8 TH CONFERENCE ON FAST FIELD CYCLING NMR RELAXOMETRY

www.ffcrelax.com

MOLECULAR BIOTECHNOLOGY CENTER

23 25 MAY 2013 TURIN ITALY

PROGRAM AND ABSTRACTS

PRECEEDING MEETING OF

EMIM 2013

the 8th European Molecular Imaging Meeting

www.e-smi.eu

esmi imaging life

European Society for Molecular Imaging

Scientific Committee

Silvio AIME
Esteban ANOARDO
Pellegrino CONTE
David LURIE
Gianni FERRANTE
Bertil HALLE
Rainer KIMMICH
Jean-Pierre KORB
Sigfried STAPF

Università di Torino

MBC

Molecular Biotechnology Center

STELAR

We are very pleased to welcome you to Turin from May 23 to 25, 2013. The 8th Conference on Fast Field Cycling NMR Relaxometry will be a good occasion for exchanging new ideas and presenting numerous and varied applications in a very open field of interest. As in the past, this 8th conference is gathering people with active interests in nuclear and electron spin relaxation, fast magnetic field switching experiments, low field magnetic resonance, nuclear quadrupole resonance and magnetic resonance imaging. The discussion will focus on nuclear magnetic field cycling experimental techniques, data interpretation and theory, as well as applications performed by other low-frequency and time-domain and low resolution NMR techniques. Topics range from experimental issues, interpretative foundations and applications in a variety of materials including but not restricted to solids, porous and heterogeneous systems, polymers, liquid crystals, biological and diagnostics.

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. http://www.ffcrelax.com/ffcrelax/mainpage.php?folder=history&page=index.php

The following conferences, held in Torino in 2001, 2003, 2005, 2007, 2009 and 2011 were aimed at strengthening the interaction between FC users from different scientific areas, stimulating the exchange of new ideas and technical features. In 2009, the *6th* symposium was particularly special in keeping with these objectives and the First Summer School on Field Cycling NMR Relaxometry was held in Mede (PV) - Italy in June 2009. This NMR School was intended to be a comprehensive introduction to NMR Field Cycling and NMR Relaxometry with the aim of enabling researchers of any scientific discipline to be able to apply the exceptional capacity of field cycling technology in their work. *http://www.ffcrelax.com/schoolNMR/home.php*

As in the past, the meeting will provide a most opportune setting for discussion by scientists from a broad range of disciplinary and geographic origins. Chemists, physicists and engineers will exchange ideas while incubating the seeds for the future development of the technique and its applications. The meeting has turned out to be a unique forum for the discussion of newly emerging and traditional methods while empowering innovative developments to ever more complex and challenging applications. The conference will focus on the most recent developments, with sessions devoted to some of the most exciting and topical aspects of the technique by world leaders in the respective disciplines. It will provide unique opportunities for young graduate students and postdocs to discussion their research with leaders in the field.

We hope that all attendees of the 8th Conference on Fast Field Cycling NMR Relaxometry enjoy the sessions, and that much fruitful cross-relaxation will occur among the many disciplines represented at the meeting.

The FFCrelax committee

Scientific Committee:

- Silvio Aime
- Esteban Anoardo
- Pellegrino Conte
- Gianni Ferrante
- Bertil Halle
- Rainer Kimmich
- Jean-Pierre Korb
- David Lurie

Organizing Secretariat :

-	Silla Sai	Stelar s.r.l.	sai@stelar.it
-	Rebecca Steele	Stelar s.r.l.	steele@stelar.it
-	Simona Baroni	Invento s.r.l.	simona.baroni@invento-lab.com

Language: The official language of the Symposium is be English

Conference web site: http://www.ffcrelax.com

Main sponsors

The Organizing Committee of the Symposium would like to thank the following sponsors whose support is gratefully acknowledged:

University of Torino
Molecular Biotechnology
Center www.mbcunito.it/about_mbc.php

Stelar s.r.l.www.stelar.it

Conference Program

Thursday 23 May, 2013

11:00-13:30	**Registration**	
12:30-13:00	**Lunch**	
13:30-13:40	***Opening and welcome address***	
	Chair: Robert Bryant ***Oral Presentation - Session 1***	
13:40-14:10	***Pierre Levitz–*** *PECSA, Université Pierre et Marie Curie -CNRS, Paris, France* Proton R_1 and R_2 NMRD induced by magnetic nanoparticles with high magnetocrystalline anisotropy	*O1*
14:10-14:40	***Luce Vander Elst*** *- University of Mons, Belgium* Characterization of paramagnetic and superparamagnetic nanoparticular MRI contrast agents by FFC relaxometry	*O2*
14:40-15:10	***Eliana Gianolio*** *- Università degli Studi di Torino, Italy* Paramagnetic liposomes as responsive relaxometric agents	*O3*
15:10-15:40	***Yves Gossuin*** *- University of Mons, Belgium* Fundamental and practical applications of NMRD profiles in the study of particulate MRI contrast agents	*O4*
15:40-16:10	***Dermot Brougham****- Dublin City University, Ireland* *Fast field cycling NMR relaxometry studies on magnetic nanoparticles suspensions; insights into MRI properties and approaches to design*	*05*
16:10-16:20	***Coffee break***	
	Chair: Jean-Pierre Korb ***Oral Presentation - Session 2***	
16:20-16:50	***Bertil Halle*** *- Lund University, Sweden* Transient access to the protein interior: Magnetic relaxation dispersion versus simulation	*O6*
16:50-17:20	***Fabien Ferrage*** *- Ecole Normale Supérieure, Paris, France* Sub-τ_c motions in proteins revealed by high-resolution NMR relaxometry	*O7*
17:20-17:50	***Giacomo Parigi*** *- CERM, University of Florence, Italy* Relaxometry for solution DNP and protein dynamics	*O8*
17:50-18:20	***Siegfried Stapf*** *- Technische Universität Ilmenau, Germany* Low-field NMR and relaxometry investigations of cartilage and its constituents	*09*
18:20-18 :50	***Robert Bryant****- University of Virginia,Charlottesville VA, USA* Spin-relaxation efficiency	*10*
19:00	***Welcome reception and dinner***	

Friday 24 May, 2013

	Chair: Silvio Aime ***Oral Presentation - Session 3***	
8:30-9:00	***David Lurie -*** *University of Aberdeen, Scotland, UK* Field-cycling magnetic resonance imaging	*11*
9:00-9:30	***Christopher Bidinosti*** *- University of Winnipeg, Canada* Phase-gradient coil designs for 3D TRASE MRI at low field	*12*
9:30-10:00	***Lionel Broche*** *- University of Aberdeen, Scotland, UK* Medical applications of fast field-cycling MRI	*13*
10:00-10:30	***Ludovic de Rochefort -*** *Université Paris Sud, Orsay, France* Initial characterization of a ±0.5T insertable dreMR magnet on a 1.5T clinical system	*14*

10:30-10:50 ***Coffee break***

	Chair: Siegfried Stapf ***Oral Presentation - Session 4***	
10:50-11:20	***Anthony Horsewill*** *– University of Nottingham, UK* Dynamic tunneling polarization: A quantum rotor analogue of dynamic nuclear polarization and the NMR solid effect	*15*
11:20-11:50	***Pär Håkansson*** *– University of Southampton, UK* The interplay of MD and QM calculations to elucidate singlet state relaxation	*16*
11:50-12:20	***Tomaz Apih —*** *Jožef Stefan Institute, Ljubljana, Slovenia* Broadband excitation with frequency swept pulses	*17*
12:20-12:50	***Pellegrino Conte —*** *Università degli Studi di Palermo, Italy* Water dynamics at the liquid-solid interface of biochar systems	*18*

12:50-13:50 ***Lunch***

	Chair: Pierre Levitz ***Oral Presentation - Session 5***	
13:50-14:20	***Daniel Canet*** *– Université de Lorraine, Vandoeuvre-les-Nancy, France* Complete proton dispersion curves from 0 Hz up to some hundreds of MHz and some relaxometry stories	*19*
14:20-14:50	***Ioan Ardelean*** *– Technical University of Cluj-Napoca, Romania* NMR relaxation of fluids confined inside porous media with magnetic impurities	*20*
14:50-15:20	***Dominique Petit*** *– Ecole Polytechnique-CNRS, Palaiseau, France* How to separate hydric state, wettability and geometric confinement on moisture transport using FFC relaxometry	*21*

15:20-16:40 ***Coffee Break and POSTER SESSION***

	Chair: Esteban Anoardo ***Oral presentation - Session 6***	
16:40-17:10	***Pascal Fries*** *– CEA, INAC, SCIB, Grenoble, France* Theory and applications of the fast electronic relaxation of complexed paramagnetic lanthanide Ln^{3+} ions, but Gd^{3+}, in solution	*22*
17:10-17:40	***Gabriele Rolla*** *– Università del Piemonte Orientale “Amedeo Avogadro”, Alessandria, Italy* ^{1}H and ^{17}O NMR relaxometric study of a series of macrocyclic Mn(II) complexes in aqueous solution and of their lipophilic derivatives	*23*
17:40-18:10	***Mark Woods*** *– Portland State University, USA* Using relaxometry to probe the traditional SBM paradigm	*24*

20:30 ***Conference dinner to be held at***
“GOLDEN PALACE HOTEL”, Via dell’Arcivescovado 18, Turin
www.goldenpalace.it

Saturday 25 May, 2013

Chair: David Lurie — **Oral Presentation - Session 7**

9:00-9:30	***Jean-Pierre Korb*** - *Ecole Polytechnique-CNRS, Palaiseau, France* Dynamics of bulk and confined crude oils	*25*
9:30-10:00	***Danuta Kruk*** – *Universität Bayreuth, Germany / University of Warmia & Mazury in Olsztyn, Poland* NMR relaxometry and translation diffusion in condensed matter	*26*
10:00-10:30	***Ralf Ludwig*** – *University of Rostock, Germany* Transport properties and molecular motion of triglyme-lithium salt mixtures – Experiments and simulations	*27*
10:30-11:00	***Marco Geppi*** – *Università di Pisa, Italy* Dynamics of P3HT in homopolymers and blends by ^{1}H and ^{13}C relaxation	*28*

11:00-11:20 ***Coffee break***

Chair: Bertil Halle — **Oral Presentation - Session 8**

11:20-11:50	***Esteban Anoardo*** - *Famaf – Universidad Nacional de Córdoba, Argentina* Proton field cycling NMR relaxometry of lipid bilayer membranes containing cholesterol. FFC membrane elastometry	*29*
11:50-12:20	***Janez Seliger*** - *Jožef Stefan Institute, Ljubljana / University of Ljubljana, Slovenia* Field-cycling double-resonance spectroscopy of quadrupole nuclei in hydrogen bonded cocrystals, salts and crystal polymorphs	*30*
12:20-12:50	***Stanislav Sykora*** **-** *Extra Byte, Castano Primo, Italy* Seven conjectures of NMR relaxometry	*31*

12:50-13:00 ***Concluding remarks***

ORAL PRESENTATIONS

Proton R_1 and R_2 NMRD induced by magnetic nanoparticles with high magnetocrystalline anisotropy

M. Levy (1), S. Neveu (2), M. Devaud (1), F. Klaus(2), Claire Wilhelm (1), J. Fresnais (2), A-L. Rollet (2), V. Dupuis(2), Florence Gazeau (1) and P. Levitz (2)

(1) MSC, Université Paris Diderot-CNRS-Paris France
(2) PECSA, Université Pierre et Marie Curie -CNRS, Paris, France

pierre.levitz@upmc.fr

Magnetic Nanoparticles (NPs) play a growing role in different fields of application especially in medicine as contrast agents or therapeutic nanoparticles for hyperthermia. The inner magnetic dynamics of these colloids coupled with the solvent diffusion around the particle can be probed by field cycling relaxometry. In this context, these nanoparticles can also be used as “nano spies” providing valuable information on the local confinement where they are localized.

NMR relaxation induced by iron oxide NPs in the superparamagnetic regime, i.e. governed by thermally activated Neel fluctuations, have been well understood by the seminal theory, developed by Roch, Muller and Gillis which is built on an original outersphere theory including a Curie relaxation. In this context, diluted suspensions of γFe_2O_3 NPs with a characteristic magnetic size from7 nm to 10 nm (weak magnetocrystalline anisotropy) display a high-frequency maximum, as predicted theoretically for the R_1 NMR Dispersion curves (NMRD). It is no longer the case for $CoFe_2O_4$ NPs of the same size (strong magnetocrystalline anisotropy) where the R_1 NMRD profiles continuously decrease with frequency. Such a shape can hardly be interpreted in the framework of existing analytical high anisotropy NMRD models.

In this presentation, we present a theoretical analysis of R_1 and R_2 NMRD explaining the disappearance of the high-field maximum in the case of highly anisotropic NPs. Importantly, our model stresses the dominant contribution of the transverse fluctuations of the NP magnetic moment, treated in a non quantum approximation, to the proton NMR relaxation.

Our model is quantitatively compared to a series of experiments performed on various suspensions of $CoFe_2O_4$ NPs. Our results highlight the potential of Brownian nanostructures, beyond the superparamagnetic regime, as highly effective MRI contrast agents.

Finally, the possibility to extend this model in the case of all coupling strengths between magnetic moment and the NP crystal is outlined.

CHARACTERIZATION OF PARAMAGNETIC AND SUPERPARAMAGNETIC NANOPARTICULAR MRI CONTRAST AGENTS BY FFC RELAXOMETRY

L. Vander Elst[1], E. Lipani[1], S. Belaïd[1], A. Hannecart[1], S. Laurent[1], R.N. Muller[1,2]

[1]Department of General, Organic and Biomedical Chemistry, NMR and Molecular Imaging Laboratory, University of Mons, 7000 Mons, Belgium
[2] Center for Microscopy and Molecular Imaging (CMMI), 6041 Gosselies, Belgium

Contrast agents for Magnetic Resonance Imaging are either paramagnetic compounds (usually Gd-complexes) or superparamagnetic nanoparticles (iron oxide nanoparticles). The first ones are mainly used as T1 agents whereas the last ones are used as T2 agents. The interest of NMRD profiles for the characterization of such systems will be illustrated by three examples.

The first topic concerns tunable-sized silica nanoparticles synthesized by the microemulsion-mediated pathway and used as carriers for the paramagnetic and the luminescent probes. The near infrared luminescent agent is a ruthenium complex that was directly entrapped in the silica shell and the paramagnetic activity comes from a Gd-DTPA derivative that is grafted on the silica surface. NMRD profiles show a strong relaxivity enhancement when the paramagnetic complex is grafted at the nanoparticle surface.

Secondly, the interest of nuclear magnetic resonance (NMRD profiles) to follow and understand the formation of nanocrystalline magnetite by the thermal decomposition of $Fe(acac)_3$ in the presence of oleic acid and oleylamine surfactants at high temperature during the synthetic process will also be reported.

Finally, the influence of the nature of the coating (hydrophilic or hydrophobic) of iron oxide nanoparticles on their relaxivity will be demonstrated through the example of temperature-responsive iron oxide nanoparticles.

Paramagnetic Liposomes as responsive relaxometric agents

Eliana Gianolio[a], Simona Baroni[b], Simonetta Geninatti[a] and Silvio Aime[a]

[a]*Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy.*

[b] *Invento srl, University of Torino, Via Nizza 52, Torino, Italy*

The term "responsive" refers to diagnostic agents whose relaxometric properties are sensitive to a given physico-chemical variable that characterizes the micro-environment in which the probe distributes. An accurate *in vivo* MRI assessment of these parameters may be of clinical value for both diagnosis and selection/monitoring of therapy. To act as responsive systems, MRI agents have to act without a prior knowledge of the actual concentration of the paramagnetic probe. This work deals with different systems based on the use of paramagnetic liposomes loaded with Gd(III)-complexes whose relaxometric properties are affected by a given parameter of interest (e.g. pH and redox state). In the pH responsive system, liposomes are loaded with an amphiphilic metal complex, which contains a moiety whose protonation changes the coordination properties of the metal chelate and which experiences a different intraliposomial distribution depending on the pH conditions. The pH of the solution can be unambiguously identified exploiting the peculiar characteristics of the resulting NMRD profiles and a ratiometric pH-responsive method has been set-up by comparing the relaxation enhancement at different magnetic field strength.

The redox responsive system exploits the effects on the water proton relaxation rates upon changes in the water membrane permeability of liposomes loaded with Gd(III) complexes.

Finally, an in vitro application of paramagnetic liposomes as relaxation probes able to assess the level expression of folate receptors on tumor cells will be reported.

1) Terreno, E.; Delli Castelli, D.; Viale, A.; Aime, S. Challenges for Molecular Magnetic Resonance Imaging, Chem. Rev. 110, 3019-3042, 2010
2) Gianolio, E. ; Stefania, R. ; Di Gregorio, E.; Aime, S. MRI Paramagnetic Probes for Cellular Labeling, EUROPEAN JOURNAL OF INORGANIC CHEMISTRY, 12, 1934-1944, 2012

Fundamental and practical applications of NMRD profiles in the study of particulate MRI contrast agents

Yves Gossuin, Olivier Sandre, Rémy Guillet-Nicolas, Jean-Luc Bridot, Freddy Kleitz, Quoc Lam Vuong

Magnetic nanoparticles can be used to enhance the contrast in Magnetic Resonance Imaging. This is related to their ability to shorten water proton relaxation times. The evolution of the relaxation rates with magnetic field (the NMRD profile) is bearing important information about these systems. Of course it allows a direct estimation of the efficiency of the magnetic particles at multiple magnetic fields, but this is not their only advantage.

Iron oxide (maghemite) superparamagnetic particles[1] are intensively used in preclinical imaging as well as in cellular imaging. Thanks to the development of relaxation models, the NMRD profile provides - through an appropriate fitting of the curve - an estimation of the characteristics of the system, as particle size and magnetization. Moreover, as the relaxation of magnetic particles is very sensitive to the clustering, NMRD profiles can also be used to check the stability in time of a colloidal suspension.

New paramagnetic particles (based on rare-earth ions) are currently developed and tested in animal models[2]. These must be divided into two groups. The gadolinium containing particles (oxide, hydroxide and fluoride) on the one hand, that could be used as T_1 contrast agents at clinical imaging fields. On the other hand, one finds particles containing dysprosium, holmium, erbium and terbium that could be used as T_2 or T_2^* agents at high fields[3,4]. Besides the magnetic susceptibility and the size of the particles, the imaging magnetic field has a tremendous influence on the relaxation efficiency of paramagnetic particles even for T_2, which is not the case for iron oxide particles. The theoretical modelling of the relaxation induced by these compounds helps determining *a priori* which particles will be suited for a given experiment. In this context, NMRD profiles are essential to test the relaxation models. But they can also help monitoring the release, by the paramagnetic particles, of rare-earth ions, which could result in a serious toxicity of these compounds.

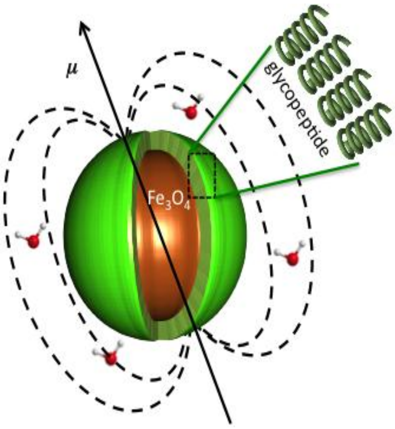
1. Vuong, Q. L., Berret, J.-F., Fresnais, J., Gossuin, Y., Sandre, O. *Advanced Health Materials* **1**:502-512 (2012).
2. Faucher, L., Gossuin, Y., Hocq, A., Fortin, M.-A. *Nanotechnology* 22 : 295103 (2011).
3. Norek, M., Pereira, G.A., Geraldes, C.F.G.C., Denkova, A., Zhou, W., Peters J.A. *J. Phys. Chem. C* **111**, 10240-10246 (2007).
4. Vuong, Q. L., Van Doorslaer, S., Bridot, J.-L., Argante, C., Alejandro, G., Hermann, R., Disch, S., Mattea, C., Stapf, S., Gossuin, Y. *MAGMA* **25**, 467-78. (2012).

Fast field cycling NMR relaxometry studies on magnetic nanoparticles suspensions; insights into MRI properties and approaches to design

Tsedev Ninjdadgar,[1] *Eoin Fox,* [1] *Jacek Stolarczyk,*[2] *Tushar Borase,* [1] *Andreas Heise*[1]
and Dermot Brougham[1]

1. School of Chemical Sciences, Dublin City University, Glasnevin, Dublin 9, Ireland.
dermot.brougham@dcu.ie
2. Department of Physics, Ludwig-Maximilians-University, Munich, Germany

The physicochemical properties of nanostructures in the fully hydrated form in suspension are critical to their performance in biomedical applications. Work from our laboratory, amongst others[1], shows that ^{1}H NMR relaxation time measurements of the solvent using fast field-cycling NMR relaxometry can provide insight into the extent of hydration, the magnetisation, and the magnetic order. This is possible because the diffusing solvent molecules interact dynamically with the nanostructure.[1] Some examples, which demonstrate the sensitivity of ^{1}H NMR to structure and surface chemistry of fully dispersed nanoparticles[2-4] and of nanoparticle assemblies[5-7] will be described. The implications of these findings for the assembly of nanocomposites and for developing applications in hyperthermia and MRI will be discussed.



Schematic of glycopeptide grafted Fe_2O_3 nanoparticles.

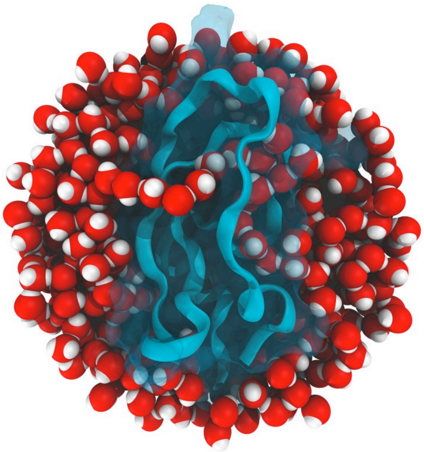
1. Theory of proton relaxation induced by superparamagnetic particles. A. Roch, R. N. Muller, P. Gillis ***J. Chem. Phys.*** 1999, 110, 5403-5411.
2. Stable aqueous dispersions of glycopeptide grafted magnetic nanoparticles of selectable functionality. Tushar Borase, Tsedev Ninjbadgar, Antonios Kapatenakis, Sandra Roche, Robert O'Connor, Christian Kerskens, Andreas Heise, Dermot F. Brougham. ***Angew. Chem. Int. Ed.***, 2013, 52, 3164-3167.
3. Epoxy ring opening phase transfer as a general route to water dispersible superparamagnetic Fe3O4 nanoparticles and their application as positive MRI contrast agents. T. Ninjbadgar, D. F. Brougham. ***Adv. Func. Mat.***, 2011, 21, 4769-4775.
4. Cooperative organization in iron oxide multi-core nanoparticles potentiates their efficiency as heating mediators and MRI contrast agents. L. Lartigue, P. Hugounenq, D. Alloyeau, S. P. Clarke, M. Lévy, J.-C. Bacri, R. Bazzi, D. F. Brougham, C. Wilhelm, F. Gazeau. ***ACS Nano*** 2012, 6(12), 10935–10949.
5. Water-Soluble Superparamagnetic Magnetite Nanoparticles with Biocompatible Coating for Enhanced Magnetic Resonance Imaging (MRI). L. Xiao, J. Li, D. F. Brougham, E. K. Fox, N. Feliu, A. Bushmelev, A. Schmidt, N. Mertens, F. Kiessling, M. Valldor, B. Fadeel, S. Mathur. ***ACS Nano*** 2011, 5(8) 6315-6324.
6. Hierarchical gold-decorated magnetic nanoparticle clusters with controlled size C. J. Meledandri, J. K. Stolarczyk, D. F. Brougham. ***ACS Nano***, 2011, 5(3), 1747-1755.
7. Controlled growth of nanoparticle clusters through competitive stabilizer desorption. J. K. Stolarczyk, S. Ghosh, D. F. Brougham. ***Angew. Chem. Int. Ed.***, 2009, 48(1), 175-178.

TRANSIENT ACCESS TO THE PROTEIN INTERIOR: MAGNETIC RELAXATION DISPERSION VERSUS SIMULATION

Filip Persson and Bertil Halle
Dept of Biophysical Chemistry, Lund University, SE-22100 Lund, Sweden

Many proteins rely for their function on rare structural fluctuations whereby solvent and other small molecules gain transient access to internal cavities. In magnetic relaxation dispersion (MRD) experiments, water molecules buried in such cavities can be used as intrinsic probes of the intermittent protein motions that govern their exchange with external solvent. While this has allowed a detailed characterization of exchange kinetics for several proteins,[1] little is known about the exchange mechanism. Here,[2] we use a millisecond all-atom MD trajectory[3] to characterize water exchange from the four internal hydration sites in the protein BPTI.

Using a recently developed stochastic point process approach,[4] we compute the survival correlation function probed by MRD experiments as well as other quantities designed to validate the exchange-mediated orientational randomization (EMOR) model used to interpret the MRD data. The EMOR model is found to be quantitatively accurate and the simulation reproduces the experimental mean survival times for all four sites with activation energy discrepancies in the range 0 – 3 $k_B T$. On the other hand, the simulated hydration sites are somewhat too flexible and the water flip barrier is underestimated by up to 6 $k_B T$. The simulation reveals that water molecules gain access to the internal sites by a transient aqueduct mechanism, where single-file water chains migrate through transient (< 5 ns) tunnels and pores (see MD snapshot below).



---

[1] E Persson & B Halle, *J Am Chem Soc* **130**, 1774 (2008).

[2] F Persson & B Halle, *J Am Chem Soc*, in press.

[3] DE Shaw *et al.*, *Science* **330**, 341 (2010).

[4] B Halle & F Persson, *J Chem Theory Comput*, in press.

Sub-τ_c motions in proteins revealed by high-resolution NMR relaxometry

Cyril Charlier,[a] Shahid Nawaz Khan,[a] Thorsten Marquardsen,[b] Philippe Pelupessy,[a] Volker Reiss,[b] Dimitrios Sakellariou,[c] Geoffrey Bodenhausen,[a,d] Frank Engelke[b] and Fabien Ferrage[a]

[a] Ecole Normale Supérieure, Département de Chimie, UMR 7203 CNRS-UPMC-ENS, Laboratoire des Biomolécules, 24 rue Lhomond, 75231 Paris Cedex 05 (France)
[b] Bruker BioSpin GmbH, Silberstreifen 4, D 76287 Rheinstetten (Germany)
[c] CEA Saclay, DSM, IRAMIS, UMR CEA/CNRS 3299 – SIS2M, Laboratoire Structure et Dynamique par Résonance Magnétique, F-91191, Gif-sur-Yvette Cedex (France)
[d] Institut des Sciences et Ingénierie Chimiques,Ecole Polytechnique Fédérale de Lausanne, BCH, 1015 Lausanne (Switzerland).

The function of a protein is governed not only by its tri-dimensional structure but also by its internal dynamics. NMR relaxation is a powerful technique to characterize such dynamics. Traditional high-field measurements of relaxation rates provide high-resolution information but limited sampling of fast motions over narrow frequency ranges of the spectral density of motions. On the other hand, conventional relaxometry allows one to explore motions over a broad range of frequencies, albeit at the sacrifice of high resolution. High-resolution relaxometry, as introduced by A. G. Redfield, can, in principle, combine the best of both worlds but the ability to record relaxation in proteins at low magnetic fields has been limited so far by signal losses during sample motions.

Here, we report the design and performance of a new shuttle system installed on a 600 MHz spectrometer, where the polarization and detection take place at high field and relaxation at various points of the stray field. We have measured longitudinal nitrogen-15 relaxation rates in ubiquitin over nearly two orders of magnitude of magnetic field from 0.33 to 14.1 T. In order to analyse low field relaxation rates and correct for the effects of relaxation during shuttling, we have developed a protocol called Iterative Correction and Analysis of Relaxation Under Shuttling (ICARUS).

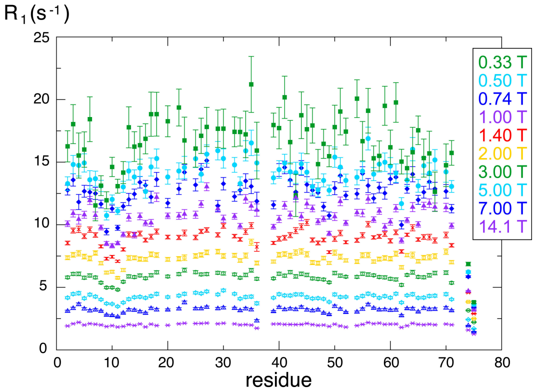


Figure 1: Longitudinal relaxation rates R_1 of ^{15}N in the backbone amide groups of ubiquitin as a function of the static magnetic field. Note that the rates increase with decreasing field and become more and more differentiated and more informative about local dynamics.

We show than some key regions of ubiquitin, in particular the β1-β2 turns, are more dynamic on a nanosecond timescale than previously thought. This study demonstrates that high-resolution relaxometry with fast sample shuttling offers unprecedented information about local motions in proteins on timescales that are faster than their overall tumbling.

Relaxometry for solution DNP and protein dynamics

Giacomo Parigi

Magnetic Resonance Center (CERM), University of Florence,
Via Luigi Sacconi 6, 50019 Sesto Fiorentino, Italy

The analysis of the relaxation profiles of paramagnetic complexes in solution represents a valuable way for the characterization of polarizing agents for solution DNP experiments. The relaxation profiles of solvent water protons in the presence of nitroxide radicals or paramagnetic metal complexes have been analyzed to obtain the structural and dynamic parameters needed for determining the coupling factor, on which the solvent DNP enhancement mainly depends [1-5]. ^{1}H relaxometry thus represents an easy way to estimate the DNP enhancement achievable at full electron saturation as a function of the applied magnetic field.

Relaxivity profiles can provide reorientation times of solute molecules up to the microsecond range, so that the tumbling time of proteins as large as hundreds kDa can be accessed [6]. In sedimented proteins [7], they can provide information on the intervening motions [8].

Recent applications of relaxometry also comprise the analysis of the spectral density of water protons for the characterization of contrast agents [9], and for acquiring information on protein aggregation and dynamics in folded and intrinsically disordered proteins. The analysis of the collective spectral density of protein protons in D_2O solutions is also feasible [10] to obtain information on protein dynamics in terms of reorientation time and generalized order parameter.

[1] P. Höfer, G. Parigi, C. Luchinat, P. Carl, G. Guthausen, M. Reese, T. Carlomagno, C. Griesinger, M. Bennati, “Field Dependent Dynamic Nuclear Polarization with Radicals in Aqueous Solution”, *J. Am. Chem. Soc.* (2008) 130, 3254-3255.

[2] M. Bennati, C. Luchinat, G. Parigi, M.-T. Türke, “Water proton relaxation dispersion analysis on a nitroxide radical provides information on the maximal signal enhancement in Overhauser Dynamic Nuclear Polarization experiments”, *Phys.Chem.Chem.Phys.* (2010) 12, 5902-5910.

[3] M.-T. Türke, G. Parigi, C. Luchinat, M. Bennati, “Overhauser DNP with ^{15}N labelled Frémy’s salt at 0.35 Tesla”, *Phys. Chem. Chem. Phys.* (2012) 14, 502-510.

[4] P. Neugebauer, J.G. Krummenacker, V.P. Denysenkov, G. Parigi, C. Luchinat, T.F. Prisner, “Liquid State DNP of Water at 9.2 T: An Experimental Access to Saturation” *Phys. Chem. Chem. Phys* (2013) in press.

[5] C. Luchinat, G. Parigi, E. Ravera, “Can metal ion complexes be used as polarizing agents for solution DNP? A theoretical discussion” *J. Biomol. NMR* (2013) in press.

[6] E. Ravera, G. Parigi, A. Mainz, T.L. Religa, B. Reif, C. Luchinat, “Experimental determination of microsecond reorientation correlation times in protein solutions”, *J. Phys. Chem. B* (2013) in press.

[7] I. Bertini, C. Luchinat, G. Parigi, E. Ravera, B. Reif, P. Turano, “Solid State NMR of proteins sedimented by ultracentrifugation”, *Proc. Natl. Acad. Sci. USA* (2011) 108, 10396-10399.

[8] C. Luchinat, G. Parigi, E. Ravera, “Water and protein dynamics in sedimented systems: a relaxometric investigation”, *ChemPhysChem* (2013) in press

[9] D.J. Mastarone, V.S.R. Harrison, A.L. Eckermann, G. Parigi, C. Luchinat, T.J. Meade, “A Modular System for the Synthesis of Multiplexed Magnetic Resonance Probes”, *J. Am. Chem. Soc.* (2011) 133, 5329-5337.

[10] C. Luchinat, G. Parigi, “Collective relaxation of protein protons at very low magnetic field: a new window on protein dynamics and aggregation”, *J. Am. Chem. Soc.* (2007) 129, 1055-1064.

LOW-FIELD NMR AND RELAXOMETRY INVESTIGATIONS OF CARTILAGE AND ITS CONSTITUENTS

Erik Rössler, Carlos Mattea, Siegfried Stapf

Department of Technical Physics II, TU Ilmenau,
PO Box 100 565, 98684 Ilmenau, Germany

The layered structure of mammalian articular cartilage is reflected by a pronounced depth dependence of T_2, the spin-spin relaxation time, which is a consequence of different degrees of order of the collagen fibers but also of a gradient of water and glycosaminoglycan (GAG) concentration, respectively. The orientational order results in an angular dependence of T_2 that becomes less pronounced at greater distance from the joint surface [1]. T_1, the spin lattice relaxation time, at conventional laboratory field strengths shows little variation in comparison.

In this study, the dependence of magnetic resonance relaxation times in bovine articular cartilage is investigated at a low magnetic field strength of 0.27 T using a portable scanner. While a systematic variation of T_2 is found that is in agreement to similar mammalian cartilage observed at high fields, T_1 also shows a strong depth dependence that correlates with the separation of the tissue into three distinct zones. This pronounced effect is explained by the increased T_1 contrast commonly found towards smaller magnetic field strengths, a consequence of slow and anisotropic molecular reorientations that dominate the relaxation dispersion at low magnetic resonance frequencies [2].

Superposed onto the power-law dependence of T_1 are the so-called quadrupolar dips, significantly reduced relaxation times in the region between about 10 and 70 mT which indicate cross-relaxation of protons with the partially immobilized nitrogen nuclei in amino acids in collagen and glycosaminoglycans (GAGs). Varying the composition, water content or structural integrity of cartilage affects both the general frequency dependence of T_1 and the shape of the quadrupolar dips, providing a possible diagnostic access to arthropathies such as osteoarthritis (OA). A statistical correlation between the degree of OA and the magnitude of the quadrupolar dips has been identified [3], but it remains unclear whether this dependence must be assigned to changes in the GAGs, collagen or both.

In the second part of this work, the effect of enzymes onto cartilage and its constituents is investigated as a model for osteoarthritis. While trypsin is known to separate GAGs from the proteoglycan backbone, collagenase attacks the collagen structure exclusively. Nitrogen nuclei in both substances are shown to contribute to the quadrupolar dips in a similar way. Experiments for both constituents as well as fresh and enzyme-treated bovine articular cartilage were carried out and the relaxivity in the region of the quadrupolar dips were quantified. The observed strong dependence on water concentration is interpreted by a fast-exchange model and is discussed in conjunction with the low-field imaging results.

[1] Y. Xia, *Magic-angle effect in magnetic resonance imaging of articular cartilage: a review*, Invest. Radiol. **35**, 602–621 (2000).
[2] E. Rössler, C. Mattea, A. Mollova, S. Stapf, *Low-field one-dimensional and direction-dependent relaxation imaging of bovine articular cartilage*, J. Magn. Reson. **213**, 112-118 (2011).
[3] L.M. Broche, G.P. Ashcroft, D.J. Lurie, *Detection of osteoarthritis in knee and hip joints by fast field-cycling NMR*, Magn. Reson. Med. **68**, 358-362 (2012).

Spin-Relaxation Efficiency

Robert G. Bryant
University of Virginia
Charlottesville, VA USA

Interfaces may change the local dynamics of adjacent liquid molecules in several ways. We have studied the surface dynamics of water at phospholipid interfaces by taking advantage of the proton-proton dipolar coupling between lipid protons and rare residual protons in deuterium oxide. The lipid surface changes the character of the water diffusion and decreases the water diffusion constant by almost a factor of ten. However, the total coupling is very weak supporting the conclusion that the effects of natural biological membranes on water-spin relaxation rates are dominated by the surface cofactors such as embedded proteins and saccharides.

The limitations to spin-relaxation efficiency are of fundamental interest in magnetic imaging among other fields. We have measured the dipolar effects of endofullerenes *unmodified* for water solubility but loaded with gadolinium(III). The solvent-proton-spin relaxation is dominated by the long range diffusive modulation of the electron-nuclear dipolar coupling, which is weak and is consistent with the large distances of closest approach imposed by the carbon cage.

The magnetic-relaxation dispersion and the ESR spectra for variety of iron(III), Mn(II), and Gd(III) complexes and particulate systems have been re-examined with the goal of identifying the critical features that control paramagnetic contributions to water proton spin-lattice relaxation. These data provide an important insight to the processes that control the electron-spin relaxation times, and therefore, limit the spin-relaxation efficiency of metal based magnetic relaxation agents.

Field-Cycling Magnetic Resonance Imaging

David J. Lurie, Lionel M. Broche, Gareth R. Davies, Brett W.C. Kennedy,
Kerrin J. Pine and P. James Ross

Aberdeen Biomedical Imaging Centre, University of Aberdeen, AB25 2ZD, Scotland, UK

http://www.ffc-mri.org

The use of Fast Field-Cycling (FFC) in combination with magnetic resonance imaging (MRI) has been increasing gradually in recent years [1].

The first use of FFC-MRI was in conjunction with Proton-Electron Double-Resonance Imaging (PEDRI) to image the distribution of free radicals in biological samples, making use of the Overhauser effect. Field-cycling allows the ESR irradiation to be applied at low field (hence relatively low frequency, and low non-resonant absorption), while NMR signal detection and imaging is carried out at higher field, to preserve SNR [2,3,4].

Relaxometric FFC-MRI aims to obtain spatially-resolved T_1-dispersion data, by collecting images at a variety of evolution field strengths [1,5,6,7]. We have demonstrated methods for implementing relaxometry from localised regions defined on a pilot image [8]. We have also shown that FFC relaxometry can detect the formation of cross-linked fibrin protein from fibrinogen *in vitro*, in a model of the blood clotting process [1,9]. This relies on ^{14}N-^{1}H cross-relaxation phenomena, also known as “quadrupole dips” in the T_1-dispersion plot [10]. These reductions in T_1, occurring at water proton Larmor frequencies equal to the ^{14}N nuclear quadrupole resonances, reveal information about the concentration and conformation of immobilised protein molecules. In recent work, we have demonstrated the potential of FFC NMR and MRI for the detection of changes in cartilage due to osteoarthritis [11].

FFC-MRI relaxometry is inherently relatively slow, since image data must be collected at a range of evolution magnetic field strengths. We have been investigating a combination of FFC with rapid MR imaging methods such as turbo spin-echo, and have succeeded in speeding up data acquisition significantly, with minimal reduction in image quality or the fidelity of T_1-dispersion data [12].

Developments in FFC-MRI have demonstrated this technique’s ability to extract extra information that is not obtainable from conventional, fixed-field techniques. In addition to bio-medical applications, field-cycling magnetic resonance may have applications in the characterisation and monitoring of industrial processes, for example in the preparation of foodstuffs.

[1] Lurie D.J., Aime S., *et al.*, Comptes Rendus Physique **11**, 136-148 (2010).†
[2] Lurie D.J., Hutchison J.M.S, *et al.*, J. Magn. Reson. **84**, 431-437 (1989).
[3] Lurie D.J., Foster M.A., *et al.*, Phys.Med.Biol. **43**, 1877-1886 (1998).†
[4] Lurie D.J., Davies G.R., *et al.*, Magn.Reson.Imaging **23**, 175-181 (2005).†
[5] Carlson J.W., Goldhaber D.M., *et al.*, Radiology **184**, 635-639 (1992).
[6] Lurie D.J., 1st Symposium on Field-Cycling NMR Relaxometry, Berlin, p5, (1998).†
[7] Ungersma S.E., Matter N.I., *et al.*, Magn.Reson.Med. **55,** 1362-1371 (2006).
[8] Pine K.J., Davies G.R. and Lurie D.J., Magn.Reson.Med. **63**, 1698–1702 (2010).†
[9] Broche L.M., Ismail S. *et al.*, Magn.Reson.Med., **67**, 1453–1457 (2012).†
[10] Kimmich R., Winter F. *et al.*, J.Magn.Reson., **68**, 263-282 (1986).
[11] Broche L.M., Ashcroft G.P and Lurie D.J., Magn.Reson.Med. **68**, 358-362 (2012).†
[12] Ross P.J. *et al.*, Proc. ISMRM 21st Annual Mtng., Salt Lake City, USA, p4217 (2013).†

†These references are available at *www.ffc-mri.org/publications.html*

Phase-gradient coil designs for 3D TRASE MRI at low field

Jesse Bellec[b], *Scott B. King*[c], *and Christopher P. Bidinosti*[a,b],
[a]*Department of Physics, University of Winnipeg, Winnipeg, Canada*
[b]*Department of Physics and Astronomy, University of Manitoba, Winnipeg, Canada*
[c]*National Research Council of Canada, Winnipeg, Canada*

Transmit Array Spatial Encoding (TRASE) is a new MR imaging technique that utilizes B_1 phase-gradient fields to manage spatial encoding, rather than the standard B_0 magnitude-gradient fields [1]. The method offers a means to eliminate some of the disadvantages associated with the generation of rapidly pulsed B_0 imaging gradients: namely, equipment expense and power consumption, mechanical vibration and acoustic noise, and nerve stimulation in patients. In a similar spirit, the on-going development of low field NMR/MRI [2] is also strongly motivated by the increased functionality that can be achieved through simplified, lightweight, and low-cost apparatus. As a result, low field MRI appears to be an ideal application of TRASE worthy of investigation.

The main requirement for TRASE is the generation of B_1 fields that have uniform magnitude and linearly varying phase over the volume of interest. For multi-dimensional TRASE MRI, two phase-gradient coils are typically needed for each image encoding direction [1]. We have previously explored the general design principles of phase-gradient coils using a target field method [3]. Based on this work we have developed an array of current structures (resonators for higher frequencies; wire-wound coils for very low frequencies) that generate all 6 phase-gradients needed for 3D imaging (Fig. 1 & 2).

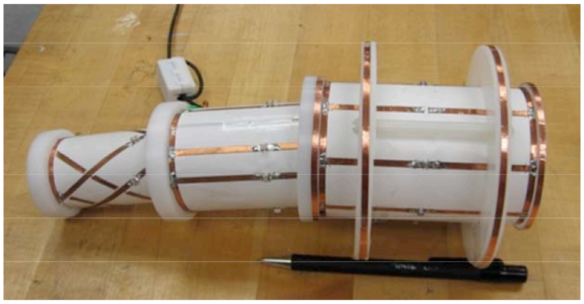


Figure 1: A recent prototype array with spiral, birdcage, and Maxwell resonant structures. Such structures have inherently low inductance and cannot be tuned for very low field/frequency operation.

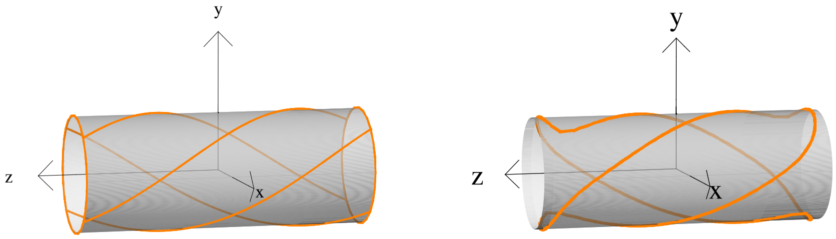


Figure 2: Resonant structures (left) can be replaced with wire-wound equivalents (right) for very low field/frequency operation.

References:

[1] JC Sharp and SB King, Magn. Reson. Med. **63**, 151 (2010).
[2] B Blümich *et al.*, Chem Phys Lett **477**, 231 (2009); KP Pruessmann, Nature **455**, 43 (2008); J Clarke *et al.*, Annu Rev Biomed Eng **9**, 389 (2007).
[3] J Bellec, C-Y Liu, SB King, and CP Bidinosti, Proc. Int. Soc. Magn. Reson. Med. **19**, 723 (2011).

Medical applications of fast field-cycling MRI

Lionel M. Broche[1], George P. Ashcroft[1], David Boddie[2], Sinclair Dundas[2], Tanja Gagliardi[1], Steve D. Heys[2], Brett W.C. Kennedy[1], David J. Lurie[1], Campbell Maceachern[3], Teena McKenzie[2], Iain Miller[2], Kerrin J. Pine[1], P. James Ross[1]

[1] *School of Medicine and Dentistry, University of Aberdeen, Aberdeen, UK*
[2] *Division of Applied Medicine, University of Aberdeen, Aberdeen, UK.*
[3] *Aberdeen Orthopaedic Trauma Unit, Aberdeen Royal Infirmary, UK*

Purpose

Fast-field cycling MRI (FFC-MRI) is a new imaging technique that opens up many possibilities for new molecular-based contrast in images [1]. It also benefits from decades of research in FFC NMR that have shown how versatile this technique can be. In particular, field-cycling allows non-invasive and contrast-agent-free detection of certain immobile proteins thanks to cross-relaxation effects between water protons and ^{14}N. Previous pilot studies have shown that this is the case with proteoglycans, albumin and fibrin, to name a few. Here we present the results of several studies that use FFC-MRI for detection or characterisation of diseased tissues in osteoarthritis, cancer, muscle atrophy, and thrombosis [2, 3].

Methods

The studies make use of two features: the quadrupolar signal and the profile of the spin-lattice dispersion curve over 3 decades of magnetic field. These features were measured from imaging experiments performed on a 59 mT field-cycling scanner [4], while FFC NMR data acquisition were performed on a SMARtracer relaxometer (Stelar, Italy). In most studies we made use of both platforms, with additional high-field scans on a 3T MRI scanner (Achieva, Philips Healthcare, Netherlands) and Raman spectroscopy in the case of osteoarthritis samples.

Results

Significant differences were observed between healthy and diseased tissues in all pathologies explored so far. Most tissues show quadrupolar signal, with variations between individuals and conditions. In particular, significant differences in the level of quadrupolar signals were observed between healthy and diseased cartilage, normal and swollen muscle, and normal and cancerous tissues.

Conclusions

FFC-MRI demonstrated capabilities in the detection of certain disease mechanisms, some of which are difficult to observe on conventional fixed-field MRI devices. Field-cycling is a promising tool for medical research, and has already shown abilities for quantitative detection of proteins.

References

[1] Lurie, D.J., Aime, S. et al., C R Phys (2010), 11:136-148
[2] Broche, L.M., Ashcroft, G.P, Lurie, D.J., Magn Reson Med (2012), 68:358-362
[3] Broche, L.M., Ismail, *et al.*, Magn Reson Med (2012), 67:1453–1457
[4] Lurie D.J., Foster M.A., *et al.*, Phys Med Biol (1998), 43:1877-1886

Initial Characterization of a ±0.5T Insertable dreMR Magnet on a 1.5T Clinical System

L. de Rochefort[1]*, E. S.M. Lee*[2]*, M. Pollelo*[3]*, R. Rolfi*[3]*, C. Sébrié*[1]*, L. Darrasse*[1]*, G Ferrante*[3]*, B. K. Rutt*[2]
[1]*Univ. Paris-Sud, CNRS, UMR8081, IR4M, Orsay, France;* [2]*Department of Radiology, Stanford University, Stanford, California, USA;* [3]*Stelar s.r.l., Mede, Italy.*

INTRODUCTION

Delta relaxation-enhanced magnetic resonance imaging (dreMR, [1-3]) uses fast field-cycling to produce contrast from dispersive agents. While ΔB can be achieved with an insertable field-cycling magnet, mutual coupling to MR structure induces eddy current (EC) that cause unintended change to the effective main field. Here, we present initial characterization of the coupling to the main magnet through image acquisitions, dreMR imaging of dispersive samples and preliminary in-vivo results.

MATERIAL AND METHODS

MR systems Experiments were conducted using a clinical 1.5T Philips system. A fast-field cycling magnet with dual-layer, solenoidal coil (40-mm clear bore), fitting inside a 20 cm-diameter, 30 cm-long mechanical housing, was positioned at the main magnet's isocenter. The insert was capable of producing ΔB = ±0.5 T at 320 A current with ramp times <2 ms while cooled by perfluorocarbons. A birdcage coil with an effective imaging region of 28 mm-diameter was used.

EC characterization A multi-phase spoiled gradient echo imaging sequence was modified to allow triggering of the FFC magnet amplifier. A transverse slice was applied with a low pixel bandwidth (96 Hz) to sensitize image displacement due to EC. 50 phasic images up to 700 ms after B_0 pulses (at up to ±15 MHz and pulse width of 400 ms). The effective main magnet offset was calculated from image spatial shifts in the readout direction that were estimated from images using cross-correlation. A mono-exponential decay was fitted to extract EC time constant and amplitude.

dreMR experiments A phantom comprising NMR tubes filled with solutions of gadofosveset (albumin-binding) contrast agent, with and without human serum albumin (HSA), was prepared. Inversion- and saturation-recovery spin-echo sequences were modified to trigger B_0 pulses during the relaxation periods.

In vivo experiments A 30 g swiss white mouse was anesthetized. The saturation-recovery spin echo sequence was modified to allow for slice-tracking: 90° and 180° pulse frequencies were shifted to follow EC. Transverse slices within the neck were acquired after 100-ms relaxation period at 1.1, 1.5 and 1.9 T.

RESULTS

The temporal evolution of EC induced frequency shift followed a mono-exponential decay (Fig.1, $T_0 = 90.6 \pm 3.3$ ms) characterized by a step response of 165 Hz/MHz*exp(-t/T_0). Image deformation was limited to a rigid-body spatial shift, and field variation was uniform within the entire bore. EC effects on imaging can thus be compensated for by tracking the frequency in the readout and slice directions. dreMR images could be obtained using inversion-recovery and saturation-recovery approaches (Fig.2, ±15 MHz) with an enhanced sensitivity to dispersive agents. EC-induced field shift can be compensated during in vivo imaging (Fig.3, ±18 MHz) indicating that an unshielded FFC insert is a viable methodology for in vivo dreMR imaging of small animals.

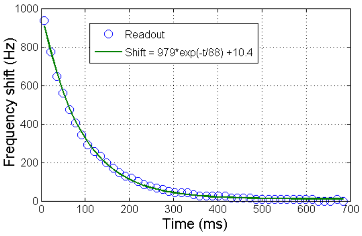


Fig. 1: Measured shift (markers) and exponential shift (line) obtained after a 100 ms long 235 mT pulse.

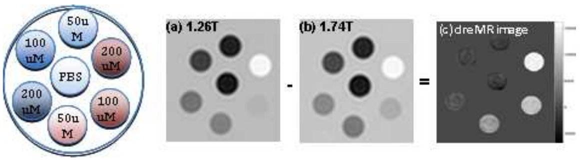


Fig. 2: dreMR experiments with ±0.36T B0 pulses.

DICUSSION AND CONCLUSION

dreMR imaging was demonstrated by interfacing an FFC insert to a Philips 1.5T system. Although the unshielded insert couples significantly to the main bore resulting in spatial shifts in images after a ΔB pulse, these effects can be compensated by the described frequency tracking method. The presented method is viable for achieving large ΔB dreMR imaging for improved contrast specificity.

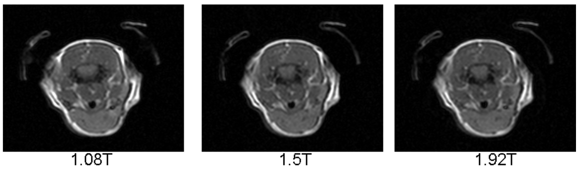


Fig. 3: Initial in vivo results demonstrating the ability compensate EC effects through frequency tracking.

REFERENCES 1. Alford, JK et al. MRM 2009; **2.** Hoelscher et al., MAGMA 2012, **3.** Hoelscher et al., MAGMA 2013

AKNOWLEDGEMENTS 2011-2012 France-Stanford collaborative projects;

Dynamic Tunneling Polarization: A Quantum Rotor Analogue of Dynamic Nuclear Polarization and the NMR Solid Effect

A.J. Horsewill, S.M.M. Abu-Khumra, B. Zhang
School of Physics & Astronomy, University of Nottingham, Nottingham, NG7 2RD. UK

1. Introduction

In NMR we are familiar with the concept of manipulating the quantum states of nuclear spins with sequences of resonant rf pulses. Similar to a spin-½ nucleus, the ground state of a hindered three-fold quantum rotor such as CH_3 is characterized by two energy levels but in this case its angular momentum properties are associated with molecular rotation rather than nuclear magnetism. An interesting question arises whether it is possible, analogously to NMR, to manipulate the rotational tunneling states of a CH_3 rotor in a prescribed manner with an experimental procedure?

We report a quantum rotor analogue of the dynamic nuclear polarization (DNP) experiment in NMR. [1] Whereas in DNP the effect is driven by electron-nuclear spin interactions, in the quantum rotor analogue the effect is mediated by interactions between the tunneling methyl groups and the nuclear spins. By suitable design of an experiment we shall show how dynamic polarization of the CH_3 spin-symmetry states can be created and we assign the phrase Dynamic Tunneling Polarization (DTP) to describe the phenomenon.

2. Spin-symmetry species

The eigenstates of tunneling CH_3 rotors are characterized by spin-symmetry species labeled A and E. Because of space-spin entanglement a change in spin-symmetry state involves simultaneous changes in space and spin eigenfunctions. Therefore on its own, electromagnetic radiation does not have the requisite symmetry properties to mediate A↔E transitions. However, the dipole-dipole interaction does have the requisite properties being determined by products of space and spin variables. By operating at low magnetic field where dipolar, tunneling and Zeeman interactions have similar magnitude, spin-forbidden transitions become weakly allowed [2] enabling A↔E changes in tunneling state to be driven in response to rf irradiation.

3. Experimental and Results

In the experiments that will be described, the populations of the CH_3 tunneling states are manipulated in a customized manner by rf irradiation of weakly allowed sideband transitions within the manifold of tunneling magnetic levels. We shall show how substantial positive and negative polarizations of the A and E states are achieved using a specially designed double resonance field-cycling NMR pulse sequence. As part of this procedure, level crossings between the tunneling and Zeeman systems are used to measure the tunneling polarizations. As an example, in the Figure the tunneling polarization in 2-butanone is plotted as a function of the rf irradiation frequency. In this material the tunneling frequency is ν_t = 492 kHz and the spectrum recorded at a magnetic field of 0.028T reveals how large changes in the temperature of the tunneling system can be driven. It is a resonant effect and even small changes in rf irradiation frequency or applied B field can cause either substantial cooling of the tunneling system or indeed substantial heating leading to inverted populations and negative tunneling temperatures.

In an adaptation of the experiment, the lifetimes of the A and E states are measured and investigated as a function of magnetic field. Spectra reveal evidence for mechanical cogwheel-like coupling between CH_3 rotors. The contribution these new experiments make to our understanding of quantum rotors will be discussed including the outlook for possible new techniques for nuclear spin polarization.

A computational model describing the DTP effects will be described.

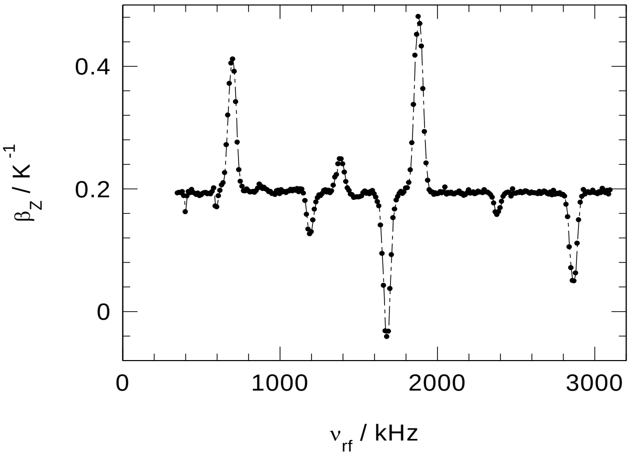


***Figure**. The DTP spectrum of 2-butanone where β_Z reports the tunneling polarization of CH_3 following equilibration of tunneling and Zeeman systems at the level crossing. B = 0.028 T. T = 4.2K.*

Acknowledgements

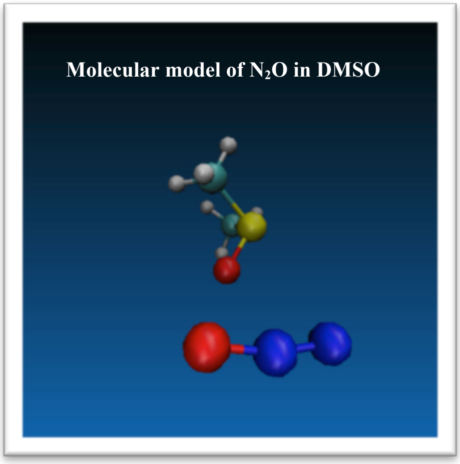
The field-cycling NMR spectrometer was constructed using grants from the Royal Society and the Engineering and Physical Sciences Research Council.

References

[1] A.J. Horsewill & S.M.M Abu-Khumra, *Physical Review Letters*. **2011**, *107*, 127602.
[2] S. Clough, A.J. Horsewill, P.J. McDonald & F.O. Zelaya, *Physical Review Letters*. **1985**, *55*, 1794.

The Interplay of MD and QM calculations to elucidate singlet state relaxation

Pär Håkansson, Giuseppe Pileio, and Malcolm H Levitt
Department of Chemistry, University of Southampton, SO17 1BJ, Southampton, UK
(e-mail: p.hakansson@soton.ac.uk)


Molecular model of N_2O in DMSO

Under certain conditions systems of two spin-1/2 support singlet states that are immune to the intra-pair dipolar relaxation superoperator therefore often showing characteristic decay constants T_S which exceed T_1 by an order of magnitude or more. These enhanced lifetimes are of particular interest as polarization (and indeed hyperpolarization) can be stored for longer time intervals with important application in MRI, for example. Because of the extended time regime, many other "minor" relaxation mechanism interplay to relax these states. An exact knowledge of these mechanisms can indicate the conditions to maximize and extend even further singlet lifetimes. However, even relatively small molecules in solution impose a number of challenges in the task of modeling T_1 and T_S from molecular dynamics simulation (MD) and quantum mechanics calculations QM. Computational cost is one major bottleneck. In addition, in order to accurately model long T_S, attention is required to the weak and rather poorly explored relaxation mechanisms such as spin-rotation.

In this work we use novel approaches to address chemical shift anisotropy, spin-rotation and inter-molecular dipole-dipole relaxation mechanisms within the joint framework of MD and QM calculations. We take particular care of molecular flexibility. The CSA contribution, for example, is computed using a *timescale-separated* spin Hamiltonian, paying particular attention to internal molecular degrees of freedom. In the case of spin-rotation, the explicit time dependent spin Hamiltonian is considered. We demonstrate a good quantitative agreement between experiments and calculations *without adjustable parameters*. We discuss the field-dependence of T_S and T_1.

Broadband excitation with frequency swept pulses

Alan Gregorovič and Tomaž Apih

Jožef Stefan Institute, Jamova 39, SI-1000 Ljubljana, Slovenia,
email: tomaz.apih@ijs.si

In last decade, several publications have demonstrated strong potential of ^{14}N NQR both in the field of the pharmaceutical analysis and for the detection of illicit compounds such as explosives and forbidden drugs. In some fields, such as detection of polymorphic structures, the technique could rival the vastly more popular NMR. However, the long measurement times or complicated experimental techniques, which are often required due to the low sensitivity, have limited the use of the technique to a relatively small number of specialized laboratories.

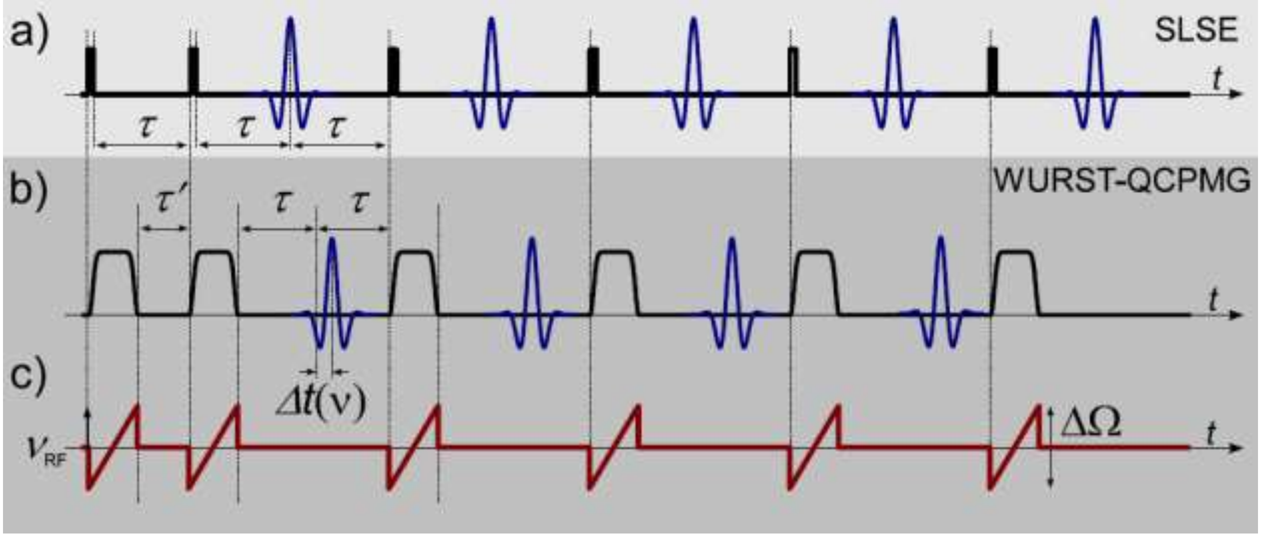


Figure: Comparison of Spin Lock – Spin Echo and WURST-CPMG pulse sequences. SLSE pulses are high power hard rectangular pulses, while WURST pulses are long low-power adiabatic frequency-swept pulses.

Here we show that a new pulse sequence WURST-QCPMG, which was recently introduced in NMR, can be effectively used to excite a train of ^{14}N nuclear quadrupole resonance ($I=½$) echo signals. The technique works also in the combination with polarization enhancement of the signal by using magnetic field cycling technique. We used WURST-CPMG to excite relatively broad 12-lines ^{14}N NQR spectrum of explosive TNT without changing the frequency. Similarly, one can use the new pulse sequence can be very effectively used to reduce the number of frequency steps in a step-by-step search for the resonance lines in a broad frequency range.

Water dynamics at the liquid-solid interface of biochar systems

Pellegrino Conte, Giuseppe Alonzo

Dipartimento di Scienze Agrarie e Forestali, Università degli Studi di Palermo, v.le delle Scienze ed. 4 90128 Palermo (Italy)

Biochar is a carbonaceous material obtained by pyrolysis of biomass feedstocks. It is applied to soils in order to improve fertility and mitigate greenhouse-gases emissions. In fact, from the one hand, biochar changes physical-chemical soil properties, thereby affecting soil fertility. From the other hand, biochar is resistant to chemical and biochemical degradation. For this reason, its use allows carbon sequestration in soils and consequent reduction of carbon dioxide to the atmosphere.

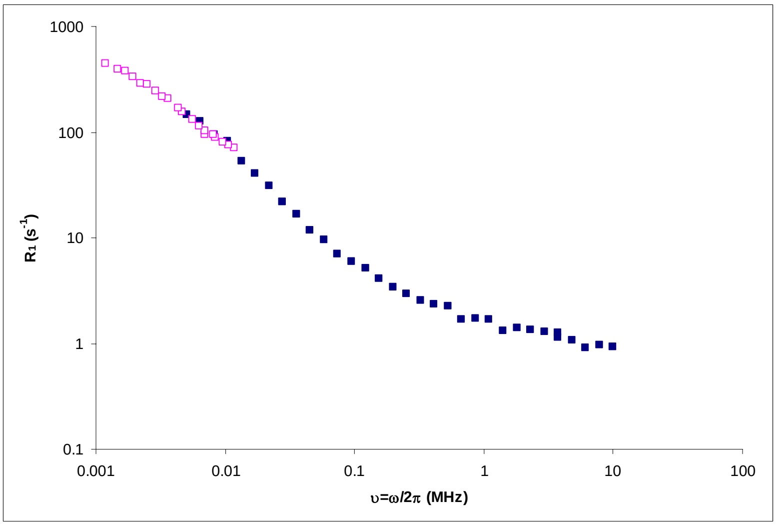
Here, dynamics of water at the liquid-solid interface of water saturated biochars is discussed. Results revealed that water dynamics is affected by the nature of biochar parent biomasses. Moreover, water undergoes to an inner-sphere interaction mechanism with biochar surface through formation of weak unconventional hydrogen bonds.

Recognition of the interaction mechanisms between water and biochar is of paramount importance in order to understand why biochar soil amendments improve soil fertility and crop production.

Complete proton dispersion curves from 0 Hz up to some hundreds of MHz and some relaxometry stories

Daniel Canet, Emilie Steiner, Mehdi Yemloul, Sabine Bouguet-Bonnet
Université de Lorraine, Vandoeuvre-les-Nancy (France)

Relaxometers are generally operative between some kHz and some tens of MHz. This frequency range can be sufficient in many instances. As an example, the detection of two hydration layers in silica gels involving hydrophobic sites will be presented[1]. If high frequencies (above 200 MHz up to 1000 MHz) are easily available with standard current instruments, the 10 MHz – 100 MHz may require old fashioned instruments. In our laboratory, this has been achieved with an old variable field electromagnet equipped with a modern home-made console and has proved especially useful for studying the solvent (toluene) dynamical behavior in an organogel phase[2]. The problem of the low frequency range, say 0 Hz – 15 kHz, is much more difficult to handle but cannot be overlooked in view of models which would predict T_1 divergence when frequency tends to zero. It is evidently out of the question to rely on T_1 measurements and the only possibility is $T_{1\rho}$ (spin-lattice relaxation time in the rotating frame) and T_2 for zero frequency. It must be noted that the latter measurement is valid as long as the spin system under investigation is devoid of J couplings. Moreover the contribution of the spectral density at the measurement frequency (200 MHz in our case) must be removed and the contribution at the frequency of interest (0 or $\nu_1 = \gamma B_1 / 2\pi$, B_1 being the amplitude of the spin-lock rf field) must be rescaled. As shown in the figure below, the method is viable[3].



Connexion of $T_{1\rho}$ measurements (empty squares, obtained by varying the spin-lock field amplitude) with T_1 measurements (filled squares, obtained by fast field cycling procedures). Relaxation rates (inverse of relaxation times) are displayed.

This approach has been successfully used for characterizing water behaviour in mesoporous materials[4].

---

[1] D. Oulkadi, M. Yemloul, S. Desobry-Banon, D. Canet, Micropor. Mesopor. Mater. 172 (2013) 213-216.

[2] M. Yemloul, E. Steiner, A. Robert, S. Bouguet-Bonnet, F. Allix, B. Jamart-Grégoire, D. Canet, J. Phys. Chem. B 115 (2011) 2511-2517.

[3] E. Steiner, M. Yemloul, L. Guendouz, S. Leclerc, A. Robert, D. Canet, Chem. Phys. Lett. 495 (2010) 287-291.

[4] E. Steiner, S. Bouguet-Bonnet, J.-L. Blin, D. Canet, J. Phys. Chem. A 115(2011) 9941-9946.

NMR relaxation of fluids confined inside porous media with magnetic impurities

I. Ardelean[a], S. Muncaci[a], C. Mattea[b], S. Stapf[b]

[a]Technical University of Cluj-Napoca, Department of Physics and Chemistry, 400114, Cluj-Napoca, Romania; [b]Ilmenau University of Technology, Department of Technical Physics II/Polymer Physics, 98684 Ilmenau, Germany

Natural or manufactured porous media may intrinsically contain heterogeneous and uncontrolled amounts of paramagnetic or ferromagnetic impurities inside their solid matrix which generate internal gradients [1]. The interpretation of NMR relaxometry data on such samples is cumbersome, and the control of magnetic impurities becomes an essential issue. That is why, in the present work, porous ceramics containing controlled and increased amount of iron oxide as magnetic impurities were manufactured, and the dynamics of water (polar) and cyclohexane (nonpolar) molecules within the pore space was investigated. The porous ceramics were fabricated using the conventional method of preparation from powders which are first dry pressed and then subject to thermal treatment [2]. Six samples (S0-S10) with increasing concentration of Fe_2O_3 were prepared by adding 0, 2, 4, 6, 8 or 10g of Fe_2O_3 to 100g of mixed powder. In order to extract the pore size distribution of the produced samples they were examined by scanning electron microscopy, the DDIF (Decay due to Diffusion in the Internal Fields) technique [1] and a new proposed technique which relies on the attenuation of the echo train in the well-known CPMG technique due to diffusion in internal gradients [3]. The magnetic characterization of the produced samples was done using a vibrating sample magnetometer indicating a linear dependence of the susceptibility constant with the Fe_2O_3 content. The solvents examined in our study were chosen in order to monitor the influence of the polarity on the surface relaxation process. The experimental relaxation dispersion curves could be compared with a two phase exchange model taking into account relaxation by interaction with paramagnetic centers on the surface of porous media [4, 5]. This comparison allowed us the conclusion that Fe_2O_3 clusters inside the porous matrix do not contribute to the relaxation in the frequency range of our experiments. It also allows the determination of the transverse diffusional correlation time at the liquid/solid interface. Moreover, a similar behavior in relaxation dispersion curves of water and cyclohexane filled samples could be observed, independently of the fact that water molecules are polar and cyclohexane molecules are nonpolar. On the other hand a longer correlation time was extracted in the case of water molecules as compared with cyclohexane. The results of this study will contribute to the interpretation of the experimental data obtained on natural or fabricated porous media with unknown magnetic properties.

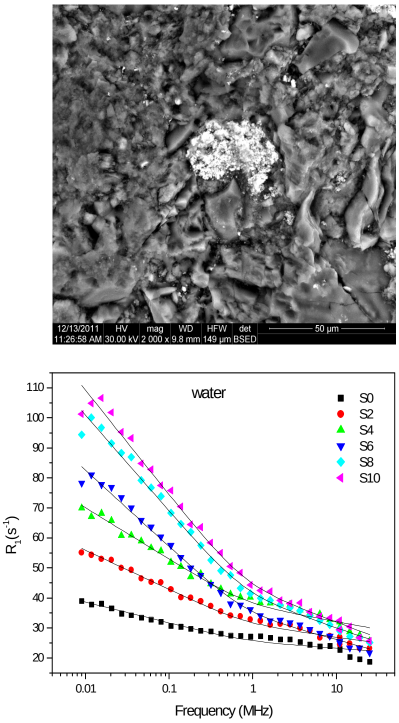


Fig.1. The SEM image of one porous ceramic (4% Fe_2O_3) and the relaxation dispersion curves recorded for the water filled samples

ACKNOWLEDGMENTS

This work was supported by a grant of the Romanian National Authority for Scientific Research, CNCS – UEFISCDI, project number PN-II-ID-PCE-2011-3-0238. Financial support by the Alexander von Humboldt Foundation is also gratefully acknowledged.

[1] Y. Q. Song, Concept. Magn. Reson. **18A**, 97-110 (2003).
[2] M. N. Rahaman, Ceramic processing and sintering, 2-nd Ed., Marcel Dekker Inc., 2003.
[3] L. J. Zielinski, J. Chem. Phys. **121**, 352-361 (2004)
[4] J. P. Korb, New J. Phys. **13**, 035016 (2011).
[5] S. Muncaci, C. Mattea, S. Stapf, I. Ardelean, Magn. Reson. Chem**.** **51**, 123-128 (2013)

How to separate hydric state, wettability and geometric confinement on moisture transport using FFC relaxometry

H. Chemmi[a], *D. Petit*[a*], *J-P. Korb*[a], *R. Denoyel*[b] *and P. Levitz*[c]

[a] *Physique de la Matière Condensée, Ecole Polytechnique-CNRS, Palaiseau 91128, France;*
[b] *MADIREL, Aix-Marseille Université CNRS-UMR 7246, Centre de St Jérôme, 13397 Marseille Cedex 20, France,*
[c] *Laboratoire de Physicochimie des Electrolytes, Colloïdes et Sciences Analytiques, UMR 7195 CNRS, Université Pierre et Marie Curie, 4 place Jussieu, 72522 Paris Cedex 5, FRANCE*

The main objective of this study is to explore the physical processes implied in the moisture transport in hardened cementitious based materials. Understanding these processes is of particular importance for improving the durability of these widely used materials[1,2,3,4]. We focus on white and grey cement pastes CEM I hardened during long periods of time (up to two years) in controlled atmosphere. In order to decouple the physical processes of moisture transport in the intricated multi-scales of these cement pastes, we have also considered calibrated porous materials in the range of micro, meso and macropores. We have insisted on the possibility of controlling *in situ* the degree of humidity inside the NMR probes and on the analysis of experimental data to extract representative parameters for the moisture transport. Here, we report fast field cycling (FFC) studies of moisture transport in three porous silicates. First, we used a MCM-41 silicate, in several hydric states, for showing the drastic impact of the geometric confinement on the moisture transport at micro-scale. Second, we have synthesized bimodal porous controlled pore glass (CPG) silicates to show how the hydric state can be an effective factor for limiting the moisture transport at meso- and macro- scales. Last, we have used a CPG coming from the same synthesis with and without calcination for modifying the grafted chemical species on pore surface. The ^{1}H NMRD profiles of the raw and calcined CPG allow quantifying the huge modification of the proton dynamics coming from the change of the wettability at interface. The analysis of the NMRD profiles in these three materials demonstrates the efficiency of the FFC relaxometry technique for characterizing the moisture transport from *nm* to half a μm and in consequence for separating hydric state, wettability and geometric confinement effects on the moisture transport.

[1] Chemmi H., Petit D., Levitz P., Korb J.−P., Berard M., Diffusion-fundamentals, 10 (2009), 4.1-4.3
[2] Chemmi H., Petit D., Levitz P., Korb J.−P., Comptes Rendus Chimie, 13 (2010), 405–408
[3] Chemmi H., Thèse de l'Ecole Polytechnique, (2011)
[4] Chemmi H., Petit D., Korb J.−P., Denoyel R., Levitz P., Micropor. Mesopor. Mater. (2013), http://dx.doi.org/10.1016/j.micromeso.2013.02.045

* Corresponding author

Theory and applications of the fast electronic relaxation of complexed paramagnetic lanthanide Ln^{3+} ions, but Gd^{3+}, in solution

Pascal H. Fries
CEA, INAC, SCIB (UMR-E 3 CEA-UJF),
Laboratoire de Reconnaissance Ionique et Chimie de Coordination,
38054, Grenoble, France

Following a precise method proposed by Aime *et al.*,[1] the very short relaxation times T_{1e} $(=T_{2e})$ of the total electronic angular momenta J of the heavy paramagnetic Ln^{3+} ions from Tb^{3+} to Yb^{3+} were recently derived in four series of isostructural complexes from the measured variation with field B_0 of the nuclear relaxation rates of selected nuclei of the ligands.[2] Combined with earlier data, these additional values of T_{1e}, in the range 0.1 – 0.63 ps, make it possible to infer a remarkable statistical ordering across the Ln^{3+} series. A theory of lanthanide electronic relaxation due to the time fluctuations of the ligand field coefficients induced by the very frequent collisions with the solvent molecules is briefly presented.[2-4] This theory, beyond the Redfield approximation, explains the surprisingly weak variation of electronic relaxation with the nature of the ligand, the solvent, the temperature, and the field. It also confirms the experimental tendency that complexes of Tb^{3+} and Dy^{3+} are most efficient to accelerate the nuclear relaxation rates. From selected examples, it is shown how such complexes can serve (i) to save time in parallel NMR arrangements,[5] which allow the simultaneous investigation of several systems during a single high-resolution experiment and (ii) to gain new supramolecular structural information around Ln^{3+} centers with atomic precision.[6] The NMR instruments and methods, which are available for measuring T_{1e} of Ln^{3+} ions, but Gd^{3+}, in complexes and for using these complexes in applications, are compared.

References

[1] S. Aime, L. Barbero, M. Botta, and G. Ermondi, J. Chem. Soc., Dalton Trans., 225 (1992).
[2] A. M. Funk, P. H. Fries, P. Harvey, A. M. Kenwright, and D. Parker, J. Phys. Chem. A **117**, 905 (2013).
[3] P. H. Fries and E. Belorizky, J. Chem. Phys. **136**, 074513 (2012).
[4] P. H. Fries, Eur. J. Inorg. Chem., 2156 (2012).
[5] P. H. Fries and D. Imbert, J. Chem. Eng. Data **55**, 2048 (2010).
[6] P. H. Fries, J. Chem. Phys. **136**, 044504 (2012).

^{1}H and ^{17}O NMR relaxometric study of a series of macrocyclic Mn(II) complexes in aqueous solution and of their lipophilic derivatives.

Gabriele A. Rolla,[a] *Lorenzo Tei,*[a] *Gilberto Mulas,*[c] *Carlos Platas-Iglesias,*[b] *Enzo Terreno,*[c] *Lothar Helm,*[d] *Mauro Botta*[a]

[a] Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale "Amedeo Avogadro", Viale T. Michel 11, 15121, Alessandria, Italy. [b]Departamento de Química Fundamental, Universidade da Coruña, Campus da Zapateira, Rúa da Fraga 10, 15008 A Coruña, Spain. [c] Centro di Imaging Molecolare, Dipartimento di Biotecnologie Molecolari e Scienze della Salute, Università di Torino, Via Nizza 52, 10126, Torino, Italy. [d] Laboratoire de Chimie Inorganique et Bioinorganique, Ecole Polytechnique Fédérale de Lausanne, EPFL-BCH, CH-1015 Lausanne, Switzerland.

In this contribution, we report a ^{1}H and ^{17}O relaxometric investigation of Mn(II) complexes with a series of cyclen-based ligands of increasing denticity. This study is devoted to expand our knowledge of the microscopic parameters describing the aqueous solution behavior of macrocyclic complexes of Mn(II) in view of a prospective application as novel MRI Contrast Agents (CAs). Using Mn(II)- instead of Gd(III)-based CAs is prompted by the reduced toxicity of Mn(II) as compared to Gd(III). To date, the development of Mn(II)-based CAs has been hindered by the arduousness of fine tuning the properties of Mn(II) complexes to combine sufficient complex stability (to ensure *in vivo* safety) with inner sphere hydration.[1] Within this context, our study investigates how structural changes in a class of macrocyclic ligands may influence the microscopic aqueous-solution parameters of the corresponding stable Mn(II)-complexes by ^{1}H and ^{17}O relaxometric techniques.[2] This study confirmed that the Mn(II) complex with the heptadentate ligand DO3A does not have inner sphere water molecules (q = 0), and therefore the metal ion is most likely seven-coordinate. The hexadentate DO2A ligand has two isomeric forms: 1,7-DO2A and 1,4-DO2A. The Mn(II) complex with 1,7-DO2A is predominantly six-coordinate (q = 0). Contrarily, in [Mn(1,4-DO2A)] a species with one coordinated water molecule (q = 1) prevails largely, whereas a q = 0 form represents only about 10% of the overall population. The Mn(II) complex of the pentadentate ligand DO1A also contains a coordinated water molecule. DFT calculations (B3LYP model) were used to support these results, as well as to determine theoretically the ^{17}O and ^{1}H hyperfine coupling constants responsible for the scalar contribution to ^{17}O and ^{1}H NMR relaxation rates and ^{17}O NMR chemical shifts. A ^{17}O NMR relaxometric study allowed the determination of the water exchange kinetics of these complexes. [Mn(1,4-DO2A)(H_2O)] complex displayed a relatively fast water exchange rate ($k_{ex}^{298} = 11.3 \times 10^8$ s^{-1}) in comparison to the [Mn(EDTA)(H_2O)]$^{2-}$ analogue ($k_{ex}^{298} = 4.7 \times 10^8$ s^{-1}), but about five times lower than that of the [Mn(DO1A)(H_2O)]$^+$ complex ($k_{ex}^{298} = 60 \times 10^8$ s^{-1}). The water exchange rate measured for the latter complex represents the highest water exchange rate ever measured for a Mn(II) complex. Further applicative development of [Mn(1,4-DO2A)(H_2O)] could be pursued by developing self aggregating amphiphilic analogues suitable for development of paramagnetic micelles and liposomes. In these systems, the parameters controlling hydration and water exchange of the coordination cage remain essentially unchanged as compared to the monomeric analogue. However, the rotational correlation time of the aggregate and the motional coupling of the coordination cage with the aggregate control the overall relaxation performance of these systems.

References

[1] Drahos, B.; Lukes, I.; Toth, E. *Eur. J. Inorg. Chem.* **2012**, *12*, 1975-1986.

[2] Rolla, G.A.; Platas-Iglesias, C.; Botta, M.; Tei, L.; Helm, L. *Inorg. Chem.* **2013**, *52*, 3268–3279.

Using Relaxometry to Probe the Traditional SBM Paradigm

Mark Woods and Mauro Botta

Department of Chemistry, Portland State University; Advanced Imaging Research Center, Oregon Health and Science University; Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale "A. Avogadro"

It is now well established the relaxivity of Gd^{3+} chelates is relatively well described by Solomon Bloembergen and Morgan theory. This in turn informs our understanding of the limitations on relaxivity of the low molecular weight Gd^{3+} chelates used in clinical practice. These agents tumble rapidly in solution which limits their relaxivity. When this rotational restriction is lifted by making the chelates tumble more slowly the relaxivity continues to be limited by the slower than optimal water exchange kinetics of the chelate. Thus it has been widely understood that in order to maximize relaxivity it is necessary to both slow molecular tumbling and optimize water exchange. This concept is often represented graphically in the manner shown in Figure 1.

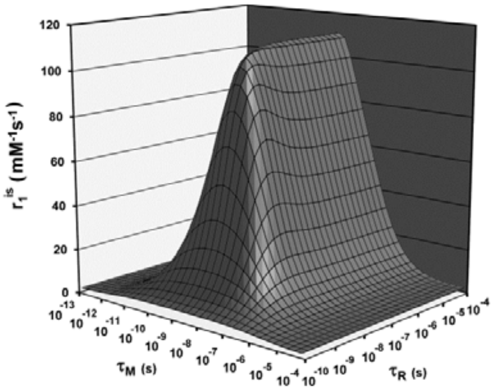


Figure 1. A simulation of relaxivity as function of molecular tumbling and water exchange.

To probe the potential gains in relaxivity that can be achieved through the optimization of water exchange kinetics we prepared two isomeric chelates of a Gd^{3+} DOTA derivative. The two chelates were designed to tumble slowly (similar τ_R) and were known to possess very similar electron spin relaxation characteristics (Δ^2 and τ_V). The primary difference between the two chelates was the water exchange rate: one was very fast the other somewhat slower. According to established theory the more rapidly exchanging isomer (τ_M = 8 ns) should afford the highest relaxivity. However, relaxometric studies of both isomers in various slowly tumbling systems have revealed that in fact the more ***slowly*** exchanging isomer (τ_M = 70 ns) affords the highest relaxivity (Figure 2). Significantly the relaxometric data affords and insight it why this unexpected result should be the case: there is a difference in the hydration state (q/r^6) between the two chelates which limits relaxivity in the most rapidly exchanging isomer.

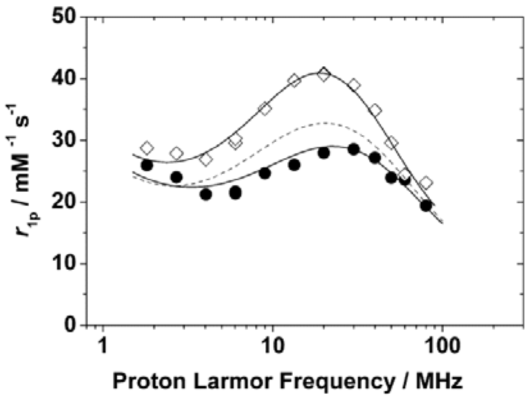


Figure 2. High field ^{1}H NMRD profiles of the fast (closed circles) and slow (open diamonds) exchanging isomers.

Dynamics of Bulk and Confined Crude Oils

Jean-Pierre Korb, Alain Louis-Joseph, Lyès Benamsili
Physique de la Matière Condensée, Ecole Polytechnique-CNRS, 91128 Palaiseau, France

Crude oils are among the most complex existing natural fluids. They contain several thousands of chemical species including hydrocarbons that come with a large range of structures and molecular sizes. They contain also asphaltene molecules that are responsible for plugging the pores of oil reservoirs and catalytic networks. These polar molecules represent a solubility class defined as the n-alkane insoluble and toluene-soluble fraction of petroleum. They are composed of a high degree of polynuclear aromatic rings that have alkyl side chains and incorporate heteroatoms (such as O, N and S). The tendency of asphaltenes to self-aggregate distinguishes them from other oil constituents. For instance, asphaltene aggregation is the cause of complex effects occurring in oil viscosity, adsorption at solid surfaces, precipitation, fluid rheology and emulsion stability. Though several analytical techniques are usually required for the analysis of the chemical structures of asphaltenes and crude oils such as chromatography and mass spectroscopy, the dynamical study of these complex natural fluids is still difficult due to the large distributions of hydrocarbon chain lengths.

Here, we propose using fast field cycling NMR relaxometry for probing the dynamics of bulk and confined crude oils with and without asphaltene. A detailed analysis of the distributions of longitudinal, T_1, relaxation times measured at different magnetic fields is proposed in terms of highly skewed bimodal (or monomodal) log-normal distributions evidencing two environments in presence of asphaltene and a single one without asphaltene. We show that these distributions are similar with the gas and gel permeation chromatography distributions, thus showing a connection of the hydrocarbon dynamics with their chain lengths. The remarkable observed features of the nuclear magnetic relaxation dispersion (*NMRD)* profiles of logarithmic averages $<1/T_1>$ for bulk and confined crude oils with and without asphaltene are interpreted with an original relaxation model of intermittent surface dynamics of proton species at proximity of asphaltene nanoaggregates and bulk dynamics in between clusters of these nanoaggregates. This allows probing the *2D* translational diffusion correlation time and the time of residence of hydrocarbons at proximity of the asphaltene nanoaggregates. This time of residence gives an average radius of exploration for the *2D* hydrocarbon diffusion of the same order of magnitude to the aggregate sizes found by *SAXS* and *SANS* in asphaltene solutions[1] and with the observation of gravitational gradients of asphaltenes in oilfield reservoirs[2]. We believe that our results are important for understanding the role of asphaltenes in the dynamics and hydrodynamics of crude oils confined in rocks.

[1] Eyssautier, J.; Levitz, P.; Espinat, D.; Jestin, J.; Gummel, J.; Grillo, I.; Barré, L. Insight into Asphaltene Nanoaggregate Structure Inferred by Small Angle Neutron and X-Ray Scattering, *J. Phys. Chem. B* **2011**, 115, 6827-6837.

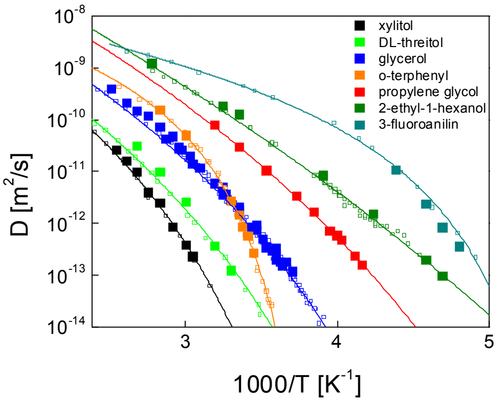
[2] Mullins, O. C.; Seifert, D.J.; Zuo, Y. Z.; Zeybeck, M. Clusters of Asphaltene Nanoaggregtaes Observed in Oilfield Reservoirs. *Energy & Fuels* **2012**, doi.org/10.1021/ef301338q.

NMR relaxometry and translation diffusion in condensed matter

A. Herrmann, M. Hofmann, D. Kruk[*], R. Meier, E.A. Rössler

Experimentalphysik II, Universität Bayreuth, 95440 Bayreuth, Germany
[*]permanent address: University of Warmia & Mazury in Olsztyn, Faculty of Mathematics & Computer Science, Sloneczna 54, PL-10710 Olsztyn, Poland

^{1}H and ^{19}F the relaxation processes are predominantly caused by magnetic dipole-dipole interactions. For dipolar relaxation one distinguishes intra- and intermolecular relaxation pathways. While the intramolecular contribution originates from interactions between nuclei belonging to one molecule, the intramolecular relaxation stems from interactions between nuclei belonging to different molecules or polymer segments. Thus, the intramolecular relaxation is associated with reorientational dynamics, while the intermolecular part provides information on translational dynamics. As the characteristic correlation time, τ_{trans}, for the translational dynamics is at least order of magnitude longer than the rotational correlation time, τ_{rot}, the intramolecular contribution to the overall relaxation dominates at low frequencies. Moreover, as $\tau_{\mathrm{rot}} << \tau_{\mathrm{trans}}$ the low frequency dispersion of the overall relaxation can be entirely attributed to the translational contribution. Thus, the translation diffusion coefficient for diamagnetic liquids and polymer melts can be straightforwardly determined from the theoretically predicted [1,2], linear dependence of the spin-lattice relaxation rate on square root of the resonance frequency. The obtained diffusion coefficients agree very well with those obtained by NMR gradient diffusiometry[3].This approach can also be applied to paramagnetic liquids (for instance containing nitroxide radicals)[4]. In this case one distinguishes three regions of linearity of the relaxation rate versus square root of frequency. Moreover, in the case of sub-diffusive motion in polymer systems, the mean square displacement as a function of time can be revealed[5,6].



Diffusion coefficient D as obtained from FC 1H NMR (full symbols) and field-gradient NMR (open symbols) for several liquids versus reciprocal temperature.[3]

1. Y. Ayant E. Belorizky P. Fries, J. Rosset, J. Phys. (France) 1977, 38, 325
2. E. Belorizky, P.H. Fries, J. Phys. C: Solid State Phys. 1981, 14, 521
3. D. Kruk, R. Meier, E.A. Roessler, Phys. Rev. E 2012, 85, 020201
4. D. Kruk, A. Korpała, A. Kubica, R. Meier, E. A. Rössler, J. Moscicki, J. Chem. Phys 2013 138, 024506
5. M. Kehr, N Fatkullin, R. Kimmich, J. Chem. Phys. 2007, 126, 094903
6. A. Herrmann, B. Kresse, J. Gmeiner, A.F. Privalov, D. Kruk, F. Fujara, E.A. Rössler, Macromolecules 2012, 45; 6516–6526

Transport Properties and Molecular Motion of Triglyme-Lithium Salt Mixtures – Experiments and Simulations

Anne-Marie Bonsa, Andreas Appelhagen, Jochen K. Lehmann, and Ralf Ludwig[1)]
Institute of Chemistry, Physical Chemistry, University of Rostock,
Dr.-Lorenz-Weg 1, D-18051 Rostock, Germany

Salvatore Bubici, Gianni Ferrante, Rebecca Steele[2)]
Stelar s.r.l., Mede (PV), Italy

Triglyme-lithium salt complexes show low volatility, high thermal stability, high ionic conductivity, and a wide potential window. It has been shown by Yoshida et al. that the mixtures of lithium bis(trifluoromethylsulfonyl)amide [Li][NTf_2] and triglyme (G3) behave like conventional room temperature ionic liquids [1,2]. In particular the equimolar triglyme-lithium complexes are presumed to be resistive against oxidation and thus thought to be promising electrolytes for lithium batteries. With a combination of experiments and molecular dynamics (MD) simulations we studied the transport properties and molecular motion of G3-lithium salt mixtures as a function of salt concentration and temperature. Self-diffusion coefficients, viscosities and ionic conductivities were measured by conventional methods. We also used fast-field-cycling NMR relaxometry to understand the molecular motion of the different components in the electrolyte system. Relaxation times T_1 have been measured on three different nuclei: ^1H of the triglyme, ^7Li of the cation and ^{19}F of the anion. The dispersion profiles were recorded in the range from 10 kHz to 30 MHz by using a Spinmaster FFC2000 instrument. The relaxation rates are sensitive for the existence of equimolar triglyme-lithium complexes as a function of temperature and salt concentration. Additional molecular dynamics (MD) simulations provide insight at molecular level about the change from glyme solutions to quasi-ionic liquids for the binary mixtures. The results can be used for tuning better electrolytes for battery systems.

[1] K. Yoshida, M. Nakamura, Y. Kazue, N. Tachikawa, S. Tsuzuki, S. Seki, K. Dokko, M. Watanabe, *J. Am. Chem. Soc.* **2011**, 133, 13121-13129.

[2] K. Yoshida, M. Tsuchiya, N. Tachikawa, K. Dokko, M. Watanabe, *J. Phys. Chem. C,* **2011**, 115, 18384-18394.

DYNAMICS OF P3HT IN HOMOPOLYMERS AND BLENDS BY ^{1}H AND ^{13}C RELAXATION

Marco Geppi,*[a] Francesca Martini,[a] Silvia Borsacchi,[a] Silvia Spera[b]
a) Dipartimento di Chimica e Chimica Industriale, Università di Pisa, v. Risorgimento 35, 56126 Pisa (Italy);
b) Centro Ricerche Per Le Energie Non Convenzionali, Istituto ENI Donegani, ENI S.p.A., Via G. Fauser 4, 28100 Novara (Italy);
email: mg@dcci.unipi.it

ABSTRACT

Polymeric solar cells (PSC's), characterized by low-cost polymeric photoactive layers, are arising a great interest in the field of solar energy, but several issues, such as the efficiency of these devices, need to be improved before their industrial breakthrough can take place [1]. The investigation of the morphology and dynamics of the polymeric photoactive layers and of the correlations between these properties and the efficiency of the final PSC's is considered of primary importance in order to develop systems with improved and optimized performances. To this aim solid-state NMR (SSNMR) is one of the most promising techniques, as demonstrated by the increasing number of applications in the field [2, 3, 4].

Blends of poly(3-hexylthiophene) (P3HT), as electron-donor, and [6,6]-phenyl-C_{60}-butyric acid methyl ester (PCBM), as electron-acceptor are one of the most performing photoactive materials developed so far, and were object of several studies in the literature [2, 3]. In this work we investigated in detail the dynamic properties of P3HT in the frequency range of MHz in both the neat polymer and the photoactive blends P3HT/PCBM before and after annealing with the final aim to find correlations between these properties and the efficiency of the correspondig devices. In particular, ^{1}H and ^{13}C T_1's were measured at different temperatures by means of low-resolution and high-resolution experiments, respectively, and were simultaneoulsly fitted by means of a suitable model using a home-made software. This analysis allowed the main reorientational motions of P3HT alkylic side-chains and the twisting motion of P3HT main-chain to be characterized, and the corresponding correlation times and activation energies to be quantitatively determined. Moreover, the phase separation behaviour of the blends were investigated by following the proton spin diffusion process through proton spin-lattice relaxation times.

Comparing the results obtained for the neat P3HT and the P3HT/PCBM blends, it was found that the dynamic behaviour of P3HT significantly changes among the different systems, and possible correlations between the mobility of P3HT side-chains in the blends before and after annealing, the phase separation behaviour, and the increase of efficiency of the final PSC following annealing were proposed [5].

References

[1] R. Po, M. Maggini, and N. Camaioni *J. Phys. Chem. C* **114**, 695-706 (2010)
[2] C. Yang, J. G. Hu, and A. J. Heeger *J. Am. Chem. Soc.* **128**, 12007-12013 (2006)
[3] R. Mens, F. Demir, G. Van Assche, B. Van Mele, D. Vanderzande, P. Adriaensens *J. Polym. Sci. Pol. Chem.* **50**, 1037-1041 (2012)
[4] S. Chambon, R. Mens, K. Vandewal, E. Clodic, M. Scharber, L. Lutsen, J. Gelan, J. Manca, D. Vanderzande, P. Adriaensens *Sol. Energ. Mat. Sol. C* **96**, 210-217 (2012)
[5] F. Martini, S. Borsacchi, S. Spera, C. Carbonera, A. Cominetti, M. Geppi *J. Phys. Chem. C* **117**, 131-139 (2013)

Proton field cycling NMR relaxometry of lipid bilayer membranes containing cholesterol. FFC membrane elastometry.

Esteban Anoardo
Laboratorio de Relaxometría y Técnicas Especiales (LaRTE)
Famaf – Universidad Nacional de Córdoba.
Instituto de Física Enrique Gaviola – CONICET
Córdoba – Argentina

It was previously demonstrated that fast field cycling (FFC) ^{1}H NMR spin-lattice relaxation rate dispersions of liposomes can be explained through a physical model that accounts for the molecular dynamics of the lipids [1,2]. The model was successfully compared with experimental measurements of liposomes prepared with different lipids (DMPC and DOPC), sizes (100-200nm) and temperatures (within the fluid liquid crystalline phase), using values for the different physical constants and parameters available in the literature. Then, the FFC NMR method was shown to be a useful tool for the study of the molecular dynamics of lipids and the viscoelastic properties of biological membranes. In the presence of cholesterol, two different pictures can be considered:

a- The cholesterol modulates the viscoelastic properties of the membrane, and consequently, the observed value of the mesoscopic involved physical parameters [3].

b- The cholesterol molecule exerts a strong influence in the lipids around it, thus separating the lipid population in two groups (cholesterol-ordered and disordered) [4].

The two pictures can be confronted with the model previously tested in cholesterol-free membranes, validating its extension to the present case.

Based on these studies, a method for the measurement of the bending elastic modulus of liposome membranes has been considered. An experiment was performed in order to test the feasibility of these measurements at limiting technological conditions (low cost/low size & fast measuring instrumentation).

[1]- Meledandri, C.J.; Perlo, J.; Farrher, E.; Brougham, D.F.; Anoardo, E. *J. Phys. Chem. B*, **2009**, 113, 15532.
[2]- Perlo J., Meledandri C. J., Anoardo E., Brougham D. F. *J. Phys. Chem. B*, **2011,** 115, 3444.
[3]- Filippov A., Orädd G., Lindblom G. *Biophys. J.* **2003**, 84, 3079.
[4]- Dai J., Alwarawrah M., Huang J. *J. Phys. Chem. B*, **2010,** 114, 840.

Field-cycling double-resonance spectroscopy of quadrupole nuclei in hydrogen bonded cocrystals, salts and crystal polymorphs

Janez Seliger[1,2] and Veselko Žagar[1]
[1] »Jozef Stefan« Institute, Jamova 39, 1000 Ljubljana, Slovenia
[2] University of Ljubljana, Faculty of Mathematics and Physics, Jadranska 19, 1000 Ljubljana, Slovenia

Engineering of crystalline materials with desired physical, chemical, or pharmaceutical properties includes the formation of cocrystals and crystal polymorphs.

Cocrystals are the crystalline structures formed by two or more components bound by non-covalent bonds, usually hydrogen bonds, π-π stacking, and van der Waals forces. In a cocrystal homosynthons and heterosynthons generally occur. Their occurrence depends on the molecular architecture and the positions and properties of functional groups. The properties of a cocrystal usually differ from the properties of the cocrystal formers.

Polymorphism is the ability of a solid material to exist in more than one crystal structure. Single-component crystals and cocrystals may exist in various polymorphic forms which in general differ in macroscopic properties.

Various polymorphs and cocrystals are usually characterized by powder X-ray diffraction, optical spectroscopy and NMR. Here we use ^{14}N and ^{17}O NQR as a method for characterization of cocrystals and polymorphs and for investigation of hydrogen bonding between molecules. We present the results of NQR studies of

(i) Two polymorphs of cocrystal isonicotinamide - oxalic acid (2:1) that is characterized by strong short O-H…N hydrogen bonds,

(ii) Various polymorphs and cocrystals of carbamazepine, an anticonvulsant and mood stabilizing drug and a model system for the study of polymorphism and

(iii) Cocrystals and salts of 2-amino-4,6-dimethylpyrimidine and various carboxylic acids, model systems for the study of hydrogen bonded supramolecular motifs, that are important in the protein-nucleic acid recognition and drug-protein recognition processes.

The experimental results show that NQR clearly distinguishes between crystal polymorphs of a given substance and provides a method for the study of stability of metastable crystal polymorphs. The differences in the NQR spectra of various polymorphs may be related to the differences in molecular conformations and intermolecular bonding patterns. The difference in the NQR spectra of a cocrystal and cocrystal formers is the consequence of the intermolecular interactions and may reflect the desired macroscopic properties of a cocrystal. NQR gives a unique view of proton position in hydrogen bond.

References:

1. J. Seliger, V. Žagar, J. Phys. Chem. A **114**, 12083-12087 (2010)
2. J. Seliger, V. Žagar, Solid State Nucl. Magn. Reson. **47-48**, 47-52 (2012)
3. J. Seliger, V. Žagar, T. Asaji, Hypefine Interactions (2013)
   DOI: 10.1007/s10751-012-0665-9

Seven Conjectures of NMR Relaxometry

Stanislav Sykora, Extra Byte, Castano Primo, Italy

The theory of [variable field] NMR relaxometry is notoriously cumbersome. Though the generic QM mathematical formulation is relatively simple, its practical applications require the combination of one or more types of spin interactions (I) and one or more types of dynamic processes (D) which modulate the interactions in a stochastic way and thus enable the relaxation. Each pair {I,D} represents a “relaxation channel” with its own relaxation rate formula. In addition, since relaxation is a second-order process, there are also cross-relaxation formulas for every pair of possible relaxation channels. The total number of potentially useful formulas is therefore extremely large (hundreds, even considering just the most common types of I’s and D’s).

Comparing such models among themselves one notices that they exhibit common regularities, some of which can be derived from first principles, while others are not yet proved, but apparently confirmed empirically. Such regularities can be useful in complex situations when there is no chance that a convincing relaxation model could be developed, or when there are insufficient resources to develop one.

I would like to present several such conjectures, some universal and some applicable only to homonuclear systems containing no unpaired electrons and no quadrupolar glitches. The talk will of course include supporting argumentation and evidence for the conjectures, and also promote the DLL representation (differential log-log) of NMR dispersion profiles.

LIST OF POSTERS

POSTER 1

D.G. Gadian, K.S. Panesar, A.J. Perez Linde, A.J. Horsewill, W. Köckenberger, J.R. Owers-Bradley
Preparation of highly polarised nuclear spin systems using brute-force and low-field thermal mixing

POSTER 2

A. Louis-Joseph, L. Benamsili, J.-P. Korb
Multi-dynamics study of crude oils by high field 2D-NMR DOSY and relaxometry

POSTER 3

C.C. Fraenza, E. Anoardo, C. Meledandri, D. Brougham
The effect of cholesterol on membrane molecular dynamics in unilamellar vesicles: a fast field-cycling NMR relaxometry study

POSTER 4

M. Yamaguchi, A. Ohira
Application of FFC-NMR relaxometry to catalyst layer materials of proton exchange membrane fuel cells

POSTER 5

C. Rizzi, J. Sirieix-Plénet, L. Gaillon, A-L. Rollet, D. Petit, P. Levitz
Aggregation of a redox amphiphilic ionic liquid observed by NMR relaxation times and electrochemistry studies

POSTER 6

H. Chemmi, A. Louis-Joseph, D. Petit, J.-P. Korb, P. Levitz
Multiscale dynamics of free and confined ionic liquids

POSTER 7

O.M. Dada, O.B. Awojoyogbe
Application of the time – dependent Bloch Flow equation and WKB approximation to NMR relaxometry

POSTER 8

V. Sapunov, A. Denisov, D. Saveliev, S. Kiselev, E. Narkhov, Y. Mitelman
Field-Cycling Overhauser Dynamic Nuclear Polarization for Geophysical Magnetometers

POSTER 9

O.B. Awojoyogbe, O.M. Dada, O.P. Faromika
Analytical solution of the NMR diffusion equation for relaxation studies of diatomic molecules undergoing rotational diffusion

POSTER 10

A. Aluculesei, C. Cruz, F. Vaca Chávez, P.J. Sebastião , D.M. Sousa, A. Roque, M.G. Tamba, G.H. Mehl

Angular dependent Fast Field-Cycling NMR Relaxometry in liquid crystals 8CB and CB-C9-CB

POSTER 11

C. Fraenza, G. Farrher, E. Anoardo, A. Ordikhani-Seyedlar, C. Mattea, S. Stapf, R. Glisoni, A. Sosnik

Molecular dynamics studies in polymeric micelles using fast field-cycling NMR relaxometry

POSTER 12

S. Kruber, G. D. Farrher, E. Anoardo

A straightforward concept for the design of incomplex notch-coil magnet systems for fast-field cycling NMR

POSTER 13

F. Martini, S. Borsacchi, G. Ruggeri, A. Pucci, M. Geppi

Phase transitions in polymeric luminescent indicators with a threshold temperature through variable-temperature SSNMR and fluorescence spectra

POSTER 14

B.W.C. Kennedy, L.M. Broche, G.P. Ashcroft, D.J. Lurie

Fast-field cycling NMR is sensitive to the method of cross-linking in BSA gels

POSTER 15

L. Bordonali, T. Kalaivani, K.P.V. Sabareesh, C. Innocenti, E. Fantechi, C. Sangregorio, M.F. Casula, L. Lartigue, J. Larionova, Y. Guari, M. Corti, P. Arosio, A. Lascialfari

Local spin dynamics and magnetic anisotropy in nearly monodispersed ferrite nanoparticles: an NMR-D study

POSTER 16

P.J. Ross, L.M. Broche, D.J. Lurie

Rapid field-cycling MRI using fast spin-echo

POSTER 17

K.J. Pine, D.J. Lurie

Towards a quality framework for localized FC relaxometry

POSTER 18

J. Leblond, M. Fleury, B. Nicot, M. Djabourov, S. Bubici

NMR relaxation-viscosity relationship in PEO melts

POSTER 19

S. Kaieda, B. Halle

Slow conformational dynamics of myoglobin as seen by internal water molecules

POSTER 20

A. Korpala, D. Kruk, S. Mehdizadeh Taheri, S. Förster, E.A. Rössler

^{1}H relaxation in solutions of superparamagnetic nanoparticles

POSTER 21

J. Perlo, G. Dominguez, E. Anoardo

Measurement of the bending elastic modulus in unilamellar vesicles membranes by fast field cycling NMR relaxometry

POSTER 22

D. Pooke, J. de Feijter, M. Mallett, S. Bubici

Cryogen-free superconducting magnet design for NMR

POSTER 23

S. Bubici, R. Steele, G. Ferrante

Fast field cycling relaxometry: moving from research towards industrial applications

POSTER 24

S. Bubici, R. Steele, G. Ferrante

Method for NMR relaxometry on hetero-nuclei at very low fields

POSTER 25

G. Ferrante, R. Cernuschi, R. Rolfi, R. Gatti, J. Barras, G. Kyriakidou, J.A.S. Smith, K. Althoefer

Authentication of medicines by Nuclear Quadrupolar Resonance (NQR) analysis; A portable system for non-destructive control of packaged pharmaceutical products

POSTER 26

D. Alberti, M. Van't Erve, R. Stefania, M.R. Ruggiero, S. Baroni, S. Geninatti Crich, S. Aime

R-ELISA: A quantitative relaxometric version of the ELISA test for the measurement of cell surface biomarkers based on the water proton T_1 measurements

Preparation of highly polarised nuclear spin systems using brute-force and low-field thermal mixing

Gadian DG[1], Panesar KS[2], Perez Linde AJ[2], Horsewill AJ[2], Köckenberger W[2], and Owers-Bradley JR[2]

[1]Institute of Child Health, University College London, WC1N 1EH, UK
[2]School of Physics & Astronomy, University of Nottingham, NG7 2RD, UK

Several strategies have been developed for generating highly polarised nuclear spin systems, including dynamic nuclear polarisation, optical pumping, and methods exploiting parahydrogen. We report here on investigations using an alternative strategy based on a 'brute-force' approach. The central notion of 'brute-force' NMR is that as the temperature is reduced and the field is increased, the equilibrium nuclear polarisation will increase, according to the Boltzmann distribution. The main problem is that it may take an extremely long time for the nuclear polarisation to approach thermal equilibrium at low temperatures and high fields, since nuclear relaxation becomes very slow. Cross-polarisation techniques can alleviate this problem.

Experiments were carried out using (i) a rapid field-cycling spectrometer that operates at temperatures down to 4.2K and delivers magnetic field switches of 10 Ts^{-1}, and (ii) a millikelvin spectrometer that operates at any chosen field up to 15T, and at temperatures as low as 10mK. Field cycling on this system can be carried out at rates of 1T min^{-1}. Experiments were carried out on [1-^{13}C] sodium acetate, either in the form of a powder, or dissolved in a 50/50 water/glycerol solution. In some experiments, sodium phosphate was also added to the water/glycerol solution.

We show that low-field thermal mixing can be used to transfer polarisation from the relatively rapidly relaxing ^{1}H reservoir to more slowly relaxing ^{13}C and ^{31}P nuclei. The effects are particularly dramatic for the ^{31}P nuclei, which at 2T and 4.2K showed a 75-fold enhancement in their effective rate of approach to equilibrium, and an even greater (150-fold) enhancement in the presence of a relaxation agent. The mixing step is also very effective in terms of the amount of polarisation transferred – 70-90% of the maximum theoretical value in the experiments reported here. These findings [1] have important implications for brute-force polarisation. We also show that the ^{1}H reservoir can be tapped repeatedly through a number of consecutive thermal mixing steps; this could provide additional sensitivity enhancement in solid-state NMR.

[1] Gadian DG, Panesar KS, Perez Linde AJ, Horsewill AJ, Köckenberger W, and Owers-Bradley JR (2012). Phys. Chem. Chem. Phys. 14: 5397-5402.

Multi-dynamics study of crude oils by high field *2D*-NMR DOSY and relaxometry

Alain Louis-Joseph, Lyès Benamsili and Jean-Pierre Korb
Physique de la Matière Condensée, Ecole Polytechnique-CNRS, 91128 Palaiseau, France

We propose using a set of non-invasive multiscale NMR techniques for probing the structure and dynamics of bulk and confined crude oils with and without asphaltene. High field NMR spectroscopy identifies the proton species. *2D* NMR *DOSY* spectra for bulk crude oils in presence or absence of asphaltene favor an interpretation of two populations of hydrocarbon aliphatic chains in two environments. In the presence of asphaltene, an analysis of the distributions of longitudinal relaxation time, T_1, in terms of a bimodal log-normal distribution, confirms the two environments clearly evidenced by varying the Larmor frequency. The remarkable features of the nuclear magnetic relaxation dispersion *(NMRD)* of $<1/T_1>$ for bulk and confined crude oils with and without asphaltene have been interpreted with an original model of intermittent surface dynamics of proton species at the surface of asphaltene nanoaggregates and bulk dynamics in between the clusters of these nanoaggregates.

The effect of cholesterol on membrane molecular dynamics in unilamellar vesicles: a fast field-cycling NMR relaxometry study.

Carla C. Fraenza and E. Anoardo

Laboratorio de Relaxometría y Técnicas Especiales (LaRTE), Facultad de Matemática, Astronomía y Física, Universidad Nacional de Córdoba and IFEG (CONICET), Córdoba, Argentina

C. Meledandri and D. Brougham

National Institute for Cellular Biotechnology, School of Chemical Sciences, Dublin City University, Dublin 9, Ireland

Fast field cycling (FFC) ^{1}H NMR spin-lattice relaxation rate dispersions of liposomes have been explained by a physical model that accounts for the molecular and collective dynamics of the lipids [1,2]. The FFC NMR method turned to be a useful tool for the study of the molecular dynamics of lipids and the viscoelastic properties of membranes composed of a single lipid type. It has been claimed that in the case of cholesterol containing membranes, the system remains in the disordered liquid crystalline phase (l_d) up to a certain concentration of the sterol [3,4]. However, other authors define a region around each cholesterol molecule within which lipids become strongly ordered, partitioning the lipid population into affected and unaffected pools, depending on the proximity to a cholesterol molecule [5-9]. The unaffected lipids are considered to be in the l_d phase, while the affected lipids are described as being in an ordered liquid crystalline phase (l_o). In this work we confront both interpretations with new experimental data, as a further refinement of our model. We analyze experimental FFC relaxation rate dispersion curves obtained at 298 K for liposomes of radius between 68 and 80 nm composed of DOPC and cholesterol at 10 and 25 mol%. The consistency obtained by this analysis suggests that the model, previously used to explain the relaxation rate dispersions in single lipid membranes, can be extended for the study of cholesterol containing liposomes.

References:

[1] Meledandri C. J., Perlo J., Farrher E., Brougham D. F., Anoardo E., *J. Phys. Chem. B*, 2009, 11, 15532.
[2] Perlo J., Meledandri C. J., Anoardo E., Brougham D. F. *J. Phys. Chem. B*, 2011, 115, 3444.
[3] Filippov A., Orädd G., Lindblom G. *Biophys. J.* 2003, 84, 3079.
[4] Filippov A., Orädd G., Lidblom G., *Langmuir* 2003, 19, 6397.
[5] Edholm O., Nyberg A. M., *Biophys J.* 1992, 63, 1081.
[6] Robinson A. J., Richards W. G., Thomas P. J., Hann M. M. *Biophys J.* 1995, 68, 164.
[7] Chiu S. W., Jakobsson E., Mashl R. J., Scott H. L. *Biophys J.* 2002, 83, 1842.
[8] Jedlovszky P., Mezei M., *J. Phys. Chem. B*, 2003, 107, 5311.
[9] Dai J., Alwarawrah M., Huang J. *J. Phys. Chem. B*, **2010,** 114, 840.

Application of FFC-NMR relaxometry to catalyst layer materials of proton exchange membrane fuel cells

Makoto Yamaguchi[a], *Akihiro Ohira*[a,b]

[a]*Fuel Cell Cutting-Edge Research Center, Tokyo, Japan*
[b]*National Institute of Advanced Industrial Science and Technology (AIST), Osaka, Japan*

In proton exchange membrane fuel cells catalyst layers work as either a cathode for oxygen reduction or an anode for hydrogen oxidation. They consist of platinum catalyst particles dispersed on carbon black particles and coated with ionomer thin films. Application of pulsed field gradient NMR which made great success to measure self diffusion coefficients of the membranes would be difficult due to their complex structure in nanoscales. Recently we reported preliminary results on NMR relaxometry of the catalyst layers which showed NMRD profiles quite different from the ionomer membranes due to strong interation of protons with the platinum particles [1]. However, due to their complex structure more detailed studies are necessary for their components and here we report two recent results on application of NMR relaxometry. NMRD profiles were measured at Larmor frequencies from 0.001 to 40 MHz by using Spinmaster FFC-2000 (Stelar s.r.l.).

1. Perfluorinated sulfonic acid ionomer membranes at low water content: Perrin et al. observed changes in NMRD profiles by the type of surface interaction as well as water content down to λ=3.4 (λ=[H_2O]/[RSO_3H]) in the case of Nafion membranes [2,3]. As water content would become lower in the catalyst layers due to diffusion of gaseous reactants, we measured ^{1}H NMRD profiles of H-Nafion membranes (DuPont NR212) of λ=1. The membranes were evacuated at room temperature and sulfonic acid sites are assumed to form dimers of ion pairs as $(RSO_3^-H_3O^+)_2$. The ^{1}H relaxation rates gradually decreased with temperature and the NMRD profiles became less steeper from power law to logarithmic frequency depenence. They are fitted by formula corresponding to renormalized Rouse model [4] which seems to be consistent with the assumption of restricted motions of protons in bridged side chains.

2. Effect of acidity on proton relaxation by interaction with platinum surface: Proton spin lattice relaxation rates of aqueous solutions contacting platinum particles were found to be dependent on their acidity. In acid solutions relaxation rates become gradually larger than water towards higher frequency and NMRD profiles are less steep. No significant effect of associated anions was identified as surface diffusion of water would not be affected by weak interaction of diffusion water and anions. In contrast, hydronium ions concentrated in the vicinity of the metal surface would strongly affect surface diffusion of water by hydrogen bond formation.

This work was financially supported by the Ministry of Economy, Trade and Industry (METI) and the New Energy and Industrial Technology Development Organization (NEDO), Japan.

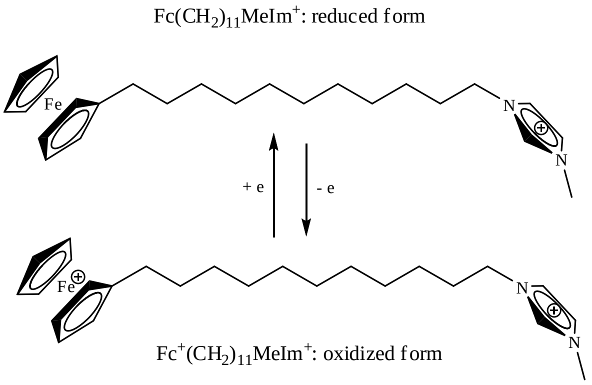
[1] Yamaguchi, M., Ohira, A., MRPM11 (2012).
[2] Perrin J.-C., Lyonnard, S., Guillermo, A., Levitz, P., J. Phys. Chem. B 110 (2006) 5439-5444.
[3] Perrin J.-C., Lyonnard, S., Guillermo, A., Levitz, P., Magn. Reson. Imaging 25 (2007) 501-504.
[4] Fatkullin, N., Kimmich, R., Weber, H. W., Phys. Rev. E 47 (1993) 4600-4603.

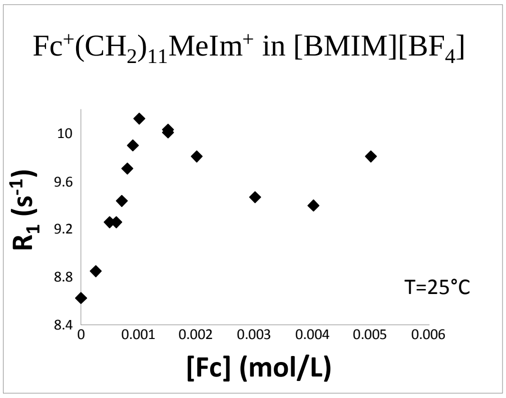
Aggregation of a redox amphiphilic ionic liquid observed by NMR relaxation times and electrochemistry studies

Cécile Rizzi[1], Juliette Sirieix-Plénet[1], Laurent Gaillon[1], Anne-Laure Rollet[1], Dominique Petit[2], Pierre Levitz[1].
(1) PECSA laboratory, UPMC-CNRS-ESPCI, 4 place Jussieu, 75005 Paris, France
(2) Physique de la Matière Condensée laboratory, École Polytechnique, France
Email: anne-laure.rollet@upmc.fr

Room Temperature Ionic liquids (RTILs) offer competitive substitutes to classical organic solvent in synthesis, separation processes or electrochemistry. They may be considered as polar solvents when exhibiting water-like properties. It was notably observed that in RTIL media, long hydrocarbon chain surfactants could self-organize to form micelles or other aggregates[1,2,3]. In RTIL media, such aggregates could significantly improve solutes solubility, modulate transport properties or allow nanoscale materials design.

We synthesized an amphiphilic RTIL exhibiting a redox moiety: the 1-(11-ferrocenylundecyl)-3-methylimidazolium bromide, which ability to aggregate or dissociate, according to its oxidation state, was already demonstrated in water[4]. Electrochemical measurements evinced that in RTILs such behaviour pertains though the critical aggregation concentration CAC is different.





The investigation of the aggregation of $Fc(CH_2)_{11}MeIm^+$ and $Fc^+(CH_2)_{11}MeIm^+$ in imidazolium based RTILs is challenging. Usual techniques as surface tension, ionic conductivity are unable to evidence the change of the physico-chemical properties upon aggregation because of the remarkable properties of RTILs, such as low surface tension, high conductivity and high ionic strength. Furthermore, the chemical similarity between $Fc(CH_2)_{11}MeIm^+$ and the RTIL blind neutrons and synchrotron scattering, and high field NMR techniques. Nevertheless, NMR relaxivity induced by the paramagnetic centre of the oxidized form ($Fc^+(CH_2)_{11}MeIm^+$) is modulated by the aggregation of the latter. By measuring the ^{1}H relaxation times it has been possible to determine precisely the CAC in agreement with the electrochemical results.

The relaxation was further investigated by recording the NMRD curves before and after the CMC.

---

[1] S. Thomaier and W. Kunz, J. Mol. Liq., 130, **2007**, 104-107.
[2] K. A. Fletcher and S. Pandey, Langmuir, 20, **2004**, 33-36.
[3] T. L. Greaves and C. J. Drummond, Chem. Soc. Rev., 37, **2008**, 1709-1726.
[4] B. Chamiot, C. Rizzi, L. Gaillon, J. Sirieix-Plénet and J. Lelièvre, Langmuir, 25, **2009**, 1311-1315.

Multiscale dynamics of free and confined ionic liquids

H. Chemmi[a], *A. Louis-Joseph*[a], *D. Petit*[a*], *J.-P. Korb*[a], *P. Levitz*[b]

[a] *Physique de la Matière Condensée, Ecole Polytechnique, CNRS, Palaiseau 91128, France*
[b] *Université Paris 06, CNRS, Laboratoire PECSA, F-75252 Paris, France*

Ionic liquids are known for their appealing properties such as high ionic conductivity, negligible vapour pressure, thermal stability, none-flammability and wide electrochemical stability window [1]. These properties lead to a broad field of applications such as optical devices, catalysts, sensors and electrolyte membranes [2]. They have recently been used as electrolytes in solar and fuel cells [3, 4] and lithium batteries [5]. For such applications, these ionic liquids have been immobilized in a solid matrix [6, 7] leading to composite materials called ionogels. However, the molecular dynamics of these liquid-like ions within a disordered solid matrix is still unknown. Here, we choose the 1-butyl-3-methylimidazolium bistrifluoromethyl-sulfonylimide [BMI][TFSI] as an cation-anion pair of ionic liquid, free or confined within a silica-like meso-porous matrices made by a sol-gel route from hydrophobic methyl groups precursors (ionogels made from tetramethoxysilane, methyltrimethoxysilane; lithium salt Li TFSI was added). The Li cation, the proton-bearing cation [BMI], and the proton-free anion [TFSI] temperature dependence dynamics are investigated by a multiscale NMR approach of ^{7}Li, ^{1}H and ^{19}F respectively. We use high field spectroscopy and relaxation NMR at 8.6 T to characterize the micro-scale dynamics. The meso-scale dynamics is followed by nuclear magnetic relaxation dispersion (NMRD) between 10 kHz and 20 MHz [8, 9, 10]. Pulse Field Gradient measurements allow investigating the macro-scale dynamics. In order to illustrate the drastic impact of the confinement on the ionic dynamics, we report studies of both the ionogel and the ionic liquid alone and we focus on the dynamics at meso-scale explored by fast field cycling relaxometry.

This work is supported by the Agence National de la Recherche ANR-2011-Blanc-(NanoChalco)

[1] P. Hapiot, C. Lagrost, Chem. Rev. 108, 2238 (2008).
[2] A. Vioux, L. Viau, S. Volland, J. Le Bideau, C. R. Chimie 13, 242–255 (2010).
[3] B. O'Reagan and M. Graetzel, Nature 353, 737-740 (1991).
[4] H. Nakamoto and M. Watanabe, Chem. Commun. 2339-2541 (2007).
[5] M.Diaw, A. Chagnes, B. Carre, P. Wilmann and D. Lemordant, J. Power sources 146, 682-684 (2005).
[6] J. Le Bideau, P. Gaveau, S. Bellayer, M.A. Néouze and A. Vioux, Phys. Chem. Chem. Phys. 9, 5419-5422 (2007).
[7] M.-A. Neouze, J. Le Bideau, P. Gaveau, S. Bellayer and A. Vioux, Chem. Mater., 2006, 18, 3931–3936.
[8] D. Petit, J.-P. Korb, P. Levitz, J. LeBideau and D. Brevet, Diffusion Fundamentals 10 (2009) 7.1 – 7.3
[9] D. Petit, J.-P. Korb, P. Levitz, J. LeBideau and D. Brevet, C. R. Chimie 13 (2010) 409–411
[10] D. Petit, J-P. Korb, P. Levitz, J. Le Bideau, D. Guyomard, A. Vioux, Magnetic Resonance in Porous Media, AIP Proceedings 1330 (2011) 85-88.

* Corresponding author: dominique.petit@polytechnique.fr

APPLICATION OF THE TIME – DEPENDENT BLOCH FLOW EQUATION AND WKB APPROXIMATION TO NMR RELAXOMETRY

O.M. Dada and O.B. Awojoyogbe*

Department of Physics, Federal University of Technology, Minna, Niger State, Nigeria E-mail: *awojoyogbe@yahoo.com*

INTRODUCTION

One of the key goals in molecular imaging using magnetic resonance is to understand the molecular dynamics that leads to establish the structure-properties relationships, which are important in order to improve and design new molecular imaging techniques for different applications. The dynamics of molecules is unique to the species they belong to and the interaction in which they are participating. All these are embedded in the relaxation times T_1 and T_2.

MATHEMATICAL FORMULATION

We study the flow properties of the modified time dependent Bloch NMR flow equations which describes the dynamics of the hydrogen atom under the influence of rf magnetic field as follows [1].

$$\frac{d^2M_y}{dt^2}+\frac{1}{T_0}\frac{dM_y}{dt}S(t)M_y=\frac{M_0\gamma B_1(t)}{T_1} \tag{1}$$

where $S(t)=\gamma^2B_1^2(t)+\frac{1}{T_1T_2}$, $\frac{1}{T_0}=\frac{1}{T_1}+\frac{1}{T_2}$

We shall assume a stream function of the form:

$$M_y(t)=\psi(t)e^{kt} \tag{2}$$

where $k=-\frac{1}{2T_o}$, v is the fluid instantaneous velocity and $\psi(t)$ is a special function of the transverse magnetization. At the point when maximum NMR signal is received (maximum values of M_y and $B_1(t)$ respectively), $M_o \approx 0$ and eqn (1) becomes

$$\frac{d^2\psi(t)}{dt^2}+\gamma^2B_1^2(t)\psi(t)=0 \tag{3}$$

Eqn (3) is subject to the following conditions: (i) $e^{kt}\neq 0$
(ii) $\gamma^2B_1^2(t)>>\left(T_g-T_v\right)$ where $T_g=\frac{1}{T_1T_2}$, $T_v=\frac{1}{4T_0^2}$

γ, T_1 and T_2 retain their usual meaning. Eqn (3) becomes [1]:

$$\frac{d^2\psi(t)}{dt}+G^2(t)\psi=0 \text{ where } G^2(t)=\gamma^2B_1^2(t) \tag{4}$$

The rf B_1 field is designed such that $G^2(t)$ vanishes at a single point $t = t_o$ only. Then

$$\begin{aligned} G^2(t)&>0 \quad \text{for} \quad t>t_o \\ G^2(t)&<0 \quad \text{for} \quad t<t_o \end{aligned} \tag{5}$$

It is required that the boundary condition holds $\psi(t)\to 0 \;\; as \;\; t\to\infty$ (indicating the nature of the FID after a long time). If the applied rf field is complex and we may set $t_0 = \infty$, the WKB approximation gives:

$$\psi(t)=\frac{D}{\sqrt{\omega_1(t)}}\exp\left(-\int_\infty^t|G(s)|ds\right) \quad \text{for } t<t_0 \tag{6}$$

$$\psi(t)=\frac{D}{\sqrt{\omega_1(t)}}\exp\left(\int_t^\infty|G(s)|ds\right) \quad \text{for } t<t_0 \tag{7}$$

where D is a constant, $\omega_1(t)=\gamma B_1(t)$ represents the frequency of the RF – induced rotation (by the applied B_1 field) [2]. Using the Larmour condition and Eqn (2) in Eqns (6) and (20), we have:

$$M_y(t)=\frac{D}{\sqrt{\omega_0(t)}}\exp\left(\int_t^\infty|G(s)|ds\right)\exp\left(-\frac{t}{2T_0}\right) \tag{8}$$

ANALYSIS OF RESULTS

The biggest challenge in the computation of relaxation parameters is the determination of the autocorrelation function. If we draw a simple analogy with the cumulant expansion treatment of relaxation [2], the transverse magnetization function is given as:

$$F(t)=\exp\left(-\int_0^\infty(t-\tau)\sum_{m=-2}^{2}[3-m(m+1)/2]\exp(im\omega_0\tau)G_m(\tau)d\tau\right) \tag{9}$$

where $\int_0^\infty\sum_{m=-2}^{2}[3-m(m+1)/2]\exp(im\omega_0\tau)G_m(\tau)d\tau=\int_t^\infty G(s)ds-\frac{t}{2T_0}$,

$\int_t^\infty G(s)ds$ depend on the nature of the applied rf field and m is the spin flip index (corresponding to different transitions between energy states [3]). Using this method [2],

$$\frac{1}{T_1}=\sum_{m=-1}^{2}m^2\int_{-\infty}^{\infty}G_m(\tau)\exp(im\omega_0\tau)d\tau, \quad \frac{1}{T_2}=\sum_{m=-1}^{2}\left[3-\frac{m^2}{2}\right]\int_{-\infty}^{\infty}G_m(\tau)\exp(im\omega_0\tau)d\tau$$

This expression implies that

$$\frac{1}{T_0}=\sum_{m=-1}^{2}\left[3+\frac{m^2}{2}\right]\int_{-\infty}^{\infty}G_m(\tau)\exp(im\omega_0\tau)d\tau \tag{10}$$

The term $J_m(m\omega_0)=\int_{-\infty}^{\infty}G_m(\tau)\exp(im\omega_0\tau)d\tau$ (11)

is the spectral density function. Hence, $\frac{1}{T_0}=\sum_{m=-1}^{2}\left[3+\frac{m^2}{2}\right]J_m(m\omega_0)$

It is then very easier to compute the correlation time (τ_c) from here based on the prevailing condition of the dynamic system. If an exponential $G_m(\tau)$ is observed [3],

$$J_m(m\omega_0)\propto\frac{\tau_c}{1+\tau_c^2(m\omega_0)^2} \tag{12}$$

CONCLUSION

We have been able to relate the relaxation parameter $1/T_0$ to the spectral density function and the correlation time. The crucial challenge this study presents is the determination of the appropriate correlation function; once this is found, every other computation follows very easily. It is observed that both T_1 and T_2 contribute to the transverse magnetization according to equation (1) and this implies that we can always determine both times from a single NMR signal sampling.

REFERENCES

[1] Awojoyogbe, O.B. (2007) A quantum mechanical model of the Bloch NMR flow equations for electron dynamics in fluids at the molecular level. *Physica Scr.* 75: 788–794.
[2] Cowan, B. P. (1997). Nuclear Magnetic Resonance and Relaxation, First Edition (Cambridge: Cambridge University Press).
[3] Silvennoinen M.J. (2002) A Study of NMR Relaxation in Blood - Mechanistic Considerations and Implications for Quantitative Functional MRI. PhD Dissertation, University of Kuopio, Finland.

Field-Cycling Overhauser Dynamic Nuclear Polarization for Geophysical Magnetometers

Sapunov V., Denisov A., Saveliev D., Kiselev S., Narkhov E., Mitelman Y.

Quantum Magnetometry Laboratory of Ural Federal University
Mira str., 21, Ekaterinburg, 620002, Russia
E-mail: sva@dpt.ustu.ru

The FC NMR technology is widely used in a proton precession magnetometers of the Earth magnetic field intended for geological and geophysical exploration. The main method used in the devices is the Packard & Varian free precession method. Considerable improvement of the modern proton magnetometers is reached by using the Overhauser dynamic nuclear polarization (ODNP). Absolute accuracy up to 0.1 nT at sensitivity up to 0.01 nT which corresponds to 0,00001% at a measurement cycle of 1-3 seconds can be obtained**.** In this report we present modern magnetometer designs (including those developed in QM Laboratory [www.magnetometer.ru]).

Potential sensitivity of Overhauser DNP magnetometers can be essentially improved (degree 3/2 from a measurement cycle for the optimized signal processing algorithms [1]), optimal concentration and/or continuous signal by the Salvi & Glenat method. It will be interesting to the decision of fundamental problems [2].The methods of DNP hyperpolarization [3, 4] and modern radical solutions used in ODNP magnetometers are important. For some substances HF saturation of the superhyperfine ESR structure at the spin exchange interactions is reached easily (*Effect of DNP easy pumping*). The report discusses technical details of maintenance of high absolute accuracy of the ODNP magnetometers; it also presents special device, namely the standard of the low magnetic field based on multilayer magnetic screen, and FC DNP spectrometer of a weak and zero field for substance research.

Modifications of ODNP vector magnetometers measuring both the field module and the absolute field components are another FC NMR application to in magnetometer methods for geophysical exploration [5]. It is based on the usage of special bias FC magnetic fields at precession signal pick up with a subsequent calculation of field component.

Other examples of application FC NMR of low magnetic field include oil well logging and cores exploration in which ODNP magnetometers provide stability of the spin echo signals in the conditions of an unstable Earth magnetic field [6].

1. Denisov, A., Sapunov, V., Dekusar, O. Calculation of proton magnetometer measurement error. (1999) *Geomagn. Aeron*, 39 (6), pp. 68-73
2. Ledbetter, M.P., Pustelny, S., Budker, D., Romalis, M.V., Blanchard, J.W., Pines, A. Liquid-state nuclear spin comagnetometers. (2012) *Physical Review Letters*, 108 (24)
3. Lingwood M.D., Han, S. Solution-State Dynamic Nuclear Polarization , *Annual Reports on NMR Spectroscopy*, (2011), 73, pp. 83-126
4. V. A. Sapunov, A. K. Chirkov, Sov. *J. Chem. Phys*., (1991), 7, 1447
5. V. Sapunov, J. Rasson, A. Denisov, D. Saveliev, S. Kiselev S. Theodolite-borne vector Overhauser magnetometer: DIMOVER. (2006). *Earth Planets Space*. V.58, №6., P.711-716
6. V. Sapunov, G. Takkand, E. Ligus and T. Khismetov. The development of geomagnetic field nuclear magnetic log. *Magnetic Resonance Imaging*. (2005). V. 23, N 2, p. 404-405

ANALYTICAL SOLUTION OF THE NMR DIFFUSION EQUATION FOR RELAXATION STUDIES OF DIATOMIC MOLECULES UNDERGOING ROTATIONAL DIFFUSION

***O.B. Awojoyogbe*[1]*, O.M. Dada*[1] *and O.P. Faromika*[2]**
[1]***Department of Physics, Federal University of Technology, Minna, Niger State, Nigeria***
[2]***Department of Physics, Federal University of Technology, Akure, Ondo State, Nigeria***
E-mail: awojoyogbe@yahoo.com

INTRODUCTION

Rotational diffusion is a process by which the equilibrium statistical distribution of the overall orientation of molecules is maintained or restored. The random re-orientation of molecules is an important process for many biophysical probes. The rotational diffusion of molecules in the presence of static magnetic and rf fields can described by the NMR diffusion equation.

MATHEMATICAL FORMULATION

The NMR diffusion equation within a spherical cavity is given as follows [1]:

$$\frac{\partial M_y}{\partial t}=D\left(\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial M_y}{\partial r}\right)+\frac{1}{r^2\sin^2\theta}\frac{\partial^2 M_y}{\partial\phi^2}+\frac{1}{r^2\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial M_y}{\partial\theta}\right)\right) \quad (1)$$

A tumbling molecule exhibits rotational diffusion which describes the tumbling motion of the molecules. If r is fixed such that $r = R$,

$$\frac{\partial M_y}{\partial t}=D_r\left(\frac{1}{\sin^2\theta}\frac{\partial^2 M_y}{\partial\phi^2}+\frac{1}{\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial M_y}{\partial\theta}\right)\right) \quad (2)$$

where $D_r=\frac{D}{R^2}$ is the rotational diffusion coefficient and R is the fixed radius of a molecular sphere. Using the method of separation of variables [2], we have the solution:

$$M_y(\phi,\theta,t)=Ae^{-D_r l(l+1)t}Y_l^m(\phi,\theta) \quad (3)$$

This expression represents the transverse magnetization of the diffusing molecule which is making a tumbling motion [2].
The above expression gives the general solution of Eqn (1). It should be noted that we may relate the expression above to the time constant τ or decay time (or the effective relaxation time) as follows [3]:

$$\frac{1}{\tau_l}=\frac{D}{R^2}l(l+1)=D_r l(l+1) \quad (4)$$

Eqn (4) thus becomes: $M_y(\phi,\theta,t)=Ae^{-t/\tau_l}Y_l^m(\phi,\theta)$ (5)

Since the radial parameter R is constant, we may assume that $A=M_0e^{-R}$. If we sum over all m and l, we have:

$$M_y(\phi,\theta,t)=\sum_{l,m}M_0e^{-R_m^l}e^{-t/\tau_l}Y_l^m(\phi,\theta) \quad (6)$$

If at t = 0, $(\phi,\theta)=(\phi_0,\theta_0)$, we write:

$$M_y(\phi,\theta,0)=\sum_{l,m}M_0e^{-R_m^l}Y_l^m(\phi,\theta)=\delta(\phi,\theta-\phi_0,\theta_0) \quad (7)$$

Then, the delta function may be expanded such that [3]:

$$\delta(\phi,\theta-\phi_0,\theta_0)=\sum_{l,m}Y_l^{m*}(\phi_0,\theta_0)Y_l^m(\phi,\theta);\ M_0e^{-R_m^l}=Y_l^{m*}(\phi_0,\theta_0) \quad (8)$$

$$M_y(\phi,\theta,t)=\sum_{l,m}Y_l^{m*}(\phi_0,\theta_0)Y_l^m(\phi,\theta)e^{-t/\tau_l} \quad (9)$$

APPLICATION TO NMR RELAXOMETRY

For this system, the autocorrelation function may be given as [3]:

$$G(t)=\frac{12\pi}{20}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\hbar^2\gamma^4}{r^6}\left\langle Y_2^{m*}(\phi,\theta)Y_2^m(\phi,\theta)e^{-t/\tau_l}\right\rangle \quad (10)$$

The angle bracket is the average over the transverse magnetization of the rotating molecules. This average is given as [3]:

$$\frac{1}{4\pi}\int d(\phi,\theta)\int d(\phi_0,\theta_0)\sum_{l,n}Y_l^{n*}(\phi_0,\theta_0)Y_l^m(\phi,\theta)Y_2^m(\phi_0,\theta_0)Y_2^{m*}(\phi,\theta)e^{-t/\tau_l} \quad (11)$$

If we perform the integral, Eqn (17) becomes [3]: $\frac{1}{4\pi}e^{-t/\tau_l}$ (12)

$$G(t)=\frac{K}{3}e^{-t/\tau_l} \quad (13)$$

where $\tau_l=\frac{R^2}{6D}=\frac{1}{6D_r}$, $K=\frac{9}{20}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\hbar^2\gamma^4}{r^6}$ is the second moment of interaction and r is the separation between two nuclear spins. The spectral density function is the Fourier transformation [3] of Eqn (13),

$$J(\omega)=\frac{2}{3}\left(\frac{K\tau_l}{1+\omega^2\tau_l^2}\right) \quad (14)$$

$$\frac{1}{T_1}=K\tau_l\left(\frac{2/3}{1+\omega^2\tau_l^2}+\frac{8/3}{1+4\omega^2\tau_l^2}\right) \quad (15)$$

$$\frac{1}{T_2}=K\tau_l\left(1+\frac{5/3}{1+\omega^2\tau_l^2}+\frac{2/3}{1+4\omega^2\tau_l^2}\right)$$

MAPPING OF EQUILIBRIUM MAGNETIZATION

From Eqn (8), we can map M_0 as a function of the radius of the rigid rotator R (which is also dependent on θ_0 and ϕ_0). It is noteworthy that Eqn (1) is solved for the condition that exists immediately the rf field is removed. At that point, M_0 starts building up from its lowest value. For multi-voxel imaging, R may be changing with different tissue conditions and it could be very important the influence of this changes on M_0. The following plots show the changes in M_0 with assumed ranges for R.

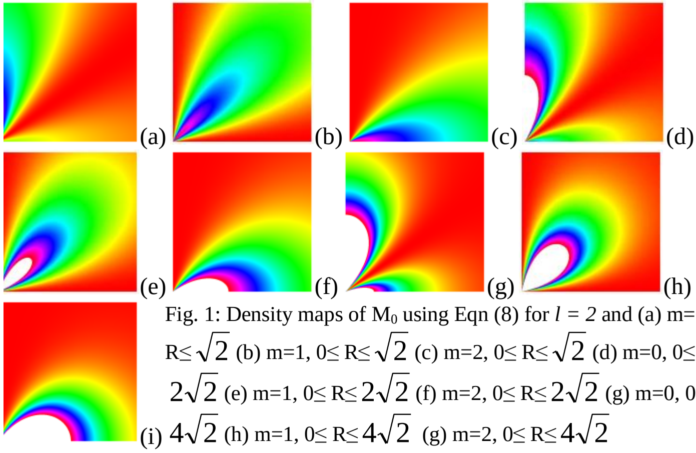


Fig. 1: Density maps of M_0 using Eqn (8) for *l = 2* and (a) m=0, 0≤ R≤ $\sqrt{2}$ (b) m=1, 0≤ R≤ $\sqrt{2}$ (c) m=2, 0≤ R≤ $\sqrt{2}$ (d) m=0, 0≤ R≤ $2\sqrt{2}$ (e) m=1, 0≤ R≤ $2\sqrt{2}$ (f) m=2, 0≤ R≤ $2\sqrt{2}$ (g) m=0, 0≤ R≤ $4\sqrt{2}$ (h) m=1, 0≤ R≤ $4\sqrt{2}$ (g) m=2, 0≤ R≤ $4\sqrt{2}$

CONCLUSION

We have derived the standard parameters of NMR relaxometry of diatomic directly from the NMR diffusion equation. The advantage of this study is that we have obtained the autocorrelation function and the spectral density function without the use of the rigorous method of probability distribution function.

REFERENCES

[1] Awojoyogbe O.B., Dada O.M., Faromika O.P., Dada O.E. Mathematical Concept of the Bloch Flow Equations for General Magnetic Resonance Imaging: A Review; Concepts in Magnetic Resonance Part A, Vol. 38A (3) 85–101 (2011).
[2] Awojoyogbe O.B, Faromika OP, Folorunsho OM, Dada M, Fuwape I. A, Boubaker K. Mathematical model of the Bloch NMR flow equations for the analysis of fluid flow in restricted geometries using the Boubaker polynomials expansion scheme, Current Applied Physics; 10: 289-293 (2010).
[3] Cowan, B. P. (1997). Nuclear Magnetic Resonance and Relaxation, First Edition (Cambridge: Cambridge University Press).

Angular dependent Fast Field-Cycling NMR Relaxometry in liquid crystals 8CB and CB-C9-CB

A. Aluculesei [1,2], C. Cruz [1,2], F. Vaca Chávez [2], P. J. Sebastião [1,2] , D. M. Sousa[3], A. Roque[3], M. G. Tamba[4], G. H. Mehl[4]

[1] *Department of Physics, Instituto Superior Técnico, Technical University of Lisbon, Av. Rovisco Pais, 1049-001 Lisbon, Portugal*
[2] *Centro de Física da Matéria Condensada, Av. Prof. Gama Pinto 2, 1649-003 Lisbon, Portugal*
[3] *DEEC & INESC-ID, Instituto Superior Técnico, TU Lisbon, Av. Rovisco Pais, 1049-001 Lisbon, Portugal*
[4] *Department of Chemistry, University of Hull, Cottingham Road, Hull HU6 7RX, United Kingdom*

Fast Field Cycling Relaxometry is a powerful technique for the study of molecular dynamics of soft matter systems, especially when combined with standard NMR high Larmor frequency measurements. In anisotropic materials such as liquid crystals, the use of T_1 measurements dependent on the angle between the external magnetic field and the preferred alignment axis of the material is particularly important for the analysis of the experimental data in the scope of appropriate NMR relaxation models. The new advances in FFC NMR experimental setups have allowed for the study of spin-lattice relaxation as a function of the sample's alignment in the magnetic field [1]. A set of proton NMR relaxation measurements as a function of Larmor frequency, temperature and angle of the known LC material 8CB and of the dimeric LC system CB-C9-CB will be presented. The angular dependence obtained for 8CB confirms self-diffusion as the main relaxation mechanism at 100 kHz. CB-C9-CB exhibits a weak first order nematic-nematic transition, confirmed by polarising optical microscopy, DSC and X-ray diffraction [2]. The structure of the low temperature nematic, N_x, phase is of significant interest due to the fundamental questions related to the formation a second nematic phase and due to potential applications such as microsecond switching of such materials [3]. The relaxation results in N_x phase, indicate a molecular dynamics behaviour, which is clearly different from that in the standard nematic phase N_u of this and other LC materials. The angular dependence results for the N_x phase differ significantly from those of the N_u phase. As the molecular dynamics is considerably influenced by the molecular organization within the LC phase, the analysis of the relaxation results contribute to the understanding of the physical behaviour of this system both with respect to fundamental and application aspects.

These experiments were performed taking advantage of the recent technological improvements introduced in the low power FFC NMR setup [1], which presents an overall performance that opens the possibility of using the FFC NMR technique in up to date unexplored molecular systems. In addition to the portability of the equipment, the magnet field homogeneity has been improved since new materials had been incorporated on it [4].

[1] D.M. Sousa, G.D. Marques, J.M. Cascais, P.J. Sebastião *Solid State Nucl.Magn.Reson.*, **38**, 36-43 (2010).

[2] V. P. Panov, M. Nagaraj, J.K. Vij, Yu. P. Panarin, A. Kohlmeier, M. G. Tamba, R. A. Lewis and G.H. Mehl, Phys. Rev. Lett. 105, 167801 (2010); C. S. P. Tripathi, *et al.* , Phys. Rev. E 84, 041707 (2011).

[3] M. Cestari, S. D. Berart, D. A. Dunmur, A. Ferrarini, M. R. de la Fuente, D. J. Jackson, D. O. Lopez, G. R. Luckhurst, M. A. P. Jubindo, R. M. Richardson, J. Salud, B. A. Timimi and H. ZimmermannPhys. Rev. E 84, 031704 (2011); V. P. Panov *et al.*, Appl. Phys. Lett**99**, 261903, (2011)

[4] A. Roque, S. Ramos, J. Barão, V. M. Machado, D. M. Sousa, E. Margato and J. Maia, Journal of Superconductivity and Novel Magnetism, Springer, Volume 26, pp. 133-140 (2013).

Molecular dynamics studies in polymeric micelles using fast field-cycling NMR relaxometry.

C. Fraenza, G. Farrher and E. Anoardo

Laboratorio de Relaxometría y Técnicas Especiales (LaRTE), Facultad de Matemática, Astronomía y Física, Universidad Nacional de Córdoba and IFEG (CONICET), Córdoba, Argentina

A. Ordikhani-Seyedlar, C. Mattea and S. Stapf

Fakultät für Mathematik und Naturwissenschaften, Technische Universität Ilmenau, Ilmenau, Germany

R. Glisoni and A. Sosnik

BIONIMED. Departamento de Tecnología Farmacéutica. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires.

The administration of drugs presenting low solubility in biological fluids still reptresents a crucial biopharmaceutic limitation for the pharmaceutical industry, being the case for about 50% of the approved drugs and 70% of those in the pipeline. Among the existing strategies to overcome this problem, inclusion of hydrophobic drugs into polymeric micelles is one of the most attractive and versatile alternatives. Amphiphilic poly(ethylene oxide)–poly(propylene oxide) block copolymers are thermoresponsive materials that display unique aggregation properties in aqueous medium. Due to their ability to form stable micellar systems in water, these materials are broadly studied for the solubilization of poorly water-soluble drugs. In this work, molecular dynamics of triblock copolymers (commercial name Pluronic block copolymers) F68 ($EO_{80}PO_{27}EO_{80}$), F108 ($EO_{141}PO_{44}EO_{141}$), and F127 ($EO_{101}PO_{56}EO_{101}$) at different concentrations (10-22.5% w/v) and temperatures (3-25°C) were analyzed using fast field-cycling NMR relaxometry. The frequency range was from 8 KHz to 20 MHz, considering that the measured local field values were lower than 1 KHz for all the samples. This study was complemented with NMR spectroscopy, NMR measurements in the rotating frame, atomic force microscopy (AFM), transmission electron microscopy (TEM) and dynamic light scattering (DLS) techniques. Although proton NMR spin-lattice relaxation rate dispersions showed a weak dispersion in the laboratory frame and no dispersion in the rotating frame, they evidenced a bi-exponential behavior that has been attributed to different relaxation of PEO and PPO groups in agreements with other authors [1]. Also, it was observed that the larger the ratio *R,* defined by number of protons of PPO divided number of protons of PEO, the less evident bi-exponentiality. Efforts will be done in order to explain, using a physical model, this weak dispersion in relaxation times and its bi-exponential behavior.

References:

[1] Ma J., Guo C., Tang Y., Xiang J., Chen S., Wang J. Liu H., *Journal of Colloid and Interface Science*, **2007,** 312, 390.

A Straightforward Concept for the Design of Incomplex Notch-Coil Magnet Systems for Fast-Field-Cycling NMR

S. Kruber, G. D. Farrher and E. Anoardo
Laboratorio de Relaxometría y Técnicas Especiales (LaRTE)
FaMAF – Universidad Nacional de Córdoba.
Instituto de Física Enrique Gaviola – CONICET
Córdoba – Argentina

Notch-coil magnet systems where considered between the first options for fast-field-cycling (FFC) NMR apparatus [1,2]. Newer and more sophisticated designs which perform better on the balance of the FFC NMR requirements were developed in the subsequent years [3,4]. Beside their eminent performances, it has to be mentioned that their technical feasibilities are fairly complex (fabrication processes, machining tools, etc.).

Here we discuss a new magnet design with an incomplex technical feasibility, which in addition provides the possibility to passively or actively readjust the homogeneity of the magnetic field. The design consists of cylindrical thick-wall conductors with an uniform helical cut inside. Thereby, these conductors are arranged, so that they form a notch-coil magnet system. Together with a straightforward optimization method to determine the best geometry of the magnet system, while approximating the conductor geometry as realistic as possible, the design of a notch-coil magnet system which performs efficiently on the FFC-NMR requirements is feasible. The resulting designs are compared with other existing FFC-NMR magnet designs [4,5] to show that the concept can yield competitive results.

[1] C. Grossl, F. Winter and R. Kimmich: *Optimisation of magnetic coils for NMR field-cycling experiment.* Journal of Physics E: Scientific Instruments **18** (4) (1985) 358.

[2] F. Noack: *NMR field-cycling spectroscopy: principles and applications*. Progress in NMR Spectroscopy **18** (1986) 171.

[3] K. Schweikert, R. Krieg and F. Noack: *A high-field air-cored magnet coil design for fast-field-cycling NMR*. Journal of Magnetic Resonance **78** (1) (1988) 77.

[4] O. Lips, A. Privalov, S. Dvinskikh, F. Fujara: *Magnet Design with High B_0 Homogeneity for Fast-Field-Cycling NMR Applications.* Journal of Magnetic Resonance **149** (1) (2001) 22.

[5] G. Ferrante, S. Sykora: *Technical Aspects of Fast Field Cycling*. Advances in Inorganic Chemistry, Vol. 57, Academic Press, 2005, pp. 405 - 470.

This work is being supported by FONCYT (PICT 2008 1810), CONICET (PIP 11220090100663) and Scyt-UNC from Argentina.

Phase transitions in polymeric luminescent indicators with a threshold temperature through variable-temperature SSNMR and fluorescence spectra

Francesca Martini,[1,2] Silvia Borsacchi,[1,2] Giacomo Ruggeri,[1] Andrea Pucci,[1] Marco Geppi[1,2]

[1] Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Risorgimento 35, 56126 Pisa, Italy
[2] INSTM-Consorzio Interuniversitario Nazionale per la Scienza e Tecnologia dei Materiali, Via Giusti 9, 50121 Firenze, Italy

Solid State NMR (SSNMR) is a very powerful technique for the study of polymeric materials, thanks to the possibility to observe lots of different nuclear properties, such as ^{13}C chemical shifts, ^{13}C and ^{1}H relaxation times etc., which are very sensitive to the phase and dynamic properties of polymeric domains [1].

^{1}H T_2 relaxation time has the property to increase monotonically with the degree of mobility of the system, and the fitting of the ^{1}H FID acquired under on resonance condition, i.e. low magnetic field, (FID analysis) allows to identify domains characterized by different ^{1}H T_2, and therefore by different phase and dynamic properties [2].

In this work we investigated the phase transitions occurring in polymeric films (PLA-PBS-BBS) of poly(lactic acid) (PLA) (85 wt%) and poly(1,4-butylene succinate) (PBS) containing a small amount of the chromophore 4,4'-bis(2-benzoxazolyl)stilbene (BBS) through the combination of ^{13}C CP/MAS spectra and the analysis of ^{1}H FID acquired at different temperatures. These materials showed a luminescent response under heating at about 80-90°C due to the formation of BBS aggregates [3], and the aim of this study was to get further insights into the morphological processes occurring in the polymeric matrix which could lead to BBS aggregation. The study was carried out on both the final PLA-PBS-BBS film and neat PLA in film and pellets.

The phase and dynamic properties of PLA domains were found to significantly change under heating. The occurrence of PLA cold crystallization at about 80°C was observed in the PLA-PBS-BBS, in agreement with previous DSC results [3], being a possible driving force for BBS aggregation. Interesting correlation between the increase of mobility of the amorphous PLA domains and the increase of the fluorescence emission of BBS aggregated were suggested.

Financial support by POLOPTEL project, Fondazione Cassa di Risparmio di Pisa, is acknowledged.

[1] Geppi, M.; Borsacchi, S.; Mollica, G.; Veracini, C.A. *Appl. Spectrosc. Rev.* **2009**, *44*, 1-89.

[2] Hansen, E. W.; Kristiansen, P. E.; Pedersen, N. *J. Phys. Chem. B* **1998**, *102*, 5444-5450.

[3] Pucci, A.; Signori, F.; Bizzarri, R.; Bronco, S.; Ruggeri, G.; Ciardelli, F. *J. Mater. Chem.* **2010**, *20*, 5843–5852.

Fast-field cycling NMR is sensitive to the method of cross-linking in BSA gels

Brett W. C. Kennedy [1], Lionel M. Broche [1], G. Patrick Ashcroft [2] and David J. Lurie [1]
[1]Division of Applied Medicine, [2]School of Medicine and Dentistry, University of Aberdeen, UK
www.ffc-mri.org

Introduction

In contrast to conventional nuclear magnetic resonance (NMR) experiments where a static magnetic field is applied to a sample, the applied field in field-cycled NMR is altered during the experiment. Field-cycling allows measurements, for example of spin-lattice relaxation rate (R_1), to be made as a function of the applied field. At several discrete field strengths the ^{1}H NMR and ^{14}N nuclear quadrupole resonance (NQR) frequencies coincide, allowing effective relaxation of the magnetisation from bulk water protons *via* quadrupolar ^{14}N nuclei [**1**]. Therefore, in a plot of R_1 *versus* field, 'quadrupolar peaks' are often observed at these fields.

It has been suggested that quadrupolar peaks in proteinous samples result from interactions between sufficiently-bound nitrogenous functional groups and low-mobility water protons [**2**]. Furthermore, the amplitude of the quadrupolar peak has been shown to be proportional to protein concentration [**3**]. In this study, the quadrupolar peaks of bovine serum albumin (BSA) gels formed by boiling or chemical cross-linking were examined.

Methods

BSA gels (final concentration 9% w/v) in 20.5 mM bicarbonate buffer (pH 7.3) were prepared by boiling or addition of formalin or glutaraldehyde (final concentration 12.5% w/v). Measurements of R_1 were made between 0.047–187.89 mT at 37 °C on a SMARtracer relaxometer (Stelar S.r.l., Mede, Italy). A power-law with Lorentzian-bell algorithm, derived from the literature [**3,4**], was fit to the data (Matlab 2012a, The Mathworks, Cambridge, UK; scripts developed by Lionel M. Broche, Aberdeen, UK).

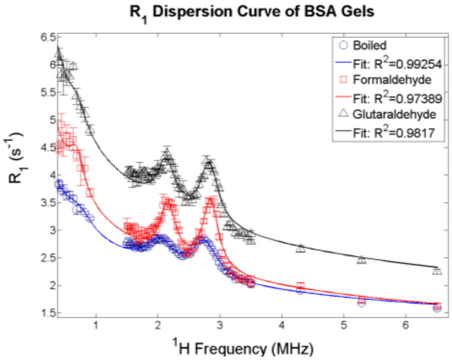


Figure 1: Dispersion curves of BSA gels generated by different cross-linking methods.

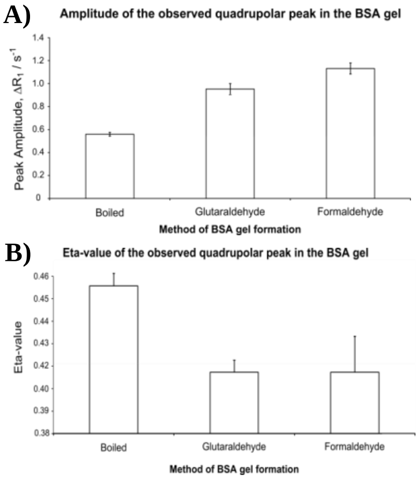


Figure 2: **A)** Amplitude and **B)** eta-value of the quadrupolar peak of cross-linked BSA gels.

Results

Dispersion curves were dependent on the method of gel formation (Figure 1). The quadrupolar peak amplitude was largest with formaldehyde (Figure 2A). The eta-value, describing the shape of the quadrupolar peaks, was similar with chemical cross-linking but larger if boiled (Figure 2B).

Discussion

Boiled BSA gels likely contain denatured protein in a network of fragments, monomers and higher aggregates [**5**] linked by various functional groups (e.g. amino, amide and sulphhydryl groups). Glutaraldehyde gels may contain BSA aggregates in a native configuration *via* the majority of free amino-groups [**6**]. Formaldehyde gels are likely cross-linked in a heterogeneous manner, involving fewer free amino-groups [**7,8**]. Therefore, quadrupolar peak amplitude and shape may be related to the macroscopic protein network, and/or the functional groups involved in gel cross-linking. These observations may be pertinent in the analysis of fixed tissue samples by field-cycled NMR, where any observed quadrupolar signals may be affected by the method of tissue fixation.

Acknowledgements

This work was supported by ARUK (grant number 19689).

References

[1]Winter, F. and Kimmich, R. (1982); 719(2), 292-298 **[2]** Sunde, E.P. and Halle, B. (2010); 203(2), 257-73 **[3]** Broche, L. M., Ismail, S. R., Booth, N.A. et al. (2012); 67(5), 1453-1457 **[4]** Korb, J-P. and Bryant, R. G. (2002); 48, 21-26 **[5]** Aoki, K., Hiramatsu, K., Kimura, K., et al. (1969); 47(4), 274-282 **[6]** Hopwood, D. (1970); 24, 50-64 **[7]** Fraenkel-Conrat, H. and Mecham, D. K. (1949); 177, 477-486 **[8]** Fraenkel-Conrat, H. and Olcott, H. S. (1948); 70(8), 2673-2684

Local spin dynamics and magnetic anisotropy in nearly monodispersed ferrite nanoparticles: an NMR-D study

L. Bordonali[1], T. Kalaivani[2,3], K. P. V. Sabareesh[1,2,3], C. Innocenti[4], E. Fantechi[4],
C. Sangregorio[4,5], M F. Casula[6], L. Lartigue[7], J. Larionova[7], Y. Guari[7], M. Corti[1,3],
P. Arosio[1,2], A. Lascialfari[1,2,3]

[1]INSTM and Department of Physics, Università di Pavia, I-27100 Pavia, Italy
[2]INSTM and Department of Physics, Università degli Studi di Milano,
via Celoria 16, I-20134Milano, Italy
[3]S3-CNR, Institute of Nanosciences, via Campi 213/A, I-41125 Modena, Italy
[4]INSTM and Department of Chemistry 'U Schiff', Università di Firenze, via della Lastruccia 3,
Sesto Fiorentino, I-50019 Firenze, Italy
[5]CNR-ISTM, via C Golgi 19, I-20133 Milano, Italy
[6]INSTM and Department of Chemical Sciences, Università di Cagliari, Cittadella Universitaria,
Monserrato, I-09042 Cagliari, Italy
[7]Institut Charles Gerhardt Montpellier, UMR 5253 CNRS-UM2, Chimie Moleculaire et
Organisation du Solide, Universite Montpellier II, Place E Bataillon, F-34095 Montpellier cedex 5,
France

We present a systematic experimental comparison of the superparamagnetic relaxation time constants of ferrite-based nanoparticles, obtained by means of dynamic magnetic measurements and ^{1}H-NMR relaxometry. Our investigation has been carried out on a broad selection of samples varying in chemical composition (Magnetite, Mn-Ferrites, Co-Ferrites), core size and employed solvents. The application of a heuristic model for the longitudinal relaxivity r_1 allowed a direct comparison between the reversal time of magnetization as seen by NMR and the results from the AC susceptibility experiments. Neel relaxation times, as measured by NMR, lie in the superparamagnetic range, as expected; a phenomenological Vogel–Fulcher law had to be applied for the AC susceptibility data analysis to recover a satisfactory agreement between NMR and AC data, since Neel's model breaks down in concentrated solutions and powders due to sizable dipolar interparticle interactions.

Key parameters obtained from the relaxivity model have been exploited to evaluate the impact of the contribution of the magnetic anisotropy to the relaxivity curves, and estimate the minimum approach distance of the bulk solvent. Indeed, the importance of this experimental validation resides in the possibility of tracking the effect of the crystal's internal anisotropy energy, dampening the low-field dispersion of r_1, with the magnetic core size of the particles. We successfully extracted the relative weights of Neel and Curie contributions (P/Q ratio) to the ^{1}H nuclear magnetization and studied their dependence on the magnetic core diameter and ion species, showing a marked decrease of the P/Q ratio as the magnetic anisotropy energy per particle increases, as a consequence of both an increased core diameter and increased magnetic anisotropy energy density.

Rapid Field-Cycling MRI using Fast Spin-Echo

P. James Ross, Lionel M. Broche, David J. Lurie
Aberdeen Biomedical Imaging Centre, University of Aberdeen, AB25 2ZD, Scotland, UK
www.ffc-mri.org

Introduction: Fast Field-Cycling MRI (FFC-MRI)[1] is an emerging technique that aims to combine the capabilities of MRI and FFC-NMR by making it possible to rapidly vary B_0 during an imaging sequence. Conventional relaxometric imaging is limited by lengthy scan times, since to estimate R_1 at least two images (i.e. IR and SR) must be acquired at each field strength. In this work we describe an adaptation of the well known Fast Spin-Echo imaging sequence[3] for FFC-MRI, named Field-Cycling Fast Spin Echo (FC-FSE) which enables relaxometric imaging in a fraction of the time that would otherwise be required.

Methods: Imaging was carried out on a home-built whole-body field-cycling imager with a 59 mT detection field[4]. The system uses a commercial console (SMIS Ltd., U.K.).

For each experiment a saturation recovery and inversion recovery image are acquired at the detection field. A single field-cycling inversion recovery image is then acquired for every evolution field of interest. R_1 is estimated at each field using a two-point method. For validation of results relaxometry was also performed on small samples using a commercial bench-top field-cycling relaxometer (SMARtracer, Stelar s.r.l., Italy).

Results: There is good agreement between the R_1 dispersion results (Figure 1) obtained using the FC-FSE sequence and those obtained using the relaxometer for a phantom consisting of crosslinked bovine serum albumin (BSA). FC-FSE images from a volunteer's thighs using an echo train length of 4 (Figure 2) exhibit virtually no artifacts from field-instability. A dispersion curve (Figure 3) obtained from the outlined region-of-interest in muscle shows pronounced quadrupole peaks, arising due to ^{1}H-^{14}N cross-relaxation in immobile protein molecules within the muscle. The total scan time was ~30 minutes compared to the 4 hours that would have been required using conventional relaxometric imaging.

Conclusions: This work has demonstrated that relaxometric imaging can be performed up to 8 times faster relative to the basic procedure, with virtually no sacrifice in the accuracy of R_1 determination. This paves the way for clinical relaxometric studies with acceptable scan times.

Acknowledgements: The author acknowledges funding from the EPSRC through the Centre for Doctoral Training in Integrated Magnetic Resonance.

References

[1] Lurie, D.J. *et al.*, *C.R. Physique* 11, 136-148, 2010.
[2] Pine, K.J. *et al.*, *Magn Reson Med*, 63, 1698-1702, 2010.
[3] Hennig, J. *et al.*, *Magn Reson Med*, 3, 823-833, 1986.
[4] Lurie, D.J. *et al.*, *Phys Med Biol*, 43, 1877-1886, 1998.

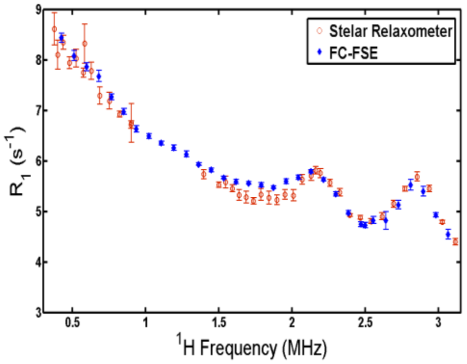


Figure 1: Dispersion curves for a phantom of cross-linked BSA obtained using the FC-FSE sequence (solid dots) show good agreement with results from a commercial relaxometer (open circles).

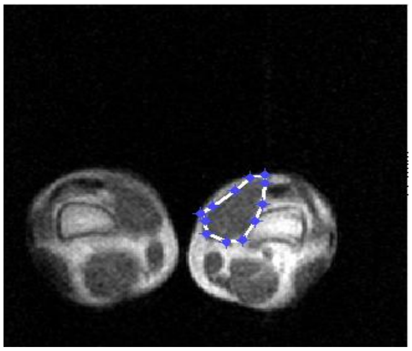


Figure 2: Image of a volunteer's thighs obtained using the FC-FSE sequence with a speed up factor of 4. RoI delineates muscle, from which a dispersion curve was obtained.

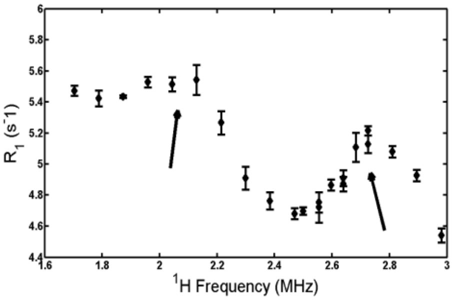


Figure 3: R_1 dispersion curve for the RoI shown in Figure 2. The quadrupole peaks arising due to immobile proteins in muscle are clearly visible (see arrows).

Towards a quality framework for localized FC relaxometry

K. J. Pine, D. J. Lurie
Aberdeen Biomedical Imaging Centre, University of Aberdeen, Scotland.
http://www.ffc-mri.org

Quality assurance (QA) concerns the accurate and repeatable production of data that meets the requirements of the user. In MRI, quality control checks are well established and ubiquitous, especially in the clinical environment where QA is mandatory for the diagnosis and management of disease. Complete guidelines for routine checks have been produced by various organisations, most notably by the American College of Radiology (ACR), American Association of Physicists in Medicine (AAPM), and the Institute of Physics and Engineering in Medicine (IPEM)[1-3]. However, despite the relevance of quality in MR relaxometry to increasingly critical applications in industry and research (including biomedicine) no equivalent consensus has been achieved. Apart from assuring data accuracy from any one experiment, QA is essential for multi-site studies and particularly useful for identifying degradation in the performance of equipment over time.

While certain routine QA tests within the scope of MRI are equally important for localized relaxometry (e.g. SNR, geometric accuracy), further application-specific quality checks can be postulated depending on the approach. The two vastly differing approaches to localized T_1 dispersion measurement in heterogeneous samples are either to acquire images following evolution at a chosen magnetic field strength and combine them to produce a calculated T_1 map, or to apply single-voxel techniques to acquire signals from a volume of interest (VOI) directly. To assure accuracy, test results should be compared against 'gold standard' methods (e.g. for T_1, flip-angle-invariant inversion-recovery with a small uniform sample and long TR). Action levels should be set such that neither deficiencies in accuracy nor instrumental variance exceed the inherent variation expected between samples and subjects.

For biomedical applications, two befitting phantoms are (a) a sphere incorporating a hollow cylinder through which a smaller sample slides (for localization profiling), and (b), a sphere containing thin-walled cubes of various sizes. All vessels are then filled with stable, inert substances with bio-equivalent relaxation parameters. Suggested checks using (b) include:

- For image-based localized relaxometry, at various field strengths and for each cube in (b), pixel counts correctly classified within actual T_1 ±10%; with those incorrectly classified broken down into internal and edge pixel counts.
- For spectroscopy-style localized relaxometry, contamination quantified by measuring T_1 within a voxel that is coincident with a cube in (b).
- For both, routine checks of accuracy and repeatability across the entire field range.

References
[1] American College of Radiology, *MRI Quality Control Manual*, 2004.
[2] American Association of Physicists in Medicine, *AAPM Report No. 100*, 2010.
[3] Institute of Physics and Engineering in Medicine, *Report No. 80*, 1999.

NMR Relaxation-Viscosity Relationship in PEO Melts.

Jacques Leblond[1], Marc Fleury[2], Benjamin Nicot[1,2], Madeleine Djabourov[1], Salvatore. Bubici[3]

[1] Laboratoire de Physique Thermique, ESPCI, Paris, France
[2] IFP Energies nouvelles, Rueil-Malmaison, France
[3] Stelar Srl, Mede, Italy

For many viscous liquids, proton NMR relaxation techniques can be used to estimate viscosity. However, the usual semi-empirical correlation $T_2 \propto \eta^{-1}$ fails in polymer melts due to the specific molecular dynamics of these complex fluids. We present a combined viscosity-NMR study on a model system, a melt of polyethylene oxide polymers of increasing molecular weights M ranging from 0.06 M_c to 12 M_c relative to the critical mass above which entanglements occur. On these polymers, we measured viscosity, NMR self-diffusion, $T_{1\rho}$, T_1 dispersion and T_2 at 23.7 MHz.

For $M > M_c$, we show that the rheology of these liquids behaves as expected from the dynamics of entangled linear polymers. Besides viscosity, proton longitudinal and transversal relaxation times clearly display the entanglement transition at $M_c \sim 4000$ g/mol. The expected power laws are verified both for viscosity and diffusivity versus molecular weight. However, temperature and viscosity dependences of the transverse relaxation time T_2 are different from simple liquids and we established a new relationship combining T_1 and T_2 to predict viscosity at a Larmor frequency of 23.7 MHz (Figure 1).

The new viscosity relationship can be explained qualitatively from the calculation of the correlation time function together with the reptation theory. For the calculation of the correlation time function, the intra-molecular interaction term is deduced from literature (fast motion of the CH_2 ethyl group and slower motion of the skeleton bonds). The inter-molecular interaction term is the most important and gives the dependence with the molecular weight. It has been calculated using the formulation proposed by Kimmich and Fatkullin (1998). With a unique set of parameters, we were able to reproduce NMR dispersion data collected at various frequencies (Figure 2). An important consequence of the theory is that the new viscosity relationship is only valid in a narrow frequency bandwidth around 23 MHz.

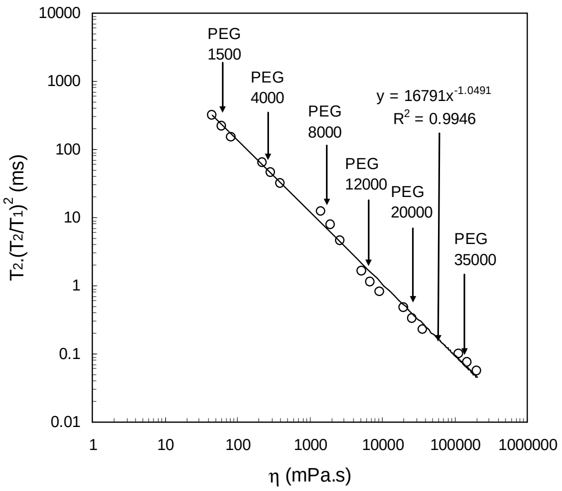


Figure 1: Measured NMR relaxation – viscosity relationship for PEO melts at 23.7 MHz (T>60°C).

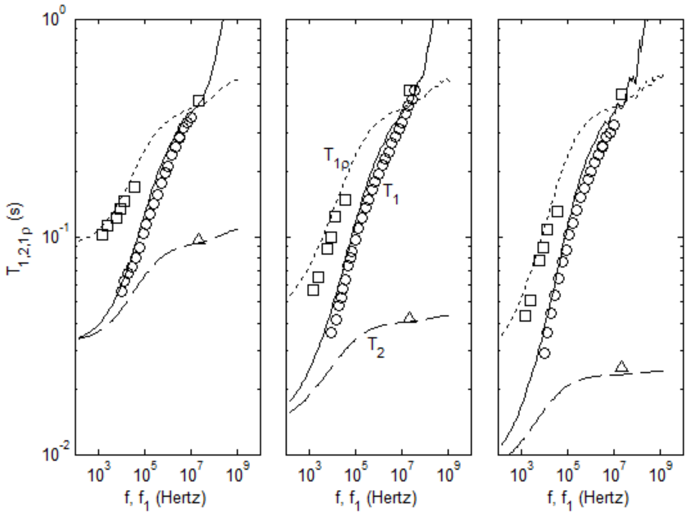


Figure 2: Dispersion data and comparison to model for 3 molecular weights (from left to right, M_w = 8433, 24584 and 41872 g/mole)

Reference: Kimmich R., Fatkullin N., Seitter R.-O. and Gille K., *J. Chem. Phys.*, 108, 5, 1 (1998)

Slow conformational dynamics of myoglobin as seen by internal water molecules

<u>Shuji Kaieda</u> and Bertil Halle
Biophysical Chemistry, Lund University, Sweden

Ever since its atomic-resolution structure was determined in the 1950s, myoglobin (Mb) has served as a prototype for biophysical studies of protein dynamics. The main function of Mb is to transport oxygen in muscle tissues. O_2, as well as other diatomic molecules like CO and NO, interacts with the buried haem iron, but the pathway along which the ligand migrates to and from this binding site is not apparent from the static mean structure. Ligand entry and exit must therefore be controlled by conformational fluctuations, but the details of this "gating" process have not been firmly established. To shed new light on conformationally gated ligand migration in the haemoprotein, we have used the water magnetic relaxation dispersion (MRD) method on freely tumbling and immobilized Mb. Since the exchange of internal water molecules is also conformationally gated, water MRD can be used to probe conformational dynamics. In particular, when the protein is rotationally immobilized by chemical cross-links, the MRD method can access the elusive nanosecond – microsecond time scale.[1] Previous crystallography and MD simulation studies indicate at least partial water occupancy in some of the internal cavities of Mb.[2,3] Most of these cavities have been implicated in ligand migration.[4] Our MRD results show that Mb contains *ca.* four internal water molecules with exchange time of ~ 5 μs. The temperature dependence of the MRD data suggests that conformational gating of water exchange is rate-limited by entropy reduction rather than disruption of hydrogen bonds. The results suggest that the water molecules are distributed over the cavities in Mb and that they exchange with external solvent via the same microsecond gating mechanism that controls ligand access to the haem.

1. E. Persson & B. Halle, *J. Am. Chem. Soc.* **130**, 1774–1787 (2008).
2. K. Chu et al., *Nature* **403**, 921–923 (2000).
3. M. A. Scorciapino *et al.*, *J. Am. Chem. Soc.* **132**, 5156–5163 (20010).
4. J. Z. Ruscio *et al.*, *Pro. Natl. Acad. Sci. USA* **105**, 9204–9209 (2000).

^{1}H relaxation in solutions of superparamagnetic nanoparticles.

A. Korpala[1], D. Kruk[2,3], S. Mehdizadeh Taheri[4], S. Förster[4], E.A. Rössler[3]

[1]Institute of Physics, Jagiellonian University, Reymonta 4, 30-059 Krakow, Poland
[2]University of Warmia & Mazury in Olsztyn, Faculty of Mathematics & Computer Science,
Sloneczna 54, PL-10710 Olsztyn, Poland
[3]Universität Bayreuth, Experimentalphysik II, 95440 Bayreuth, Germany
[4]Universität Bayreuth, Department of Physical Chemistry I, 95440 Bayreuth, Germany

^{1}H spin-lattice relaxation dispersion profiles for toluene solutions of superparamagnetic nanoparticles have been collected in temperature range of 257K - 298K. The nanoparticles consist of iron oxide core coated with polyisoprene shell. ^{1}H spin-lattice relaxation in solutions of nanoparticles of different core size (5nm, 6.5nm, 9nm,14nm), core shape (spheric and cubic) and thickness of the polymer shell (from 2nm to 4nm) has been measured.

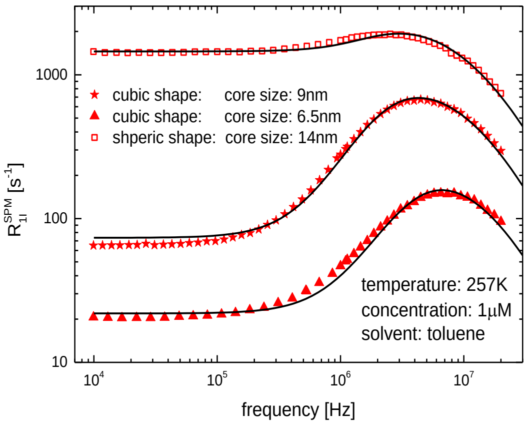


Figure 1: Experimental relaxation dispersion profiles for 1μM toluene solutions of different superparamagnetic nanoparticles at 257K.

The observed features of ^{1}H spin-lattice relaxation dispersion are a combined effect of magnetic properties of the nanoparticles (electron spin, anisotropy energy and electronic relaxation rates) and dynamical properties of the solvent (translational diffusion).

The ^{1}H spin-lattice relaxation is caused by dipole-dipole interactions between magnetic moments of the proton and of the nanoparticle. The dipolar interaction fluctuates in time due to translational dynamics of the participating molecules and relaxation of the electronic spin of the nanoparticle.

The theory of ^{1}H relaxation induced by dipolar coupling to superparamagnetic nanoparticles including the both sources of fluctuations of the dipolar interactions has been proposed by P. Gillis *et al.* [1]. As far as the translation diffusion is concerned, the theory uses force-free-hard-sphere diffusion model according to which the interacting particles are treated as hard spheres undergoing Fick diffusion [2]. This description (with independently obtained translation diffusion coefficients of the solvents [3]) has been applied to the large set of experimental data (illustrative fits are shown in Figure 1). The analysis gives the effective electronic spin of the nanoparticle *S* and the electronic relaxation times τ_{S1} and τ_{S2}. The electronic spin stays constant with changing temperature. The electronic relaxation times τ_{S1} and τ_{S2} (referred as longitudinal and transverse relaxation time respectively) are weakly dependent on temperature or in some cases remain unchanged and τ_{S2} is shorter than τ_{S1} almost by an order of magnitude. The overall picture of the proton relaxation processes and the obtained parameters are consistent as it will be presented and discussed in details.

Acknowledgments

The project was funded by National Science Center, DEC-2012/05/N/ST3/03174.

References:

1. P. Gillis, A. Roch, R.A. Brooks, J. Magn. Reson. **137**, 402-407 (1999).
2. L. P. Hwang, and J. H. Freed, J. Chem. Phys. **63**, 4017 (1975).
3. G. Hinze, H. Sillescu, J. Chem. Phys. **104**, 314 (1996).

Measurement of the bending elastic modulus in unilamellar vesicles membranes by fast field cycling NMR relaxometry

Josefina Perlo, Gabriela Dominguez y Esteban Anoardo
Laboratorio de Relaxometría y Técnicas Especiales (LaRTE)
Famaf – Universidad Nacional de Córdoba.
Instituto de Física Enrique Gaviola – CONICET
Córdoba – Argentina

Lipid vesicles can be used as idealized model systems of real biomembranes. They have attracted much interest in biophysical research, particularly for the study of different processes related to the viscoelastic and mechanical properties of the membrane. Different experimental techniques are implemented for the analysis of membrane elasticity. However, easy available benchtop instruments (generally based on optical microscopy) are only useful for giant unilamellar vesicles. On the other hand, successful techniques used in large/small (LUV/SUV) unilamellar vesicles turned to be based on large scale instrumentation like conventional NMR [1] or neutron spin-echo [2]. It is worth to mention the atomic force microscopy (AFM) as an exception, allowing the study of mechanical properties in LUV with small scale instrumentation, although more invasive than the previous [3]. Low cost reliable benchtop instruments allowing precise determination of the bending elastic modulus and/or other viscoelastic parameters in LUVs and SUVs are thus very much attractive within this picture.

Previous studies of unilamellar liposomes using proton NMR field-cycling relaxometry suggested that the collective nature of the lipid dynamics should be considered for a consistent interpretation of the measured relaxation disperssions [4,5]. Later, it turned to be clear that relevant information about the elastic properties of the membrane can be extracted from the collective dynamics contribution within a restricted Larmor frequency-range [6]. In the ideal situation, this should be done in a small benchtop dedicated instrument. To test this concept, the proton spin-lattice relaxation rate (R_1) was scanned within a restricted Larmor frequency range (typically 200kHz to 2MHz), but using a standard instrument with degraded magnet homogeneity (lower than 350ppm/cm^3), thus simulating extreme conditions for the relaxometry experiment. The potentiality of *NMR relaxometry at inhomogeneous field conditions* is analyzed within this picture and for this particular case, i.e., low magnetic field homogeneity, proton diluted sample & low signal to noise ratio.

[1]- G. Althoff, O. Stauch, M. Vilfan, D. Frezzato, G. Moro, P. Hauser, R. Schubert and G. Kothe, J. Phys. Chem. B 106, 5517 (2002).

[2]- Z. Yi, M. Nagao and D. P. Bossev, J. Phys.: Condens. Matter DOI: 10.1088/0953-8984/21/15/155104 (2009).

[3]- N. Delmore and A. Fery, *Phys. Rev. E* DOI: 10.1103/PhysRevE.74.030901 (2006).

[4]- C. Meledandri, J. Perlo, E. Farrher, D. Brougham and E. Anoardo, J. Chem. Phys. B 113, 15532 (2009).

[5]- J. Perlo, C. Meledandri, E. Anoardo and D. Brougham, J. Chem. Phys. B 115, 3444 (2011).

[6]- Josefina Perlo, PhD. Thesis. Universidad Nacional de Córdoba (2011).

Cryogen-Free Superconducting Magnet Design for NMR

Dr Donald Pooke, Jacob de Feijter, Mike Mallet - HTS-110 Ltd
Salvatore Bubici - Stelar Srl

For NMR applications, fields above 1.5 tesla are only practical with superconducting magnets. It has long been thought that the challenges of vibration, stability, and robustness made traditional superconducting magnets impractical for industrial NMR applications. We report the development and successful operation of cryogen-free High Temperature Superconducting (HTS) magnets for NMR operating at 4.7 T (200MHz) and 3 T (125MHz) that address these issues.

To overcome the burden of helium and nitrogen refills, cryogen-free magnets are attractive for materials research applications such as beamline magnets and hard disk drive materials research. The availability of high capacity HTS conductors has made development of magnets suitable for NMR application possible. NMR systems using self-shielded HTS-NMR magnets have now accumulated several years of successful operation in five different countries. In particular the 3T system for relaxometry provides a vital tool in the development of new contrast agents for magnetic resonance imaging.

Fig. 1 200MHz mobile NMR system

Fig. 2 3T relaxometry magnet

Magnets were manufactured using BSSCO superconductors and exhibit homogeneity of 0.25 ppm before electric shimming for FT-NMR applications and 15 ppm for variable field relaxometry application. High capacity cryocoolers enable rigid coil supports to be used whilst maintaining operating temperatures at 15-30 K, where the wire performance can sustain the desired high fields. HTS magnets do not operate in a persistent-current mode, special high stability power supplies are used to operate the magnet at any desired field strength.

These magnets will form the basis of a new class of NMR instrument for industrial environments, enabling innovative solutions that combine variable field relaxometry with FT-NMR. Future developments will include higher fields for both variable field relaxometry and FT-NMR.

Fast Field Cycling Relaxometry: Moving from Research towards Industrial Applications

[a] Salvatore Bubici, [a] Rebecca Steele, [a] Gianni Ferrante

[a] Stelar srl, Via E. Fermi 4, 27035 Mede (PV); E-mail: ferrante@stelar.it

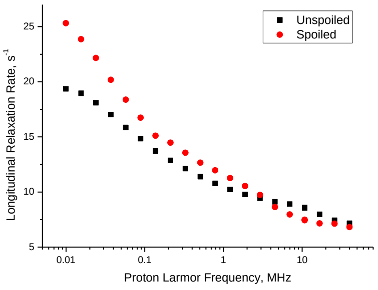
Fast Field Cycling Relaxometry (FFCR) is a NMR technique used to determine the longitudinal relaxation time (T_1) over a range of B_0-fields spanning about six decades, from about 10^{-6} Tesla up to ~ 1 Tesla, or 3 Tesla, without varying the frequency of the spectrometer [1,2]. The main information that can be extracted from nuclear magnetic resonance dispersion (NMRD) curves, T_1 or R_1=1/ T_1 versus the Larmor frequency ω ($\omega=\gamma B_0$, γ is the gyromagnetic ratio), is that concerning molecular motions characterized by temperature-activated frequencies and described by means of the spectral density J(ω).

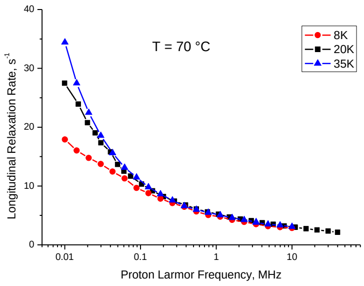
The data obtained may, therefore, be correlated directly to the physical/chemical proprieties of complex materials. The use of radio frequency allows the easy penetration of most materials, thus permitting, the exploration of slow dynamics which are often difficult to study in heterogeneous materials (including liquids, solids and gels) by other spectroscopic methods.

Furthermore, the benefit of exploring the range of low Larmor frequencies is to detect typical relaxation features associated with molecular processes characterized by very long correlation times, such as molecular surface dynamics and collective effects. The FFCR technique shows greatest potential where the characteristics of a sample depend intimately on the molecular dynamics and / or the state of aggregation.

Herein we show developments in the FFCR method and discuss some contributions of NMRD profiles towards the fundamental understanding of classes of materials and phenomena predicted by theoretical models. We show in practice how relaxation experiments can be applied for qualitative structural diagnostics in solutions, quantitative structural determinations, recognitions of weak intermolecular interactions and studies of molecular mobility. The findings that have been established more recently are noteworthy for their potential industrial use in quality assessment and off-line process monitoring.

FFCR is a technique which has remained as a research tool and practically unexploited in industry, and thus an important challenge is the transfer of this important technique towards more industrial applications.





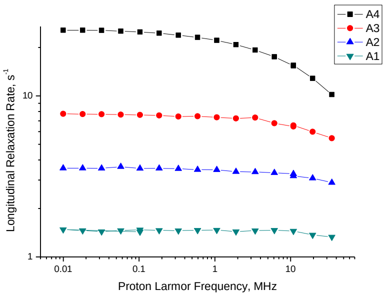


Figure 1. The FFCR NMR method is able to differentiate between unspoiled and spoiled foods.

Figure 2. FFC ^{1}H NMR was applied to study the spectrum of re-orientational and diffusional dynamics in melts of polyethylene glycol (PEG) with different molecular weights (8000, 20000 and 35000).

Figure 3. FFC ^{1}H NMR was applied to study the transport properties and molecular motions of electrolyte solutions including ionic liquids as a function of salt concentration. These results could be used to find improved electrolytes for battery systems.

References
[1] Ferrante and Sykora Adv. *Inorg. Chem*. Vol. 57, p. 405.
[2] R. Kimmich and E. Anoardo *Progress in Nuclear Magnetic Resonance Spectroscopy* 44 (2004) 257-320.

Method for NMR Relaxometry on Hetero-nuclei at Very Low Fields

[1] Salvatore Bubici, [1] Rebecca Steele, [1] Gianni Ferrante

[1]Stelarsrl, Via E. Fermi, 4 27035 Mede (PV); E-mail: ferrante@stelar.it

Up to now most applications of NMR relaxometry involved the study of protons due to the low sensitivity of other nuclei (hetero-nuclei) and to technical difficulties mainly related to signal to noise ratio (SNR) problems caused by the low acquisition frequency.

The technique of Fast Field Cycling permits the direct observation of hetero-nuclei with low receptivity and detectability, due to the fact that the magnetic field strength can be switched without the need to vary the frequency of the spectrometer.

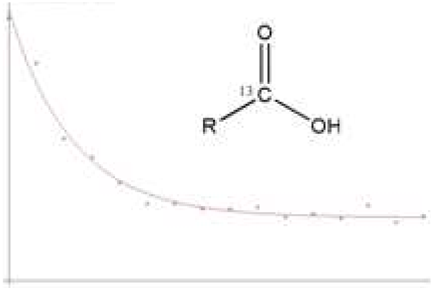
Fast Field Cycling Relaxometry (FFCR) is a NMR technique used to measure the spin relaxation curves over a range of B_0-fields, spanning about six decades, from about 10^{-6}Tesla up to ~ 1 Tesla or 3 Tesla, thus information concerning molecular motions characterized by temperature-activated frequencies and described by means of spectral density J(ω), can be obtained directly.

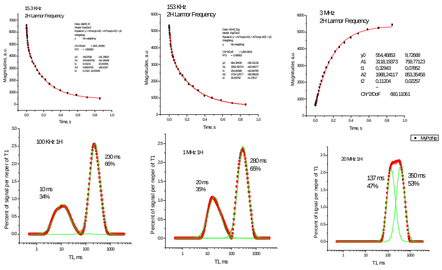
This multi-nuclear approach expands the potential of Fast Field Cycling NMR applications and allows exploration of the field dependence of the spin-lattice relaxation time T_1 of important hetero-nuclei within substances, especially at low Larmor frequencies (down to 10 ^{1}H kHz), where other conventional NMR experiments present severe signal-to-noise (S/N) ratio degradation.

The FFCR technique allows investigation of the content and /or the ability to characterize compounds containing important NMR-sensitive nuclei, such as ^{2}H, ^{7}Li, ^{13}C, ^{19}F, ^{31}P, ^{23}Na.The presence of such nuclei in a limited number of positions can be explored, therefore providing important structural information.

The possibility of measuring nuclear spin relaxation, on nuclei other than ^{1}H, over a wide range of frequencies presents a new advance in the possible applications of TD-NMR and the possibility for new channels of research.

Herein we show the applicability of FFCR for the acquisition of the longitudinal relaxation rate ($R_1 = 1/T_1$) as a function of the applied magnetic field strength (as called Nuclear Magnetic Resonance Dispersion or "NMRD") of some important hetero-nuclei.





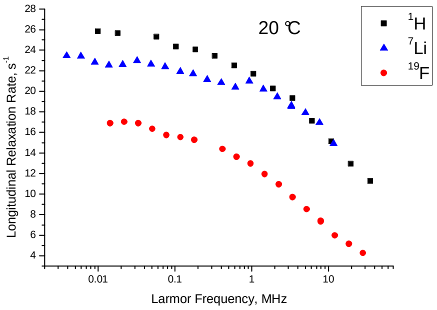


Figure 1.Longitudinal decay curve,obtained by a ^{13}C NMR signal of enriched samples, at 2.35 mT (0.1 ^{1}H MHz) and -120 ℃ of a carboxylic acid.

Figure 2.Longitudinal relaxation data at the three different fields (0.0023 T, 0.023 T and 0.5 T) on ^{2}H and relative T_1distribution in terms of Laplace Inverse Transform of fuel cell membranes, measured directly on solid sample.

Figure 3.NMRD profiles on three different nuclei (^{1}H, ^{19}F and ^{7}Li) belonging to the same sample of an electrolyte solution for a battery system.

Authentication of medicines by Nuclear Quadrupolar Resonance (NQR) Analysis;

A portable system for non-destructive control of packaged pharmaceutical products

Gianni Ferrante†, Riccardo Cernuschi†, Roberto Rolfi†, Riccardo Gatti†

Jamie Barras*, Georgia Kyriakidou*, John Alec Sydney Smith*, Kaspar Althoefer*

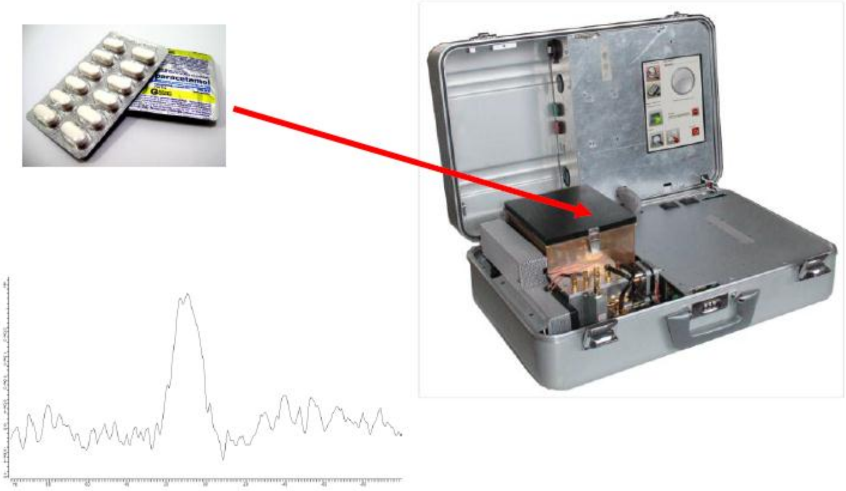
†Stelar s.r.l., Via Enrico Fermi 4, Mede (PV), Italy;

* King's College London, UK

Counterfeit and substandard medicines constitute a serious threat to public health, for example the use of substandard medicines can lead to therapies failing, and the emergence of medicine-resistant forms of infectious agents. This work aimed to develop a robust, economical and portable Quadrupole Resonance (QR) device for the non-invasive, non-destructive authentication of packaged pharmaceutical products, particularly bottles and blister packs [1], [2], [3], [4].

The system gives the operator an answer in a few seconds to a few minutes depending on the medicine or quantity.

The instrumental concepts and methods as well as real data will be presented in the poster.



Paracetamol authentication: 1 Box of 16 pills /1000 mg

[1] J. Barras, K. Althoefer, M. D. Rowe, I. J. Poplett, and J. a. S. Smith, "The Emerging Field of Medicines Authentication by Nuclear Quadrupole Resonance Spectroscopy," *Applied Magnetic Resonance*, Mar. 2012.

[2] E. Balchin, D. J. Malcolme-Lawes, I. J. F. Poplett, M. D. Rowe, J. a S. Smith, G. E. S. Pearce, and S. a C. Wren, "Potential of nuclear quadrupole resonance in pharmaceutical analysis," *Analytical chemistry*, vol. 77, no. 13, pp. 3925–30, Jul. 2005.

[3] J. A. S. Smith, "Nuclear quadrupole interactions in solids," *Chemical Society Reviews*, vol. 15, no. 2, p. 225, 1986.

[4] J. Barras, D. Murnane, K. Althoefer, S. Assi, M. D. Rowe, I. J. F. Poplett, G. Kyriakidou, and J. A. S. Smith, "Nitrogen-14 Nuclear Quadrupole Resonance Spectroscopy: A Promising Analytical Methodology for Medicines Authentication and Counterfeit Antimalarial Analysis," *Analytical chemistry*, Feb. 2013.

R-ELISA: A quantitative relaxometric version of the ELISA test for the measurement of cell surface biomarkers based on the water proton T_1 measurements.

Alberti Diego, Van't Erve Mark, Stefania Rachele, Ruggiero Maria Rosaria, Baroni Simona, Geninatti Crich Simonetta, Aime Silvio
University of Turin, Department of Molecular Biotechnology and Health Sciences - Turin, Italy

Introduction

Quantitative measurement of marker expression in diseased cells is still a topic of considerable interest and different methodologies are currently under intense scrutiny. Our work aims at developing an *in vitro* method based on the release of paramagnetic species from relaxometrically "silent" liposomes operated by the action of a Phospholipase A_2 (PLA_2) previously targeted to the epitope of interest. The release of the paramagnetic species is proportional to the number of PLA_2 bound to the cell outer surface. The released paramagnetic species causes an increase of the longitudinal water proton relaxation rate. Thus the quantification of the epitopes of interest relies on the amplification effect associated to the release of the paramagnetic payload from the liposomes operated by the action of the targeted phospholipase. The measure of water proton T_1 is a well established methodology and can be carried out on any NMR instrument. Multiple samples can be simultaneously measured by acquiring T_1-weighted MR images by extrapolating T_1 values from the observed signal intensity values.

Methods

Stable liposomes were prepared using the following lipid composition: 95% DSPC, 5% DSPE-PEG 2000. Their inner aqueous cavity contains a Gd-HPDO3A solution (200mM). The used phospholipid formulation yielded systems characterized by a very low water exchange rate (relaxometrically "silent" liposomes). PLA_2 was conjugated to folic acid residue through a PEG 3000 linker (folate-PLA_2). IGROV and Hela cells with different folate receptor (FR) expression have been incubated with the folate-PLA_2. After washing out of the unbound enzyme, aliquots of "silent" liposome were added to the cells. Enzyme induced liposome destabilization has been measured by relaxometry at 0.5T (Stelar Spinmaster) and at 1 T (Aspect M2).

Results

Gd-loaded "silent" liposome suspension yielded a stable, low relaxivity of $0.6mM^{-1}s^{-1}$.Upon adding PLA_2 (1.5uM) to this suspension, the observed relaxivity increases to $4.2mM^{-1}s^{-1}$ in ca. 40h. The attained value corresponds to the known relaxivity of free Gd-HPDO3A. Two millions IGROV cells were incubated in the presence of folate-PLA_2 for 1h. After washing, the amount of the enzyme that remained bound to cells was assessed by adding Gd-loaded "silent" liposomes for 20h. The observed relaxation rate increased from $0.55s^{-1}$ to $1.4s^{-1.}$ On the basis of this result it was possible to estimate the number of FR expressed by the different ovarian cancer cell lines.

Conclusions

R-ELISA assay can detect in cell suspension nM receptor concentrations. Its sensitivity can be further improved using more efficient contrast agents (i.e. Mn^{2+} ions) inserted the inner aqueous cavity of "silent" liposomes.