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Swept-frequency two-pulse phase modulation for heteronuclear dipolar decoupling in solid-state NMR

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Abstract

We introduce a heteronuclear dipolar decoupling sequence for application in solid-state nuclear magnetic resonance. The sequence, called swept-frequency two-pulse phase modulation (SW_f-TPPM), is based on one of the decoupling sequences, TPPM. The sequence is robust in performance with respect to various experimental parameters, such as, the pulse flip angle, pulse phase, and offset and a comparison is made with other decoupling schemes, namely TPPM, SPINAL, and XiX, on a sample of U–^{13}C-labelled tyrosine for magic-angle spinning speeds up to 14 kHz.

1. Introduction

High-resolution solid-state NMR spectra of rare nuclei such as ^{13}C in unaligned samples are routinely obtained with the combined use of magic-angle spinning (MAS) and appropriate radio-frequency (RF) irradiation on the abundant ^{1}H spins to decouple the ^{1}H–^{13}C dipolar coupling [1,2]. A continuous burst of RF irradiation, called the CW decoupling [1], was used for heteronuclear dipolar decoupling till the efficiency of which got improved by the introduction of two-pulse phase modulation (TPPM) scheme [3] and a variant of it, namely, small phase incremental alteration (SPINAL) [4]. SPINAL has been shown to perform better than TPPM over a wide range of MAS rates [5,6]. The recently introduced decoupling sequence XiX [7], an elaboration of an amplitude-modulated decoupling scheme suggested by Tekely [8], has been found to be better at high MAS rates, $\omega_r > 25$ kHz.

Efficient heteronuclear dipolar decoupling is very important in many applications, particularly in the solid-state NMR of biomolecules to get narrower ^{13}C or ^{15}N spectra. Efforts are also underway to understand the principles of decoupling, such as, the factors causing residual line broadening, the influence of homonuculear ^{1}H–^{1}H dipolar coupling, and both higher-order and cross-terms of and among the various spin interactions [9–11]. Hence, the area of decoupling is an emergent topic with newer sequences and modifications of the existing ones being introduced to enhance spectral resolution [12–18].

Ease of implementation, robustness with respect to MAS rates and RF inhomogeneities, and a performance index comparable to or better than SPINAL are certain desirable features of newer decoupling sequences. With these general guidelines and basic block of TPPM at hand we present here an alternative decoupling sequence which will be shown to be comparable to SPINAL for the range of MAS rates, RF amplitudes, and off-resonance values investigated.

The Letter is structured along the following lines: construction of the new decoupling sequence, an intuitive understanding of its performance based on the Fourier picture, and experimental comparison of various decoupling sequences.

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2. Design of the new pulse sequence

For the design of the new decoupling sequence we consider TPPM as the building block which is $R_\phi R_{-\phi}$. In other words, the phase is square wave modulated at the RF nutation frequency, ω_1, if the flip angle R is 180°. Often in experiments R is found to be close to 165° which means that the modulation is only approximately ω_1. Experimentally both R and the phase ϕ need to be optimised.

SPINAL-64 is of the form $Q\overline{Q}\,\overline{Q}Q\overline{Q}QQ\overline{Q}$ with $Q \equiv R_\phi R_{-\phi}$, $R_{\phi+5}R_{-\phi-5}$, $R_{\phi+10}R_{-\phi-10}$, $R_{\phi+5}R_{-\phi-5}$. In experiments, optimal R and ϕ are generally 165° and 10°, respectively. XiX consists of two-pulses of phases x and $\bar{x}$ with a pulse duration $\tau_\mathrm{p} > 1.5\tau_\mathrm{r}$ (rotor period) that needs to be optimised.

The first step towards improving on TPPM is to understand the reason(s) for its efficiency. The first term in the Fourier expansion of its phase modulation is $\frac{4}{\pi}\sin(\omega_\mathrm{c}t)$, where ω_c is the modulation frequency. It is interesting that independently, and from a completely numerical approach, the Emsley group also arrived at cosine modulation of the phase as a means to improved decoupling [9]. The RF Hamiltonian, in the rotating frame of such phase-modulated sequences, may be represented by

$$\mathscr{H}_\mathrm{RF} = \omega_1\left\{\sum_i I_x^i\cos(\phi(t)) + \sum_i I_y^i\sin(\phi(t))\right\} \tag{1}$$

We analyse the case where the RF phase $\phi(t)$ is $a\cos(\omega_\mathrm{c}t)$, where a and $\omega_\mathrm{c}(t)$ are the modulation depth and frequency, respectively. The analysis is only marginally different for other sinusoidal modulation patterns. The system Hamiltonian consists of four parts: one S spin, often ^{13}C, chemical shift, many I spins, often ^{1}H, chemical shifts, the heteronuclear (I_iS), and homonuclear (I_iI_j) dipolar coupling terms, and is given by

$$\begin{aligned}\mathscr{H}_\mathrm{sys} &= \omega_s(t)S_z + \sum_i \omega_i(t)I_z^i + \sum_i \omega_{iS}(t)2S_zI_z^i \\ &\quad + \sum_{i,j}\omega_{ij}(t)[2I_z^iI_z^j - (I_x^iI_x^j + I_y^iI_y^j)]\end{aligned} \tag{2}$$

The time dependence is a result of MAS. In a frequency modulated frame defined by $T = \exp(-\mathrm{i}\phi(t)\sum_i I_z^i t)$ the RF Hamiltonian becomes time independent, $\omega_1 I_x$, whilst the I spin offsets become $(\omega_i(t) - \dot{\phi}(t))$. If the RF Hamiltonian is large relative to the offsets, we may transform into an interaction frame, $T' = \exp(-\mathrm{i}\omega_1\sum_i I_x^i t)$, defined by the former. All the action happens in this frequency-modulated interaction frame. Barring the frequency-modulation, the analysis thus far is identical to CW decoupling [1]. In this frame, only the I spin offsets, on which we focus our attention, show any difference from the CW decoupling case and are given by

$$(\omega_i(t) - \phi(\dot{t}))(I_z^i\cos(\omega_1 t) + I_y^i\sin(\omega_1 t)) \tag{3}$$

For cosine modulation, $\phi(\dot{t}) = -a\omega_\mathrm{c}\sin(\omega_\mathrm{c}t)$. The modulation frequency is often close, if not equal, to ω_1. At resonance, when the equality holds, the average Hamiltonian over the nutation period $\tau_1 = 2\pi/\omega_1$ is of the form $-a\omega_\mathrm{c}/2I_y$, which looks like an additional RF term.

We now perform a second averaging about this term. This is justified as there is a time scale separation between τ_r and τ_1 ($\tau_\mathrm{r} \gg \tau_1$). Interesting and documented resonance phenomena arise when $\omega_1 = n\omega_\mathrm{r}$ with n equal to 1/2 or 1. Here $a\omega_\mathrm{c}/2 = \omega_1$. The case of $n = 1/2$ leads to homonuclear rotational recoupling (HORROR) [20] and $n = 1$ to rotary resonance recoupling (R^3) [21] with the former being important here. At the HORROR condition, the homonuclear proton dipolar coupling is reintroduced leading to efficient spectral spin diffusion. Prior studies have established the connection between enhanced spin diffusion over the proton network and improved decoupling efficiency [9,1,22]. Reintroduction of the proton homonuclear coupling at the HORROR condition in the second-averaged frequency-modulated interaction frame accounts for the improved efficiency of all the phase-modulated decoupling sequences over CW decoupling. It also explains heretofore unexplained observations such as, for example, the poor decoupling performance of the frequency-modulation phase modulation (FMPM^R) sequence of Gan and Ernst [19] in contrast with FMPM^L. We must remark here that Paëpe et al. [9] have realised the importance of the HORROR condition in their cosine-modulated sequence but, to the best of our knowledge, have not attributed its central importance in other phase-modulated decoupling sequences.

Obviously, improvements could be made to the existing phase-modulated sequences by making the HORROR condition broadbanded in much the same way that conventional HORROR can. One needs to only look as far as the dipolar recoupling enhancement through amplitude modulation (DREAM) sequence [23]. The approach is simple and borrows the idea from adiabatic pulses: sweep through the HORROR condition as efficiently as possible. Varying the modulation depth, a, or the modulation frequency, ω_c, achieves this sweep. In SPINAL, a is varied [4]. Here, we introduce a sequence, swept frequency-TPPM (SW$_\mathrm{f}$-TPPM), where ω_c is varied.

With TPPM as building block there are various ways to generate a frequency modulation. One that is straightforward, and employed here, is to vary the pulse width. The modulation profile was chosen to crudely resemble a tangential sweep (in analogy with the DREAM scheme) which we implemented with the sequence {[$0.78\tau_\phi$-$0.78\tau_{-\phi}$] [$0.86\tau_\phi 0.86\tau_{-\phi}$] [$0.94\tau_\phi 0.94\tau_{-\phi}$] [$0.96\tau_\phi 0.96\tau_{-\phi}$] [$0.98\tau_\phi 0.98\tau_{-\phi}$] [$\tau_\phi\tau_{-\phi}$] [$1.02\tau_\phi 1.02\tau_{-\phi}$] [$1.04\tau_\phi 1.04\tau_{-\phi}$] [$1.06\tau_\phi 1.06\tau_{-\phi}$] [$1.14\tau_\phi 1.14\tau_{-\phi}$] [$1.22\tau_\phi 1.22\tau_{-\phi}$]} where a good guess for τ_ϕ was the optimal TPPM value, corresponding to 165°, with a phase ϕ. Consequences of its variation will be discussed in the next section.

The superior performance of SPINAL over TPPM was attributed to large number of frequency components in the former [4]. Although with the present knowledge this may be contested it is still instructive to compare the power

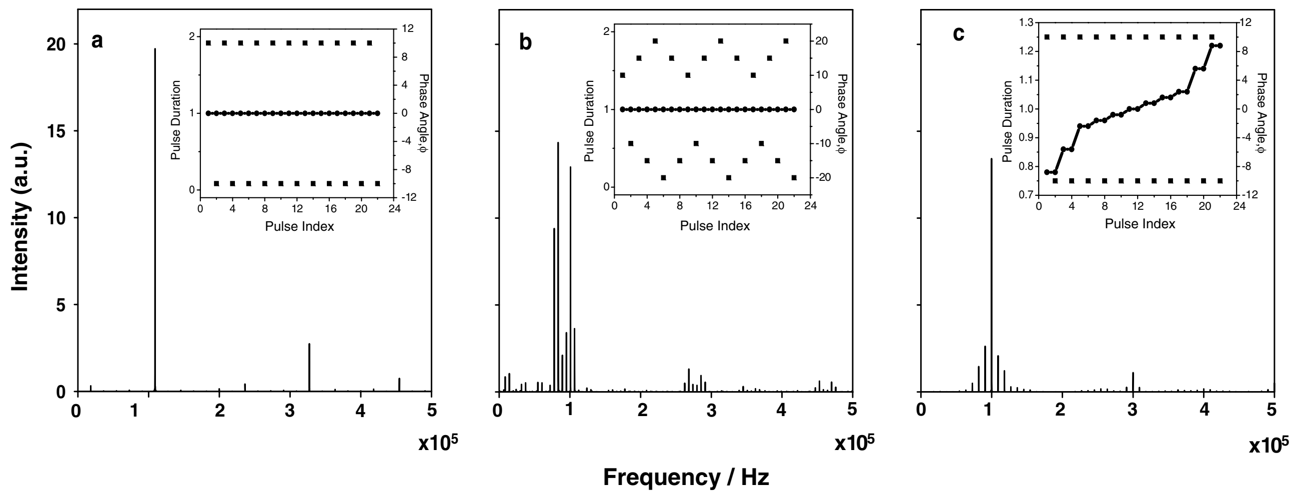

Fig. 1. Power spectrum of: (a) TPPM, (b) SPINAL-64, and (c) SW_f-TPPM sequences with $\omega_1 = 100$ kHz, flip angle of 165°, and $\phi = 10°$. The sampling time was 1 μs. The insets of each plot show time domain and phase profile of a set of 11 pairs of pulses for each of the sequences.

spectrum of TPPM, SPINAL-64, and SW_f-TPPM shown in Fig. 1. Both SPINAL-64 and SW_f-TPPM have more Fourier components than TPPM.

A way to an improved decoupling sequence would be to generate a distribution of frequency components, in its power spectrum, about the HORROR condition in the modulated frame. SW_f-TPPM achieves this with a modulation of pulse duration such that the sweep is faster when further away from the optimal τ_ϕ and slower around τ_ϕ. The insets of Fig. 1a–c show the variation of pulse duration and phase angle, for 11 pairs of pulses that form the basic unit of SW_f-TPPM, for the three schemes. The optimal distribution for efficient decoupling is far from obvious but intuitively one is inclined to think of a normal or uniform distribution. From Fig. 1 the frequency components in SW_f-TPPM are significantly more normally distributed than SPINAL-64 and less power is present in higher harmonics. We now explore if these improvements are reflected in experimental performance.

3. Experimental

All experiments were performed on a Bruker AV500 MHz spectrometer equipped with a 4 mm triple-resonance CPMAS probe. A U–^{13}C-labelled tyrosine was used for these experiments with a relaxation delay of 120 s to avoid any saturation effects. Results from the new sequence are compared with TPPM, SPINAL-64, and XiX. The experiments were performed in the MAS range of 6–14 kHz.

4. Results and discussion

Fig. 2 shows the signal intensity of the CH_2 (top row) and CH (bottom row) peaks (at 38 and 138 ppm, respectively) as a function of ω_r for three different ω_1, 100 kHz (left panel), 90 kHz (middle panel), and 70 kHz (right panel). The performance of both SPINAL-64 and SW_f-TPPM is fairly comparable, with SW_f-TPPM slightly outperforming SPINAL-64. The performance of TPPM gets better with higher ω_r. The performance of SW_f-TPPM deteriorates at ω_1 lesser than 70 kHz, a feature which will be examined in detail later. XiX data is only shown for $\omega_1 = 100$ kHz as its performance deteriorated for lower ω_1.

The homonuclear dipolar couplings are stronger in the case of the CH_2 group compared with the CH group. In the former case SW_f-TPPM, being broad-banded by design, is able to recouple the ^1H–^1H dipolar couplings more efficiently than the other sequences giving it an advantage. The oscillations in the intensity profile of the CH_2 group in Fig. 2 arise from rotational-resonance effects at some of the ω_r values investigated. Because the sample was uniformly ^{13}C-labelled, finding rotor speeds that avoid any rotational-resonance conditions was far from straightforward. In the case of the CH group there is not much difference among all the sequences with respect to efficiency due to both weaker homonuclear ^1H–^1H and heteronuclear ^1H–^{13}C dipolar couplings. Hence, TPPM is able to recouple ^1H–^1H dipolar couplings to an extent that is not bettered further by either SPINAL or SW_f-TPPM.

To investigate further the efficiency of SW_f-TPPM, we have plotted in Fig. 3 the intensity of the CH_2 peak as functions of pulse duration in (a), ^1H off-resonance irradiation frequency in (b), and the phase angle ϕ in (c) (for SW_f-TPPM the pulse duration implies the duration of the central pulse pair) for $\omega_1 = 100$ kHz and $\omega_r = 14$ kHz. The dependence of the decoupling efficiency of SW_f-TPPM with variation in the RF offset is less marked than both SPINAL and TPPM as can be seen from Fig. 3b. An interesting feature results from (a) and (c). Whilst TPPM is robust with respect to variation in ϕ, SPINAL is robust with respect to variation in the flip angle (pulse duration). SW_f-TPPM has the nice feature of being broad-banded with respect to both the pulse duration and ϕ making it easier to implement.

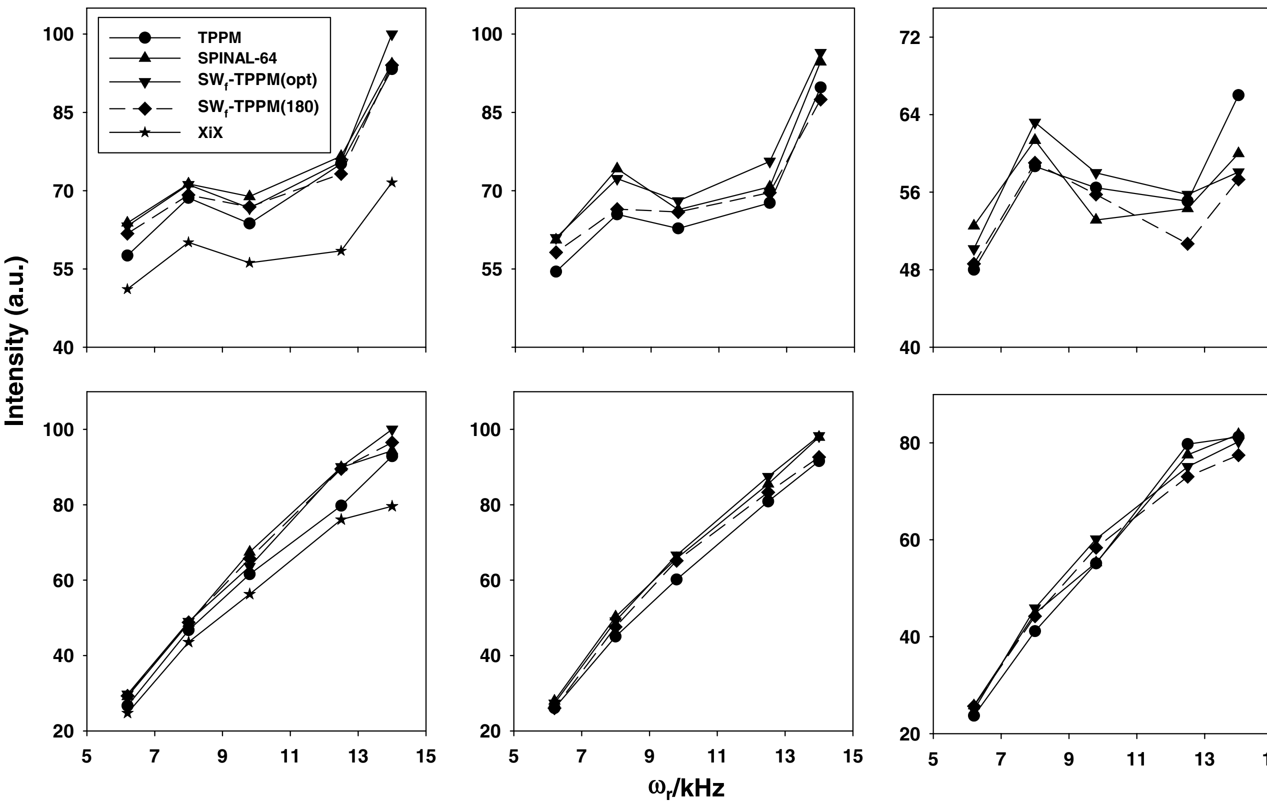

Fig. 2. Spectral intensity comparison of the CH_2 peak (at 38 ppm), top panel, and the CH peak (at 138 ppm), bottom panel, with TPPM (filled circle), SPINAL-64 (upper triangle), XiX (star), and SW_f-TPPM (lower triangle) sequences plotted as a function of the MAS frequency, $\omega_r = 6.2$, 8.0, 9.8, 12.5, and 14.0 kHz. Left, middle, and right columns correspond to experiments with $\omega_1 = 100$, 90, and 70 kHz, respectively, for which the optimal value of the pulse duration was 4.8, 5.8, and 6.4 μs, respectively, corresponding to a flip angle of ca. 165°. Whilst the phase angle ϕ for SW_f-TPPM was 12.5°, it was 10° for SPINAL-64, and suitably optimised for TPPM between 5° and 10° depending on the values of ω_r and ω_1. The dashed lines correspond to the implementation of SW_f-TPPM where the flip angle was 180°. ω_1 was determined by performing a nutation experiment on a sample of adamantane.

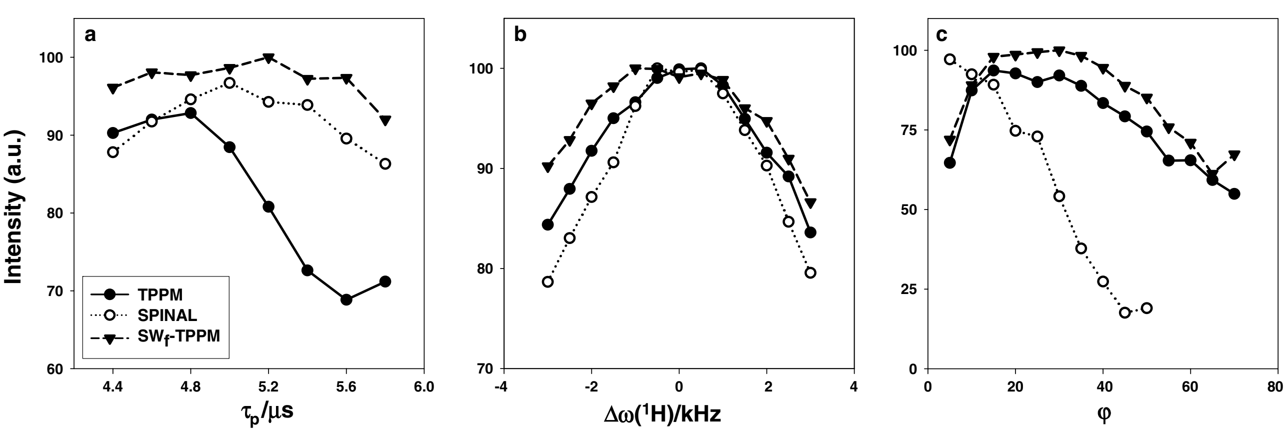

Fig. 3. Intensity of the CH_2 peak monitored as a function of: (a) the pulse duration (flip angle) τ_ϕ, (b) ^{1}H off-resonance irradiation, and (c) the phase angle ϕ for TPPM (filled circle), SPINAL-64 (empty circle), and SW_f-TPPM (lower triangle). All intensities are normalised with respect to those of SW_f-TPPM.

A point of concern in the implementation of SW_f-TPPM would be the selection of the pulse durations τ_ϕ. The only aspect to take note of is the general shape of the modulation profile in Fig. 1c, *i.e.*, slow in the middle and fast at the ends. To reiterate, one just needs to select a few values around the optimal value of τ_ϕ. The dashed lines in Fig. 2 show results of an implementation of SW_f-TPPM with τ_ϕ corresponding to a flip angle of 180°. The results show that although the performance of SW_f-TPPM deteriorates, like other sequences, at low RF power levels it is still comparable to SPINAL.

The 'tangential sweep' that SW_f-TPPM tried to mimic is unlikely to be the most optimal. A bimodal Floquet analysis of TPPM and SW_f-TPPM to complement the zeroth-order average Hamiltonian theory employed here is in progress, which is expected to give a version of SW_f-TPPM with an optimal modulation profile.

5. Conclusions

The improved decoupling characteristics of phase-modulated sequences like TPPM has been shown here to arise from a HORROR condition involving an RF-like term in a modulated frame and the rotor frequency, which reintroduces proton–proton dipolar couplings. With this insight we have proposed a TPPM variant, SW_f-TPPM, in which the modulation frequency is varied by modulating the pulse widths. An intuitive understanding of the performance of SW_f-TPPM was made on the basis of a Fourier picture. Detailed experimental characterisation upto 14 kHz of spinning speed shows that SW_f-TPPM is on par, if not better, than SPINAL and better than TPPM. SW_f-TPPM has the desirable feature of ease of implementation.

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