

Communication

Simultaneous measurement of D and T_2 using the distant dipolar field

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Abstract

The presence of long-range dipolar fields in liquids is known to introduce a non-linear term in the Bloch–Torrey equations which is responsible for many interesting effects in nuclear magnetic resonance as well as in magnetic resonance imaging. We show here, for the first time, that the diffusion coefficient D and the spin–spin relaxation time T_2 can be obtained simultaneously from the time evolution profile of the long-range dipolar field refocused signal. In a COSY Revamped by Z-asymmetric Echo Detection sequence, the analytical first-order approximation solution of the Bloch–Torrey equations modified to include the effect of the distant dipolar field is used to demonstrate the technique in an experiment using doped water.

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1. Introduction

The diffusion-attenuated signal refocused by the presence of long-range nuclear dipolar interactions in liquids has many interesting properties. Recently, diffusion measurements free from external motion artifacts [1] and diffusion–attenuation in the presence of the distant dipolar field (DDF) have been reported in the literature [2–5]. In the prototype CRAZED [6] sequence (diagrammed in Fig. 1) the evolution of intermolecular multiple quantum coherences (iMQCs) during the evolution time t_1 has been shown to make the signal sensitive to susceptibility variations, diffusion, and transverse relaxation mechanisms in a way that depends on the ratio n of the area under the gradient pulses utilized to create the DDF [7,8]. Remarkably, the sensitivity to diffusion occurs not only during the evolution time t_1 but also during the detection interval t_2 . Furthermore, the signal dependence can be described analytically only in limited regimes [3–5] and a complete solution addressing the

diffusion contribution to the NMR signal in the presence of the DDF resorts to numerical calculations [9].

In this communication we show for the first time, both theoretically and experimentally, the possibility of obtaining both the diffusion constant D and the transverse relaxation time T_2 in a single experiment setup using the signal refocused by the distant dipolar field. The solution of the Bloch–Torrey equations including the DDF in a first-order perturbation approximation [5] is utilized to analyze the data. To demonstrate the technique, the signal evolution of doped water for the case $n = 2$, associated with the intermolecular double-quantum coherences (iDQCs), is investigated at a 9.4 T polarizing field. The data obtained from the signal temporal evolution provide values for D and T_2 in agreement with data obtained by conventional techniques.

2. Theory

The detection of iMQCs in liquids is based on the idea that the existence of a modulation helix in the magnetization can break the angular symmetry of the dipolar interaction and recover the long-range part of the motionally

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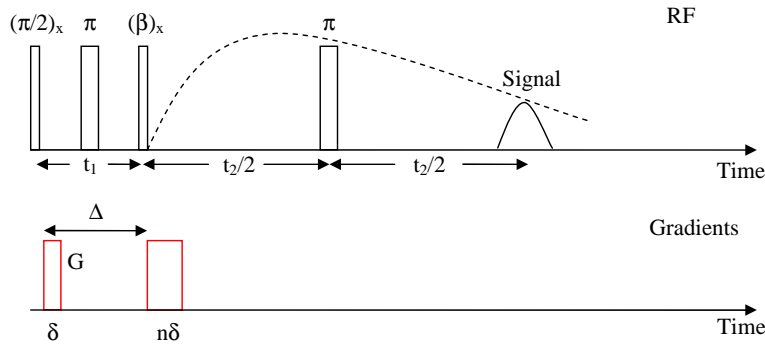


Fig. 1. Gradient and radio frequency pulses in the CRAZED sequence. The dashed line is the envelop of the signal echo-peaks obtained by varying t_2 .

averaged dipolar field among the spins in separate molecules. This long-range dipolar field is responsible for converting the iMQCs into observable signal. The theoretical framework for evaluating the detected signal follows two conceptually different views: the quantum and the classical approach, which have proven to produce the same results at least for non-confining geometries [10]. The classical approach, where the effect of the dipolar field interactions are considered, via a mean-field theory, as a non-linear additional term in the Bloch–Torrey equations [11] is commonly adopted since it offers a straightforward approach to incorporating diffusion effects.

Since the pioneering work of Robyr and Bowtell [12], the analytical solution available for the role of diffusion during the acquisition period has been limited to $t_2 \ll \tau_d$ or to a regime where the effect of the diffusion signal-attenuation is much stronger than the recovering caused by the dipolar field [3–5]. These strengths can be quantified in time by two parameters: the diffusion-attenuation characteristic time $1/Dk^2$ and the dipolar characteristic time $\tau_d = 1/\mu_0\gamma M_0$, respectively. μ_0 is the vacuum permeability, γ is the gyromagnetic ratio of the spin-bearing nucleus, M_0 is the equilibrium magnetization density, and D the diffusion coefficient, $k = \gamma G\delta$ denotes the wave vector of spatial modulation magnetization caused by the magnetic field gradient, G is the gradient pulse intensity with duration δ .

Fig. 1 shows schematically a CRAZED pulse sequence composed of two radio-frequency (RF) pulses $\pi/2$ and β and modified to include π pulses during the evolution period t_1 and the acquisition echo-time period t_2 to refocus any evolution in the presence of magnetic field inhomogeneities while retaining the dipolar interactions. The first and second gradient pulses have the same amplitude G and widths δ and $n\delta$, where n is an integer. Assuming the polarizing field along the z -axis, one is interested in the time evolution of the transverse magnetization density $M^+ \equiv M_x + iM_y$. In a regime where the first-order approximation for the effect of the DDF in the presence of diffusion is valid, an analytical expression can be obtained for the NMR signal [5]. This regime comprises experiments where the diffusion contribution to the signal is significant compared with that of the DDF. This is a condition naturally matched in the type of experiment described here. For $n = 2$, the DDF

refocused signal in this limit, including the effects of relaxation, is given by [3,4]

$$\overline{M^+(t_1, t_2)} = \frac{M_0}{2} \sin^2 \frac{\beta}{2} \times \frac{e^{-[Dk^2 + 1/T_2]t_1}}{[2Dk^2 + 1/T_1]\tau'_d} \left[e^{-t_2/T_2} (1 - e^{-[2Dk^2 + 1/T_1]t_2}) \right]. \quad (1)$$

We have defined $\tau'_d \equiv \tau_d(e^{[Dk^2 + 1/T_2]t_1})/\sin\beta\Delta_s$ as an effective dipolar time and $\Delta_s = \frac{1}{2}(3\cos^2\theta - 1)$ is the dipolar angular dependence. θ is the angle between the modulation gradient G and the polarizing field B_0 . T_1 and T_2 are, respectively, the spin–lattice and spin–spin relaxation times and β is the third RF pulse in the CRAZED sequence indicated in Fig. 1. The overline means an average over the whole sample. It can be noticed in Eq. (1) that for t_2 values where the exponential argument $(2Dk^2 + 1/T_1)t_2 \gg 1$, the remaining signal-decay comes only from the T_2 relaxation contribution. This key characteristic permits us to obtain the T_2 relaxation time without any decaying effect caused by diffusion. Experimentally, in a log-normal plot of the normalized signal versus t_2 the slope of the linear decay for $t_2 \gg 1/(2Dk^2 + 1/T_1)$ permits us to obtain the value of T_2 directly. When the long-time decay is not linear there is an indication that Eq. (1) is not valid in that experimental regime or extra effects such as radiation damping must be considered [3].

The time t_2^* where the maximum signal-amplitude occurs can be easily predicted from $\frac{\partial \overline{M^+}}{\partial t_2}$ in Eq. (1) yielding $t_2^* = (\ln[T_2(2Dk^2 + 1/T_1 + 1/T_2)]) / (2Dk^2 + 1/T_1)$. If the regime $2Dk^2 \gg 1/T_1$ is valid, the following relation can be established:

$$\exp[2Dk^2 t_2^*] = T_2(2Dk^2 + 1/T_2). \quad (2)$$

The left side and the right side of this expression are monotonically growing functions. Plotting the two functions separately for an interval of values for the diffusion coefficients ($D > 0$) makes the point of intersection of the two curves determines the value for D .

Experimentally, D can be obtained using a single gradient intensity G , which makes the DDF approach presented here drastically different from the pulsed gradient spin-echo approach, where conventionally the intensities of

the gradients used are varied to obtain the diffusion–dispersion curve [2]. Eq. (1) is limited to the first-order approximation regime obtained by a time-dependent perturbative expansion of the distant dipolar field contribution in the modified Bloch–Torrey equations [5]. For the case $n = 2$, this regime is given by the upper-bound condition $(Dk^2\tau_d')^{-2} \ll 1$ which is less restrictive than was previously reported [3]. This looser restriction can be explained by considering that, for $n = 2$, the second-order term in the expansion of the DDF contribution gives zero observable signal [5] and the next non-zero contribution comes from the third-order term contribution.

3. Experiments and discussion

The experiments were conducted at room temperature in a Varian Inova animal scanner equipped with a transmission-detection birdcage coil of 38 mm (i.d.) at a magnetic field of 9.4 T. A glass sphere (Wilmad) of 8 mm (i.d.) was employed to null any effect of dipolar field related to the shape of the sample and also to make the RF field homogeneous by positioning the sphere at the center of the coil. The NMR parameters of interest (T_2 , T_1 , and D) were measured separately using the conventional CPMG, inversion-recovery, and PGSE sequences, respectively [13]. In a sample of water doped with CuSO_4 the values measured were $T_2 = 250$ ms, $T_1 = 289$ ms, and $D = 2.15 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$.

A four-step phase cycling was implemented to select for the double-quantum coherences. We cycled the first pulse ($x, y, -x, -y$) and the receiver ($x, -x, x, -x$) leaving all other pulse phases unchanged. In fact, for the range of gradient intensities used here, the ratio $n = 2$ filters the single-quantum contribution very well and the necessity of phase cycling can be relaxed at least for non-structured systems [14]. A repetition time TR of 3 s was used to avoid possible stimulated echo contamination [14] and four averages per scan were acquired in all measurements.

The length scale of diffusion for the water spins during the longest period of measurements was $\sqrt{2Dt_2} \approx 50 \mu\text{m}$ indicating that the experiment was in the free-diffusion limit. The gradients employed to create the DDF were applied parallel to the polarizing field with intensities $G = 0.1, 0.15$, and 0.2 T/m and durations of $\delta = 2$ and 4 ms for the first and second pulse, respectively. The range of gradient intensities utilized guaranteed the condition $kL \gg 1$, where L is the characteristic sample distance along the gradient modulation. This ensures the local form approximation of the DDF [11]. The temporal evolution of the NMR signal in the presence of the DDF was investigated using a fixed $\Delta \approx t_1 = 5$ ms, $\beta = \pi/2$, $n = 2$ and collecting the echo-peaks refocused at t_2 values varying from 18 to 612 ms.

Fig. 2A shows the experimental DDF refocused signal-amplitude (open circles) versus the acquisition time t_2 for the case $n = 2$ related to the iDQC evolution. The solid lines are plots of Eq. (1) where the values of T_2 , T_1 , and D used to fit the data were obtained experimentally by con-

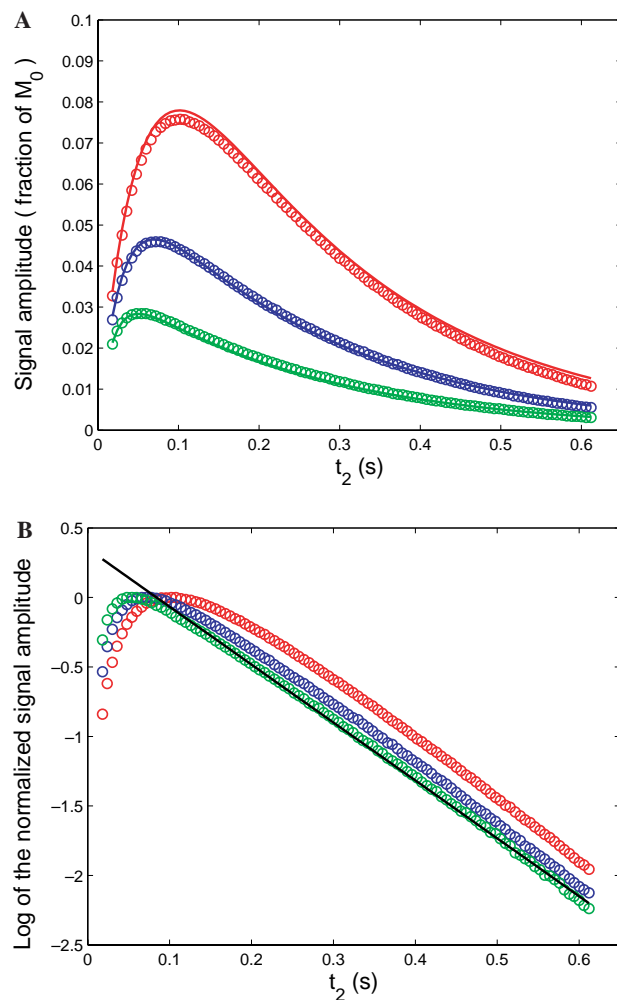


Fig. 2. The open circles represent experimental data for the signal amplitude versus t_2 for the case $n = 2$, $G \parallel B_0$, and $\beta = \pi/2$ at 9.4 T where $\tau_d' \approx 100$ ms. From top to bottom, for each panel, $(2Dk^2 + 1/T_1)^{-1} = 63, 32$, and 19 ms, where $G = 0.1, 0.15$, and 0.2 T/m , respectively. (A) Signal amplitude (fraction of M_0) versus t_2 . The solid lines are based on Eq. (1) using the parameters (D , T_2 , and T_1) obtained by the conventional techniques described in the text. (B) Log-normal plot for the maximum-normalized signal amplitude versus t_2 . The solid black line is an exponential decay where the inverse of the slope gives $T_2 = 240$ ms. The value $D = 2.19 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ is obtained via Eq. (2) as described in the text considering T_1 infinite. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

ventional NMR techniques as described above. The agreement with the theory indicates that the expression for the first-order approximation for the contribution of the DDF can be used in the regime studied. The discrepancies in the fitting at longer t_2 values is likely related to Eq. (1) being a first-order approximation for the DDF effects relative to those caused by diffusion. This assertion is supported by the increase in these discrepancies as G decreases (see Fig. 2A). However, the decaying effect in our experiments also seems to be related with radiation damping effect [3,15] since curves (data not shown) for samples with long T_2 relaxation exhibit this effect more pronounced at the same experimental conditions.

Fig. 2B shows the same experimental data in a log-normal plot. The signal is normalized by its maximum which makes the dependence on the pulse angles and the magnetization density disappear. Furthermore, since the regime of validity for Eq. (1) is established, no adjustable parameters are necessary to obtain T_2 or D from the experiment. The data for $G = 0.2$ T/m (green open circles), between $t_2 = 100$ and 612 ms was fit to a linear function of t_2 (solid black lines). This fitting gives the value of $T_2 = 240$ ms which agrees with that obtained by the CPMG method within a 5% error. The data are plotted for different gradient intensities, which does not change the value of T_2 obtained but controls, via the parameter $(2k^2D + 1/T_1)^{-1}$, the time interval above which the decay is linear and independent of D . In the regime where $2Dk^2 \gg 1/T_1$, the diffusivity can be evaluated by varying the value of D until the left and right side in Eq. (2) agree. Using the experimental value $t_2^* = 51$ ms where, for $G = 0.2$ T/m (green open circles), the signal exhibits a peak (zero-amplitude point in the normalized log-normal curve), and with $T_2 = 240$ ms obtained by the slope of the decaying signal, results in a diffusivity $D = 2.19 \times 10^{-9}$ m² s⁻¹. This value agrees with the PGSE result within a 5% error.

4. Conclusion

An interesting property inherent to the presence of long-range dipolar fields in liquids is reported here for the first time. A way to obtain simultaneously T_2 and D in a simple experiment setup using the signal refocused by the distant dipolar field was described. The theoretical result obtained for the iDQC refocused signal is in agreement with the experiment, where no additional adjustable parameters are necessary to obtain D and T_2 . The regime of validity of the first-order expansion, which exhibits the important characteristic responsible for the effects described, is established without too much restriction and within reasonable experimental conditions.

Since the DDF refocusing properties do not change when the magnetization is submitted to the application of π pulses, a combination of this technique with fast acquisition methods, e.g., CPMG [16], could in principle provide D and T_2 information in a single scan acquisition. This could become an important tool in NMR spectroscopy and fast T_2 - and/or D -maps acquisition [17,18]. Fundamentally, the limitation to the technique seems to be the inherently low signal-to-noise ratio of the iMQC recovered signal. Systems where $T_2 \ll \tau_d$ constitute a challenge for the technique since in this regime the amount of signal refocused by the distant dipolar field is around the noise level. In addition, if the values of D are small in a way that the condition $2Dk^2 \gg 1/T_1$ is not tenable for the gradients available, the value of T_1 has to be considered in Eq. (2).

The validity of the linear approximation for the contribution of the distant dipolar field in the presence of diffusion seems to be more flexible than previously discussed in the literature. For instance, the condition $1/Dk^2\tau_d \ll 1$ used in [3] to guarantee the validity of Eq. (1) is not respect-

ed in the experiments performed here. However, the theory gives excellent agreement with the data. A perturbation theory approach indicates that this condition is only sufficient but not necessary for the validity of the first-order limit. Work along this line is currently in progress.

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