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Efficiency of heteronuclear dipolar decoupling schemes in solid-state NMR: Investigation of effective transverse relaxation times

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ABSTRACT

We here compare the T_2' values of various heteronuclear dipolar decoupling schemes commonly used in solid-state nuclear magnetic resonance experiments. Swept-frequency two-pulse phase modulation scheme is shown to give longer T_2' values for the majority of the magic-angle-spinning frequencies and radiofrequency amplitudes considered here. The longer T_2' values obtained are shown to yield spectra with higher resolution in experiments, such as INADEQUATE, which incorporate spin-echo blocks. Such blocks normally constitute the indirect dimension of a multidimensional experiment during which heteronuclear dipolar decoupling is applied, thereby making the relevance of T_2' manifest clearly. Experimental results are shown on samples of glycine, alanine, and Aβ_{42}.

1. Introduction

Heteronuclear dipolar decoupling is imperative in most solid-state nuclear magnetic resonance (NMR) experiments where spectra of rare spins, such as ^{13}C and ^{15}N, dipolar coupled to abundant spins, such as ^{1}H are recorded. Several approaches exist in this regard [1–6]. One of the recently introduced schemes, namely, swept-frequency two-pulse phase modulation (SW$_f$-TPPM) [7] has been shown to perform better in terms of resolution and sensitivity than many of the existing schemes particularly for magic-angle-spinning (MAS) frequencies (ν_r) in the range of 5–35 kHz [8]. More importantly, it was shown that SW$_f$-TPPM has a broad-banded performance efficiency in terms of variations in pulse duration, phase angle, and irradiation offset, thus making it easier to optimise than many other schemes [9]. However, it was also shown recently that most of the popular decoupling schemes provide nearly the same sensitivity and resolution for high MAS frequency of 60 kHz [10]. This is true whether one works in the high radiofrequency (RF) amplitude regime ($\nu_1/\nu_r \geqslant 3.0$) or low RF regime of say 10–20 kHz ($0.3 \geqslant \nu_1/\nu_r \geqslant 0.1$). Hence, outwardly it seems there is no difference among these decoupling schemes at high MAS frequencies thus making the choice of a particular scheme mainly an academic interest. Notwithstanding this fact, it remains as already shown, that the SW$_f$-TPPM scheme still is the most robust making the case for a routine application of this at all MAS and RF regimes.

The group of Emsley has shown the importance of refocused line width and the associated rate constant T_2' as a parameter to estimate the efficiency of heteronuclear dipolar decoupling schemes [11,12]. Although, at high MAS frequencies, the limiting line width seems to have been reached for the existing decoupling schemes, it is quite possible that the decoupling schemes have an influence on the transverse relaxation times. This in turn will have an impact on many of the multidimensional experiments, such as REDOR (Rotational Echo Double Resonance) [13] and INADEQUATE (Incredible Natural Abundance Double Quantum Experiment) [14,15] that rely on the refocused line width, i.e., on the line width corresponding to the dephasing time measured in a spin-echo experiment. It is believed that a major factor in limiting line width arises from the residual coherent interactions due to incomplete dipolar averaging with MAS and heteronuclear dipolar decoupling. It is, hence, useful to investigate the efficiency of various decoupling schemes to average out these residuals by observing the coherence time scales in a spin-echo experiment involving a particular decoupling scheme.

We here compare the performance of TPPM [2], SPINAL [3], SW$_f$-TPPM [7], SW$_f$-TPPM-sc (supercycled SW$_f$-TPPM) [16], XiX [17], and

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PISSARRO [18] decoupling schemes for MAS frequencies 10, 22, and 60 kHz using high (ν_1 = 196 kHz) and low (ν_1 = 10 kHz) decoupling RF amplitudes with respect to the T_2' values. Decoupling efficiency using low RF amplitudes at high spinning frequencies has been explored in the past also [10,19–22]. Here, SW$_f$-TPPM scheme is shown to have a relatively better performance with regard to the T_2' values under all the regimes investigated. The observations also manifest in INADEQUATE type of experiments performed on $^{13}C_2$-, ^{15}N-L-glycine and $^{13}C_3$-, ^{15}N-L-alanine and in frequency-selective ^{13}C–^{15}N REDOR experiments [23] performed on amyloid β (Aβ_{42}) fibrils.

2. Experimental

All solid-state NMR measurements were performed at magnetic fields of 16.43 T (^{1}H Larmor frequency of 700 MHz) using Bruker AVIII NMR spectrometer and 11.74 T (^{1}H Larmor frequency of 500 MHz) using Bruker AV NMR spectrometer. A 2.5 mm triple-resonance probe was used for experiments at MAS frequencies of 10 and 22 kHz. For experiments at 60 kHz of MAS, 1.3 mm double-resonance standard-bore probe was used. Experiments were done on commercially purchased 2-^{13}C-, ^{15}N-L-glycine, $^{13}C_2$-, ^{15}N-L-glycine, and $^{13}C_3$-, ^{15}N-L-alanine all used without any further purification. A sample of commercially available adamantane was used for the calibration of RF amplitude using nutation experiments.

Solid-phase peptide synthesis was employed to synthesise the 42-amino-acid long amyloid β (Aβ_{42}) peptide according to 9-fluorenylmethoxycarbonyl (Fmoc) protocol. The peptide was isotopically labelled at specific positions, Ser8, Val12, Phe20, Asp23, Lys28, Met35, and Ile41, using uniformly ^{13}C- and ^{15}N-labelled amino acids, and His14 which was uniformly ^{15}N labelled. Synthesis products were purified to >95% by HPLC as confirmed by mass spectrometry. To obtain amyloid fibrils of Aβ_{42}, a 400 μM solution of purified peptide in HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) buffer (pH = 7.4) was kept at room temperature with mild rotation (10 rpm) for 4 days. Fibril formation was confirmed by electron microscopy as shown elsewhere [24].

T_2' measurements were carried out by monitoring peak height of a single resonance in the 1D ^{13}C spectrum of 2-^{13}C-, ^{15}N-L-glycine recorded after a spin-echo scheme, the pulse sequence for which is shown in Fig. 1a. ^{1}H decoupling during the spin-echo and acquisition period was achieved by using one of the aforementioned decoupling sequences. The observed ^{13}C peak height was plotted as a function of the spin-echo duration which was incremented in a non-rotor-synchronised fashion to obtain what is called *transverse dephasing curves*. These curves were then fitted to a single-exponential decay function to obtain transverse dephasing times (T_2' values). Two-dimensional (2D) *z*-filtered refocused INADEQUATE [25,26] spectra were recorded by acquiring 128 points in the t_1 dimension. ^{1}H decoupling during evolution and acquisition periods was achieved by using one of the aforementioned ^{1}H decoupling schemes. A total of 128 scans per t_1 increment was recorded with an inter-scan delay of 2 s. Dwell times of 7.95 and 15.9 us were used in t_1 and t_2 dimensions, respectively. The τ delays in the first and second echo periods and the *z*-filter delay were set to 6 and 5 ms, respectively [26].

Frequency-selective ^{13}C–^{15}N REDOR experiments were performed at a spinning frequency of 10 kHz using the pulse sequence

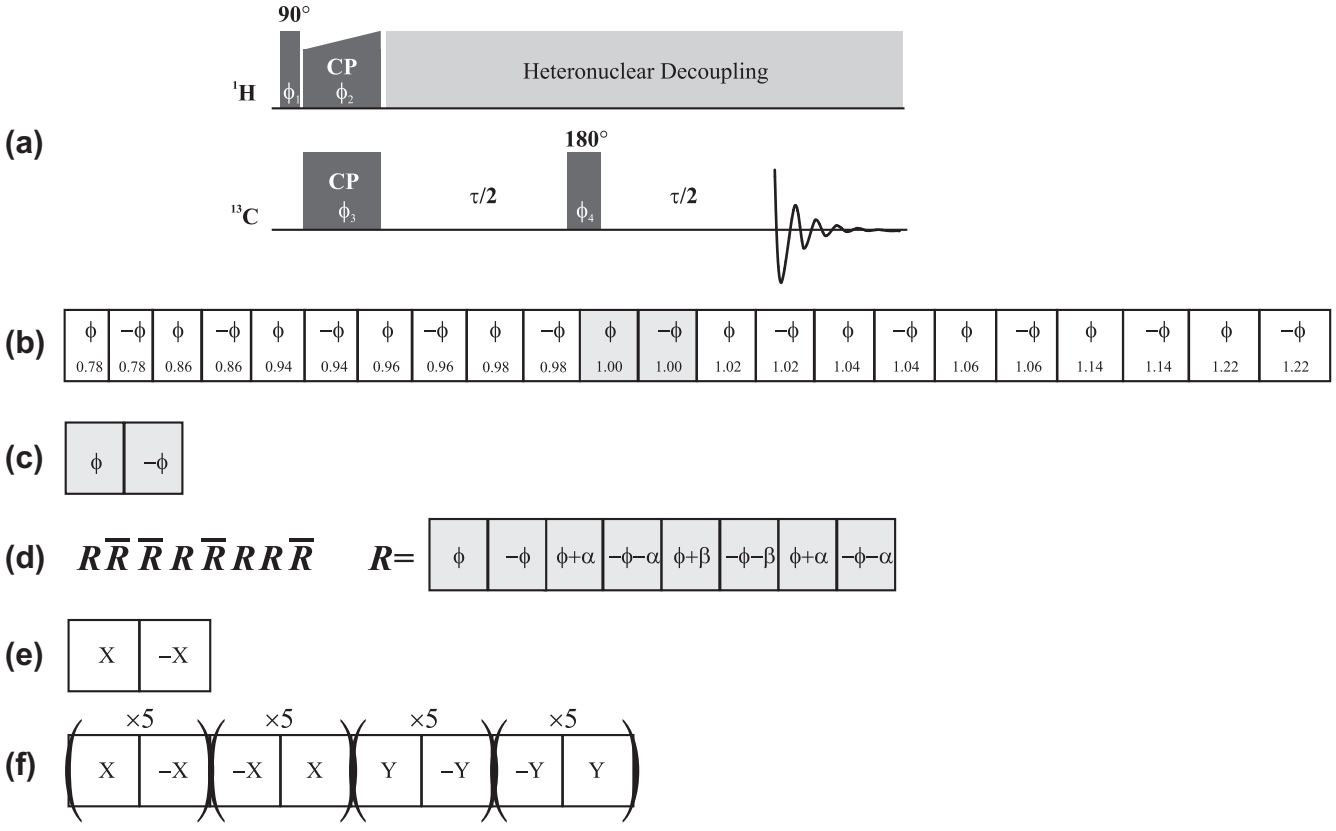

Fig. 1. (a) Schematic of the spin-echo pulse sequence used for the measurement of T_2'. $\tau/2$ was incremented in a non-rotor synchronised fashion to obtain transverse dephasing curves whilst ^{1}H decoupling was implemented during both spin-echo and acquisition periods. A 32 step phase cycling was employed as following: $\phi_1 = y, -y, \phi_2 = x, x, y, y, -x, -x, -y, -y, \phi_3 = x, \phi_4 = x$ (8), y (8), $-x$ (8), $-y$ (8), $\phi_{rec} = x, -x, -y, y, -x, x, y, -y, -x, x, y, -y, x, -x, -y, y$. Schematic representation of (b) SW$_f$-TPPM, (c) TPPM, (d) SPINAL64, (e) XiX, and (f) PISSARRO decoupling schemes.