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ABSTRACT

Heteronuclear spin decoupling is a highly important component of solid-state NMR experiments to remove undesired coupling interactions between unlike spins for spectral resolution. Recently, experiments using a unification strategy of standard decoupling schemes were presented for high radio-frequency (RF) amplitudes and slow-intermediate magic-angle-spinning (MAS) frequencies, in the pursuit of deeper understanding of spin decoupling under phase-modulated RF irradiation [A. Equbal *et al.*, J. Chem. Phys. **142**, 184201 (2015)]. The approach, unified two-pulse heteronuclear decoupling (UTPD), incorporates the simultaneous time- and phase-modulation strategies, commonly used in solid-state NMR. Here, the UTPD based decoupling scheme is extended to the experimentally increasingly important regime of low RF amplitudes and fast MAS frequencies. The unified decoupling approach becomes increasingly effective in identifying the deleterious dipole-dipole and, in particular, J recoupling conditions which become critical for the low-amplitude RF regime. This is because J coupling is isotropic and therefore not averaged out by sample spinning unlike the anisotropic dipole-dipole coupling. Numerical simulations and analytic theory are used to understand the effects of various nuclear spin interactions on the decoupling performance of UTPD, in particular, the crucial difference between the low-phase and high-phase UTPD conditions with respect to J coupling. In the UTPD scheme, when the cycle-frequency of the pulse-sequence is comparable to the RF nutation frequency, the existence of a non-zero *effective rotation* in the basic two-pulse scheme becomes an essential feature for the efficient and robust averaging out of the scalar J coupling. This broad viewpoint is expected to bring different optimum low-power decoupling pulse schemes under a common footing.

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I. INTRODUCTION

Efficient heteronuclear spin decoupling is indispensable to obtain highly resolved solid-state NMR spectra under magic-angle-spinning (MAS) conditions, especially for rare nuclei like ^{13}C and ^{15}N where resolution is limited by strong dipole-dipole and J couplings with ^1H spins. This calls for efficient and robust decoupling using radio-frequency (RF) pulses (spin rotation) in addition to MAS (sample rotation). An optimal decoupling pulse sequence averages out the direct as well as the indirect coupling interactions.^{1–15}

The most essential consideration for efficient decoupling with simultaneous spin and spatial manipulation is “skirting” the interference between the physical/spatial rotation by MAS and the spin rotation by RF irradiation.^{16–18} This is typically achieved by setting the RF field amplitude (ν_1) several times higher than the MAS frequency, ν_r (i.e., $\nu_1 > 4\nu_r$) or lower ($\nu_r > 4\nu_1$).^{19,20} In addition, there are several other higher-order interactions that may impede the decoupling performance of a pulse scheme. This makes it extremely challenging to have one particular pulse scheme which can minimize all the deleterious effects and across all the experimental conditions

including spinning frequency, radio-frequency, and spin system (samples).^{1–3}

Continuous-wave (CW) decoupling,⁵ the simplest irradiation technique, is still used in the indirect dimension of NMR experiments in certain cases, especially to avoid the interference between simultaneous pulses on different nuclear spins.^{1–3,21,22} But its application in the direct dimension, i.e., during signal acquisition, is very rare owing to its inefficacy. Phase-modulated schemes like two-pulse phase-modulation (TPPM)⁶ decoupling, X-inverse-X (XiX),^{7,8} or refocused continuous-wave (rCW)^{23,24} schemes and/or their variants, such as SW_f-TPPM,²⁵ SPINAL64,¹¹ PISSARRO,¹⁶ and rCW^{APPA},²⁶ have been demonstrated to be much more efficient across all spinning and RF regimes. All these pulse schemes were originally designed for the high- ν_1 -slow- ν_r regime, but interestingly they remain efficient even for the low- ν_1 -fast- ν_r regime.^{27–29} Whilst the optimum TPPM parameters (pulse phase and length) remain similar in both the experimental regimes, low- ν_1 -fast- ν_r and high- ν_1 -slow- ν_r , the XiX²⁸ and the rCW²⁷ schemes have different optimum parameters in the two experimental regimes. This is mainly

attributed to J couplings which will be addressed here. The optimum TPPM decoupling is obtained by optimization of the pulse-phase and the flip-angle around 20°–30° and 180°, respectively, in both the regimes. On the other hand, in XiX and rCW, the decoupling optimization is achieved only in terms of synchronization of the pulses with respect to the rotor period (τ_r) in the high- ν_1 -slow- ν_r regime. The actual flip angle of the pulse is not important making the optimum decoupling independent of the ν_1 value. However, in the low- ν_1 -fast- ν_r regime, the situation is opposite. Here, the actual flip angle of the pulses in the XiX and the rCW sequences is a more important factor than rotor synchronization. An obvious question that arises here is: why does the optimum decoupling conditions change for the XiX and the rCW schemes but not for the TPPM scheme in the two experimental regimes? Also, are there, in general, more efficient decoupling conditions than the basic TPPM, rCW, and XiX in the two pulse regime?

Addressing these intriguing questions is the focus of this manuscript. In this pursuit, we adopt the framework of the unified two-pulse decoupling (UTPD) scheme³⁰ which previously was

FIG. 1. (a) General schematic of the UTPD pulse scheme. (b) Numerically simulated peak height of ^{13}C resonance of the $^{13}\text{CH}_2$ spin system under the UTPD irradiation scheme for different values of $(\phi - \theta)$ under the experimental conditions of a 700 MHz ^1H Larmor frequency with $\nu_1 = 10$ kHz and $\nu_r = 50$ kHz, respectively. For the given RF amplitude, 360° flip angle corresponds to $\tau = 100 \mu\text{s}$. The dotted circles and dotted squares in the plots correspond to the parameters of conventional schemes and UTPD schemes, respectively, as listed in Table I.

introduced for the high- ν_1 -slow- ν_r regime. The basic UTPD pulse scheme comprises two pulses with different phases and, in general, having different pulse lengths, as shown in Fig. 1(a). The essential idea was to develop a comprehensive understanding of all the two-pulse phase-modulated decoupling schemes, complementary to the theoretical depiction of the TPPM scheme by the group of Ernst.^{15,31} In this manuscript, we extend the UTPD approach to the fast spinning and low RF amplitude ($\nu_r > 4\nu_1$) regime, which not only addresses the above posed questions but also combines all the basic two-pulse decoupling solutions in vogue and illustrates the transition in the optimum decoupling conditions with the changes in the UTPD parameters.

In general, two-pulse irradiation can be considered to form the basic building block of all the major decoupling schemes presented to date. Within a two-pulse scheme, the strategies of relative (i) phase modulation, (ii) RF amplitude modulation, and (iii) time (pulse length/flip-angle) modulation have been used to obtain different decoupling schemes. Using the UTPD scheme, it is shown that just phase modulation and time modulation of the two basic pulses are sufficient to obtain complete decoupling solutions to the first-order Hamiltonian. RF amplitude modulation^{32,33} adds another dimension to UTPD, but it is left out of consideration, as its implications come only in the higher-order Hamiltonian. Extensive numerical simulations have also been performed to understand the influence of various spin interactions on the decoupling performance. These are corroborated with experimental demonstration. The tolerance of the two-pulse decoupling scheme toward offset is also shown here experimentally. Toward the end, the essential difference that originates owing to the J coupling interaction between UTPD schemes with low- and high-phase differences is highlighted and analyzed theoretically using Fourier analysis of the UTPD pulse scheme in the RF interaction frame.

II. NUMERICAL RESULTS AND DISCUSSION

First, we examine the features of the decoupling profile of UTPD under the low- ν_1 -fast- ν_r regime using SIMPSON^{34,35} based numerical simulations. The aim is to essentially delineate the gradual changes in the resonance or optimum decoupling conditions as the UTPD parameters are varied. We notate the UTPD schemes as UTPD $[(\phi - \theta), \tau_1, \tau_2]$, where $(\phi - \theta)$ is the relative phase between the two constituent pulses whose duration is τ_1 and τ_2 [Fig. 1(a)]. The cycle time of the scheme is notated as τ_c , as indicated in Fig. 1(a).

A. UTPD $[(\phi - \theta), \tau_1, \tau_2]$

In order to illustrate the effects of simultaneous phase- and time-modulation of RF pulses on the heteronuclear spin decoupling efficiency, multiple two-dimensional numerical simulations were performed as a function of pulse lengths, τ_1 and τ_2 , and the relative pulse phase $(\phi - \theta)$. The gradual changes in the resonance conditions or optimum conditions, as $(\phi - \theta)$ increases from 30° to 180° , are investigated in Fig. 1(b). The figure maps the numerically simulated normalized peak height of ^{13}C resonance in a $^{13}\text{CH}_2$ spin system with $(\phi - \theta)$ increasing from a small value of 30° to the maximum possible value, 180° , i.e., from UTPD $[30^\circ, \tau_1, \tau_2]$ to UTPD $[180^\circ, \tau_1, \tau_2]$. These simulations were done with ν_1 and ν_r

equaling 10 kHz and 50 kHz, respectively, using the spin parameters described in Sec. V.

In general, at small values of $(\phi - \theta)$, efficient decoupling is observed when τ_c (sum of the pulse lengths, τ_1 and τ_2) corresponds to a total rotation of 360° or its integral multiple for the given ν_1 (as depicted by dashed boxes in Fig. 1). Here, 360° corresponds to $100\ \mu\text{s}$ as ν_1 is 10 kHz. The special case of τ_c around 360° and $\tau_1 = \tau_2 = \tau_c/2$ conforms to the TPPM solution as marked with dotted circles in the contour plots. The optimum solution for TPPM is when the flip-angle of each of the pulses, β_1 and β_2 , is $\sim 180^\circ$. This is justified later in Fig. 6 and also by the fact that all the first- and second-order coupling interactions, including J couplings, are averaged out at $\beta_1 = \beta_2 \sim 180^\circ$ for a small relative phase (Sec. IV).

However, when $(\phi - \theta)$ is incremented toward larger values, the decoupling performance gets attenuated at lower values of τ_c and enhanced for higher τ_c . This is clearly evident in cases of $(\phi - \theta) = 90^\circ$ and higher values. Also, as can be noticed, for $(\phi - \theta) < 90^\circ$, good decoupling condition is observed along the main diagonal (left-top to right-bottom). By contrast, for $(\phi - \theta) > 90^\circ$, optimum decoupling conditions build up along the opposite diagonal (left-bottom to right-top). A strikingly different decoupling regime is detected when $(\phi - \theta)$ approaches 90° , which is complementary to the results obtained with high RF condition.³⁰ For larger $(\phi - \theta)$, a very robust decoupling region is observed for $\tau_1 + \tau_2$ close to $n \times 360^\circ$ (n is an integer) and $\tau_1 \neq \tau_2$. This is clearly evident for $(\phi - \theta) = 180^\circ$ where the most efficient decoupling is obtained when the net flip angle ($\beta_1 + \beta_2 = \beta_c$) is $2 \times 360^\circ$ but $\tau_1 \neq \tau_2 \neq 360^\circ$. The XiX condition, i.e., UTPD $[180^\circ, \tau_1, \tau_2]$ with $\tau_1 = \tau_2$, is not very robust, owing to the presence of the second-order cross term and J coupling as will be discussed later. As compared to the $\tau_1 = \tau_2$ diagonal condition, there are several other off-diagonal conditions with $\tau_1 \neq \tau_2$ in UTPD $[180^\circ, \tau_1, \tau_2]$ which are more robust and more efficient solutions (shown by dotted squares).

B. Effect of various spin interactions in UTPD $[(\phi - \theta), \tau_1, \tau_2]$

In order to get better insights into the decoupling mechanism of the UTPD scheme, its decoupling efficiency was numerically simulated under the influence of various nuclear spin interactions. The aim here is to know which interactions are deleterious to efficient decoupling within the UTPD parameter space. Here, we consider a $\text{CH}_2\text{-H}$ spin system to incorporate the effect of the extended H-H spin network. Figure 2 shows the decoupling performance of UTPD $[(\phi - \theta), \tau_1, \tau_2]$ for five different values of $(\phi - \theta)$: 30° , 60° , 90° , 120° , and 180° , under four different types of spin interactions assuming experimental conditions of 700 MHz of ^1H Larmor frequency with ν_1 and ν_r equaling 10 and 50 kHz, respectively.

First, the case where all the interactions, $^1\text{H}\text{-}^{13}\text{C}$ heteronuclear dipole-dipole and J couplings, $^1\text{H}\text{-}^1\text{H}$ homonuclear dipole-dipole coupling, and ^1H chemical-shift anisotropy (CSA) interaction are present is considered in Fig. 2(a). The plots are essentially similar as in Fig. 1, but the resonance conditions are more smeared in the $\text{CH}_2\text{-H}$ case. This is due to the ^1H homonuclear coupling network which leads to self decoupling. To deconvolute the effect of ^1H CSA and $^1\text{H}\text{-}^1\text{H}$ homonuclear dipole-dipole couplings on the decoupling performance of the UTPD scheme, these interactions are

FIG. 2. Numerically simulated peak height of ^{13}C resonance of the $^{13}\text{CH}_2\text{-H}$ spin system under UTPD irradiation for different values of $(\phi - \theta)$ under the conditions of (a) all interactions ($^1\text{H}\text{-}^{13}\text{C}$ dipole-dipole and J coupling, ^1H CSA, and $^1\text{H}\text{-}^1\text{H}$ dipole-dipole coupling) present, (b) ^1H CSA turned off, (c) $^1\text{H}\text{-}^1\text{H}$ dipole-dipole coupling turned off, (d) $^1\text{H}\text{-}^{13}\text{C}$ J coupling turned off, and (e) ^1H CSA, $^1\text{H}\text{-}^1\text{H}$ dipole-dipole coupling, and $^1\text{H}\text{-}^{13}\text{C}$ heteronuclear J-couplings turned off. τ_1 and τ_2 were optimized in terms of flip angle in steps of 5° .

sequentially turned on/off and decoupling performance is monitored over the entire UTPD parameter space.

In Fig. 2(b), the ^1H CSA interaction is turned off while all the other interactions are present. Here, for small values of $(\phi - \theta)$, the decoupling efficiency shows remarkable improvement over the entire values of timing parameters (except for rotary-resonance recoupling conditions³⁶) and becomes weaker as the cycle time τ_c increases owing to decrease in the magnitude of the Fourier coefficient of the time-dependent $^1\text{H}\text{-}^{13}\text{C}$ dipole-dipole coupling operator in the RF interaction frame. This is well illustrated in a previous publication.³⁷ The low-phase UTPD schemes are, hence, least affected by the $^1\text{H}\text{-}^1\text{H}$ homonuclear dipole-dipole and J couplings. In fact, this observation is similar to the high ν_1 regime³⁰ and is extensively mentioned in the literature in the context of TPPM and CW irradiation.^{1,31} Decoupling performance for high $(\phi - \theta)$ close to 180° remains very similar in the presence or absence of ^1H CSA at the optimum condition. However, for smaller τ_c , decoupling efficiency is significantly improved in the absence of ^1H CSA but the resonance conditions essentially remain the same.

Next, the case where all the $^1\text{H}\text{-}^1\text{H}$ homonuclear dipole-dipole couplings are turned off is analyzed in Fig. 2(c). Here, for small values of $(\phi - \theta)$, the presence of CSA of the irradiated spins severely hampers the decoupling performance as compared to Fig. 2(b) where CSA was turned off. This indicates that low-phase UTPD schemes do not fully refocus the residual dipole-dipole coupling originating from the cross term between ^1H CSA and $^1\text{H}\text{-}^{13}\text{C}$ dipole-dipole coupling for the low ν_1 regime, similar to the high ν_1 regime. This is clearly reflected in the reduced performance efficiency of CW and TPPM decoupling at high magnetic field where CSA effects are enhanced. The presence of $^1\text{H}\text{-}^1\text{H}$ coupling does not have a deleterious influence on the decoupling profile for the low-phase UTPD scheme ($\phi - \theta < 90^\circ$) but rather provides an advantageous self decoupling effect. However, a drastic difference is observed for larger values of $(\phi - \theta)$ where a marked improvement in the decoupling performance is observed along the opposite diagonal in comparison with the case in Fig. 2(a) where $^1\text{H}\text{-}^1\text{H}$ coupling is present.

To remove the effect of all the indirect interactions on the decoupling efficiency, both ^1H CSA and $^1\text{H}\text{-}^1\text{H}$ couplings are

removed in Fig. 2(d). Clearly, the decoupling performance is improved over the entire parameter space of UTPD. Only some recurrent small dips are observed for the conditions $k(\tau_1 + \tau_2) = n\tau_r$, that are mainly due to recoupling of the dipole-dipole Hamiltonian to the first order, where τ_r is the rotor period and n and k are Fourier indices associated with the modulation of coupling operator because of MAS and RF, respectively. The positions and the magnitude of these dips depend on the magnitude of scaling factors or the magnitude of Fourier coefficients at the respective recoupling conditions as illustrated by Ernst *et al.* using tri-modal Floquet theory.³¹

In case of $\phi - \theta = 180^\circ$, an additional large dip is observed along the diagonal $\tau_1 = \tau_2$. Clearly this dip is a result of ^1H - ^{13}C J since it vanishes in Fig. 2(e) where ^1H - ^{13}C J is also turned off in addition to the ^1H - ^1H homonuclear dipole-dipole couplings and ^1H CSA (i.e., only ^1H - ^{13}C heteronuclear dipole-dipole couplings are present). This confirms that in addition to the ^1H - ^1H dipole-dipole coupling, the high phase UTPD ($\phi - \theta = 180^\circ$) is also impeded by J coupling when $\tau_1 = \tau_2$, i.e., the XiX condition, or when $\tau_1 = \tau_2$ corresponds to 360° rotation. However, the lower-phase UTPD schemes are not affected by the ^1H - ^{13}C J couplings. The rationale behind this observation will be explained later in Sec. IV.

Overall, it can be concluded from this numerical analysis that lower-phase UTPD offers the most efficient decoupling conditions when CSA is not the limiting factor, and higher-phase UTPD is optimum when the homonuclear dipole-dipole couplings and the heteronuclear J-couplings are not an impeding factor. At higher phases, the most efficient decoupling conditions correspond to unequal timing parameters of the two pulses in UTPD, which remove the deleterious effect of ^1H - ^{13}C J coupling and ^1H - ^1H homonuclear dipole-dipole coupling.

III. EXPERIMENTAL RESULTS AND DISCUSSION

The simulations, done on a small model spin system, need to be validated experimentally. To this end, the decoupling performance of the UTPD scheme was recorded as a function of the relative phase, $(\phi - \theta)$, and the pulse lengths, τ_1 and τ_2 .

A. UTPD $[(\phi - \theta), \tau_1, \tau_2]$

The relative phase was varied by fixing the phase of the first pulse, θ to 0° , and performing phase modulation by changing the phase of the second pulse, ϕ only. In order to validate the simultaneous effects of phase- and time-modulations, signal intensity of $^{13}\text{C}_\alpha$

FIG. 3. Experimentally obtained peak height of $^{13}\text{C}_\alpha$ resonance of 1,2- ^{13}C -glycine ethyl ester using UTPD $[(\phi - \theta), \tau_1, \tau_2]$ irradiation for different values of $(\phi - \theta)$ ranging from 30° to 180° under the conditions of 700 MHz of ^1H Larmor frequency with ν_1 and ν_r equaling 10 and 50 kHz, respectively. For the given RF amplitude, the 360° flip angle corresponds to $\tau = 100 \mu\text{s}$. The dotted circles and dotted squares in the plots correspond to the parameters of conventional schemes and UTPD schemes, respectively, as listed in Table I.

resonance in the 1,2- ^{13}C -glycine ethyl ester sample was observed as a function of pulse lengths τ_1 and τ_2 for different ϕ , as in Fig. 1. The experiments were recorded under the same conditions as in Fig. 1, i.e., with ν_r and ν_1 set to 50 kHz and 10 kHz, respectively, and at a magnetic field corresponding to 700 MHz of the ^1H Larmor frequency. All the 2D contour plots shown in Fig. 3 were normalized to the highest peak intensity which was obtained in case of UTPD[180°, τ_1 , τ_2].

The experimental results are very similar to those obtained from the numerical simulations in Fig. 1. The resonance conditions and the optimum decoupling conditions change gradually with the change in $(\phi - \theta)$. A distinct change in the decoupling profile is observed as ϕ changes from a small value to a large value. The advantages of incorporating time modulation of the two pulses in addition to phase modulation are also clear. In general, at the lower relative phase, $\phi - \theta = 30^\circ$, or $60^\circ < 90^\circ$, efficient decoupling is observed for the total flip-angle of both the pulses ($\beta_1 + \beta_2$) being 360° , represented by dashed squares. In this case, a 360° rotation is achieved for a pulse duration of $100\ \mu\text{s}$. The special case of τ_c around 360° and $\tau_1 = \tau_2 = \tau_c/2$ corresponds to the TPPM solution (highlighted by circle in the contour plot). Increasing ϕ toward larger values attenuates decoupling efficacy at lower values of τ_c and enhances it for higher values of τ_c . For $\phi > 90^\circ$, optimum decoupling conditions build up along the opposite diagonal, i.e., the left-bottom to the right-top. In general, a large number of optimum decoupling conditions are found at larger relative phase, $(\phi - \theta)$, but the rotary-resonance conditions also become more influential there. Clearly, $\tau_1 = \tau_2$ conditions must be avoided for large ϕ . It is quite evident that the basic XiX condition, i.e., $(\phi - \theta) = 180^\circ$ (marked by circle), is less efficient and less robust compared to the condition: $\beta_1 + \beta_2 = 360^\circ$ and $\tau_1 \neq \tau_2$ (shown by dotted rectangles in UTPD180°). The experimental findings in Fig. 3 show that ideally at on-resonance conditions, efficient heteronuclear decoupling can be achieved for all the values of $(\phi - \theta)$. However, in a practical situation, the choice would depend on the spin system. For a spin system, where CSA interactions are dominant, like at large B_0 field or in case of ^{19}F nuclear

FIG. 4. ^1H offset dependence of various decoupling schemes monitoring the $^{13}\text{C}_\alpha$ resonance of 2- ^{13}C -labeled glycine with the best decoupling parameters obtained from 2D optimization and performed under conditions of 700 MHz of ^1H Larmor frequency with $\nu_1 = 10\ \text{kHz}$ and $\nu_r = 50\ \text{kHz}$.

spin, high-phase $(\phi - \theta)$ UTPD should be the choice. However, if homonuclear coupling is dominant, low-phase UTPD will be a more suitable choice.

B. Robustness of UTPD scheme toward offset

In general, low RF amplitude decoupling sequences are preferred owing to instrumental challenge and deleterious sample heating, in particular, for biological samples. However, the typical ν_1 employed in the low- ν_1 scenario is of the same order of magnitude as the range of typical proton chemical shifts. This situation might have detrimental effects on the performance of decoupling sequences because the effective rotation of spins is different for different resonance offsets, and the most optimum decoupling conditions can never be achieved simultaneously for all the protons

FIG. 5. Normalized spectra of $^{13}\text{C}_\alpha$ resonance of 2- ^{13}C -labeled glycine recorded using different decoupling sequences under the experimental conditions of $\nu_r = 50\ \text{kHz}$ and $\nu_1 = 10\ \text{kHz}$ and 700 MHz of ^1H Larmor frequency.

TABLE I. Suggested experimental parameters for the UTPD scheme in the two different MAS regimes, slow and fast, with $\tau_c = \tau_1 + \tau_2$.

UTPD ($\theta - \phi$)	Conventional schemes	Slow MAS ($\nu_1 > 4\nu_r$)	Fast MAS ($\nu_1 < 4\nu_r$)
30°	TPPM	$\tau_1 = \tau_2 = \tau_c/2$ $\tau_c \sim (\nu_r/\nu_1)^* \tau_r$	$\beta_1 = \beta_2 \sim 180^\circ$
30°	...	$0 < (\tau_1 - \tau_2) < 0.05\tau_c$ $\tau_c = (\nu_r/\nu_1)^* \tau_r$	$0^\circ < (\beta_1 - \beta_2) < 100^\circ$ $\beta_1 + \beta_2 = 360^\circ$
90°	rCW ^A	τ_1 or $\tau_2 = \tau_\pi$ $\tau_1 + \tau_2 = 1.05\tau_r$	$(2\tau_1 + \tau_2)/\tau_r = \text{integer}(2\nu_r/\nu_1)$ $\beta_2 = 270^\circ$
90°	...	τ_1 or $\tau_2 = \tau_\pi$ $\tau_1 + \tau_2 = 1.05\tau_r$	$(\beta_1 - \beta_2) = 144^\circ$ or $\beta_1 + \beta_2 = 2^*360^\circ$
180°	XiX	$\tau_1 = \tau_2 \sim 1.8^* \tau_r$	$\beta_1 = \beta_2 \sim 360^\circ$
180°	...	$\tau_1 + \tau_2 \sim 2\tau_r$ $0.04\tau_r < (\tau_1 - \tau_2) < 0.06\tau_r$	$\beta_1 + \beta_2 = 2^*360^\circ$ $\beta_1 - \beta_2 = \sim 140^\circ$

with different chemical shifts which, therefore, would result in an offset-dependent line broadening.^{14,15} Figure 4 compares the offset dependence for different low-power decoupling sequences over an offset range of ± 8 kHz under the conditions of ν_1 and ν_r of 10 kHz and 50 kHz, respectively. Each of these sequences was first optimized individually at on-resonance condition. The comparison shows that offset dependence of all these schemes are similar. In general, the decoupling efficiency severely drops as offset increases. However, in UTPD[180°, τ_1 , τ_2], this drop in efficiency is relatively slower. This trend is similar to AM-XiX³³ where amplitude modulation of the two XiX pulses leads to better decoupling especially at the off-resonance conditions. Finally, to emphasize that efficient decoupling can be obtained across the entire phase space of the UTPD scheme with the incorporation of time modulation, the NMR spectra of ¹³C α -glycine, acquired with individually optimized schemes, are compared in Fig. 5. All the schemes perform similarly, except for XiX which is $\sim 20\%$ less efficient than others. Time modulation can lead to better performance of XiX just like amplitude modulation. The rationale behind the advantage of incorporating time modulation of the two pulses is discussed from a theoretical perspective in Sec. IV. Finally, to provide some guidelines from a practical point of view, a listing of various UTPD conditions in the two different experimental regimes is made in Table I. The parameters corresponding to the conventional and UTPD schemes are indicated in Figs. 1 and 3 by dotted circles and dotted squares, respectively. Herein, τ_1 , β_1 and τ_2 , β_2 correspond to the lengths and flip angle of the individual pulses. The phases of the individual pulses are represented by θ and ϕ .

IV. THEORY

Here, the important phase dependence of the UTPD pulse scheme on dipole-dipole and J couplings is explained using effective

Hamiltonian analysis. For consistency, we follow the well-established theoretical framework used in our earlier analysis of heteronuclear decoupling schemes,^{27,38,39} similar to that introduced by Ernst and co-workers.³¹ Here, it is sufficient enough, to the first order of approximation, to consider only the heteronuclear spin coupling interaction between two spins, I and S , whilst the I spin is being irradiated with the RF field to achieve decoupling. Under MAS, these interactions are defined by the time-dependent Hamiltonian

$$H(t) = \underbrace{\omega_I I_z S_z}_{\text{J coupling}} + \underbrace{\sum_{n=-2}^2 \omega_D^{(n)} e^{in\omega_r t} I_z S_z}_{\text{Dipole-dipole coupling; } n \neq 0} + \underbrace{\omega_1(t) I_{\phi(t)}}_{H_{RF}}, \quad (1)$$

where ω_I and ω_D^n refer to the J coupling magnitude in angular frequency units and the n -th order Fourier coefficients of the $I - S$ heteronuclear dipole-dipole coupling, respectively. $\omega_1(t)$ and $\phi(t)$ are the RF amplitude and phase of decoupling pulses, respectively, in the UTPD scheme. The effect of RF can be best analyzed by transforming the Hamiltonian into the interaction frame of the UTPD pulses using the propagator $U_{RF}(t) = \hat{T} e^{-i \int_0^t H_{RF}(t') dt'}$, where $\hat{T}$ is the Dyson time-ordering operator.⁴⁰

The RF Hamiltonian can influence only the I spin operator which is present in the two coupling terms as I_z . Therefore, calculating the transformed I_z operator in the RF interaction frame at different times is all what we need. The I_z operator under the UTPD scheme will transform as a linear combination of I_x , I_y , and I_z

$$\begin{aligned} U_{RF}^{-1}(t) I_z U_{RF}(t) &= a^x(t) I_x + a^y(t) I_y + a^z(t) I_z \\ &= \sum_{\sigma=x,y,z} a^\sigma(t) I_\sigma, \end{aligned} \quad (2)$$

where the coefficients $a^x(t)$, $a^y(t)$, and $a^z(t)$ are the time-dependent components (trajectories) of I_x , I_y , and I_z operators, respectively,

such that the norm $\sqrt{a^x(t)^2 + a^y(t)^2 + a^z(t)^2} = 1$ at any time t since U_{RF} is an unitary operator. The normalized values of these coefficients depend on the phase difference between the two pulses in UTPD, the length of the pulse scheme ($\tau_c = \tau_1 + \tau_2$), and RF amplitude of the pulses. These trajectories are shown for two UTPD schemes, UTPD[45°, τ_1 , τ_2] and UTPD[180°, τ_1 , τ_2], with τ_1 and τ_2 corresponding to 180° flip in Fig. 6.

In the case of UTPD[45°, τ_1 , τ_2], the trajectories are non-cyclic, but they are cyclic for UTPD[180°, τ_1 , τ_1] and $\tau_1 = \tau_2$. This implies that the time-dependent coefficient $a^\sigma(0) \neq a^\sigma(\tau_c)$ for UTPD[45°, τ , τ], but $a^\sigma(t) = a^\sigma(t + \tau_c)$ for UTPD[180°, τ , τ]. Whether these trajectories are cyclic or non-cyclic has a crucial role in determining the performance of a given decoupling scheme especially in the presence of J coupling which can be refocused only using RF and not by MAS. One can understand this in the following way: “the time average of a cyclic trajectory when repeated over several blocks of the pulse scheme remains the same as for one block of the basic pulse scheme. But when a non-cyclic trajectory is repeated by concatenating it multiple times, the resultant average of the Hamiltonian over several cycles becomes zero, even when the average in each cycle itself is non-zero, assuming that effective cycle time is not too long as compared to coherence decay time.” This subtle concept is crucial in determining the robustness of the low-phase or time-modulated UTPD scheme toward J coupling, as discussed below.

In the case of UTPD[180°, τ , τ], the average of $a^\sigma(t)$ is non-zero in the interval from 0 to τ_c . As this scheme is cyclic in nature (i.e., $a^\sigma(t) = a^\sigma(t + \tau_c)$), this non-zero average remains the same even when the basic sequence is repeated multiple times. In the case of UTPD[45°, τ , τ], owing to its non-cyclic nature, the non-zero average of $a^\sigma(t)$ and $a^\sigma(t)$ changes with concatenation of each block of the basic UTPD[45°, τ , τ] pulse scheme. Eventually, by repeating the basic unit multiple times, the average of $a^\sigma(t)$ can become zero. With four blocks of UTPD[45°, τ , τ] and with τ equaling π rotation, complete averaging of all the $a^\sigma(t)$ components can be achieved and, therefore, an interaction like J coupling which is modulated by just the RF is always averaged out in a non-cyclic UTPD scheme. However, in case of a cyclic scheme with zero effective rotation, like UTPD[180°, τ , τ] with equal flip angles, the J coupling,

in general, is not averaged out to zero. Only under certain conditions, when the average in each cycle itself is zero, the overall average will be zero even when the sequence is repeated. This can also be understood in terms of resonance conditions as exploited extensively by the group of Ernst.¹ The standard way to identify whether an RF pulse sequence is cyclic or not and whether the average value of the trace is zero or non-zero over each cycle is to rewrite the time-dependent coefficients of the trajectories in terms of a Fourier series.

In general, the Fourier coefficients associated with the RF modulations are non-cyclic for the duration τ_c , i.e., $a^\sigma(t) \neq a^\sigma(t + \tau_c)$. Or in other words, there is non-zero, effective rotation of the interaction frame Hamiltonian per unit of the pulse scheme. In general, the Fourier series for $a^\sigma(t)$ can be constructed using two basic frequencies, the pulse-modulation frequency ($\omega_c = 1/\tau_c$) and the effective-rotation frequency ω_{eff} . The effective-rotation is calculated here using the Quaternion formalism.^{15,41} Accordingly,

$$a^\sigma(t) = \sum_{k=-\infty}^{\infty} \sum_{\ell=-1}^1 a_{k,\ell}^\sigma e^{ik\omega_c t} e^{i\ell\omega_{eff} t} \quad (3)$$

for $\sigma \equiv \{x, y, z\}$. The effective rotation $\beta_{eff} = \frac{\omega_{eff}}{2\pi} 360^\circ \tau_c$ (in degrees) for different values of $(\phi - \theta)$ in UTPD[($\phi - \theta$), τ_1 , τ_2] is plotted in Fig. 7. The contour plot shows that β_{eff} for the high-phase UTPD scheme is zero along the diagonal ($\tau_1 = \tau_2$) in contrast to low-phase UTPD which has non-zero β_{eff} except for conditions where pulse flip angles are integer multiples of 360°.

Using Eqs. (1)–(3), the RF interaction frame Hamiltonian becomes

$$\hat{H}(t) = \sum_{k=-\infty}^{\infty} \left(\omega_J S_z + \sum_{n=-2}^2 \omega_D^{(n)} e^{in\omega_c t} S_z \right) I_\sigma a_{k,\ell}^\sigma e^{ik\omega_c t} e^{i\ell\omega_{eff} t}. \quad (4)$$

Notably, the J coupling is modulated by two frequencies and the dipole-dipole coupling by three frequencies in the RF interaction frame. This Hamiltonian becomes dominant and causes line broadening only when its time average is non zero. So for J coupling, when the first order average

FIG. 6. Time dependent trace or the trajectories, $a^\sigma(t)$ for $\sigma \equiv x$ (red), y (blue), and z (black), in the RF interaction frame for (a) UTPD[45°, τ , τ] and (b) UTPD[180°, τ , τ], with τ corresponding to the 180° flip angle.

FIG. 7. Effective rotation in degrees for different UTPD schemes calculated using the Quaternion formalism.

$$\bar{H}_J(t) = \int \sum_{k=-\infty}^{\infty} a_{k,\ell}^{\sigma} e^{ik\omega_c t} e^{i\ell\omega_{\text{eff}} t} dt = 0,$$

the J coupling is averaged out per cycle of the UTPD scheme, i.e., when the condition $k\omega_c + \ell\omega_{\text{eff}} \neq 0$ is satisfied, and/or the scaling factor $a_{k,\ell}^{\sigma} = 0$. A general condition for this will be fulfilled when the frequencies are not commensurate, $k\omega_c \neq \ell\omega_{\text{eff}}$, for small k and ℓ , or when the effective-rotation frequency $\omega_{\text{eff}} \neq 0$. The latter condition is met by low-phase UTPD- the effective rotation per unit cycle time (τ_c) is non-zero. By contrast, for high-phase UTPD, the effective rotation is nearly zero along the diagonal condition (i.e., $\tau_1 = \tau_2$) and therefore J coupling is not averaged out, in general, unless when the scaling factor $a_{k,\ell}^{\sigma} = 0$. Only at the off-diagonal conditions, $\tau_1 - \tau_2 \neq n * 360^\circ$ (for integer n), the effective rotation is non-zero. The above justification clearly states out why time modulation is a must for obtaining maximum resolution especially with the high-phase UTPD condition. In general, creating an effective rotation by using either time-, phase-, and/or amplitude-modulation in the basic two-pulse scheme is an essential characteristic of an efficient and robust decoupling scheme in the low-power regime. In case of dipole-dipole coupling, the resonance condition is governed

by three simultaneous modulations. The dipole-dipole Hamiltonian gets recoupled when $n\omega_r + k\omega_c + \ell\omega_{\text{eff}} = 0$ is satisfied, and the extent of recoupling depends on the magnitude of the coefficient $a_{k,\ell}^{\sigma} \omega_D^{(n)}$. When the modulation frequencies become more and more different from each other, the scaling factor becomes progressively smaller. Overall, spinning helps in averaging out the dipole-dipole coupling and it is possible to easily find the conditions for all phases of UTPD where interference can be avoided and good resolution can be obtained. These resonance conditions have been discussed in detail by the group of Ernst.^{15,31}

V. METHODS AND MATERIALS

All simulations were performed using the SIMPSON^{34,35} open-source simulation package for typical parameters of a CH₂ spin system (assuming conditions of a 700 MHz ¹H Larmor frequency): $\delta_{\text{H}}^{\text{CSA}} = -3050$ Hz, $\delta_{\text{C}}^{\text{CSA}} = 0$, $\eta_{\text{C}}^{\text{CSA}} = 0$, $\delta_{\text{H1}}^{\text{iso}} = 0$, $\delta_{\text{H2}}^{\text{iso}} = 200$ Hz, $\delta_{\text{C}}^{\text{iso}} = 0$, $\omega_{\text{HC}}^{\text{D}}/2\pi = -23.3$ kHz, $\omega_{\text{HH}}^{\text{D}}/2\pi = -21.3$ kHz, $\omega_{\text{HC}}^{\text{J}}/2\pi = 130$ Hz, and $\omega_{\text{HH}}^{\text{J}}/2\pi = 13$ Hz. For the CH₂-H spin system, $\delta_{\text{H}}^{\text{CSA}} = -2000$ Hz,

the additional $\omega_{\text{H,C}}^D/2\pi = -3$ kHz, and the additional $\omega_{\text{H,H}}^D/2\pi$ couplings were -6.9 kHz and -3.8 kHz, keeping heteronuclear J couplings fixed at 130 Hz. The decoupling performance of a sequence does not depend on the CSA of less abundant carbon spins up to second-order in the effective Hamiltonian. For the same reason, CSA of carbon was not taken into consideration. Spin parameters were obtained using the SIMMOL package.⁴²

All the experiments were carried out at 16.43 T (^1H Larmor frequency of 700 MHz) using the Bruker AV III NMR spectrometer. A 1.3 mm double resonance standard Bruker MAS probe was used for experiments at MAS frequencies of 50 kHz and an RF amplitude of 10 kHz. The experiments were carried out on commercially available 2- ^{13}C -glycine (Sigma-Aldrich) and its derivative 1,2- ^{13}C -glycine ethyl ester powder samples. Ramped-amplitude cross-polarization (CP)⁴³ was used to achieve ^1H - ^{13}C polarization transfer. Heteronuclear decoupling pulses were applied during the detection of the ^{13}C free-induction decay (FID). During decoupling, the ^1H carrier frequency was placed on resonance to aliphatic protons. The individual pulse durations (τ_1 , τ_2) in UTPD[($\phi - \theta$), τ_1 , τ_2] were optimized from 0.1 μs to 160.1 μs with a step size of 2 μs . Peak heights obtained after Fourier transformation of the FID were used for quantitative comparisons.

VI. CONCLUSION

The decoupling efficiency profile of the two pulse scheme (UTPD) over the entire pulse phase and length parameters is elucidated here in the low- ν_1 -fast- ν_r regime. It turns out that for typical spin parameters of the $^{13}\text{CH}_2$ (glycine) spin system, multiple efficient decoupling conditions exist. In general, the lower-phase UTPD[($\phi - \theta$), τ_1 , τ_2] schemes are more tolerant toward second-order deleterious effect of ^1H homonuclear dipole-dipole coupling and higher-phase schemes are more tolerant toward high CSA effect of ^1H , similar to the high- ν_1 -slow- ν_r regime. We have also demonstrated that for higher phases, the time modulation plays a cardinal role in significantly improving the decoupling efficiency and robustness owing to an *effective rotation* which refocuses the signal dephasing induced by second-order ^1H homonuclear coupling and first-order ^1H - ^{13}C J coupling. In our perspective, the presence of effective rotation is the crux of efficient and robust decoupling in the low-power regime.

In the context of next generation solid-state MAS NMR experiments (high B_0 and fast ν_r), we want to assert that since CSA increases linearly with the strength of B_0 and second-order residual dipole-dipole terms scale down with fast MAS, the tolerance toward J coupling and ^1H offset will become the major parameters influencing the decoupling performance of a pulse scheme. In such a scenario, the technique of pulse flip-angle modulation (by incorporating time or amplitude modulation) and super-cycling of the high phase UTPD scheme will become important. Sc-AM-XiX and rCW^{ApA} are existing examples of this, but there still lies significant scope of improvement especially in achieving better offset tolerance.^{27,33} This is being investigated currently.

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