between the rock and fluid, $\Delta\chi = \chi_{rock} - \chi_{fluid}$. As χ_{fluid} and χ_{rock} become much different, $\Delta\chi$ becomes proportional to ion concentration. Over the range of concentrations tested, for the $PrCl_3$ solutions, the change in linewidth with concentrations is linear, but for $MnCl_3$ solutions it is not. $MnCl_3$ solutions also decrease the relaxation times and at concentrations above 0.02 molar, the linewidth in the unconsolidated samples we used may be dominated by the natural linewidth of the solution. One thing is certain; the linewidth increases faster than the chemical shift for both $PrCl_3$ and $MnCl_3$ solutions. We tested a few other shift reagents and found that the linewidth increased faster than the chemical shift as well.

We unfortunately must conclude that the use of chemical shift reagent to enhance the distinguishability of oil and water in porous media will not work and we must look for another method.

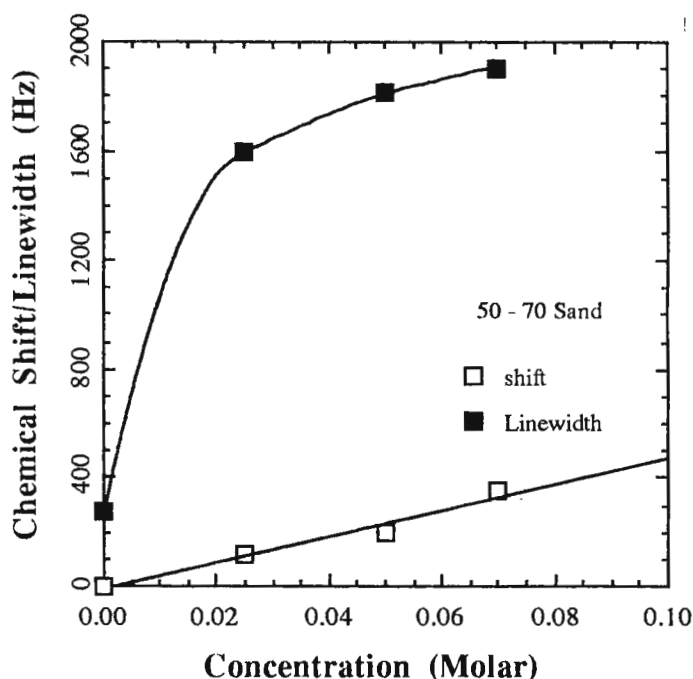


Figure 2: Chemical Shift and Linewidth of $MnCl_3$ Solutions in 50-70 mesh sand. Shift calculated as first moment of the line.

Sincerely,

Carl M. Edwards

Sincerely,

C-T. Chang

Sincerely,

John Robinson

cme/gl

1. Cockrill, A.F., et. al., Chemical Reviews 73, 553(73)
2. Wayne, R.C., and Cotts, R. M. Phys. Rev. Lett. 151, 264(66)
3. Drain, L.E., Proc Phys. Soc. 80, 1380(62)
4. Glasel, J.A., Lee, K.H., J. Amer. Chem. Soc. 96, 970(74)



EXPLORE THE ALTERNATE ROUTE...!

**QUALITY REFURBISHED
NMRs**

BRUKER . JEOL . VARIAN

PERMANENT MAGNETS . ELECTRO MAGNETS . CRYO MAGNETS

.....

CURRENTLY IN STOCK: **BRUKER WM-360WB, NR-80**

VARIAN FT-80A

ALSO AVAILABLE: **VARIAN EM-390, EM-360A, VXR-400**

JEOL FX-90Q

FOR FURTHER DETAILS CALL: (708) 913-0777

International Equipment Trading Ltd.
960 Woodlands Parkway, Vernon Hills, IL 60061
FAX: (708) 913-0785

Call Now for the Best Value!

New and Reconditioned
Analytical Instruments

INVENTORY UPDATE SPRING 1990

X-RAY

Philips AXS Fluorescence
spectrometer + 3100 generator
Rigaku D/MAX-AV automated vertical
diffractometer
Siemens SRS 200 Fluorescence
spectrometer + 805 generator
Stoe, Bragg-Brentano Diffractometer

GAS CHROMATOGRAPHS:

Hewlett Packard 5830A, dual FID
Hewlett Packard 5840A with 7671A
Hewlett Packard 5880A with FID,
ECD, NPD
Hewlett Packard 3392A integrator
Perkin Elmer Sigma 1B, dual TCD
Perkin Elmer Sigma 2000 with
HS-100 auto-injector
Perkin Elmer 3920B, dual FID
Tekmar ALS II Autosampler
Tekmar LSC II Purge and Trap
Tracor 540 with ECD, FID
Varian 6000 FID, FPD capillary and
packed column with model 8000
autosampler

H.P.L.C.:

Beckman 345
Dionex 2000Vsp ion chromatograph
Hewlett Packard diode array
detector 1040M + HP 9000
(9843A), 20 Meg drive and printer
Perkin Elmer LC-75 UV detector
Perkin Elmer LC-85 UV detector
Varian Varichrome UV detector
Varian 5060 + UV-100 and Vista 401
Waters 6000A pump
Waters 440 detector
Waters 441 detector
Waters 710B wisp Autosampler

MASS SPECTROMETERS:

Finnigan 4021
Finnigan 1020/1050
Hewlett Packard 5987 with 5890 GC
with RTE-6 operating system

UV-VIS:

Bausch & Lomb Spectronic 2000
Beckman DU-7
Hitachi 100-80
Perkin Elmer Lambda 3B
Varian 2290

ATOMIC ABSORPTION:

Instrumentation Labs 457 with D2
and 440 AVA
Jarrell Ash 951 with D2
Jarrell Ash 655 Atomizer
Jarrell Ash EDL Power Supply
Jarrell Ash Smith-Hieftje Video 12E
with 188 Furnace Atomizer and
440 AVA
Leeman Labs Plasma Spec III
simultaneous and sequential
Perkin Elmer EDL Power Supply
Perkin Elmer 403
Perkin Elmer 373 with D2
Perkin Elmer 560 with D2
Perkin Elmer 703 with D2
Perkin Elmer 2380 with printer
Perkin Elmer 5000 with D2
Perkin Elmer HGA-400
Perkin Elmer HGA-500
Perkin Elmer HGA-2200 furnace
Perkin Elmer AS-40 Autosampler
Perkin Elmer AS-50 Autosampler
Perkin Elmer Data System 10 for AA
Varian 875 with graphite furnace
and computer

DISPERSIVE IR:

Beckman Acculab 2
Perkin Elmer 1330 Perkin Elmer 297

FT-IR:

Digilab FTS-15B +10 cm-1 option
Nicolet 20SX Nicolet 20DX

RESONANCE

SPECTROMETERS:

Bruker WM-360 NMR
Bruker CXP-200 NMR
JEOL FX-90Q NMR
Varian CFT-80 NMR
Varian EM-360L NMR

ELECTRON MICROSCOPES:

Cambridge 120B SEM
Hitachi H-300 TEM
ISI SS-60 SEM + Kevex 8000 III EDS
ISI 100
JEOL 35C SEM
Philips 400 STEM with EDS

NUCLEAR INSTRUMENTS:

Beckman 5000 scintillation counter
Tracor Gamma Trac 1290

THERMAL ANALYZERS:

Dupont 1090 with 910 DSC

BIOTECHNOLOGY

Applied Biosystems (ABI) Protein
Sequencer 477A with 120A
ABI Peptide synthesizer 430A
ABI Analytical HPLC 150A
ABI DNA synthesizer 380B-02
ABI Separation system 130A
ABI HPLC 151A
Beckman J2-21M Centrifuge
FTS Systems freeze-dryer

MISCELLANEOUS:

A.O. model 820 microtome
Aminco SPF-500 spectrofluorometer
Best Power 3KVA UPS
Bicron M92, M95, M86 surveyors
Blue M deluxe floor oven with
Touch-Matic controls
Hiac Royco 4100 with 3200 sampler
346 BCL sensor
Jarrell Ash Deluxe Varisource
L & N Microtrack 7995-12
Technicon InfraAlyzer 400 moisture
analyzer
Perkin Elmer LS-3 spectrofluorometer
Perkin Elmer 240C CHN analyzer
Reichert Zetopan phase contrast and
fluorescence microscope
Zeiss Photomicroscope III
Zeiss ICM 405 microscope

Above equipment carries a
90-day warranty

Availability is subject to
prior sale.



International Equipment Trading Ltd.

960 Woodlands Parkway
Vernon Hills, Illinois 60061

(708) 913-0777

FAX: 913-0785 TELEX: 754500 IET UD

SERVING THE
SCIENTIFIC COMMUNITY
FOR 10 YEARS
1980-1990

John Cavanagh
Department of Molecular Biology
Phone: 619-554-4311
FAX: 619-554-9822

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

August 10, 1990.
(received 8/13/90)

Sensitivity Improvement in 2D Heteronuclear Correlation Spectra

Dear Prof. Shapiro:

A major consideration in the application of any experimental NMR method is the inherent sensitivity of the technique. The biological applications of high resolution NMR spectroscopy are, with increasing frequency, being limited by the sensitivity of the techniques due, for example, to the desire to study molecules which can only be obtained in small quantity, have low solubilities or give rise to large resonance linewidths.

With this in mind we have developed a method that significantly improves the sensitivity of 2D N-H correlation spectra, for heteronuclei with a single geminal proton, such as amides. The increased signal-to-noise ratio arises because two in-phase orthogonal proton magnetization components can be refocussed at the end of a pulse sequence, rather than the usual one component, and can subsequently be processed to give a pure phase spectrum. Figure 1a shows a conventional heteronuclear single quantum coherence (HSQC) pulse sequence used for recording N-H correlation spectra. At the end of this sequence one in-phase proton magnetization component is present and recorded. Also present is an unobservable heteronuclear multiple quantum term. Figure 1b shows the sensitivity enhanced pulse sequence we have developed that refocusses the heteronuclear multiple quantum term to in-phase proton magnetization in addition to retaining the normal in-phase proton magnetization component. A second experiment is recorded with phase inversion of the heteronuclear pulse immediately following t_1 , which changes the sign of one of the two components. Addition and subtraction of the two separate

experiment gives two data sets that can be processed to yield two pure phase, conventional, 2D heteronuclear correlation spectra. Addition of these two spectra doubles the size of the resonances, whilst the noise adds independently and increases only by a factor of $2^{1/2}$. Thus a sensitivity enhancement of up to $2^{1/2}$ should be observed. Experimentally, due to relaxation effects during the longer enhanced sequence, an enhancement of slightly less than $2^{1/2}$ is obtained. Figure 2 shows a slice parallel to the F_2 axis through resonances in the natural abundance N-H correlation spectrum of BPTI (20mM, 308K, 90/10 H_2O/D_2O , pH=4.8) recorded using the HSQC sequence of Fig. 1a. Figure 2b shows the corresponding slice from the sensitivity enhanced spectrum recorded using the pulse sequence of Fig. 1b. Both experiments took 20 hours to record, and both slices are plotted on the same absolute scale. The signal-to-noise ratio increase seen here is about 30%.

Please credit this contribution to the account of Peter Wright.

Sincerely yours



John Cavanagh



Arthur G. Palmer III.

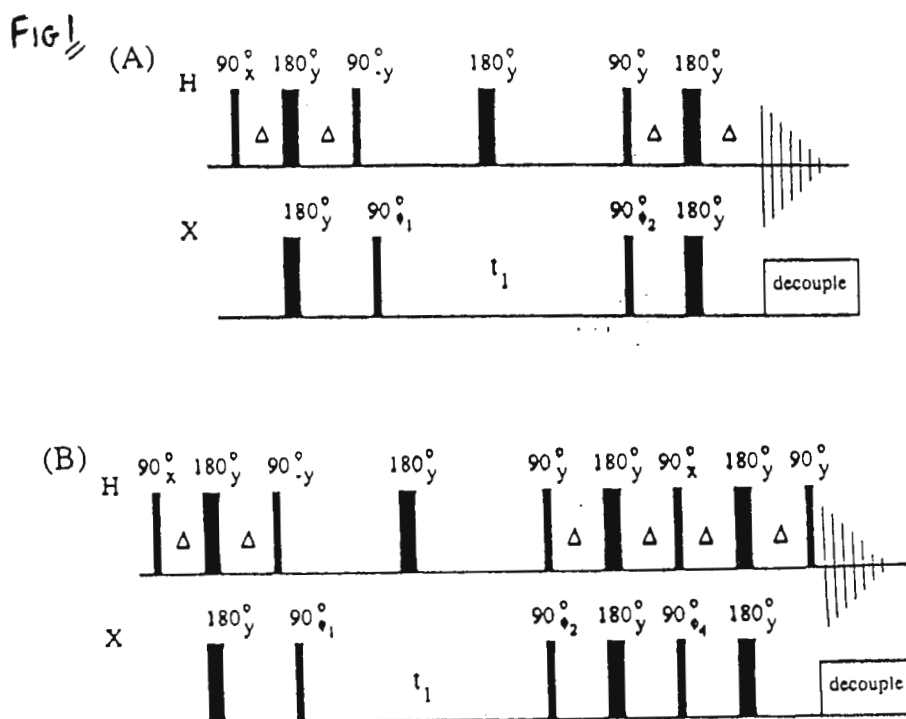
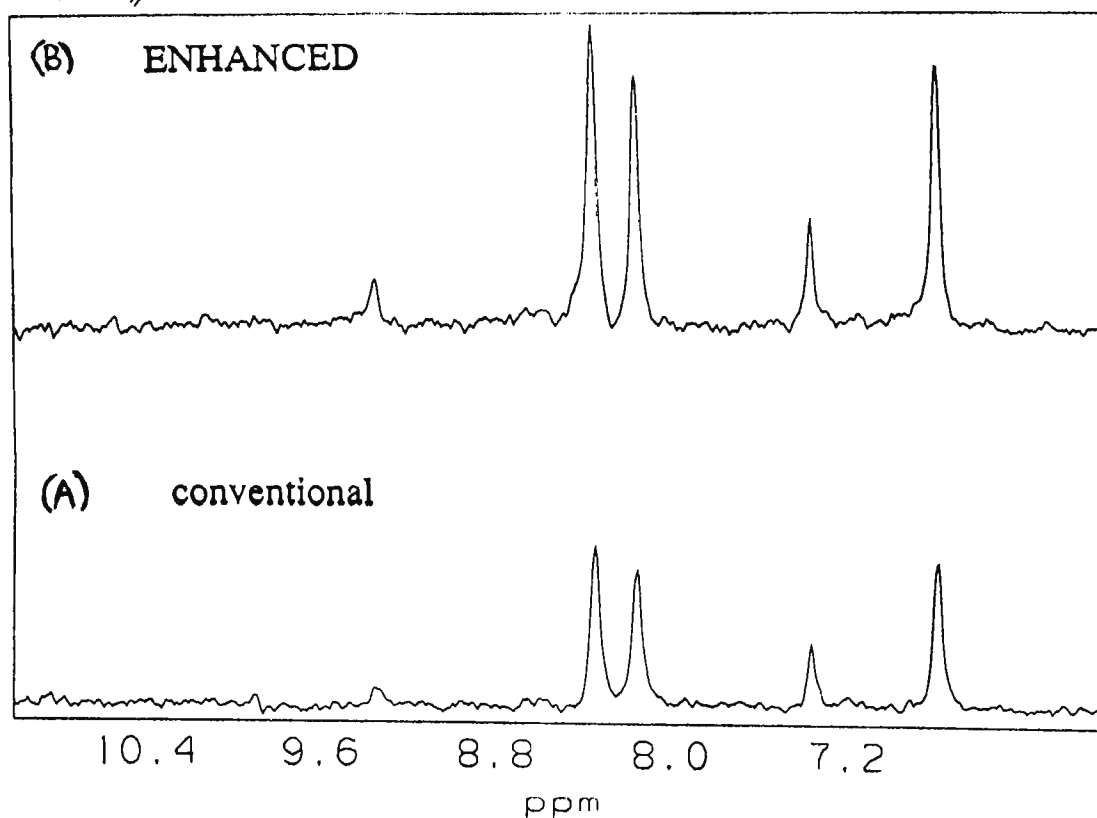


FIG 2



Postdoctoral Position Available

The NMR laboratory of the Biotechnology Research Institute (BRI) is seeking a postdoctoral scientist to participate in our ongoing research in the development of advanced NMR methods (2D and 3D transferred NOE and isotope-edited spectroscopy) for applications in drug design. The position will be available for two years and is supported by CIBA-GEIGY Corporation (USA and Canada). Specific projects include transferred NOE-based determination and refinement of the dynamic structure of enzyme-bound inhibitors and the development of new 2D and 3D NMR techniques for the study of the interaction of inhibitors with large protein assemblies. The successful candidate will work closely with peptide and computational chemists at BRI. Our laboratory is equipped with two Brüker (AM-500 and AMX-500) NMR spectrometers. We also have access to a Brüker AMX-600 spectrometer located in the NRC laboratories in Ottawa. These instruments are connected to a Vax cluster and an Iris 4D/280 graphics computer for data processing and molecular modelling. Interested candidates should contact Dr. Feng Ni at (514)-496-6729 or send a CV and 2 letters of reference to:

Dr. Feng Ni
Biotechnology Research Institute
6100 Royalmount Avenue
Montréal, Québec
Canada H4P 2R2

TAMU NMR Newsletter

Editor/Publisher: Bernard L. Shapiro

966 Elsinore Court, Palo Alto, California 94303, U.S.A. (415) 493-5971

Mailing Label Adornment: Is Your Dot Green?

If the mailing label on your envelope of this issue is adorned with a large green dot: this decoration means that payment for your 1990-91 subscription has not been received as of 17 September 1990. Unpaid subscriptions will be suspended before the November issues are mailed. If you are green dotted, please arrange to have your payment executed without delay, or at least contact me to arrange for uninterrupted Newsletter flow. This notice applies to all Subscribers, but not to Sponsors or Advertisers.

Another (?) Mailing Label Adornment: Is Your Dot Red?

If the mailing label on your envelope of this issue is adorned with a large red dot or circle: this decoration means that you will not be mailed any more issues until a technical contribution has been received by me.

Page Length Request Instruction

Attention overseas subscribers: If you must use paper which is longer than 11", *please* take care that all material (including signatures, addresses - everything!) ends no more than 10" from the top of each of your pages. It is costly to make reductions, and henceforth I reserve the right to chop the excess length off any page, no matter what the result. Beware of the dreaded guillotine! Your cooperation in this matter will be greatly appreciated. Thank you.

All Newsletter Correspondence

Should Be Addressed To:

Dr. Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303, U.S.A.
(415) 493-5971

DEADLINE DATES *

No. 386 (November) -----12 October 1990
No. 387 (December)-----9 November 1990
No. 388 (January)-----7 December 1990
No. 389 (February)----- 18 January 1991

* *Please note that these deadline dates have been moved a bit forward from those previously in effect.*

*

*

*

*

*

CSI 2T Applications

Shielded Gradients: Theory and Design

NMR imaging and localized spectroscopy depend on the use of pulsed magnetic field gradients. As these techniques have grown more complex, it has become apparent that eddy currents created in the magnet cryostat and other structures by pulsed gradients have become the chief limitation to many sophisticated applications.

Figure 1a illustrates the design problem for unshielded gradients. Figure 1b illustrates the shielded gradient arrangement. Figures 2 and 3 show the contours of constant flux for an unshielded and shielded Z gradient coil, respectively. This demonstrates that, for the shielded gradients, most of the flux has been kept away from the magnet bore.

The dramatic reduction of eddy currents which can be made over the conventional, unshielded gradients is shown in Figures 4a, b. These graphs show frequency as a function of time following the application of a long, constant amplitude gradient pulse which is suddenly cut off. Soon after cut off, a 90° pulse is applied and the complex FID recorded. The instantaneous frequency is then obtained from the FID and normalized by dividing by the frequency offset at the sample during the gradient pulse.

Figure 4a shows a typical decay of extra magnetic fields in a CSI 2T instrument caused by eddy currents in the conventional, unshielded gradient set with compensation.

Figure 4b shows the decay of the uncompensated shielded Z gradient and Figure 4c shows the Z gradient decay with compensation. Note that the time scale for 4b and 4c is five times shorter than that for the unshielded gradients.

Fig. 1a.

CONVENTIONAL GRADIENT COIL

- Currents are constrained to flow on a single cylinder.
- There is only one degree of freedom.



Fig. 1b.

SHIELDED GRADIENT COILS

- Currents on two cylinders.
- Two degrees of freedom.

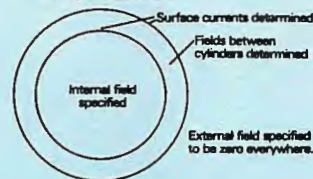


Fig. 1a—Design problem for unshielded gradients. The field inside the winding is specified to be a linear gradient and the current pattern on the cylinder is determined. **Fig. 1b**—Design arrangement for shielded gradients. The field inside the inner cylinder is specified to be a linear gradient and the field beyond the outer cylinder is specified to be close to zero. The current patterns on both inner and outer cylinders are then determined.

Fig. 2.

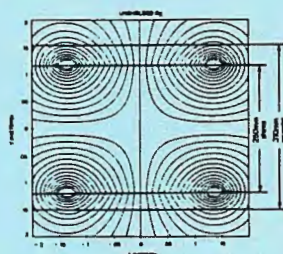
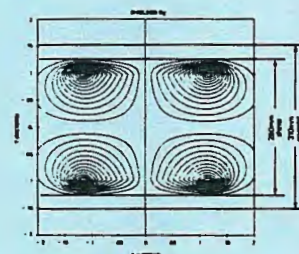


Fig. 3.



Lines of constant flux for Z-gradient. **Fig. 2**—Unshielded gradient. Note that flux lines extend well beyond the cryostat bore. **Fig. 3**—Shielded gradient. Flux lines are kept within the outer gradient cylinder.

Fig. 4a.

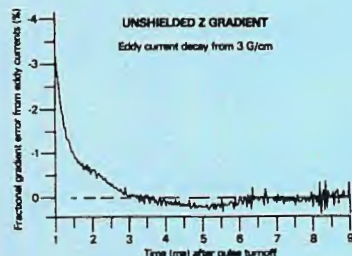


Fig. 4b.

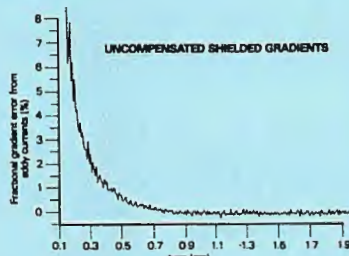


Fig. 4c.

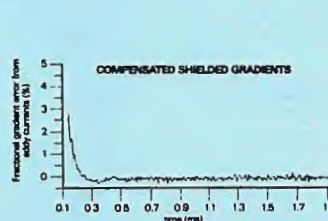


Figure 4b

Decay of field following application of square gradient pulse. **Fig. 4a**—Unshielded gradients. **Fig. 4b**—Shielded S150 gradient with no waveform compensation. **Fig. 4c**—Shielded S150 gradient with waveform compensation.

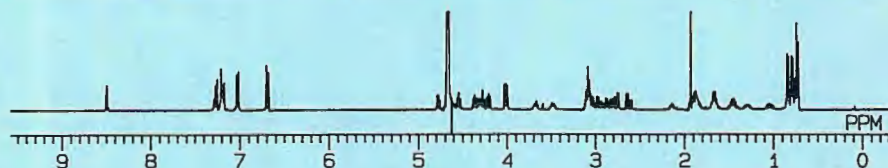
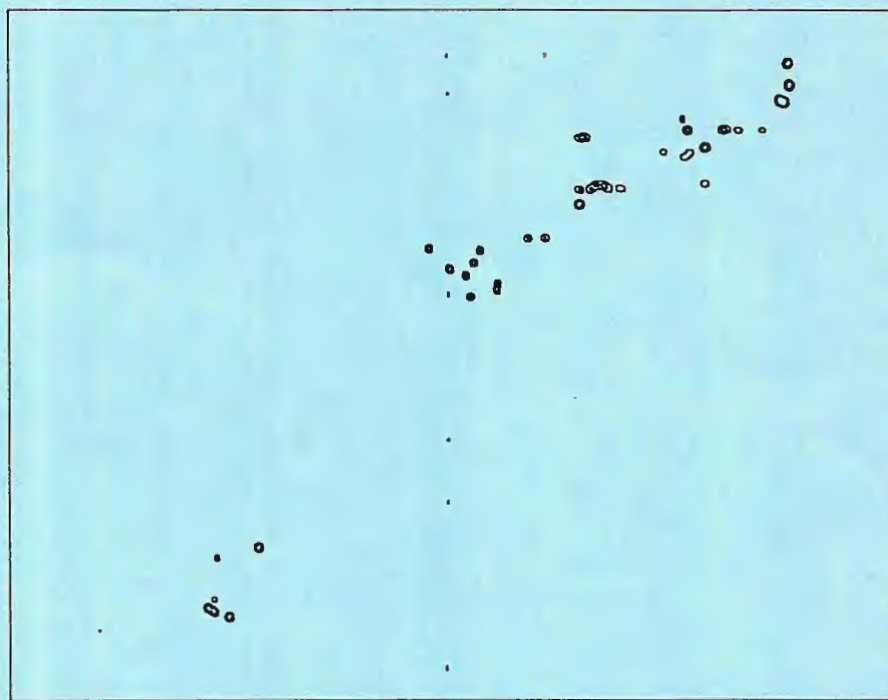


GE NMR Instruments

AFTER THE WORK IS FINISHED...

THE OTHER CPF COMES OUT TO PLAY

When all of the day's production samples have been run and the piles of spectra plowed through, JEOL's CPF can quickly switch operation modes. This same highly automated machine which is used for all of the production work can produce very high quality research data for those non-routine problems that always seem to appear. In many cases all that is necessary to make the change is to log into the research account. This changes the CPF from an automated, limited instrument into a wide-open research-grade spectrometer. With the addition of the appropriate accessories the low cost CPF is capable of running the most sophisticated research type experiments including CP MAS solids. Now that the CPF is available at a field strength of 400 MHz in addition to the very popular 270 MHz, the high field research spectrometer has become very affordable. The above 400-CPF data is a reverse detection ^{13}C experiment run on Angiotensin-II. The instrument used for this experiment is a standard CPF with the addition of the optionally available reverse detection Broad Band probe. This data clearly shows that the routine need never be the only thing you can do.



For more information please contact:

JEOL

11 Dearborn Road, Peabody, MA 01960 (508) 535-5900 (Phone) (508) 535-7741 (FAX)