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Phase-modulated LA-REDOR: A robust, accurate and efficient solid-state NMR technique for distance measurements between a spin-1/2 and a quadrupole spin

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ABSTRACT

Distances between a spin-1/2 and a spin > 1/2 can be efficiently measured by a variety of magic-angle spinning solid state NMR methods such as Rotational Echo Adiabatic Passage Double Resonance (REAPDOR), Low-Alpha/Low-Amplitude REDOR (LA-REDOR) and Rotational-Echo Saturation-Pulse Double-Resonance (R/S-RESPDOR). In this manuscript we show that the incorporation of a phase modulation into a long quadrupolar recoupling pulse, lasting 10 rotor periods that are sandwiched between rotor-synchronized pairs of dipolar recoupling π pulses, extends significantly the range of the values of the quadrupole moments that can be accessed by the experiment. We show by a combination of simulations and experiments that the new method, phase-modulated LA-REDOR, is very weakly dependent on the actual value of the radio-frequency field, and is highly robust with respect to off-resonance irradiation. The experimental results can be fitted by numerical simulations or using a universal formula corresponding to an equal-transition-probability model. Phase-modulated LA-REDOR $^{13}C\{^{11}B\}$ and $^{15}N\{^{51}V\}$ dipolar recoupling experiments confirm the accuracy and applicability of this new method.

1. Introduction

The knowledge of a distance between atoms is essential for understanding structure, dynamics, bond character and other properties of individual molecules or more complex materials. One of the primary Magic Angle Spinning Nuclear Magnetic Resonance (MAS NMR) methods for obtaining the distance between two atoms is the Rotational Echo Double Resonance experiment (REDOR [1]). One way in which the recoupling of the dipolar interaction can be obtained with REDOR, is by the application of two π-pulses every rotor period to the detected spin, with the exception of the middle pulse, which is applied to the coupled spin. This sequence of pulses leads to a recoupling signal $S(t)$. Elimination of the pulse on the coupled spin results in averaging of all internal interactions (assuming a small chemical shift anisotropy and neglecting the homonuclear interactions), leaving only relaxation effects, and gives a reference signal $S_0(t)$. If the coupled atom does not possess a quadrupole interaction, or if this atom has a spin larger than one half but its quadrupole frequency is sufficiently small with respect to the radio-frequency (rf) field, full recoupling of the dipolar interaction is obtained at long times. The dipolar constant D can be extracted from the curve $\Delta S/S_0(t) = 1 - S(t)/S_0(t)$, and therefore the interatomic distance is obtained.

With increased values of the quadrupole frequency, the maximum achievable value of $\Delta S/S_0$ decreases until it becomes too small making the experiment ineffective. Increased recoupling efficiency can be obtained by using a selective REDOR. In this experiment, the π pulse on the quadrupolar nucleus is applied selectively to the central transition (thus for a quadrupolar nucleus with an integer spin such as ^{14}N this method cannot be used). The efficiency of this method depends on the value of the spin of the quadrupolar nucleus and, for a spin-3/2, a maximum of 50% is obtained [2] (for other spins this value is smaller). In order to further improve the efficiency of the experiment in such conditions, other approaches have been utilized. Sequences like TRAPDOR [3], REAPDOR [4], SPIDER [5], R-RESPDOR [6], S-RESPDOR [7] and LA-REDOR [8], all have a limit of $\Delta S/S_0 \sim 2S/(2S+1)$, where S is the quadrupole spin quantum number. REAPDOR (Rotational Echo Adiabatic Passage Double Resonance) is efficient for recoupling the dipolar interaction when adiabatic conditions are fulfilled during the pulse applied to the quadrupolar nucleus. Adiabaticity requires that $\nu_1^2/\nu_R\nu_Q \geqslant \alpha_{min}$, where ν_1, ν_R and ν_Q are the rf field strength, spinning speed and quadrupolar frequency, respectively, and α_{min}

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is ~0.5. That is to say, this sequence can be used when the nucleus has a relatively small quadrupole frequency, or the experimental conditions use low spinning speeds and high rf fields. The difference between REDOR and REAPDOR is the width of the pulse on the quadrupolar nucleus; when the REAPDOR pulse length $\tau_p = T_R/3$, the number of adiabatic transfers is optimized and REAPDOR can be simulated with a universal formula that depends only on the dipolar interaction [9–12]. In the sudden passage limit, where $\alpha < \alpha_{min}$, REAPDOR becomes inefficient and alternative experiments have been devised that can recouple efficiently the dipolar interaction. These experiments are based on a similar effect; a simple extension of the pulse to at least 1.5 rotor periods or more mixes the populations of the quadrupole spin, and the overall curve can be approximated with an equal-transition-probability model. This model is based on the assumption that during the pulse, the probability of a transition between two spin states is random, and therefore equal for all transitions and all crystallites. We have shown before that this assumption is not necessarily correct [13], since different crystallites have different transfer properties. Nevertheless, the overall integrated signal behaves very close to this random model in certain cases, allowing for a general universal formula to be devised accordingly [7]. The LA-REDOR experiment (Low-Alpha/Low-Amplitude REDOR) differs from REAPDOR only by the width of the pulse on quadrupolar nucleus: $\tau_p = \varepsilon T_R$, $\varepsilon \in [1.5{:}4]$. The Rotational-Echo Saturation-Pulse Double-Resonance (R/S-RESPDOR) methods employ in addition to the long quadrupolar-recoupling pulse, also symmetry-based recoupling of the dipolar interaction. In these experiments, rotary resonance recoupling [6,14] or an $SR4_1^2$ block [15] are applied to the detected spin one-half nucleus thereby reducing the dependence on spinning speed stability and suppressing the homonuclear dipolar interaction between the detected spins while keeping the heteronuclear dipolar interaction to the quadrupolar nucleus intact. Due to this type of irradiation the dipolar interaction is scaled giving $D_{eff} = kD$, $k < 1$ and, therefore, longer recoupling times. The shortcoming of LA-REDOR and RESPDOR is the requirement for specific values of ν_1 and ν_R for given ν_Q values if optimal performance is desired [13]. Therefore, unlike REAPDOR, these methods are more susceptible to errors due to rf inhomogeneity and offset. Also, these sequences are limited by the maximal strength of the quadrupole coupling, and show reduction in efficiency at high spinning speeds.

In this manuscript, we present a new method, the phase-modulated LA-REDOR. As will be shown below, extension of the pulse in addition to phase modulation results in a recoupling curve that is very robust with respect to rf inhomogeneity, offset and spinning rate, makes the method applicable to very large values of the quadrupole interaction of any spin $S > 1/2$, and permits modeling of this experiment with a simple universal formula corresponding to a random transition model [7,9].

2. The phase-modulated LA-REDOR experiment

Extending the width of the pulse on the quadrupolar nucleus from $T_R/3$ in REAPDOR to $1.5T_R - 4T_R$ in LA-REDOR/RESPDOR gave an opportunity to carry out experiments under non-adiabatic conditions [6–8]. As simulations show, further extension of the width of the pulse reduces its efficiency. On the other hand, pulses with alternating amplitude and phase can also be explored. Such pulses can be made adiabatic [16–20]. The mechanism by which such pulses work is the smooth adiabatic variation of the amplitude and the phase generating level anti-crossings and therefore exchange of populations. The phase-modulated LA-REDOR pulse was designed based on the form of the Lorentzian adiabatic pulse [17]; it combines phase modulation (Blocks B, C in Fig. 2) with a

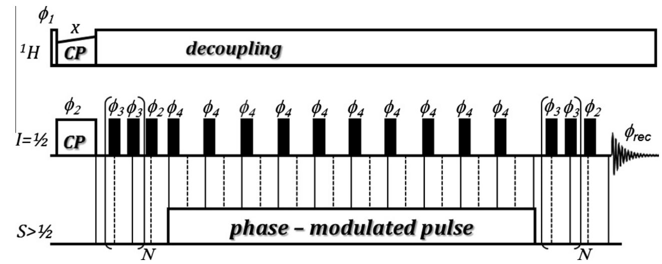

Fig. 1. The phase modulated LA-REDOR sequence employing a long pulse with phase modulation on the coupled quadrupole *S*-spin and *xy*8 phase cycle on the detected, spin-1/2, *I*-spin (represented by the phases ϕ_3 and ϕ_4). The following phase cycle has been implemented: $\phi_1 = y, \bar{y}$; $\phi_2 = x, x, y, y, \bar{x}, \bar{x}, \bar{y}, \bar{y}$; $\phi_3 = \phi_4 = x, y, x, y, y, x, y, x$; $\phi_{rec} = x, \bar{x}, y, \bar{y}, \bar{x}, x, \bar{y}, y$; ($\phi_3$ and ϕ_4 are incremented within a single scan of the sequence while the other phases are incremented in the regular fashion, between consecutive scans). Dashed and solid lines represent half and full multiples of the rotor period. During the pulse on spin *S*, 10 rotor-synchronized π-pulses are applied to the *I* spin that decouple the offset, chemical shift anisotropy and dipolar interaction. The index *N* is incremented in the indirect dimension, and the total dephasing time is given by $t_1 = (2N + 2)T_R$, where T_R is the spinning rotation period. This time reference assumes that no dipolar dephasing occurs during t_1, as discussed in the text.

nutation period and supercycling, taking a total width of $10T_R$. As will be shown below, this alternation makes the pulse robust with respect to many experimental parameters although the contribution of adiabatic transfers during this pulse in the experiment is not entirely clear, and the mechanism by which it works is currently under investigation.

The phase modulated LA-REDOR (mod. LA-REDOR) experiment is shown in Fig. 1. The basic dipolar recoupling units prior and after the pulse are similar to REDOR; however, a long phase modulated recouping pulse that lasts 10 rotor periods is used in the middle of the sequence, replacing the prior options of either a π pulse, a pulse lasting $T_R/3$ or a pulse lasting more than a single rotor period. During the recoupling pulse, both the dipolar and chemical shift interactions must be refocused and, therefore, a train of rotor synchronized echo π pulses is used, similarly to the CPMG experiment. This approach is somewhat different than in LA-REDOR, where the pairs of π pulses were maintained during the entire experiment.

The recoupling pulse is of constant amplitude and varied non-smooth phase. The value of the phase is given by

$$\phi(t) = \phi_0 + \kappa f(\tau) \tag{2.1}$$

It consists of 12 alternating blocks: 8 blocks with varied phase ($\kappa \neq 0$, $\phi_0 = 0$) and a width $0.875T_R$, and 4 blocks with constant phase ($\kappa = 0$, $\phi_0 = 225$) and a width $0.75T_R$. Each block within the varied phase is divided into 8 parts (the width of each part is $0.109375T_R$) and has the same values of $f(\tau)$:

$$f(\tau) = 360^\circ\{\tau \tan^{-1}(\tau) + 0.5\ln(1+\tau^2)\},$$
$$\tau = \frac{2t}{T_R} - 3; \quad \frac{t}{T_R} = 0.125, 0.25 \ldots 1.125 \tag{2.2}$$

The actual values of κ and the order of the blocks are described in Table 1, and the explicit values of Eq. (2.2) are shown in Table 2. These values are graphically presented in Fig. 2 and have been implemented in the pulse sequence.

3. Results and discussion

3.1. Phase modulated LA-REDOR efficiency and its analytical form

The optimal performance of REAPDOR, LA-REDOR/RESPDOR and that of the new phase-modulated LA-REDOR (mod. LA-REDOR) sequence is bound by complete randomization of spin populations. Therefore, the recoupling curve can generally be described by the

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