THE NMR NEWSLETTER

No. 509

February 2001

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PTS 040	.1-40 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$5,330.00 (1 Hz resol., OCXO freq. std.)
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PTS 160	.1-160 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$6,495.00 (1 Hz resol., OCXO freq. std.)
PTS 250	1-250 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$7,440.00 (1 Hz resol., OCXO freq. std.)
Type 1 **PTS 310** Type 2	.1-310 MHz	1 Hz	1-20μs	standard	3½"H×19"W	BCD (std) or GPIB (opt)	1 Hz resol., OCXO: $6,425.00 1 Hz resol., OCXO: $5,850.00
PTS 500	1-500 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$8,720.00 (1 Hz resol., OCXO freq. std.)
PTS 620	1-620 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$9,625.00 (1 Hz resol., OCXO freq. std.)
PTS 1000	0.1-1000 MHz	optional .1 Hz to 100 KHz	5-10μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$11,830.00 (1 Hz resol., OCXO freq. std.)
PTS 3200	1-3200 MHz	1 Hz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$14,850.00 (1 Hz resol., OCXO freq. std.)
PTS x10	user specified 10 MHz decade	1 Hz	1-5μs	standard	3½"H×19"W	BCD (std) or GPIB (opt)	$3,000.00 (1 Hz resol., OCXO freq. std.)
PTS D310	two channels .1-310 MHz	.1 Hz	1-20μs	standard	5¼"H×19"W	BCD (std) or GPIB (opt)	$8,560.00 (.1 Hz resol., OCXO freq. std.)
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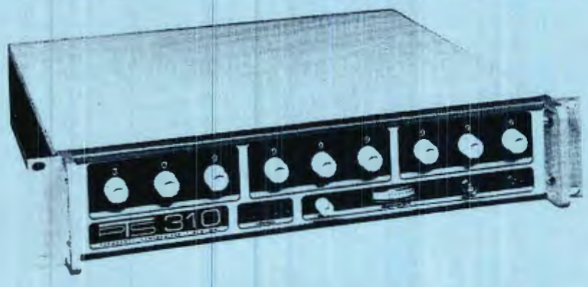

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FORTHCOMING NMR MEETINGS

PITTCON 2001, New Orleans, LA, **March 4-9, 2001**. Contact: The Pittsburgh Conference, Dept. CFP, 300 Penn Center Blvd., Suite 332, Pittsburgh, PA 15235-5503. Tel: 412-825-3220; Fax: 412-825-3224; E-mail: pittconinfo@pittcon.org.

42nd ENC (Experimental NMR Conference), Rosen Plaza Hotel, Orlando, Florida, **March 11-16, 2001**; Arthur G. Palmer, Chair: Agp6@columbia.edu; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87505; (505) 989-4573; Fax: (505) 989-1073; E-mail: enc@enc-conference.org; Web: www.enc-conference.org.

ACS National Meeting, "Symposium on High Resolution NMR Spectroscopy of Polymers, " San Diego, CA, **April 1-5, 2001**; Contact: H. N. Cheng (hcheng@herc.com) or A. D. English (alan.d.English@usa.dupont.com); See Newsletter 505, 29.

Magnetic Resonance in Chemistry and Biology, XIth International Conference, Zvenigorod, Russia, **April 20-27,2001**. Contact: http://www.nmr.de/html/conf/zelino.shtml.

ISMRM 9th Scientific Meeting and Exhibition, and ESMRMB 18th Annual Meeting and Exhibition, Joint Annual Meeting, **April 21-27, 2001**, 10th Annual Meeting of the Section for Magnetic Resonance Technologists, and 17th Annual Meeting of the British Association of MR Radiographers, **April 20-22, 2001** Glasgow, Scotland, UK; Contact: ISMRM, P.O. Box 45690, San Francisco, CA 94145-0690; http://www.ismrm.org

ISMRM 9th Scientific Meeting and Exhibition; ESMRMB 18th Annual Meeting and Exhibition, Joint Annual Meeting. Glasgow, Scotland, **April 21-27, 2001**.Contact: ISMRM Central Office, 2118 Melvia Street, Suite 201, Berkeley, CA 94704. Tel: 510-841-1899; Fax: 510-841-2340; E-mail: info@ismrm.org.

Computational Aspects of Biomolecular NMR, Gordon Conference, "Il Ciocco", Barga (Pisa) Italy, **May 6-11, 2001**. Contact: Michael Nilges nilges@embl-heidelberg.de, or Dave Cast case@scripps.edu.

continued on page 34

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LOCKHEED MARTIN

To: The NMR Newsletter
01/08/2001
(received 01/08/2001)

Optimization of Gradient Selected Phase Sensitive ^{31}P-^{31}P DQF-COSY

NMR Research Lab, Sandia National Laboratories, Albuquerque NM 87185-0888

Barry,

Our laboratory has recently been involved in obtaining high resolution ^{31}P NMR of phosphorous containing polymers and glass composites. It was shown that the ^{31}P-^{31}P connectivity within phosphate backbones could be obtained for Zn-phosphate glass systems that had been dissolved in EDTA containing solutions.[1] In order to improve the resolution in these ^{31}P NMR spectra we investigated the use of gradient selected phase sensitive double quantum filtered (DQF) ^{31}P-^{31}P COSY. Ultimately one wants to optimize the gradient refocussing pulse that is used as a multiple quantum filter in the DFQ-COSY experiment. Unfortunately gradient optimization on the actual samples being investigated proved too time consuming or difficult. Instead it was found that a 50 mM sodium tripolyphosphate ($Na_5O_{10}P_3$), 60 mM EDTA aqueous solution was a perfect sample for optimization of the ^{31}P-^{31}P DQF. Figure 1 shows the 1D ^{31}P NMR spectra for this polyphosphate sample revealing the doublet from the two end-group phosphates (δ = -4.3 ppm), and the triplet arising from the bridging phosphate group (δ = -19.0 ppm). Note there is a small diphosphate impurity species observable at δ = -5 ppm. The inset of Figure 1 shows an expansion for the 1D ^{31}P-^{31}P DQF-COSY experiment with the anti-phase doublet clearly evident corresponding to a J = 18.9 Hz. In Figure 2 the resulting optimized ^{31}P-^{31}P DQF-COSY is shown. Note that the diagonal resonance of the impurity diphosphate group is suppressed. This sample allows the optimization of the DQF experiments in a very short time, and should prove useful for other ^{31}P-^{31}P correlation experiments.

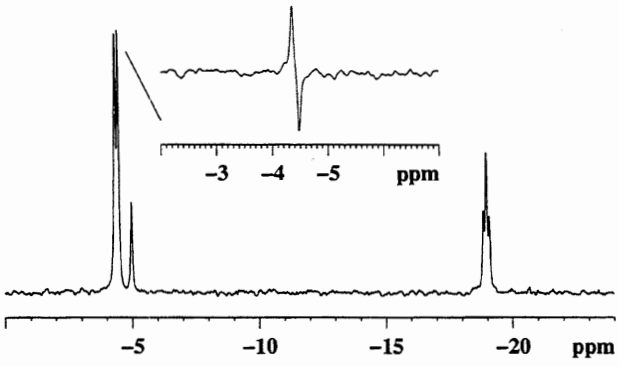

Figure 1

Sincerely,

Todd M. Alam Brad Tischendorf

[1]J.W. Wiench, M. Pruski, B. Tischendorf, J. U. Otaigbe, B. C. Sales, *J. Non-Cryst. Solids*, 263&264 **(2000)** 101-110.

Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy under Contract DE-AC04-94AL85000.

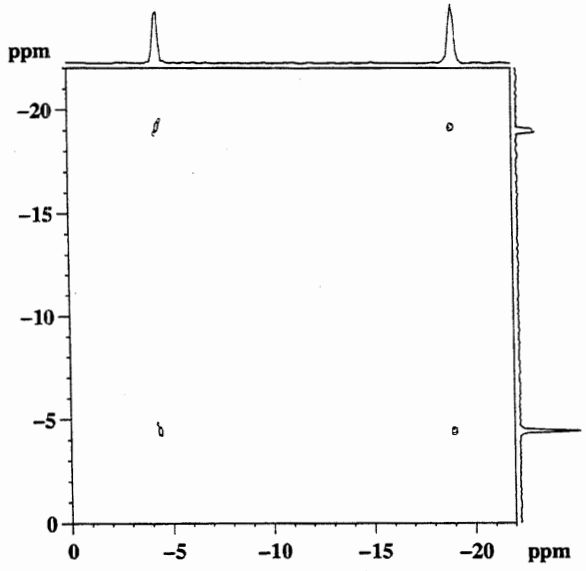

Figure 2

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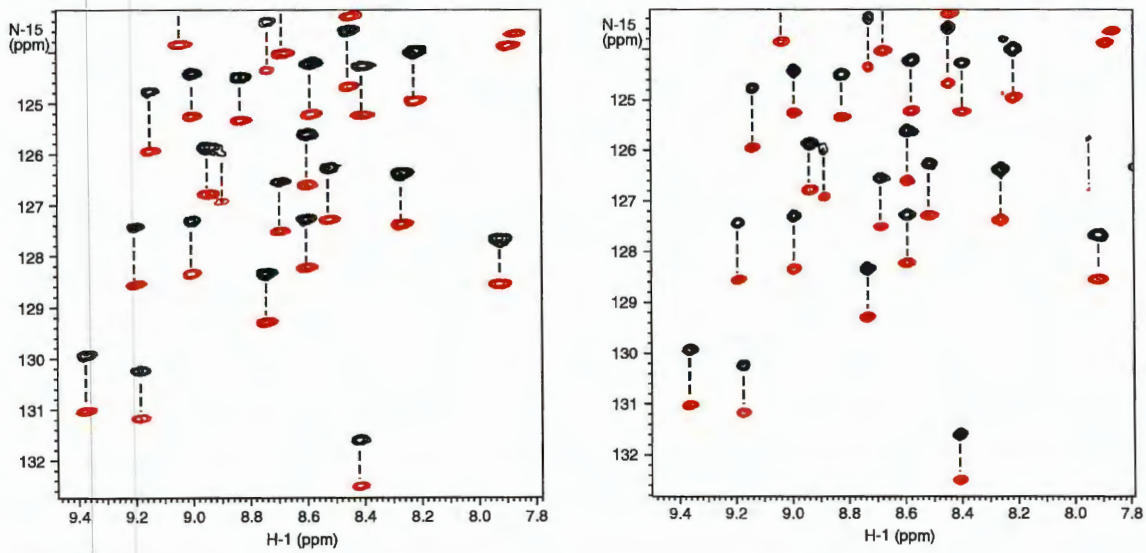
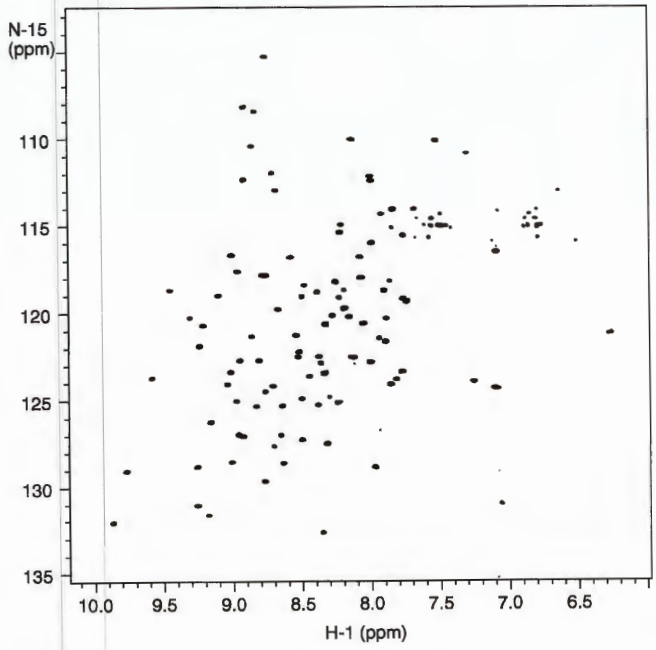


Measurement of residual dipolar N-H couplings at 900 MHz in partially oriented proteins with (right) and without the use of band-selective homonuclear decoupling.

TROSY at 900 MHz



The ^{15}N-^{1}H TROSY correlation spectrum of 6F1 1F2 module pair from the gelatin-binding domain of fibronectin. Sample courtesy of Prof. .I.D. Campbell of Oxford University.

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UNIVERSITY OF ALBERTA

(received 1/11/2001)

Department of Biochemistry
University of Alberta
Edmonton, Alberta
T6G 2H7

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

Stereospecific Assignment of the Methyl Groups of Leucine and Valine using Constant Time {^{1}H, ^{13}C}-HSQC

Dear Dr. Shapiro:

Stereospecific assignments of methyl groups of valine and leucine are an important step in the process of protein structure determination using NMR. These methyl groups make important hydrophobic contacts with other residues that form the core of the protein. Furthermore, stereospecific assignments increase the precision of the entire structure by eliminating the use of large pseudoatom corrections. Neri *et. al.*[1] first pioneered an ingenious technique that utilizes the stereoselectivity of biochemical pathway to selectively ^{13}C label a particular methyl group in leucine and valine. If the microorganism that is expressing the protein of choice is grown in a medium that contains 33% ^{13}C labeled glucose and 67% unlabelled glucose, stereoselectivity of biosynthetic pathway and the law of probability govern that if the *pro*-R methyl group is ^{13}C labeled, there is a 99% chance that the adjacent carbon atom is also ^{13}C labeled. On the other hand, if the *pro*-S methyl group is ^{13}C labeled, there is only a 1% chance that the adjacent carbon atom is ^{13}C labeled. Figure 1 illustrates the pairs of non-random labeling pattern that can result from fractional ^{13}C-labeling.

Traditionally, these stereospecific differences in labeling patterns between the pairs of methyl groups are visualized with a conventional {^{1}H, ^{13}C}-HSQC, in which the crosspeak corresponding to the *pro*-R methyl group is a doublet with a splitting of 33Hz in ω_1 frequency axis. Here, we report an alternative way of visualizing these differences using constant time {^{1}H, ^{13}C}-HSQC. In constant time {^{1}H, ^{13}C}-HSQC, the phase of a methyl crosspeak is determined by the number of ^{13}C atoms attached to the methyl group. Thus, if a crosspeak corresponds to a *pro*-S methyl group in the protein, its phase in the CT-HSQC of the fractional ^{13}C-labeled version of the protein will be opposite to the phase of the same crosspeak in the CT-HSQC of the fully ^{13}C-labeled version of the protein. On the other hand, the phase of a crosspeak corresponding to a *pro*-R methyl group would not change as we go from fractionally ^{13}C-labeled biosynthetic protein to 100% ^{13}C-labeled protein. This concept is illustrated using constant time {^{1}H, ^{13}C}-HSQC of C-terminal domain of cardiac troponin C, shown in Figure 2. It is interesting to note that in these spectra, the crosspeak corresponding to Cδ1, Hδ1# of leucine 121 (a *pro*-R methyl group) is overlapping with the crosspeak corresponding to Cδ1, Hδ1# of leucine 117 (a *pro*-S methyl group). In the conventional {^{1}H, ^{13}C}-HSQC, the doublet of L121.Cδ1,Hδ1# is covered up by the L117.Cδ1,Hδ1#

crosspeak, making its visualization slightly more difficult. However, in the constant time {^{1}H, ^{13}C}-HSQC of the same sample, it is not difficult to tell that one methyl group is *pro*-R while the other is *pro*-S since the two peaks practically cancelled each other out in the constant time {^{1}H, ^{13}C}-HSQC spectrum.

Yours Truly

Xu Wang **Dr. Leo Spyracopoulos** **Dr. Brian D. Sykes**

email: brian.sykes@ualberta.ca

Reference:

1. Neri *et. al.*, *Biochemistry*, **28**(1989), 7510-7516.

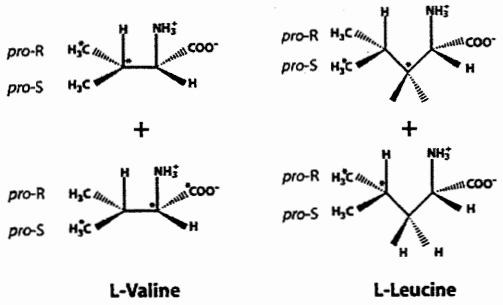


Figure 1. The 2 types of valine and leucine that can be produced as a result of fractional 13C labeling. The asterik indicate that the atom is ^{13}C-labeled.

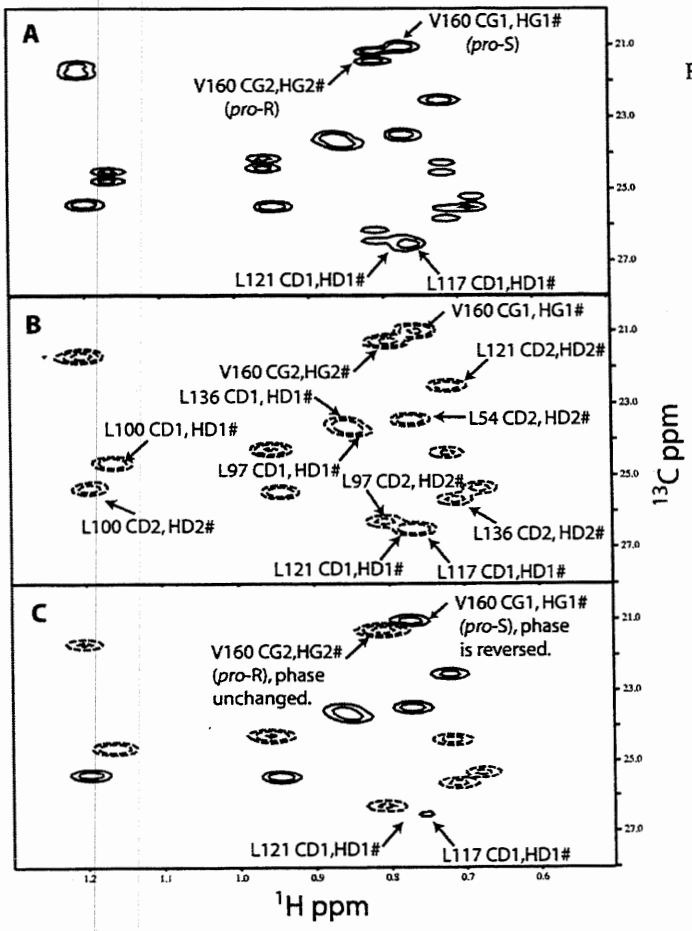
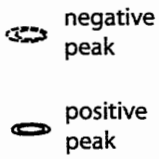


Figure2. Comparisons between {^{1}H, ^{13}C}-HSQCs of C-terminal domain of cardiac troponin C. A) conventional {^{1}H, ^{13}C}-HSQC, B)CT-HSQC of full ^{13}C-labeled protein, C) CT-HSQC of fractionally ^{13}C-labeled protein. Note the canceling of L117.CD1, HD1# crosspeak with L121.CD1, HD1# crosspeak in CT-HSQC of fractionally ^{13}C-labeled protein.



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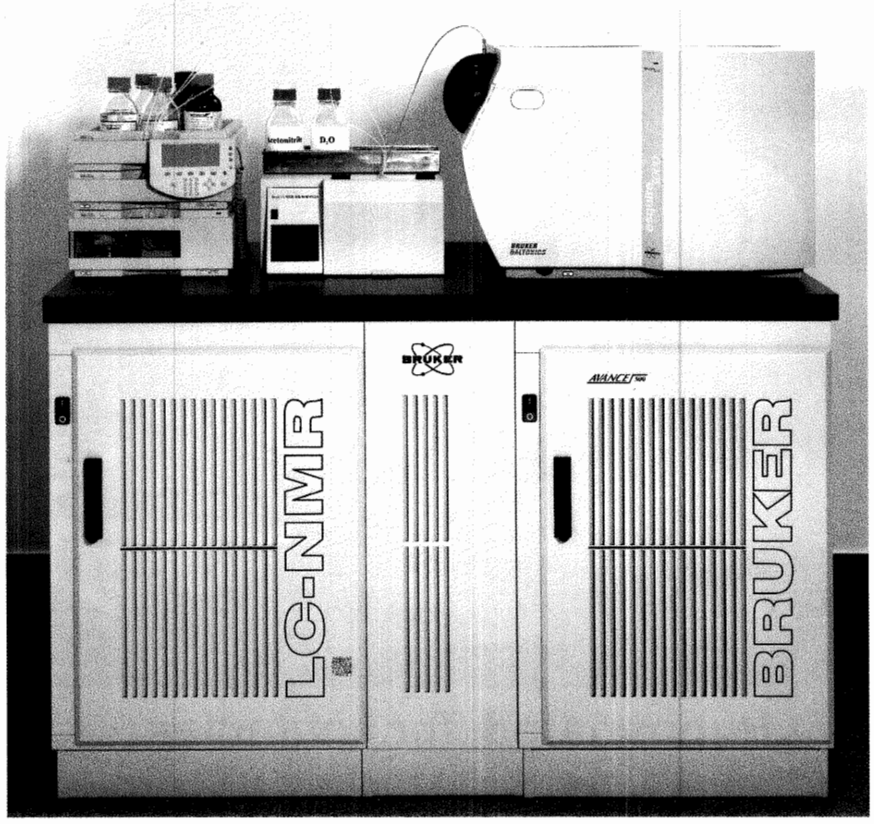

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DAVIS, CALIFORNIA 95616

(received 1/18/2001)

Professor Barry Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto CA 94303-3410

RE: Respiratory Gated Mouse Images With New Bruker Biospec

Dear Professor Shapiro,

We recently completely upgraded our 7 Tesla/183mm bore scanner. This involved replacing the entire instrument except for the magnet. The old General Electric NMR console, probes, shims, and gradients were discarded and replaced with a Biospec console and probes, shims, and gradients purchased from Bruker. We would like to report that we have been very happy with the quality of the images produced by the new Bruker Biospec, the speed of data collection and processing, and the ease of use of the Paravision software. An additional benefit has been Bruker's respiratory gating capability, handled by the PhysioTool module in Paravision.

As a test of the respiratory gating we collected spin-echo images of a normal mouse abdomen, using Bruker's 35 mm diameter 10-slot birdcage resonator and G0-60 mm microimaging gradients. Figures 1A and 1B compare identical non-gated (A) and respiratory gated (B) images of the mouse abdomen; motion artifacts are pronounced (as expected) in A but nearly eliminated in B. Image C shows a longer respiratory gated scan (NEX=8) of the abdomen with the slice position through the mouse kidneys. The image quality and S/N is excellent. The image was collected with just a 1 mm slice thickness and a matrix of 512 points over a 2.5 mm FOV, clearly showing excellent internal anatomical detail of the kidneys. Renal cortex, medulla, and blood vessels are seen. Gray and white matter of the spinal cord can also be readily distinguished.

Sincerely,

Kazutaka Yamada
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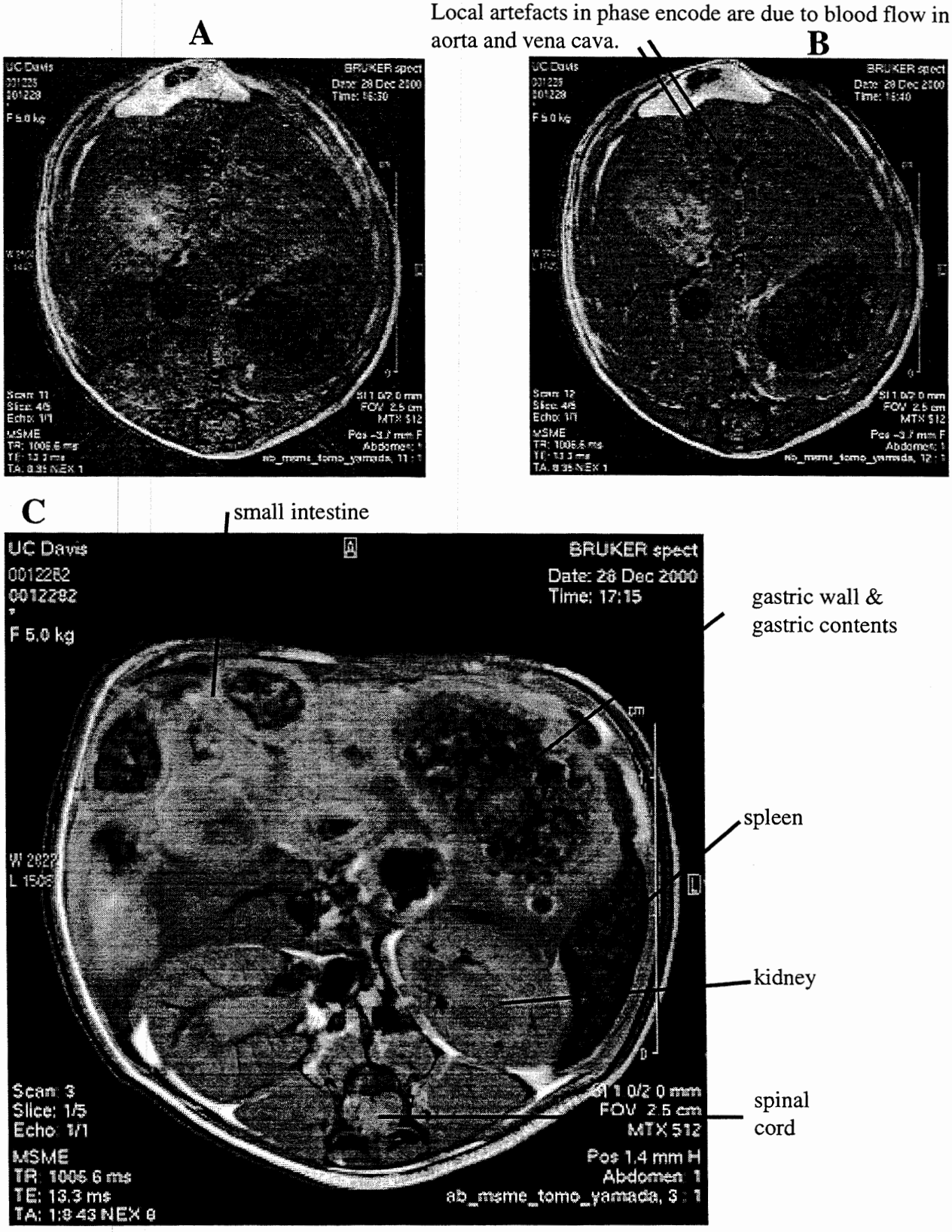

Figure 1: Spin-echo images of mouse abdomen at 7 T on a Bruker Biospec. (**A**) Collected with no gating, NEX=1, (**B**) with gating, NEX=1, (**C**) with gating, NEX=8. All data collected with FOV=2.5 cm, slice=1 mm, 512*512 points, TR=1s, TE=13 ms.

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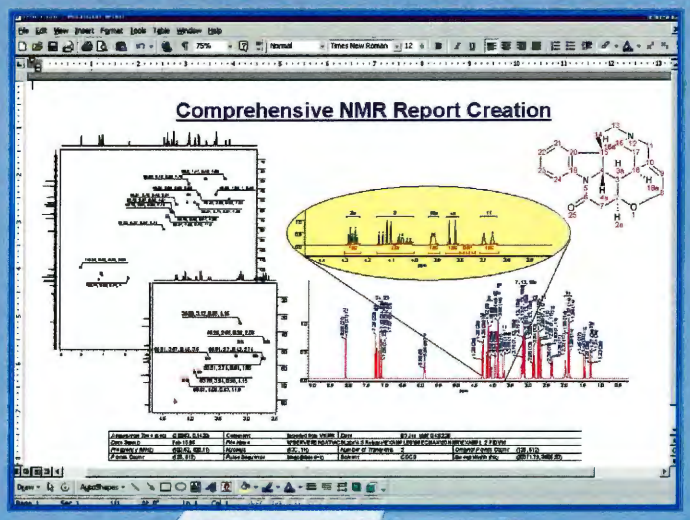

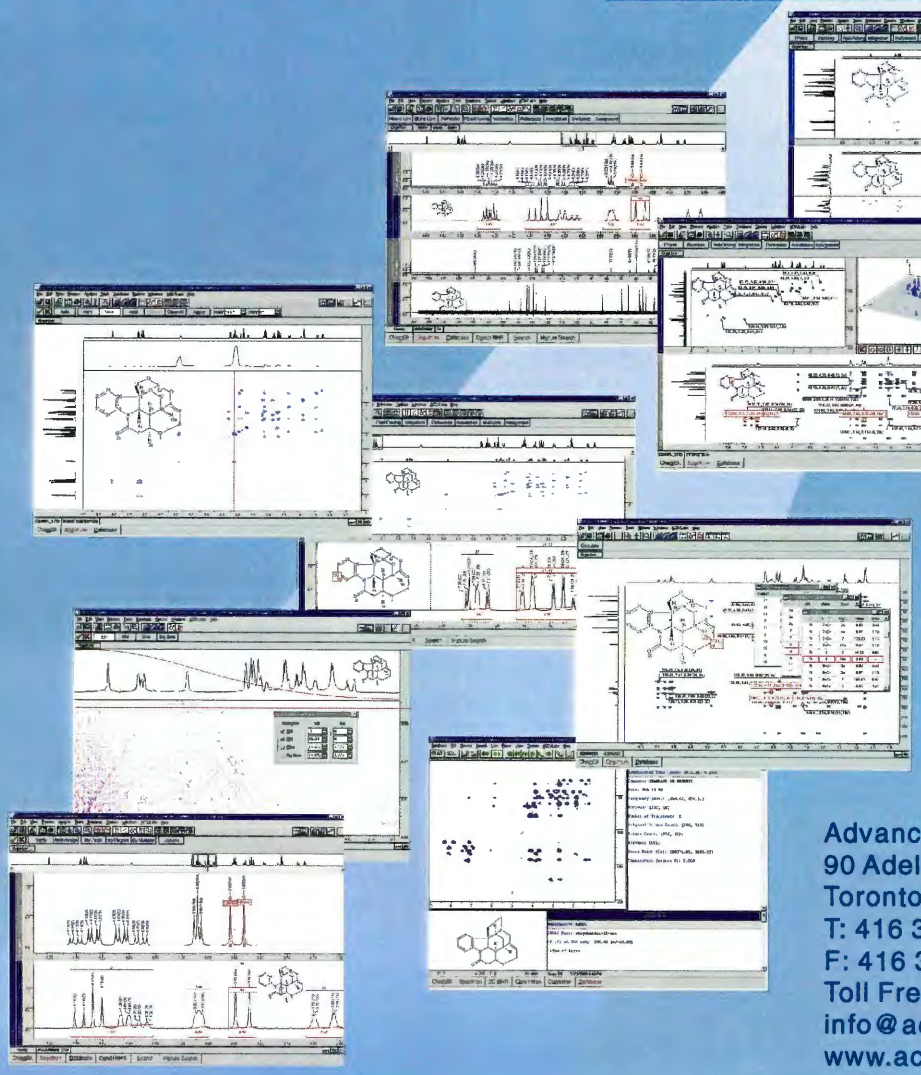

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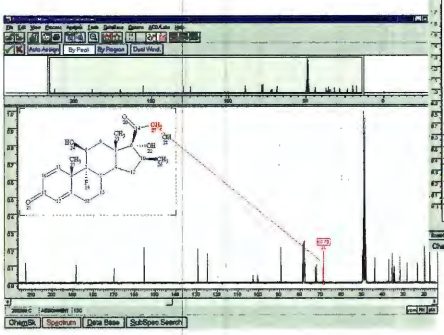

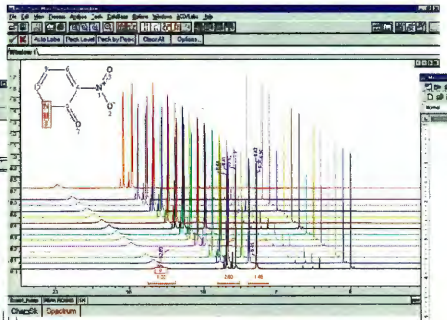

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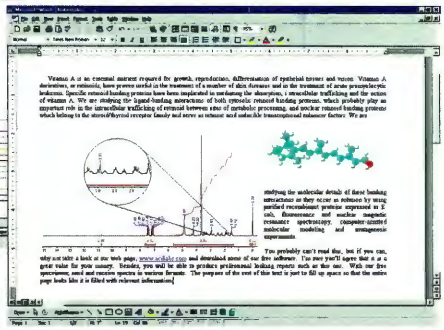

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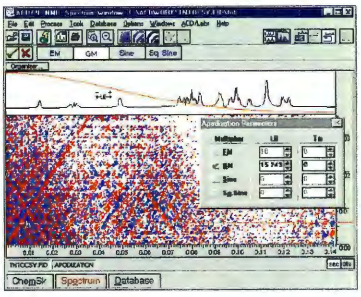

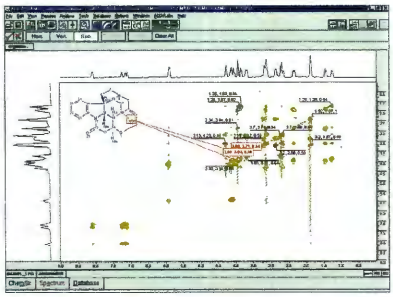

Assign 2D spectra to structures

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(received 1/19/2001)
January 8, 2001

Gadolinium Enhanced MRI of Matrix Formation in Cartilage Treated with Therapeutic Agents

Dear Barry,

We have been hard at work looking into the effects of ibuprofen and aspirin on the growth of cartilage in a hollow-fiber bioreactor (HFBR) system [4] which is NMR-compatible. We are interested in the subject because a variety of therapeutic agents are currently used in clinical practice to ease pain and swelling in patients suffering from osteoarthritis (OA). These agents, however, have been shown in cell culture to damage cartilage. We found in the literature that NSAID (non-steroidal anti-inflammatory) drugs have been found to deplete important molecules in the cartilage extracellular matrix (ECM), the tissue surrounding cartilage cells (chondrocytes) [1-2]. Clinical studies to correlate the use of NSAID's with the progression of OA do not give any definitive answers [3]. Two-dimensional culture studies have looked at these effects, but do not allow for the study of the diffusion of therapeutic agents into three-dimensional cartilage. MRI and the HFBR system are perfect for these studies because we can look at three-dimensional cartilage in a non-invasive fashion.

We isolated chondrocytes from the sterna of 16 day-old chick embryos and then injected them into a HFBR, a sealed glass tube of 5 mm diameter that provides a chamber for cell growth. The bioreactor contained six porous fibers and was continuously supplied with tissue culture medium (TCM) to which we added ibuprofen (35 μg/ml) or aspirin (180 μg/ml). Images of control and treated cartilage were taken at four weeks after inoculation. MRI microscopy experiments were performed on our microimaging equipped Bruker DMX spectrometer operating at 9.4T.

We found that ibuprofen drastically reduced the amount of tissue that grew both directly around each fiber ("tissue layer") and in the parenchymal space between fibers ("parenchymal layer"). Figure 1 and 2 show T_1 weighted, gadolinium enhanced images of cartilage grown in the presence and absence of ibuprofen, respectively. The extracellular matrix in the control image appears dark due to the exclusion of Gd-DPTA. This can be quantified in terms of matrix fixed charge density (Table 1) [5]. In general, the ibuprofen FCD values were lower than both aspirin and control. Aspirin values were also lower than control. None of these, however, reached statistical significance except for the ibuprofen parenchymal value which was significantly lower than control ($p<0.05$).

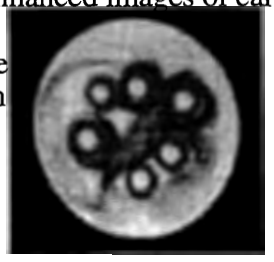

Figure 1

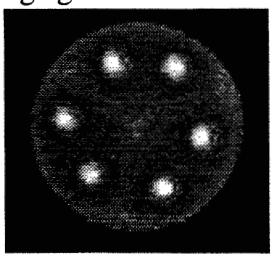

Figure 2

	MT Tissue	MT Parenchymal	MFC Tissue	MFC Parenchymal
Control	0.56 ± 0.11*	0.73 ± 0.12@	-110.61 ± 33.66	-133.48 ± 44.03^
Ibuprofen	0.40 ± 0.22	0.27 ± 0.16@	-44.69 ± 5.14	-24.13 ± 8.55^
Aspirin	0.14 ± 0.13*	N/A	-89.31 ± 15.6	-82.80 ± 16.06

Above: (*, @, ^ indicate p<0.05 within columns).
Table 1. Magnetization Transfer (MT, k_m, s^{-1}) and Matrix Fixed Charge Density (MFC, mM) values for bioreactor cartilage grown in presence of aspirin and ibuprofen.

The trend for the FCD values can be appreciated qualitatively. In the T_1 weighted images shown on the previous page both the tissue and parenchymal layers appear brighter for ibuprofen than for control. In both images the fiber lumens appear bright due to the perfusion of gadolinium through the bioreactor system.

We also found other interesting quantitative trends. The MT k_m tissue value for aspirin, for example, was lower than that for both control ($p<0.5$) and ibuprofen (NS). Ibuprofen was slightly lower than the control (NS). The MT k_m parenchymal value for aspirin was not calculated due to a small sample size.

We can conclude from the images and values that ibuprofen seems to decrease chondrocyte proliferation and leads to a drastic reduction in tissue growth.

Previous studies have shown that MT results are sensitive to the collagen content of the tissue [5]. The reduced FCD suggests that there is a decrease in cartilage proteoglycan. These two results combined indicate that both aspirin and ibuprofen affect the two major components of the extracellular matrix in a three-dimensional culture system.

These interesting results suggest that therapeutic agents may damage cartilage in various ways. Further studies with other drugs including COX-2 inhibitors are currently underway. These, along with more clinical data, may influence how clinicians decide to treat patients with symptomatic OA. This knowledge may help physicians treat the symptoms of OA without furthering the progression of disease.

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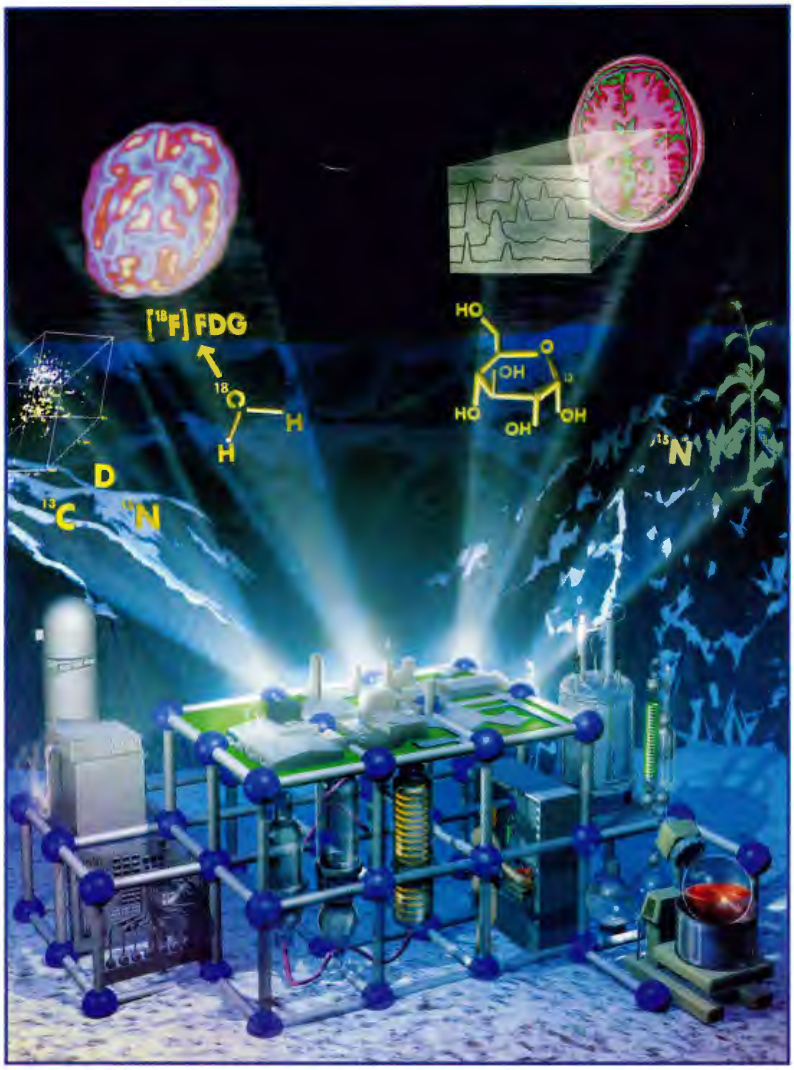

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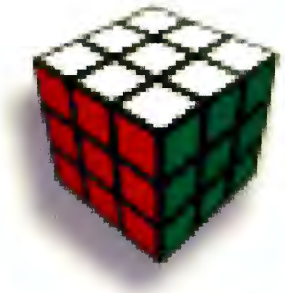

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(received 1/9/2001)

January 4 2001

Surface Area measurements of porous materials with Laser-Polarized Xe NMR

Dear Barry,

Holiday greetings to you, and many thanks for another colorful present. Despite your desire to go electronic in the new millennium, I'll stick to paper once more as its quicker than getting my signature scanned in!

I have been in the process of moving my collaborative research here in Boston from Brigham and Women's Hospital to MIT, where it appears they have magnets they want me to fix and make work! In the meantime, I will tell you a little of some work we had done previously at Brigham and Women's Hospital, in collaboration with some lung physiologists over there. It sprung from the desire of Sam Patz and myself to look for a useful contribution from inhaled laser-polarized gas NMR over and above the pretty pictures that the radiologists make of human lungs. (Although, it must be said, they do make extremely impressive images of the human lung structure using this technique of imaging the inhaled gas.)

I had been using PGSE-style measurements of the time-dependent diffusion coefficient ($D(t)$) of Xe gas in model porous media to determine surface-area/volume (S/V) ratios of the enclosing sample. This spun off into the idea of looking at S/V ratio in lung tissue, after discussions with Jim Butler from the Harvard School of Public Health, and George Topulos, an anesthesiologist at BWH, both lung physiology experts. They impressed upon us the need for such a non-invasive measurement to study lung function, and the inability of any current technique to provide this information. We had originally thought of applying similar diffusion-style experimental techniques in the lung, to derive such information. However, as I showed in my last letter to you (May 2000) problems with the PGSE narrow pulse approximation, in the case of gas-phase diffusion measurements, can lead to misleading $D(t)$ results in the short-diffusion-time regime, the area which provides the S/V data. In human lungs, the need to use the gas at atmospheric pressure, rather than elevated pressures, and the low-gradient strength provided in clinical scanners (2 - 4 G/cm), would serve to both increase the time of the diffusion encoding pulse and increase spin movement during this pulse. This would simply enhance any problems already seen in model porous systems when trying to accurately derive S/V from $D(t)$ measurements in this length-scale regime.

Jim Butler instead came up with a novel idea, using the fact that the Xe is reasonably soluble in tissue, and very soluble in lipid-phases in general. We would monitor the rate of xenon exchange into the tissue, and, having made some other characterizations, be able to back out the S/V from the rate of exchange. It was a very simple yet elegant solution, and one which certainly reduced the complexity of the NMR experiment required. However, being mostly chemists and physicists, we wanted to test the technique on model samples first, rather than diving straight into a human sample. Besides, access to research spectrometers is much easier than human scanners, and since grad school, the appeal of doing research at 3am is fading!

Sam made contact with Porex Corporation, in Atlanta, GA, who provided us with ideal test samples. They supply polyethylene granulate materials for a wide range of uses including filtering, wicking and chromatography. The sample is essentially a "plastic rock" - granules of polyethylene compacted and fused together to give what looks like a lump of solid polyethylene, but has a porosity of 40-50%, with pore sizes ranging from tens to a few hundred microns. Polyethylene is also very soluble for Xe, so provided us an ideal test sample.

The NMR experiment relied not only on the fast exchange of Xe from the gas phase into this polymer sample, but the fact that the highly-polarized (1% polarization - 3 orders of magnitude above thermal equilibrium) allowed us to see this exchange in a very short time period. The experiment was essentially a simple saturation recovery experiment of the type first year grad students use to measure T_1. The saturation pulses were shaped to selectively saturate the dissolved phase Xe signal (200 ppm downfield from the gas resonance) while leaving the gas signal almost untouched. A variable delay time would permit diffusion of laser-polarized Xe spins into the polymer sample, after which time the observation pulse would let us monitor this exchange. Instead of an exponential buildup of signal, however, the signal increased as a function of $\sqrt{t}$.

Jim derived the following equation, valid at short times, to link the xenon signal as a function of $\sqrt{t}$ to the S/V of the sample (1):

$$\frac{N_{diss}(t)}{N_{gas}(t=0)} = \frac{b}{\phi}\frac{S}{V}\sqrt{\frac{4D_{diss}t}{\pi}}$$

where $N_{diss}(t)$ is the number of dissolved phase Xe atoms at exchange time t (~ dissolved phase signal $S(t)$), $N_{gas}(t=0)$ is the original number of xenon gas atoms at time 0 (monitored by an initial low-flip angle pulse on the gas resonance before the saturation experiment), and b, ϕ, and D_{diss} are the partition coefficient for xenon in the material, the porosity of the sample, and the xenon dissolved phase diffusion coefficient, respectively. These latter three parameters were derived separately using thermally-polarized xenon in sealed samples of the polyethylene granulates, at elevated pressures. In the case of lung studies, ranges for some of these parameters are well known, while others (such as D_{diss}) would need to be evaluated *ex-vivo*.

An example series of spectra from one such experiment is shown in Fig.1. The spectra have all been normalized to keep the gas-phase signal at 0 ppm constant. This accommodates the principle that the gas phase provides an infinite sink of xenon for exchange, while in reality the laser-induced enhanced polarization is actually decreasing with time due to T_1 decay and RF depletion, as well as exchange itself. A series of Xe signal buildup curves for four different polymer samples is shown in Fig. 2. Fig. 3, a table, lists the derived S/V values for each sample, along with those we measured separately using confocal microscopy. The NMR and microscopy measurements agree reasonably well, but both differ markedly from the manufacturer's specifications. This is not surprising, as their data is derived from mercury intrusion porosimetry, a method that is known for being more indicative of pore-throat size than pore size itself.

This work is being readied for publication in *Phys Rev E.*, and we are making plans to apply the technique to animal models, and eventually humans. We note that a similar method has been used by the Virginia group to monitor gas-phase signal loss in animal lungs as a function of Xe exchange into tissue (2).

Best Regards,

Ross Mair, writing for Sam Patz Jim Butler George Topulos Ron Walsworth

1. R. Mair, S. Patz, J. Butler, D. Hoffmann, G. Topulos, R. Walsworth, 8th ISMRM, # 2190, Denver (2000).
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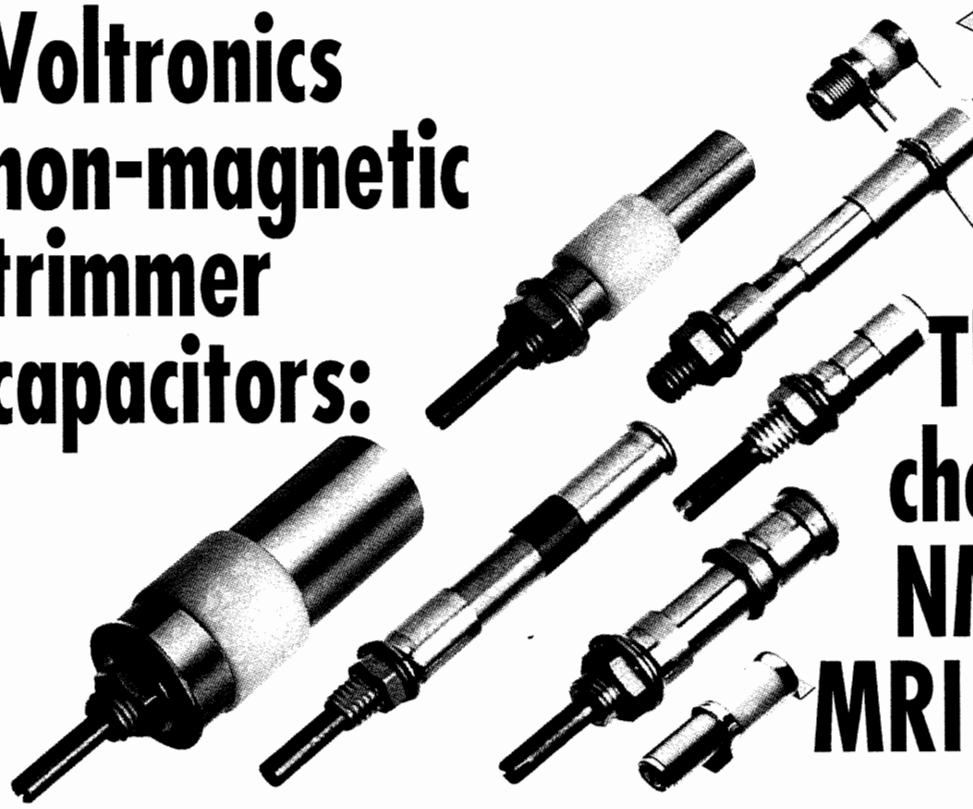

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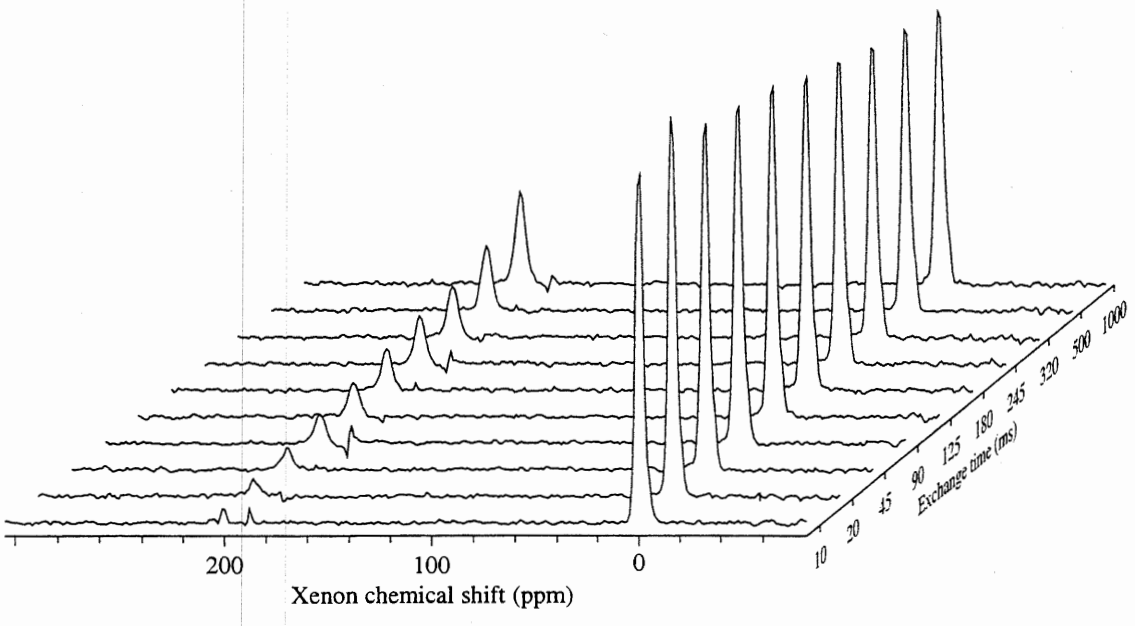

FIG. 1: Xenon interphase exchange spectra as a function of the exchange time. The peaks at 0 ppm arise from the off-center excitation of xenon in the gas phase when the dissolved-phase xenon is pulsed selectively. The dissolved-phase peaks at 200 ppm show recovery as a function of the varying exchange time after the residual magnetization is zeroed by the saturation train.

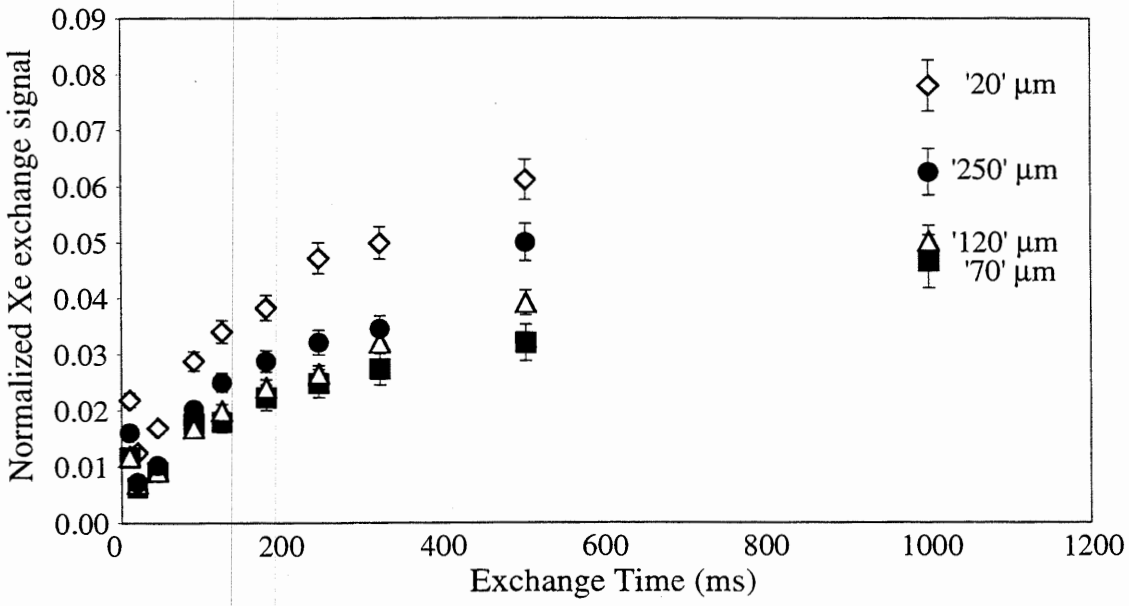

FIG. 2: Xenon interphase exchange buildup data, acquired at 4.7 T, for each of the four polymer samples used, indicated in the diagram by their nominal manufacturer quoted pore size.. Normalized xenon integral = $S_{diss}(t)\phi/(b(S_{gas}(t=0)$ / sin $\alpha))$.

Manufacturer's pore size (μm)	20	70	120	250
Microscopy *"pore size"* (μm)	87	148	168	159
Microscopy S/V (μm^{-1})	0.023	0.014	0.012	0.013
Xe NMR S/V (μm^{-1})	0.031	0.014	0.016	0.018

FIG 3: The measured values of *S/V* for each of the four polymer samples, derived from both the microscopy and Xe NMR measurements. The measured "pore size" from the microscopy measurements is actually the mean linear intercept between surfaces: $L_m = 2(S/V)^{-1}$. The manufacturer's claimed pore size is also listed.

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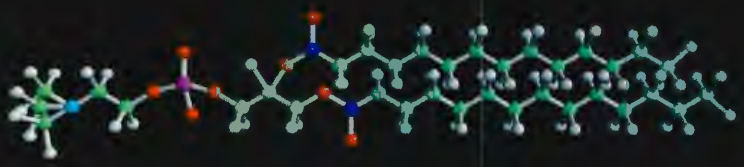

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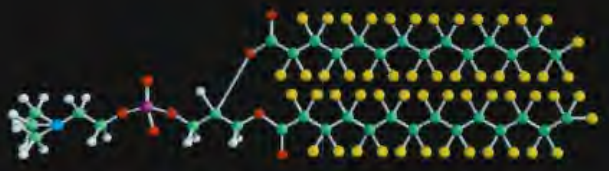

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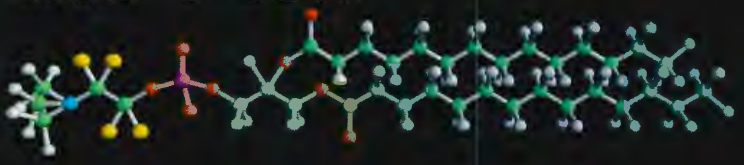

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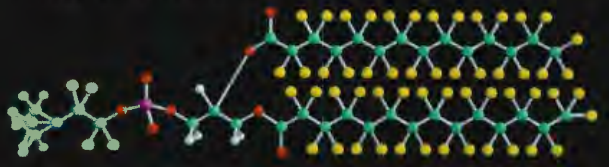

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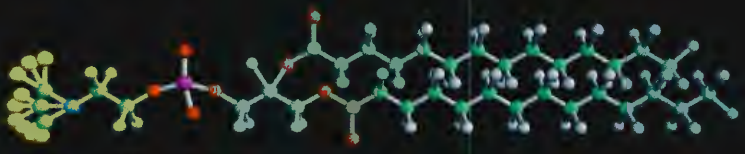

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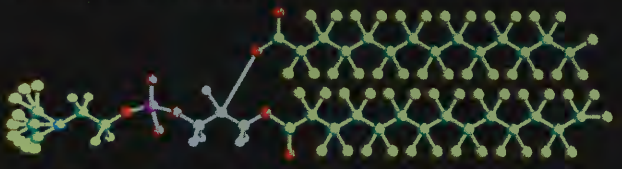

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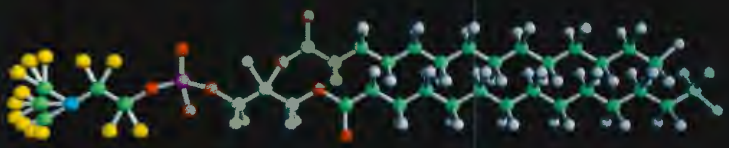

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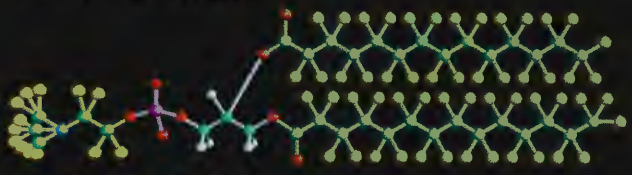

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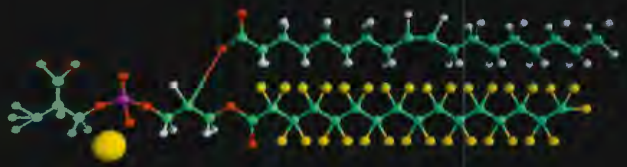
Asymmetric Fatty Acid



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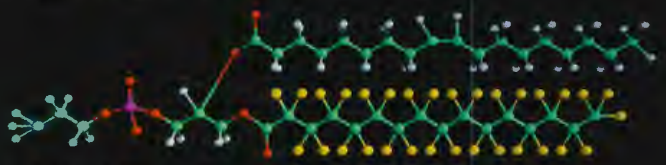

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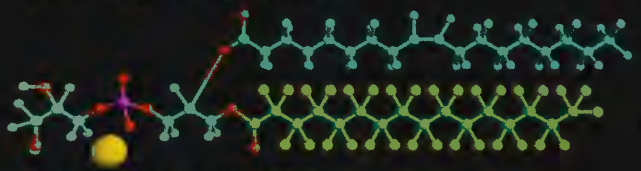

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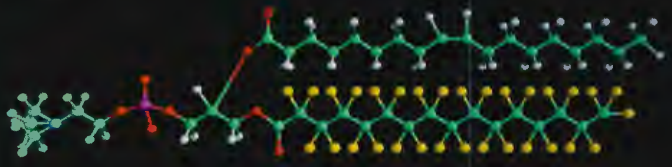

16:0-18:1 PC (D31)

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January 16, 2001

(received 1/16/2001)

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

Are Spin-Spin Coupling Constants Affected by High Applied Magnetic Fields?

Dear Barry,

Fran and I apologize for the delay of our contribution. Our output of spectroscopic data is at a minimum. However, searching through our NMR data collected a year ago, we found some data that may be of some interest to you and other readers.

Data reported several years go suggest that the crystallization of the n-alkanes in asphalts affect its low-temperature properties (1,2,3). Since no one has yet measured the amounts of normal and branched alkanes in asphalts, we undertook the task of trying to measure the amounts of these two types of alkanes, which is no easy task for a complex mixture such as asphalt. To a first approximation, the hydrogens of the terminal methyl group and the hydrogens of the branched methyl groups differ significantly in chemical shifts to warrant an investigation by 1H NMR. Figure 1 shows the 1H NMR spectra of the methyl hydrogens in motor oil at 400 (4), 500 (5), and 800 (6) MHz. Motor oil was investigated because the resonances in the methyl region are similar to asphalts. The 1H spectrum of the motor oil was record at three different applied magnetic fields with the hope of separating the two different types of methyl groups and simplifying the spectrum. There appears to be some simplification in the 800 MHz spectrum.

However, what is of interest in this report is the apparent effect ofthe high applied magnetic fields on the coupling constant for the hydrogen triplet of the terminal methyl group. The spacing of the peaks in the triplet are not equal nor are they independent of the applied field Figure 2 is a plot of the data. The equations for the least-square fit of the data are:

$$J1 = 6.0508 + 0.00012262\ Bo \qquad [1]$$

$$J2 = 6.7790 + 0.00067528\ Bo \qquad [2]$$

The high-energy constant, J1, is to the left of the center peak of the triplet and low energy constant, J2, is to the right of the center peak. We thought the spacing in a triplet were to be equal and independent of the applied field (7). According to the equations, at low applied magnetic fields (used many years ago) the effect would probably be within the experimental error of the measurements. We don't know if the observed changes in the coupling constant is real and/or if others have observed the same effect in "pure" compounds. If anyone has an explanation, we would like to hear from them.

Sincerely,

D. A. Netzel
dnetzel@uwyo.edu

F. P. Miknis
fmiknis@uwyo.edu

1. D. A. Netzel, F. P. Miknis, J. C. Wallace, Jr., C. H. Butcher, and K. P. Thomas, "Molecular Motions and Rheological Properties of Asphalts: An NMR Study", Chapter 2 in Handbook of Asphalt Science and Technology (A. Usmani, ed.), Marcel Dekker , New York (1997).

2. L. C. Michon D. A. Netzel, T. F. Turner, D. Martin, and J-P Planche, "A 13C NMR and DSC Study of the Amorphous and Crystalline Phases in Asphalts", Energy & Fuels, 13(3), 602 (1999).

3. D. A. Netzel, "Low Temperature Studies of Amorphous, Interfacial, and Crystalline Phases in Asphalts using Solid State 13C Nuclear Magnetic Resonance", Transportation Research Record 1638, 23 (1998).

4. University of Wyoming.

5. NuMega Resonance Labs, Inc.

6. Stanford University School of Medicine.

7. J. A. Pople, W. G. Schneider, H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance", McGraw-Hill, New York, 1959, p.92

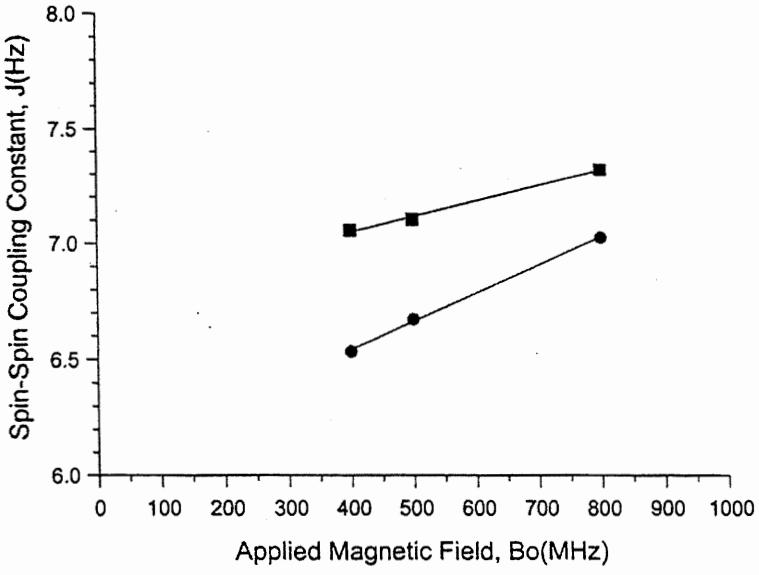

Figure 2. Spin-spin coupling constant versus the applied magnetic field for the terminal methyl group hydrogens for n-alkanes in motor oil: ● J1; ■ J2.

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References: (1) Whistler, R.; BeMiller, J. *Methods in Carbohydrate Chemistry*; New York, NY, 1980. (2) Duffin, G. et al. *J. Chem. Soc.*, Perkin Trans., *1*, **2000**, 2237 (3) Halliday, D.; Bodamer, O. *Eur. J.of Pediatr.*, **1997**, *13*, 35. (4) Phalakornkule C., Domach M. M. ^{13}C *NMR Analysis on Flux Regulation in Bacillus subtilis*. 20th Annual Chemical Engineering Symposium, Carnegie Mellon University, October 1998.

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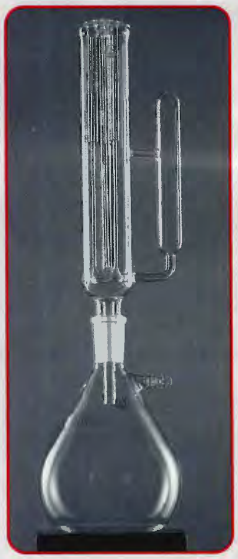

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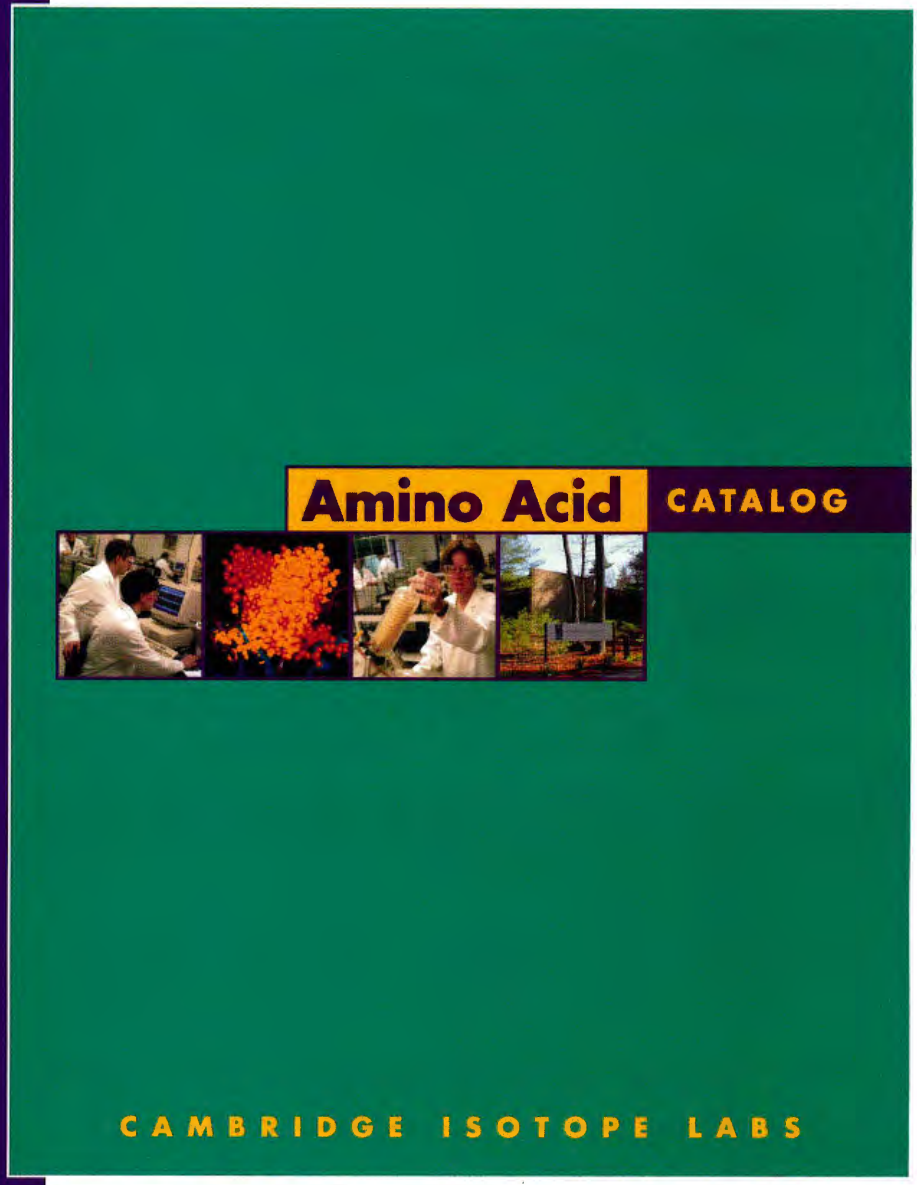

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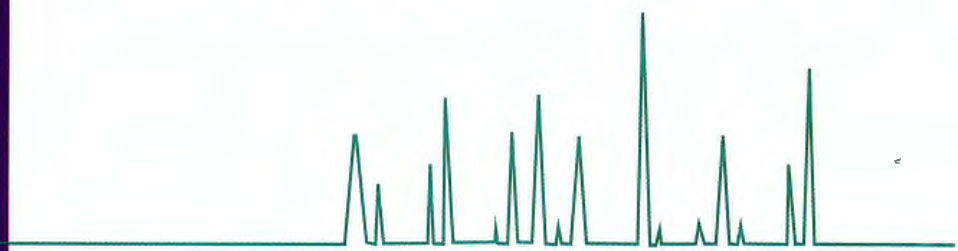

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PRELIMINARY AGENDA

Sunday March 11, 2001 1:00 to 6:00 pm
The Rosen Centre Hotel Orlando, Florida

Measurement of Long-Range ^{1}H - ^{31}P Coupling Constants in Oligonucleotides and Oligosaccharides
Charlotte H. Gotfredsen, Axel Meissner and Jens O. Duus
Carlsberg Laboratory, Copenhagen

Dipolar Couplings and Sidechain Conformation in Proteins
Georg Kontaxis and Ad Bax, NIH

Flexible Automation Solution for a Mercury VX Console Equipped with SMS Autosample Changer and Nalorac PulseTune™ Probe
Donald V. Eldred and Richard B. Taylor, Dow Corning Corporation

Multidimensional NMR of Fluoropolymers: Problems and Solutions
Peter L. Rinaldi and Olivier Assemat, The University of Akron

Flow NMR of Biofluids to Rapidly Evaluate Toxicity in Vivo
Michael D. Reily, Pfizer Global Research

Long-Range Heteronuclear Coupling Constants: Where to Get Them and What They are Good For
R. Thomas Williamson and Frank E. Koehn, Wyeth Ayerst

Interplay of Protein Dynamics with Structure, Stability and Ligand Binding
Martin Stone, Indiana University

Cryogenic Probes - Nuts and Bolts
Atholl Gibson, Toby Zens and Jim Carolan, Nalorac Corporation

Determining Global and Local Structure in Nucleic Acids with Residual Dipolar Couplings
Arthur Pardi, University of Colorado

Probing Slow Timescale Dynamics at Sidechain Positions in Proteins
Frans A. C. Mulder, Nikolai Skrynnikov, Bin Hon,
Frederick W. Dahlquist and Lewis E. Kay
University of Toronto

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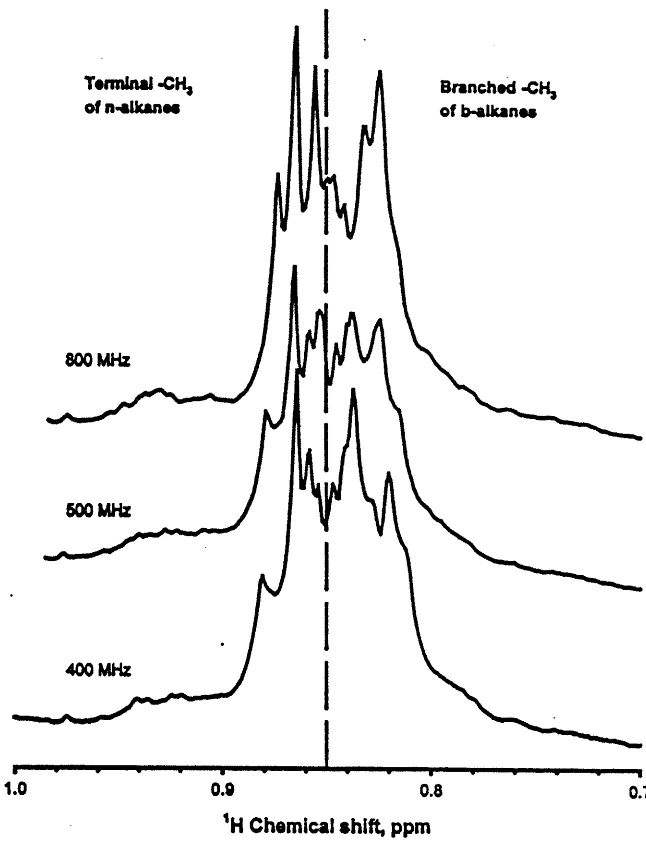

Figure 1. ^{1}H NMR spectra of the methyl hydrogens in motor oil at 400, 500, and 800MHz.

NMR Manager Position
& Post-Doctoral Fellowships in NMR Spectroscopy

The Department of Biochemistry at Wake Forest University School of Medicine (Bowman-Gray) is in the process of making a major investment in Biological NMR Spectroscopy and Structural Biology. We recently installed a Bruker 600 MHz NMR spectrometer configured for multidimensional NMR studies of biological macromolecules including proteins, nucleic acids and lipids. A cryoprobe for this system will be delivered in 2001. We are also developing core laboratory multi-user facilities for X-ray crystallography and MR imaging. We recently made a faculty appointment to David Horita from Andy Byrd's lab at NCI whose research interests are in the area of NMR spectroscopy of proteins. My own research interests are in the area of nucleic acid structure and function while Professor Mike Thomas is interested in NMR of lipids. We are seeking an outstanding individual with broad expertise in NMR spectroscopy for an NMR manager position. We also have immediate openings for post-doctoral researchers interested in application of NMR to problems of biological importance. Wake Forest is in a great environment with easy access to the Smoky Mountains and the North Carolina Beaches. Interested candidates should send their CV and the names of at least two references to:

William H. Gmeiner, Ph.D.
Professor and Chairman
Department of Biochemistry
Wake Forest University School of Medicine
Winston-Salem, NC 27157
bgmeiner@wfubmc.edu

University of East Anglia

From The Dean
Professor N. Sheppard F.R.S.

School of Chemical Sciences
University Plain, Norwich NOR 88C
Telephone Norwich (0603) 56161
Telegraphic Address UEANOR

17th March, 1972

Dear Barry,

NMR Studies of Activation Parameters

and Energy Differences associated with Internal Rotation in

Substituted Ethanes

I am replying to your recent letter reminding me that another contribution is due from us for the NMR Newsletter.

Audrey Purdie and I have been looking at the variable-temperature NMR spectra of a series of ethanes substituted by Me or Cl groups with a view to determining the activation parameters of internal rotation, and the energy differences between spectroscopically distinguishable isomers.

Since starting this work, we have recently discovered two other groups which are interested in similar ranges of compounds under Professor J D Roberts of Cal Tech and Dr J E Anderson of University College, London. The table below gives the values of the free energy of activation ΔG^* at the coalescence temperatures, for the compounds where our work has overlapped. Results from different laboratories are approximately the same, taking solvent differences into account.

A surprising and somewhat disappointing feature about the values so far obtained is that they seem to lie within two ranges, namely 7 - 8.5 kcal/mole and 10 - 11.5 kcal/mole for the penta- and hexasubstituted ethanes respectively. We had hoped to see some well defined trends in the size of the ΔG^* as one type of substitutent is systematically replaced by the other as an indication, for example, of the relative strengths of methyl...methyl, chlorine...chlorine and methyl...chlorine interactions across the central C-C bond. However, we have to hear in mind that ΔG^* is a relative energy term, dependent on the energy of the ground state conformer as well as that of the transition state. With interaction of the non-bonded substituents to be considered in both states, the overall picture is perhaps more complex than we originally envisaged.

We have been finding that in cases where the molecule has more than one isomer, the more stable form is the one in which the number of gauche interactions involving Me...Me and Cl...Cl is at a minimum, in favour of Me...Cl interactions. This tends to support the argument that the interaction between Me...Cl is less than that for Me...Me and Cl...Cl, as argued for data for energy differences in 1,2 disubstituted ethanes[3].

Professor B L Shapiro, 17th March, 1972

We are continuing our NMR study of a number of related compounds as well as complementing this and previous work with Raman and infra-red studies. From the latter we hope to identify torsional frequencies, from which alternative data the barrier to internal rotation may also be determined.

Yours sincerely,

Norman Sheppard

COMPOUND	AP	Roberts	Anderson
$Me_3C-CHMe_2$	~7.4		7.1
$Me_3C-CClMe_2$	10.3	9.8	10.4
Me_3C-CCl_2Me	11.4	10.8	
$Me_2CH-CCl_2Me$	8.5		8.4
$Me_3C-CMeCl-CMe_3$		11.4	11.4

Values of ΔG^* in kcal/mole at the coalescence temperatures

1. J D Roberts et al, JACS 93, 4472 (1971)
2. J E Anderson and H Pearson, Chem Comm 871 (1971); JCS (B), 1209 (1971)
3. N Sheppard, Adv Spectroscopy (1959) 1, 288

Professor B L Shapiro,
Texas A & M University,
College of Science,
College Station,
Texas 77843,
USA.

NS/SIC

Position Available

The U.S. Customs Laboratory located in Savannah, GA has recently acquired a Bruker 500 MHz NMR. We have also acquired from Eurofins, in France, equipment that will enable us to do SNIF (Site-specific Natural Isotope Fractionation) work. The Savannah Laboratory has acquired this equipment to do research into determining the geographic origin agricultural products (e.g., fruit juices, sugar, peanuts, etc.) based on the hydrogen: deuterium ratio of derivatives as it relates to latitude. We currently have a vacancy in the laboratory and are seeking candidates for employment who are experienced in high field NMR. The primary responsibility of the position will be to conduct geographic origin studies aimed and determining the country of origin of imported agricultural products.

Time is of the essence. The current Vacancy Announcement opened on February 7, 2001 and will close on March 7, 2001. Information on how to apply can be found on the Internet at www.customs.treas.gov/career/car_opps.htm. The vacancy announcement number is HQDEU/01-006CJG. Alternatively, anyone interested could call us at 912-447-6545 and we will be happy to discuss the position. If a highly qualified candidate is interested and contacts us before the closing date, we can very likely extend the closing date.

Depending on the education and/or experience the position will be filled at the GS-11 or GS-12 level. The journeyman grade for the position is GS-12. Salary range for GS-11 is $43.3K to $56.3K; for GS-12, it is $51.9K to $67.5K. The Savannah Laboratory is a new facility constructed in 1999. The laboratory has a staff of 22 (17 scientist and 5 admin. staff). The jobs are very stable. In Savannah, the cost of living is low and the quality of life in high. The laboratory has very flexible work hours and leave policy. Leave can be taken at just about any time and in units of as little as one hour at a time. Arrival time at work and quitting time are flexible.

Please contact Carson Watts at (912) 447-6545 if you are interested.

Positions Available

Postdoctoral Positions in NMR Spectrometry and Bio-inspired Nanotechnology

We are currently seeking postdoctoral fellows for research positions in the area of solution-state NMR spectroscopy at New York University, Department of Chemistry, located in New York City, USA. The candidates should be recent Ph.D. graduates with research expertise in multidimensional NMR spectroscopy of proteins, polypeptides, or polymers. Experience in pulse sequence design is also desirable.

Our research centers on high-field NMR structural determination of biomineralization-related protein and polypeptide sequences that have application to nanostructured materials. These NSF, ARO funded positions are for 2 years, with the possibility of a third year, and the salaries are negotiable based upon experience and qualifications. The start date is May 1, 2001, or thereafter.

Interested candidates should forward their CV and the names and contact information of three references to Professor John S. Evans at jse@dave-edmunds.dental.nyu.edu. Deadline for receipt of application is March 1, 2001. Applicants will be requested to send hardcopy materials after their initial contact. New York University is an equal opportunity employer.

Forthcoming NMR Meetings, continued from page 1:

13C Symposium and Training IX: Hepatic Gluconeogenesis, University of Texas Southwestern Medical Center, Mary Nell and Ralph B. Rogers Magnetic Resonance Center, Dallas, Texas, Thursday, **May 10, 2001**. Contact Janet Thach at janet.thach@utsouthwestern.edu. Please check our web page at http://www2.swmed.edu/rogersmr at a later date for details.

Gordon Research Conference on Magnetic Resonance, **June 17-22, 2001**, Roger Williams University, Bristol, Rhode Island (note the new, improved location !!!). Contacts: Rob Tycko, Chair, 301-402-8272, tycko@helix.nih.gov, and Kurt Zilm, Vice-Chair, kurt.zilm@yale.edu. Site description and application information available at http://www.grc.uri.edu.

IXth International Symposium on Magnetic Resonance in Colloid and Interface Science, St. Petersburg, Russia, **June 26-30, 2001**. Contact: Mrs. L. Ya. Startseva, Secretariat of ISMRCIS, Boreskov Institute of Catalysis, 5, Prosp. Akad. Lavrentieva, Novosibirsk, 630090, Russia. Tel: +7 (3832) 34-12-97; Fax: +7 (3832) 34-30-56; E-mail: star@catalysis.nsk.su.

Royal Society of Chemistry: 15th International Meeting on NMR Spectroscopy, Durham, England, **July 8-12, 2001**; Contact: Mrs. Paula Whelan, The Royal Society of Chemistry, Burlington House, London W1J 0BA, England; tel: +44 (0) 207-437-8656; fax: +44 (0) 207-734-1227; Email: conferences@rsc.org\; Use the subject header '01NMR15'

ESR and Solid State NMR in High Magnetic Fields, Stuttgart, Germany, **July 22-26, 2001**. Contact: Prof. Hans Paus, 2 Physikalisches Institut, Universität Stuttgart, Pfaffenwaldring 57, D-70550 Stuttgart, Germany. Tel: ++49-711-685-5223 or -5217; Fax: ++40-711-685-5285; E-mail: ampere2001@physik.uni-stuttgart.de.

43rd Rocky Mountain Conference on Analytical Chemistry, Denver, CO, **July 29 – August 2, 2001**; www.milestoneshows.com/rmcac

ISMAR 2001, Jerusalem, Israel, **August 19-24, 2001**; See http://www.tau.ac.il/chemistry/ISMAR.html.

14th European Symposium on Polymer Spectroscopy, Dresden, Germany, **September 2-5, 2001**. Contact: Institut für Polymerforschung Dresden e. V., ESOPS 14, Postfach 12 04 11, 01005 Dresden, Germany. Tel: +49 351 4658-282; Fax: +49 351-4658-214; E-mail: espos@ipfdd.de.

Sixth International Conference on Magnetic Resonance Microscopy, Nottingham, UK, **September 2-5, 2001**. http://www.magres.nottingham.ac.uk/conferences/2001/icmrm/

Fourth International Conference on Molecular Structural Biology, Vienna, Austria, **September 5-9, 2001**. Contact: Andreas Kungl, Austrian Chemical Society (GÖCH), Biochemistry Subgroup, c/o Institute of Pharmaceutical Chemistry, Univeristy of Graz, Universitätsplatz 1, A-8010 Graz, Austria. Tel: +43 316 380 5373; Fax: +43 316 382541; E-mail: andreas.kungl@kfunigraz.ac.at.

2nd Alpine Conference on Solid-State NMR, Chamonix-Mont Blanc, France, **September 9-13, 2001**; Contact: Alpine Conference Secretariat, Laboratoire STIM, Ecole Normale Supérieure de Lyon, 46 allée d'Italie, 69364 Lyon Cedex 7, France; alpine.SSNMR@ens-lyon.fr; Tel. +33-(0)4 72-72-84-86/ 83 84; Fax. +33 (0)4 72 72 84 83; http://ens-lyon.fr/STIM/alpineweb,html

XXth International Conference on Magnetic Resonance in Biological Systems, Toronto, Ont., **August 25-30, 2002**. For further information check www.uwo.ca/chem/icmrbs/, or contact: mgordon@julian.uwo.ca

Additional listings of meetings, etc., are invited.

Address all Newsletter correspondence to:

Dr. B. L. Shapiro
The NMR Newsletter
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650-493-5971* - *Please call only between 8:00 am and 10:00 pm, Pacific Coast time.*

Deadline Dates

No. 510 (Mar.)	23 Feb. 2001
No. 511 (Apr.)	23 Mar. 2001
No. 512 (May)	27 Apr. 2001
No. 513 (June)	25 May 2001
No. 514 (July)	22 June 2001

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

* E-mail: shapiro@nmrnewsletter.com

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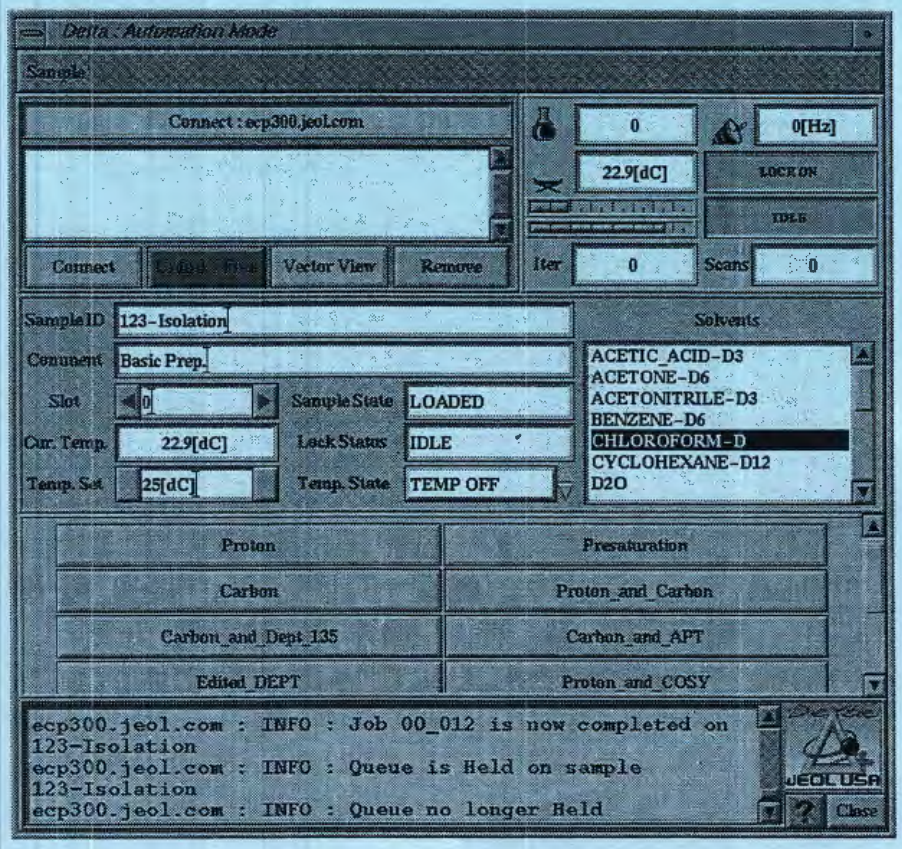
If the mailing label on your envelope is adorned with a large **red dot**: this decoration means that you will not be mailed any more issues until a technical contribution has been received.

JEOL Can Give You the Data You Need From Your Desktop PC or MAC



The **Eclipse+** NMR Spectrometer can be operated anywhere there is a computer on the local network. The **Single Window Automation** pictured above can be used with a single mouse click to select the sample from the auto-sample changer, gradient shim on any probe, run the selected experiment, and plot the data on any network postscript printer. Need more data, click another button and the **Eclipse+** is off to do your work - and you have not left your office. Contact us at nmr@jeol.com or visit or web site at www.jeol.com.

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