4th Conference on Field Cycling NMR Relaxometry

Turin (Italy)
May 26-28, 2005

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The ***First symposium on Field Cycling NMR Relaxometry*** was held in Berlin 1998, with the purpose of:
- bringing together all the researchers practicing FC methods with those who do not yet but are interested in applying this technique in the future
- forming a discussion forum promoting and cultivating the description of molecular motions in complex system by spectral densities in relation to recent condensed matter theories and
- dissemination of the information on the technique as well as the potential of its applications

and it proved to be a big success.

The ***2nd*** *and* ***3dt*** meeting, held in Torino in 2001 and 2003, were aimed with the intention of strengthening the interaction between FC users of different areas, stimulating the exchange of new ideas and technical features.

This year, following the big success of the previous meetings, the ***4tht*** symposium wants to congregate again the fast growing and enthusiastic community of FC users & developers.

The purpose of this 4th workshop is :

- to gather people with active interests in nuclear and electron spin relaxation, fast magnetic field switching experiments, low field magnetic resonance, nuclear electric quadrupole resonance, and magnetic imaging.
  - to focus discussion on magnetic field cycling experimental techniques, data interpretation and theory, as well as applications performed by other low-frequency and low resolution NMR techniques.
- to span a range of topics including experimental issues, interpretative foundations, liquids, solids, porous and heterogeneous materials, polymers, biological materials, and diagnostics.

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The official language of the Symposium will be English

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Program

Thursday May 26,2005

10,00-18,00	- Registration	
18,00	- Welcome to the participants	
18.10	- Awarding of FFC2005 conference prize to Prof. Reiner Kimmich :	
18,20	- *Conference opening lecture* ***R. Kimmich -*** *University of Ulm – Germany* Nano- and micropore confinement effects detected by field-cycling NMR relaxometry	*O1*
19,20-21,30	***Welcome party and poster session***	

Friday, May 27, 2005

	Chair: R. Kimmich	
8,30-9,00	***J.P. Korb -*** *Ecole Polytecnique – Palasieau,Frence* Microstructure and texture of hydrated cement-based materials: a field cycling relaxometry approach	*O2*
9,00-9,30	***K. Mueller*** *- Institut of Physical Chemistry – Stuttgard,Germany* Structure, Dynamics and Order-Disorder-Phenomena in Solids: Applications of Solid-State NMR Spectroscopy	*O3*
9,30-10,00	***M. Geppi -*** *University of Pisa-Italy* Dynamics of polymers through a unified analysis of multi-frequency 1H and 13C spin-lattice relaxation times	*O4*
10,00-10,30	***S. Stapf*** *- ITMC RWTH - Aachen, Germany* ^{1}H and ^{2}H relaxation dispersion of partially deuterated polyisoprene - master curves of site-specific molecular dynamics	*O5*
10,30-10,45	***Coffee break***	
	Chair : R.Muller	
10,45-11,15	***D. Lurie –*** *University of Aberdeen – U.K.* Protein Quantitation by Field Cycling MRI	*O6*
11,15-11,45	***Sharon Ungersma*** *– Stanford University – USA* In vivo MR Imaging with T1 Dispersion Contrast	*O7*
11,45-12,15	***H.M. Vieth*** *– Free University of Berlin – Germany* Dynamic nuclear polarization at variable Magnetic Field	*O8*
12,15-12,45	***F. Casanova -*** *ITMC RWTH - Aachen, Germany* Advances in material characterization by ex situ NMR	*O9*
12,45- 14,00	***Lunch break***	
14,00-15,00	***Poster session***	
	Chair: A. Horsewill	
15,00-15,30	***J.Seliger*** *- Jozef Stefan Institute – Ljubljana, Slovenia* Field cycling measurements of ^{14}N NQR frequencies	*O10*
15,30-16,00	***E.Anoardo*** *- Universidad Nacional de Cordoba – Cordoba, Argentina* Acoustic stimulated NMR relaxometry studies in thermotropic liquid crystals	*O11*
16,00-16,30	***P. Sebastiao*** *– Centro de Fisica de Materia Condensada – Lisboa,Portugal* Molecular Dynamics in Liquid Crystals with Peculiar Polymorphisms: Experimental Techniques and Model Fitting	*O12*
16,30-16,45	***Coffee break***	

	Chair: R.Bryant	
16,45-17,15	***T. Apih*** - *Jozef Stefan Institute – Ljubljana, Slovenia* Detection of nitrogen based explosives by field-cycling and quadrupole resonance techniques	*O13*
17,15-17,45	***A.Lundin -*** *Siberian State Technological University - Krasnoyarsk, Russia* NMR-Relaxation in aqueous and alcohol solutions of inorganic salts.	*O14*
17,45-18,15	***E.Sigmud*** *– Schlumberge r- Doll Research – Ridgefield, Usa* Rapid mesaurement of slow NMR relaxation times in the fringe field regime	*O15*
19,30	***Conference dinner***	

Saturday, May 28, 2005

	Chair: S. Aime	
8,30-9,00	***B.Halle*** *- Lund University – Sweden* The mechanism of magnetic relaxation in aqueous gels and tissues	*O16*
9,00-9,30	***R.. Bryant*** *- University of Virginia – Charlottesville, Usa* Fast Field Cycling Applications in Protein and Lipid-Protein Systems	*O17*
9,30-10,00	***M.Fasano*** *– University of Insubria – Busto Arsizio, Italy* Field cycling ^{1}H NMR relaxometry of transferrins	*O18*
10,00-10,30	***C. Luchinat*** *–University of Florence – Sesto Fiorentino, Italy* Direct proton NMRD of biological macromolecules	*O19*
10,30-10,45	***Coffee break***	
	Chair: J.Kowalewski	
10,45-11,15	***D. Kruk*** *– Technical University – Darmstadt, Germany* Field dependent relaxation processes in crystal lattices containing dipolar and quadrupole spins	*O20*
11,15-11,45	***A. Horsewill*** *– University of Nottingham – UK* The influence of heteronuclear dipolar interactions on field-cycling NMR measurements of spin-lattice relaxation:^{13}C,^{19}F,^{2}H and ^{1}H studies of proton tunnelling in the hydrogen bond	*O21*
11,45-12,15	***P. Belton –*** *University of East Anglia – Norwich, UK* Relaxation Time Measurements in Sugar Glasses	*O22*
12,15-12,45	***C. Mattea*** *– University of Ulm – Germany* Hydrodynamic dispersion in the nanoscopic vicinity of surfaces in porous materials investigated by field-cycling	*O23*
12,45-14,00	***Lunch***	
14,00-15,00	***Poster session***	
	Chair B.Halle	
15,00-15,30	***J. Kowalewski*** *– University of Stockholm – Sweden* NMRD and ESR data for slowly-rotating paramagnetic complexes: can we obtain a consistent interpretation?	*O24*
15,30-16,00	***L.Helm*** *– EPFL Lausanne – Switzerland* Water -soluble Gd@C60 derivatives and their proton relaxivities	*O25*
16,00-16,30	***P. Gillis*** *– University of Mons Hainaut –Mons, Belgium* The Paradoxical Relaxivity of Ferritin	*O26*
16,30-16,45	***Coffee break***	
	Chair M. Botta	
16,45-17,15	***J.Desreux*** *– University of Liege – Belgium* Actinide ions investigated by nuclear magnetic relaxation dispersion	*O27*
17,15-17,45	***R. Sharp*** *– University of Michigan - Ann Arbor, Usa* Central Role of Tetragonal 4th-Order ZFS Coupling in the Mechanism of NMR Paramagnetic Relaxation for S>3/2 Ions	*O28*
17,45-18,00	Final discussion	

Oral Presentations

Nano- and micropore confinement effects detected by field-cycling NMR relaxometry

Rainer Kimmich[1], *Carlos Matted*[1], *Nail Fatkullin*[2]

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[2]*Kazan State University, Department of Molecular Physics, 420008 Kazan, Tatarstan, Russia*

It will be shown that the confinement of polymer melts in nanopores leads to chain dynamics dramatically different from bulk behavior. This so-called **"corset effect"** occurs both above and below the critical molecular mass and induces the dynamic features predicted for reptation. A spinodal demixing technique was employed for the preparation of linear poly(ethylene oxide) (PEO) confined to nanoscopic strands which in turn are embedded in a quasi-solid methacrylate matrix. Chain dynamics of the PEO in the molten state was examined with the aid of field-gradient NMR diffusometry (time scale: 10^{-2} s … 10^{0} s) and field-cycling NMR relaxometry (time scale: 10^{-9} s … 10^{-4} s) [1]. The dominating mechanism for translational displacements probed in the nanoscopic strands by either technique is shown to be reptation. A corresponding evaluation formalism for NMR diffusometry is presented. It permits the estimation of the mean PEO strand diameter. Depending on the chemical composition of the matrix, the diameters range from 8 to 58 nm. A "tube" diameter of only 0.6 nm was concluded to be effective even when the strand diameter was larger than the radius of gyration of the PEO random coils. This "corset effect" is traced back to the lack of the local fluctuation capacity of the free volume in nanoscopic confinements [2].

In the second part, the **"flow-relaxation effect"** of a polar fluid confined to pores of a diamagnetic, polar solid material will be reported: It will be demonstrated that hydrodynamic flow reduces the spin-lattice relaxation rate of the fluid in the kHz to MHz frequency regime. The effect was predicted by an analytical theory, and was verified both by field-cycling NMR relaxometry and Monte Carlo simulations of model pore spaces. Adsorbate molecules diffusing in the vicinity of pore surfaces can perform adsorption, desorption and readsorption cycles effectively leading to displacements along the surface. Since the surface determines the orientation of the adsorbed molecule relative to the external magnetic field, desorption at one site and readsorption at another site of a non-planar surface will cause molecular reorientation. This is the basis of the "reorientation mediated by translational displacements" (RMTD) relaxation mechanism. Due to the RMTD process, spin-lattice relaxation dispersion curves reflect the topology of the pore surface. If hydrodynamic flow is superimposed to surface diffusion the RMTD process will be accelerated in a sort of rotational analogue to translational hydrodynamic (or Taylor/Aris) dispersion [3]. In field-cycling NMR relaxometry experiments, this reveals itself by a prolongation of spin-lattice relaxation times at low frequencies. Using a HPLC pump, the effect was measured in a porous monolithic silica material [4]. The flow-relaxation effect takes place in the vicinity of the pore surfaces in a range between molecular distances and distances less than a few hundred nanometers.

[1] R. Kimmich, N. Fatkullin, Advan. Polym. Sci. 170, 1 (2004). **[2]** C. Mattea, N. Fatkullin, E. Fischer, U. Beginn, E. Anoardo, M. Kroutieva, R. Kimmich, Appl. Magn. Reson. 27, 371 (2004). **[3]** M. Sahimi, Rev. Mod. Phys. 65, 1393 (1993). **[4]** C. Mattea and R. Kimmich, Phys. Rev. Lett. 94, 024502 (2005).

Microstructure and texture of hydrated cement-based materials: A field cycling relaxometry approach

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We show how the measurement of proton nuclear magnetic spin-lattice relaxation as a function of magnetic field strength or nuclear Larmor frequency can provide reliable information on the progressive setting of the microstructure of cement-based materials. The remarkable features of the relaxation dispersion support an interpretation in terms of coupled solid-liquid relaxation at pore interfaces, surface diffusion and nuclear paramagnetic relaxation. The measurement does not require any drying of temperature modification and is sufficiently fast to be applied continuously during the progressive hydration of the material. Coupling this method with the standard proton nuclear spin relaxation, 2D T_1-T_2 correlation and high resolution NMR allows us to follow the long-time texturation of the material.

Structure, Dynamics and Order-Disorder-Phenomena in Solids: Applications of Solid-State NMR Spectroscopy

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Dynamic solid-state NMR techniques are applied to characterize various types of solids in terms of their structural and motional behavior over a large temperature range. The studies primarily rely on variable-temperature measurements comprising broad line ^{2}H NMR techniques (line shape, spin-spin and spin-lattice relaxation experiments). The application of suitable simulation programs allows in most cases a quantitative data analysis from which detailed information about the structural (orientational, conformational order) and motional features (intramolecular, overall molecular motions) of the system under investigation can be achieved.

The present contribution reports on representative results from variable-temperature solid-state NMR studies of inclusion compounds. These systems are well-known guest-host materials which can be used for the examination of small organic molecules under confined spatial conditions. Here, we report on inclusion compounds with urea, thiourea, cyclophosphazene and perhydrotriphenylene as host component. The guest components are small (selectively or perdeuterated) organic molecules, such as benzene, pyridine, branched alkanes, bromoalkanes or distyrylbenzene.

It is demonstrated that, in general the guest species are highly mobile, and quite often only become rigid on the NMR time-scale upon cooling to cryogenic temperatures. They exhibit various motional processes, which depend on the actual system under investigation. Thus, we were able to identify and to quantify (local) conformational as well as (overall) rotational motions, the latter of which are directly related to the symmetry properties of the guest molecules and the surrounding host matrix. In fact, depending on the system highly restricted or almost unhindered overall motions were evaluated. In addition, molecular fluctuations were found to play a prominent role for the motional behavior of the guest species. It could be demonstrated that solid-solid phase transitions are not only accompanied by distinct structural changes of the host matrix. Rather, they give rise to pronounced changes of the dynamic features of the guest species, which can be assigned to dynamic order-disorder phenomena.

The ordering behavior of the guest molecules is a consequence of the spatial constraints imposed by the surrounding host matrix. In this context, it was demonstrated that unusual conformational states are stabilized in such guest-host systems. For instance, for branched n-alkanes in urea and thiourea inclusion compounds ecliptic chain conformations could be unequivocally detected, which otherwise are energetically very unfavorable.

If time permits, we will also briefly report on variable-temperature ^{11}B NMR studies on dodecaborate clusters $B_{12}X_{12}^{2-}$, which differ in the substituents X = H, Cl, Br, I as well as the respective counter ions (Na, K, Rb, Cs, NH_4). It could be shown that the dodecaborate clusters undergo thermally activated icosahedral jumps, while the positional order remains unaltered. The derived kinetic parameters were found to depend strongly on the actual chemical structure of the $B_{12}X_{12}^{2-}$ clusters, i.e., substituent X or counter ion. A comparison with the structural data proves that this is a direct consequence of the packing effects in these dodecaborate systems.

Dynamics of polymers through a unified analysis of multi-frequency ^{1}H and ^{13}C spin-lattice relaxation times

Marco Geppi[1], Claudia Forte[2], Marco Malvaldi[1], Giulia Mollica[1], Carlo Alberto Veracini[1]

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2 *Istituto per i Processi Chimico Fisici, CNR, Area della Ricerca, via Alfieri 1, 56010 Ghezzano, Pisa, Italy.*

A new approach to extract reliable quantitative dynamic information from NMR relaxation data of amorphous polymers has been recently presented[1], consisting of the simultaneous fitting of ^{1}H and ^{13}C T_1 vs temperature curves, obtained at different frequencies, by means of unified motional models. The reliability of the dynamic parameters obtained by this approach is substantially increased with respect to the single curve and/or single nucleus analysis because of the possibility of both investigating motions over a wide frequency range and combining relaxation times carrying either global (^{1}H) or local (^{13}C) dynamic information.
Here, the dynamics of three ethylene-propylene amorphous random copolymer, at different ethylene/propylene ratios, was investigated by analyzing proton relaxation times measured by wideline NMR techniques at three Larmor frequencies (25, 300 and 400 MHz), and carbon T_1's measured by high-resolutions techniques (MAS and High-power proton decoupling) at two Larmor frequencies (75 and 100 MHz). The measurements were carried out as a function of the temperature in the temperature range 238-358 K, just above the glass-transition temperature.
The experimental data were analyzed in terms of segmental main-chain motion, rotation of the methyl groups about their ternary symmetry axes, and libration of C-H bonds, described by suitable models.

[1] C. Forte, M. Geppi, M. Malvaldi, V. Mattoli, *J. Phys. Chem. B* **2004**, *108*, 10832-10837

^{1}H and ^{2}H relaxation dispersion of partially deuterated polyisoprene – master curves of site-specific molecular dynamics

Sobiroh Kariyo, Siegfried Stapf

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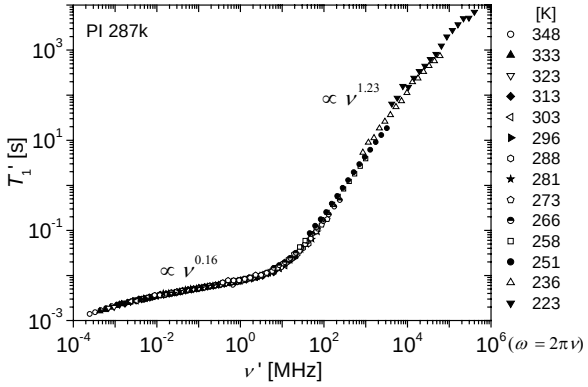
The proton T_1 frequency dependence in polyisoprene has been reported [1] to be significantly weaker than that described for a range of other polymers [2]; in fact, available theories do not support such a weak dependence [3,4]. On the other hand, this characteristic feature is found also in polyisoprene-based elastomers so that a more thorough investigation seemed worthwhile. For these reasons, polyisoprene has been taken as a test case to pursue a detailed study of molecular mobility employing a set of differently labelled polyisoprene standards (methyl deuterated, main-chain deuterated, and perdeuterated [5]) and comparing the ^{1}H as well as ^{2}H relaxation dispersions over a frequency range as wide as possible.



By applying the time-temperature superposition principle, master curves of the relaxation dispersion covering about nine orders of magnitudes in frequency were generated. The two features dominating the dispersion of polyisoprene – a weak frequency dependence on the low-field region and a steep slope indicating local motions at higher fields – is shown at right for the fully protonated sample. The essential question one has to ask is whether the comparatively small value of the exponent does indeed reflect the spectrum of reorientational motions, or is the consequence of some other effect. This could be a strong intermolecular contribution to the relaxation, possibly possessing a different frequency dependence, or a particular effect of the methyl group, as the structurally similar polybutadiene follows the expected frequency dependence. Both possibilities could be ruled out by partial and full deuteration of the material: apart from small differences which can be attributed to isotope effects, the ^{1}H dispersion exponent was found to be the same for all samples, and ^{2}H relaxation showed exactly the same value. While a pure steric influence of the methyl group on the chain mobility may exist, the reorientational spectrum of the methyl group is identical to that of the backbone, and the equivalence of proton and deuteron results rules out intermolecular interactions of different frequency dependence.

[1] S. Kariyo, S. Stapf, *Macromolecules* **35**, 9253 (2002).
[2] H. W. Weber, R. Kimmich, *Macromolecules* **26**, 2597 (1993).
[3] M. Doi, S.F. Edwards, *The Theory of Polymer Dynamics*, Clarendon, Oxford, 1986.
[4] N. Fatkullin, R. Kimmich, *J. Chem. Phys.* **101**, 822 (1994).
[5] F. Alvarez, J. Colmenero, R. Zorn, L. Willner, D. Richter, *Macromolecules* **36**, 238 (2003).

Protein Quantitatation by Field-Cycling MRI

G.R. Davies, G.C. Cameron and D.J. Lurie, Bio-Medical Physics, University of Aberdeen, UK

Introduction:

It is well known that "quadrupole dips" occur in the T_1-dispersion plots of samples containing immobilised protein molecules [1,2]. The markedly-reduced T_1 values are due to enhanced ^{1}H relaxation at those field strengths where the ^{1}H NMR frequency coincides with one of the ^{14}N NQR frequencies.

When T_1-dispersion data is plotted as relaxation rate ($R_1 = 1/T_1$) versus magnetic field, peaks occur at the "quadrupole dip" field strengths. Jiao and Bryant [2] previously showed that the size of these peaks, ΔR_1, is proportional to a sample's protein concentration, where

$$\Delta R_1 = R_1^{QD} - R_1^0 \qquad (1)$$

Here, R_1^{QD} is the measured R_1 value at the field where a dip should occur (e.g. 65 mT) and R_1^0 is the predicted R_1 value at the same field in the absence of the effect (obtained by interpolation).

In this work we have extended these ideas in order to generate "ΔR_1" images, the intensity of which should be proportional to the concentration of immobilised protein [2].

Methods:

A field-cycled inversion-recovery imaging pulse sequence was used. An initial polarisation period at 450 mT was applied, at the end of which the magnetisation was inverted by a 10 ms adiabatic fast passage (AFP). (AFP was used for inversion, to provide immunity from B_1 and B_0 field inhomogeneity.) The field was then switched to its evolution value, around 65 mT, for approximately 150 ms. Then the field was returned to 450 mT and the signal was read out using a 90° pulse. In imaging experiments, gradients were also applied during this detection period. In order to generate a ΔR_1 image, k-space data was collected with and without inversion at three evolution magnetic field values: 56 mT, 65 mT and 75 mT. The R_1^0 value at 65 mT was calculated by linear interpolation of the R_1 values measured at 56 mT and 75 mT. R_1^{QD} was calculated directly from the data obtained at an evolution field of 65 mT, and a ΔR_1 image was generated via Eq. 1, using software written in IDL.

The imager used for these experiments was a new home-built field-cycled MRI system with signal detection at 450 mT [3], suitable for samples up to 60 mm diameter.

Results and Conclusion:

Figure 1 shows an R_1 dispersion curve obtained from a sample of heat-treated hen's egg albumin; the peaks at 49 mT and 65 mT are clearly visible. The dashed line indicates the linear fit of R_1 between 56 mT and 75 mT, from which ΔR_1 was calculated. Figure 2 shows a calculated ΔR_1 image of a test-object composed of tubes (11 mm i/d) filled with protein-containing gels (various concentrations of BSA or egg albumin). Initial results show good correlation between ΔR_1 (from the image) and protein concentration.

In conclusion, our initial results confirm the feasibility of non-invasive, quantitative protein concentration imaging.

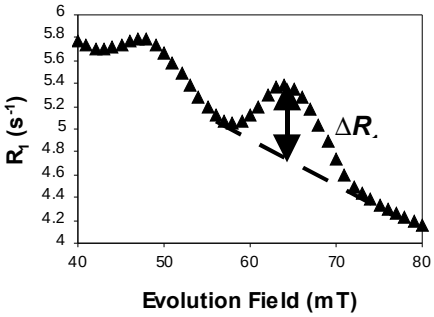


Figure 1: Measured R_1 dispersion of heat-treated hen's egg albumin.

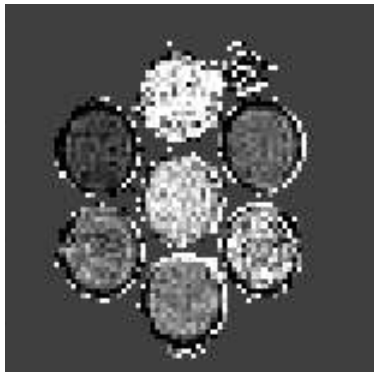


Figure 2: Section from calculated ΔR_1 image of multi-sample gel sample.

References:

[1] Kimmich R. *et al.*, Phys. Med. Biol. **29**, 593 (1984).
[2] Jiao X. & Bryant R.G., Magn. Reson. Med. **35**, 159 (1996).
[3] Lurie D.J. *et al.*, Magn. Reson. Imaging **23**, 175-181 (2005).

In vivo MR Imaging with T_1 Dispersion Contrast

S.E. Ungersma[1], N.I. Matter[2], A. Macovski[2], S.M. Conolly[3], G.C.Scott[2]
[1]Department of Applied Physics, [2]Department of Electrical Engineering, Stanford University, CA, USA
[3]Department of Bioengineering, UC Berkeley, CA, USA

Introduction. We are investigating a new contrast mechanism to provide protein contrast for MRI. This technique uses a prepolarized MRI scanner composed of two pulsed electromagnets: a strong magnet to polarize the sample and a low-field homogeneous magnet for signal readout [1]. For tissues whose T_1 varies with magnetic field (T_1 dispersion), changing the field strength allows the tissue magnetization to decay with a new value of T_1. The difference between two images taken after allowing the magnetization to evolve at different field strengths yields an image with T_1 dispersion contrast: tissues with flat T_1 dispersion curves are dark and tissues with rapidly changing T_1 dispersion curves are bright [2]. In particular, tissues with high protein content, such as muscle tissue or myelin, exhibit rapid changes in their T_1 dispersion curves near 50 mT and 65 mT due to cross-relaxation with nitrogen nuclei in the protein backbone [3,4]. We have created images with protein content contrast from differences in T_1 dispersion between fat or unbound water (no protein content), which have roughly constant T_1 over a small field range, and muscle tissue (high protein content), which has a rapidly varying T_1 near the quadrupole dips. We demonstrate this technique on *ex vivo* samples [5] and *in vivo* on a normal volunteer.

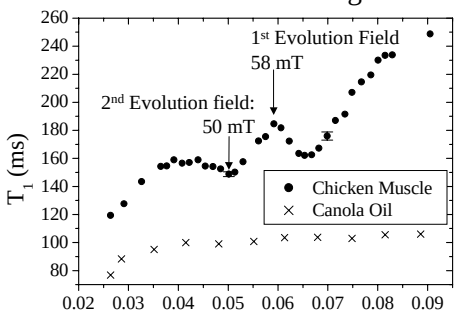


Figure 1.

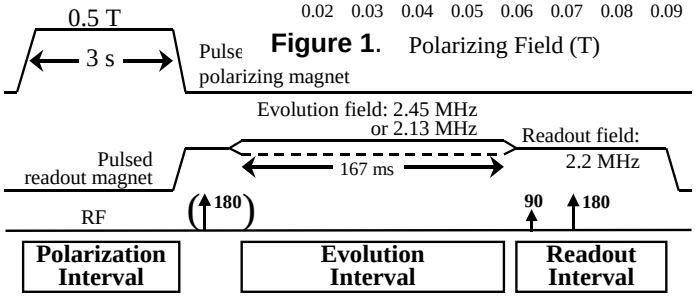


Figure 2. Pulse sequence of PMRI magnets.

Methods. Figure 1 shows T_1 dispersion measurements taken with our prepolarized MRI scanner on muscle and fat samples [6]. Between the two evolution fields (indicated with arrows), the T_1 of the muscle tissue changes by ~35 ms (20%), while the T_1 of the fat sample stays virtually constant. We exploit the different slopes of the two T_1 dispersion curves using the pulse sequence shown in Fig. 2. A strong polarizing pulse (0.5 T) is followed by an evolutionary pulse (50 mT or 58 mT), and then the RF excitation and readout is performed at an intermediate field (52 mT). The final image with T_1 dispersion contrast is created either by direct subtraction between the high and low field data sets or by cluster analysis. Cluster analysis can determine which voxels had different T_1 values in the two images; masking removes voxels whose T_1 was the same in each image.

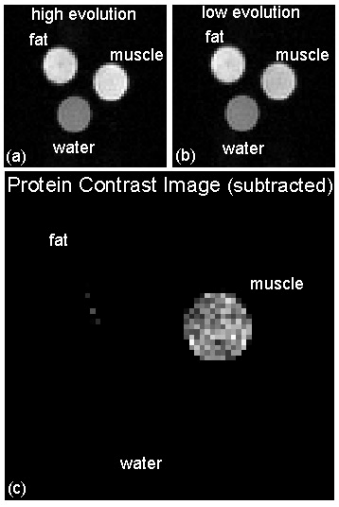


Figure 3. 4 cm FOV (64×64), 2D projections. Samples are 1 cm diameter, 3 cm in depth.

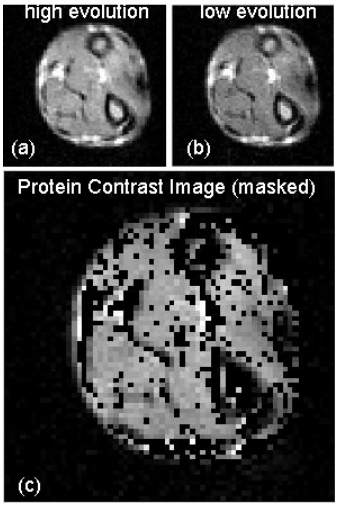


Figure 4. 8 cm FOV (64×64), 2 cm slice thickness.

Results. In our *ex vivo* test, we imaged three samples: muscle tissue and fatty tissue (chicken), and water doped with copper sulfate (T_1~100 ms). Figure 3(a,b) shows two images taken with different evolutionary field strengths: (a) 58 mT evolutionary field, and (b) 50 mT evolutionary field. Figure 3(c) shows the direct subtraction of the two images. In the resulting image, the signal from the fat and water samples (no protein content) has been almost entirely subtracted out, while the signal from the muscle sample (high protein content) is still significant.

We also imaged the arm of a normal volunteer. Figure 4(c) shows a T1 dispersion image generated by cluster analysis; the high evolution field image was masked to eliminate pixels that had the same intensity in both images. The masking threshold was determined by calculating the theoretical difference in intensity between muscle tissue in the high and low field evolution images (23%), and then setting the threshold halfway between the calculated difference and unity (meaning identical T_1 in the two images). Regions of fat (no protein content) which appear bright in the original images (a,b) are dark in the image with T_1 dispersion contrast. This technique may provide a new contrast mechanism for imaging disorders that affect protein content, such as myopathies in muscle tissue, demyelinating diseases in white matter, or diseases which cause protein deposition in the major organs.

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Dynamic Nuclear Polarization at Variable Magnetic Field

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The NMR spectra of reaction products resulting from a radical reaction often exhibit an anomalous intensity pattern because of transient spin polarization generated in the course of the reaction. While other well-known mechanisms of dynamic nuclear polarization, e.g. the Overhauser effect, rely on pumping of electron spin transitions this Chemically Induced Dynamic Nuclear Polarization (CIDNP) results from spin-selective reaction steps and it has been widely used for analyzing intermediate reaction stages. For reasons of resolution and sensitivity the CIDNP is usually studied at the fixed external magnetic field of the NMR spectrometer. Such a practice limits the potential of the CIDNP method because the polarization efficiency strongly depends on the external magnetic field strength. For exploiting the full scope we perform our experiments at variable magnetic field. This opens the opportunity of determining the mechanism of polarization and extracting magnetic resonance parameters of the radical intermediates responsible for the CIDNP formation. While the high field part of the CIDNP depends on both the g-factor and the hyperfine interactions (HFI) of the radicals, the CIDNP at low field is conditioned solely by the HFI. Therefore, the analysis of the low field CIDNP provides information on the HFI constants. Once the HFI constants have been determined, the g-factor of the radical can be obtained from the CIDNP at high field. Thus, such a strategy allows one to extract the desired magnetic resonance parameters from the field dependence of the CIDNP. Because all individual field dependencies of the nuclei in a radical pair are simulated together with one common set of parameters, the fitting procedure is sensitive in spite of the large number of parameters.

Necessary for such experiments is a field cycling NMR spectrometer with high spectral resolution that operates over a wide field range and allows light irradiation. We designed a mechanical field cycling set-up employing digitally controlled rapid positioning of the NMR probe in the fringe field of the 7T cryomagnet of our 300 MHz spectrometer used for detection. It permits the observation of NMR-spectra under permanent slow sample-rotation (0-150Hz) or MAS (up to 5 kHz) while allowing spin evolution at any desired magnetic field strength between earth magnetic field and 7T. At a field below 0.1 T, where a high homogeneity of the magnetic field across the sample volume is required, the field setting is achieved by control of the electric current through a pair of auxiliary Helmholtz coils placed under the cryomagnet. Details of the design will be discussed.

One application was the investigation of various amino acid radicals generated as a result of quenching the triplet state of a photoexcited dye molecule by histidine, tyrosine, tryptophan or methionine. In aqueous solution different radical species and reaction pathways are observed at variation of the pH. Other studies to be presented include the identification of the polarization mechanism and its change when the molecular mobility is reduced.

Advances in material characterization by ex situ NMR

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Nuclear Magnetic Resonance is a established analytical tool widely used for structural and conformational determination in chemistry, biology, medicine and material science. Material characterization is carried out by measuring NMR parameters like chemical shift, nuclear spin relaxation times, dipolar couplings, and self-diffusion coefficients. NMR methods are mainly developed to work in the strong and homogeneous field of superconducting magnets, but the limited working volume of these devises dramatically restricts the application field of NMR techniques for *in situ* studies. In contrast to conventional NMR, where the sample is adapted to fit into the probe, inside-out NMR uses open magnet geometries specially adapted to the object under study. The advantage of such analysis is that limitations of sample size and transportability no longer prevail, but an accompanying handicap is that the static magnetic field is necessarily spatially inhomogeneous. This circumstance has two important consequences. First, the NMR spectrum of the sample becomes strongly broadened to the extent that a spectroscopic characterization of the sample seems impossible in this case. Second, non-uniform gradients in the static magnetic field make single-sided Magnetic Resonance Imaging (MRI) particularly troublesome. As a natural result, most applications to date have been constrained to use relaxation parameters as qualitative indicators of the material composition or structure.

During the last years, a sustained effort in the design of dedicated single-sided NMR probes as well as the development of suitable techniques to be used in the presence of inhomogeneous magnetic fields has lead to an important step ahead in the characterization of arbitrarily large objects in situ. In this work we will give an overview of the most recent achievements in this field. In particular, we will present the development of methodologies for imaging and ex-situ spectroscopy, giving particular emphasis to the important role of the magnet design in the final performance of these techniques.

Field cycling measurements of ^{14}N NQR frequencies

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Various nuclear quadrupole double resonance techniques based on magnetic field cycling may be used to determine the ^{14}N nuclear quadrupole resonance frequencies in solids and in ordered liquids. The choice of the technique as well as its sensitivity strongly depend on the experimental parameters. Some most useful techniques will be discussed in details and illustrated in cases of 4,4'-azoxyanisole (PAA), 4,4'-bis(heptyloxy)azoxybenzene (HpAB), nicotinic acid and sulfamerazine.

ACOUSTICALLY STIMULATED NMR RELAXOMETRY STUDIES IN THERMOTROPIC LIQUID CRYSTALS

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The study of NMR relaxation in the presence of sonication can be used to display new features of the underlying molecular dynamics. In this context, liquid crystals are particularly interesting due to their relative molecular simplicity and observable couplings between the director and acoustic fields [1-3]. A strong coupling between the sonic field and order director fluctuations (ODF) exist trough density modulation across the sample volume [4]. The frequency spectrum of the hydrodynamic modes corresponding to the collective dynamics can be modified through the ultrasonic field, while the observation of these processes can be conveniently performed in a broad dynamical range. This experiment can conveniently be implemented through field-cycling NMR relaxometry [1,5-8], thus allowing to extend the study into the kHz Larmor frequency range, where ODF´s can be better observed through the proton spin-lattice relaxation time T_1 [9]. The topic will be revisited and new physical insights will be discussed.

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Molecular Dynamics in Liquid Crystals with Peculiar Polymorphisms: Experimental Techniques and Model Fitting

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Liquid crystalline compounds containing a strong polar terminal group often exhibit peculiar polymorphisms including different types of smectic A and C mesophases and reentrant behaviour of nematic, smectic A and C phases [1]. These systems are particularly interesting from the molecular dynamics study point of view, since with just one system it is possible to study the molecular dynamics in different mesophases, or mesophases of the same type but which appear in a reentrant sequence.

A short review of the molecular dynamics studies in three liquid crystalline systems exhibiting different polymorphisms including N, SmA1, SmAd, SmA2, SmC2, reentrant N and reentrant SmA phases with different periodicities is presented [2]. The experimental techniques used to obtain the experimental results and some aspects of the model fitting process will be described.

The combined use of classical and fast field-cycling NMR techniques to obtain the spin-lattice relaxation dispersion over a very large frequency range from the kHz to hundreds of MHz allows for a better separation of the different mechanisms contributing to the relaxation [3]. The analysis of the experimental results can be greatly improved if, in addition to the frequency dispersion, temperature and angular T1 dependences are also considered in the model fitting performed simultaneously to all T1 experimental results using a global-target least-square minimization procedure [4].

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Detection of nitrogen based explosives by field-cycling and quadrupole resonance techniques

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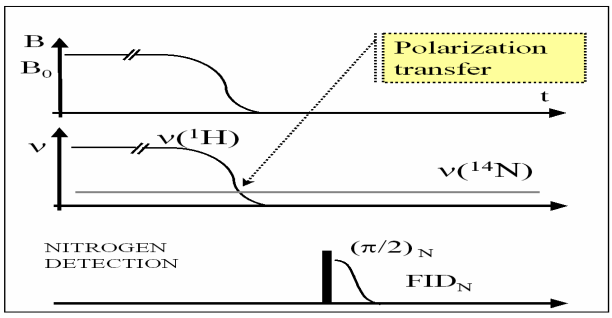
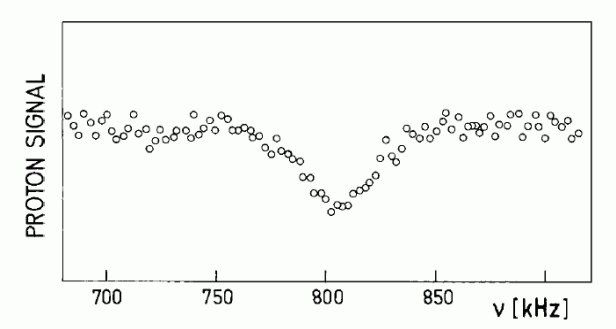
Practically all of the explosives used in landmines (Trinitrotoluene (TNT), Hexogen (RDX), Octogen (HMX), Nitropenta (PETN) or combinations of those) contain nitrogen, which is a quadrupole nuclei (I=1). This opens up an exciting possibility of developing a nuclear quadrupole resonance based mine detection technique, which would not depend on the presence of metal in the booster, landmine shape, its dielectric or temperature capacity difference to soil, but would rather detect the presence of the explosive itself. While remote detection of RDX (with ν_{NQR} between 3.4 and 5 MHz) has been successfully demonstrated, detection of the most commonly used explosive TNT is hampered by the low sensitivity due to sub-MHz ν_{NQR}.

To overcome the low sensitivity problem of TNT detection, we have used two methods for the detection of sub-MHz ^{14}N NQR signals:

1. ***Polarization enhanced NQR (PE-NQR)***. In this experiment, ^{14}N NQR is directly detected in zero field, but signal is enhanced by the transfer of the nuclear polarization from ^{1}H nuclei, polarized in high magnetic field. Here, enhancement factor of 7 was achieved on the 0.98 MHz ^{14}N NQR line in 4-nitrobenzoic acid.



2. ***Proton-nitrogen nuclear quadrupole double resonance (NQDR) with magnetic field cycling***. Here, ^{1}H NMR signal is measured after coupling with ^{14}N by means of field cycling and rf irradiation, achieving S/N increase up to 30.



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NMR-RELAXATION IN AQUEOUS AND ALCOHOL SOLUTIONS OF INORGANIC SALTS

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Here some results on investigations of structure and dynamics of aqueous and alcohol solutions of inorganic salts studied in the NMR-group of Physics Department of Siberian State Technological University using NMR-relaxation are presented [1-10]. It is well known that the theory of liquid state is far from closing. Therefore the experimental methods and, in particular, NMR-relaxation to study this state are very necessary. NMR relaxation data can be used to extract information about the composition of the hydration spheres near paramagnetic (diamagnetic) ions, the distances and the lifetimes of water molecules around ions, etc. One of the important interactions between solvent (water) and dissolved substance is hydrophobic hydration [1], which does not involve the formation of chemical bonds between the solute and solvent. The concept of negative and positive hydration [2, 3] is used in solving the problems of the liquid state. For the ions with so called positive hydration the mobility of the water molecules in the first hydration sphere being lower compared to that in the free water and vice versa for the ions with negative hydration. But this is mainly theoretical predictions which have not good experimental confirmation. It is important also in this connection to investigate the rate of protons exchange between water molecules.

In the work [4] the structural and dynamics characteristics of the Cu (II) solvate complex in aqueous solutions were studied. To improve the accuracy of determination of structural and dynamics characteristics of solvate complexes we suggest the procedure and fulfilled experiments at low temperatures (~ 140 - 220 K). At the bottom of this range the solutions were in vitrified state and at the top - in the state of metastable liquid. In the work [5] the structure and dynamic characteristics of aqueous solutions near the Cu (II) and Ni (II) ions in the wide temperature range were studied and in [6] - near the ions Cu (II) and Mn (II). The results of investigation of the same solutions at a constant ionic strength of solutions are described in [7]. The article [8] is devoted to the study by 1H and 17O NMR and NMR-relaxation the rate of proton exchange in solvates of alkali metals in water and methanol solutions and [9] - to the study of the aqueous solutions of ethanol using PMR-relaxation. In [10] the results of investigations of aqueous solutions of Praseodymium salts by high resolution and broad line NMR as well as by 1H and 17O NMR-relaxation are presented. Now the study of aqueous solutions containing some other lanthanides is in progress and the obtained results will be published in the near future.

The experiments were performed with the use of the equipment provided by the Collective Use Center of the Siberian Division of the Russian Academy of Sciences.

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Rapid measurements of slow NMR relaxation times In the fringe field regime

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The measurement of T_1 plays a key role in the study of biological materials, porous media, and biomedical imaging. The necessity of tracking the magnetization evolution from excitation to full recovery, however, makes the T_1 sequence problematic. Shortening this intervals below several T_1 typically leads to fit errors from confusion with full magnetization M_0, since the short time (t) behavior of a recovering signal does not distinguish the two:

$$M(t) = M_0\left(1 - e^{-t/T_1}\right) \approx M_0 \frac{t}{T_1} \tag{1.1}$$

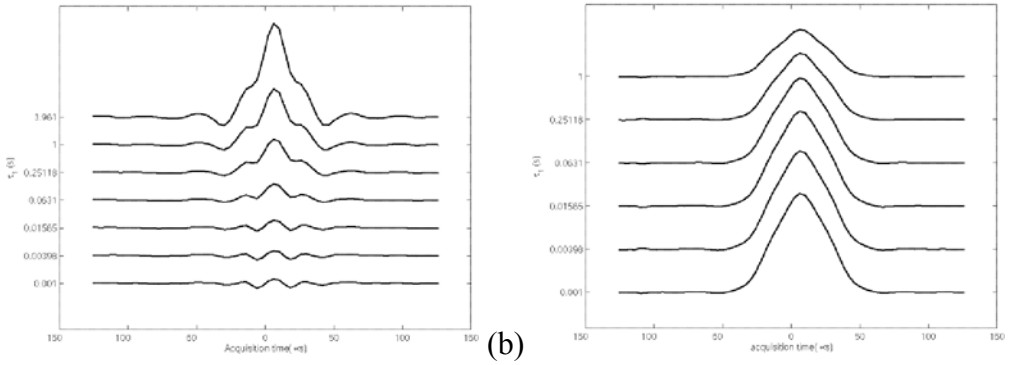
Many techniques address this issue, including the approach to steady-state magnetization, progressive steady-state saturation, field gradient signal separation for simultaneous acquisition, or timing optimization of the standard inversion/saturation recovery.

NMR well-logging is a unique regime, including (1) a static, inhomogeneous field, (2) acquisition in a moving tool, and (3) presence of very slowly relaxing materials—e.g. bulk water. These conditions require a specialized technique for fast T_1 measurement. The method we describe focuses upon shortening both the measurement period dramatically without loss of accuracy in T_1.

The evolution of the longitudinal magnetization following any excitation carries two components: (1) a "recovery" component from fresh magnetization growth, and (2) a "decay" component from the return to equilibrium of perturbed spins:

$$M_z(\tau) = \underbrace{M_0(1 - e^{-\tau/T_1})}_{\text{recovery}} - \underbrace{M_0' e^{-\tau/T_1}}_{\text{decay}} \tag{1.2}$$

We describe several pulse sequences isolate these two components experimentally. The clear advantage the "decay" component is its single exponential form. We discuss demonstration of this technique as well as its extension to distributed relaxation rates and multi-component systems.



(a) (b)

Fig. 1 : Time dependences of fringe-field echo shapes for two different T1 experiments. (a) Standard saturation recovery. (b) FIR/SR decay signal. The decay channel features a simple, time-independent shape that provides accurate T1 with short time measurements only.

The mechanism of magnetic relaxation in aqueous gels and tissues

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In magnetic resonance imaging of soft tissue, intrinsic contrast is generated mainly by spatial variations of water ^{1}H spin relaxation rates, which are linked to the molecular structures and dynamics of the tissue. Previous work on magnetic relaxation in tissues and tissue-like model systems has been dominated by single-field, steady-state magnetization transfer experiments, which do not provide sufficient information to elucidate the molecular mechanisms and are usually interpreted in terms of phenomenological models with little predictive power. A few groups have also reported magnetic relaxation dispersion (MRD) data, but the observed ^{1}H R_1 dispersion profiles have been fitted to empirical expressions or rationalized in terms of explicit relaxation models that have not been decisively tested. A quantitative, molecular-level understanding of the mechanistic basis of intrinsic image contrast is therefore not available.

Our approach to this problem has three main ingredients. First, we study model systems – agarose and gelatin gels – that share the essential features of soft tissue (such as high water content and immobilized macromolecules) but otherwise are as simple and well-characterized as possible. By studying these systems as a function of pH, we can identify the species responsible for the observed relaxation effects. Second, we acquire both ^{1}H and ^{2}H dispersion profiles (over 4–5 frequency decades), complemented with ^{17}O MRD data. Because quadrupolar (^{2}H and ^{17}O) relaxation only involves single spins, it is easier to analyze than dipolar (^{1}H) relaxation, where cross relaxation comes into play. Third, we analyze the data in terms of relaxation theory that is rigorously valid for the investigated systems. This requires a stochastic Liouville approach that goes beyond the conventional motional narrowing approximation as well as a new perspective on cross-relaxation.

The principal conclusions emerging from this work are as follows:

1. The R_1 dispersion is mainly due to long-lived internal water molecules in the agarose double helix and to labile OH and NH hydrogens in the collagen triple helix.

2. All our relaxation data can be quantitatively rationalized in terms of a single relaxation-inducing motion: exchange between bulk water and trapped water molecules (μs time scale) or labile hydrogens (ms time scale). There is thus no need to invoke macromolecular motions.

3. Cross-relaxation between exchanging (water or OH/NH) protons and directly dipole-coupled nonlabile macromolecular protons quenches the secular spectral density that would otherwise contribute at high frequencies. Unlike previously discussed cross-relaxation models for biological macromolecules, here it is the exchange itself that provides the relaxation sink.

4. Because the exchange rates are smaller than the (residual) dipolar/quadrupolar frequency, the motional-narrowing approximation breaks down. For ^{1}H relaxation due to labile proton exchange on the ms time scale, the stochastic theory predicts that the dispersion occurs at the dipolar frequency, rather than at the motional frequency (inverse correlation time).

5. The ability to quantitatively describe the ^{1}H and ^{2}H relaxation over 5 frequency decades in terms of water and labile hydrogen exchange (and nothing else) in polysaccharide and polypeptide gels (systems that are frequently used as MRI phantoms) suggests that spin relaxation in tissues can be understood in terms the same molecular mechanisms.

Fast Field Cycling Applications in Protein and Lipid-Protein Systems

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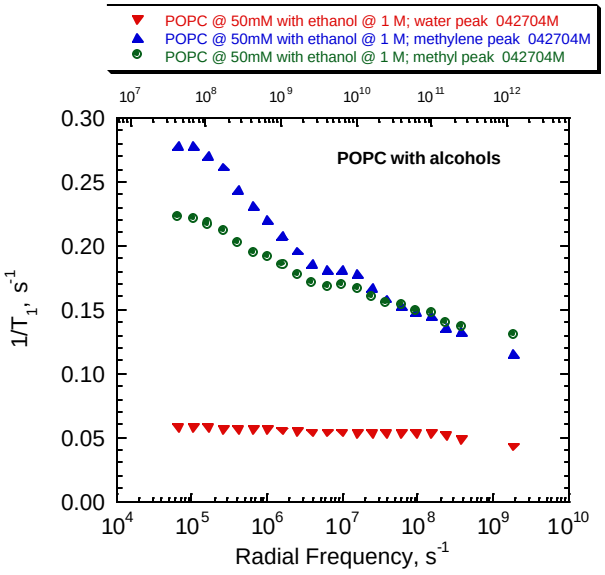
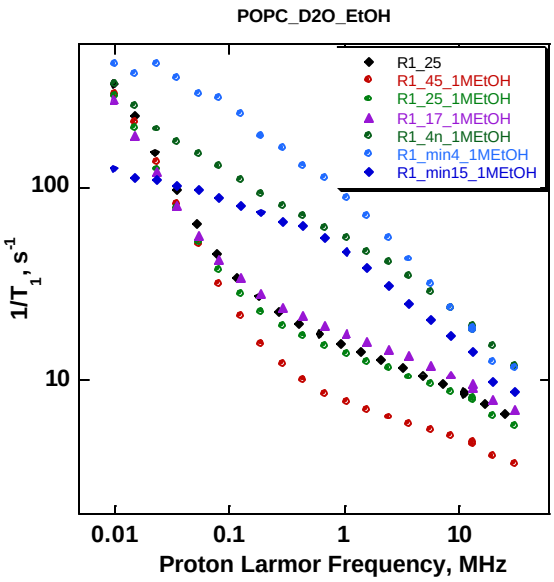
High resolution field cycling permits examination of individual relaxation dispersion profiles of multicomponent solutions. The ^{1}H spin-lattice relaxation of ethanol protons and residual water protons in D_2O preparations of phosphatidyl choline vesicles is dominated by the magnetic couplings at the vesicle-solvent interface. However, the relaxation dispersion data show that the relaxation detected in the small molecule spin systems is not simply the result of a magnetization transfer from the bilayer lipid protons to the small molecule protons. The lipid proton relaxation is distinctly different from the co-solvent molecule relaxation so that the relaxation dispersion of the small solutes reports the interfacial dynamics rather than the lipid chain dynamics.

A limitation of sample shuttling methods for providing high resolution MRD is the problem of high relaxation rates at low fields, which may destroy the magnetization during transit even if the target field is not low. This problem makes recording the complete relaxation dispersion profile for a solution phase protein difficult because as the magnetic field falls below the rotational dispersion, the protein spin relaxation rate becomes very large. A strategy to record complete relaxation-dispersion profiles is to control the relaxation rate of a labile observe ligand that samples the macromolecule sites by chemical exchange as in a transferred NOE experiment. If the thermodynamics and dynamics of the labile ligand are appropriately chosen, the magnetic field dependence of particular intramolecular vectors may be examined in detail over a complete magnetic field profile. We will discuss several aspects of this strategy in the context of protein and membrane bound protein dynamical studies.

Proteins are reported to suffer a glass transition at low temperature. The proton MRD profile in both dry and hydrated proteins provides important insights to the character of this transition in proteins at low temperature. The proton MRD profiles on serum albumin recorded as a function of temperature between 150 K and 315 K demonstrate the crucial participation of water in the definition of the protein structure and dynamics.





Field cycling ^{1}H NMR relaxometry of transferrins

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Transferrins are an extended family of iron binding proteins. This family includes different subtypes: serum transferrin (Tf) is found predominantly in mammalian blood and appears to be the main iron regulatory/transfer molecule; lactotransferrin (Lf) is found in mammalian milk, tears, saliva and vaginal secretions and is involved in host defence mechanism related to the non-immune defence system against pathogenic bacteria, fungi, protozoa, both directly and through regulation of the inflammatory response; ovotransferrin is capable of delivering iron to cells and inhibiting bacterial moltiplication.
These proteins are all glycoproteins with molecular weight of about 80 kDa. They fold in two lobes that show sequence homology with each other and can bind one ferric ion per lobe. Ferric ions are far from each other and magnetically non-interacting. Iron ions are coordinated by two tyrosine residues, one aspartate, and one histidine, together with two oxygen atoms from a bridged HCO^-_3. This set of ligands provides an ideal coordination scheme for stable and reversible iron binding. The paramagnetic contribution to the NMR rate of solvent water protons is useful for a better characterization of the molecular environment of the Fe(III) binding site and of its dynamics.
NMRD profiles of transferrins are characterized by a rather complex functional form. This is in part due to the rather anisotropic spin Hamiltonian of the Fe(III) ions in the coordination scheme of lactoferrin. Relaxivity values of lactoferrin are much higher than those reported for human and ovotransferrin, and NMRD profiles are sensibly different.
Results shown here are consistent with a closest distance for a single water hydrogen atom of 3.1 Å. By looking at the X-ray structure of Lf (PDB ID code:1BLF) we can locate two water oxygens at 3.95 and 4.27 Å from each Fe(III), respectively. Temperature dependence data suggest that an important contribution to the overall paramagnetic contribution to the solvent water relaxation rate arises from one or more second sphere water molecules in slow exchange with the bulk. A decreasing value of the exchange rate is obtained, ranging from 1.2 to 0.7 μs in the observed temperature range (25 –65 °C),with an activation enthalpy of 7.3 ±0.8 kJ mol^{-1}. The low exchange rate obtained from NMRD data can be explained by the observation that both water molecules are bound to several polar groups of the protein backbone and side chains. By increasing the pH from 6.5 to 12 two distinct titrations are observed, consistent with sequential removal of both water molecules. Structural data indicate a pair of Lys residues (Lys210 and Lys301) that are present in Tf as well, although they assume a different orientation in Tf. This discrepancy could explain the different pH behaviour of Lf compared to Tf in the mechanism of iron release.

Direct proton NMRD of biological macromolecules

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The improvement in sensitivity currently achieved by the FFC relaxometer, and the further increases that we can reasonably expect in the near future, suggest that we will be increasingly able to tackle systems that were not practically amenable until the recent past. Among them are relatively diluted D_2O solutions of proteins and of other biological macromolecules or aggregates. Being able to directly observe a proton signal from a biological solute under close to physiological conditions allows us to obtain a more direct (although averaged) information on the spectral density, and possibly information on the dynamics and aggregation properties of the system. Encouraging results recently obtained on different protein samples will be discussed (1). Further increases in the signal to noise will also allow detecting non-exponential decays of the collective proton magnetization of the macromolecule, and hopefully to attempt bi-exponential fits thereby further increasing the information content of the NMRD experiment (2). A proper analysis in terms of bi-exponential decay will also improve our understanding of the NMRD of liquid but viscous foodstuff such as olive oil (3).

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Field dependent relaxation processes in crystal lattices containing dipolar and quadrupole spins.

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In multispin systems containing both quadrupolar ($I >= S$) and dipolar ($I=½$) nuclei coupled by mutual dipole-dipole interactions, transitions of the dipolar spins leading to their longitudinal relaxation are accompanied by quadrupole spin transitions between energy levels determined by static quadrupole interactions together with Zeeman couplings. Only in the high field limit, when the Zeeman coupling of the quadrupole spin is much stronger than its quadrupole interaction, the S spin is quantized in the laboratory frame. Thus, the 'classical' Solomon-Blombergen-Morgan (SBM) approach [1-4] to dipolar relaxation, developed under the assumption of a Zeeman energy structure for both interacting spins, may not be treated as a proper description of frequency dependent relaxation processes of the dipolar spins. In addition, the high spin nucleus usually provides through its own relaxation mechanism an additional source of relaxation for the dipolar nuclei.

From the perspective of the spin ½ the relaxation processes of the quadrupole spin contribute to time fluctuations of the mutual dipole-dipole coupling in a manner similar to other stochastic processes like jump diffusion. The quadrupole spin exhibits complex, multiexponential relaxation, which can be described under certain motional conditions within the framework of the Redfield perturbation approach [5]. Since the dipolar spin senses various relaxation rates corresponding to particular quadrupole spin modes and coherences, fluctuations of the mutual dipole-dipole coupling cannot be described by one characteristic time constant.

We present a general description of spin - lattice relaxation of a dipolar spin ½ induced by its coupling to an ensemble of quadrupole spins, valid for an arbitrary magnetic field and arbitrary quadrupole spin quantum number. Our approach includes the effects of the quadrupole spins being quantized in a frame determined by a superposition of the quadrupole and Zeeman interactions, as well as the multiexponential quadrupole relaxation. We provide in this way a general tool appropriate for interpretation of field-dependent relaxation studies for a wide class of solid state systems containing dipolar as well as quadrupole spins with mutual dipole-dipole couplings.

Essential elements of the theoretical framework follow the formalism of the paramagnetic relaxation enhancement theories [6-8].

We apply the general approach to interpret fluorine relaxation profiles for LaF3 single crystals.

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The influence of heteronuclear dipolar interactions on field-cycling NMR measurements of spin-lattice relaxation: ^{13}C, ^{19}F, ^{2}H and ^{1}H studies of proton tunnelling in the hydrogen bond

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In Nottingham we have designed and built a current-switched superconducting field-cycling NMR spectrometer for studying the role of quantum tunnelling in molecular dynamics. [1] The instrument is designed for work in the solid state with sample temperatures extending from 4K up to 300K. The maximum field-switching rate is $10Ts^{-1}$. Among the systems studied is molecular rotation in symmetrical groups such as the methyl rotor, the rotations of the hydrogen molecule in various environments and proton transfer in the hydrogen bond. [2,3,4] The latter will form the focus of this paper and the emphasis will be on the methodology of field-cycling relaxometry in cases where the sample possesses two spin species so that heteronuclear dipolar interactions are dominant.

Tunnelling matrix elements are exponentially dependent on the barrier properties and the particle mass, therefore isotope effects can provide useful insight into the fundamental mechanism underlying the dynamics. Direct isotope effects, involving deuteration of the hydrogen atoms implicated in the proton transfer, have recently been published. [3] However, of topical interest is the possibility of secondary isotope effects arising from isotopic substitution of the molecular skeleton. Proton transfer in the hydrogen bond is accompanied by the motion of the heavier framework atoms of the molecule; the motion is properly described as one over a multi-dimensional potential energy surface. We have studied the proton transfer tunnelling dynamics via the ^{13}C NMR of ^{13}C substituted benzoic acid with the aim of observing small isotope effects in the tunnelling rate. This is experimentally challenging and represents what we believe is the first field-cycling study of ^{13}C. [5]

The introduction of a second spin species has a significant effect on the spin-lattice relaxation of the first spin species (and vice-versa). Compared with homonuclear systems, the spectral density acquires additional components characterised by the sum and difference Larmor frequencies of the two nuclei. Further, instead of a single relaxation rate, the spin-lattice relaxation is characterised by a 2 x 2 relaxation matrix. Therefore, the magnetisation recovery becomes biexponential and the initial polarisation state of the second nucleus strongly affects the magnetisation recovery of the nucleus which is being observed in the spin-lattice relaxation measurement. We shall report on the results of spin-lattice relaxation investigations on ^{1}H-^{13}C, ^{1}H-^{19}F and ^{1}H-^{2}H heteronuclear systems. The role of heteronuclear interactions in spin-lattice relaxation and the methodology of field-cycling relaxometry will be discussed.

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Relaxation Time Measurements in Sugar Glasses

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Sugar and carbohydrate glasses are important in nature as protection against desiccation and in pharmaceuticals and foods. Glasses are thought to be heterogeneous on the 5 to 10 nm scale and would be expected to show a distribution of correlation times for motion. We have compared results of NMR relaxation time studies of the crystalline and glassy states of the rhamnose and methyl rhamnose and shown that there is no evidence for either heterogeneity or distributions of correlation times. However in the glassy state the motions of water and the methyl groups in the glass are decoupled from the motion of the sugar backbone. A region just above the glass transition can also be identified that is not truly a viscous liquid or a glass. Using the data motional maps can be made which describe the motions of the various components across then temperature range. The results reported here, which were obtained at constant field and variable temperature are compared to the some reported fast field cycling results.

The flow-relaxation effect: Hydrodynamic dispersion in the nanoscopic vicinity of surfaces in porous materials investigated by field-cycling NMR relaxometry and Monte Carlo simulations

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We report on a new effect of spin-lattice relaxation of a polar fluid confined to pores of a diamagnetic, polar solid material: It is demonstrated that slow hydrodynamic flow with velocities of a few centimetres per second or less reduces the spin-lattice relaxation rate of the fluid. The effect was predicted by an analytical theory and is verified both by field-cycling NMR relaxometry and Monte Carlo simulations of model pore spaces. Adsorbate molecules diffusing in the vicinity of pore surfaces can perform adsorption, desorption and readsorption cycles effectively leading to displacements along the surface. Since the surface determines the orientation of the adsorbed molecule relative to the external magnetic field, desorption at one site and readsorption at another site of a non-planar surface will cause molecular reorientation. This is the basis of the "reorientation mediated by translational displacements" (RMTD) relaxation mechanism. The effective displacements along the surface where shown to be of a Lévy walk type [1,2]. Due to the RMTD process, spin-lattice relaxation dispersion curves reflect the topology of the pore surface [3]. If hydrodynamic flow is superimposed to surface diffusion the RMTD process will be accelerated in a sort of rotational analogue to translational hydrodynamic (or Taylor/Aris) dispersion [4]. In field-cycling NMR relaxometry experiments, this reveals itself by a prolongation of spin-lattice relaxation times at low frequencies. Using a HPLC pump, the effect was measured in a porous monolithic silica material [5]. The flow-relaxation effect takes place in the vicinity of the pore surfaces within molecular distances and distances less than a few hundred nanometers. This picture was verified and examined in detail with the aid of Monte Carlo simulations of a number of model pore spaces [6]. As conclusions we state that (i) the RMTD relaxation mechanism of fluids in porous materials was proven, (ii) that hydrodynamic dispersion affects molecular displacements at surfaces, and (iii) that interfacial slip in the sense of a molecular hopping, i.e. desorption/readsorption process takes place.

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NMRD and ESR data for slowly-rotating paramagnetic complexes: can we obtain a consistent interpretation?

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Two methods for predicting proton NMRD profiles in paramagnetic complexes with zero-field spiltting (ZFS) in aqueous solution have been extended to also simulate the ESR lineshapes. The first approach (the "Swedish slow motion approach") is valid under a fairly general set of conditions[1], the second is a Redfield limit theory[2]. In both models, the ZFS is assumed to consist of a static and a transient part, with respect to the molecular frame. In the first model, the two components are affected by two dynamic processes: the complex rotation and distortion (pseudorotation). In the second model, the transient ZFS is modulated by the pseudorotation and causes multiexponential electron spin relaxation, while the rotation is assumed slow. The static ZFS does not contribute to electron spin relaxation but influences the energy levels of the electron spin in an orientation-dependent manner. The orientation-dependence of relaxation properties is powder-averaged in the final step of the calculations.
Comparisons of NMRD and ESR data in slowly-rotating (protein-bound) Gd(III) complexes were recently reported by Westlund and co-workers[3,4]. We use their data in our modelling and find indications that a consistent interpretation using our models may be possible.

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Water-soluble Gd@C_{60} Derivatives and Their Proton Relaxivities

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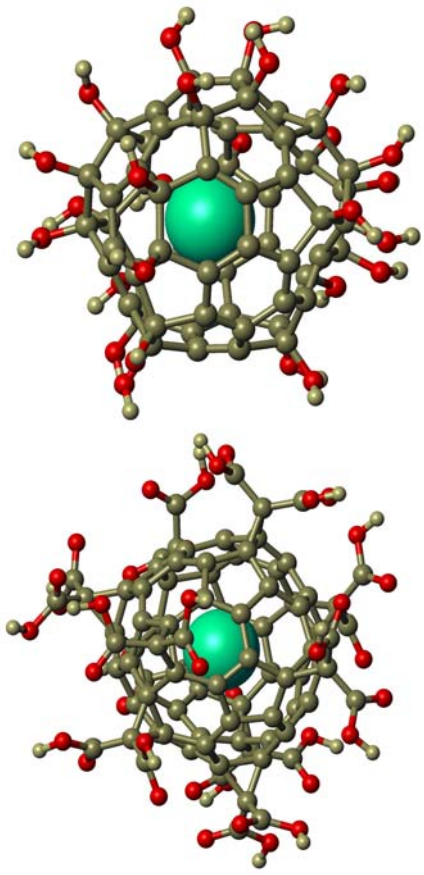
Water-soluble fullerene derivatives possess potential for biomedical applications as antioxidants, anti-HIV drugs, X-ray contrast agents, bone-disorder drugs and photosensitizers for photodynamic therapy. In addition, endohedral metallofullerenes (M@C_{2n}) have been suggested as nuclear medicines (M = Ho^{3+}), fluorescent tracers (M = Er^{3+}) and MRI contrast agents (M = Gd^{3+})[1,2] largely because the closed fullerene cage insures against toxic metal-ion release *in vivo*. Water-soluble members of the Gd@C_{60} family of metallofullerenes have recently been shown to achieve their large proton relaxivities (r_1) though pH-controlled self-aggregation.[2] In fact, self-aggregation may well be a common feature of all water-soluble fullerene chemistry, and its understanding is, therefore, of general importance for fullerene-based drug delivery. Proton nuclear magnetic relaxation dispersion (NMRD) measurements for the water-soluble metallofullerenes, Gd@$C_{60}(OH)_x$ (x≈27), and Gd@$C_{60}[C(COOH)_2]_{10}$ can be used as a reporter to probe the aggregation (or disaggregation) characteristics of water-soluble fullerene materials in the presence of physiologically-encountered agents.



Molecular models of Gd@$C_{60}(OH)_{26}$ (top), and Gd@$C_{60}[C(COOH)_2]_{10}$ (bottom).

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THE PARADOXICAL RELAXIVITY OF FERRITIN

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Ferritin, the iron-storing protein, speeds up proton transverse magnetic relaxation in aqueous solutions. This T_2–shortening is used in magnetic resonance imaging to assess iron concentration in the brain and in the liver.

Extrapolating the successful theory of relaxation induced by iron oxide nanoparticles, that effect was long assigned to water diffusion within the inhomogeneous local field created by the magnetized iron cores. However, experimental data contradict that explanation, *in vitro* as well *in vivo*: the most unexpected observation is the linear dependence of the transverse relaxation rate with B_0 (1). We first showed that exchange between an adsorbed proton fraction and the bulk dominates the relaxation, thanks to relaxation measurements made in water-methanol solutions (2). We then built a proton exchange dephasing model (PEDM) which allows a first–order relaxation mechanism (3); that model explicitly accounts for the antiferromagnetic structure of the ferrihydrite nanometric core of the protein (4).

For the same iron concentration, relaxation caused by ferritin *in vivo* appears to be more efficient than in solutions (5). This significant difference between tissues and solutions was assumed to be due to clustering. That conjecture is now confirmed by recent measurements of relaxation in solutions where ferritin is agglomerated by trypsin, an enzyme degrading the proteinic shell.

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ACTINIDE IONS INVESTIGATED BY NUCLEAR MAGNETIC RELAXATION DISPERSION

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The actinides and the lanthanides formally have the same electronic structure but they differ in many respects. The 5*f,* 6*d*, 7*s*, and 7*p* orbitals of the actinides have comparable energies and overlap spatially, so that bonding can involve any or all of them. Moreover, because the 5*f* orbitals have a much greater spatial extension, the actinides are more prone to form partially covalent bonds, their redox chemistry is much richer and the exact nature of the ground state of the solvated ions is still a subject of debate despite recent theoretical studies. The electronic structure of an actinide ion may even depend on the nature of the surrounding ligands.

The studies on the actinide compounds are thwarted by the intense radioactivity of the available nuclides and advanced methods had to be developed to gain information on these compounds. Nuclear magnetic relaxation dispersion is relatively straightforward to use with highly radioactive solutions and sheds some light on the properties of actinide ions in solution. This technique has been applied to an investigation of the simple ions U^{4+}, Np^{4+}, Pu^{3+} and Cm^{3+} and to the oxy ions NpO_2^{+}, NpO_2^{2+} and PuO_2^{2+} in water. Shortenings of the electronic relaxation times due to stronger spin-orbit couplings and admixtures of higher energy levels to the ground states are deduced from the NMRD measurements. Changes in oxidation states, complexation processes and radiolysis phenomena are also investigated by NMRD.

Central Role of Tetragonal 4th-Order ZFS Coupling In the Mechanism of NMR Paramagnetic Relaxation for S>3/2 Ions

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The tetragonal 4th-order zero field splitting (zfs) interaction plays a central role in the mechanism of NMR paramagnetic relaxation produced by S=2, 5/2, and 7/2 transition metal ions. The physical mechanism is entirely different for integer (S=2) and noninteger (S=5/2, 7/2) electron spins. For integer spins in the vicinity of the zfs-limit, the tetagonal 4th-order zfs coupling splits the $m_S=\pm2$ non-Kramers doublet, driving $\langle S_z \rangle$ into oscillation at the frequency of the doublet splitting. This motion of $\langle S_z \rangle$ disrupts the resonant dipolar coupling of the electron and nuclear spins with the result that NMR-paramagnetic relaxation enhancement (NMR-PRE) is strongly depressed. The application of a Zeeman field of a strength at which the Zeeman energy exceeds the $m_S=\pm2$ doublet splitting collapses the doublet, thereby producing a profound increase in the NMR-PRE. This is the principal feature of the MRD profile of the S=2 complex, Mn(III)-TSPP (tetra-sulfonatophenylporphyrin). For half-integer spins, S=5/2 and S=7/2, the 4th-order tetragonal zfs coupling is likewise an important factor determining the form of the MRD profile, although by an entirely different physical mechanism, which involves zfs-induced wavefunction mixing of the $m_S=\pm5/2$ and $m_S=\pm1/2$ levels. This mechanism is illustrated in an experimental study of Fe(III)-TSPP. Model calculations suggest that zfs-induced wavefunction mixing is likely also to be important for Gd(III) and Mn(II) complexes.

Posters

EFFECT OF THE INTRACELLULAR LOCALIZATION OF A Gd-BASED IMAGING PROBE ON THE RELAXATION ENHANCEMENT OF WATER PROTONS

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Introduction

MRI visualization of cells labeled with Gd-based imaging probes appears a promising route for pursuing novel applications in the field of cellular and molecular imaging. In fact, it has been shown that the problems associated with the intrinsic low sensitivity of MRI can be overcome by the intracellular accumulation of a high number of paramagnetic Gd(III) chelates. A simple method for entrap 10^8-10^9 Gd-chelates per cells consists of incubating the cells with the imaging agent at 25-50 mM concentration.(1) By this route, Gd-chelates are entrapped into endosomic vesicles, and it has been noted that the observed relaxivity is "quenched" in the presence of high amounts of internalized Gd-chelates.(1,2) This drawback clearly represents a limitation to the proposed method of cell labeling and needs to be investigated in more detail. In order to ascertain whether the observed relaxivity "quenching" is dependent upon the localization of the paramagnetic agent inside the endosomes, it has been carried out parallel internalization experiments by using the electroporation procedure in which the imaging probe is localized into cytosol.

Methods

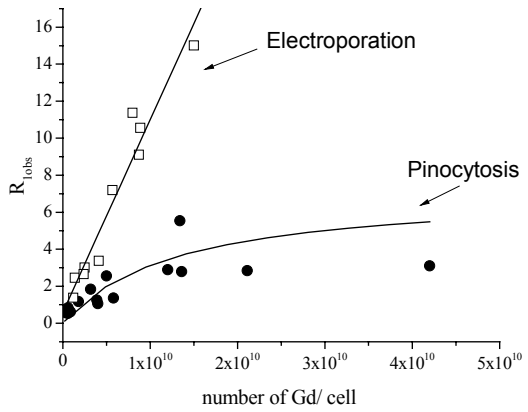
The internalization of Gd-HPDO3A (ProHance®, Bracco Imaging) into a rat hepatocarcinoma cell line (HTC) was carried out by pinocytosis (the cells were incubated for 16-24 hours in culture media containing the Gd-complex) or by electroporation (an electric pulse is applied to a cell suspension containing the Gd-complex in order to induce the membrane permeation). T_1 of water protons were measured on the resulting cellular pellets at 0.5 T and 25°C on a Stelar Spinmaster spectrometer. MR-images were acquired on a Bruker Avance300 spectrometer (7 T) equipped with a Micro 2.5 microimaging probe. The time dependence of longitudinal magnetization has been analyzed according to theoretical models(3) which describe the relaxometric behavior of multi-compartment systems.

Results

The localization of the imaging probe was assessed by acquiring Confocal Microscopic images of HTC cells labelled with the fluorescent Eu-HPDO3A analog. As expected, the relaxation efficiency of Gd-HPDO3A internalised by pinocytosis shows a drastic decrease upon increasing the amount of complex entrapped into endosomes (Figure 1). A significantly higher efficiency was observed for Gd-HPDO3A internalized by the electroporation route. The different relaxation enhancement displayed by HTC pellets was confirmed by acquiring MR images of phantoms containing the labeled cells dispersed in agar. These experiments allow us to establish that the minimum number of HTC cells labeled with GdHPDO3A detectable by MRI is *ca.* 500 cells/μl in the case of electroporation and *ca.* 5000 cells/μl for pinocytosis (figure 4b)respectively.

Conclusions

The obtained results remark the importance of the procedure used for labelling cells and demonstrate that the cytosol confinement of the probe yielded higher relaxing efficiency, thus allowing the MRI detection of a smaller number of cells with respect to the entrapment into endosomes.



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A New Generation of High Relaxivity q=2 MRI Contrast Agents based on the eptadentate AAZTA ligand

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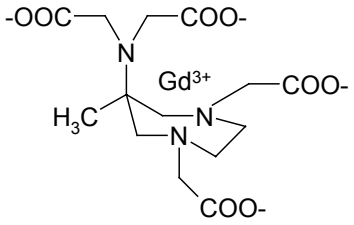
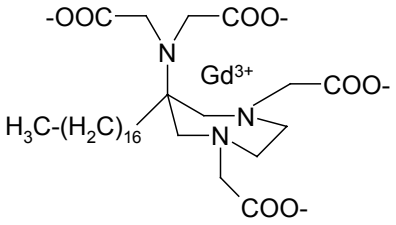
Introduction

The attainment of high relaxivity is of fundamental importance for pursuing novel applications of Gd(III) chelates as MR Imaging Probes. The most straightforward route to high relaxivities is provided by systems containing two water molecules in the inner coordination sphere of the paramagnetic ion. However, the increased hydration must not have negative consequences on the overall stability of the complex neither it has to favor the formation of ternary complexes with endogenous negative ions. Few systems have shown to possess these requisites. Gd-AAZTA owns these properties and, moreover, it displays a relatively fast exchange of the coordinated water molecules. On the basis of these favorable features, a derivative of Gd-AAZTA containing a long aliphatic chain has been synthesized and its relaxometric properties investigated in detail.



Gd-AAZTA



Gd-AAZTA-C17

Methods

The synthesis of AAZTA ((6-amino-6-methylperhydro-1,4-diazepinetetraacetic acid)) and of its hydrophobic derivative is simple, and relies on available and cheap chemicals. The key step is the reaction of $RCH_2CH_2NO_2$ with formaldehyde and N,N'-dibenzylethylenediamine, followed by hydrogenation and insertion of the four carboxymethyl moieties. The Gd(III) complexes were prepared by reacting stoichiometric amounts of the ligands with Gd(III) trichloride. The ligand pK_a values and the stability constant of the complex were determined by potentiometric titration at 298K in KCl 0.1 M. Relaxometric measurements were carried out on a Stelar Spinmaster Relaxometer operating at variable frequencies between 20 and 80 MHz and on a Stelar Field Cycling Relaxometer in the frequency range 0.01-40 MHz. The binding to HSA was investigated by the Proton Relaxation Enhancement (PRE) method. The exchange lifetime of the coordinated water molecules was evaluated by measuring the temperature dependence of the water ^{17}O transverse relaxation rate of 20 mM solutions on a JEOL Spectrometer operating at 90 MHz.

Results

The complex $[Gd(AAZTA\text{-}C17)]^-$ showed to have the outstanding properties of the parent complex, namely: i) two inner sphere water molecules in fast exchange with the bulk, ii) high thermodynamic stability in aqueous solution and iii) a nearly complete inertness towards the influence of bidentate endogenous anions. The functionalization with the hydrophobic chain induces the formation of micelles already at sub-millimolar concentrations (cmc 0.1 mM). The relaxivity of the self-assembled complex is 30 $mM^{-1}s^{-1}$ at 20 MHz and 298K. Moreover Gd-AATZA-C17 displays a high affinity binding to Human Serum Albumin ($2.4\times10^4 M^{-1}$). The relaxivity shown by the Gd-AATZA-C17/HSA adduct is ca. 80 $mM^{-1}s^{-1}$ at 20 MHz and 298K.

Conclusions

A novel Gd(III) chelate based on the unprecedented and easily obtained AAZTA ligand has been reported as a prototype of a new class of highly sensitive agents. The simple and straightforward synthesis of the AATZA ligands, together with the good stability and excellent relaxation enhancement capabilities of their Gd(III) chelates suggest that these systems may have a huge potential in the development of high performance MRI contrast agents.

SPIN-LATTICE RELAXATION DUE TO DIRECTOR FLUCTUATIONS IN THE NEMATIC PHASE: TOWARDS A SOLUTION OUTSIDE THE SMALL ANGLE APPROXIMATION.

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Spin-lattice relaxation in the nematic phase can be explained in terms of isotropic motions like those driving NMR relaxation above the clearing point, and collective motions associated to order fluctuations of the mesophase´s director (OFD). The collective dynamic is characterized by long-range cooperative modes (or hydrodynamic modes), associated with order fluctuations [1-2]. The ODF model (and rear improved versions) has been used by many authors to discuss different features related to the spin-lattice relaxation dispersion in nematic specimens [3-5]. So far the ODF mechanism was successfully used within the small angle approximation.

In recent experiments, the collective dynamics of nematic compounds was studied under ultrasonic excitation [5-8]. The inclusion of an acoustic free energy term was used to explain ODF enhancement within the small angle limit. However, the validity of this analysis requires a careful examination due to a probable violation of this assumption.

In the present work, the statistical interdependence of the faster rotational reorientation of the individual spin-bearing molecules and the slower ODF [9] is reanalyzed within this context. The analysis is presented in terms of a Krammers equation, that is, a type of Fokker-Plank equation. This formalism gives a first insight into the resolution of the general and complex problem of the spin-lattice nuclear magnetic relaxation in nematic compounds, without making use of the small fluctuation approximation.

Economic support from Conicet, Fundación Antorchas and Secyt – UNC is acknowledged.

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* CONICET

HYDROXYPYRIDINONE-BASED GADOLINIUM COMPLEXES FOR MRI. EFFECTS OF SUBSTITUENTS ON RELAXIVITY PROPERTIES

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Tripodal hydroxypyridinone (HOPO) based Gadolinium complexes have shown promise as contrast agents for Magnetic Resonance Imaging due to their high relaxivity and stability. Heteropodal complexes containing a 2,3-dihydroxy-terephthalamide (TAM) moiety have the further advantage that the terminal acid can be easily functionalized with, for instance, targeting or solubilizing moieties. Several functionalized Gd-TREN-bisHOPO-TAM-X complexes where X is either a negatively or positively charged pendant group, have been synthesized. We present here the effect of the charged terminal group on the relaxivity behavior of the complex. In particular, the selectivity of the complex with regards to physiologically available anions as a function of its charge and the modulation of the hydration number are discussed.

Theoretically, the optimal water residence time of HOPO-based complexes enables them to achieve high relaxivity upon slowing down their molecular tumbling.[1] This can be achieved by grafting the Gd chelate to a rigid, spherical macromolecule such as a protein or a dendrimer. However, the solubility of a dendrimer is primarily determined by that of its terminal groups. The poor water-solubility of the parent complex therefore requires that it be grafted upon a "water-solubilizing dendron" primarily terminated by hydrophilic hydroxyl groups. Furthermore, in order to fully take advantage of the structure of the dendrimer, it has to be as rigid or compact as possible to avoid the Gd^{III} chelate from freely rotating or folding back.

We present therein the synthesis and relaxivity study of a mono-disperse and rigid block dendrimer containing one gadolinium chelate, Gd-TREN-bisHOPO-TAM-Asp-Asp_2-12OH.

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Dendrimeric Gd(III) complex of a monophosphinated DOTA analogue: optimizing relaxivity by reducing internal motion

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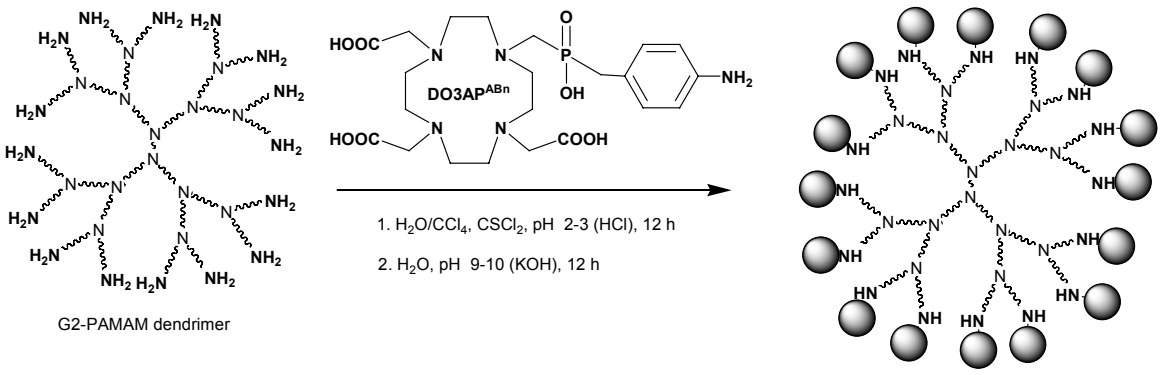
Most of the currently approved Gd-based MRI contrast agents suffer from a rather low efficiency mainly due to a fast molecular tumbling and a slow water exchange rate. Recently, examples of low molecular weight systems with rather fast rate of water exchange have been reported. However, upon binding to a macromolecular carrier the expected relaxivity enhancement is often limited. This effect may arise from a reduced water exchange rate of the Gd(III) complex in the macromolecular adduct and from a certain degree of internal mobility around the spacer connecting the complex to the macromolecular backbone. To overcome these difficulties, the design of bifunctional chelate maintaining fast water exchange rate when loaded on the appropriate carrier is necessary. Once this requirement is fulfilled, the limitation of the internal motion is of primary importance for achieving significant relaxivity enhancement.

Here we present an example where a marked increase of relaxivity has been observed upon rigidifying the internal frame of Gd-containing PAMAM dendrimers: the effect has been attained by either protonation of the dendrimer or by forming supramolecular adducts with cationic polyaminoacids. We characterized the compounds by relaxometric measurements (variable-temperature ^{17}O and ^{1}H NMRD) and found that the water residence lifetime was slightly increased (~ 40 ns) as compared to the parent complex DO3AP^{ABn} (24 ns), but still close to the optimal region. We also found that the internal motion can be modulated as a function of pH or by interaction of the conjugates with positively–charged macromolecules, such as polyarginine.



Acknowledgement: We thank to GAČR (No. 2003/02/0493 and 2003/03/0168), MIUR (FIRB) and NATO (Collaborative grant No. PST.CLG 980045).

Analysis of uniformity in magnetic fields generated by saddle compensating coils for field-cycling NMR

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In certain NMR relaxometry experiments, external magnetic field contributions must be compensated. For this aim, the two in-plane components of the compensating magnetic field may be generated by a saddle coil set. The implemented compensating system may have to be as uniform as possible or, in some cases; a small gradient may be introduced through a proper current unbalance. Saddle shaped coils have been widely used in the past to generate uniform magnetic fields and magnetic field gradients in NMR experiments.

In the present work, the magnetic field generated by a saddle coil system was exactly calculated in the whole space and experimentally tested in two different spatial planes (central and top planes) of the coil. The uniformity of the three components of the magnetic field was separately studied using Taylor series expansions around the geometric center of the coil. The optimum geometry was determined taking in consideration the first two terms of the Taylor expansions. It was found that the maximum uniformity of the field produced by the saddle coil system is achieved when $z_o=4R$ and $\varphi_o=\pi/3$ [1]; where z_o, R and $2\varphi_o$ are the height, radius and the aperture angle of the coil, respectively.

The fourth term of the Taylor expansion was calculated in order to obtain an approximated manipulable analytical expression of the magnetic field within the sample. Fourth order Taylor series and exact expressions were compared in different regions of the coil. A noticeab le agreement between them (differences minor than *1.5 %*) was encountered when distances from the center of the coil do not exceed *R/2*. Therefore, the magnetic field in the central zone of the saddle coil system (usually occupied by the sample) can be easily and accurately obtained with a pocket calculator via the fourth order Taylor expansion.

Deviations of the magnetic field produced by an optimum compensating saddle coil system were contrasted with typical NMR magnet field inhomogeneities. Possible influences of such deviations were determined to be negligible in NMR experiments.

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2- Fellow of CONICET.

Charge-Carrier Dynamics in Polyaniline-based Conducting Polymers using NMRD

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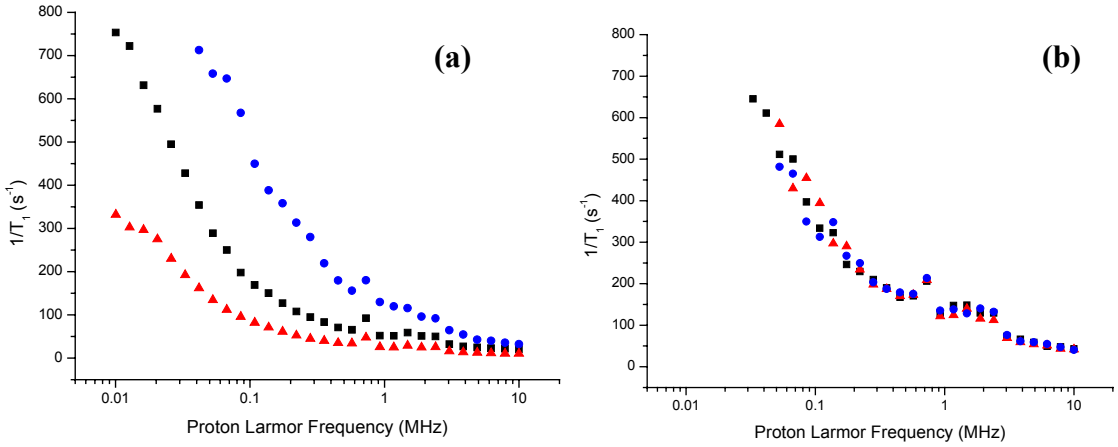
Inherently Conducting Polymer, ICP's, are polymers that show conductivity slightly higher than normal polymers due to conjugation along the backbone. On doping with an organic modifier the conductivity increases by a factor of 10^6-10^{10}. The doping is spatially non-homogeneous, so the polymer consists of highly doped, crystalline, conducting regions of a nanometer scale and amorphous poorly conducting regions of lower dopant concentration. Conductivity is limited by the passage of charge carriers through these amorphous regions by inter-chain hopping.

In the ICP, polyaniline-TFSA, the charge carriers are polarons; spin ½ radical species that are created and stabilised by the anionic dopants. The polarons diffuse along a single chain with a diffusion coefficient, $D_{\parallel}$, or hop from chain to chain with a diffusion coefficient, $D_{\perp}$. ^{1}H relaxation in moderate to highly doped solid polyaniline samples is due to the dipolar interactions between the mobile polarons and the protons on the polymer backbone. While in the partially and un-doped samples relaxation is due to ^{1}H-^{1}H dipolar interactions modulated by molecular motions, in the normal way.

Published relaxation data for ICPs were fitted to a fractal power-law appropriate for anomalous diffusion, and the powers obtained in these studies were related to the dimensionality of polaron motion. The powers obtained for polyaniline-TFSA in our study are not in agreement with the literature. However, our measured powers can be correlated with the AC conductivity. There exists a percolation threshold in dopant concentration, NMRD response and conductivity. For samples of both high and low conductivity there is an NMRD cutoff frequency in the low MHz range. Below this cutoff there is a change in frequency dependence of T_1, thought to be due to intrachain hopping. The temperature and dopant concentration dependencies of the NMRD profiles will be discussed.



NMRD profiles showing the temperature response at 50^{0}C (▲), 24^{0}C (■) and –20^{0}C (●), of highly doped polyaniline-TFSA (a) and low dopant concentration polyaniline-TFSA (b)

Magnetic Nanoparticle Assemblies

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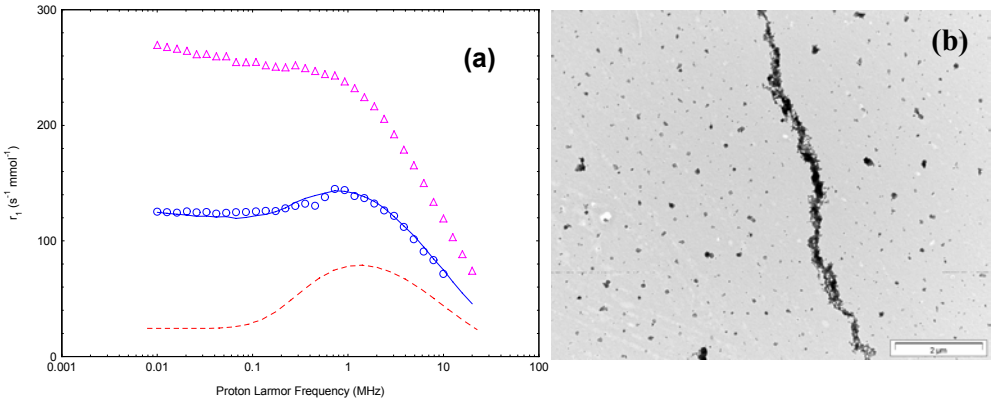
Magnetic nanoparticle assemblies are objects of considerable scientific interest for basic research, but also for applications in ICT and biotechnology which range from magnetic memory storage to contrast agent development. The final stage of fabrication of a device incorporating such assemblies would usually involve attaching them to a surface, but the initial cluster growth takes place in suspension. NMRD, in conjunction with other techniques, can provide insight into the nature of the nanocluster in suspension and into the mechanisms of growth.

Control of the architecture of such assemblies is critical to the development of new devices. 2D and 3D assemblies have been extensively researched, while reports on 1D assemblies are comparatively rare. In this work we report the preparation of magnetic nanoparticles formed in the presence of single-stranded herring sperm DNA. The DNA acts as a template for the preparation of magnetic nanowires whose suspensions exhibit high relaxivity at low field. We also present work on fatty acid stabilised nanocomposites. For these materials the NMRD response is sensitively dependent on the size of the primary nanoparticle, but not of the nanocluster.



(a) NMRD response of single stranded- (△) and double stranded hs-DNA (○)
(b) TEM images of single stranded hs-DNA-magnetite nanocomposites subjected to a magnetic field

ON THE ACOUSTIC – DIRECTOR FIELDS INTERACTION ENERGY IN THE SMECTIC-A PHASE

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It was recently recognized that when an acoustic wave propagates in a liquid crystal, the induced fluctuations of the density couple with the director field giving rise to a molecular orienting free energy term. A theoretical model was proposed for the corresponding interaction energy in the nematic phase, being possible to verify its consistency by means of nuclear magnetic relaxation and optical experiments [1-3]. The model was later extended into the smectic A phase, showing a good agreement with nuclear magnetic relaxation experiments [4,5]. Even after considering relevant own aspects concerning the elastic free energy at smectic order, a detailed smectic description of the acoustic interaction energy was still not taken into account.

In this work we propose a refined model in order to consider sound-induced smectic layer displacements, and the coupling between these and density fluctuations. Here we add new terms to the energy, which account for the layers - local director interactions and layers - local density interactions. This result can be compared with the free smectic A energy obtained by de Gennes [6]. The understanding of this interaction process is a crucial step in the way for inducing controlled hydrodynamic processes within the smectic order. The impact of the new term in the corresponding spectral density is also analyzed.

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DEVELOPMENT AND DESIGN OF NMR-RELAXOMETER

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Some 15 years ago in our NMR-group in Siberian State Technological University the systematic works on application of NMR-relaxometry to study and control the properties of matter were started [1, 2]. And at the same time we began developing and design of different techniques in order to measure NMR-relaxation times and adequately process and store different information in this field [3, 4]. In this report the results of developing of a laboratory NMR-Relaxometer using a pulse programmer (PP) with unique possibilities to operate the apparatus are presented. PP is one of the most important part of NMR-relaxometer: it must have a possibility to form and set all possible tasks and gather, process and store all necessary information.

The programmer capable to generate all specific multiple pulse sequences to measure spin-lattice and spin-spin relaxation times was built using the so called field-programmable gate array (FPGA). The FPGA is an integrated circuit which may be programmed to perform a specific task. But in spite of great possibilities for application in different electronic devices the FPGA chips as far as is known did not yet used in PP of NMR-relaxometers on the PCI bus.

The created hardware consists of two chips FPGA in which configuration files are stored. The necessary pulse sequence is send to the PP through the PCI bus of the personal computer. For development of PP the program Qartus II 4.0 exposed on the Internet site of company Altera (www.altera.com) was used. For description of the logic circuit of the device the language AHDL (Altera Hardware Description Language) was utilized.

Concrete hardware realization of the PP is based on use FPGA of two Altera families. It is connected with the fact that FPGA chips of family Cyclone having plenty enough of gates and the built - in RAM the working output voltage can't be established more than 3,3V. But the majority of parent electric parameters of interface PCI correspond to standard TTL, that is, a voltage of an input/output must be equal +5V, that is impossible for FPGA of family Cyclone. Therefore for maintenance of compatibility of electric parameters of interface PCI it has been used FPGA MAX7128S, supporting a voltage on output 5 V and 3,3 V. On FPGA Cyclone EP1C3T100C8 the program of generation of pulse sequences was created.

The developed device successfully works in a hardware-software complex of registration and processing of all necessary information. The apparatus generates multiple rectangular coherent pulses, with the set time parameters. Management is carried out by developed specialized software specifying parameters necessary for work of NMR-relaxometer: pulse sequences of required duration of pulses and delays between them and also the data specifying an initial phase of radio-frequency synchronized with external frequency of the transmitter filling each pulse. The PP built has 8 independent output channels, with resolution of 10 ns, which is also the minimum duration of each pulse.

The created laboratory equipment works at the temperatures of a sample from - 170°C till +200°C. It gives the possibility to see and process the relaxation curve, calculates measured relaxation times in an automatic way and exposes the results on the display.

Now the work on the development of a table NMR-relaxometer with mini magnet is in progress.

The work is supported by Russian Foundation for Basic Research (project no. 03-03-32819).

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^{1}H NMR characterization of myristic acid interaction with Mn(III)heme human serum albumin

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Human serum albumin (HSA), the most prominent protein in plasma, is best known for its exceptional ligand binding capacity. HSA abundance (its concentration being 45 mg/mL in the serum of human adults) makes it an important determinant of the pharmacokinetic behaviour of many drugs. HSA binds a broad variety of ligands as aminoacids, hormones, metal ions and it is responsible for the transport of heme, bilirubin, medium and long chain fatty acids. Fatty acids are required for the synthesis of membrane lipids, hormones and second messengers, and serve as an important source of metabolic energy. HSA is able to bind several moles of fatty acids and it is clear that protein has multiple fatty acids binding sites of varying affinities [(1)].
The heme-HSA complex is obtained by binding of Mn(III)heme to HSA. Mn(III)heme binding to HSA endows the protein with peculiar spectroscopic properties and it is used as spectroscopic probe to follow a number of events involving the conformation of the protein[(2)].
The paramagnetic effect of the buried water cluster has been used to follow conformational changes due to variable pH and temperature of defatted Mn(III)heme-HSA, Mn(III)heme-HSA fatty acid complexes, ternary Mn(III)heme-HSA-myristate complexes formed at 1:1: 3 and 1:1: 6 molar ratio.
Results obtained here show a different contribution to relaxivity depending on the conformational state of the protein and on the occupancy of the myristic acid binding sites. Moreover, temperature dependence data suggest that an important contribution to the overall paramagnetic contribution to the solvent water relaxation rate is due to water molecules in fast exchange with the bulk.
The relaxivity change is more significant between pH 5.5 and 8, where HSA is in its native form (N). This is in part due to the increase of myristic acid molar ratio that makes easier water accessibility to paramagnetic centre, Mn(III)heme. The relaxivity of Mn(III)heme-HSA complex decreases with decrease of myristic acid molar ratio. It is clear that without myristic acid water access to paramagnetic centre is either not allowed, or it occurs on a timescale faster than the molecular correlation time of the protein.
In the range of pH between 8.3 and 11.9, corresponding to the HSA basic form (B), the contribution to relaxivity of Mn(III)heme-HSA fatty acid complexes and ternary Mn(III)heme-HSA-myristate complex does not change significantly from defatted Mn(III)heme-HSA. Therefore, we can assume that myristate binding does not affect the B form of HSA.

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Direct detection of proton solute relaxation

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Measurements of proton longitudinal relaxation of proteins and liposomes diluted in D_2O in millimolar concentration have been performed to directly monitor the spectral density function of solute protons. In theory, each protein/liposome proton has its own relaxation rate, and the magnetization decay detected from relaxometric measurements is the sum of the magnetization decays for all protons in the sample. Theoretical calculations performed with the program CORMA indicate that the distribution of relaxation rates is bimodal. A good fit for all the magnetization decays was indeed obtained with the modeled bimodal relaxation rate distribution. The experimental low field relaxation rate values so obtained were significantly smaller than the theoretical predictions calculated by CORMA. This was ascribed to internal local motions quenching proton contribution to R_1 (1). The experimentally obtained spectral density functions have been analysed as a sum of Lorentzian functions and compared to theoretical expectation. It was possible in this way to obtain information on the global order parameter of the system and on the aggregation state of the solute through a safe estimation of the solute reorientational time.

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Multi-exponential fit of NMRD data for olive oil analysis

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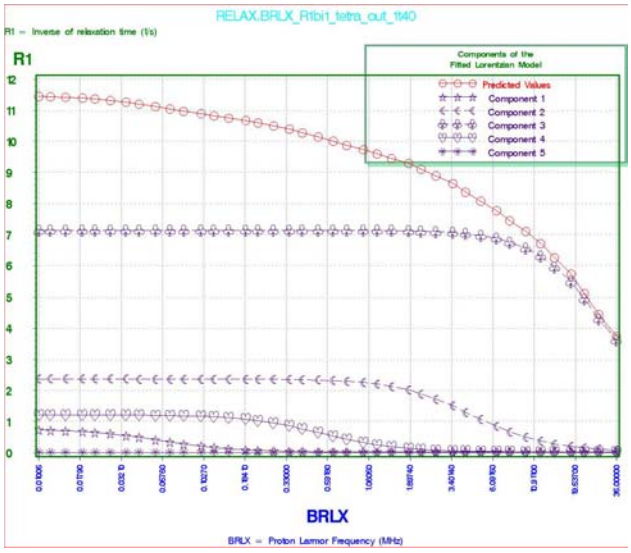
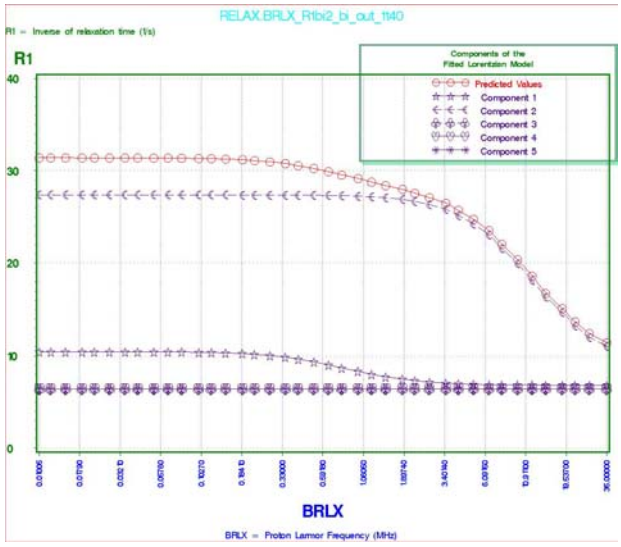
NMRD profiles of Tuscan olive oil samples have been acquired for their relaxometric characterization. Software programs have been written to analyze the magnetization decays detected by the relaxometer thought multi-exponential models. We found that a monoexponential function provides a poor fit in the whole accessible range of frequency. The decays could be indeed well fitted with a biexponential function. Inclusion of a third exponential term did not reduce the sum of the differences between experimental and back-calculated values. The developed model comprises a protocol for the determination of the weighting factor of the two exponential functions. Such weighting factor is proportional to the number of nuclei relaxing with about the corresponding rate. In this way, two relaxation rate profiles for each set of data were determined as a function of the magnetic field. The profiles were then analysed as a sum of Lorentzian functions (see graphs below).





Correlation times from 100 to 1 ns with different weights were obtained. Comparative analysis of the NMRD profiles of different types of oils is in progress, to investigate whether the quality of the different oils may be correlated to the parameters related to relaxometric properties.

A dedicated NMR apparatus for non-invasive and non-destructive measurements of great dimension cores

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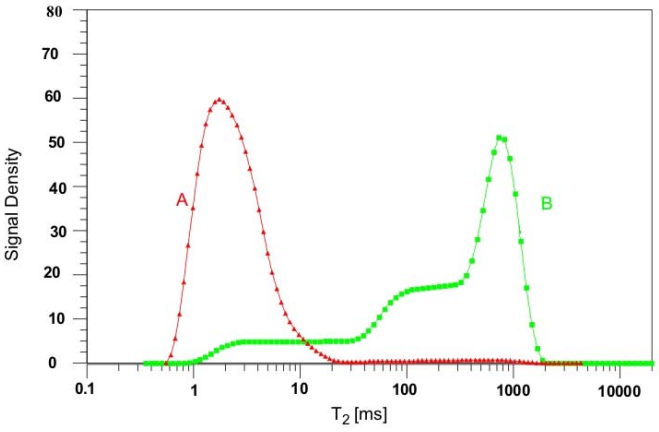
Nuclear Magnetic Resonance Relaxometry is a universally accepted technique for the determination of structural and transport properties of porous media in a non-destructive and non-invasive way. In particular, it allows one to determine[1] porosity, permeability and irreducible saturation. The increasing use of this methodology requires new types of equipment making it possible to investigate samples with particular characteristics, such as large, full-size cores.

In order to perform relaxation measurements on full size cores, an apparatus has been designed and built. It is composed of a versatile SpinMaster console, a permanent magnet with large bore and good field homogeneity over the whole sample volume, and several RF coils combining large volume with short dead time with high B_1 field homogeneity. The apparatus is compatible with the cores of up to 12 cm in diameter.

To further improve the performance of the apparatus, we have implemented special measurement pulse sequences, such as Logarithmically distributed Aperiodic Pulse Saturation Recovery (LAPSR) and Inversion Recovery with Composite Inversion Pulse (IR-CP) and CPMG with Composite Inversion Pulses (CPMG-CP).



In order to evaluate the system performance, we have performed measurements using phantoms with known NMR parameters, as well as non-consolidated cores (10 cm in diameter and 15 cm high).

The Figure shows two T_2 relaxation time distributions, obtained evaluating raw data by UPEN[2], for two different samples: sample A is a fine sand, while sample B is a gravel. As expected, sample A is characterized by a single peak at very short times, whereas sample B shows a wide distribution covering three decades.

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Field-cycling and rotating frame relaxometry of mesoscopic polymer melt layers

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Polymer chain dynamics changes dramatically from bulk to mesoscopically confined melts. Model polymer theories help us understand this dynamical behaviour of polymers in bulk and confined state [1]. The Rouse and Renormalized Rouse theories describe the behaviour of bulk polymers while the Tube or Reptation theory explains the dynamics of confined polymers. The Rouse model visualising beads and springs in a viscous medium, successfully models polymers below the critical molecular weight, where so-called chain "entanglements" are absent. Longer polymer chains with molecular weight greater than the critical molecular weight and having entanglement effects are modelled by the renormalized Rouse formalism. The tube or reptation theory describes the dynamics of polymers geometrically confined in mesoscopic length scales that is from nano- to micrometers [2]. The aim of our work is to see the transition from Rouse to reptation dynamics in confined polymer layers, by a variation of the effective layer thickness.

In our work we prepare polymer melt layers confined between thin film foils (KAPTON) of 7.5µm thickness by a simple roll-coating technique [3]. A solution of our polymer, a perflouropolyether, with a very compatible volatile solvent like 2,3dihydrodecaflouropentane is prepared and is roll coated on the Kapton foil using a motor to rotate at constant velocity. The velocity of the motor and the solution concentration are the parameters which control the final polymer melt layer thickness as predicted by the Landau-Levich-Derjaguin formula for thin film roll-coating [4],[5].

The molecular weights of the polymers selected were less than the critical molecular weight. The spin lattice relaxation was measured in the frequency range 1 kHz to 10 MHz and the relaxation curves of the bulk melts are shown to fit well with the Rouse model. The polymers then confined in fine layers exhibited effects of confinement in the field cycling relaxation data. As the signal to noise ratio tends to become poor with very thin polymer layers, rotating frame relaxation technique was used in the low frequency regime of 1 to 10 kHz to study the relaxation behaviour. Translational diffusion measurements using both pulsed field gradients and in the fringe field with a gradient of 60T/m [1] were also done and the results are presented.

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Synthesis and Characterization of a New Gd-DTPA Derivative with a Fast Water Exchange

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The water residence time (τ_M) is a decisive parameter of the efficiency of MRI paramagnetic contrast agents but the effects of chemical modification on this factor are still controversial. In this study, a new Gd-DTPA derivative (GdL1) with an additional carboxylate group (Figure 1) was synthesized and characterized by multinuclear NMR

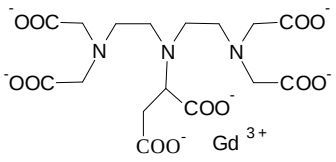

Figure 1: Structure of the Gd-complex GdL1

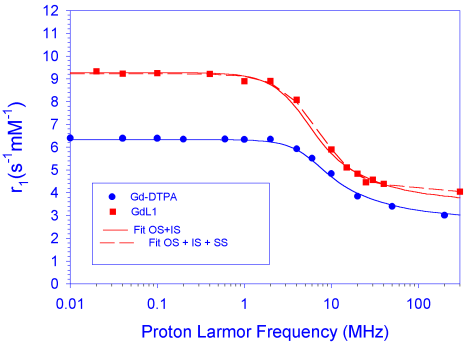

Figure 2: proton NMRD profile of GdL1 and Gd-DTPA at 310 K

The analysis of the ^{17}O NMR data results in a water residence time of GdL1 almost 5 times smaller than that of the parent compound Gd-DTPA (τ_M^{310}=32 ns). The proton relaxivity of GdL1 at 20 MHz is 25 % larger than the Gd-DTPA one at 310 K.
Using the classical innersphere and outersphere theories, the theoretical adjustment of the proton NMRD profile needs a high value of the electronic relaxation time at low field (τ_{SO}) as well as a reduction of the distance between Gd^{3+} ion and the coordinated water hydrogens (Figure 2). Since the presence of the additional carboxylate group could be responsible of a second hydration sphere whose molecules are exchanging very fast with the bulk, second sphere water molecules were included in the theoretical model used above. The following parameters are obtained : τ_R=65 ps, τ_{SO}=100 ps, τ_V=8 ps, 4 water molecules in the second sphere at a distance of 0.4 nm and a correlation time for these second sphere molecules equal to 29 ps.
Thanks to its short water residence time, this new Gd-complex appears thus as a good candidate to a macromolecular coupling.

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Physicochemical Characterization of C-functionnalized Gd-TTDA Complexes, Potential New Contrast Agents for MRI

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The efficacy of gadolinium complexes as MRI contrast agents relies on their ability to enhance the water proton relaxation rate. Several parameters among which the water residence time τ_M have to be optimised to obtain a maximum efficacy at a given magnetic field. Ideally at 310K, τ_M should be equal to ca 10 to 30 ns. Recent works have shown that derivatives of Gd-TTDA have τ_M in this range [1,2] but their stability is not satisfactory for in vivo use. This work reports the physicochemical characterization of four new Gd-TTDA complexes with potentially short τ_M and increased stability.

The τ_M of the gadolinium complexes at 310 K, as calculated from the oxygen-17 transverse relaxation rate of water at 7.05 T are 13 ns, 43 ns, 3 ns and 56 ns for compounds **1**, **2, 3** and **4** respectively. Both methyl derivatives **1** and **3** and the parent compound **5** have quite similar relaxivities at low and high fields whereas the low field relaxivity of both phenyl derivatives **2** and **4** is similar and larger (figure 2).

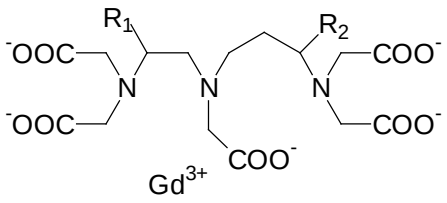

Figure 1 : Structure of
Gd-C_4-Me-TTDA **1** (R_1=CH_3, R_2=H),
Gd-C_4-Phe-TTDA **2** (R_1=C_6H_5, R_2=H),
Gd-C_9-Me-TTDA **3** (R_1=H, R_2=CH_3),
Gd-C_9-Phe-TTDA **4** (R_1=H, R_2=C_6H_5)
and Gd-TTDA **5** (R_1=H, R_2=H)

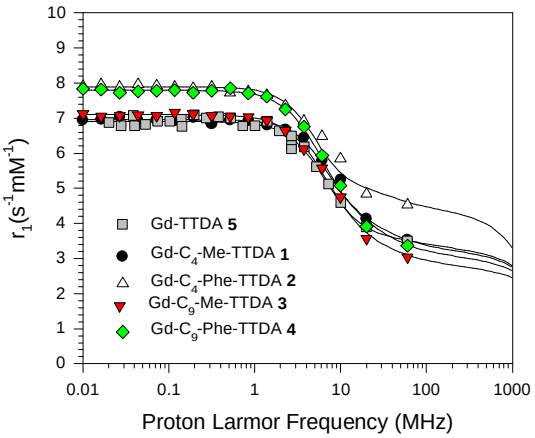

Figure 2: ^{1}H NMRD profiles of aqueous solutions of Gd-C_4-Me-TTDA **1**, Gd-C_4-Phe-TTDA **2,** Gd-C_9-Me-TTDA **3,** Gd-C_9-Phe-TTDA **4,** Gd-TTDA **5**

For the isomers **3** and **4**, reasonable values of τ_R^{310} were obtained by increasing the value of r to 0.32 nm whereas for **2**, r had to be decreased 0.30 nm to get a reasonable τ_R^{310}. It seems thus that the C_9 substitution has a harmful effect on the distance r whereas a C_4 substitution is rather beneficial.

The stability of complex **2** versus transmetallation by zinc(II) ions, although sligthly better than that of Gd-TTDA, is still lower than that of Gd-DTPA-BMA but complex **4** is characterized by a better stability.

In conclusion, both phenyl derivatives **2** and **4** and more particularly complex **4** seem thus to be good candidates for in vivo use.

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Field Cycling Relaxometry in the Earth's magnetic field

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An Earth's field nuclear magnetic resonance apparatus based on the design presented in [1] and applying the method of Packard and Varian [2] is used to measure ^{1}H relaxation times. The device is built in a way that it can be used in a normal laboratory environment with its natural occurring interfering influences such as electric wires and metal from reinforced concrete or furniture. Self compensation against external alternating fields is achieved by a construction of two identical coils that are wound in opposite directions with respect to each other and connected in series (first order gradiometer). In this way external magnetic field noise common to both coils is cancelled out and the signal from the 20ml sample in one of the coils can be detected with minimal interference. Furthermore a 4mm thick aluminium shielding around the coils protects against low frequency alternating electrical fields. Three pairs of gradient coils (Maxwell pairs) are placed around the aluminium shielding to homogenise the Earth's magnetic induction in the sample volume. To keep the sample at a constant temperature the coils and the sample are cooled by air. By means of varying the polarising current, the apparatus can be used as a field cycling relaxometer.

The NMR device is still in a set-up phase, but from the first test measurements it can be concluded that this apparatus is able to measure transversal relaxation times in the Earth's magnetic field from about 10ms up to several seconds. The transversal relaxation time is directly derived from the digitised free induction decay (FID) signal with a signal to noise ratio of about 100. The ^{1}H Larmor frequency ($\gamma B_o/2\pi$) in the laboratory of the University of Bremen was determined to be 2058Hz, corresponding to a magnetic field strength of 48μT. A single ^{1}H free induction decay signal measured by this apparatus and obtained from the protons of a 20ml water sample at room temperature is shown in Figure 1. Longitudinal relaxation times longer than about 20ms can be measured in a range from about 70μT to 0.07T, corresponding to Larmor frequencies from 3kHz to 3MHz.

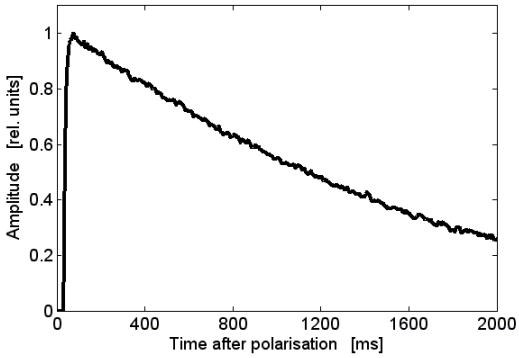

Figure 1: A single ^{1}H FID signal in the Earth's magnetic field from a 20ml water sample at 22°C

The planned application of the apparatus is the investigation of saturated and unsaturated porous model systems and soils by determining longitudinal and transversal relaxation times. Furthermore, the influences of large molecules in porous systems such as organic substances in soil will be explored by studying the longitudinal relaxation time dispersion.

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NMR relaxometry of partially immobilized polymers – grafted chains and block-copolymers

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Common theories that describe the molecular dynamics of polymers are based on the assumption of a free melt, i.e. a random arrangement of molecules without any further external constraints. Introducing defined conditions that reduce the mobility of the chains can serve as a means to investigate how the dynamics of an individual polymer chain is influenced by the local environment. One possibility to generate such conditions is the chemical fixation of one or both chain ends, either by grafting to the surface of a solid object or by linking it to a second polymer which forms a solid-like phase. The time-dependence of segmental fluctuations and, as a consequence, the frequency dependence of the NMR relaxation time is expected to be influenced by these restrictions.

Polydimethylsiloxane (PDMS) chains were grafted onto SiO surfaces which generated short loops of typically less than 10 monomer units between grafting points [1,2]. Increasing grafting density led to the complete suppression of the well-known power-law relation of T_1 on Larmor frequency which is characteristic for semi-local and coherent motion at intermediate frequencies, while the high-frequency behaviour ($> 10^7$ Hz) remained mostly unaffected. The temperature dependence of the relaxation dispersion of phase-separated and grafted polymers is presented and is compared with longitudinal and transverse relaxation time measurements at high magnetic fields.

A different approach was chosen by synthesizing block-copolymers of well-defined chain lengths which were know to undergo phase separation [3]. Polybutadiene (PB) and polystyrene (PS) of similar molecular weights were used to generate block-copolymers that formed lamellar structures consisting of a glassy PS phase and a soft PB phase; the results were compared to PS-PB-PS triblock copolymers and to PB melts as a reference. Over a wide range of temperatures, PS remained in the glassy state so that its signal contribution could be filtered out easily. Only the dynamics of PB was investigated systematically by variation of Larmor frequency, temperature and chain length. The power-law dependence which was found for pure bulk PB was observed to be changed in the block copolymers, in particular the range of the intermediate region of tube-affected motion was reduced in width. Spin diffusion between the PS and the PB phases could be ruled out to explain this finding, so that the change in the dispersion must be assigned to an actual variation of the reorientational spectrum subject to the given geometrical restrictions.

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NMR RELAXATION STUDY OF *HYPOLYTRUM PUNGENS*

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It is very common for people to prepare tea from herbs as a medicine for different types of diseases that occur in heart, stomach, liver and others. It is well known that some tea has potential health benefits. There are studies showing that the antioxidants present in tea help to reduce the risk of heart disease and kinds of cancers. The antioxidants also help to prevent the potentially cell-damaging effects of certain substances in the body [1].

The *Hypolytrum pungens* is used to prepare tea for diabetic's control. In popular medicine it is believed that the tea of this herb has substances, which promote the elimination of the glucose excess from the blood stream. However, the use of this type of teas does not have a specific concentration and also it is not know the quantity that should be drunken along the day. Thus, as everything related to these teas is empiric, scientific studies still have to be done to obtain information on their components that are related to their pharmacological activity and the best way to use them [2].

This study focuses on the investigation of the *Hypolytrum pungens* to understand its dynamical behavior, which is a part of a methodology in development to study these compounds. For this purpose, we have chosen to first analyze the presence of molecular domains mobility.

The material for analysis was collected in Magé, Rio de Janeiro. The herb was washed, dried and maintained at low temperatures. The analyses were carried out in a short period of time (one day), to ensure that no external changes would influence the results. The hydrogen relaxation times of leaf, stem and seed were carried out on Resonance MARAN Ultra 23 spectrometer, operating at 23 MHz for hydrogen, using a inversion recovery pulse sequence (180° - τ - 90°), T_1, with a range of τ varying from 100 ms up to 5,000 ms and Carr-Purcell-Meiboom- Gill (90° - τ - 180°), T_2, with τ = 0.1 ms.

T_1 relaxation time data and the distribution of domains obtained for the herb regions are shown in Table1.

Table 1 – Measurements of T_1 data of leaf stem and seed at 27°C

Sample	T_1 (ms)	number of domains
Leaf	23.4	2
Stem	162.2	4
Seed	60.9	1

The first information on the relaxation data is related to the spin-lattice relaxation time, which showed that the stem relaxation mechanism is controlled by a rigid component that is probably the cellulose. The seed shows T_1 value higher than leaf, because the polysaccharides control the spin-lattice relaxation process.

According to the number of distribution domains it can be seen that the stem presents a larger quantity of domains with different molecular mobility, which are responsible for the relaxation process. The leaf present at least two domains that control the relaxation process and in the seed one predominant domain constituted by the starch is responsible for the relaxation mechanism. With respect to the T_2, the behavior of this parameter corroborates the information obtained from T_1.

Novel Approaches to the Timing of FFC-NMR experiments

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Compared with a HR-NMR spectrometer, a Fast-Field-Cycling NMR Relaxometer imposes a number of extra requirements on the timing of acquisition sequences [1]. This is because the field-switching cycles become more sophisticated (field waveforms profiling) and because FFC-NMR is used to investigate all kinds of samples, including liquids, solids, granular materials and combinations of them with very different FIDs (required sampling rates range from 1 kHz to 10 MHz).

Consider, for example, samples with several phases (e.g., a rigid matrix, a bulk water phase, and an adsorbed water layer). In such cases it would be convenient to split the FID into two or more temporal windows and apply in each of them quite different signal-acquisition parameters (such as the dwell time and filter width values). In this way one could, in fact, optimize the final S/N ratio of each sample component [2]. This approach implies, however, a real-time control of the dwell time, the filter settings and other receiver parameters.

With the ongoing development of variable-field relaxometry, we expect that there will soon arise the need for a second and even third RF irradiation channel and that all such channels will need to be synchronized with the rest of the system. We provide dynamically controlled (not just digitally pre-settable) frequency, phase and amplitude of all the channels and offer the User additional possibilities such as composite, profiled, and chirp pulses.

To meet all these requirements, we have adopted a number of innovative engineering solutions, centered around the modern FPGA based **system-on-chip (SOC)** concept and trying to place all the most speed critical discrete electronic devices close to each other on the same board. The heart of the system is a powerful FPGA chip running at up to 210 MHz clock speed. A **single chip** system provides us with considerable timing advantages such as **direct signal digitization up to 90 MHz** and a **complete run-time control of all relevant acquisition parameters** with **temporal resolution of 20 ns.** The FPGA chip is located on a **PCI board** together with **pulser controlled ADC, DAC's, RF attenuators, RAM** and relative analog and digital circuits.

In order to control slower devices such as magnetic field pulse shapers it was found more expedient to use dedicated small pulse sequencers placed on the corresponding slow device's boards and remotely synchronized from the main pulser.

The FPGA system chip incorporates:

- **Quadrature Digital Down Converter** (phase detector), as well as **pulser controlled digital CIC and FIR filter blocks**.
- A versatile **pulser controlled data accumulator** with an ample **choice of accumulation modes** [2].
- Three independent, **pulser-controlled** digital RF-generation channels.
- Safety interlocks and external events controller **interfaced with pulser**.
- Pulse sequences generator, implemented as a **hard-wired sequence-timing sub-processor** with **128 bits wide "words"**, specifically designed to handle all the tasks discussed above as well as many others. The generator has **96 output channels** available for **hardware control** which permit synchronization with other boards and external devices. It supports **run-time re-programming**, **unconditional and conditional jumps** and **execution of sub-sequences**. It also supports **nested cycles** to a depth of 7 levels, ensuring **very compact and fast loading sequence programs**. The **running sequences can be dynamically updated and reprogrammed**. The sequencer **can react in sophisticated ways to run-time internal and external events** such as signal overflows, safety interlocks and timing triggers.

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Novel Approaches to Signal Acquisition and Accumulation in FFC-NMR experiments

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Among the particularities of FFC-NMR relaxometers is the extreme dynamics of the magnet system which, while essential for the technique [1], makes the acquisition field somewhat unstable (noisy). Further field reproducibility problems arise also from the thermal and mechanical stresses on the magnet during operation.

All this deteriorates signal coherence between successive scans and thus reduces the efficiency of the data accumulation process (FID shortening). The close link between magnetic field stability and reproducibility and the achievable sensibility is of considerable importance because low S/N ratios still limit many of the inviting potential applications of FFC NMR relaxometry. The limit is particularly felt when measuring relaxation profiles of nuclides with low γ and/or low abundance, such as ^{2}D, ^{7}Li, ^{17}O, ^{13}C, etc.

Improving the S/N ratios has been one of the principle goals of many recent Stelar efforts, such as the development of FFC magnets with ever higher maximum fields (higher initial polarization), better cooling systems (improved field stability), higher acquisition frequencies (improved probe sensitivity), solenoid probes (better sensitivity for small-volume samples), novel null-biased sequences (reduced noise propagation in data evaluation algorithms) and, last but not least, novel signal acquisition and accumulation methods implemented on the new SOC (system-on-chip) PCI board to be used on future Stelar instruments.

The features implemented on this board include a complete digital receiver capable of direct signal digitization up to 90 MHz and including a dual digital down converters in quadrature and programmable filters (CIC and FIR) which can be switched in real time even during signal acquisition. The switchover to complete digital handling, by itself, eliminates many of the artifacts typical of all types of NMR, such as those due to offsets and quadrature misadjustment.

Another avenue leading to a S/N improvement regards samples with several phases (e.g., a rigid matrix, a bulk water phase, and an adsorbed water layer) in which it is convenient to divide the FID into several temporal windows and apply in each of them quite different signal-acquisition parameters (such as the dwell time and filter width values). This is made possible by the novel timing-control features of the on-the-chip pulser sub-processor.

Moreover, we have implemented novel data accumulation modes intended to combat the field stability and reproducibility problems which, as mentioned above, are specific for FFC NMR relaxometry. In particular, the new system adopts a number of data accumulation schemes, some of which are substantially different from the usual averaging of the Cartesian components of the complex signal. Thus, for example, it is possible to average (in separate buffers) the magnitudes and phases at each FID point and thus remove most of the field instability effects and drastically extend the usable portion of the FID. It is even possible to average simultaneously the two Cartesian coordinates as well as the magnitude-phase pairs in four distinct buffers. Mathematical algorithms for proper exploitation of all this information are under development but there is no doubt that the impact on achievable S/N ratios will be quite considerable.

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LOCAL MAGNETIC FIELD COMPENSATION FOR LOW-FIELD RELAXOMETRY

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3 – School of Chemical Sciences, Dublin City University, Dublin 9, Ireland.

In a previous work [*1*] an experimental NMR procedure was proposed which is capable of detecting and quantifying the additional magnetic field contributions from external sources in the ULF band. This field has both normal and parallel components and is present in the laboratory during a Field Cycling (FC) experiment. A suitable hardware system to compensate for these components was also proposed.

A certain degree of external magnetic field contribution is always present in the laboratory. This field is not solely a result of the earth's magnetic field but is made up of many different sources. It is, in fact, the main obstacle for the acquisition of a NMRD profile in the KHz region as it prevents the measurement of relaxation times at those magnetic fields which have comparable signal strengths.

From our experience [*2*] the most problematic region is from 10 KHz down depending on the laboratory environment. This can pose a frustrating problem for many FC applications unless a countermeasure is adopted which can compensate for this.

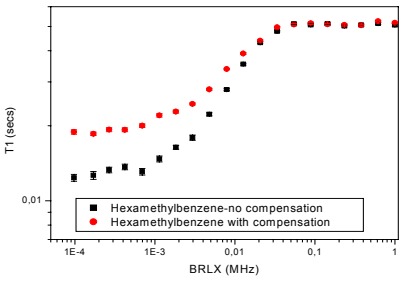
In this poster we present the development of a hardware/software compensation system and its integration in a Stelar Spinmaster FFC2000 relaxometer. The system [*1*] is capable of automatically compensating for the environmental magnetic fields at the position of the sample.

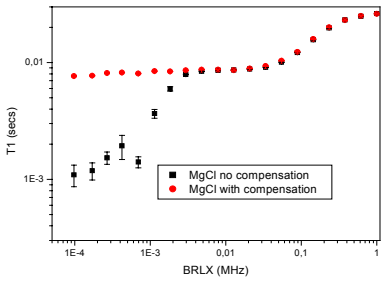
The hardware system is based on a set of oppositely opposing saddle coils, [*3*] driven by a 4 channel current source, which is controllable and programmable by the software of the system. The coils create a rotating magnetic vector in the x,y plane in order to compensate the normal component of B_o.

The compensation procedure is done by minimizing the NAFID (Non Adiabatic FID) which can be observed using special conditions with a pre-polarized Field Cycling experiment.

In addition, the parallel component is detected by NMR and it can be compensated using the bipolar current offset settings of the electromagnet.

Description of hardware and preliminary results regarding the normal and parallel compensation of the local fields in a NMRD profile are presented here.





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Gianni Ferrante, Stanislav Sykora, Advances in inorganic Chemistry, volume 57, 2005 Elsevier Inc.
[3] Optimum saddle coils for external magnetic field compensation in field-cycling NMR
F. Bonetto, E. Anoardo, M. Polello, in press

Null-Biased Fast-Field-Cycling Sequences

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The standard pre-polarized and non-polarized measurement sequencies used in fast-field-cycling (FFC) NMR relaxometry [1] suffer from two major drawbacks:

(a) Due to the magnetization evolution during switching intervals, the longitudinal magnetization evolves with increasing τ towards non-zero values. Consequently, FFC-NMR decay curves must be fitted with an adjustable 'offset' parameter, in addition to the decay rates and weights of individual sample components (for example, three parameters in the case of a mono-exponential fit).

(b) Measurements are carried out using different sequences at high relaxation fields (NP) and at low relaxation fields (the crossover field being approximately half of the polarization field). For reasons which are not yet quite clear, this sometimes leads to a statistically significant discrepancy between the two 'sections' of the resulting NMRD profile.

We propose new measurement sequences consisting in a combination of RF pulse-phase cycling, receiver cycling and magnetic field cycling, such that all switching-time interval effects get cancelled, while the sample pre-polarization effects and the subsequent decay are enhanced.

In such sequences, the acquired signal $S(\tau)$ decays rigorously to zero for $\tau \rightarrow \infty$ (which is why we call them ***null-biased***). Essentially all classical FFC-NMR sequences can be cast in this way (the basic NP/PP, IR, IR_CPMG, ...), some of them in a way which does not at all reduce the efficiency of the measurement (i.e., the total signal range which can be achieved in a given time).

The null-biased sequences offer several important advantages:

(1) Since $S(\infty)$ is strictly null and does not have to be estimated experimentally, there is no need to acquire portions of the decay curve where the signal is already almost stable (this leads to a time saving).

(2) For the same reason, the data can be fitted without the adjustable offset parameter (for example, a two-parameter fit is sufficient in the case of a mono-exponential decay). Considering the effect of number of adjustable parameters on their confidance intervals, this fact alone improves the precision of the estimated T_1 by a large factor (~10).

(3) In most cases, the same sequence can be used to acquire the NMRD profile over the complete range of field values (for example, from 5 kHz to 40 MHz). As a result, the measured NMRD profiles are internally more coherent and no discrepancy between high-field data and low-field data can occur.

We discuss also an apparent drawback of the new sequences consisting in the fact that they enhance the visual impact of random field variations between consecutive scans. Analysis shows, however, that traditional measurements are burdened by the same instabilities, even though they are to a large extent masked by the switching-interval signal components.

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