THE NMR NEWSLETTER

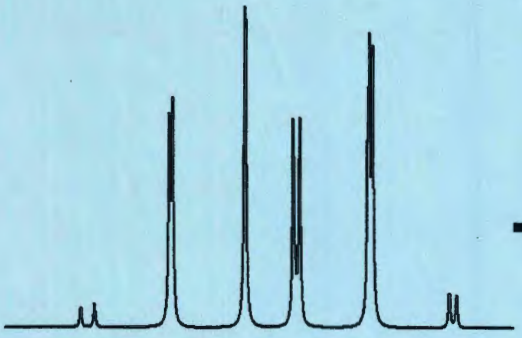
No. 512

May 2001

NUTS - Toolbox for NMR data processing

Illustration of different ways to copy and paste spectra

Choosing the right tool makes a big difference!



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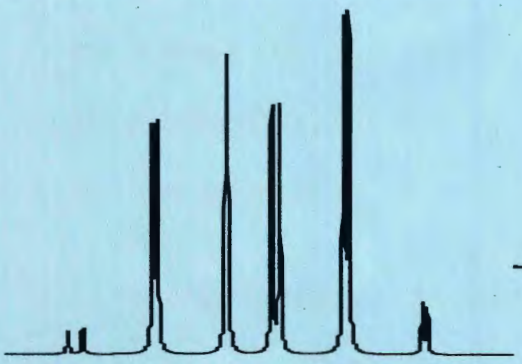
The image is captured as pixels on/off, giving low resolution and leading to distortion when the figure is resized.



Metafile at screen resolution

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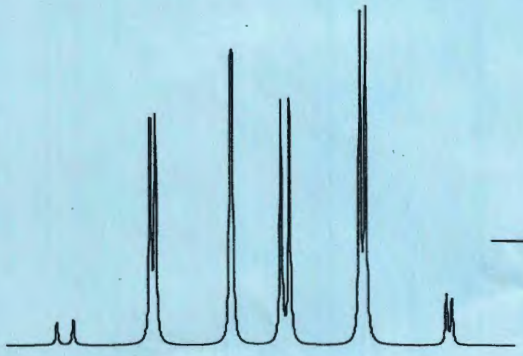
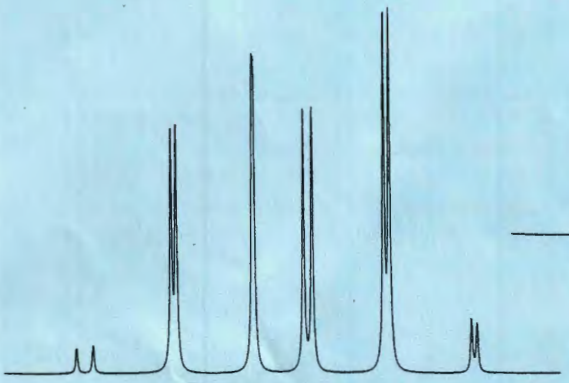
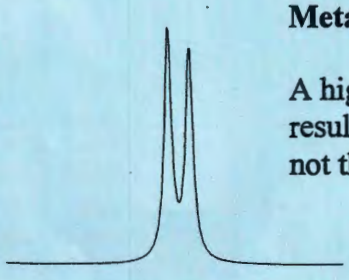


Metafile with 300 dpi printer "device context"

The printer's resolution is higher than the screen's, so the round-off distortion is reduced.





Metafile with 2438 dpi printer "device context"

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FORTHCOMING NMR MEETINGS

9th Chianti Workshop on Magnetic Resonance – Nuclear and Electron Relaxation, Tirrenia (Pisa), Italy, **May 26 – June 1, 2001**; http://www.cerm.unifi.it/chianti/chianti9.html. *Note: changed location.*

Fast Field Cycling Magnetic Relaxation Conference, Torino, Italy, **June 1-3, 2001**; http://nmr.ch.unito.it/meeting/ffcrelax/.

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, Rhodes, Greece, **August 19-24, 2001**; See http://www.tau.ac.il/chemistry/ISMAR.html. *Note: New Location. See Newsletter 511*, 14.

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.

continued on inside back cover

NORTHWESTERN UNIVERSITY

Joseph B. Lambert
Clare Hamilton Hall Professor of Chemistry

April 2, 2001
(received 4/10/2001)

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

Title: Propeller Rotation

Dear Barry:

In our studies of silyl and stannyl cations, we have had occasion to prepare several systems with bulky aryl groups surrounding the atoms silicon and tin. Mislow, Ōki, and others previously studied such systems, of which triphenylmethane (Ph_3CH) is the prototype. The phenyl rings assume a propeller arrangement around the center atom. This spatial arrangement is chiral but is subject to rapid racemization by rotation around the aryl-C bond. The barrier is raised substantially by replacing the ortho hydrogen atoms by methyls, as in the mesityl group (2,4,6,-trimethylphenyl, Mes).

We have systematically varied three aspects of the general structure Ar_3MX: aryl substitution Ar, the central atom M, and the fourth substituent X. Barriers are measured by decoalescence of the resonances of ortho or meta groups. At slow rotation, the two ortho or the two meta groups on a single ring are nonequivalent, but, at fast rotation, they become equivalent. Resonances of groups at the para position do not vary.

Substitution of silicon for carbon and then of tin for silicon progressively lowers the barrier in trimesitylaryl systems: Mes_3CH (21.9 kcal mol^{-1}), Mes_3SiH (12 kcal mol^{-1}), and Mes_3SnH (<ca. 8 kcal mol^{-1}). We were unable to freeze out rotation in the tin system in the temperature range available to us. The reduction likely results from the longer M-aryl bond lengths in the order C-C < C-Si < C-Sn. Longer bonds decrease ortho/ortho interactions and lower the barrier to aryl rotation.

Replacement of mesityl with duryl (2,3,5,6-tetramethylphenyl, Dur) tends to enhance steric interactions through the buttressing effect. The meta methyls render the ortho methyls less flexible in their response to steric interactions. Angle distortion that might relieve ortho-ortho interactions is reduced or prohibited. We were able to make two pairwise comparisons, of the chlorides and the allyl compounds: Mes_3SiCl (ca. 12.5 kcal mol^{-1}) vs. Dur_3SiCl (15.0 kcal mol^{-1}) and $Mes_3Si(allyl)$ (11 kcal mol^{-1}) vs. $Dur_3Si(allyl)$ (13.4 kcal mol^{-1}). The buttressing effect by the meta methyls thus appears to be worth about 2-2.5 kcal mol^{-1}.

The effect of the fourth group (we had H, Cl, and allyl) is less easily rationalized, as the allyl group provided a lower barrier in comparison with H and Cl. The overall order was allyl < H < Cl.

Sincerely,

Joseph B. Lambert

Lijun Lin

McMaster University

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April 4, 2001

(received 4/10/2001)

Dr. B.L. Shapiro
The NMR Newsletter
966 Elsinore Court
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U.S.A. 94303-3410

Adventures in Iteration

Dear Barry,

The iterative version of MEXICO is running, and I have been playing with it. MEXICO is a chemical exchange lineshape simulation program I have been working on for a while now. The latest non-iterative version is already available through my web page, and depending on how speedy the NMR Newsletter's publication is, the iterative version may well be.

The program will do lineshape simulations for two-site chemical exchange of coupled spin systems. The populations may or may not be equal, and the program will automatically recognize mutual exchange. The program is written in C, with dynamic memory allocation, so there is no theoretical limit to the size of the spin system, but 6 spins represents a practical limit. The iterative version uses a Nelder and Mead simplex algorithm (Marquardt is coming soon, I hope), and almost all the parameters can be varied. For more details, see my web page.

The simplex lives up to its reputation as inefficient, but robust. I have been fitting my favourite data set (*1,2*), and typical results are shown in the figure. It may take 30 to 40 iterations to converge, but converge it will. The question is the precision and accuracy of the rates that come out.

The precision is wonderful. Repeated fittings with random initial values, using both the rate and the chemical shift difference as variables gave an average rate of 89.8 s^{-1}, with a standard deviation of 0.1 s^{-1} ! I am not quite sure whether to believe an error in a rate measurement of 0.11%, but the difference plot indicates an excellent fit.

The issue, of course, is accuracy. The value of this rate depends on assumptions of the natural linewidth. For this data set, the natural linewidth and the rate are so strongly correlated that they can not be separated. This is no surprise, but if we can get reliable estimates of natural linewidth, or do reference deconvolution (*3,4*), we should be able to get very accurate and precise rates.

So I am continuing to test the program - if any one has some challenging data they would like me to attack, I'd be interested in hearing from them.

Yours truly,

Alex D. Bain
bain@mcmaster.ca
http://www.chemistry.mcmaster.ca/faculty/bain/

References

1. Fauconnier T, Bain AD, Hazendonk P, Bell RA, Lock CJL. Structure and dynamics of azapropazone derivatives studied by crystallography and nuclear magnetic resonance. Can J Chem 1998; 76: 426-430.

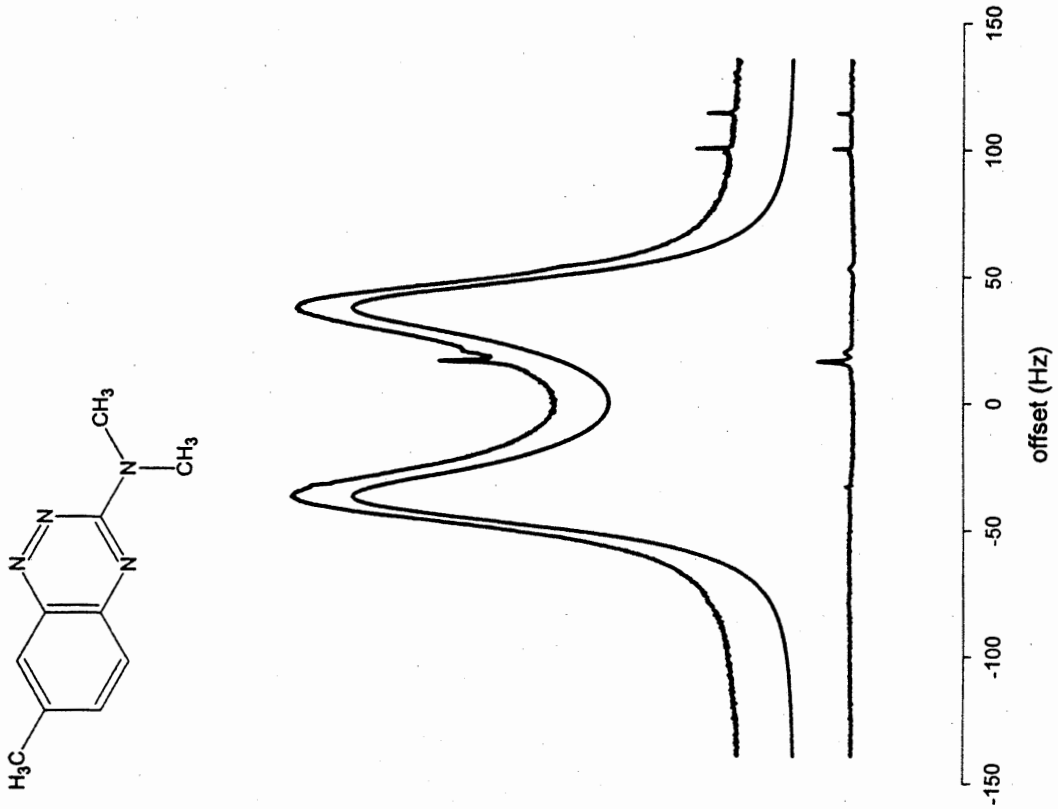
2. Bain AD, Rex DM, Smith RN. Fitting dynamic NMR lineshapes. Magn Reson Chem 2001; 39: 122-126.

3. Barjat H, Morris GA, Swanson AG, Smart S, Williams SCR. Reference deconvolution using multiplet reference signals. J Magn Reson 1995; 116 A: 206-214.

4. Denkova PS, Dimitrov VS. Combined use of complete lineshape analysis of 1D spectra subjected to reference deconvolution and linear prediction, 2D-EXSY spectra and a double fitting method for the study of chemical exchange. Application to an eight-site exchange system. Magn Reson Chem 1999; 37: 637-646.

Figure

Experimental and calculated spectra of the exchanging methyl groups in an azapropazone derivative, from reference (*1*). Top: experimental; middle: calculated; bottom: difference spectrum.



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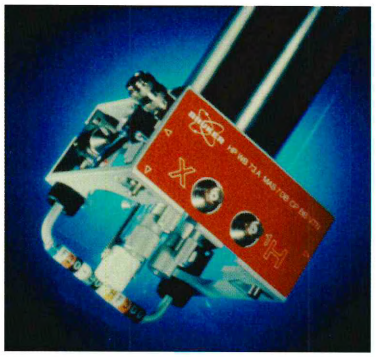

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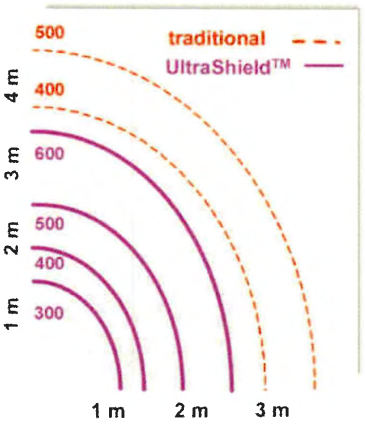

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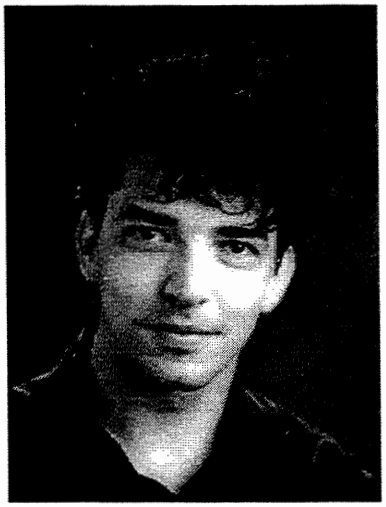
2001 Laukien Prize

A major highlight of the 42nd ENC, March 11 – 16 in Orlando, Florida was the presentation of the third annual Günther Laukien Prize. The prize honors the memory of Professor Günther Laukien, a co-founder of Bruker Instruments, who died in May of 1997. Professor Laukien founded the Bruker company in Germany in 1960, and oversaw its growth into one of the largest manufacturers of analytical and medical NMR instrumentation, as well as other scientific instrumentation. This prize, which carries a monetary award of $15,000 generously provided by Bruker, is intended "to recognize and reward new cutting-edge experimental NMR research with a very high probability of enabling beneficial new applications."

The 2001 Günther Laukien Prize was awarded to Drs. Prüssmann, Weiger, and Boesiger from the ETH in Zürich for their breakthrough work in parallel imaging, which has led to the development of the so-called SENSE (SENSitivity Encoding) technique (1).



Their approach allows the faster acquisition of magnetic resonance imaging (MRI) and spectroscopy data by using arrays of small coils and a reduced image field of view (FOV), allowing a reduction in the number of phase encode steps in the imaging scheme that is proportional to the number of coils. For example, when using two coils, the speed can be doubled, etc. The pitfall of choosing a phase-encoding FOV that is smaller than the sample size is the induction of strong aliasing artifacts due to violation of the Nyquist sampling theorem. The idea behind the SENSE method is to use the sensitivity profiles of each receiver coil to spatially encode the information and therefore to allow the "un-aliasing" of the image by means of linear algebra. The strength of the SENSE approach lies in its simplicity and its general applicability to all multiple coil systems, independent of coil arrangements. The developed theoretical formalism allows for a better theoretical understanding of the parallel imaging process and includes other parallel imaging techniques, such as the SMASH (2), as a particular case of the whole theory.

The awardees have shown the applicability of the SENSE method through the demonstration of fast cardiac imaging, fast three-dimensional functional imaging, and fast contrast-enhanced MR angiography, and are extending their work to fast spectroscopic imaging. Several of the major MRI manufacturers are now starting to develop the specialized coil systems needed to make SENSE technology generally accessible to the MRI centers in the world. It is expected that this will lead to an explosion in SENSE technologies and applications, exactly the type of high impact methodological development that is the hallmark of the Laukien prize.

References:

(1) Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P, SENSE: Sensitivity encoding for fast MRI, MRM 42:952-962 (1999)
(2) Sodickson DK, Manning WJ. Simultaneous acquisition of spatial harmonics (SMASH): fast imaging with radiofrequency coil arrays. Magn. Reson. Med. 38: 591-603 (1997).

Peter Boesiger received a Ph.D. in solid-state NMR from the University of Zurich, Switzerland, in 1977. After research fellowships in the Netherlands and the United States, he joined the Institute of Biomedical Engineering of the University and ETH Zurich, where he was appointed as Professor and Head of the Biophysics Division in 1991.

Klaas Prüßmann was born in 1969 and studied Physics and Medicine at the University of Bonn, Germany. In the year 2000 he received his Ph.D. degree in Physics from ETH Zurich and is currently a postdoctoral fellow at the Institute of Biomedical Engineering in Zurich.

Born in 1967, **Markus Weiger** studied Physics at the University of Wurzburg, Germany, and started to work in the field of MRI at the Philips Research Laboratories in Hamburg. In 2000 he received his Ph.D. degree from the ETH Zurich and currently holds a postdoctoral position at Oxford University.

2002 GÜNTHER LAUKIEN PRIZE – CALL FOR NOMINATIONS

The nominated work should be published within the last three years. In some special cases, the award may be for cumulative achievements over a longer period.

Nominations should include the following and be submitted by October 31:

1. Name of nominee, the nominee's affiliation, address, phone, fax and e-mail.
2. Name of nominator, address, phone, fax and e-mail.
3. A brief (no more than 200 words) description of the work serving as the basis for the nomination.
4. A list of relevant publications (no more than 5).

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March 23, 2001
(received 4/2/2001)

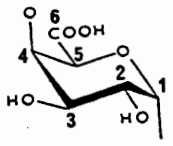
Dr. B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303-3410

Dear Dr. Shapiro:

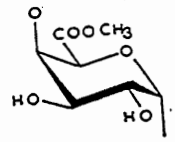
NMR Analysis of Pectin

Pectin is a natural polysaccharide extracted from citrus peels, apple pomace, and other plant materials[1]. It contains mostly a (1-4)-α-D-galacturonic acid (G) backbone with various levels of methyl esterification (E). (It also contains other sugars and side chains.)

G =



E =



As an illustration, the ^{13}C NMR spectrum of a pectin sample is given above. The ^{1}H and ^{13}C NMR spectra can be analyzed to obtain the triad sequence distribution, involving G and E. In a recent paper[2], the NMR triad sequences for a number of pectin samples were reported. It was shown[2,3] that pectin is compositionally heterogeneous, and that the NMR data cannot be analyzed satisfactorily by the simple statistical models, such as Bernoullian, first-order Markovian, second-order Markovian, or enantiomorphic-site models. Instead, the NMR data may be treated with a more complex model, such as a multicomponent model[4,5] or a perturbed Markovian model[6,7].

For a compositionally heterogeneous material, it is preferable to fractionate the material and obtain the NMR data of fractions. In the earlier paper[2], the NMR data of two pectin fractions (C1 and C2) were reported. These are given in Table 1. Also given in Table 1 are the calculated values from some two-component and three-component models[2,3]. From the mean deviations, it appears that the three-component first-order Markovian (**M1/M1/M1**) model gives the best fit.

Table 1. Observed and calculated triad intensities for 2-component Bernoullian (**B/B**), 3-component Bernoullian (**B/B/B**), and 3-component 1st-order Markovian (**M1/M1/M1**) models

Fraction/Triad	Obsd	Calc (**B/B**)	Calc.(**B/B/B**)	Calc.(**M1/M1/M1**)
Fraction C1				
EEE	43.4	43.4	43.4	43.4
EEG	27.2	27.2	26.2	27.2
GEG	3.2	4.6	4.0	4.3
EGE	16.1	13.6	13.1	15.5
GGE	4.9	9.2	8.0	4.8
GGG	5.2	2.1	5.2	4.9
Fraction C2				
EEE	32.6	32.6	32.6	32.6
EEG	27.5	24.3	26.9	27.0
GEG	8.5	7.4	5.9	5.9
EGE	10.3	12.2	13.5	13.4
GGE	11.8	14.9	11.8	11.8
GGG	9.4	8.6	9.4	9.4
Mean deviation		1.8	1.2	0.7

The first-order Markovian probabilities for the three components are summarized in Table 2. All three components are nearly random in distribution. However, component 1 has a slight tendency towards alternation ($P_{GE} + P_{EG} = 1.118$), whereas components 2 and 3 are slightly blocky ($P_{GE} + P_{EG}$ being 0.950 and 0.932, respectively). The component weight factors for the two pectin fractions are given below.

Fraction C1: $w_1 = 0.905$, $w_2 = 0.051$, $w_3 = 0.044$

Fraction C2: $w_1 = 0.294$, $w_2 = 0.650$, $w_3 = 0.056$

Table 2. 1st order Markovian probabilities for the three components in pectin

Component	P_{GE}	P_{EG}	E	G	Tendency
1	0.883	0.235	0.790	0.210	Slightly Alternating
2	0.620	0.330	0.653	0.347	Slightly Blocky
3	0.002	0.930	0.002	0.998	Slightly Blocky

Thus, pectin contains *at least* three separate Markovian components, according to this analysis. For more information, please consult refs. 2 and 3. This work was done in collaboration with Tom Neiss of DuPont Pharmaceuticals Company.

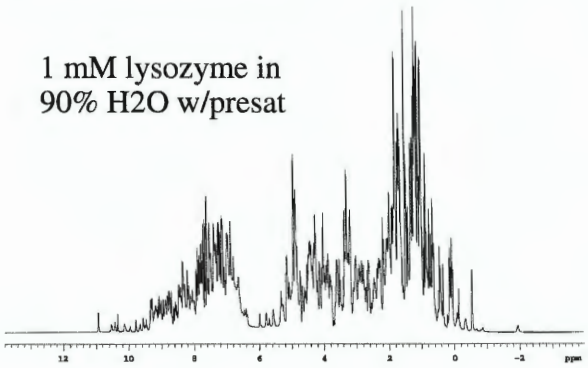
Very truly yours,

H. N. Cheng
(email: hcheng@herc.com)

References

1. For example, Rolin, C. "Pectin", in Whistler, R. L.; BeMiller, J. N. eds., *Industrial Gums*, 3rd Ed., Academic Press: San Diego, 1993, pp. 257-293.
2. Neiss, T. G.; Cheng, H. N.; Daas, P.; Schols, H. A. *Macromol. Symp.* **1999**, *140*, 165.
3 Neiss, T. G.; Cheng, H. N., *ACS Polym. Prepr.*, **2001**, *42*(1), 76.
4 Cheng, H. N. *J. Appl. Polym. Sci.* **1988**, *35*, 1639.
5 For example, Cheng, H. N. *Makromol. Chem. Theor. Simul.* **1992**, *1*, 415 and **1993**, *2*, 901.
6 Cheng, H. N. *Macromolecules* **1992**, *25*, 2351.
7 Cheng, H. N. *Macromolecules* **1997**, *30*, 4117.

Varian and Oxford Instruments are pleased to announce the establishment of a joint applications laboratory located in Oxford, U.K. The new laboratory features the Inova 900 MHz NMR spectrometer.



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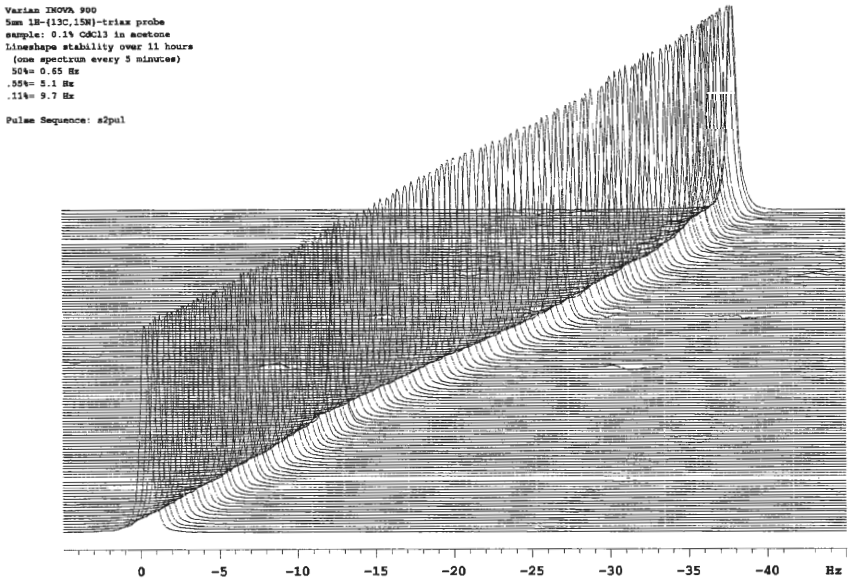

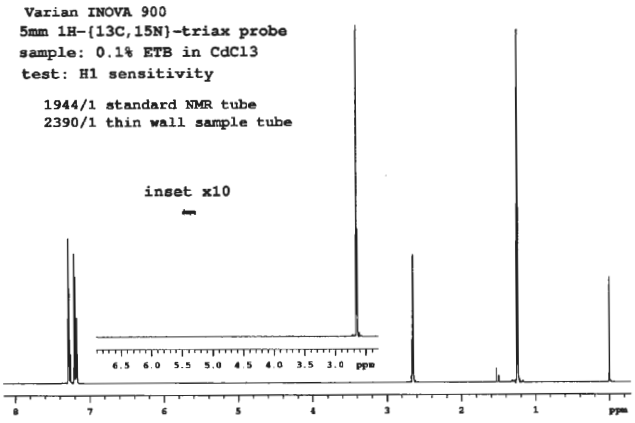

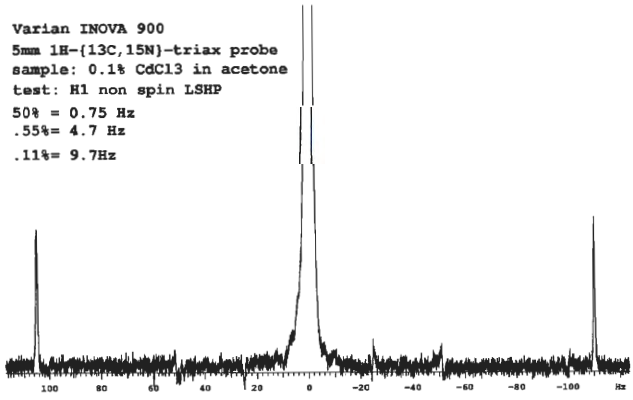

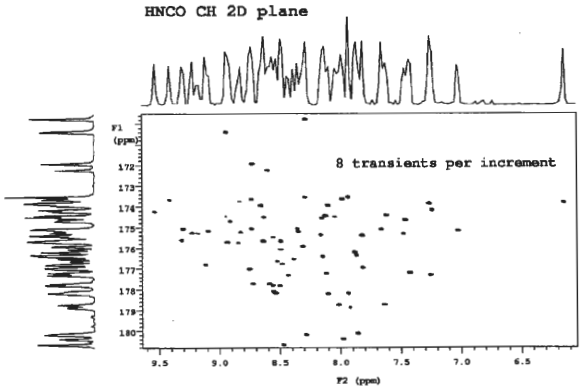

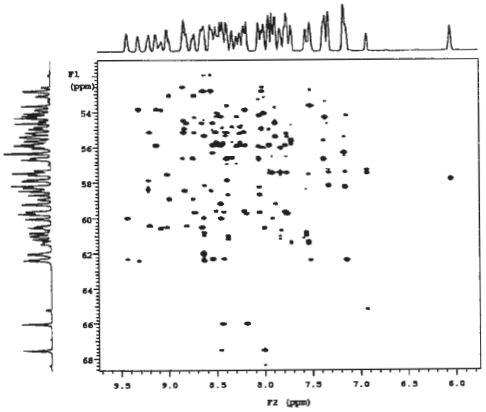

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(received 4/21/2001)

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

Leipzig, 06.04.01

TMS as a diffusion reference

Dear Barry,

We have been working in the application of DOSY-NMR experiments to study molecular association in organic solutions.[1,2] We were mainly interested in following the changes in the diffusion of a particular solute, capable of being involved in H-bond, upon a modification in the composition of the solution by the addition of a H-bond donor or acceptor. A modification of the solution composition is expected to induce changes in the viscosity, and the effective determination of the separate contributions of the changes in viscosity, and molecular size, to the determined value of the diffusion, frequently involves additional experimental work to measure the viscosity of the solutions. However, the use of a diffusion reference compound that is not able to be involved in H-bonding allows to determine to what extend the diffusion of the other solutes is affected by changes in viscosity and/or H-bond, given the fact that the former affects equally all compounds in the solution.

We propose the use of tetramethylsilane (TMS) as a standard for such diffusion referencing in organic solvents, since it will not be involved in H-bond and because it is the normal internal standard used for chemical shift referencing in organic solvents due to its non-interacting properties.

With this procedure a simple quantitative description of the modifications in the solute structure can be made through the use of the Stokes-Einstein equation[3] ($D = k_BT/(6\pi\eta r_H)$), and changes in hydrodynamic radii can be determined. The ratio of the diffusion of a particular solute (D) and the TMS (D_{TMS}) will be independent of the viscosity: $D/D_{TMS} = r_{HTMS}/r_H$. This ratio allows the direct comparison of values among solutions after the addition of a H-bond donor or acceptor ($D'/D'_{TMS} = r_{HTMS}/r'_H$), and since the hydrodynamic radius of TMS (r_{HTMS}) is considered to be constant, any changes in this ratio may be attributed to modifications in the hydrodynamic radius of the solute in study ($\Delta r_H = r'_H/r_H$). This provides a quantitative insight into the changes in the aggregation of the components forced by H-bonding.

As an example we present here the result of the application of this procedure to a mixture of phenol (**1**) and toluene (**2**), two compounds with very similar hydrodynamic radius and molecular weight, but where only one can be involved in H-bonding. The behaviour of such a mixture was studied upon the addition of hexamethylphosphoramide (**3**) (HMPA) as a H-bond acceptor.

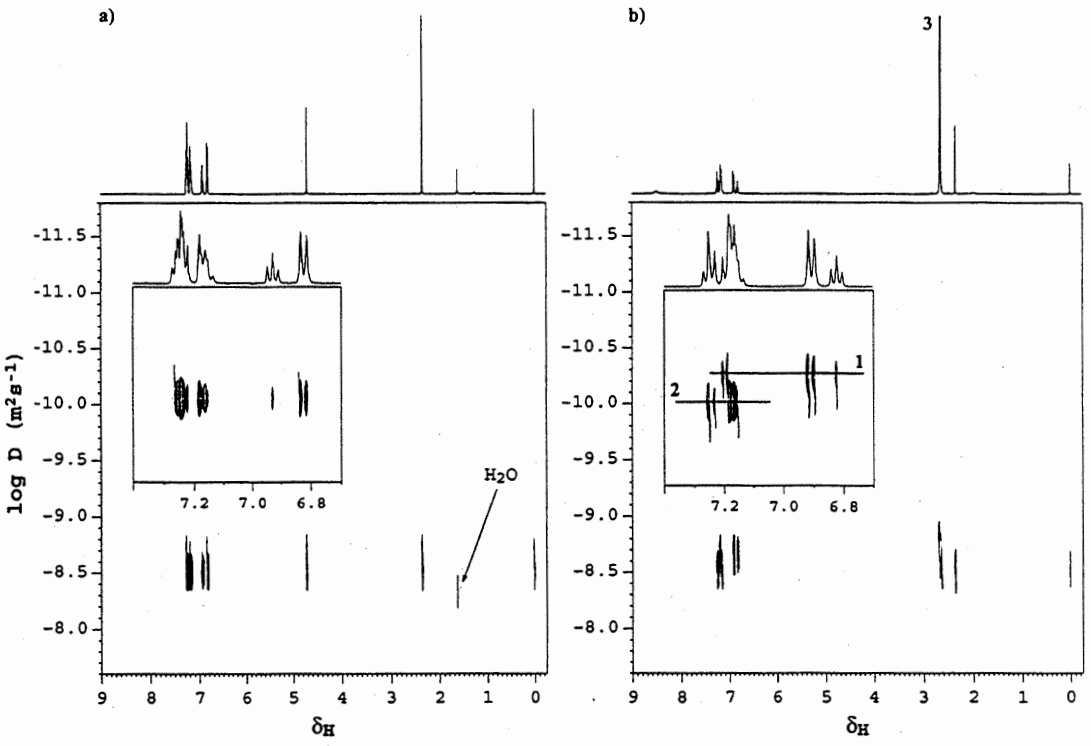

Figure (**a**) The ^{1}H-DOSY of an equimolar mixture of phenol and toluene in $CDCl_3$ containing TMS as a reference; and (**b**) the ^{1}H-DOSY of the same mixture after the addition of HMPA. In both cases an expansion of the aromatic region is shown.

	Before HMPA addition		After HMPA addition		
Compound	$D/10^{-9}$ m^2s^{-1}	D/D^{TMS}	$D/10^{-9}$ m^2s^{-1}	D/D^{TMS}	Δr_H
TMS	2.92	1.00	2.30	1.00	1.00
Toluene	2.94	1.01	2.30	1.00	1.00
Phenol	2.94	1.00	1.68	0.73	1.37

Sincerely yours

[Eurico Cabrita]

[Stefan Berger]

[1] Kapur GS, Cabrita EJ, Berger S, *Tethrahedron Lett.*, 2000, **41**, 7181-7185.
[2] Diaz MD, Berger S, *Carbohydrate Research,* 2000, **329** 1-5.
[3] Johnson CS, In *Encyclopedia of Nuclear Magnetic Resonance*, Grant, DM, Harris, RK (eds), John Wiley & Sons, 1996, **3**, 1626-1644.

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April 5, 2001
(received 4/5/2001)
Dr. Barry L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, California 94303-3410

Carbon-Proton Cross-Polarization in Solid Amino Acids

Dear Barry,

Here are data gathered by Jeff Smith, an undergraduate in the laboratory, that show effects characteristic of the cross-polarization experiment in glycine and alanine. The data were gathered at room temperature under matched conditions. The experimentally determined cross-polarization time constants, T_{CH}, and apparent proton spin-lattice relaxation time constants, $T_{1\rho H}$, are given below.

Amino acid carbon	$T_{1\rho H}$ (msec.)	T_{CH} (microsec.)
Glycine carboxyl	30±3	870±100
Glycine α carbon	27±3	170±20
Alanine carboxyl	1.3±0.1	360±40
Alanine α carbon	1.8±0.3	90±10
Alanine methyl carbon	1.51±0.15	200±20

The presence of a methyl group always significantly shortens the apparent $T_{1\rho H}$, as observed for other solid organic materials. The protonated carbons cross-polarize faster than the nonprotonated carboxyl carbons, as would be expected. These generalizations are true for the other amino acids examined – isoleucine, valine and cysteine. Comparison of magnitudes of time constants for various amino acids shows qualitative trends with structure that Jeff is examining further by investigation of other solid amino acids.

In other news, we await the installation of a new 600 MHz spectrometer, the impending arrival of which has made us realize again the limitations of 10'6" ceiling heights for NMR spectroscopy. Needless to say, this installation has entailed major changes.

Best regards, as always.

Yours truly,

Cecil Steve

Cecil Dybowski
Professor

Shi Bai
NMR Spectroscopist

Departments of Radiology & Pathology

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UAMS MEDICAL CENTER

April 18, 2001
(received 4/23/2001)

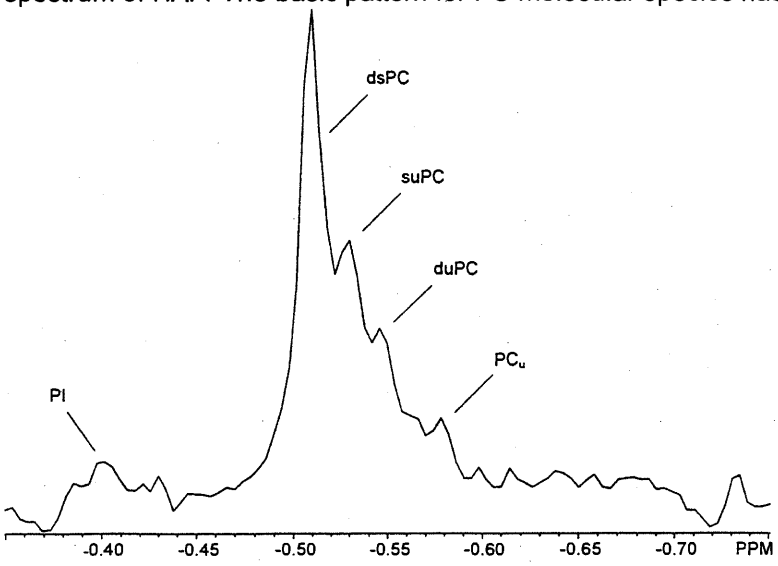
Barry Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303-3410

Title: ^{31}P NMR of Oxidized Phospholipids

Dear Barry:

In previous contributions to *The NMR Newsletter*, I have described some of our work in characterizing phospholipid (PL) mixtures from natural sources using ^{31}P NMR spectroscopy. High resolution ^{31}P NMR spectra are obtained in an organic-solvent system to resolve PL classes (headgroups) and subclasses (linkage type at the sn-1 position of glycerol), and in a sodium-cholate, aqueous dispersion system to resolve phosphatidylcholine (PC) molecular species (acyl chain unsaturation) (Pearce and Komoroski, *Magn. Reson. Med.* **44**, 215-223, 2000).

Little work has been done on oxidized PLs, which may be important to characterize in a number of disease processes. We previously acquired the ^{31}P NMR spectrum of the oxidation product of 16:0/20:4-PC with soybean lipoxidase. The product, 16:0/15'-HPETE-PC, is the derivative of 16:0/20:4-PC with a hydroperoxy group at C-15 of the sn-2 acyl chain (20:4 = ETE = eicosatetraenoic acid). Its ^{31}P resonance occurs at -0.575 ppm, which is reasonably well resolved from the main group of PC molecular species resonances. Although in our initial studies we have seen no evidence for the oxidized species above in the ^{31}P NMR spectra of human or rat brain PLs, on occasion we have seen evidence for a signal in this region in ^{31}P spectra of human amniotic fluid (HAF). Some HAF spectra exhibit weak signals in the vicinity of -0.575 ppm, consistent with a PC species such as 16:0/15'-HPETE-PC. The figure below shows one such ^{31}P NMR spectrum of HAF. The basic pattern for PC molecular species has been determined previously (Pearce and Komoroski, *Magn. Reson. Med.* **29**, 724-731, 1993). It arises from PCs with 2 saturated (dsPC), 1 saturated and 1 unsaturated (one or two double bonds) (suPC), and 2 unsaturated (one or two double bonds per chain) (duPC) acyl side chains. PI denotes the resonance of phosphatidylinositol. The resonance labeled PC_u may arise from oxidized species. Maturing fetal lung tissue is the primary source of PC species in HAF, and oxidized PLs are not unexpected in lung tissue. Additional studies of highly unsaturated model PLs, other oxidized species, and HAF samples are necessary to confirm assignments in this region.



With best regards,

Rich

Richard A. Komoroski

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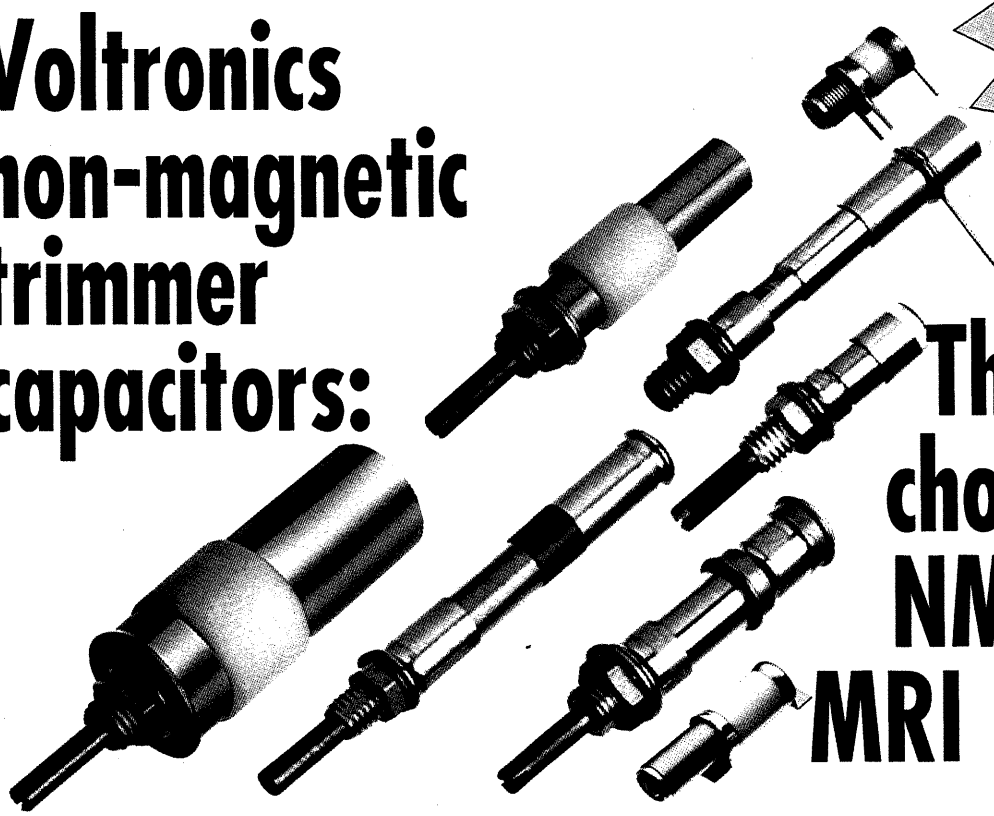

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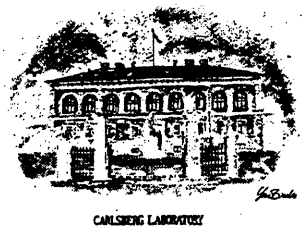


Prof. B.L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto CA 94303, **USA**

April 25, 2001
(received 4/25/2001)

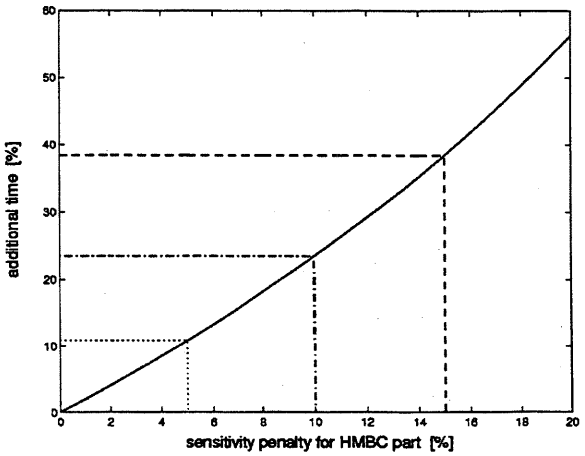
How much sensitivity loss is acceptable in combined experiments?

Dear Barry:

Combining two NMR experiments into one in the sense that two different spectra can be extracted from the same data set is a potential spectrometer time saver. However, time saving can be deceptive if there is a penalty of reduced sensitivity for the combined experiment. The question is how much the sensitivity can drop before the apparent time saver becomes a time loser.

Let us by way of example consider combining HMBC and HSQC in the sense that a one-bond correlation spectrum can be extracted from an HMBC-type data set. HMBC is the least sensitive of the two so that is the experiment where the sensitivity is critical. Suppose there is a sensitivity penalty of x% for the HMBC part of the combined experiment. Then the combined experiment needs to run $\left(1-\frac{x}{100}\right)^{-2}$ times the time for the regular HMBC-type experiment in order to achieve the same signal-to-noise ratio. Of course, it is a bad deal if the added time exceeds the time it would take to record a separate HSQC spectrum.

The diagram to the right shows the additional time for the combined experiment as a function of the sensitivity loss of x% suffered for the HMBC part of the combined experiment. For example, "minor" sensitivity losses of x = 5, 10, or 15% requires that the combined experiment runs 11, 23, or 38% longer to achieve the same signal-to-noise ratio as in a separate HMBC-type experiment. The reference for judging the sensitivity in a spectrum should be the weakest signal of interest. Clearly, in order to estimate the practical value of a given combined experiment it is most helpful to know what its number x is.



The approach MBOB (Multiple-Bond and One-Bond correlation: *Magn. Reson. Chem.* **38**, 981-984 (2000); *The NMR Newsletter*, No. 508, January 2001; http://www.crc.dk/nmr/) for extracting a (broadband) HMBC spectrum and a one-bond correlation spectrum from the same data set is a full time saver as there is zero sensitivity penalty associated with this combined experiment.

Sincerely yours, Thomas Schulte-Herbrüggen Axel Meissner Ole W. Sørensen

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The NMR Newsletter - Book Reviews

Book Review Editor: István Pelczer, Dept. of Chemistry, Princeton University, Princeton, NJ 08544

"Modern Techniques in Protein NMR"

(*Biological Magnetic Resonance*, Vol. 16)

Eds.: **N. Rama Krishna** and **Lawrence J. Berliner**

1998, Kluwer Academic/Plenum Publishers (www.wkap.nl)

ISBN: 0-306-45952-1; 387pp., USD 145.00, EUR 136.00

The excellent series *Biological Magnetic Resonance* has been covering MR applications over a wide range of topics in biomolecular research for many years. Now it presents two consecutive volumes (nos. 16 and 17 - see also the following review by Valérie Copié), that focus on modern protein NMR methods, structure calculations and dynamics. These new books continue with the tradition of high quality summary of methods and developments in this field. Given the rapidly moving target, it shows the ability and hard work of the editors, who managed to bring together an excellent group of authors. Some of the chapters in Volume 16 may look somewhat familiar from earlier publications, and there is some overlap between the topics, but the collection is well selected and highly educational.

Volume 16 consists of two major sections. In the first, the leading theme is studying very large protein systems, including complexes and membrane proteins. In second part, bearing the title of "Pulse Methods", the real subject is coupling between nuclei, its suppression (decoupling), and approaches to its accurate measurement and its use to determine dihedral angle restraints. The book also provides 14 pages of contents of previous volumes in the series, and 5 pages of index.

In the first chapter, Marius Clore and Angela Gronenborn summarize the general strategy for determining structures of large systems, such as proteins and protein complexes, as well as of nucleic acids. They discuss multidimensional NMR, access to various structural restraints, isotope-filtering approaches, and they lay out a detailed strategy for structure refinement, including long-range structural restraints. This outstanding summary is illustrated by impressive examples from their own laboratories.

Isotope labeling is the subject of the following two chapters, in particular labeling large proteins with ^2H. Two leading laboratories present an overview and illustrative summary of some of their results; Kevin Gardner (now at UTSW Medical Center) and Lewis Kay from the Toronto "NMR-fortress", and Sandy Farmer (Bristol-Myers Squibb) accompanied by Ron Venters (Duke). These two chapters have significant overlap, but they are very informative, while some differences in the viewpoint and applications (such as detailed studies of methyl dynamics, and the strategy for rapid determination of overall folding) are quite educational. In the fourth chapter Marassi, Gesell, and Opella summarize multidimensional NMR methods for structural studies of membrane proteins, which field has grown tremendously in recent years.

The next section begins with the excellent summary of homonuclear decoupling by Ēriks Kupče in collaboration with Hiroshi Matsuo and Gerhard Wagner. Kupče has been a pioneer in developing decoupling techniques and sequences (working on such projects also with Ray Freeman), which became indispensable for studies at very high fields. This chapter gives us a well-organized insight how these highly sophisticated multipulse methods are designed and how they work. Attractive examples illustrate the capacity of these methods.

continued

The following chapter is presented by Geerten Vuister and co-workers on measuring coupling constants, a topic developed in large part at the NIH in Ad Bax's laboratory. The experiments presented in this chapter provided the foundation of significant improvement in structure determination of proteins (and all kinds of large biomolecules) in recent years. Using quantitative J-correlation methods opened the door for essential future applications not discussed in this book, such as J-couplings through H-bonds.

In the last chapter Christian Griesinger and his co-authors present an extensive and exhaustive summary of methods that can be used to determine torsion angle restraints in large (and also not that large) molecules. They provide an integrated overview of how these restraints can be extracted taking advantage of various interactions of spins, including conventional NOE/ROE data, J-coupling values, cross-correlated relaxation, other relaxation information, residual dipolar couplings, and chemical shifts. A rich variety of methods, both experimental and those taking advantage of systematic data processing, is presented. The specific examples are about labeled RNA and perdeuterated proteins. The last pages deal with relaxation-based applications.

The rapid development in the field of biomolecular studies by NMR continues with a speed that is difficult to follow by lengthy publications such as a book. There are some methods, which have become very popular lately but are missing from the presentation, or seem to show greater potential than what one would assess from the chapters, such as use of residual dipolar couplings, and measurement of couplings through H-bonds, for example. TROSY type experiments are certainly badly missing from the picture. However, Volume 16 (together with the following volume) presents a very good summary of the fundamental strategies and most of the essential tools for biomolecular structural studies by NMR spectroscopy. I recommend these books warmly to all who are practitioners in this field, and also as reference books in teaching.

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The NMR Newsletter - Book Reviews

Book Review Editor: István Pelczer, Dept. of Chemistry, Princeton University, Princeton, NJ 08544

"Structure Computation and Dynamics in Protein NMR"

(*Biological Magnetic Resonance*, Vol. 17)

Eds.: **N. Rama Krishna** and **Lawrence J. Berliner**

1999, Kluwer Academic/Plenum Publishers (www.wkap.nl)

ISBN: 0-306-45953-1; 384pp., USD 145.00, EUR 136.00

The book presents a series of diverse chapters focusing on areas of actively pursued research within the field of biological NMR. The first section of the book emphasizes novel computation methods that are currently being developed to improve the often cumbersome and tedious NMR approaches presently used to solve the structures of large proteins. The second section, which is much shorter than the first one, covers recent developments in the field of protein dynamics and novel approaches used to investigate hydration in complex biological systems. The book is extended with fifteen pages listing contents of previous volumes in the series and ten pages of Index.

The first chapter of the book presents important concepts about modeling structures on the basis of NMR and x-ray diffraction data. The next two chapters deal with automated resonance assignment protocols. This is an area of considerable interest for the NMR community since the traditional methods of peak picking, NOE assignments, and evaluation of inter-proton distance estimates are very labor intensive and inefficient, especially when analyzing NMR spectra from multiple 2D, 3D, and 4D NMR data sets. First, Braun and co-workers review several approaches being developed to combine automated assignment procedures of multidimensional NMR spectra and calculation of proteins' 3D structures. In particular, they focus on application of the self-correcting distance geometry method and the usefulness of the NOAH-DIAMOD program developed in their laboratory. In a subsequent chapter, Montelione and collaborators describe the AUTOASSIGN program, which is designed to derive backbone H^N, H^α, C', C^α, ^{15}N, and side chain C^β resonance assignments from a specific set of triple-resonance experiments.

A section by Nilges and O'Donoghue follows and describes methods to calculate structures of symmetric protein oligomers from NMR data. The challenge here is to be able to distinguish between intra-unit, inter-unit, and mixed NOE signals. For dimers, this difficulty can be tackled using asymmetric labeling strategy. But ambiguities remain for higher-order oligomers. Nilges and collaborators present a new calculation method, called the symmetry-ADR (ambiguous distance restraints) method, to overcome this problem. The last three chapters in this first section pertain to improved computational methods for structure refinements. The first one, from Gorenstein's group, discusses the use of hybrid-hybrid matrices for 3D NOESY-NOESY data refinement. The next chapter is presented by Thomas James and co-workers, and describes the use of conformational ensemble calculations to generate accurate and precise dynamical structures of proteins by NMR. Lastly, Rama Krishna (one of the book editors) and colleagues review the theory and application of the CORCEMA formalism for the quantitative analysis of transferred-NOESY spectra of reversibly forming ligand-receptor complexes.

continued

In the book's second section, the focus switches to the dynamics of protein structures and to the study of protein-bound water. Prestegard and colleagues lead this second part by presenting exciting new approaches to measure residual dipolar couplings in weakly oriented systems. The authors discuss the benefits of measuring reduced dipolar couplings at high fields, and present applications of residual dipolar coupling measurements to the improvement of NOE-based protein 3D structure refinements, and to the investigations of protein internal motions and dynamics.

A subsequent chapter is a contribution from Heinz Rüterjans and Jan Engelke, in which they discuss recent developments in ^{15}N and ^{13}C relaxation time measurements as they apply to the studies of protein dynamics. Finally, the last two chapters of the book relate to the use of NMR to study protein-bound water molecules. First Bertil Halle and colleagues describe how nuclear magnetic relaxation dispersion (NMRD) methods can be used to characterize hydration states of proteins. Although NMRD has been around for a while, it is only recently that the method has become more amenable to studies of protein-bound water molecules. This chapter stresses the complementary nature of the NMRD and NOE methods for studying the hydration of proteins in solution. It is fair to say that Halle is one of major contributors to the development of NMRD for this purpose. I would enthusiastically recommend this chapter for any reader who would not have the time to read this book in its entirety (hope you do, however!). The book finishes with a chapter by Gottfried Otting, who describes the use of intermolecular water-solute NOEs in the study of bound water molecules.

This book should receive wide interest from anyone involved in solution NMR studies of protein structures and dynamics. I would encourage all interested in new developments in biological NMR to read it.

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Montana State University
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FEBRUARY 16, 2001- FOR IMMEDIATE RELEASE

SIGMA-ALDRICH ACQUIRES ISOTEC TO ENHANCE LIFE SCIENCE CAPABILITIES

February 16, 2001—Sigma-Aldrich Corporation (NASDAQ: SIAL), a $1+ billion life science and high technology company, enhanced its leadership position in life sciences through the acquisition of Isotec, Inc. Founded in 1979 and based in Miamisburg, Ohio, Isotec is a leading producer and supplier of stable isotopes and isotopically labeled compounds used in life science research, medical diagnostics and PET imaging applications. Matheson Tri-Gas, a member of the Nippon Sanso Corporation, previously owned Isotec.

Isotec offers over 2,000 products and is a major raw material supplier for the production of Carbon-13 and Nitrogen-15 labeled compounds, in addition to selling these and other stable isotopes direct to end users. The acquisition is expected to add $15 million to 2001 sales, increasing at least 10% annually for the next several years. The purchase price of $35.6 million was paid in cash. The acquisition will result in no initial charges, have no adverse affect on earnings in 2001 and be accretive thereafter.

David Harvey, Chairman, President and CEO of Sigma-Aldrich said: "Isotec is an excellent addition to our life science portfolio. Their products have high growth potential and will make us one of the leaders in the stable isotope market. Many of our current customers in life science, medical imaging and the manufacture of diagnostic test kits depend on Isotec's products, so this acquisition helps broaden our product relationships with them."

Sigma-Aldrich develops, manufactures and distributes the broadest range of high quality biochemicals, organic chemicals, chromatography products and diagnostic reagents available in the world. Our products are used in high tech research and development in the life sciences, at universities and in industry, for the diagnosis of disease, and as specialty chemicals for pharmaceutical and other manufacturing purposes in more than 160 countries. We are committed to the success of our customers, employees and shareholders through life science, technology and service.

This release contains forward-looking statements relating to future performance, goals, strategic actions and initiatives and similar intentions and beliefs which involve assumptions regarding Company operations, investments and acquisitions and conditions in the markets the Company serves. Although the Company believes its expectations are based on reasonable assumptions, such statements are subject to risk and uncertainty, including, among others, certain economic, political and technological factors. Actual results could differ materially from those stated or implied in this news release, due to, but not limited to, such factors as changes in the business environment in which the Company operates, changes in research funding, uncertainties surrounding government healthcare reform, government regulations applicable to the business and the impact of fluctuations in foreign currency exchange rates. The Company does not undertake any obligation to update these forward-looking statements.

For more information about Sigma-Aldrich, please visit our award-winning web site at www.sigma-aldrich.com.

For questions, contact: Kirk A. Richter, Treasurer 314-286-8004

Fast Field Cycling Magnetic Relaxation Conference
Second Announcement

We are organizing a discussion meeting to be held June 1,2 and 3, Torino, Italy following the Chianti Workshop (May 26-June 1,2001 in Pisa, http://www.cerm.unifi.it/chianti/chianti9.html). The gathering will include poster presentations as well as oral presentations that will focus on discussions of technique, theory, and interpretation of the magnetic field dependence of nuclear spin-lattice relaxation rate constants.

Program Outline:

Friday June 1 12:00 pm Registration
2:00 pm Scientific Sessions Begin

Saturday June 2
Oral Presentations and Discussions
Conference Dinner

Sunday June 3
Final Scientific Sessions, Conference ends at 1:00 pm.

Arrangements:

The meeting will be held at Villa Gualino, which is associated with the Institute for Scientific Exchange. You may see the location at: http://www.isi.it/get.html

The meeting is being arranged electronically. All details for the meeting including the registration are available at the meeting website: http://nmr.ch.unito.it/meeting/ffcrelax/
At this site you may: Register for the meeting, Submit an abstract, Get travel instructions, View the updated scientific program as it develops.

We encourage you to visit this web site and register now if you plan to attend.

We will provide another announcement shortly and update you on the scientific program.

Organizing Committee

Silvio Aime
Robert Bryant
Gianni Ferrante
Claudio Luchinat

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Position Available

U.S. Customs Laboratory

Vacancy Announcement Extended – Now Looking for a Primary Instrument Operator

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. 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 scientists 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.

Position Available

A postdoctoral position is available in July 1, 2001 at the Department of Biochemistry, Case Western Reserve University, Cleveland, Ohio. The research focuses on NMR studies of molecular structure, folding and dynamics in proteins. Applicants should have a Ph.D. in biophysics, biochemistry or molecular biology, with experience in one or more of the following areas: multi-dimensional NMR, protein resonance assignments, protein structure determination from NMR-based restraints, protein expression and purification, pulse sequence modification or other biophysico-chemistry methods, such as fluorescence, circular dichroism, DSC etc.

NMR spectrometers in The Cleveland Center of Structural (CCSB) include two Varian INOVA 600 MHz and one 500 MHz NMR spectrometers. Also available are an 800 MHz NMR facilities at the Ohio State University. CCSB will obtain a 900 MHz NMR instrument in 2003.

Please send a curriculum vitae, two letters of reference, and copies of pertinent publications to:

Qingxin Hua, Ph. D.
Dept. of Biochemistry. Rm-W261
Case Western Reserve University
2109 Adelbert Road.
Cleveland, OH 44106
qhua@biochemistry.cwru.edu Fax: (216) 368-4458

Address all Newsletter correspondence to:

Dr. B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303.
650-493-5971* - *Please call only between 8:00 am and 10:00 pm, Pacific Coast time.*

Deadline Dates

No. 513 (June)	25 May 2001
No. 514 (July)	22 June 2001
No. 515 (Aug.)	20 July 2001
No. 516 (Sept.)	24 Aug. 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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Forthcoming NMR Meetings, continued from page 1:

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.

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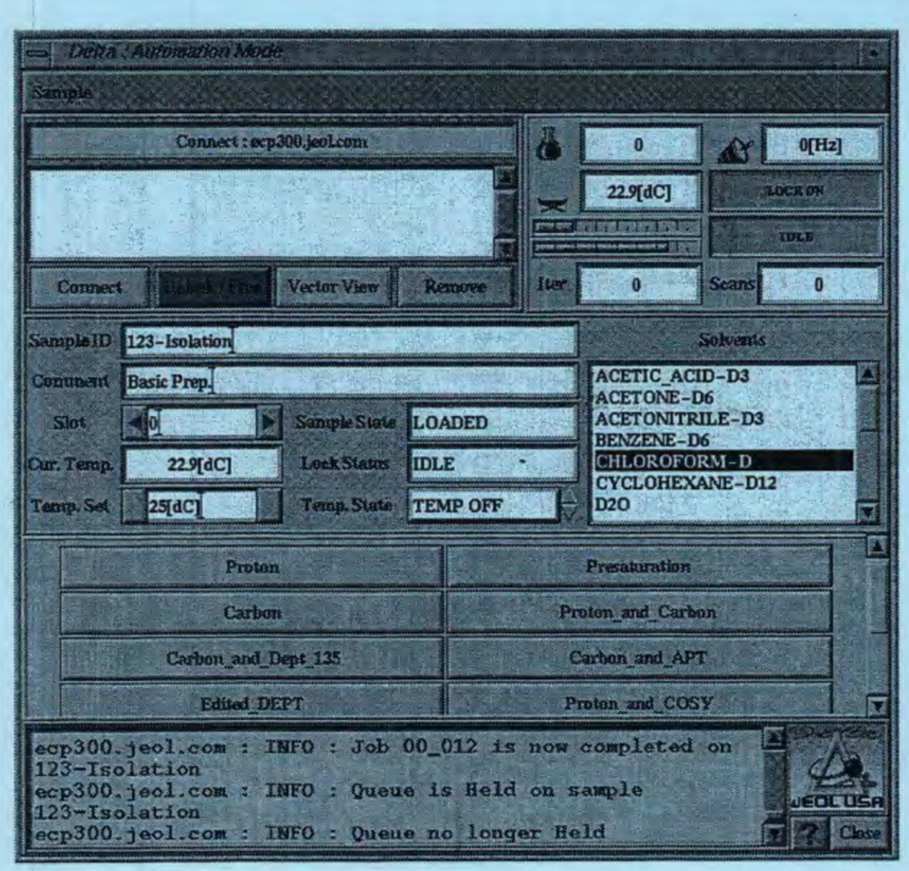

The **Eclipse+** NMR Spectrometer can be operated anywhere there is a computer on the local network. The **Single Window Automation** pictured above can be used with a single mouse click to select the sample from the auto-sample changer, gradient shim on any probe, run the selected experiment, and plot 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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