TEXAS A&M UNIVERSITY

NMR NEWSLETTER

No. 415

April 1993

Continued on Inside Back Cover

PTS
FREQUENCY SYNTHESIZERS

NMR-MRI HIGH PERFORMANCE DIRECT SYNTHESIZERS

The accuracy, stability and low noise you need for any experiment. Most widely accepted line of high-reliability frequency synthesizers. Thousands in use worldwide.

PTS 040

Range: 0.1–40 MHz
Resolution: 0.1Hz–100KHz (opt)
Switching: 1–20μs

Output: +3 to +13dBm; 50ohm
Spurious Outputs: –75dBc
Phase Noise: –75dBc (0.5Hz–15KHz)

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: $5,125.00*

PTS 120

Range: 90–120 MHz
Resolution: 0.1Hz–100KHz (opt)
Switching: 1–20μs

Output: +3 to +10dBm; 50ohm
Spurious Outputs: –75dBc
Phase Noise: –75dBc (0.5Hz–15KHz)

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: $5,125.00*

PTS 160

Range: 0.1–160 MHz
Resolution: 0.1Hz–100KHz (opt)
Switching: 1–20μs

Output: +3 to +13dBm; 50ohm
Spurious Outputs: –75dBc
Phase Noise: –63dBc (0.5Hz–15KHz)

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: $6,245.00*

PTS 250

Range: 1–250 MHz
Resolution: 0.1Hz–100KHz (opt)
Switching: 1–20μs

Output: +3 to +13dBm; 50ohm
Spurious Outputs: –70dBc
Phase Noise: –63dBc (0.5Hz–15KHz)

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: $7,155.00*

PTS 310

Range: 0.1–310 MHz
Resolution: 1Hz
Switching: 1–20μs
Phase Continuous: 1Hz–100KHz steps

Output: +3 to +13dBm; 50ohm
Spurious Outputs: Type 1 –70/65 (typ/spec) Type 2 –65/60dBc
Phase Noise: –68dBc (0.5Hz–15KHz) –63dBc

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: Type 1 $6,175.00* Type 2 $5,625.00*

PTS 500

Range: 1–500 MHz
Resolution: 0.1Hz–100KHz (opt)
Switching: 1–20μs

Output: +3 to +13dBm; 50ohm
Spurious Outputs: –70dBc
Phase Noise: –63dBc (0.5Hz–15KHz)

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: $8,385.00*

PTS 620

Range: 1–620 MHz
Resolution: 0.1Hz–100KHz (opt)
Switching: 1–20μs

Output: +3 to +13dBm; 50ohm
Spurious Outputs: –70dBc
Phase Noise: –63dBc (0.5Hz–15KHz)

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: $9,255.00*

PTS 1000

Range: 0.1–1000 MHz
Resolution: 0.1Hz–100KHz (opt)
Switching: 5–10μs

Output: +3 to +13dBm; 50ohm
Spurious Outputs: –70dBc (0.1–500 MHz), –65dBc (500–1000 MHz)
Phase Noise: –60dBc (0.5Hz – 15KHz)

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: $11,375.00*

PTS x10

Range: 10 MHz band, selected decade 0.1–100 MHz
Resolution: 1Hz
Switching: 1–5μs
Phase Continuous: 2 MHz band, even or odd steps

Output: +3 to +13dBm; 50ohm
Spurious Outputs: –65/–60dBc (typ/spec)
Phase Noise: –70dBc (0.5Hz–15KHz)

Freq. St'd: OCXO, TCXO, Ext.
Interface: BCD par. or GPIB
Price: $2,575.00*

OTHER OPTIONS

Programmable Attenuator 0–90dB (or 0–99dB with GPIB)
n x 10 MHz output (20–140 MHz) or any 10 MHz line

*Prices are US only, and include manual & remote (BCD) control, 1 Hz resolution, OCXO std.

DDS & PHASE ROTATION AVAILABLE ON ALL OF OUR MODELS

PROGRAMMED TEST SOURCES, INC.

P.O. Box 517, 9 Beaver Brook Rd., Littleton, MA 01460 Tel: 508-486-3008 FAX: 508-486-4495

TEXAS A&M NMR NEWSLETTER NO. 415, APRIL 1993 AUTHOR INDEX

TEXAS A&M NMR NEWSLETTER NO. 415, APRIL 1993 ADVERTISER INDEX

SPONSORS OF THE TAMU NMR NEWSLETTER

Abbott Laboratories
American Microwave Technology
ATI Instruments
Bruker Instruments, Inc.
Burroughs Wellcome Co.
Cambridge Isotope Laboratories, Inc.
Chemagnetics
Cryomagnet Systems, Inc.
The Dow Chemical Company
The Du Pont Merck Pharmaceutical Company
Eastman Kodak Company
E. I. du Pont de Nemours & Company
JEOL (U.S.A.) Inc., Analytical Instruments Division
The Lilly Research Laboratories, Eli Lilly & Company
Merck Research Laboratories
Millipore Corporation, Waters Chromatography Division
The Monsanto Company
Nalorac Cryogenics Corporation
Norell, Inc.
Oxford Instruments
Petroleum Recovery Institute
The Procter & Gamble Company, Miami Valley Labs
Programmed Test Sources, Inc.
Shell Development Company
Tecmag
TRIPOS Associates/New Methods Research, Inc.
Unilever Research
Union Carbide Corporation
The Upjohn Company
Varian, Analytical Instrument Division

FORTHCOMING NMR MEETINGS

11th International Meeting on NMR Spectroscopy, Sponsored by the Royal Society of Chemistry, Swansea, Wales, U.K., **July 4 - 9, 1993**; Contact: Dr. J. F. Gibson or Ms. G. B. Howlett - See TAMU NMR Newsletter 415, 5; Phone: (44-71) 437-8656; Fax: (44-71) 437-8883.

Gordon Research Conference: Magnetic Resonance, Wolfeboro, NH, **July 11 - 16, 1993**; Contact: Dr. A. M. Cruickshank, Gordon Research Center. University of Rhode Island, Kingston, RI, 02881-0801; (401) 783-4011 or -3372; Fax: (401) 783-7644.

35th Rocky Mountain Conference on Analytical Chemistry, Denver, Colorado: **July 25-29, 1993**; Contact: Patricia L. Sulik, RML, Inc., 456 S. Link Ln., Ft. Collins, CO 80524; Phone: (303) 530-1169.

12th Annual Scientific Meeting and Exhibition of the Society of Magnetic Resonance in Medicine, New York, NY, **August 14-20, 1993**; Contact: SMRM, 1918 University Ave., Suite 3C, Berkeley, CA 94704; Phone: (510) 841-1899; Fax: (510) 841-2340.

1993 FACSS Meeting, Detroit, Michigan, **October 17-22, 1993**; Contact: H. N. Cheng, Hercules, Inc., Research Center, 500 Hercules Road, Wilmington, DE 19808; Phone: (302) 995-3505; Fax:. (302) 995-4117. See TAMU NMR Newsletter 411, 10.

Pacific Conference, Pasadena, California, **October 19-23, 1993**; Contact: Ms. B. Belmont, Pacific Conference, 14934 S. Figueroa St., Gardena, CA 90248;Phone: (310) 538-9709.

12th International Meeting on NMR Spectroscopy, Sponsored by the Royal Society of Chemistry, Manchester, England, **July 2 - 7, 1995** [sic]; Contact: Dr. J. F. Gibson or Ms. G. B. Howlett - See TAMU NMR Newsletter 415, 5; Phone: (44-71) 437-8656; Fax: (44-71) 437-8883.

ISMAR 1995, Sydney, NSW, Australia, **July 16-21, 1995** [sic]; Contact: Dr. Wm. A. Bubb, Secretary, Univ. of Sydney, Dept. of Biochemistry, Sydney, NSW 2006, Australia. See TAMU NMR Newsletter 414, 8.

Additional listings of meetings, etc., are invited.

January 13, 1993 (received 3/1/93)
Dr. Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Amoco Corporation
160 West Warrenville Rd.
Naperville, Illinois 60563

Upper Stack Funnel to Aid Auto-Sampler Changer

Dear Dr. Shapiro:

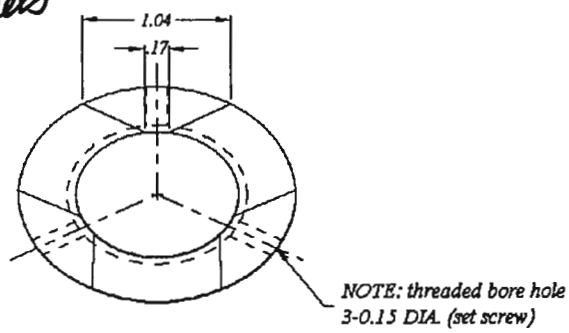
Three of our spectrometers are equipped with automatic sample changers to permit unattended operation. We occasionally encountered problems where a sample was not perfectly centered over the magnet's upper stack during insertion, causing the sample spinner to get caught on the top edge of the upper stack instead of dropping into the magnet. The automation run would proceed normally, unable to detect that the sample did not drop into the probe and proceed to autoshim on an empty probe. After many unsuccessful autoshimming attempts, the run would abort. Usually the sample would become dislodge when the eject air came on, and the robot would retrieve it and proceed to load the next sample. Although Varian provided a device (shown below) that helped direct samples into the magnet, we found that samples still got caught on its edge. We wanted to design a smooth, funnel-shape top for the upper stack that would direct samples into the magnet, with no edges for the spinner to get caught on, and to compensate for any slight robot arm misalignments when inserting samples.

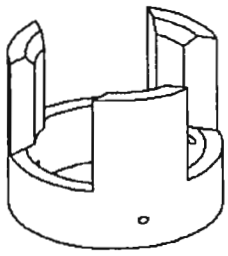
Below you will find drawings of such a funnel which has been working for us for several months without a problem. Spaces between the three "fins" allow room for the robots fingers to open and close, as well as allow a 20 mm NMR tube to pass through. Measurements are in inches. The funnel was machined out aluminum. Perhaps this will be of assistance to another lab encountering the same problems.

Best regards,

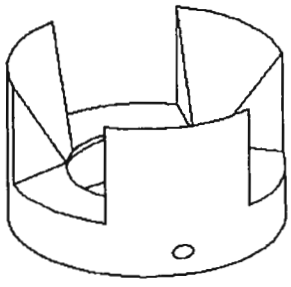
Mary L. Michaels

Rod Salazar





Original Design



New Design

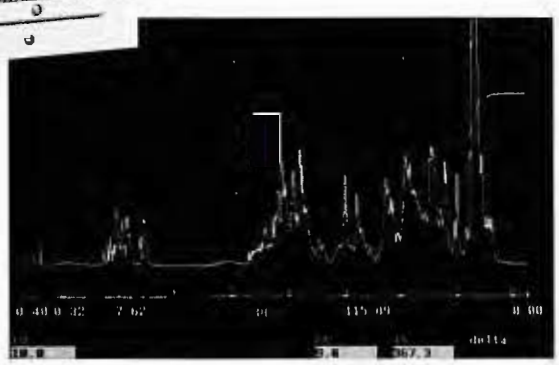
AMT Delivers More For Less!

10–90 MHz, 1000 Watt RF power amplifiers for less than $10,000

Key Features:

- Full 10–90 MHz frequency range
- 1000 watt power rating
- Linearity ±1dB
- Noise blanking in less than 2 μs
- Less than 5% pulse droop
- Dual mode, Pulse/CW operation
- Digital power meter
- Dual range power limits

Model 3426



The AMT NMR/NMRI product family

SERIES	FREQUENCY	POWER RATINGS
3130	200–500 MHz	50 to 300 W
3200	6–220 MHz	150 to 1000 W
3304	30–310 MHz	400 W
3420	10–90 MHz	1000 to 2000 W

Call Jim Lukes at AMT, or your local distributor NOW
for a price that will flip your spins!

AMERICAN MICROWAVE TECHNOLOGY

3080 Enterprise Street ■ Brea, CA 92621 ■ (714) 993-0802 ■ Fax (714) 993-1619

AMERICAN MICROWAVE TECHNOLOGY

Model 3426
10–90 MHz, pulsed, solid-state, RF power amplifier system

Electrical specifications:

Frequency range	10–90 MHz
Pulse power (min.) into 50 ohms	1000 W
CW power (max.) into 50 ohms	100 W
Linearity (±1 dB)	0–900 W
Gain (typ.)	65 dB
Gain flatness	± 2 dB
Input/Output impedance	50 ohms
Input VSWR	< 2:1
Pulse width	20 ms
Duty cycle	Up to 10%
Amplitude rise/fall time	250 ns typ.
Amplitude droop	5% to 20 ms typ.
Phase change/output power	10° to rated power, typ.
Phase error overpulse	4° to 20 ms duration, typ.
Noise figure	11 dB typ.
Output noise (blanked)	< 20 dB over thermal
Blanking delay	< 2 μs on/off, TTL signal
Protection	1. VSWR: infinite VSWR 2. Input overdrive: up to 10 dB 3. Over duty cycle/pulse width 4. Over temperature

Supplemental characteristics:

Connectors, rear panel	1. RF input: BNC (F) 2. RF output: Type N (F) 3. Noise blanking: BNC (F) 4. Interface: 25 pin D(F), EMI filtered
Indicators, front panel	1. AC power on 2. Peak power meter 3. Over pulse width 4. Over duty cycle 5. Over temperature 6. Over drive 7. CW mode
System monitors	1. Forward/Reflected RF power 2. Over pulse width/duty cycle 3. DC power supply fault 4. Thermal fault
Front panel controls	1. AC power 2. Pulse width 3. Duty cycle
Cooling	Internal forced air
Operating temperature	+10 to 40°C
AC line voltage	208/230 VAC, ±10%, 50–60 Hz
AC power requirements	2000 watts
Package	Rack mount
Size (HWD, inches)	8.75 × 19 × 20.25
Net weight	100 lbs.

03/92

3080 Enterprise Street ■ Brea, CA 92621 ■ (714) 993-0802 ■ Fax (714) 993-1619

Eleventh International Meeting on

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

University College of Swansea, Wales
4–9 July 1993

Introduction

The eleventh international meeting on NMR Spectroscopy will take place at the University College of Swansea, Wales from Monday 5 July to Friday 9 July, with participants foregathering on the afternoon and evening of Sunday 4 July 1993.

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

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

1969	Birmingham	1983	Edinburgh
1972	Guildford	1985	Cambridge
1975	St Andrews	1987	Canterbury
1978	York	1989	Warwick
1981	Exeter	1991	St Andrews

Scientific Programme

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

1 **Experimental Techniques**
Chairman: J C Lindon
Invited Lecturers: S W Homans, J Homer, J Skilling

2 **Solid-state NMR**
Chairman: R K Harris
Invited Lecturers: B Blümich, H J Jakobsen, A C Olivieri, F Taulelle

3 **NMR Imaging**
Chairman: P Morris
Invited Lecturers: T J Brady, P Mansfield, R Turner

4 **Biological NMR**
Chairman: J Griffiths
Invited Lecturers: R S Balaban, J Frahm, R J Maxwell

5 **Structure and Dynamics – Organic**
Chairman: D Neuhaus
Invited Lecturers: P E Hansen; G Morris

6 **Structure and Dynamics – Inorganic**
Chairman: M Schröder
Invited Lecturers: B T Heaton, A E Merbach

7 **Structure and Dynamics – Physical**
Chairman: T Cosgrove
Invited Lecturers: F D Blum, P Stilbs

8 **Structure and Dynamics – Biological Macromolecules**
Chairman: D L Turner
Invited Lecturers: R J P Williams, K Wüthrich

POSTER SESSIONS AND CONTRIBUTED PAPERS

Poster presentations form a vital and significant component of the meeting. Contributions were called for in Circular 1 (closing date for submission of Abstracts being 22 January 1993), and more than 160 offers have already been accepted for inclusion in the programme. Abstracts already submitted in accordance with the prescribed format will constitute the meeting 'Book of Abstracts' which will be distributed to all participants at registration on arrival. Late contributions can still be considered for poster presentation, but it will not be possible to publish any late abstracts received after the closing date for registration **Monday 31 May 1993.**

Anyone interested in submitting a late offer of a poster should send a title and brief abstract, indicating the appropriate symposium topic, (according to the proforma described in the accompanying documentation) to Dr John F Gibson, Secretary (Scientific), The Royal Society of Chemistry, Burlington House, London W1V 0BN.

Two periods in the programme which have been set aside for formal viewing and discussion of posters, the first session on **Tuesday** has been scheduled to take place at **16.10 - 17.30** and the second poster session on **Thursday** at **16.10 - 17.30.** Odd numbered posters will be presented in Poster Session 1, whilst **even** numbered posters will be presented in Poster Session 2. Numbers will be notified to the presenters in due course. The first-named author is expected to present the poster unless the organisers are informed othersie by 31 May, the closing date for applications.

-continued -

REQUEST FOR FURTHER INFORMATION

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

Tel: 071 437 8656
Fax: 071 437 8883

Please send, when available, the Second Circular and Application Form for the **11th International Meeting** on **'Nuclear Magnetic Resonance Spectroscopy'** to be held at University College, Swansea from 4 to 9 July 1993 *(available in February/March 1993).*

PLEASE WRITE YOUR NAME AND ADDRESS CLEARLY ON THIS LABEL

NAME .....

ADDRESS .....

.....

.....

.....

If undelivered, please return to:
The Royal Society of Chemistry, Burlington House,
London W1V 0BN, UK

I should like to present a short paper:

POSTER presentation preferred ☐

ORAL presentation preferred ☐

I have no preference between oral and poster presentation ☐

ORAL presentation (by graduate students only) ☐

For Symposium .....

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

A highly recommended meeting, for both scientific and other purposes. There are are always excellent social functions and well-chosen excursions, very conveniently organized. Also a good "accompanying persons" program. Take stout walking shoes and gear for the slight (hah) chance of rain. British dorm accomodations will not make you feel pampered.

BLS

The 8th International Symposium on Molecular Recognition and Inclusion will be held in Ottawa, Ontario, Canada from July 31 to August 5, 1994. For further information please contact Mrs. Huguette Morin-Dumais, Steacie Institute for Molecular Sciences, National Research Council of Canada, 100 Sussex Drive, Ottawa, Ontario, Canada, K1A 0R6. Telephone: (613) 993-1212, FAX: (613) 954-5242, E-Mail: ISMRI@NED1.SIMS.NRC.CA.

Information

The 8th International Symposium on Molecular Recognition and Inclusion will focus on the rapidly advancing field of supramolecular chemistry including all aspects of molecular recognition and inclusion. As part of the main symposium, a special "Lock and Key" symposium will be held to commemorate the 100th anniversary of Emil Fischer's seminal paper in which the lock and key analogy was first proposed. The symposium will focus on molecular recognition and will include all chemical and biological aspects (structure, catalysis, complex formation biomimetic reactions, self assembly, sensors, drug design, new and modified hosts). Additional areas to be covered include: physical methods and computation (advances and applications to molecular recognition and guest-host chemistry) and the solid state (new inclusion hosts, microporous solids, clathrates, inclusion compounds, intercalates, chemistry in confined spaces, clusters). The program will consist of 35-40 plenary and invited lectures as well as contributed presentations in poster format. Abstracts of oral and poster presentations will be available to participants in booklet form.

International Advisory Committee

G.D. Andreetti	(Parma)	J.M. Lehn	(Strasbourg)
A. Cheetham	(Santa Barbara)	Y. Murakami	(Fukuoka)
J.L. Atwood	(Alabama)	D.D. MacNicol	(Glasgow)
J.E.D. Davies	(Lancaster)	H. Ogoshi	(Kyoto)
W.L. Duax	(Buffalo)	W. Saenger	(Berlin)
G.W. Gokel	(Miami)	J. Szejtli	(Budapest)
T. Iwamoto	(Tokyo)	F. Vogtle	(Bonn)
J. Lipkowski	(Warsaw)		

Organizing Committee

P. Arya	(Ottawa)	G. Gokel	(Miami)
T. Bein	(Purdue)	L. Johnston	(Ottawa)
G. Buchanan	(Ottawa)	H. Morin-Dumais	(Ottawa)
G. Burton	(Ottawa)	J. Ripmeester	(Ottawa) (Chair)
J. Daroszewski	(Ottawa)	C. Ratcliffe	(Ottawa)
C. Detellier	(Ottawa)	F. Vogtle	(Bonn)
G. Facey	(Ottawa)	M. White	(Halifax)
T. Fyles	(Victoria)	J. Wuest	(Montreal)

NUCLEAR MAGNETIC RESONANCE INSTRUMENTS

Recent Advances in NMR Technology

You are cordially invited to attend Varian's NMR Workshop featuring new NMR techniques and their applications to structure analysis.

Throughout the day, you will have opportunities to meet with Varian's NMR Application Chemists and fellow scientists to discuss how recent trends in NMR spectroscopy might help solve your own research problems . We hope you'll join us.

May 6, 1993

8:15 am - 4:30 pm

Howard Johnson Kenmore
575 Commonwealth Avenue
Boston, Massachusetts 02215

May 25, 1993

8:15 am - 4:30 pm

Varian Ginzton Research Center
3075 Hansen Way
Palo Alto, California 94304

R.S.V.P. Please make your reservation at least two days prior to the workshop date by calling Varian at 1-800-356-4437.

Breakfast & Informal Discussions

8:15 - 9:00 Continental breakfast provided

Morning Session:
Organic Chemistry and Natural Products

9:00 - 9:10 Welcome and Opening Remarks

9:10 - 10:00 Modern Techniques for Structure Elucidation
Speaker: Steve Cheatham

10:00 - 10:20 Break

10:20 - 11:10 Total Structure Elucidation by Proton-detected Carbon/Proton 2-D Chemical Shift Correlations
Speaker: Jim Shoolery

11:10 - 12:00 New Twists on Old Experiments: Pulsed Field Gradients, Waveform Generators, Nano Samples
Speaker: Paul Keifer

Lunch & Informal Discussions

12:00 - 1:30 Buffet lunch provided

Afternoon Session:
Biomolecular Studies

1:30 - 2:20 Working in Water: Experimental Strategies for Proteins and NucleicAcids
Speaker: Steve Smallcombe

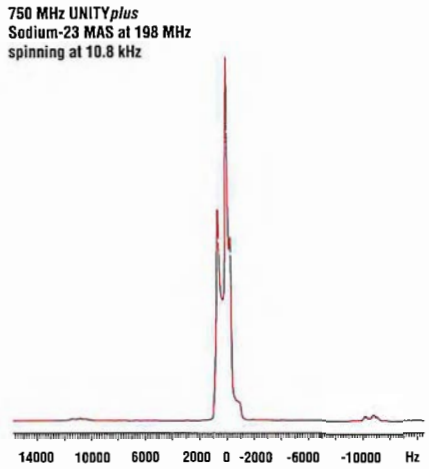
2:20 - 3:10 Experimental Strategies in Macromolecular Structure: N-Channel and N-Dimensional
Speaker: George Gray

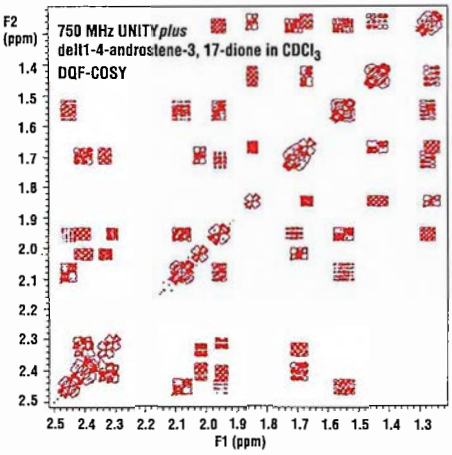
3:10 - 3:30 Break

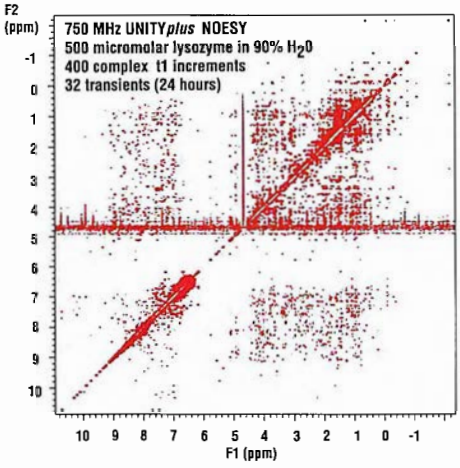
3:30 - 4:30 Software, Data Systems, and Data Processing in Modern NMR
Speaker: Steve Patt

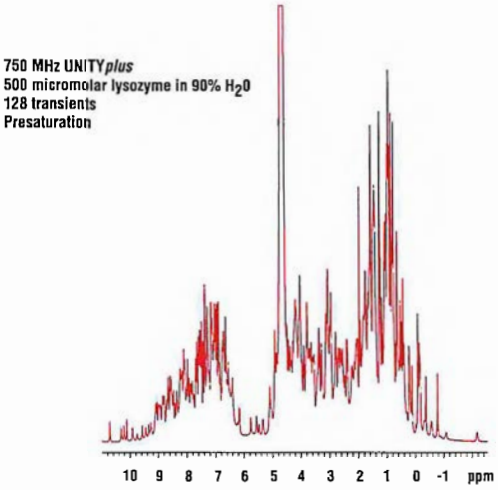
varian

Varian Delivers 750 MHz Results.









These spectra were obtained on a Varian 750 MHz UNITYplus™ NMR spectrometer.

Leadership in NMR Technology

Varian Associates, Inc. and Oxford Instruments have jointly developed the first 750 MHz NMR system.

Ideal for biomolecular and chemical applications, Varian UNITY*plus* NMR spectrometers perform the most demanding experiments at all field strengths. Oxford 750 MHz magnets provide the best long-term stability and do not require cryo-pumping. Uniquely designed as a single, no-compromise platform for liquids, solids, and microimaging at the widest range of field strengths, the UNITY*plus* offers the most advanced technology to the NMR community. Varian's exceptional probes, pulsed field gradients, and flexible software provide the ideal system for leading-edge NMR research.

For additional information, contact the Varian office nearest you.

Varian Associates 3120 Hansen Way, Bldg. 4, Palo Alto, CA 94304-1030, U.S.A. Tel: 1-800-356-4437 • **Varian International AG** Kollerstrasse 38, CH-6303, Zug, Switzerland Tel: (42) 44 88 44 • **Varian GmbH** Alsfelderstrasse 6, D-6100 Darmstadt, Germany Tel: (0 61 51) 70 30 • **Varian Instruments Ltd.** 3rd Matsuda Bldg., 2-2-6 Ohkubo-Shinjuku, Tokyo, Japan Tel: (3) 3204-1211

varian

Varian's 750 MHz Spectrometers Provide Results

Advantages

- Highest chemical shift dispersion and sensitivity in a persistent, non-pumped magnet
- Outstanding performance and stability is delivered by the UNITY*plus* NMR system
- Greatest flexibility is provided by VNMR software

Applications

- Structure determination of biomolecules
- Detection of minute sample quantities
- MAS studies of quadrupolar nuclei
- Methods development at high field strengths

Call your sales representative. Australia (3) 543 8022. Austria (1) 69 55 450. Belgium (2) 721 4850. Brazil (11) 829 5444. Canada (416) 457 4130. Denmark (42) 84 6166. France (1) 69 86 38 38. Germany (6151) 70 30. Italy (2) 753 1651. Japan (3) 3204 2111. Korea (2) 561 1626. Mexico (5) 533 5985. Netherlands (3403) 50909. Norway (9) 86 74 70. Spain (01) 430 0414. Sweden (8) 82 00 30. Switzerland (42) 44 88 44. UK (932) 24 37 41. US 800-356-4437. Other International (415)424-5424.

MAG-6055/569

varian

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

March 6, 1993 (received 3/15/93)

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

Dear Dr. Shapiro:

RE: A Pulsed Field Gradient Interface for Varian VXR Systems

The research people here at A.E. Staley are interested in diffusion in food systems. So we bought a 10mm double-tuned z-gradient probe and Techron amplifier from Doty Scientific Co. for our Varian VXR 4000.

This left us with the problem of controlling the Techron with the VXR's acquisition computer. Fortunately Varian supplies four digital lines, which can be controlled by Pascal programs. George Emtzinger of Doty Scientific graciously drew a circuit for us, that used the control lines to address a series of voltage supplies with an analog multiplexer. We expanded on his idea to build the interface diagrammed below.

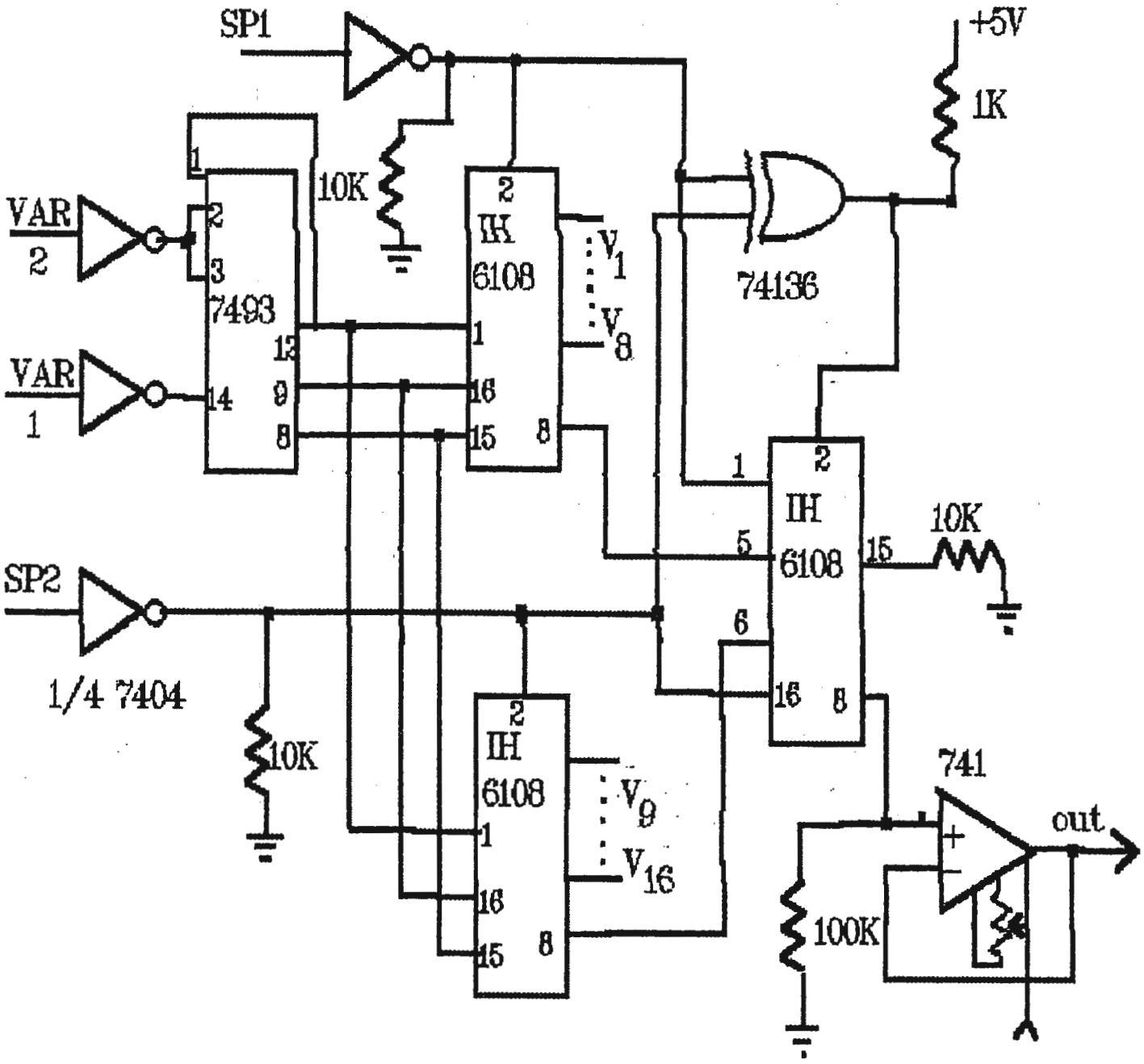
SP1 enables the positive gradient, SP2 the negative gradient. Note the inverters (7404). The PFG strength can be set to one of eight different positive values or negative values and zero. This is done by pulsing VAR1 a set number of times. The interface counts the pulses (7493) and addresses the two multiplexers(IH6108), which select two of the voltage inputs, V1 to V8 (LM317's) and V9 to V16 (LM337's). VAR2 resets the counter. The third multiplexer chooses the + or - output, gates the PFG voltage via the exclusive OR and then sends the output to the operational amplifier (741). The system has been working well for us and doesn't seem to have any bugs. We can add pre-emphasis circuitry later if we wish.

We also would like to thank two Varian people, Raymond Attwell and Philip Hornung for their help in this project.

Gary P. Juneau Paul E. Carter

Attachment

GJ:sd
h:\tarnu


SP1
+5V
1K
10K
VAR
2
7493
VAR
1
74136
IH
6108
V_1
V_8
SP2
1/4 7404
10K
IH
6108
10K
IH
6108
V_9
V_{16}
741
out
100K

Washington
WASHINGTON·UNIVERSITY·IN·ST·LOUIS

Department of Physics

415-13
Washington University
Campus Box 1105
One Brookings Drive
St. Louis, Missouri 63130-4899
(314) 935-6276
FAX (314) 935-6219

February 25, 1993
(received 3/1/93)

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

Guest Dynamics of (Thiourea)$_3CCl_4$ and (Thiourea)$_3CCl_3Br$ Inclusion Complexes

Dear Dr. Shapiro,

We have been studying the dynamics of CCl_4 and CCl_3Br molecules in thiourea host lattices at temperatures below 30 K. Our aim is to understand what role guest-guest and guest-host interactions play in the order/disorder phase transitions observed at higher temperatures in these systems.[1]

T_1 measurements of the ^{35}Cl nuclear quadrupole resonances in (thiourea)$_3CCl_4$ indicate that CCl_4 molecular reorientation is the dominant relaxation mechanism (Alexander-Tzalmona strong collision limit) for temperatures above 18 K, with an observed activation energy of only 3.7 kJmol^{-1} (~440 K). Thus, the CCl_4 guest molecules still have considerable motional freedom in the ordered state, particularly when compared to other guests in thiourea inclusion complexes[2].

We also find that the ratio of intensities of the two NQR lines is 1:1. This ratio indicates that in the ordered phase the CCl_4 molecule (T_d symmetry) sits in the thiourea adducts ("tubes" of D_3 symmetry) such that one of the molecular two-fold axes coincides with one of the adduct two-fold axes. X-ray diffraction studies[3] have revealed that in the disordered phase, the molecule spends equal time oriented along each of the three two-fold axes of the adduct. We believe that in the ordered structure, the molecule is restricted to one of these orientations. This is consistent with our NQR measurements and the R ln 2.8 value of the transition entropy obtained by Matsuo's group at Osaka.

NQR frequency-swept spin echo measurements of the (thiourea)$_3CCl_3Br$ inclusion complex reveal two broad resonances, with a 1:2 ratio of intensities. The ~300 kHz separation of the lines is the

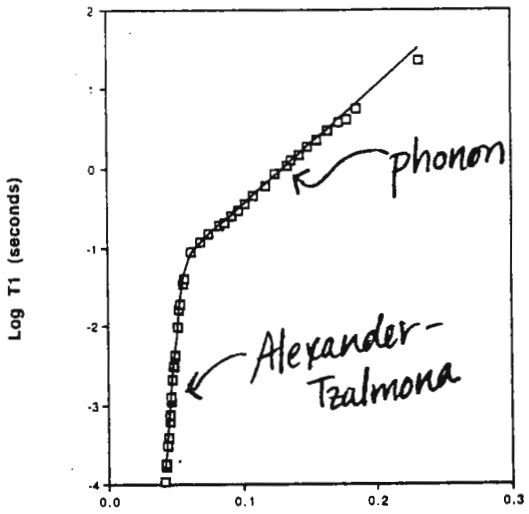
same as that observed in the CCl_4 compound. These results suggest that the ordered structure of the CCl_3Br complex is the same structure that we propose for the CCl_4 complex. The width of the lines (5 times broader than in the CCl_4 complex) suggests that the Br atoms are site disordered. Indeed, Matsuo's group has observed a glass transition at ~18 K, which they believe is the result of the freezing-out of the reorientations of the Br-C bond. We hope to learn more about the dynamics of the glassy phase of this complex from T_1 measurements which are now in progress.

Sincerely,

Natalie Adolphi & Mark Conradi
Dept. of Physics, Washington U.

Takasuke Matsuo
Dept. of Chemistry, Osaka University

1. M. Sekii, T. Matsuo and H. Suga, *J. Inclusion Phenom.* **9**, 243 (1990).
2. L. Pang and E. A. C. Lucken, *J. Inclusion Phenom.* **5**, 245 (1987).
3. J. F. Fait, A. Fitzgerald, C. N. Caughlan and F. P. McCandless, *Acta Cryst.* C**47**, 332 (1991).



^{35}Cl NQR T_1 as a function of temperature for the higher frequency line in (thiourea)$_3CCl_4$. The open squares are measured values. The solid line is an empirical fit: $T_1 = (T_{1phonon}^{-1} + T_{1alex\text{-}tzal}^{-1})^{-1}$. $T_{1phonon}^{-1} = (9.58 \times 10^{1})\, e^{-34.6/T}$ and $T_{1alex\text{-}tzal}^{-1} = (7.12 \times 10^{11})\, e^{-440/T}$. (A power law fit to the phonon-dominated regime gives an exponent of -4.5.)

CMX Multi-Channel Applications

The unique channel modularity design of the Chemagnetics™ CMX spectrometer gives you the NMR flexibility you need for solids, liquids and microimaging. The CMX offers the range of capabilities required for today's wide variety of experiments by supporting multiple channels. And the CMX design allows new channels to be added easily and affordably. All this adds up to a "no-compromise" approach to experimental capability.

Chemagnetics utilizes the latest technology to put multi-channel flexibility in the hands of the spectroscopist. Dual 16 bit, 1 MHz digitizers offer maximum dynamic range over the widest bandwidths. And each RF channel in the CMX is equipped with its own pulse programmer, so experiments are never limited by pulse programmer capacity.

The CMX is designed to start small *and* grow, providing the whole spectrum of NMR capabilities as they evolve, when you need them. Multi-channel capability with the CMX - flexibility for tomorrow, available today from Chemagnetics.

One Channel

Solids	Liquids
▪ MAS	▪ NOESY
▪ DOR	▪ TOCSY
▪ Wideline	▪ COSY
▪ CRAMPS	▪ Proton/Fluorine

Two Channels

Imaging	Solids	Liquids	Liquids+Imaging
	▪ Rotational Resonance ▪ CP/MAS ▪ HETCOR	▪ HCCH-TOCSY ▪ Reverse Detection ▪ HETCOR ▪ X-Decoupled	▪ ^{1}H, ^{19}F, Gradient Field Spectroscopy

Three Channels

Solids	Liquids	Liquids+Imaging
▪ REDOR	▪ Triple Resonance ▪ ^{1}H, ^{13}C, ^{15}N, HMQC-TOCSY	▪ H/X Gradient Field Spectroscopy

Four Channels

Liquids	Liquids+Imaging
▪ Advanced 4-channel Solution State	▪ Multi-Channel Gradient Field Spectroscopy

Corporate Headquarters
Chemagnetics, Inc.
2555 Midpoint Drive
Fort Collins, Colorado 80525
303–484–0428
1–800–4 OTSUKA
Fax 303–484–0487

Europe - U.K.
Otsuka Electronics Europe, Ltd.
Claro Court Business Centre
Claro Road
Harrogate, HGI 4BA
United Kingdom
Phone 0423 531 645
Fax 0423 531 647

Europe - France
Otsuka Electronics Europe, SARL
"Le Copernic"
Park d'Innovation
67400 Strasbourg–Illkirch, France
Phone 088 66 82 00
Fax 088 66 82 04

Japan
Otsuka Electronics Co., Ltd.
2F Hashikan-LK Building
1–6, Azuma-Cho
Hachioji, Tokyo 192
Japan
Phone 0426–44–4951
Fax 0426–44–4961

Chemagnetics

Dedicated to Design Excellence

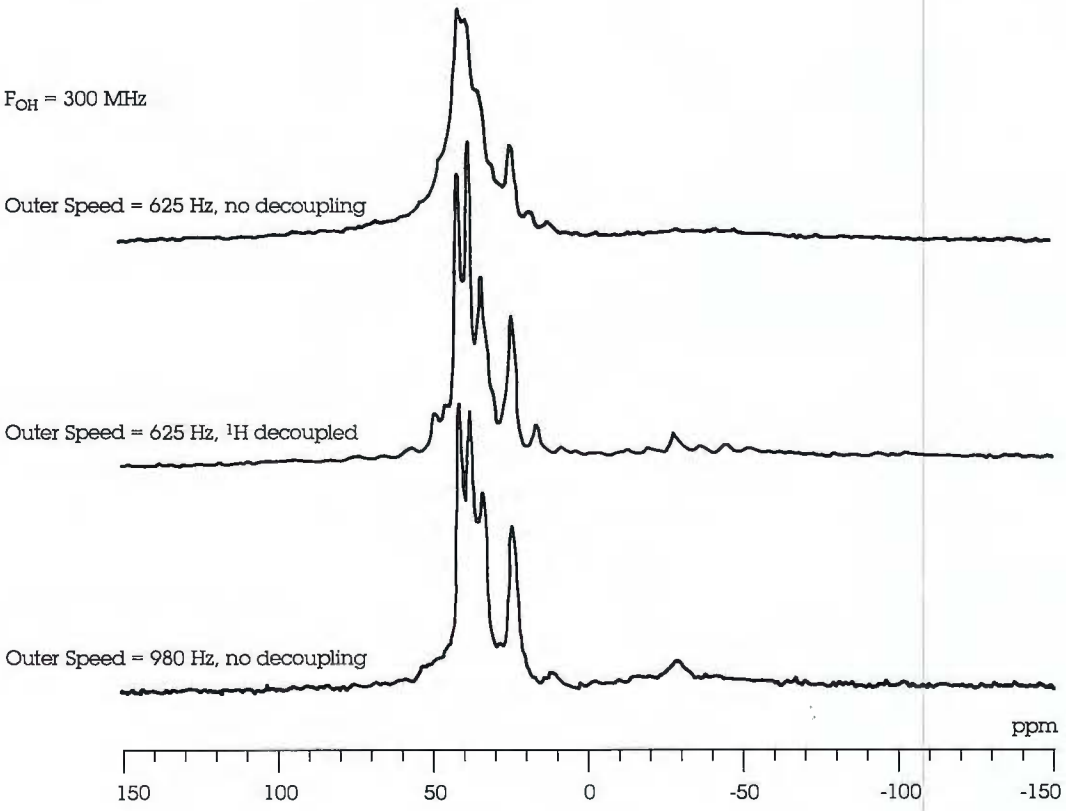
Leading the Way in Double Rotation

Double Resonance DOR from Chemagnetics

Double rotation has revolutionized the study of quadrupolar nuclei by providing structural information previously hidden by 2nd order quadrupolar broadening. When applied with proton decoupling, broadening from proton dipolar coupling is eliminated, and resolution is greatly improved. Cross polarization also enhances the signal from strongly coupled octahedral hydrated sites compared with weakly coupled tetrahedral sites.

These spectra of AlPO-11 below illustrate these effects. The top spectrum shows single resonance DOR at 625 Hz spinning. The bottom trace shows significant improvement at 980 Hz; note especially the appearance of the octahedral peak at 30 ppm. The middle trace shows 625 Hz DOR with proton decoupling; the peaks are narrower than at 980 Hz, especially the octahedral signal.

The Double Resonance DOR probe from Chemagnetics™ is available today to help you achieve the best possible resolution of chemical shifts. Call now for our latest application note on this exciting new technique.



Chemagnetics

ARGONNE NATIONAL LABORATORY

9700 South Cass Avenue, Argonne, Illinois 60439

ANL BITNET: BOTTO@ANLCHM
TELEX: 9102583285
PHONE: (708) 252-3524
FAX: (708) 252-9288

February 24, 1993
(received 3/1/93)

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

RE: **NMR Studies of Solid Organic Residues on Prehistoric Pottery**

Dear Barry:

Over the past two years, we have been collaborating on a project that involves the identification of charred crusts and other remaining organic residues on pottery from the Late Iron Age (200 BC-50 BC) in the Netherlands. Interrelationships established through paleo-environmental research have given archaeologists some insight into potential natural sources for food gathering, but they cannot always show proof of actual use of these sources. Identification of food stuffs and information about preparation and conservation would open a new chapter in the archaeology of diet and food gathering.

Archaeological studies concerning the function of pottery for storage, cooking, or as a status object are often based on variations in shape, decoration and production technology of the vessels. Chemical analyses of the organic (food) residues on pottery surfaces provide direct information on vessel use. Recent analytical pyrolysis studies[1] have revealed several groups of organic compounds in the residues: polynuclear aromatic species, free fatty acids, cholesterol and pyrolysis products indicative of proteins, polysaccharides and aliphatic lipid structures have been identified. SEM results support the hypothesis that organic residues represent the last use of the vessel.

The ^{13}C CP/MAS spectra of three representative organic residues isolated from individual pottery samples are shown in the Figure. The spectra show the characteristic fingerprints for carbohydrate char (top), a mixture of carbohydrate char and long-chain unsaturated fatty acids (middle) and proteinaceous residue (bottom). The NMR data are to be correlated with data obtained by pyrolysis- and GC-MS analyses in order to classify residues into several groups. Group classification of these residues in archaeological pottery will be used to facilitate assignment of the original use of vessel types in ancient societies.

Sincerely,

Robert E. Botto
Chemistry Division

Tania Oudemans
Institute for Prehistory Leiden
Leiden, The Netherlands

Jaap J. Boon
FOM Institute for Atomic
and Molecular Physics
Amsterdam, The Netherlands

Reference 1. Oudemans, T.F.M. and Boon, J.J. *J. Anal.App. Pyrol.* **1991**, *20*, 197-227.

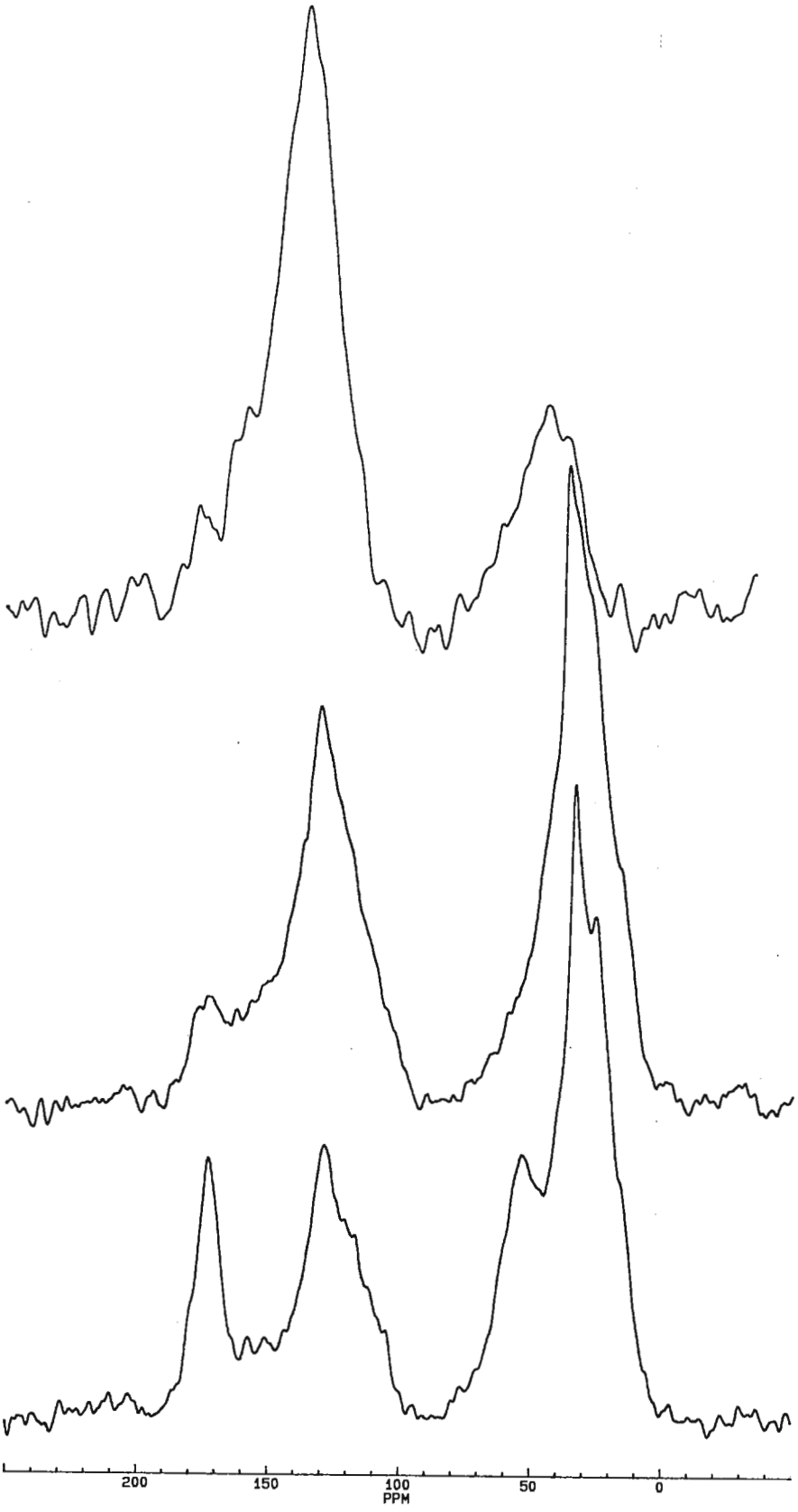


Figure 1. The 25-MHz ^{13}C CP/MAS spectra of Late Iron Age pottery residues from the Netherlands: contact time of 1.5 ms for CP; recycle delay of 1 s; 4.5 μs 90° pulse width (56 kHz proton decoupling field); spinning frequency ca. 4 kHz; sample size 40-100 mg.

LOUISIANA STATE UNIVERSITY
AND AGRICULTURAL AND MECHANICAL COLLEGE
Department of Chemistry

Dr. B.L. Shapiro, Editor
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94393

February 25, 1993
(received 3/1/93)

Hazardous Waste Solidification/Stabilization: Solid-State ^2H NMR Spectroscopy of Phenol in Portland Cement

Dear Dr. Shapiro:

A significant portion of modern industrial waste is disposed by solidification in cements and slags. To be successful, a solidification/stabilization procedure must entrain waste so as to prevent leaching, especially by ground water. Laboratory leaching studies probe the macroscopic characteristics of a solid. A complementary technique, deuterium NMR spectroscopy, that probes microscopic dynamics of the waste has been developed and is described herein for the system of phenol/portland cement. This is the first use of deuterium NMR spectroscopy to study waste solidification/stabilization. The main feature of deuterium NMR spectroscopy is the ability to monitor molecular reorientations over a wide range of reorientation rates. This technique allows one to determine if a particular deuterated organic waste is effectively solidified/stabilized and to determine the lower limit of the bond strength between the waste and the cement matrix.

The deuterium NMR results of d_5-phenol/cement (10% d_5-phenol by weight) shows that there are at least two major components present in the cement matrix: one component has a line shape characteristic of phenol bound through oxygen and undergoing rapid 180° flip motion whereas the other component has a narrow resonance corresponding to liquid-like phenol. Figure 1a shows a spectrum dominated by a single resonance due to d_5-phenol with liquid-like mobility; there are shoulders at ±65 kHz due to a phenol component having less mobility, that is, tethered phenoxide restricted to fast two-site 180° jump motion. The relative abundance of each fraction is determined by fitting the ^2H line shape to a model consisting of a narrow Gaussian resonance plus a lineshape calculated for fast two-site 180° jump motion (Figure 2). Results of the model calculations for various cure times are as follows:

10% phenol/cement cured in 5mm NMR tube @	1 month	56 (2)% liquid-like phenol
	1 year	45 (2)%
	15 month	20 (2)%
10% crushed at 2 month, oven treated at 2 month, 36 hr, 90°C @	2 month	5 (2)%

The fraction of phenol with liquid mobility is correlated with the amount of pore water in the cement. Pore waters decrease with cure time, and can be reduced by crushing the sample followed by oven drying; the ^2H NMR results for the dried sample are shown in Figure 1b.

In summary, phenol does react, as desired with cement via acid-base chemistry but is not successful in immobilizing phenol. NMR is shown to be an effective method for nondestructive monitoring of waste microscopic mobility in cements with significant advantages over EPA-mandated leaching studies, since quantitative measurements of tethered and free waste can be made. A full paper on this work has been accepted for publication in Environmental Science and Technology.

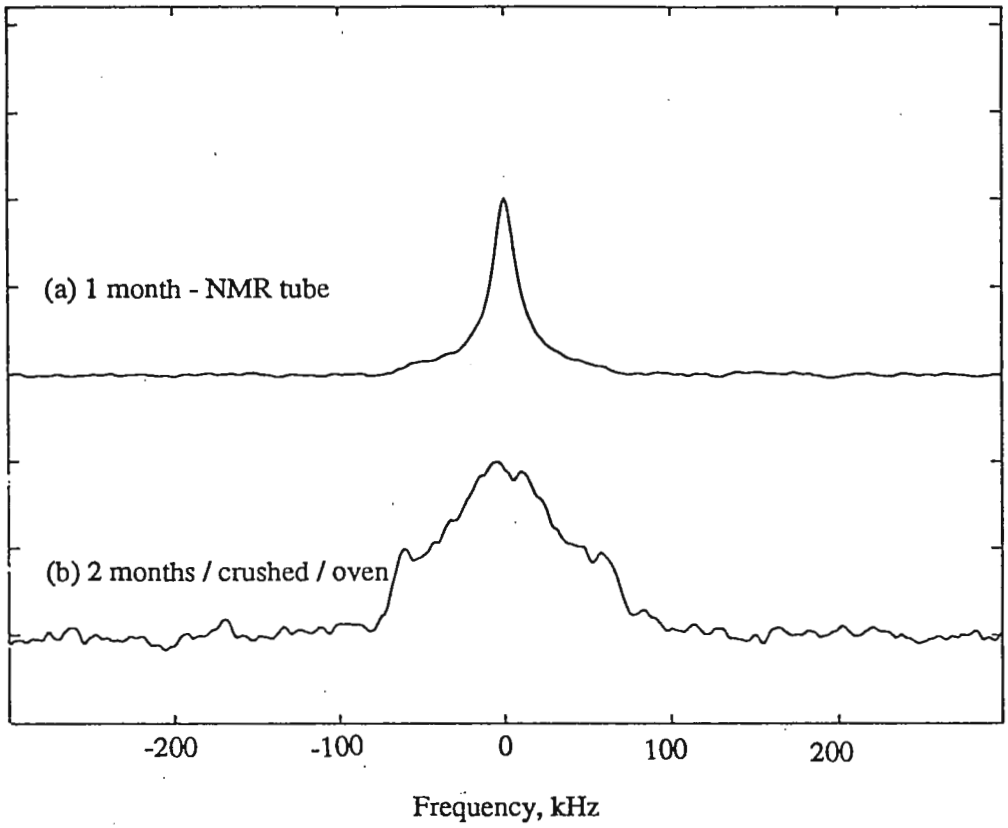
Sincerely,

Michael A. Jansa
Michael A. Jansa

Les Butler
Les Butler

Baton Rouge • Louisiana • 70803-1804 • 504/388-3361 • FAX 504/388-3458

Figure 1. Deuterium NMR of 10% phenol (by weight) in portland cement at 1 month and 2 months of cure.



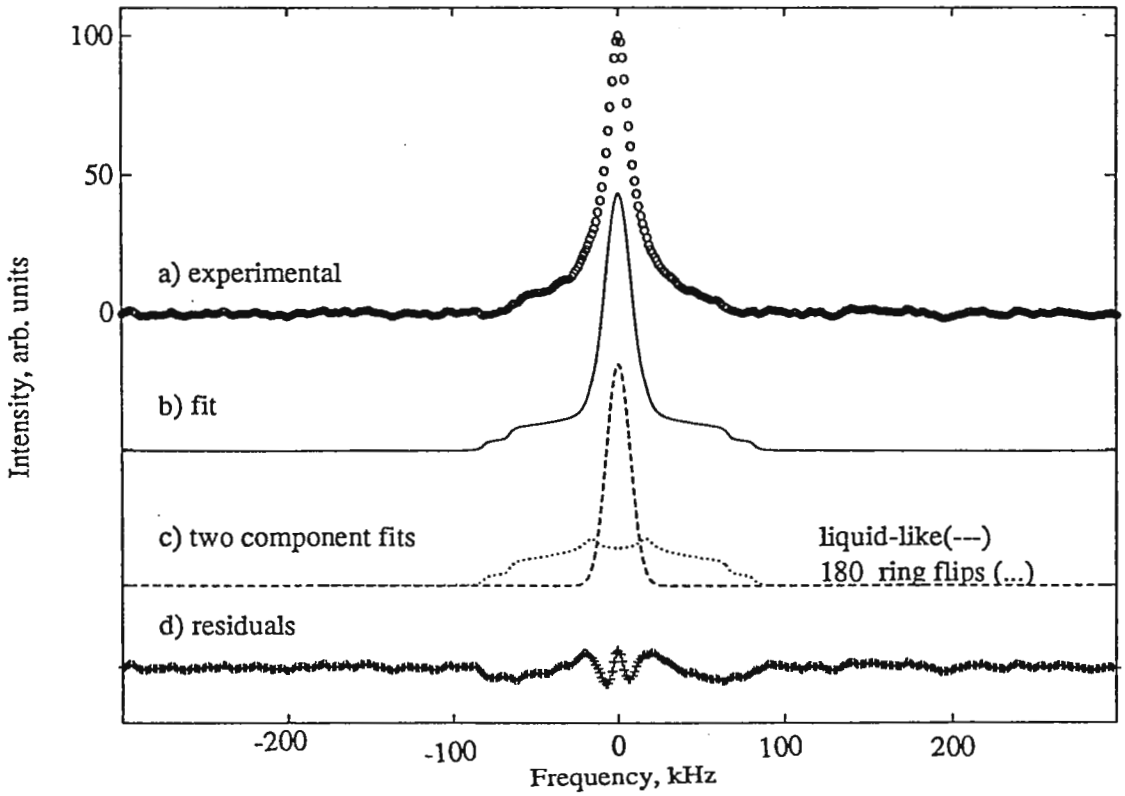


Figure 2. Deconvolution of ^{2}H NMR spectrum into two components, liquid-like and tethered through the oxygen.

SuperSonic MAS

Introducing our newest SuperSonic Spinners!

5-mm SuperSonic CP/MAS

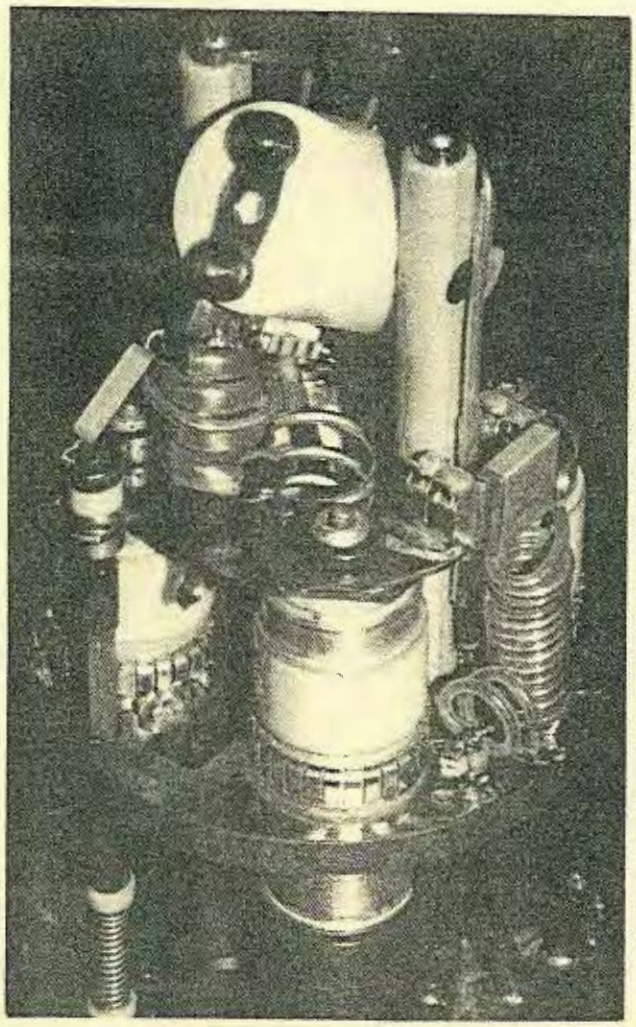
Spinning speed – 18 kHz
Sample volume – 70 µl to 110 µl

7-mm SuperSonic CP/MAS

Spinning speed – 13 kHz
Sample volume – 250 µl to 370 µl

Doty Scientific, Inc.
700 Clemson Road
Columbia, SC 29223
USA

Phone: (803) 788-6497
Fax: (803) 736-5495



Doty 5-mm SuperSonic CP/MAS Triple-tuned REDOR Probe

3.5-mm SuperSonic CP/MAS

Spinning speed – 26 kHz
Sample volume – 20 µl to 30 µl

The 3.5-mm SuperSonic spinner is available for probes 30.5 mm in diameter and larger. Applications include ^{1}H, ^{19}F and quadrupolar nuclei.

10-mm SuperSonic CP/MAS

Spinning speed – 10 kHz
Sample volume – .8 ml to 1 ml

The 10-mm SuperSonic spinner is available for supercon probes 44 mm in diameter and larger. **Also, the 10-mm can accommodate 7-mm glass ampules.**

14-mm SuperSonic

Spinning speed – 6.5 kHz
Sample volume – 2.2 ml to 2.8 ml

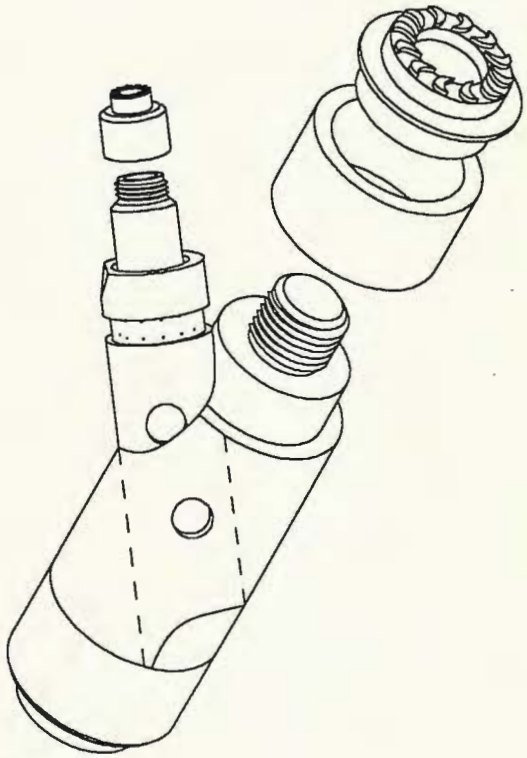
The 14-mm spinner can only be provided in wide bore probes over 70 mm. Applications include low-level constituents, such as natural abundance ^{15}N in polymers and quantitative MAS without CP.

Doty Scientific makes DOR *routine!*

High Resolution NMR of Quadrupolar Nuclei in Solids

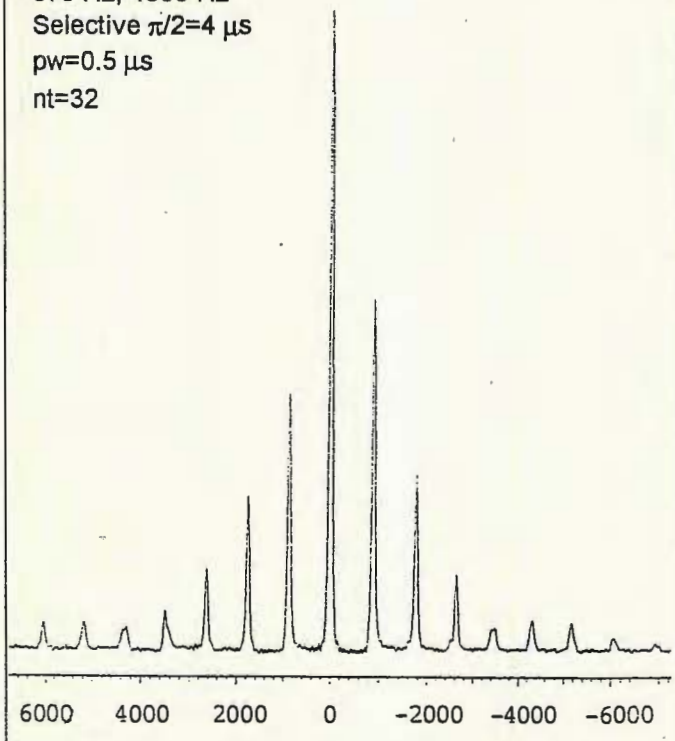
Double Rotation (DOR)

Parameter	Prior Art	Doty
Outer rotor max rate	1100 Hz	**1200 Hz**
Inner rotor max rate	6000 Hz	**7000 Hz**
Sample volume	50 µl	**100 µl**
Packing/balancing	hours	**5 minutes**
Typical rotor lifetime	hours	**2 years**
Materials	Vespel	**ZrO_2, Si_3N_4**
Dual spin rate detection	No	**Yes**
Acoustic noise	deafening	**quiet**
VT range		**-140 to +180°C**



Na_2SO_4 DOR Spectra without side-band suppression

870 Hz, 4500 Hz
Selective $\pi/2$=4 µs
pw=0.5 µs
nt=32



Spectra provided by Dr. Laima Baltusis and Varian Applications Lab, Palo Alto, California

Typical multi-X performance

Field (T)	Nuc.	Freq. (MHz)	Ring-down*	Power (W)	$\pi/2$ (µs)
4.7	^{1}H	200	5 µs	200	4
4.7	^{27}Al	52	20 µs	250	4
4.7	^{17}O	27	30 µs	700	4
9.4	^{27}Al	104	15 µs	250	4.5
9.4	^{17}O	54	20 µs	600	4.5

* Ringdown (20τ) when matched to typical preamp.
" $\pi/2$ " means maximum signal for $\frac{1}{2},-\frac{1}{2}$ transition.

Doty Scientific, Inc.
700 Clemson Road
Columbia, SC 29223 USA

Phone: (803) 788-6497 Fax: (803) 736-5495

Francis Bitter
National Magnet Laboratory
Massachusetts Institute of Technology
Building NW14-5119
Cambridge, Massachusetts 02139
Telephone 617-253- 0484
E-mail: fishbein@ccnmr.mit.edu

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

March 8, 1993
(received 3/10/93)

Dear Dr. Shapiro,

PLOTTING NMR SPECTRA ON THE MACINTOSH

Recent contributions to the Newsletter have presented several techniques for exporting graphical output in the form of HPGL or PostScript code from NMR processing software to the Macintosh for annotation. While touching up transferred HPGL code has the advantage that the time-consuming rendering of 2D plots is done on a workstation with more memory and a faster CPU than the Macintosh, the user is often forced to undo much of the plot formatting done by the NMR processing program. This process is further hampered by the difficulty in constructing macro scripts for common reformatting operations on the Mac.

As an alternative, we have found it practical to simply replot the original data on the Macintosh using Igor, a data analysis and plotting application from WaveMetrics, and the Spyglass family of 3D visualization programs. Starting with data from RNMR, our in-house NMR processing program, we can generate high quality plots with complete control over features such as fonts, axis labels, and other annotation.

Data may be read into the various Macintosh plotting programs in either binary integer or IEEE floating point format. Since neither of these formats is directly supported by our NMR acquisition and processing software, we have written a translation program, IMPORT, which converts VAX NMRi and FTNMR format files into IEEE or binary integer files. NMR processing programs which export data to either or both of these formats will not require IMPORT. Similarly, it should be possible to read data from NMRi and FELIX files created on a RISC-based computer without conversion since these machines use the same floating point representation as the Macintosh. Note that to read such files directly into a Macintosh application, one must be able to separate the real and imaginary parts of the data and to skip any header or trailer bytes. Most Macintosh plotting programs can skip a given number of header bytes but most applications require that the real and imaginary parts not be interleaved. Thus, external data conversion will sometimes be required to export data from RISC workstations.

We write converted integer or IEEE data to disk on one of our VAX/VMS workstations running the DEC PATHWORKS for Macintosh file server software, VAXshare. Similar workstation-based AppleShare file servers include XINET for HP and Sun Unix systems and PacerShare for DEC ULTRIX computers. Alternatively, one may mount a Unix file system on the Macintosh using client software such as NFS/Share. On the Macintosh, the user accesses the spectra by logging onto AppleShare in the usual way and simply reading the data via the "Open" dialog in the Mac application. The data is never copied from workstation to Macintosh, so the Macintosh need not have large disk storage capacity. However, it is advantageous for the Macintosh to have as much memory as possible, since most applications will attempt to load the entire NMR data set into RAM. While System 7 users may make use of virtual memory for plotting larger spectra, this may entail an unacceptable decrease in performance.

For plotting individual 1D spectra or stack plots of 1D spectra, we use WaveMetrics' Igor, which offers a built-in macro language for automating data importation and plotting. Stackplot, a macro we have written in Igor, takes the user through the entire process of reading the data, creating scales, and adjusting the stack offsets via dialog boxes. Once the plot is rendered, the user may modify any aspect of the graph itself, axes, labels, and so forth, as well as

add annotation with full support of technical symbols and subscripts and superscripts. Unlike most other 1D graphics applications, Igor does not impose an explicit limit on the size of the spectra and allows the frequency axis to be reversed as per NMR convention. Another useful feature is the built-in page layout window which permits multiple stack plots to be combined with text and graphics from other applications to create complete figures. The creation of composite layouts may also be automated by writing scripts or modifying display recreation macros generated internally by Igor from the user's commands. An external operation (XOP) supplied with Igor also allows 2D data to be contour plotted once the data has been packed into a 1D vector. Once generated, Igor contour plots may be customized and combined into figures in the same way as the 1D plots. Finally, Igor prints spectra at very high resolution, so complex features are not lost.

We use Spyglass Transform to render 2D spectra as contour, density, or surface plots on the Macintosh. Contours may be set at regular intervals as well as at any desired intensity. A user-definable color map may be used to distinguish the contours. While the Macintosh must have sufficient memory to load the entire 2D data set (4 bytes per point), a minimal amount of additional RAM is needed for rendering, so reasonably large data sets may be plotted in this way. For example, a Macintosh equipped with 16MB of physical memory and running System 7.0.1 can generate contour plots of 1024 X 2048 point 2D data sets. Transform generates both isometric and perspective surface plots which may be rotated arbitrarily in space interactively. Axes and annotation may be added to surface plots in Transform and to contour plots in Spyglass Format, a companion program. In addition, any plot may be exported to a CAD or page layout program as a PICT file for further manipulation. Transform allows the user to automate plot generation by defining templates, which store the current plot parameters.

Spyglass Dicer generates color/grayscale density plots of 3D spectra as pixels in a cube. One may not only display the 3D peaks in space but also plot 2D slices along any two axes. Because only one byte of RAM is required per data point and since Dicer reads the data into memory only as it is needed for rendering, 3D NMR spectra may be plotted in Dicer with a modest investment in RAM (12-16 MB). If the entire data set is too large to render, subsets of the data may be plotted individually without creating new data files. As in Transform, the user may define templates to store a particular plot style. The latest version of Dicer (2.0) can take 2D slices obliquely through the data cube and add axis labels and annotation. Again, plots may be exported to other Macintosh applications via PICT and HDF for assembling complex figures.

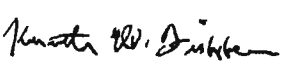
Finally, we would like to emphasize that NMR spectra plotting on the Macintosh is not a particularly slow process. For example, Dicer can render a 128 X 256 X 256 point subset of a 3D NMR spectrum in about ten minutes on a Quadra 950 with 16MB of RAM, and this time may be reduced to two minutes if the data set can be copied to a local disk before loading. Thus, replotting NMR data on the Macintosh is not prohibitive in time, disk space, or memory and allows the user to prepare figures of superior quality than through retouching HPGL or PostScript code.

Products Mentioned

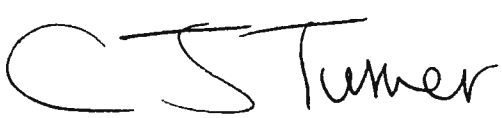
Igor 1.26, $295 WaveMetrics P.O. Box 2088 Lake Oswego, OR (503) 620-3001
Spyglass Transform 2.1, $595 list ($349 edu.), **Spyglass Format 1.1**, $235 list ($149 edu.)
Spyglass Dicer 2.0, $695 list ($399 edu.), Spyglass, Inc. P.O. Box 6388 Champaign, IL 61826 (217) 355-6000
PATHWORKS for Macintosh, Digital Equipment Corporation, 1-800-344-4825
PacerShare for ULTRIX, Pacer Software
XINET, 2560 Ninth St. Suite 312, Berkeley, CA 94710 (505) 344-0279
NFS/Share, $295, Intercon Systems Corporation, (703) 709-9890

Sincerely,

K.W. Fishbein



Christopher J. Turner



The Wellcome Foundation Ltd

The Wellcome Research Laboratories
Langley Court, South Eden Park Road,
Beckenham, Kent BR3 3BS

Wellcome

telegrams and cables
WELLAB BECKENHAM
telex WELLAB 23937 G
fax 081-650 9862
telephone 081-658 2211

DEPARTMENT FAX NO: 081-663 3788

PS/BMNC/93/10

17 February, 1993
(received 2/25/93)

Dr. B.L. Shapiro
TAMUNMR Newsletter
966 Elsinore Court
Palo Alto, California 94303

750MHz ^{1}H NMR Spectra of Biofluids

Dear Barry,

As the trend to higher and higher magnetic fields continues, it becomes necessary to ask what is the gain in information content in the NMR spectra. In the past this has been most noticeable in the improved capability to obtain three dimensional structures of small proteins, but it should not be overlooked that there are potential significant gains for small molecule studies, for instance in complex mixture situations. As part of a collaboration between Wellcome, Birkbeck College of the University of London and Bruker, we have been engaged in a comprehensive project involving body fluids both from humans with a variety of clinical conditions and from related animal studies and we have now made some exploratory measurements at a proton frequency of 750MHz where improvements are immediately visible when the results are compared with 600MHz spectra.

^{1}H NMR spectroscopy of human biofluids such as urine and blood plasma has much potential for clinical diagnosis. The importance of the increased dispersion available at the highest field strength lies in (1) the ability to see differences in the spectra which can be used as input to computer pattern recognition routines for classifying the samples - higher dispersion gives greater differences in the NMR descriptors of the samples and hence could lead to a lower chance of misdiagnosis, (2) the ease of comprehensive endogenous metabolite assignments leading to a better understanding of the biochemical condition and hence a more logical therapeutic intervention and (3) measurements at different frequencies monitor different time scales of dynamic processes such as metal, drug or macromolecule binding.

The resolving power of 750MHz ^{1}H NMR is illustrated in the figure which shows expansions of the 750MHz spectrum of a human urine from a child with an inborn error of metabolism known as α-hydroxyglutaric aciduria. This results in a very abnormal metabolite pattern in the urine and requires the best possible dispersion in order to make unambiguous resonance assignments. We have also studied 750MHz spectra of urine from people treated with standard drugs in order to probe drug metabolism and from individuals with other inborn errors of metabolism and are investigating the diagnostic potential of NMR for such studies. We have also studied blood plasma from people suffering from uraemia caused by chronic renal failure where, surprisingly, many of the toxins that accumulate in the blood still remain uncharacterised. Detailed analysis of spectra from control and uraemic patients are under way in an attempt to throw light on this problem. 750MHz ^{1}H NMR, including 2-dimensional techniques such as J-resolved spectroscopy, promises to offer significant improvement in information content over lower frequencies in all of these areas.

John

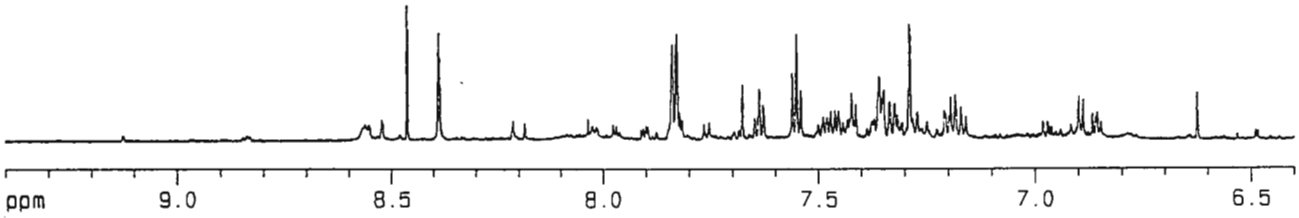
John C. Lindon
Wellcome

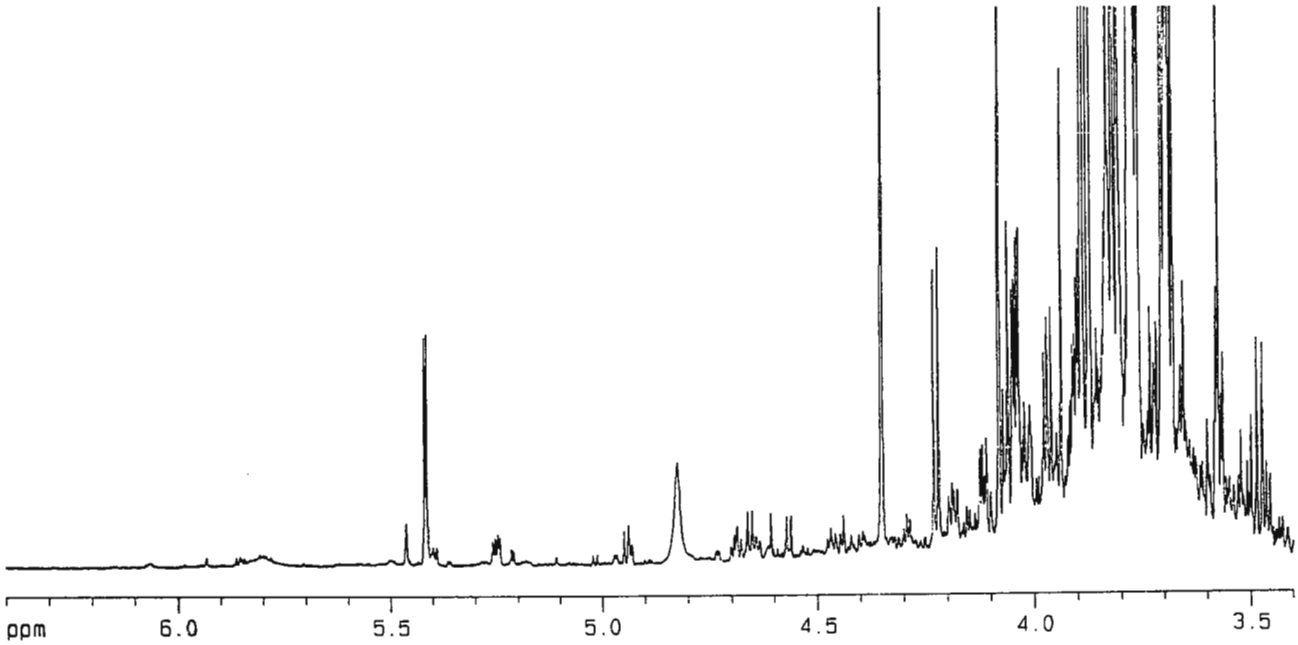
Jeremy

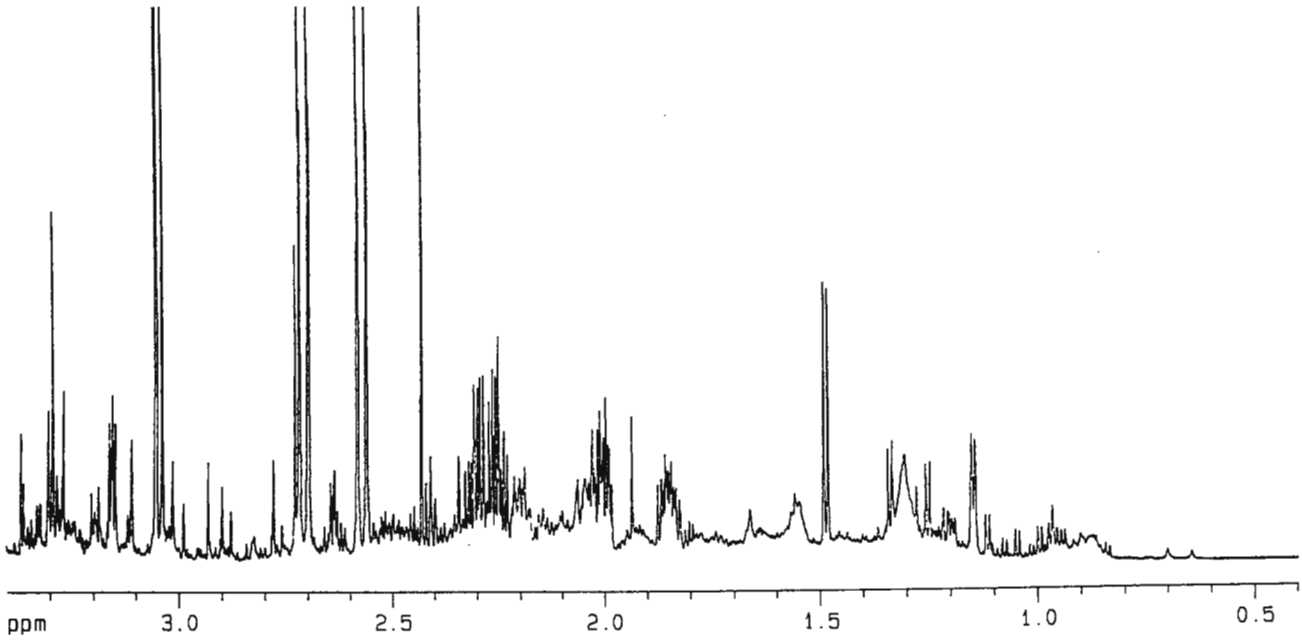
pp. Jeremy Nicholson
Birkbeck

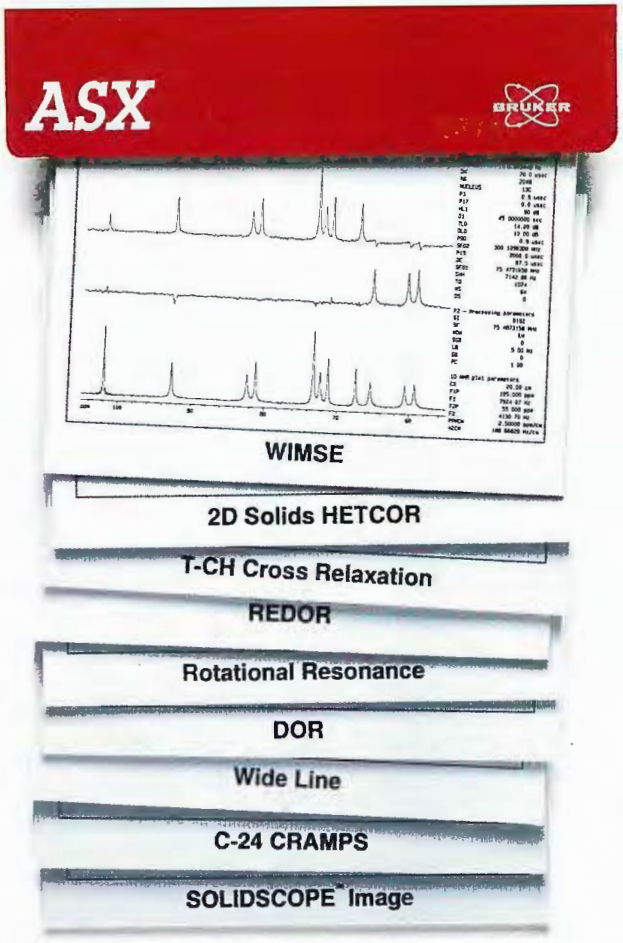
Manfred

pp. Manfred Spraul
Bruker

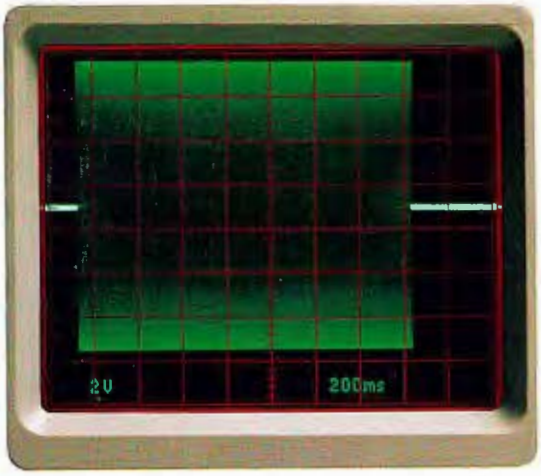

ppm
9.0
8.5
8.0
7.5
7.0
6.5


ppm
6.0
5.5
5.0
4.5
4.0
3.5


ppm
3.0
2.5
2.0
1.5
1.0
0.5



1.5 second burst of ASX rf output, power greater than 400W, with virtually no amplitude droop



In Solids NMR, what you don't see makes all the difference.

It may be that you will never see the purity of the ASX™ rf, derived from highest quality synthesizers. You may never directly observe the virtually instantaneous phase switching of Bruker's unique 4-phase modulator, or measure the 4 MHz bandwidth of Bruker's 451 MHz IF receiver. And you may never have occasion to verify the amplitude, phase and frequency pulse shaping precision of the 64 kW/channel waveform memories, or the droop-free performance of the 1 kW amplifiers (even during bursts of more than 1 second!).

But you will see cutting-edge results. Because these unique features of the ASX™ enable you to perform the widest range of solids spectroscopy and imaging experiments available in the industry.

Solids NMR redefined. Period.

In fact, it was this unmatched level of performance that allowed us to invent methods such as C-24 CRAMPS, WIMSE and HETCOR, which provide liquid-like 1D and 2D results for solids. In addition, Bruker's SOLIDSCOPE™ and STRAFI™ proprietary solids-imaging technologies have made us the undisputed leader in imaging of rigid solids.

And you won't find the UNIX-based ASX™ difficult to use. In fact, features such as pneumatic MAS sample insert/eject, microprocessor regulated rotor speed, automatic spin up/down and built-in probe tune and wobble make the ASX™ the easiest solids machine ever. Better yet, add an optional solids sample changer and go home while the ASX™ continues without you! Of course the ASX™ can easily be expanded to full AMX™ high resolution performance, as well as micro-imaging of liquids.

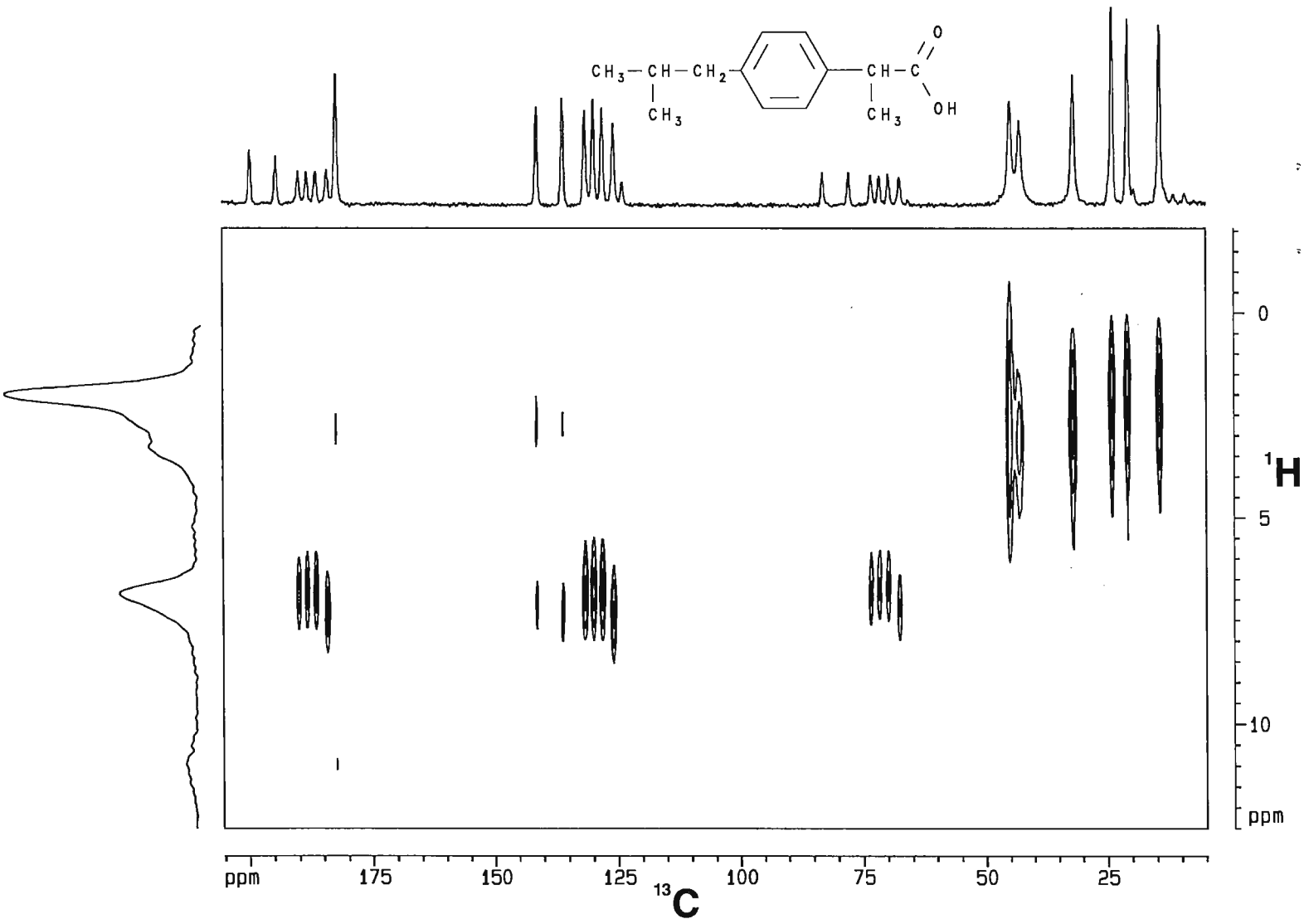
Ask for details on the ASX™. . .it's for Advanced Solids Xcellence.

Bruker Instruments, Inc.
Manning Park, Billerica, MA 01821
In Europe: Bruker Analytische Messtechnik GmbH, Silberstreifen, D-7512 Rheinstetten 4, Germany

Comprehensive Support for Innovative Systems

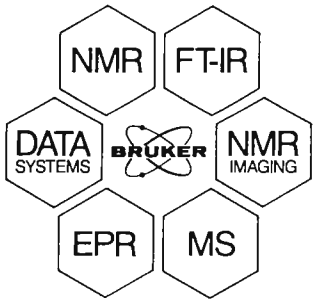
BRUKER

ASX-Advanced Solids Excellence



Solid State 2D HETCOR of Ibuprofen

In this spectrum the solid state 2D HETCOR experiment, developed in the Bruker applications laboratory, has been applied to the pharmaceutical compound ibuprofen. For comparison, 1D ^{13}C CPMAS and BR-24 ^{1}H CRAMPS spectra are displayed along the axes in place of the usual 2D projections. Strong cross peaks are visible for all of the directly bonded proton-carbon groups, as well as first order sidebands for the four aromatics. In addition, each of the three non-protonated carbons is shown to correlate to at least two long range protons. Note that minute differences in proton chemical shift, impossible to resolve in the 1D CRAMPS spectrum, are clearly visible in the 2D spectrum. 2D HETCOR requires simultaneous, fully windowless pulse sequences to be applied to both protons and carbons during the evolution and mixing periods. All the data shown here was obtained and processed on a Bruker ASX-300.



Australia: BRUKER (Australia) Pty. LTD., Alexandria, New South Wales, Tel. 02-5506422
Belgium: BRUKER SPECTROSPIN S.A./N.V., Brussels, Tel. (02) 648 53 99
Canada: BRUKER SPECTROSPIN (Canada) LTD., Milton, Ontario, Tel. (416) 876-4641
England: BRUKER SPECTROSPIN LTD., Coventry, Tel. (0203) 855200
France: SADIS BRUKER SPECTROSPIN SA, Wissembourg, Tel. (088) 73 6800
India: BRUKER INDIA SCIENTIFIC Pvt. LTD., Andheri (West), Bombay, Tel. 22-62-62-232
Italy: BRUKER SPECTROSPIN SRL, Milano, Tel. 02-70-636-370
Japan: BRUKER JAPAN CO. LTD., Ibaraki-ken, Tel. 0298-52-1234
Netherlands: BRUKER SPECTROSPIN NV, Wormer, Tel. (75) 28 52 51
Scandinavia: BRUKER SPECTROSPIN AB, Täby, Sweden, Tel. (00468) 758-03-35
Spain: BRUKER ESPANOLA S.A., Madrid, Tel. 341-259-20-71
Switzerland: SPECTROSPIN AG, Fällanden, Tel. 1-82 59 111
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. 0421-2205-0
BRUKER-SAXONIA ANALYTIK GMBH, Leipzig, Tel. 003741-239-2453
USA: BRUKER INSTRUMENTS, INC., Billerica, MA 01821, 508-667-9580, Fax: 508-667-3954
Regional Offices in Chicago, IL, (708) 971-4300 / Wilmington, DE, (302) 478-8110
Houston, TX, (713) 292-2447 / San Jose, CA, (408) 434-1190

T · H · E
OHIO
STATE
UNIVERSITY

Campus Chemical Instrument Center

176 West 19th Avenue
Columbus, OH 43210-1173
Phone 614-292-3446

March 8, 1993
(received 3/12/93)

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

Data Transfer using TCPIP with NFS between Aspect 3000's and Workstations.

Dear Barry:

The ability to transfer data from spectrometers has become increasingly important both for archival purposes and for remote processing. Fortunately the current generation of spectrometers using UNIX based computers are ideally suited for networking. But for those of us with older spectrometers not equipped with Ethernet, a method of moving both ASCII and binary files has become critical.

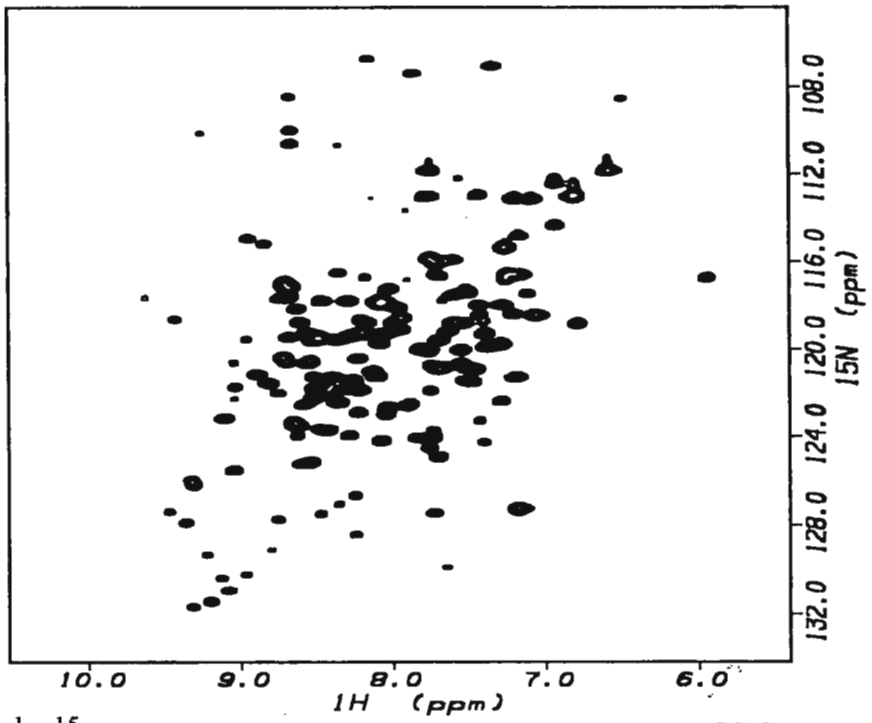
At Ohio State we have been transferring data from our Bruker spectrometers located in the College of Pharmacy, the Department of Chemistry, and my location the Campus Chemical Instrument Center both between spectrometers (more correctly first to pc's attached to the spectrometers) and to workstations. This is accomplished using a program I wrote in Pascal called **NMRNET** which runs on both an Intel based PC and an Aspect computer. The data is transferred between the computers using the high-speed parallel port on an Aspect computer and a 24-bit parallel digital I/O Metrabyte PIO-12 card inside a PC interfaced with a handshake card developed by Markley's group at Madison . A typical 32 KWord file (99072 bytes) can be transferred in four seconds and a 1 MWord file (3,146,496 bytes) can be transferred in eighty-seven seconds.

After the data is transferred to a PC, it may then be sent *via* ftp to a workstation for off-line processing or storage. This does involve a two step process, however, in that the person transferring the data must first send it from the spectrometer to a PC, then log onto some remote computer, and finally send the file(s) using the correct transfer mode, *e.g.*, binary if a data file is to be transferred. Also, unless people using this two step transfer method promptly erase their files transferred to the PC, the disk drive may very rapidly become filled with data files. Was there ever a disk drive with enough storage capacity?

Recently we have eliminated this two step process by using the Network File System or NFS software which enables a PC to access a disk drive on a remote computer, which is running an NFS server, as if the disk was directly attached to a PC. We are using several products at Ohio State both DOS and OS/2 2.0 versions of FTP's (the company) Idrive and in my case IBM's TCPIP for OS/2 with NFS. When my computer boots it automatically mounts four different UNIX workstations located in different departments on campus. These remote disks appear to my operating system as disk drives D, E, F, and G just as if they were physically installed in my computer. There may be a time penalty when using virtual or network drives, e. g., a four second

transfer might become two to four seconds longer, but the convenience outweighs any time saving.

Below is a 2-D HMQC spectrum that was acquired on our AM-500 using an inverse ^{1}H-^{15}N probe, transferred to a SGI workstation where it was processed with Felix 2.05, the spectrum was plotted as an HPGL file which was then imported into this letter written with Microsoft Word for Windows.



^{1}H-^{15}N HMQC acquired with Garp decoupling on AM-500 at CCIC.

If anyone would like copies of the software please feel free to contact me by e-mail at ccottrel@magnus.ohio-state.edu. for the best method of transferring the programs to you. Please credit this contribution to Alan Marshall's account.

Sincerely,

Chuck

Charles E. Cottrell, Ph.D.
Sr. Res. Associate

Roche

ROCHE RESEARCH CENTRE

Prof. B. L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto CA 94303 USA

Roche Products Ltd.
40, Broadwater Road
Welwyn Garden City
Herts. AL7 3AY, UK

24 December 1992 (received 3/3/93[sic])

The effects of inhibitors on the NMR spectra of larger proteins

Dear Barry,

As NMR dimensions increase, so - at least, it seems - molecules also get bigger. With the prospect of soon increasing our NMR capabilities above two dimensions, we have begun to study a 165-residue domain of recombinant human collagenase which includes the zinc-containing catalytic site (DH Williams, KMK Bottomley, A Friedlein, M Manneburg, H-W Lahm, F Winkler, A D'Arcy, G Williams and EJ Murray, J. Mol. Biol., submitted).

Our initial impressions were encouraging. Figure 1a shows a region of the 2D double-quantum spectrum of this domain; a large number of alpha-beta correlations are evident and it was hoped that the protein would be suitable for further study. However, TOCSY and NOESY (Figure 1b) spectra contained very little information and this was attributed to short single-quantum relaxation times and rapid spin diffusion.

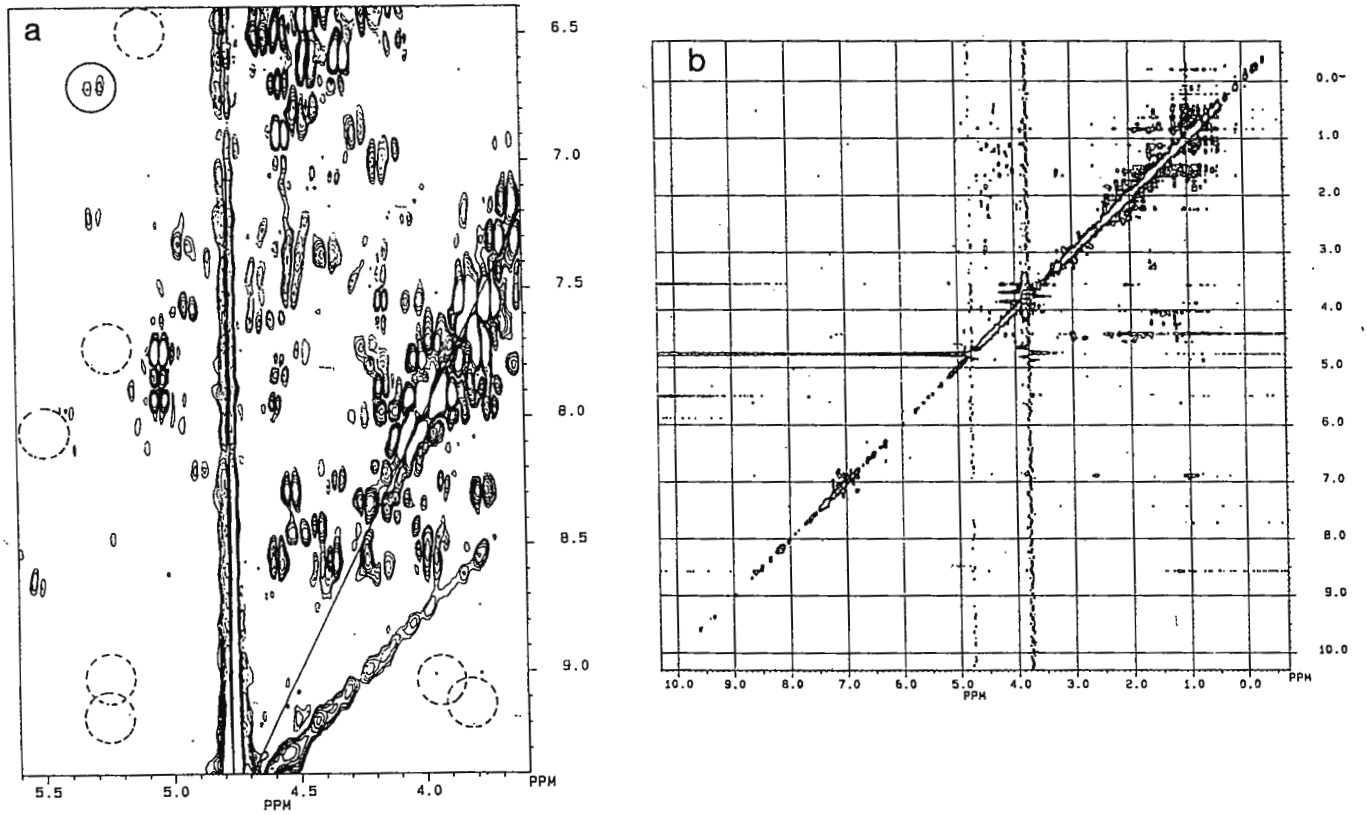


Figure 1

ROCHE RESEARCH CENTRE

Adding a low molecular weight inhibitor produced a few small changes to the 1D NMR spectrum and permitted the observation of a limited number of additional protein signals in the double-quantum spectrum (ringed in Figure 2a). The improvement in the NOESY spectrum was dramatic, however, (Figure 2b) and work is proceeding on the characterisation of the enzyme-inhibitor complex.

This change in the NOESY spectrum is presumed to arise from the damping out of a dynamic process on addition of the inhibitor. An analogous improvement in the ability to grow crystals of the collagenase domain is observed when an inhibitor is added to the protein solution.

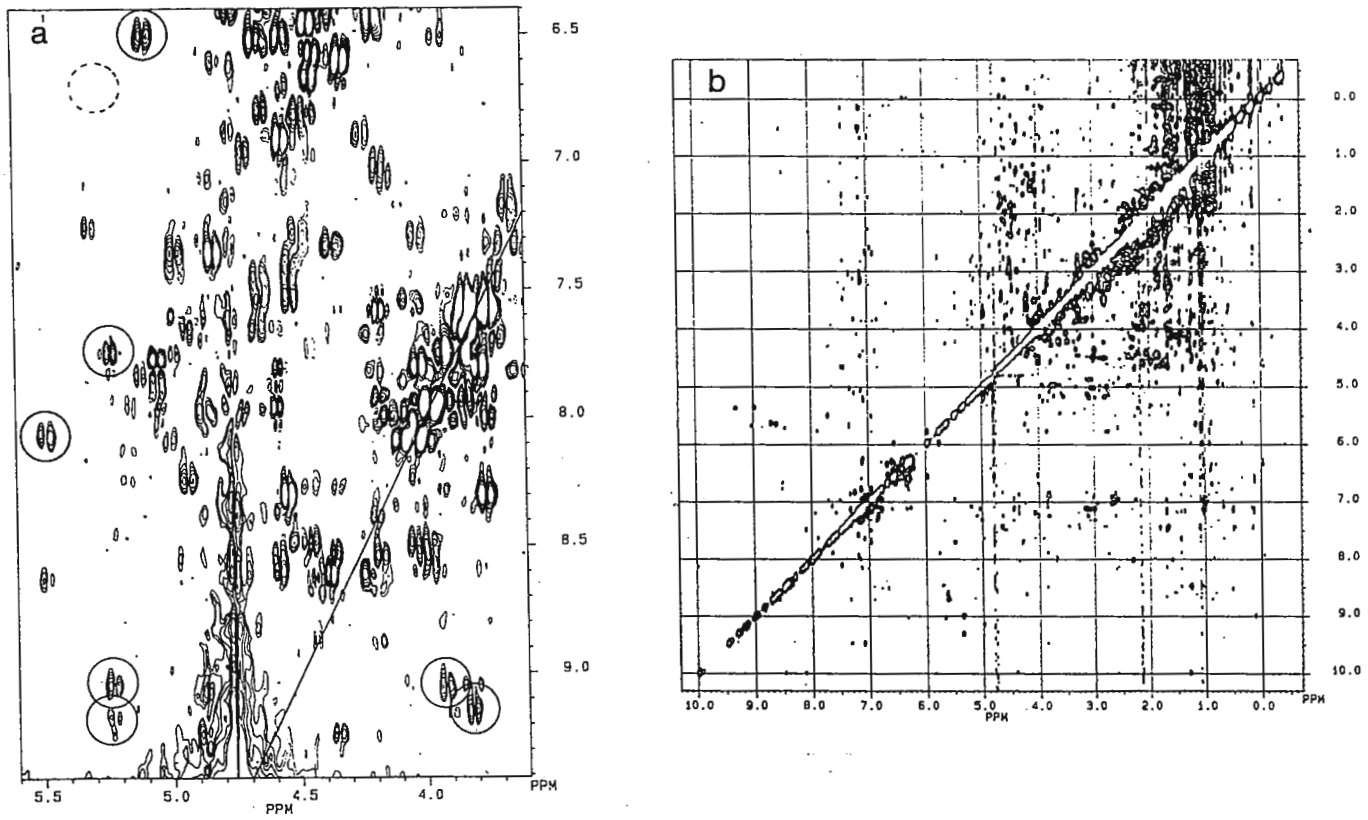


Figure 2.

Please credit this to the account of Tony Thomas.

Best wishes,

Glyn Williams

New Z•SPEC®
Microsample Probes

Announcing a complete product line of high performance ^{1}H observe, broadband observe, indirect detection (ID), and triple resonance (IDT) microsample probes. Z•SPEC® Microsample probes feature extremely short PW90's and outstanding water suppression capability. The Microsample ID Probe and Broadband Observe Microsample Probe have full X channel tuning range (^{31}P-^{15}N).

APPLICATION

The Z•SPEC family of microsample probes allow you to complete the analysis of your quantity limited samples (140µl) in one-half the normal time compared to your standard 5mm probe. Shown on the next page are HMQC data from 12µg of cryptolepine (Figure 1), HMBC data from 35µg of cryptolepine (Figure 2), HMQC data from 140µg Digoxin (Figure 3), and TOCSY data from 140µg Digoxin (Figure 4).

These 500MHz spectra demonstrate the significant gain in absolute signal to noise performance and speed of analysis that can be achieved when using the Z•SPEC Microsample Inverse Detection Probe.

COMPATIBILITY

The top loading design of the Z•SPEC microsample probe assures convenient sample changing and compatibility with automatic sample changers. Z•SPEC probes interface directly to Bruker, General Electric, or Varian spectrometers operating at a ^{1}H frequency of 200, 250, 270, 300, 360, 400, 500, or 600 MHz.

CUSTOMER SUPPORT

The staff of the Z•SPEC probe group include applications specialists who are available to install and support our products in your laboratory. For more information about Z•SPEC NMR probes, contact our marketing department.

NALORAC

837 Arnold Drive, Suite 600, Martinez, CA 94553
Tel: (510) 229-3501 • FAX 510.229.1651

Z·SPEC® Microsample Spectra

Figure 1: HMQC Spectra of 12µg of cryptolepine obtained in 16 hours with Z•SPEC MID500 probe. Normal ^1H spectrum (256 transients) for the 12µg sample plotted on top.

Figure 2: HMBC Spectra of 35µg cryptolepine obtained in 22 hours with Z•SPEC MID500 probe. Aromatic F_2 window. Normal ^1H spectrum (64 transients) for 35µg sample plotted on top.

Figure 1

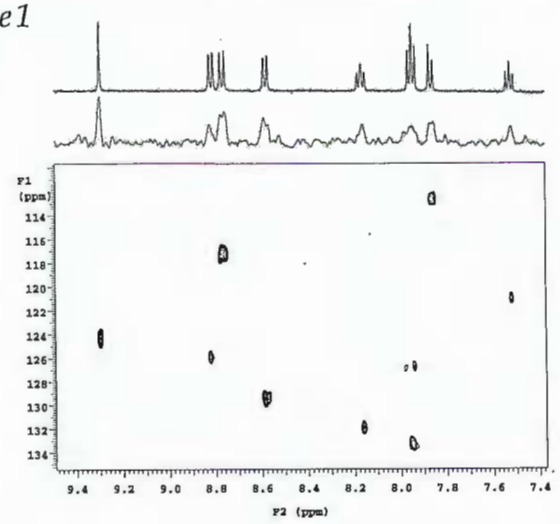
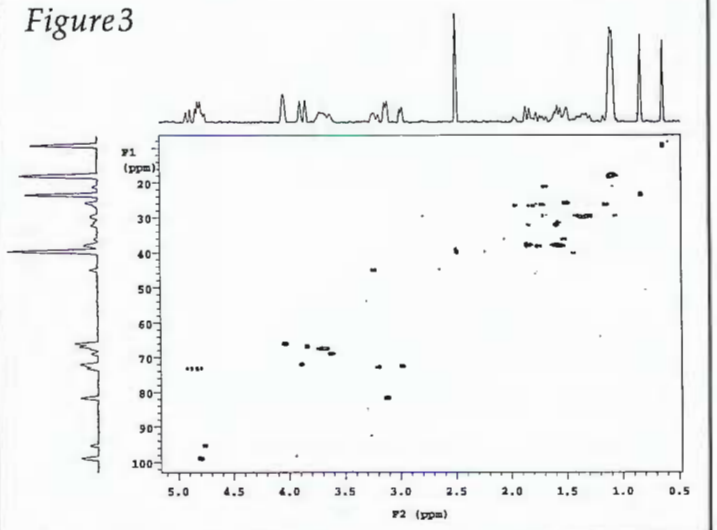


Figure 3



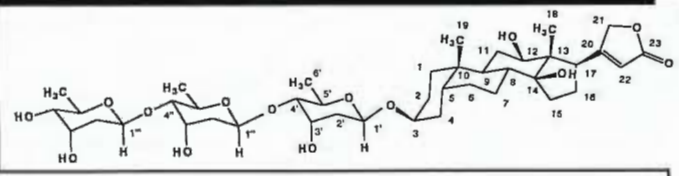


Figure 2

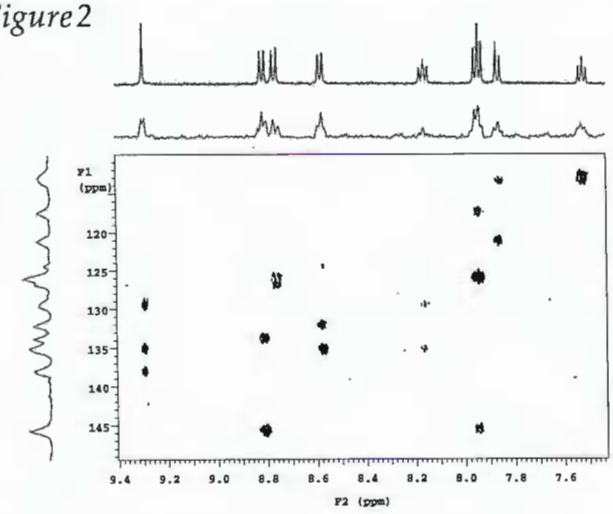


Figure 4

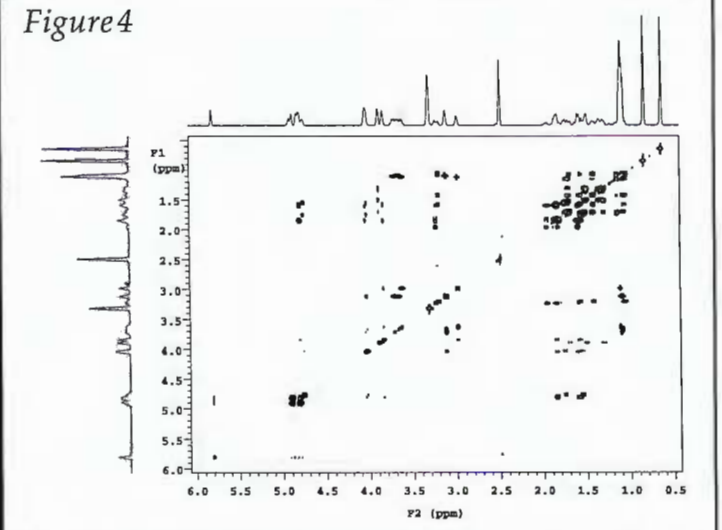


Figure 3: HMQC Spectra of 140µg Digoxin obtained in 14.5 hours with Z•SPEC MID500 probe.

Figure 4: TOCSY Spectra of 140 µg Digoxin obtained in 58 minutes with Z•SPEC MID500 probe.

Please review the following publications for additional examples of results obtained with Z•SPEC Microsample Probes: Micro Inverse-Detection: A Powerful Technique for Natural Product Structure Elucidation, Ronald C. Crouch and Gary E. Martin, *Journal of Natural Products*, **55 (9)**, pg 1343-1347 (1992); Comparative Evaluation of Conventional 5mm Inverse and Micro-Inverse Detection Probes at 500MHz, Ronald C. Crouch and Gary E. Martin. *Magnetic Resonance in Chemistry*. In press.

NALORAC

837 Arnold Drive, Suite 600, Martinez, CA 94553
Tel: (510) 229-3501 • FAX 510.229.1651

University
of Nebraska
Medical Center

The Eppley Institute for Research
In Cancer and Allied Diseases
A National Cancer Institute Designated
Laboratory Cancer Research Center
600 South 42nd Street
Omaha, NE 68198-6805
402/559-4090
Fax: 402/559-4651

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

(received 3/12/93)

Advantages/Disadvantages of PFG for imino hydrogen detection

Dear Barry - One of the principal advantages of pulsed field gradients is their utilization in solvent suppression for ^1H detection in aqueous solution. In our work on RNA and DNA structures we have compared the use of a 1D spin echo pulse sequence with pulsed field gradients

90-ΔG-δ-180-δ-ΔG-δ_2-FID (ΔG is the PFG time, δ, δ_2 are short delays)

to that obtained by using binomial solvent supression sequences. I would like to summarize some of the advantages and disadvantages to using this particular PFG-sequence for 1D solvent suppression.

1. This pulsed field gradient experiment is relatively easy to setup and temperature dependent chemical shift changes of solvent are not a problem. This is very nice when determining the Tm of a nucleic acid that ordinarily requires recalibration of parameters that effect solvent suppression at several temperatures.
2. There are no chemical shift dependent intensity or phase distortions using this pulse sequence. This may be particularly useful in 1D NOE experiments on nucleic acids where the reduced intensities for aromatic hydrogens resulting from the uneven excitation profile of binomial solvent suppression sequences makes detection of imino to aromatic hydrogen NOEs problematic.
3. It is possible to measure the exchange rates of imino hydrogens by monitoring the decrease in the signal intensity for imino hydrogens relative to non-exchangeable hydrogens. We are currently working on quantifying this process.

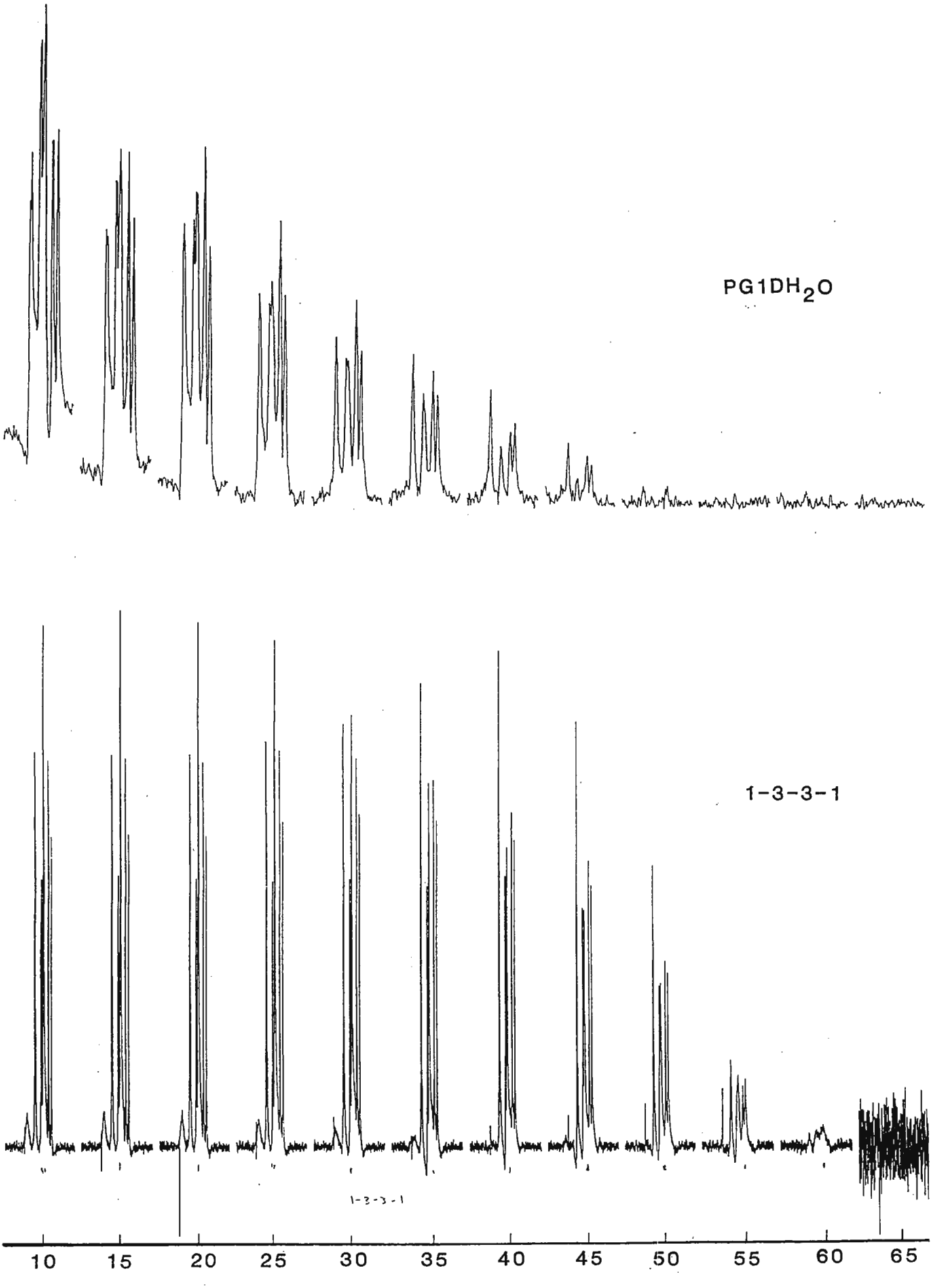
There are several disadvantages for this PFG pulse sequence.

1. Since this version of the pulse sequence is not phase sensitive the linewidths are broader. We are looking at whether linewidths are broadened from imperfections in the refousing of the pulse sequence in phase sensitive versions of this and other sequences.
2. Hydrogens that exchange very rapidly with water are severely attenuated with relatively short gradient pulses. While this is a bonus in determining exchange rates, simple detection and NOE experiments are more difficult.
3. Lower effective Tm since signal intensities in the PFG experiment are attenuated by diffusion as well as exchange. In the figure is a comparison of the temperature dependence of the 1D spectrum for a fluorinated DNA sequence obtained by using the PFG sequence and with the 1331 pulse sequence.

Sincerely,

William H. Gmeiner

415-36



JOHNS HOPKINS UNIVERSITY
SCHOOL OF MEDICINE
and
THE JOHNS HOPKINS HOSPITAL

DEPARTMENT OF RADIOLOGY
AND
RADIOLOGICAL SCIENCES

TELEPHONE: (410) 955-4221
FAX: (410) 955-9799

Mailing Address:
DIVISION OF NMR RESEARCH, , 110 MRI
600 N. WOLFE STREET,
BALTIMORE, MD 21287

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

March 8, 1993
(received 3/18/93)

IN VIVO PROTON NMR SPECTROSCOPY OF THE HUMAN LIVER

Dear Professor Shapiro,

Thank you for your recent "ultimatum". We have been predominantly interested in proton spectroscopy of the human brain over the past 2 to 3 years, but are often reminded by some of our colleagues that there are indeed other organs which might be interesting to study. However, it was our general feeling that proton spectroscopy outside of the brain was extremely difficult because of large lipid signals and problems due to respiratory (and cardiac) motion, and there have been few reports of proton spectra outside of the brain (1). Nevertheless, we recently attempted to record a spectrum from the liver of a normal volunteer, and, to our surprise, observed a large number of signals in the high field end of the spectrum (between 2 and 4 ppm) with comparative ease.

The spectrum shown below was recorded at 1.5 Tesla on a GE Signa spectrometer using the "PRESS" pulse sequence; a 5" inch surface coil placed over the liver was used for signal reception. The voxel size was 2x2x2 cm^3, with a TR of 1 second and a TE of 20 msec. After shimming, a water linewidth of 15 Hz was attained; water-suppression was then achieved using 3 "CHESS" pulses in the usual fashion. No attempt was made to suppress lipid signals. The volunteer held their breath for 8 seconds while the spectrum was being recorded (8 scans). The spectrum was apodized using exponential (-1 Hz) and gaussian (+2 Hz) filtration. We found that time-averaging over longer periods of time (with breathing) resulted in decreased resolution, and signal-to-noise ratios improved more slowly than the expected $\sqrt{n}$, presumably because of respiratory motion.

Clearly, there is a lot of information in the spectrum, and assigning the peaks should become the source of much heated discussion over the coming years! (the chemical shifts in the figure are referenced to water at 4.7 ppm). Apart from the strong lipid signals (including those at 2.81, 2.20 and 2.09ppm), based on the PCA extract spectra of Rafter et. al. (2), the signal at 3.33 ppm is assigned to betaine, and the signals at 3.81 and 3.50 to glucose. Based on a phantom study, the peaks at 3.70 and 3.62 ppm are tentatively assigned to glutathione,

Sincerely Yours,

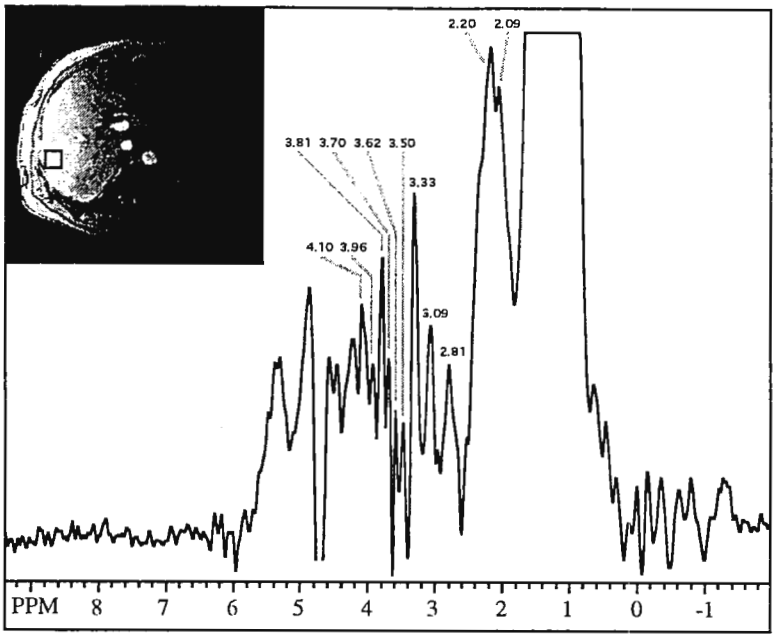
P.B. Barker.

Peter B. Barker, D. Phil.,

Brian J. Soher, B.Sc.

John C. Chatham, D. Phil.

1. M. Bär äny, B. G. Langer, R. P. Glick, P. N. Venkatasubramanian, A. C. Wilbur and D. G. Spigos, *Radiology* **167,** 839 (1988).
2. J. E. Rafter, T. E. Bates, J. D. Bell and R. A. Iles, *Biochim Biophys Acta* **1074,** 263 (1991).



Position Available

TRIPOS
SPECTROSCOPY GROUP

The Tripos Spectroscopy Group (Formerly New Methods Research Inc. in Syracuse, New York) has a position available for a Customer Support Scientist to provide direct telephone and other service to customers.

The successful candidate will have a Ph.D. in Chemistry, an allied field, or equivalent experience. Familiarity with the principles of NMR spectroscopy is an absolute requirement.

Additional demonstrated skills in the following areas are also desirable: familiarity with spectrum-molecule relationships, knowledge of SYBYL and SPL, and experience with software installation protocols on UNIX and VMS computers.

This opportunity, with a progressive company in the software development field, also provides excellent benefits and working conditions.

To apply submit resume/vitae and salary requirements to Ms. A. Tindall, Human Resources Manager, Tripos Spectroscopy Group, 6035 Corporate Drive, East Syracuse New York 13057-1016. Equal Opportunity Employer.


NMR 750
The new 750 MHz; Easy to use. Easy to operate. Easy to see why Oxford leads the field.
OXFORD
Oxford Instruments, NMR Instruments
Osney Mead, Oxford OX2 0DX, England
Telephone +44 (0) 865 269500 Fax +44 (0) 865 269501

Merck & Co., Inc.
P.O. Box 2000
Rahway NJ 07065-0900

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

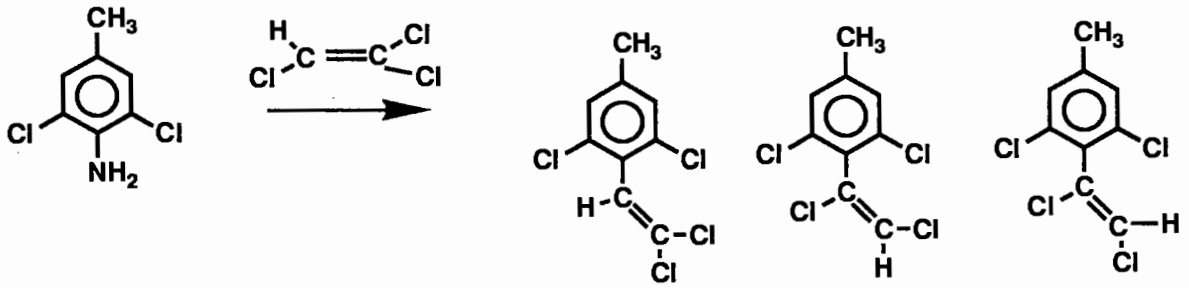
MERCK
Research Laboratories

(received 3/19/93)

Dear Barry,

Solving structure problems by ^{5}J and/or ^{7}J

Most of us who solve structure problems for a living rarely find it necessary to deal with coupling constants under one Hz. Papers that do investigate this area are generally basic studies which attempt to delineate the mechanism and stereochemical features that govern long range couplings up to seven intervening bonds (see publications by T. Schaefer: Can. J. Chem 61, 2785 (1983), J. Mag. Res. 73, 59 (1987), R. Laatikainan, Mag. Res. Chem. 24, 498 (1986) and Tet. 41, No. 21, 4919 (1985) and references therein). The unexpected, however, does arise from time to time and we wish to report an example in which a structure problem was most conveniently solved by the detection of a sub one Hz coupling. The reaction in question involved the aprotic deamination of 4-amino-3,5-dichloro toluene using trichloroethylene which could give rise to one or more of the illustrated isomers:



I II III

Although only one product was formed an identification from a routine 1D spectrum would be difficult since the three structures should show only small chemical shift differences. If, however, structure I is viewed as analogous to an ortho substituted benzaldehyde one might expect to detect the well documented five bond coupling between the (quasi aldehydic) vinyl and the $H_{2,6}$ protons. Happily, the illustrated spectrum (figure 1) showed a ^{5}J of 0.37 Hz which agrees with the published value of 0.39 Hz reported for 2,6-dichlorostyrene. Any residual doubt that the correct structure is I was eliminated by the detection of the 0.74 Hz coupling between the vinyl and methyl protons. This is readily accommodated with I since ^{7}J values up to 0.62 Hz have been reported. Structures II and III, however, would require coupling over nine bonds which is, to our knowledge, unprecedented in the styrenes. In p-methyl styrene itself any coupling between the terminal vinyl and the aromatic or methyl protons is unresolved and is estimated to be well under 0.2 Hz.

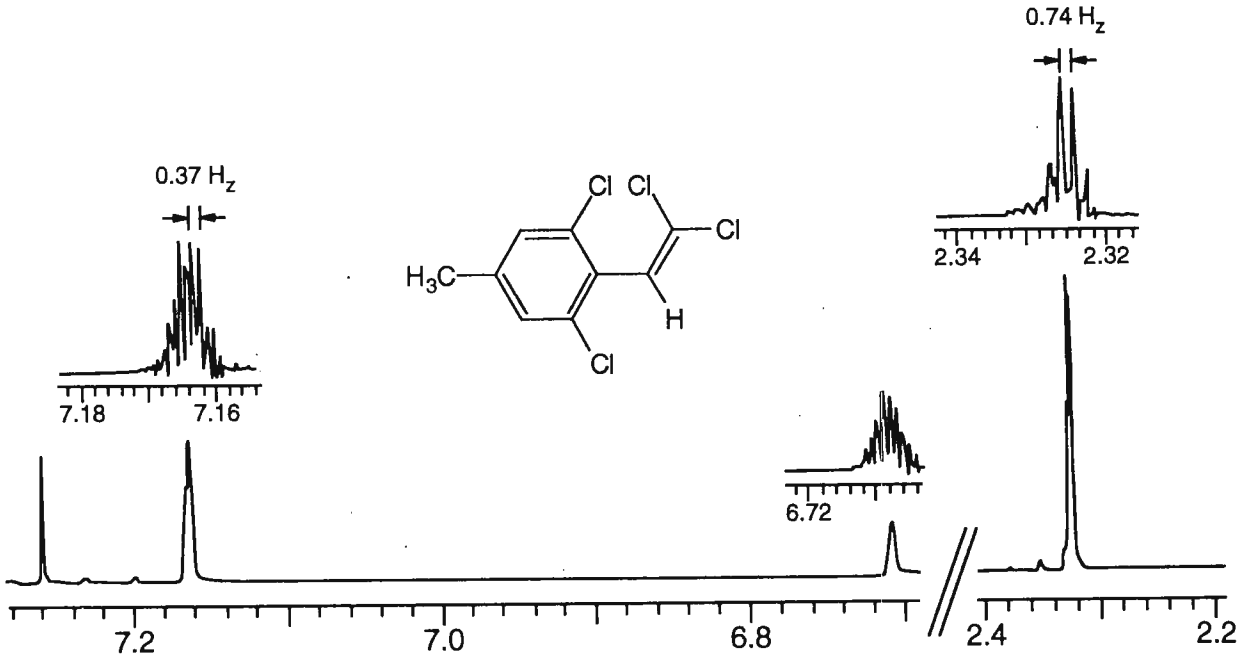
Since the stereochemical requirements for ^{7}J have not been defined to the same degree as ^{4}J, ^{5}J and ^{6}J we decided to compare ^{7}J in I with the bromomethyl and dibromomethyl analogs and the results in the accompanying table strongly suggest that a non-zero value for θ (angle of inclination from the plane of the aromatic ring) is indicated for both coupling protons.

Table

Compound	^{7}J
I	0.74
$BrCH_2Ar$-	0.4
Br_2CHAr-	ca 0

B. Arison

T. Beattie



The College of Staten Island
THE CITY UNIVERSITY OF NEW YORK
ST. GEORGE CAMPUS
130 STUYVESANT PLACE
STATEN ISLAND, NEW YORK 10301

March 1, 1993 (received 3/6/93)

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

Hindered Methyl Internal Rotation

Dear Dr. Shapiro:

Previous theory[1] provided an equation to calculate fully anisotropic overall molecular tumbling with free group internal rotation:

$$J(\omega_i) = \sum_{a}\sum_{a'b}\sum_{r} Z(\lambda_r)_{aa'} \cdot D^{(2)*}_{ab}(\alpha,\beta,0)\, D^{(2)}_{a'b}(\alpha,\beta,0)$$

$$\cdot [d^{(2)}_{b_e}(\Delta)]^2 \frac{\lambda_r + b^2 R_1}{(\lambda_r + b^2 R_1)^2 + \omega_i^2} \qquad 1$$

As a general rule, the methyl internal rotation rate is much faster than the overall skeletal reorientation. Therefore the T_1 and NOE for methyl groups usually exhibit no magnetic field dependence. However, we found that the T_1 values of the methyl groups at C-18 and C-19 of ginsenoside-Re (GR) are as much as double as the resonance frequency is raised from 50 Mhz to 100 MHz. The NOE values also increase with rising magnetic fields. To explain our experimental data, a spectral density function including hindered methyl internal rotation was developed as:

$$J(\omega_i) = \sum_{a}\sum_{a'b}\sum_{r} Z(\lambda_r)_{aa'} \cdot D^{(2)*}_{ab}(\alpha,\beta,0)\, D^{(2)}_{a'b}(\alpha,\beta,0)$$

$$\cdot [d^{(2)}_{b_e}(\Delta)]^2 \left[\frac{S^2\lambda_r}{\lambda_r^2 + \omega_i^2} + \frac{(1-S^2)(\lambda_r + b^2 R_1)}{(\lambda_r + b^2 R_1)^2 + \omega_i^2}\right] \qquad 2$$

where the definitions of S^2 adopted from reference 2, others were from reference 1. If $S^2=0$ i.e., internal rotation is unrestricted, Equation 2 reduces as expected to Equation 1. The calculation of the dynamic parameters for GR requires knowledge of the most probable conformation which was derived from molecular mechanics calculations.

Table 1 lists the calculated methyl internal rotation rates and the spatial restriction orders from Equation 2. Among the interesting trends revealed for these molecules with similar rigid frameworks, the first is that methyl internal rotation rates decreases as the side chains become longer and more complex, thus ensuring a more crowded environment around the molecular skeleton. The second and corresponding trend is the methyl rotation barriers increase substantially for more bulky sidechains. Finally, S^2 is found to be about 0.50 for GR, indicating group internal rotation that is neither completely free nor entirely restricted.

Table I Methyl Group Internal Rotation Rates and Barriers[a]

Compound	Carbon	R_i (s^{-1})	S^2	ΔE (kcal/mol)
5α-androstane[b]	C-18	6.9×10^{10}	-	3.3
	C-19	1.9×10^{11}	-	2.7
Sodium taurocholate[c]	C-18	1.8×10^{10}	-	4.0
	C-19	1.6×10^{10}	-	4.1
Ginsenoside-Re[c]	C-18	4.2×10^{9}	0.52	4.9
	C-19	2.3×10^{9}	0.50	5.3

[a] Calculated with $\alpha=\beta=90^0$ and $\Delta=70.5^0$.
[b] From Reference 10.
[c] This work.

1. Levy, G. C.; Kumar, A.; Wang, D. J. Am. Chem Soc. 1983, 105, 7536.
2. Lipari, G.; Szabo, A. J. Am. Chem. Soc. 1982, 104, 4546.

Sincerely

Dehua Wang

Dehua Wang

Ruth E. Stark

Ruth E Stark

Non-magnetic Trimmer Capacitors

Voltronics Corporation has produced non-magnetic trimmer capacitors for over 20 years. The increasing applications have impelled the company to mount an active, continuing engineering effort in this field.

NON-MAGNETIC PROPERTIES

The severe requirement for non-magnetic properties is such that in a 14,000 Gauss field the capacitors must not distort the useable field by more than one part per 600 million. To achieve this, no materials or platings exhibiting measureable magnetism, such as stainless steel or nickel, are used. Commercial brass is unacceptable. Typical magnetic susceptibility is 40 x 10^{-6} CGS units. Voltronics' strict traceability system and its testing for minute magnetism insure this essential parameter.

NON-ROTATING PISTON TRIMMER DESIGN

The capacitors have Voltronics' unique non-rotating piston design which offers 100% tuning linearity without reversals, high Q, long life, and low internal inductance. The internal bushing arms which prevent rotation also wipe on the moving piston to form a low resistance contact which can carry several amperes of RF current. **No current flows along the tuning screw as in all other trimmer capacitor designs!**

SEAL

Most of the capacitors are internally O-ring sealed so that they can withstand immersion in flux and cleaning solvents without leaking.

DIELECTRIC

There are six choices of dielectric material: annular band glass, embedded band glass, quartz, air, teflon and sapphire. Annular band glass consists of a tube of glass with metallized bands on the outside. Embedded band glass is the same as annular band with a metallic electrode embedded inside to decrease the effective dielectric thickness and thus increase capacitance. This also lowers the voltage rating. Quartz has a high voltage rating and has high Q. Sapphire's high dielectric constant combined with a high Q and voltage rating make it the best overall dielectric, but also the most expensive. Teflon has the highest voltage rating and high Q, but has a lower dielectric constant which results in lower capacitance ranges or larger sizes. Air offers high Q, small size and no organic material, a factor in some NMR tests. The NMK_HV parts with teflon offer small size, high voltage ratings and no internal air gap preventing ionization.

SPLIT STATOR AND DIFFERENTIAL STYLES

Non-magnetic split stator and differential capacitors are available . Consult the factory for detailed specifications.

100-10 FORD ROAD ▪ DENVILLE, NEW JERSEY 07834 ▪ PHONE : 201-586-8585 ▪ FAX : 201-586-3404

Voltronics CORPORATION

Non-magnetic Trimmer Capacitors

Capacitance (pF) From Below	Capacitance (pF) To Above	Q (Min.) 25 MHz	Q (Min.) 100 MHz	Peak RF Voltage Rating* 100 MHz	Dielectric	Figure	"A" Dim. ±.06	"B" Dim. ±.03
0.4	3.5	9000	2700	800	Quartz	1	0.63	0.20
0.5	3.5	9000	2700	800	Quartz	2	0.63	0.31
1.0	6.0	9000	2000	800	Quartz	2	0.63	0.31
0.6	7.0	9000	3000	500	Sapphire	3	0.50	0.15
0.8	10.0	9000	1100	1000	Quartz	5	1.21	0.38
0.8	10.0	1800	900	12000	Teflon	4	1.83	0.63
0.8	10.0	2000	1000	8000	Teflon	4	1.15	0.38
1.0	10.0	3500	900	3000	Teflon	2	1.69	0.31
1.0	10.0	3500	900	4200(Note 1)	Teflon	2	1.69	0.31
1.0	10.0	10000	5000	250	Air	6	0.29	0.23
1.0	9.0	10000	3000	1500	Teflon	6	0.29	0.23
0.9	12.0	9000	1000	1200	Quartz	5	1.45	0.45
1.0	15.0	2000	800	3000	Teflon	2	1.69	0.31
1.0	22.0	9000	800	900	Quartz	2	1.67	0.31
7.5	24.0	7000	800	1000	Quartz	5	1.48	0.40
5.0	25.0	2000	750	6000	Teflon	4	1.62	0.63
5.0	25.0	1500	700	15000	Teflon	4	1.77	1.13
3.0	30.0	1200	600	6000	Teflon	4	2.25	1.50
1.0	38.0	800	250	900	Glass	7	1.67	0.31
1.0	38.0	800	250	900	Glass	2	1.67	0.31
2.0	40.0	3000	400	700	Sapphire	2	1.30	0.31
5.0	50.0	700	350	10000	Teflon	4	2.25	1.50
1.0	70.0	650	325	6000	Teflon	4	3.00	0.70
3.0	70.0	650	325	15000	Teflon	4	3.25	1.63
5.0	85.0	600	300	6000	Teflon	4	3.25	1.50
2.0	120.0	600	95	700	Glass	8	1.76	0.31

IN	0.010	0.015	0.016	0.020	0.025	0.030	0.036	0.040	0.070	0.080	0.085	0.090	0.095	0.120	0.150	0.160	0.167	0.190	0.200	0.220	0.225	0.230	0.235	0.245	0.250	0.260	0.2
MM	0.25	0.38	0.41	0.51	0.64	0.76	0.91	1.02	1.78	2.03	2.16	2.29	2.41	3.05	3.81	4.06	4.24	4.83	5.08	5.59	5.72	5.84	5.97	6.22	6.35	6.60	7.1

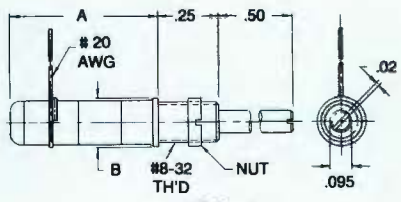


FIG. 1

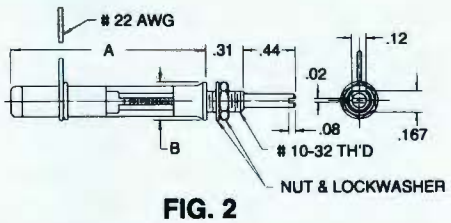


FIG. 2

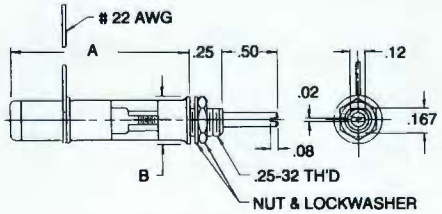


FIG. 5

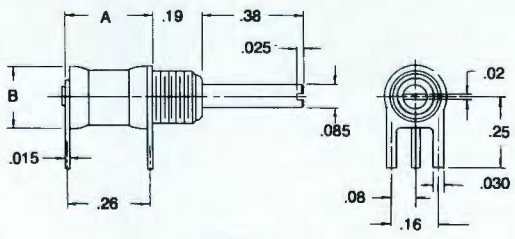


FIG. 6

Voltronics CORPORATION 100-10 FORD ROAD ▪ DENVILLE, NEW JERSEY 07834 ▪ PHONE : 201-586-8585 ▪ FAX : 201-586-3404

PART NUMBER DESIGNATIONS			
Configuration as shown on drawing	Same as drawing without extended shaft (Note 3)	Same as drawing with no lead(s)	Same as drawing with no lead(s) and no extended shaft
NMQS3GE	NMQS3G	NMQS3GENL	NMQS3GNL
NMQM3GE	NMQM3G	V2105	NMQM3GNL
NMQM6GE	NMQM6G	NMQM6GENL	NMQM6GNL
NMP8ME	NMP8M	N/A	N/A
V2236	V2010	V2102	V2276
NMNT10-12E	NMNT10-12	NMNT10-12ENL	NMNT10-12NL
NMNT10-6E	NMNT10-6	NMNT10-6ENL	NMNT10-6NL
V2145E	V2145D	V2145B	V2145F
V2145H	V2145G	V2145A	V2145I
NMKP10E(Note 2)	NMKP10	NMKP10ENL	NMKP10NL
NMKP10HVE(Note 2)	NMKP10HV	NMKP10HVENL	NMKP10HVNL
V2269	V2268	V2002B	V2002A
NMNT15E	NMNT15	NMNT15ENL	NMNT15NL
NMQM22GE	NMQM22G	NMQM22GENL	NMQM22GNL
V2271	V2270	V2101	V2272
NMNT25-6E	NMNT25-6	NMNT25-6ENL	NMNT25-6NL
NMNT25-15E	NMNT25-15	NMNT25-15ENL	NMNT25-15NL
NMNT30E	NMNT30	NMNT30ENL	NMNT30NL
V2066E	V2066	N/A	N/A
NMTM38GE	NMTM38G	NMTM38GENL	NMTM38GNL
V2274	V2273	V2050	V2275
NMNT50E	NMNT50	NMNT50ENL	NMNT50NL
NMNT70-6E	NMNT70-6	NMNT70-6ENL	NMNT70-6NL
NMNT70-15E	NMNT70-15	NMNT70-15ENL	NMNT70-15NL
NMNT85E	NMNT85	NMNT85ENL	NMNT85NL
NMTM120CE	NMTM120C	N/A	N/A

NOTES:

1. V2145H type parts are filled with silicone fluid to increase RF breakdown voltage.
2. The NMKP10E and NMKP10HVE parts have ceramic cylinders which are solder sealed. These parts may be ordered with plastic cylinders and epoxy seals. To order the plastic style, change the beginning of the part number from "NMKP" to "NMKEP", ex. NMKEP10HV.
3. For parts without extended shafts, the tuning screw will either be recessed inside the threaded bushing or will be flush with the end of the bushing.

*RF VOLTAGE RATINGS:

Because RF non-magnetic applications are pulsed, only RF pulse peak voltage ratings are listed. These are the voltages at which arcing began inside the parts. The parts were not damaged and continued to be used at slightly lower power settings. CW ratings are lower. DC ratings are substantially higher. Almost every application is different, with pulse rate, frequency and impedance varying. For substantially higher voltage ratings, consult the factory. Modifications may be possible to meet your requirements.

The RF peak voltage ratings are shown as a guide only. They are based upon a limited number of tests by an NMR lab. Voltronics does not perform these tests as part of the normal final inspection procedures.

290	0.310	0.380	0.440	0.450	0.460	0.500	0.630	0.700	1.000	1.130	1.150	1.210	1.300	1.380	1.450	1.480	1.500	1.620	1.630	1.670	1.690	1.760	1.770	1.830	2.250	3.000	3.250
37	7.87	9.65	11.18	11.43	11.68	12.70	16.00	17.78	25.40	28.70	29.21	30.73	33.02	35.05	36.83	37.59	38.10	41.15	41.40	42.42	42.93	44.70	44.96	46.48	57.15	76.20	82.55

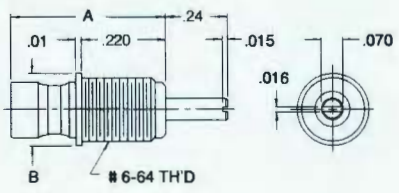


FIG. 3

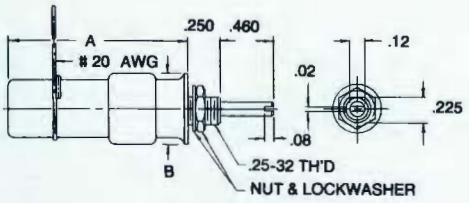


FIG. 4

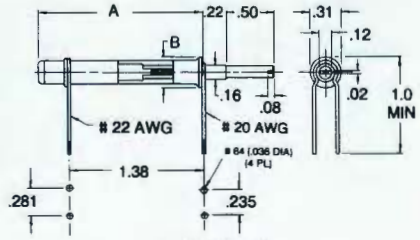


FIG. 7

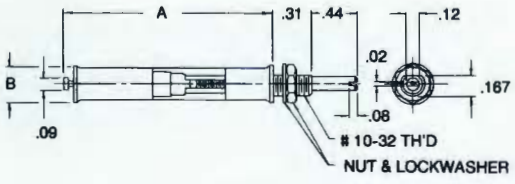


FIG. 8

100-10 FORD ROAD ▪ DENVILLE, NEW JERSEY 07834 ▪ PHONE : 201-586-8585 ▪ FAX : 201-586-3404

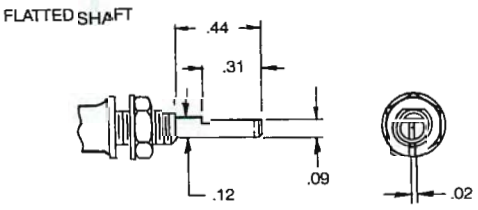
Voltronics CORPORATION

SPECIAL DESIGNS

Each of the parts shown in this catalog was developed for a specific customer application. Special parts have been designed for cryogenic applications. Many other mounting configurations are available. Call the factory to discuss your special needs.

FLATTED SHAFT OPTION

All extended shafts are available with flatted extended shafts as shown in this drawing. To order this option, add "FS" to the part number shown in the second or fourth columns in the "Part Number Designation" section (ex. V2010FS).

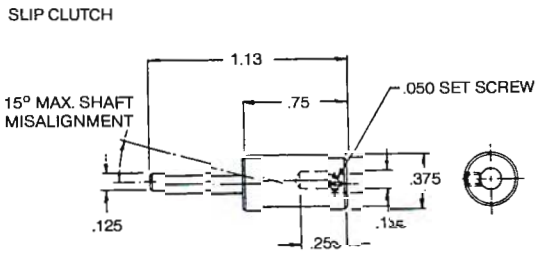


ANTENNAS AND COILS

Voltronics can produce very stable antennas and coils on glass or quartz tubes. Consult the factory with your specific requirement.

NON-MAGNETIC SLIP CLUTCH

The slip clutch prevents damage to the trimmer capacitor, especially when it is tuned by a long rod as in many probes. The trimmers' 72 turns per inch internal thread can create great forces on the positive stops which may damage the capacitors or strip the threads. The slip clutch is also able to compensate for up to 15° of misalignment between the rod and the trimmer. The clutch is pre-set to five inch ounces. All parts of the clutch are non-magnetic.



Part Number: SC375

GENERAL SPECIFICATIONS OF PAGE 2 APPLY EXCEPT:

1. Tuning torque: 0.5 to 4 inch ounces
2. Temperature coefficient: —100 to +500 ppm/°C except
   NMKP10E: 50 ±50 ppm/°C
   NMKP10HVE: —60 to +30 ppm/°C

RECOMMENDED TUNING TOOLS:

Voltronics TT-500 and TT-600 tuning tools are non-magnetic, with ceramic tips.

Voltronics CORPORATION 100-10 FORD ROAD ■ DENVILLE, NEW JERSEY 07834 ■ PHONE : 201-586-8585 ■ FAX : 201-586-3404

ROSKILDE UNIVERSITY

Associate professor Poul Erik Hansen, Institute of Life Sciences and Chemistry

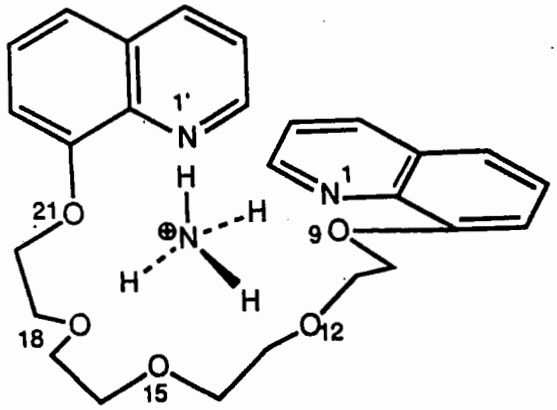
Professor B.L.Shapiro
966 Elsinor Court
Palo Alto, CA 94303
U.S.A

March 2 1993
(received 3/6/93)

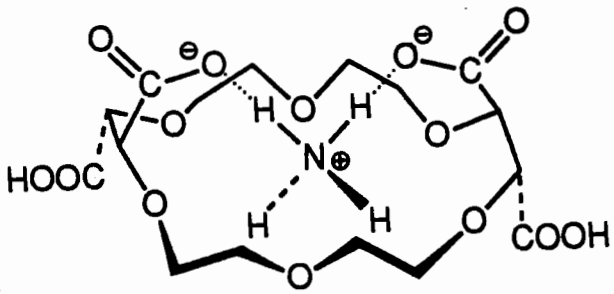
Dear Professor Shapiro

"Isotope Effects of Ammonium Ions"

We have continued to study deuterium isotope effects in ammonium ions. Two approaches have been taken. Theoretical calculations to figure out the reason for the negative two-bond deuterium isotope effect and use of inclusion complexex of ammonium ions to create well defined coordination situations.
Ab initio calculations of the LORG type showed unambigously that the negative sign is related to directional hydration at the N-D bond. Hydrogen-bonding decreases both $^2\Delta H(D)$ and $^1\Delta N(D)$ numerically and the decrease is controlled by the N...O distance. This effect can be ascribed to electric field effects.



$^2\Delta H(D)$ = -34 ppb/D



$^2\Delta H(D)$ = -10 ppb/D

An illustration of these findings is obtained in inclusion complexes. Large negative two-bond isotope effects are found in a complex with the podand K5. In this complex strong hydrogen bonds are formed, whereas small effects are seen in a complex with 18-crown-6$(COOH)_4$. In the latter two of the NH bonds are buried without forming hydrogen bonds, hence the small isotope effect. 18-crown-6 itself gives a $^2\Delta H(D)$ of -19 ppb/D.

Yours sincerely

Poul Erik Hansen

Conseil national de recherches Canada
National Research Council Canada

Institut de recherche en biotechnologie
Biotechnology Research Institute

March 17, 1993 (received 3/18/93)

CNRC · NRC

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

Protein Spin Diffusion in Transferred NOE Experiments

Dear Dr. Shapiro,

In response to your ULTIMATUM, I would like to share with your readers our recent results on the analysis of protein spin diffusion in transferred NOE experiments. The applications of transferred NOEs usually rely on the assumption of fast exchange conditions. In such cases, the observed NOEs are a direct consequence of the conformation of ligands in the protein-bound state (Landy & Rao, JMR 81, 371 1989). However, the situation can be rather complicated if the protein-ligand complex is very large, e.g. >30,000 dalton as often encountered in practical applications. First of all, one need to take into account of the effect of the finite exchange rate (Ni, JMR 96, 651-656, 1992). For a fixed mixing time, NOE intensities are attenuated by the presence of slow dynamic exchange. Spin diffusion pathways can also give rise to NOE cross peaks that cannot be assigned to direct distances between ligand protons. Relaxation matrix methods can in principle reduce the effect of spin diffusion if NOEs and exchange cross peaks between all the participating protons can be observed. In transferred NOE epxeriments, however, only ligand protons are selectively observed while the protein proton resonances escape detection as a result of the slow tumbling of protein-ligand complexes. These "silent" but relaxation-active protein protons make the relaxation analysis of transferred NOEs extremely diffucult.

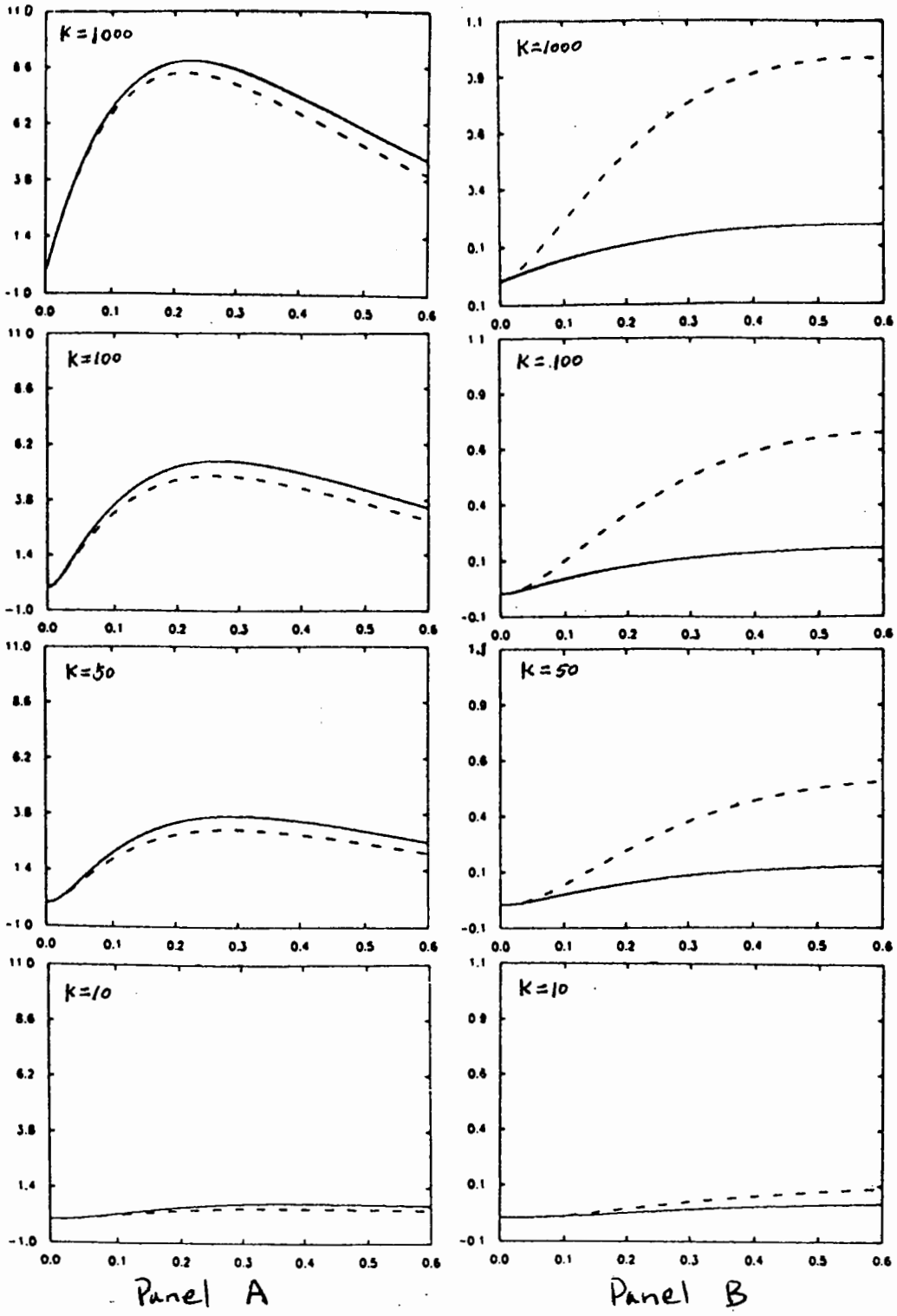
Recently, we adopted an "inverse" strategy for the analysis of transferred NOEs. In this procedure, we test the correctness of a model structure through transferred NOE simulations including all experimental parameters (Ni et al, Biochemistry 31, 11551, 1992). We extended this work to assess the contribution of protein spin diffusion as a function of the exchange rate (Ni & Zhu, JMR, submitted). Intuitively, protein spin diffusion may become less severe as the exchange rate approaches infinity (fast exchange). This, however, is not at all the case as one can see from the following figure. The solid lines represent the transferred NOE buildup between the ligand protons in the absence of protein protons. The dotted lines are the corresponding curves in the presence of protein protons. As expected, direct (strong) NOEs are attenuated in the presence of protein spin diffusion (Panel A). Weak NOEs, on the other hand, are enhanced through indirect cross relaxation mediated by protein protons (Panel B). The enhanced NOEs would produce a false distance of 3 Å between the ligand protons instead of an actual distance of 3.9 Å (Ni & Zhu, JMR, submitted).

In closing, I would like to mention that I have a few postdoctoral positions in my lab to continue studies outlined in this letter (see AD in the same issue).

6100, avenue Royalmount
Montréal, Québec, Canada
H4P 2R2

6100 Royalmount Avenue
Montreal, Quebec, Canada
H4P 2R2

Canada



Sincerely Yours,

Feng Ni, Ph.D.
Research Officer
Professor of Biochemistry
McGill University

Research Associates and Visiting Scientists: The NMR laboratory of the Biotechnology Research Institute (BRI) is seeking NMR scientists to complement our ongoing research in the development of advanced NMR methods for applications in drug design. The position will be available initially for two years and extendable up to five years. You will be leading research projects in development of 2D and 3D transferred NOE and isotope-editted NMR methods to determine and refine the dynamic structure of enzyme-bound inhibitors. Ideally, the applicants should have one or two years of postdoctoral experience (for RAs) in high-resolution and multi-dimensional NMR spectroscopy. But we also consider new Ph.D.s if they are independent enough to lead scientific projects and draft scientific publications. 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 network of Silicon Graphics workstations for data processing and molecular modelling.

The Biotechnolgy Research Institute, as a federally-funded branch of the National Research Council of Canada, is devoted to basic and applied research in protein engineering, molecular recognition and rational drug design. As an NMR spectroscopist, you will be interacting with a multi-disciplinary team of scientists composed of peptide and protein chemists, molecular biologists, medicinal chemists, molecular modellers and x-ray crystallographers. Interested candidates should contact Dr. Feng Ni at:

Phone: (514)-496-6729; Fax: (514)-496-5143
e_mail: fengni@bobino.bri.nrc.ca

or send a CV and 2 letters of reference to:

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

Your Obsolete Data Acquisition System Can Make Your NMR Spectrometer Appear to Be...

tecmag

Introduces

Q E

The QE Upgrade You've Been Waiting For...

AQUERIUS™ is the latest member of the ZODIAC™ Series specifically designed for upgrading General Electric QE 300 NMR spectrometers. It replaces the 1280 computer boards, 8" floppy disk drives, hard disk drives and the pulse programmer board. Coupled with a Macintosh II computer, AQUERIUS and the exclusive MacNMR™ software provide the capabilities of CHARM. Increased flexibility, such as hardware looping, 2048 steps, simultaneous pulses, fast processing, improved dynamic range and a choice of ADC's have been added to the system. The AQUERIUS data acquisition system gives the features QE users have been waiting for:

- The Macintosh II, an industry standard 32-bit computer (with a 3.5" floppy disk drive) .
- A wide selection of low cost, high capacity, reliable hard disk drives, removable drives, optical disk drives, and laser printers.
- Unlimited copies of MacNMR for off-line data processing stations.
- True Ethernet, AppleTalk and other LAN'S (cross mounting of disks).
- Easy to use graphical controlled user interface.
- Software support. MacNMR is updated about every 6 months.
- Fast processing. 16K complex floating-point FFT in 700 ms!
- Hardware looping (HOHAHA and ROESY capabilities).
- Choice of ADCs. 12-bit 200 kHz or 1 MHz spectral width.

Call for more details on the AQUERIUS or other ZODIAC data acquisition systems.

SPECIFICATIONS

Pulse Programmer

Minimum Pulse Width:	**100 ns**
Maximum Pulse Width:	**430 s**
Time Resolution:	**100 ns**
Loop Counters:	**5**
Steps:	**2048**

Signal Averager

ADC Resolution:	**12 bits**
No. of Channels:	**2 (simultaneous sampling)**
Min. Sampling Time:	**5 μs or 1μs per channel**
Max. Bandwidth:	**200 kHz or 1 MHz**
Memory Size:	**64 k-Word x 32 bits**

tecmag

6006 Bellaire Blvd.
Houston, TX 77081
Tel: (713) 667-1507
Fax: (713) 667-3180

EVALUATION OF NOISE WITH HISTOGRAM OF NMR SPECTRA

Alain Louis-Joseph, Alain Rouh and J.Y Lallemand

D.C.S.O
Ecole Polytechnique 91128 Palaiseau FRANCE.
Tel : 1 69 33 48 61 Fax : 1 69 33 30 10

to

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

(received 2/9/93)

4/02/93

Dear Sir,

The evaluation of noise is important in many strategies of NMR data processing (maximum entropy spectral analysis, peak picking routines ...). The usual way to perform this calculation is to select a spectral region of a 2D or 3D section assumed to be free of any NMR signal, and to calculate on this data set {X} an estimation of the statistic variance (or mean square deviation).

$$(1) \qquad \sigma^2_{classic} = \frac{1}{N} \Sigma_{n=1}^{N} (x_n - x_{mean.})^2$$

This calculation has several limitations :

- This variance is calculated for an area which must be large enough to get an accurate estimation.
- The arbitrary choice of the area is based on white noise hypothesis, that needs to be validated.
- The data set {X} region may contain unexpected NMR signal of low magnitude and the noise evaluation is thus biased.
- There is no way to check the truthfulness of the three previous hypothesis.
- This procedure is not automatic.

Considering these limitations, equation (1) is not the best estimation of the noise characteristic. We propose a method which uses the entire NMR data set (2D or 3D), and which is independant of the presence of NMR signal. This method is based on the construction of an histogram $H(x_i)$ of the spectrum as follow,

$$(2) \qquad N (F_X(x_i+c) - F_X(x_i)) = H(x_i)$$

We analyse around a number of channels, of width c, the distribution function $F_X(x_i)$ of the N sampled data x_i. In practice $H(x_i)$ is the number of occurence of magnitude x_i. If c is small enough compared to x_i we can write ;

$$(3) \qquad \frac{F_X(x_i+c) - F_X(x_i)}{c} \approx f_X(x_i)$$

$f_X(x_i)$ is the probability density function of X.

Combination of equations (2) and (3) gives :

(4) $$H(x_i) \approx N.c.\ f_X(x_i)$$

The histogram $H(x_i)$ can thus be assimilated to the probability density function.
If the noise is gaussian, $f_X(x_i)$ takes a gaussian distribution lineshape and from the maximum of the histogram we can calculate the estimated standard deviation by ;

(5) $$\sigma_{exp} = \frac{N.c}{Hmax.\ \sqrt{2\pi}}$$

- where N is the number of analysed data points ;
c, the channel width of the histogram ;
Hmax, the maximum of the histogram.

This method[1] was experimented on a 3D HOHAHA-NOE ^1H spectrum of capsicein, a 98 residus protein, with size 256x256x256 data points. The histogram built (experimental histogram), shown on figure 1.a, shows a good gaussian lineshape (centered on zero and with a σ_{exp} deduced from (5)) in good agreement with a simulated one (figure 1.b), reconstructed with the experimental σ_{exp}. The difference at the bottom of the the curves, is due to the baseline distortion, which represents systematic artifacts in NMR experiments : the data are spread around the zero level. Note that computed histogram of the spectrum after baseline correction is considerably disturbed (figure 1.c). In this example, we have used a baseline correction algorithm which enhances positive peaks versus negative ones. Hence the distribution of the negative datas are tailored toward the mean value. In that case, equation (5) is no longer valid. This displays the sensitivity of the histrogram to any processing on the data.

A direct demonstration of the usefulness of the method is examplified on figure 2.a and 2.b where a 3D cross section along $\omega 3$ has been thresholded at the level $2\sigma_{exp.}$ without lost of information and any manipulations on the contour figure levels.

We have shown that histogram calculation can easily solve automatic evaluation of noise on the entire NMR data set and allows to check the white noise hypothesis of 2D or 3D experiments. The determination of relevant threshold for 2D or 3D contour plot is direct. The method should be able to be extended to non gaussian distribution by fitting the experimental histogram with the expected one and deducing the noise level (in that case equation (5) must be deduced from each distribution).

---

[1] All this work is implemented in the GIFC software developped by Alain Rouh in our laboratory.

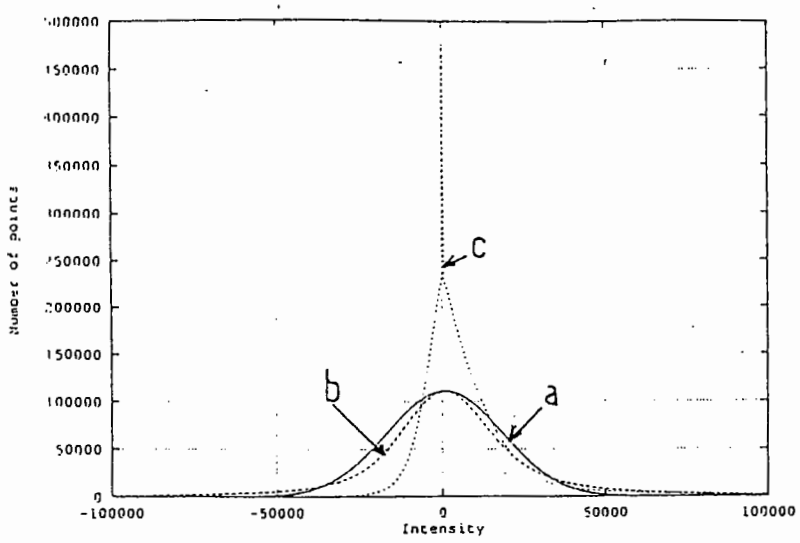
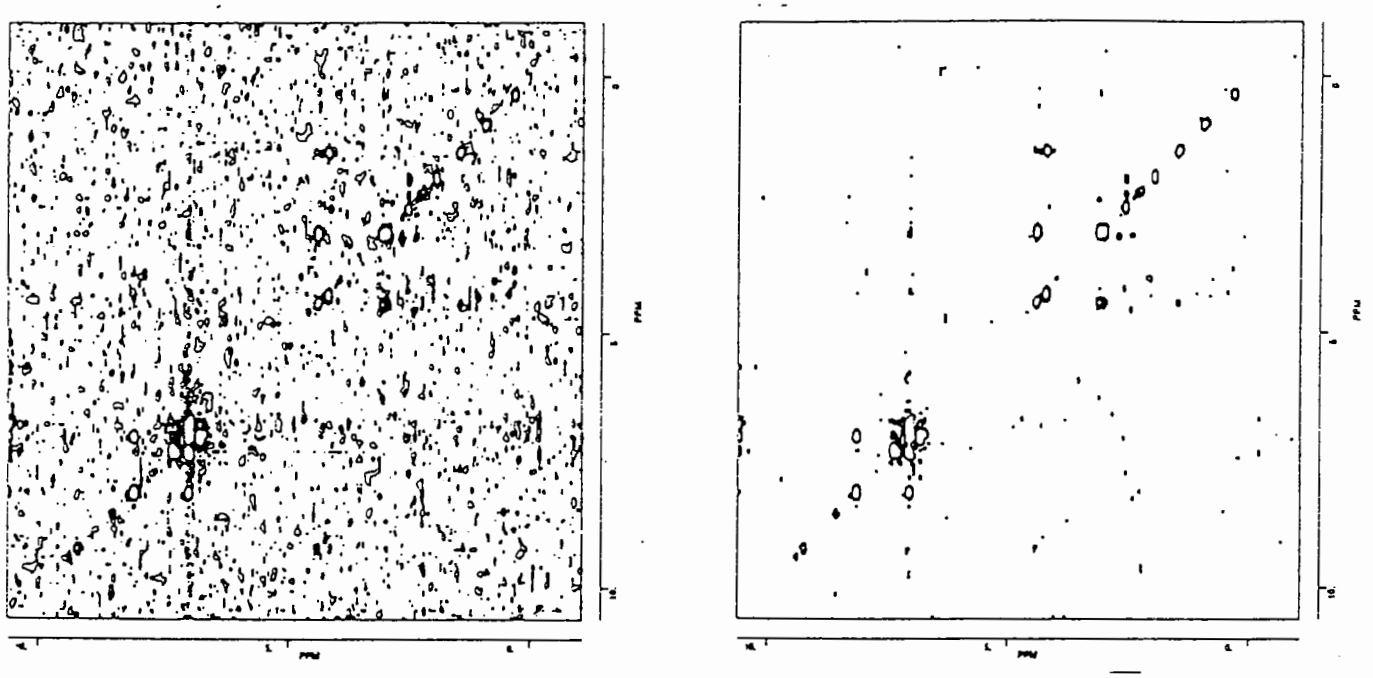


Figure 1 : Histogram on a 3D nmr experiment as described in the text.
a)... experimental histogram on the 3D without baseline correction
b)... simulated histogram from experimental σ and mean value.
c)... histogram on the 3D with its baseline corrected.



a b

Figure 2 : Comparison between the entire plane (a) and the thresholded one (b) of the 3D HOHAHA-NOE on capsicein with a 600MHZ spectrometer.
N=16430948 ; Hmax = 111202 ; C=292.9688 ; σ_{exp}=17269.56

Feb. 28, 1993
(received 3/8/93)

From: Glaxo Inc., Research Institute
5 Moore Drive
Structural & Biophysical Chemistry
Venture Center
RTP, N.C. 27709

Dear Barry,

We enjoyed putting together our first submission to the Newsletter and have entitled it **BAD BAD POINTS AND ANNOYING INTERRUPTS.**

The first problem that we would like to convey deals with off- line processing environments, which are common in many NMR Labs. In our lab we employ Felix 2.0 Beta and were working with a 16 Mbyte triple resonance HNCO dataset from a 15N/13C labeled protein. During examination of the partially processed data it became obvious the data was corrupted with bad points along interferograms in the t2 (13C) dimension (Figure 1a,b). This was determined to be the case in a number of t2 vectors and caused bad F3,F1 planes(t2) like the one illustrated in Figure 1c. At the time we were unsure what caused the bad points; was it the spectrometer, ethernet transfer or host computer introducing the error? Either one was possible, though error checking in the data transfer cast less suspicion on that suspect. Being curious types, we pushed on to diagnose the problem.

Mike began by tracing the location of a few of the bad points by performing inverse transforms on some of the vectors which were clearly afflicted. Each of the 'bad' points had a value of about 262,000, whereas the 'good' data never got over 3,000. The 32 bit integer data from the AMX spectrometer were written out in ascii and easily searched using AWK for data values greater than +/- 5,000. This examination yielded 21 exceptional values, interestingly appearing only in the real part of the data. Later, a more general software tool to examine datasets for corruption was developed. It compares each point with the mean and variance of neighboring points and flags those greater than 4 standard deviations from the mean. When he looked at the bad points themselves, it was easy to see each resulted from a single bit (the 19th) being altered in every case but one. The value of 262,395 or (hex: 00 04 00 fb) for instance, should have really been 251 (hex: 00 00 00 fb). Fortunately, the bad points stuck out like sore thumbs due to the magnitude of the error and were easily corrected with another program to modify individual words in a binary dataset (Figure 1). Corruption in the lower few bits would be undetectable if they approximated the true data values of course, but would likewise have a smaller effect on the spectra.

The closest we got to determining the exact source of the corrupted data was by tracing a path to some bad memory chips on the file server that

received the ethernet transferred data. Others using the file server also experienced corrupted data.

Having repaired the data we moved on to complete the processing with Felix 2.0 beta running on a 35Mhz personal Iris and came up against a subtle problem when using bundle mode processing in the t1 direction. The data were acquired as 512 complex pairs in t3 (NH), 32 complex pairs in t1 (15N) and 32 complex pairs in t2 (13CO). Respectively, a matrix of 512 X 128 X 128 real points was built for zero filled FT'ed data. Data in t3 were sized to 512 points, thus retaining only the low field amides; discrete access mode was employed. The second transform in t1 employed bundle mode processing using the reserved symbol, vector, and the linear prediction (LP) utility as described in the Felix manual. In this dimension we used first and last point linear prediction. Vector's value was 512x128 or 64K operations in our example. The bundle mode executed with ease half the operations, but beyond 32K operations the process slowed to a snail's pace; executing about one operation in 30 seconds. Using the osview utility on the Iris, we could see the CPU's Interrupts value going through the roof. Don Holt, our local Unix guru and network manager, recognized this as a clear sign of attempts of division by zero. Since we chose to size the matrix file to include zero filling in t1, there were zeroes in half the matrix and, evidently, the LP function in Felix can't manage these operations with zeroes in the data record. Therefore, we hard-coded into the macro a bundle loop counter of 32K rather than eliminating the use of LP in the t1 domain. If one would not use LP in this dimension, the symbol vector can be used as described in the manual without performance losses. In the final dimension (t2) the vector variable was reemployed along with LP, since all interferograms were assembled from transformed data vectors and did not have zeroed data values.

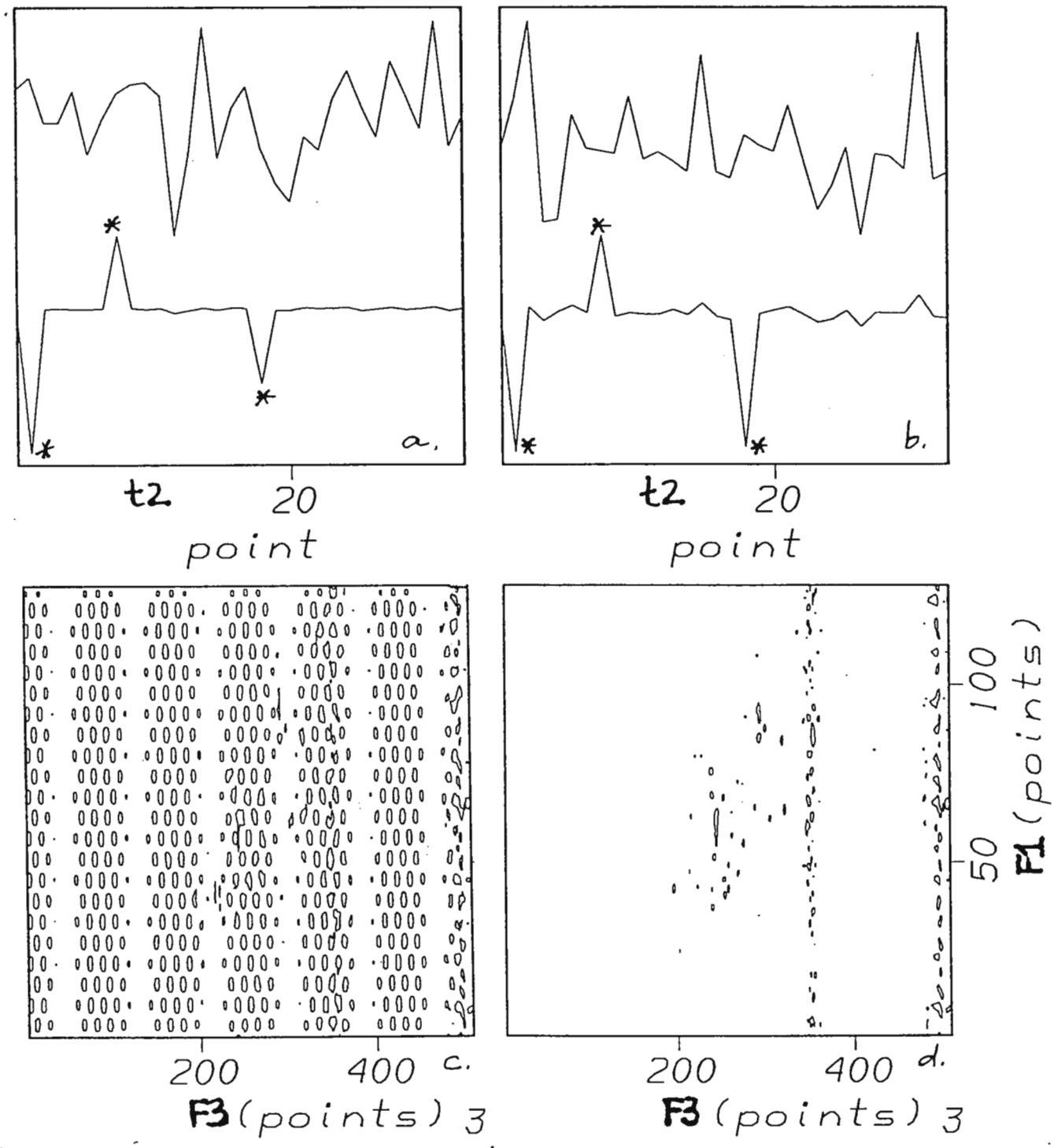
Maybe our description of these problems will assist others in detecting bad points and annoying interrupts when processing data.

Regards,

R.Gampe S.Brown D.Davis D.Holt R.Rutkowske M.Word

Robert Steve Don D. Holt Mike

Figure 1:(a,b bottom) two t2 interferograms containing three bad points (*) of large magnitude; (a,b top) same two t2 interferograms with corrected points as described in paragraph 2; (c) example of an F3,F1 plane (t2) from uncorrected data; (d) same plane as (c) with corrected data. The streak at about point 350 in F3 is an artifact from probe coil vibrations and the one at about point 500 arise from the H2O signal.



TRIAD NMR : Spectra, Spreadsheets, Structures All-in-one!

Now with DIANA and MARDIGRAS+ options

TRIAD NMR is integral to the Tripos Molecular Information Analysis System: Analytical Information Processing, Chemical Information Management, and Molecular Visualization, Design and Analysis combine to deliver an unprecedented approach to structural problem solving. Imagine the ability to simultaneously view spectra, query a 3D database, and create a molecular structure!

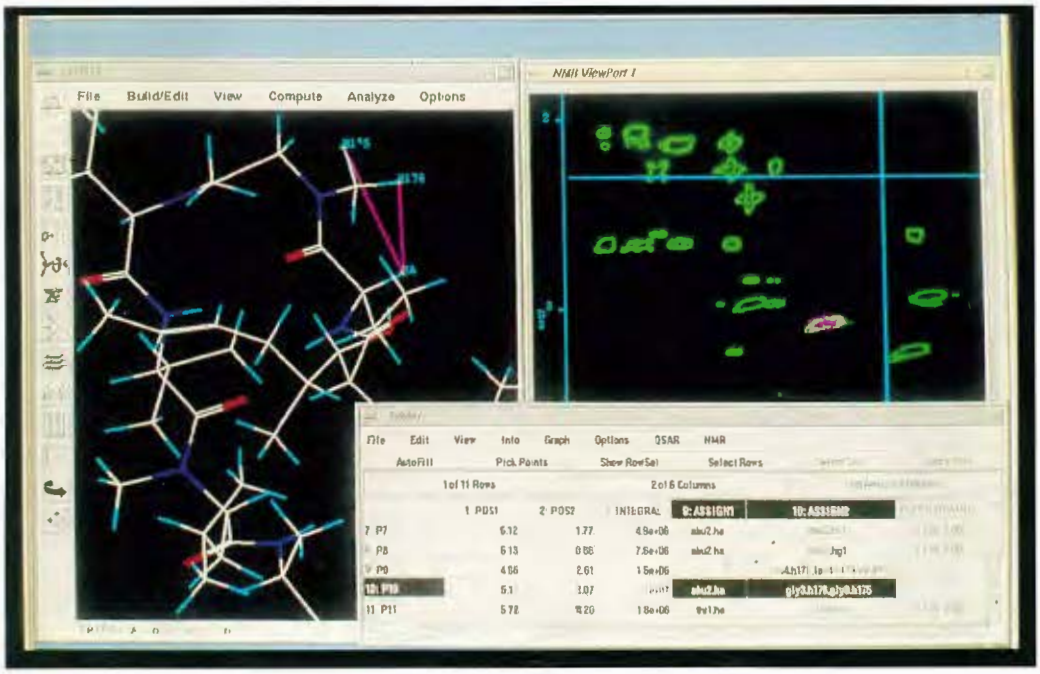
TRIAD NMR can be configured to meet your scientific and budgetary requirements: TRIAD NMR Base for 1 and 2D applications, or TRIAD NMR Advanced for multi-dimensional applications. In each case, the Tripos ***chemactive*** Molecular Spreadsheet facilitates easy data analysis and familiar data presentation.

Why choose TRIPOS?

Now TRIAD NMR delivers the power, flexibility and visualization required for efficient analysis...speeding your progress toward innovative and accurate solutions. TRIPOS provides you with unified and powerful tools to bring new products to market quickly.

Established in 1979, TRIPOS links scientific, spreadsheet and open interface tools to pioneer the field of Molecular Information Analysis Systems. We also set the standard for timely and comprehensive customer support.

A key TRIPOS innovation is our Molecular Spreadsheet, a visual database which helps researchers dynamically analyze and visualize complex scientific data across a broad range of applications.



Simultaneous highlighting in the Molecular Spreadsheet, spectra, and 3D structure reveals shared data points. In this example, ambiguous information is recorded and graphically rendered.

TRIAD NMR

TRIAD NMR *What other vendors can only promise is available TODAY at Tripos!*

TRIAD NMR :
The Molecular Spreadsheet Advantage

Only TRIAD NMR delivers the power of the Molecular Spreadsheet, specifically designed for chemistry applications. Spreadsheet efficiency and logic manage all stages of data analysis with the flexibility and query functions that fuel creative investigation in research.

You can open multiple spreadsheets sequences simultaneously to correlate spectra acquired in complementary experiments, i.e. NOESY, COSY. You can also design and label columns and rows to accommodate desired measurements or calculations specific to your chemistry.

Uses of the Molecular Spreadsheet include:

- generating peak tables with rows that represent 1D or nD cross-peaks and columns that are the resonance attributes (e.g. lineshape, chemical shifts)
- creating, editing, and maintaining accurate list of positive and negative peaks
- automatically generating structural constraints
- performing interactive and automated resonance assignments
- obtaining and identifying stereo-specific assignments

TRIAD NMR :
The Single-point Solution

Only TRIAD NMR melds data management, processing, and analysis into one unified, powerful package. The familiarity of the Spreadsheet format, the easy-to-use dialog boxes, and Recipe Builders for commonly used processing sequences allow operation by either the laboratory technician or the research scientist.

Furthermore, TRIAD NMR ensures computer hardware independence and network compatible processing through the use of distributed graphics, including both GL and high performance X-Window implementation on a variety of platforms.

Data can be transferred via ethernet, BrukNET, high-speed parallel and serial (Kermit) connections from more than 80 instrument/processor configurations. "Point and Click" data conversion programs exist to quickly convert incompatible file formats into a unified data structure. Time required for creating or modifying formats is minimized.

Twenty accurate conformations of hirudin, generated by DIANA, are displayed in SYBYL.

Szyperski et al
J. Mol. Biol.
(1992), 228, 1193-1205.

TRIAD NMR :
State of the Art Spectral Display

TRIAD NMR's design enhances views of the complex details required to obtain qualitatively and quantitatively precise measurements. Instant "rubberband zoom" and "zoom and pan" allow you to quickly zero in on peak location and volume. The "pan" is especially convenient for quickly finding related NMR peaks in different spectral regions.

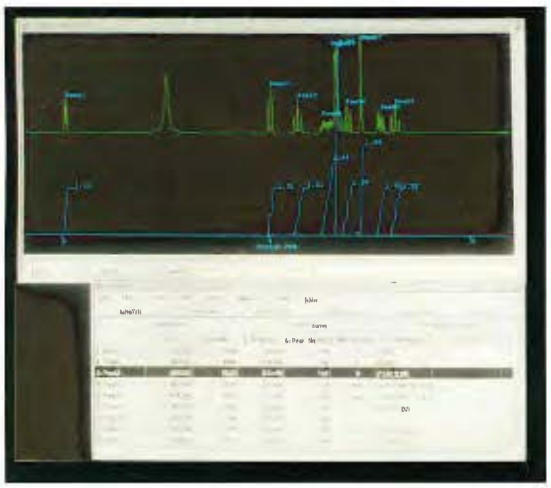
Because TRIAD NMR stores "views" of the display, you only need to generate a contour plot or series of contour plots once. Views can be saved to disk for recall at any time, allowing you to return to any analysis point without recomputation.

TRIAD NMR incorporates quick and easy NOE and ROE spectral simulation for comparison to experimental data and for the back-calculation of structures.

TRIAD NMR :
Comprehensive NMR Analysis

TRIAD NMR, the most comprehensive multi-dimensional data reduction and analysis system available, provides intelligent, automated algorithms for processing and qualifying spectral data. The widely acclaimed and powerful SPL macro language can automate repetitive procedures or provide complex user-defined protocols.

TRIAD NMR includes a variety of interactive data manipulation tools coordinated with a selection of graphics modes suitable for all circumstances. You can direct TRIAD NMR to assign spectra and quickly extract structural information. Spectral simulations and J-coupling analysis are standard. Distance constraints are automatically generated for molecular structure calculations, eliminating the need for time consuming manual entry.



TRIAD NMR's 1D analysis displays normalized intergrals. The Molecular Spreadsheet tracks multiplicity and J-coupling information.

The TRIAD NMR Recipe Builder saves time by storing common processing sequences for re-use.

MARDIGRAS+, developed in the laboratory of Professor T. James, UCSF, quickly refines NOE distances through analysis of a hybrid matrix, reducing the need for multiple NOESY experiments or the reliance on spectra acquired at short mixing times (low s/n.)

TRIAD NMR :
The 3D Molecular Design Advantage

TRIAD NMR is fully integrated with the Tripos SYBYL family of molecular design products, resulting in accelerated throughput of NMR Results to predict 3D molecular structures for simultaneous visualization and analysis. Or its open architecture lets you easily communicate with other modeling programs of your choice.

With TRIAD NMR and SYBYL, you have the unique ability to select (highlight) any row of the Molecular Spreadsheet and simultaneously view the corresponding elements in the spectra as well as the structure. Queries can also originate in either the spectral or structural window to retrieve and highlight the corresponding row(s) in the Spreadsheet.

In SYBYL, you can apply NMR-generated constraints to distance geometry, physical simulated annealing, conformational search, and molecular dynamics routines. Or use the data with COMPOSER protein homology modeling and SYBYL/QSAR activity prediction techniques. SYBYL's premier interactive graphics let you phase spectra and rotate 3D graphics for preferred viewing.

TRIAD NMR : A Scientific Knowledge Base

Within SYBYL, TRIAD NMR can be harnessed with DIANA, developed in the laboratory of Professor K. Wüthrich, ETH, for the quick and accurate calculation of protein conformation from NMR measurements. Much faster than other molecular dynamics and physical simulated annealing processes, DIANA serves as a calculation engine while SYBYL builds and displays the molecules.

Leading NMR scientists collaborated with Tripos to guide TRIAD NMR's development and verify its accuracy. At Tripos, TRIAD NMR is the product of an expert staff of Ph.D. scientists and computer scientists with unmatched experience in the field of NMR. This staff is complemented by an extensive network of field-based Applications Scientists who provide customer support.

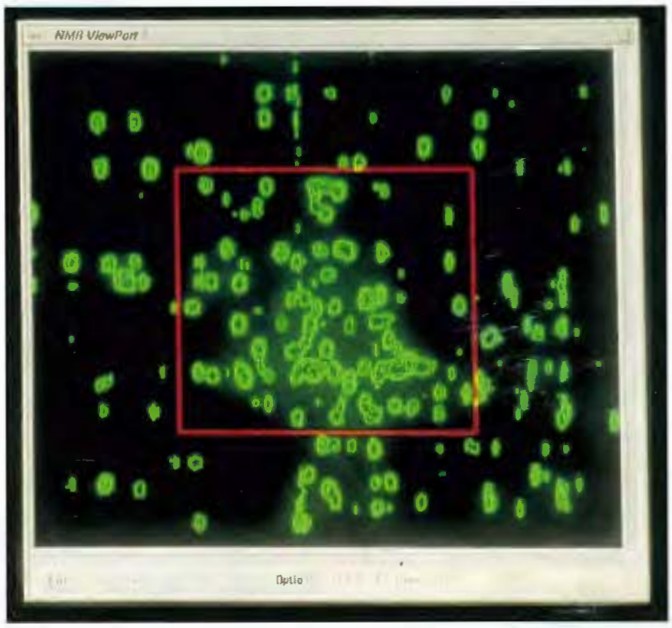
Distinctive support selections for customers include:

- specialized workshops
- structured training courses
- periodic software updates
- an industry-recognized customer hotline

TRIPOS NMR :

Delivering on the promise of tomorrow...today.

TRIAD NMR's graphics capabilities, including rubberband zoom buttons and scroll bars, promote precise and immediate viewing of complex details.



TRIPOS—pioneering Molecular Information Analysis

TRIPOS Associates, Inc.

a subsidiary of Evans & Sutherland

	Phone:	Fax:
•1699 S. Hanley, Suite 303 St. Louis, MO 63144-2913	1 800 323-2960 1 314 647-1099	1 314 647-9241
• Munich, Germany	+49 89 420-03030	+49 89 451-03039
• Palaiseau Z.I., France	+33 1 69 191670	+33 1 69 320947
• Bracknell, UK	+44 344 300144	+44 344 360638
• Rigong International, Inc Korea	+82 2 516-2636	+82 2 516-5362
• Sumisho Electronics Co., Ltd. Japan	+81 3 5228 5525	+81 3 5228 5526
• M &Vactek Corp. Taiwan, R.O.C.	+886 2 7883836	+886 2 7836255

COMMISSARIAT A L'ENERGIE ATOMIQUE

DIRECTION DES SCIENCES DE LA MATIÈRE
DEPARTEMENT DE RECHERCHE FONDAMENTALE SUR LA MATIERE CONDENSÉE

SERVICE D'ÉTUDE DES SYSTÈMES ET ARCHITECTURES MOLÉCULAIRES (SESAM)
Laboratoire des Macromolécules Végétales

(received 2/27/93)

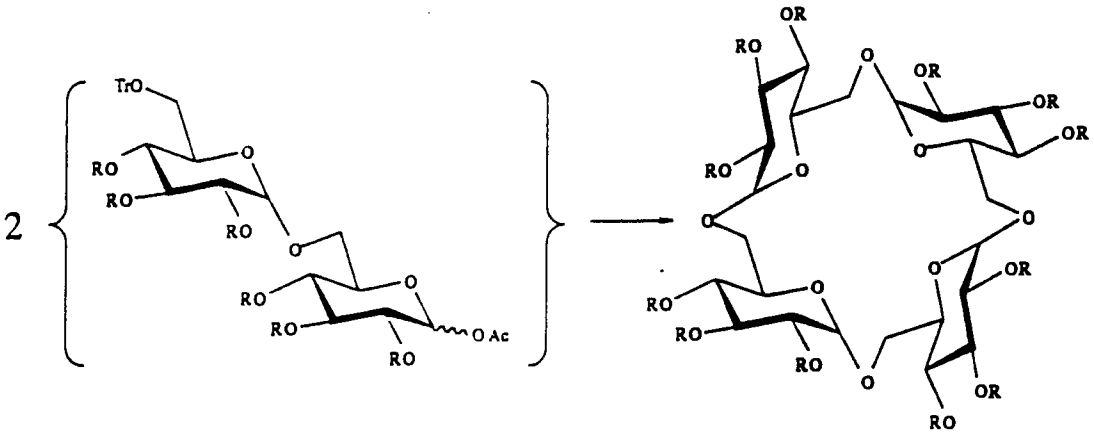
Dr B. L. SHAPIRO
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303
USA

Dear Dr Shapiro,

Local mobility in CDs analogs

Cyclodextrins or substituted cyclodextrins are known to be rigid molecular structures having a hydrophobic cavity able to welcome a variety of neutral molecules.

We have designed a synthesis of cyclo-oligosaccharides, analogs to natural CDs which, on the contrary, could present more structural mobility of the internal macrocycle. The α(1,6) configuration of the glycosidic linkage was chosen for this purpose (Scheme).



Scheme

A low temperature ^{1}H and ^{13}C NMR study of the perbenzylated cyclotetraisomaltoside (CID4Bn) clearly shows the existence of two energetically favoured conformations at 183K for proton (400MHz, Figure Ia) and at 240K for carbon (100MHz, Figure Ib).

More surprising is the fact that this observed mobility seems to be restricted to the C_5-C_6-O_6-C_1 portion of the macrocycle and appears already at room temperature on the 400MHz spectrum as shown by the unresolved doublet of the anomeric proton (H-1, 5.25ppm). The signal is still resolved at 200MHz (Figure II).

Didier Gagnaire Stephan Houdier Philippe Vottéro

CENTRE D'ETUDES NUCLÉAIRES DE GRENOBLE
SESAM/ MV - 85 X - 38041 GRENOBLE CEDEX FRANCE
TÉL. (33) 76 88 38 33 FAX (33) 76 88 50 90

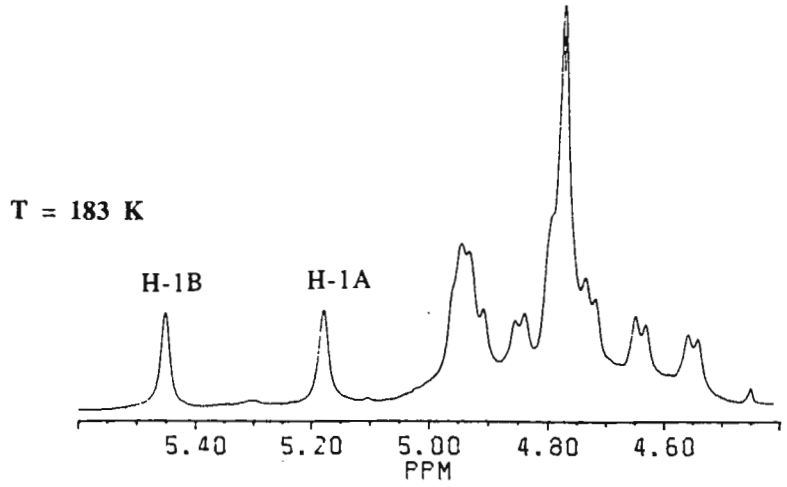


Figure Ia : Proton NMR spectrum of CID4Bn at 400 MHz (aceton-d_6)

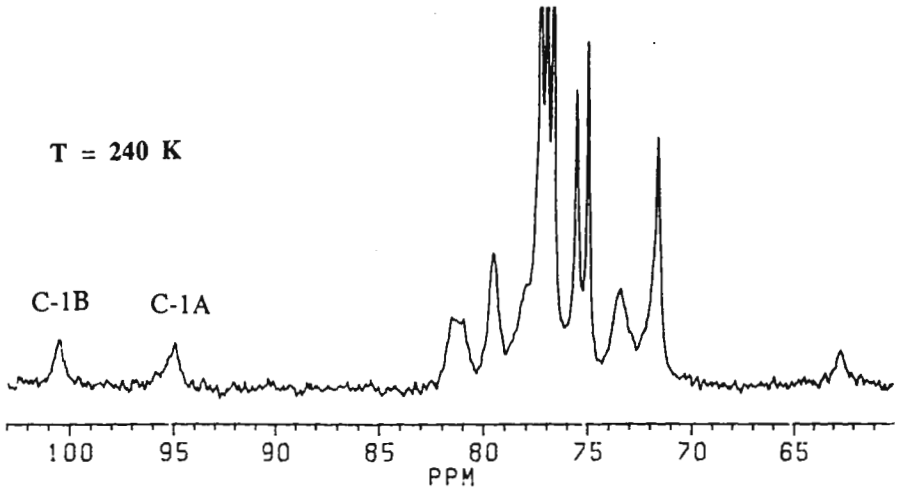


Figure Ib : Carbon NMR spectrum of CID4Bn at 100 MHz ($CDCl_3$)

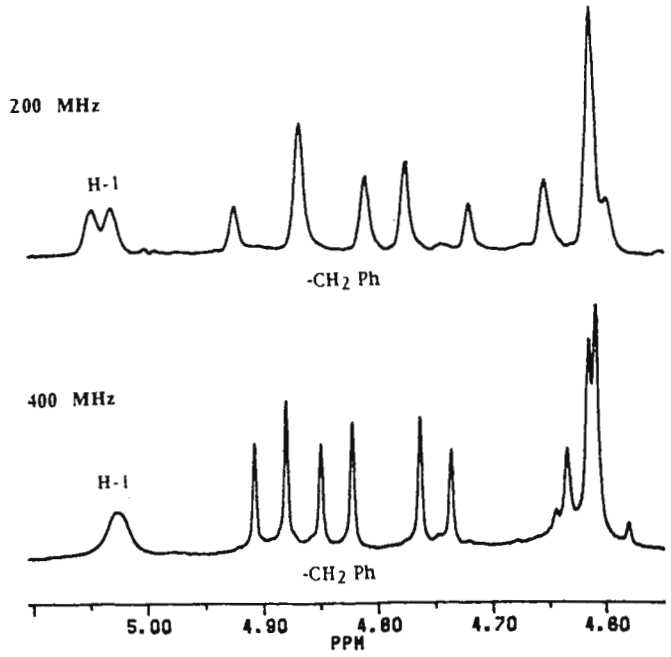


Figure II : Proton NMR spectra of CID4Bn
at 200 and 400 MHz ($CDCl_3$; T = 298 K)

UNIVERSITÀ DEGLI STUDI DI MILANO

Dipartimento di Scienze Molecolari Agroalimentari

DISMA Via Celoria, 2 I-20133 Milano Tel. 02-2663662 /2365029 /2362721

March 11, 1993
(received 3/16/93)

Professor Bernard L. Shapiro
Texas A&M University NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

^{31}P NMR NOESY EXCHANGE EXPERIMENTS TO MEASURE THE AVERAGE LIFETIME OF ANTITUMOR DRUGS IN THE INTERCALATION COMPLEX WITH OLIGONUCLEOTIDES

Dear Barry,

the kinetics of association and dissociation between drugs and nucleotides are usually investigated by fluorescence techniques. It has been shown that even for short oligonucleotides, the association mechanism is very complex. In the case of anthracyclines the slow steps, corresponding to the dissociation, appear to be important for determining the cytotoxicity and the antitumor activity and are more difficult to be analysed by fluorescence techniques.

We have used ^{31}P NMR spectroscopy to study the intercalation complex of daunomycin with the DNA fragment d(CGTACG)[1]. Actually ^{31}P resonances have appeared very sensitive probes for the conformational changes induced in the double helix structure by intercalating molecules[2].

Thus we used the NOE exchange technique to measure the dissociation rate constant of the slow steps for the anthracyclines/d(CGTACG) intercalation process.

Some analogues of daunomycin and doxorubicin (Adriamycin) were examined, including two 3'-desamino-3'-morpholino derivatives, which present an outstandingly potent antimitotic activity in experimental models and 9-deoxydoxorubicin, an analogue endowed with very low cytotoxicity.

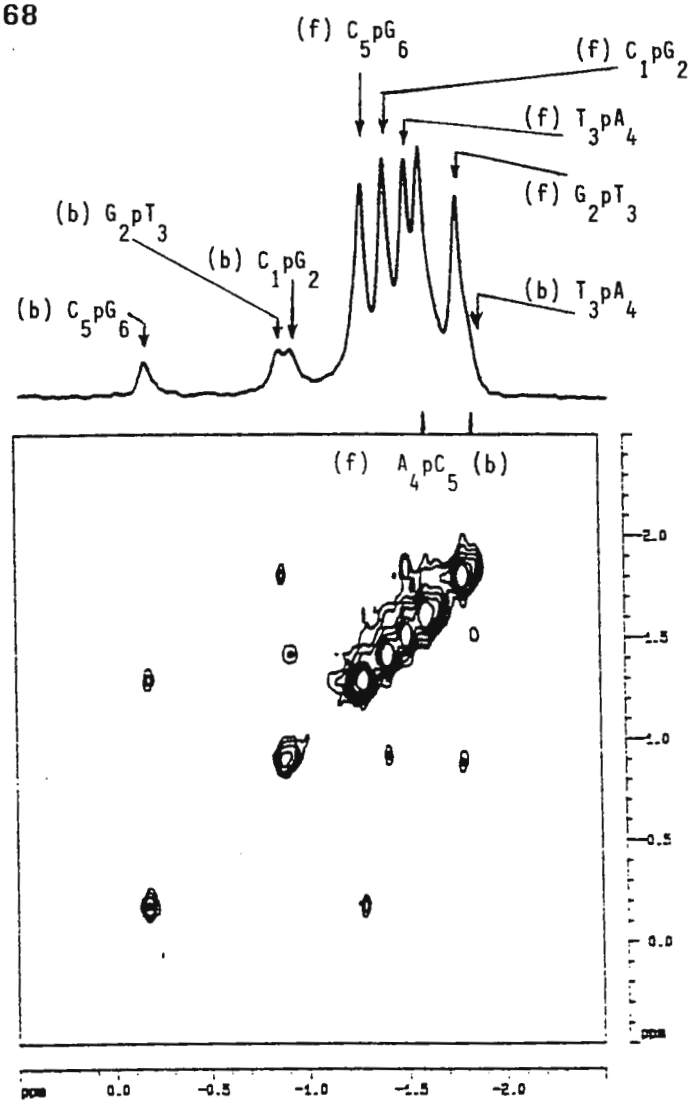
The individual phosphates were assigned, in the free nucleotide, by 2D ^{31}P/^{1}H shift correlation, and in the complex, by following each ^{31}P signals on addition of increasing amount of drug. The new resonances at low field (see Figure), thus attributed to C_5pG_6, G_2pT_3 and G_1pG_2, are connected by chemical exchange to the corresponding signals of the free nucleotide. This allowed to identify the intercalation sites, which resulted to be the same for all anthracyclines, i.e. between the terminal CG base-pairs of the helix (two molecules of drugs per douplex).

The lowfield shift (1.11 and 0.90 ppm for C_5pG_6 and G_2pT_3) indicate significant distortions at these sites as a consequence of the intercalation, while minor local deformations should be experienced by C_1pG_2 ($\Delta\delta$ = 0.47 ppm).

The rate constants were then obtained by quantification of the signal intensities of the NOESY experiments at different mixing times[3].

The average lifetime of the drug in the intercalation site greatly increases for morpholino derivatives ($k_{off} = 2s^{-1}$) compared with the parent doxorubicin ($k_{off} = 15\ s^{-1}$) and daunomycin ($K_{off} = 50s^{-1}$), and can be related to the higher activity found for them. It is also significant that 9-deoxydoxorubicin, which is endowed with very low activity, shows a lifetime so short that the k_{off} could not be measured.

415-68



FIGURE

2D ^{31}P NOESY exchange spectrum at 242.94 MHz of a complex d(CGTACG)/morpholino doxorubicin (Drug/nucleotide ratio = 0.5, NaCl 1M and phosphate buffer in water, pH 6.7, 25.4 °C, τ_{mix} ms) (b) and (f) are the signals of the bound and free phosphates respectively.

Reference

[1] E.Ragg, R.Mondelli, C. Battistini, A. Garbesi, F.P. Colonna, FEBS Letters, 236, 231 (1988).
[2] D.G. Gorenstein and K. Lai, Biochem., 28, 2804 (1989).
[3] R.R. Ernst, G. Bodenhausen, A. Wokaun, Principles of Nuclear Magnetic Resonance in One and Two Dimensions, Clarendon Press, Oxford, 1987.

with our best greetings
sincerely yours

Enzio Ragg
Enzio Ragg

Stefania Mazzini
Stefania Mazzini

Rosanna Mondelli
Rosanna Mondelli

POSTDOCTORAL POSITION

A postdoctoral position is available immediately to study synthetic polymer blends, composites and mixtures by solid state NMR. Some simple polymer synthesis will also be required. Good knowledge of solid state NMR is necessary and basic knowledge of polymer chemistry is preferable. Applicants must have a recent Ph. D. The initial appointment will be for one year and renewable for a second year. The salary will depend on qualifications and will not be lower than Can. $ 23,000/year. Interested candidates should send a resume and the names, phone and fax numbers or e-mail addresses of two or three references to : Prof. A. Natansohn, Department of Chemistry, Queen's University, Kingston, Ontario, K7L 3N6, CANADA. Fax: (613) 545-6669, phone: (613) 545-2008, e-mail: natansoh@qucdn.queensu.ca

Table of Contents, cont'd.

* * * * *

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. 417 (June)----------21 May 1993
No. 418 (July)---------- 25 June 1993
No. 419 (August)---------- 23 July 1993
No. 420 (September)-------- 20 August 1993

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.

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.

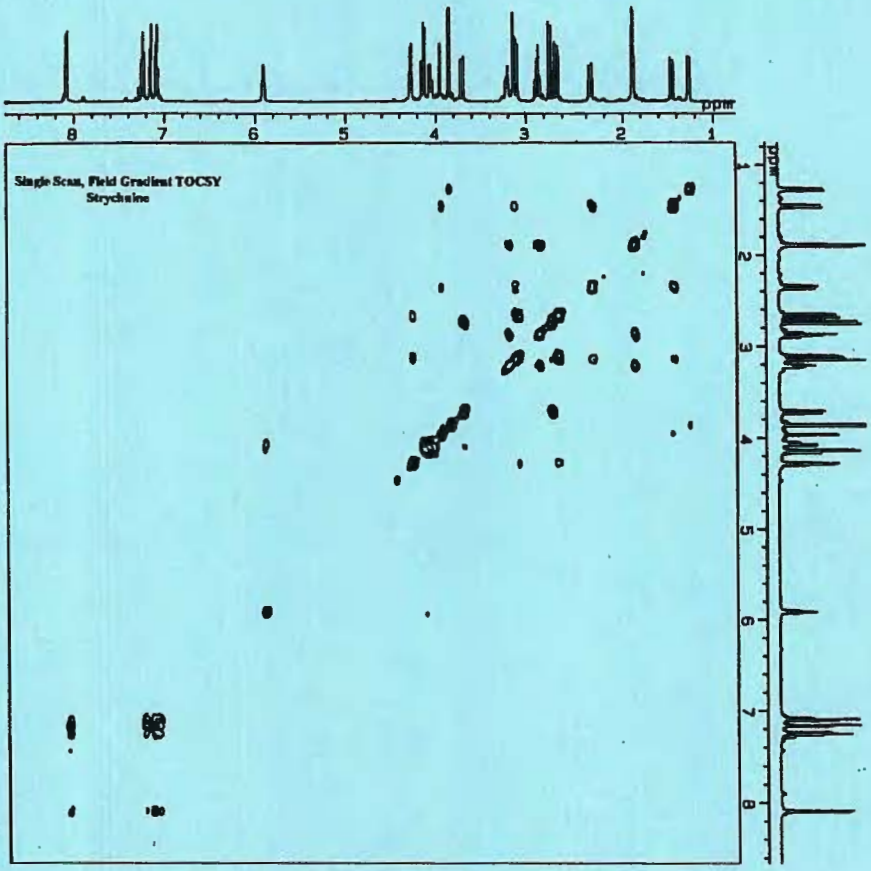
PLEASE **Page Length Instruction**

Attention overseas subscribers: If you must use paper which is longer that 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.

NMR

FROM JEOL USA

Gradient Probes



The above data is a 512 by 512 *TOCSY* spectrum and was obtained on an **Alpha**- 500 in less than 5 minutes with **JEOL**'s gradient probe. This same probe is also designed to do reverse and water suppression experiments. Pulse shaping, three channel operation, dynamic Rf control, matrix shims, as well as unsurpassed field reliability are all standard with the **Alpha**.

ALPHA FIRST IN PERFORMANCE, FIRST IN TECHNOLOGY

JEOL, USA
11 Dearborn Rd.
Peabody, MA 01960
508/535-5900
FAX 508/535-7741

JEOL, NJ
23 E. Brunswick Dr
East Brunswick, NJ
908/254-7028
FAX 908/254-8850

JEOL, CA
3500 West Bayshore Rd
Palo Alto, CA 94303
415/493-2600
FAX 415/493-0581

JEOL, IL
9801W. Higgins Rd Suite 220
Rosemont, IL 60018
708/825-7164
FAX 708/696-2559

JEOL NMR

Soquelec, Ltd.
5757 Cavendish Blvd
Suite 101
Montreal, Quebec
Canada H4W2W8
514/482-6427
FAX 514/482-1929

JEOL, DE MEXICO
Insurgents Sur #953
Col. Napoles
03810 Mexico D.
525/515-2616
FAX 525/515-3261