

Communication

# Heteronuclear decoupling under fast MAS by a rotor-synchronized Hahn-echo pulse train

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## Abstract

A new heteronuclear decoupling mechanism under fast magic-angle spinning MAS is introduced. It is based on refocusing the coherences responsible for the dephase of low- $\gamma$  nuclei ( $^{13}\text{C}$ ,  $^{15}\text{N}$ ) transverse spin-polarization in the presence of strongly dipolar-coupled protons, and has the advantage that can be implemented by pulsed techniques, with all the benefits resulting from a reduced duty cycle compared with conventional decoupling by continuous *rf* irradiation. The decoupling efficiency of a simple rotor-synchronized Hahn-echo pulse train is analyzed both theoretically and experimentally. It was found that a substantial improvement in sensitivity and resolution can be achieved in compounds with small  $^1\text{H}$  chemical shielding parameters even at moderate sample spinning, and some interesting applications are shown. It is also shown that much faster spinning frequencies, or alternative refocusing sequences, are needed for applications on rigid organic solids, i.e., in systems with larger  $^1\text{H}$  chemical shifts.

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**Keywords:** Solid-state NMR; Fast MAS; Heteronuclear decoupling; Hahn-echo; High-resolution

## 1. Introduction

Achieving high spectral resolution by designing more powerful heteronuclear decoupling techniques is an essential prerequisite for the efficient application of the modern solid-state nuclear magnetic resonance (SS-NMR) methodology to complex systems, such as biological macromolecules. For many years until recently, high-power continuous wave (CW) decoupling represented the common way to achieve heteronuclear decoupling in SS-NMR under magic-angle spinning (MAS)—for a review see [1]. The introduction of two-pulse phase-modulated (TPPM) decoupling by Bennett et al. [2] initiated renewed interest in understanding the decoupling process in rotating solids and started the development of more sophisticated phase- (and/or amplitude) modulation schemes [3–14]. Yet, the

improvement in resolution is by far not as spectacular as expected, which might indicate that decoupling through continuous *rf* irradiation on the proton channel has reached limitations originating from its basic averaging mechanism.

In the present work, we explore the possibility of employing a different heteronuclear decoupling mechanism, which is based on refocusing the coherences responsible for the dephase of low- $\gamma$  nuclei ( $^{13}\text{C}$ ,  $^{15}\text{N}$ ) transverse spin-polarization, and thus for the observed residual broadening. It is shown here, that a simple rotor-synchronized Hahn-echo pulse train (RS-HEPT) can achieve this goal even in the presence of a strongly dipolar-coupled  $^1\text{H}$  network, provided that protons have negligible small chemical shielding parameters, and the spinning frequency is sufficiently high. The refocusing properties of RS-HEPT under these conditions are quantitatively analyzed by numerical simulations on model ( $^{13}\text{C}$ ,  $^1\text{H}$ ) spin systems. Subsequently, they are demonstrated in practice by the  $^{13}\text{C}$  CP/MAS

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spectrum of adamantane acquired at 25 kHz spinning frequency, where a substantial line narrowing compared to the CW decoupled spectrum was obtained. Numerical simulations performed under more realistic conditions, i.e., by taking proton chemical shift values typically found in organic solids, have shown that RS-HEPT can outperform CW or TPPM decoupling only under a very fast ( $\nu_R \sim 40$  kHz), and a hypothetically extremely fast ( $\nu_R \sim 100$  kHz) spinning regime, respectively.

Efforts aimed at reducing the decoupling power are not new, and they have resulted in developing equivalent, low-*rf* power (and fast MAS), versions of the classical decoupling techniques [15]. Within this context, pulsed heteronuclear decoupling represents an attractive alternative to the conventional decoupling by continuous *rf* irradiation on the  $^1\text{H}$  channel due to its reduced duty cycle. The results presented here demonstrate that such an approach is in principle feasible, but for routine practical applications on rigid organic solids new pulse sequences that are more robust to  $^1\text{H}$  chemical shielding at moderate sample spinning are needed. Although RS-HEPT does not meet this requirement is still preferable to be used on samples like adamantane, where it enables a better shimming, or a more accurate calibration of the  $^1\text{H}$  *rf* field strengths.

## 2. Results and discussion

In the following, we discuss the evolution of dilute nuclear spins, such as  $^{13}\text{C}$  or  $^{15}\text{N}$ , under a rotor-synchronized Hahn-echo pulse train (RS-HEPT) applied on the  $^1\text{H}$  channel. First, numerical simulations of the  $^{13}\text{C}$  FID acquired on resonance, and sampled every half of the separation  $\tau = 2\tau_R$  between adjacent  $\pi$ -pulses in the sequence, are performed under various experimental conditions in a C-H8 spin system. The atomic coordinates correspond to a  $-\text{NH}-\text{CH}-\text{CH}_2-\text{CH}-\text{CH}_3$  molecular fragment, where only the  $\text{CH}_2$  carbon is considered a  $^{13}\text{C}$  isotope. Since no relaxation is accounted for in the simulations, any deviation of the computed NMR signal from a constant, non-decaying, function will quantify the achieved decoupling efficiency. All the simulations presented in this work have been performed using the *Spinevolution* program [16].

In Fig. 1, the CW decoupled  $^{13}\text{C}$  NMR signal is compared with the FID obtained under decoupling by RS-HEPT at  $\nu_R = 25$  and 40 kHz spinning frequencies. As clearly demonstrated in [17,18], the dominant contribution to residual broadening under CW decoupling is determined by interference terms between  $^1\text{H}$  chemical shielding, and  $^1\text{H}-^{13}\text{C}$  heteronuclear dipolar interactions. Qualitative arguments indicate that  $^1\text{H}$  chemical shielding interaction will represent the main cause for residual broadening under RS-HEPT as well. In terms of an effective Hamiltonian associated to the decoupling

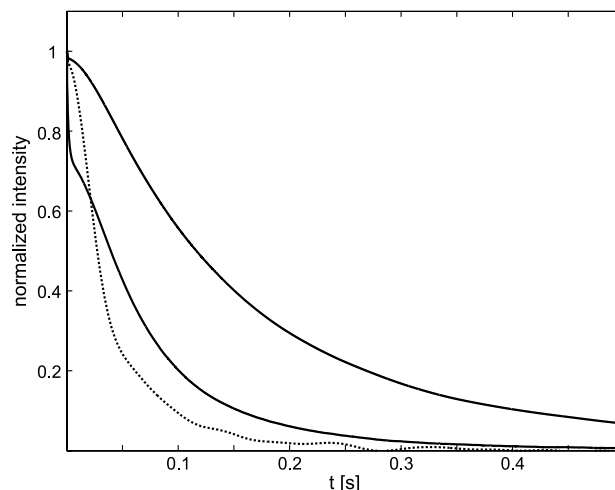


Fig. 1. Numerical simulations of the  $^{13}\text{C}$  FID acquired on resonance in a C-H8 spin system, of which structure and interaction parameters are described in the text. The three curves correspond to different heteronuclear decoupling conditions: *dotted line*, CW decoupling ( $\nu_{\text{H}} = 45$  kHz,  $\nu_{\text{R}} = 10$  kHz); *continuous lines*, RS-HEPT decoupling ( $\nu_{\text{H}} = 83.3$  kHz) at two different spinning frequencies,  $\nu_{\text{R}} = 25$  kHz (the lower curve) and  $\nu_{\text{R}} = 40$  kHz (the upper curve), respectively.

sequence, the leading contribution to the  $^{13}\text{C}$  NMR signal decay comes from third order cross-terms between  $^1\text{H}-^1\text{H}$  homonuclear dipolar,  $^1\text{H}-^{13}\text{C}$  heteronuclear dipolar, and  $^1\text{H}$  chemical shielding interaction, respectively. Under  $\pi$ -pulses, the former remains unchanged, but the latter two contributions will both change their sign. Overall, the cross-term as a whole is  $\pi$ -pulse invariant, and thus cannot be refocused by the RS-HEPT sequence. To account for this effect, also a distribution of isotropic and anisotropic chemical shifts has been assigned to the eight protons in the system. For the particular case discussed here, however, only a small variation of these interaction parameters was considered, namely, 0–0.1 ppm and 0–0.5 ppm for the isotropic, and the anisotropic  $^1\text{H}$  chemical shifts, respectively. As can be seen from the figure, there are two distinct contributions to the RS-HEPT decoupled signals: a fast decaying component, leading to a very broad line (often hidden into the baseline), and also a slow decaying component, which gives the desired high-resolution line. The contribution of the low-resolution component to the total signal is still significant at  $\nu_R = 25$  kHz, but it can be made negligible small in a fast spinning regime (in our example,  $\nu_R = 40$  kHz). Nevertheless, even at 25 kHz spinning frequency one expects an improved decoupling efficiency by RS-HEPT compared to CW, as the decay rate of the high-resolution component in the former case is lower than it is in the latter.

The above theoretical predictions are fully confirmed in the case of the  $^{13}\text{C}$  NMR spectrum of adamantane acquired under RS-HEPT at  $\nu_R = 25$  kHz. As can be seen from the Figs. 2 and 3, a substantial gain in sensitivity

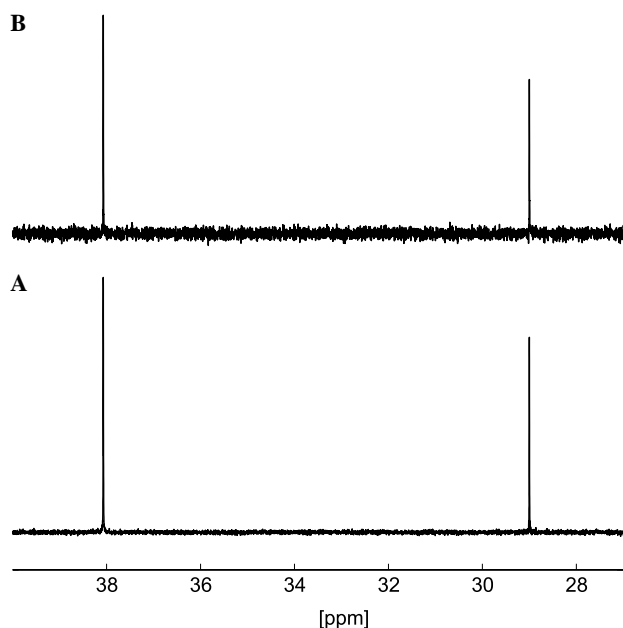


Fig. 2. The  $^{13}\text{C}$  CP/MAS spectrum of adamantane obtained under different heteronuclear decoupling conditions: (A) RS-HEPT decoupling ( $\nu_{1\text{H}} = 83.3$  kHz,  $\nu_{\text{R}} = 25$  kHz), (B) CW decoupling ( $\nu_{1\text{H}} = 45$  kHz,  $\nu_{\text{R}} = 10$  kHz). A number of 16384 points were acquired with a dwell time of  $80 \mu\text{s}$  ( $2\tau_{\text{R}}$ ), and 64 scans have been accumulated in the both cases with a recycle delay of 30 s. Since a long acquisition time ( $t_{\text{acq}} = 1.3$  s) was employed to minimize the artifacts caused by the FID truncation, this requirement is particularly critical in the case of CW decoupling for preventing the coil damage. A more reasonable recycle delay of 3 s could be, however, safely employed in the case of RS-HEPT decoupling, and this was actually done during its calibration. An optimization with respect to the  $rf$  decoupling field offset was performed to minimize the contribution of the  $^1\text{H}$ - $^{13}\text{C}$  scalar couplings to the residual broadening.

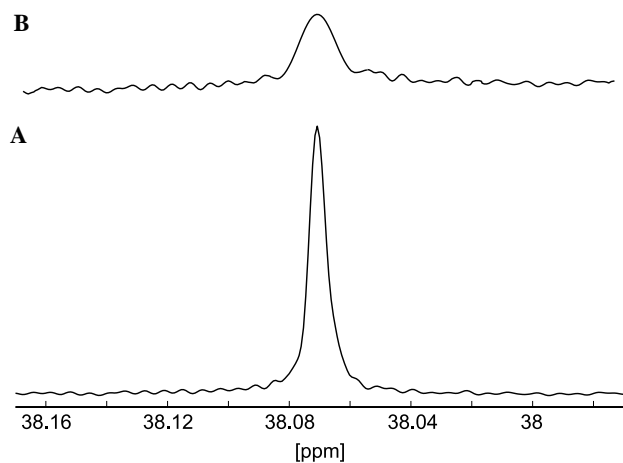


Fig. 3. A blow up of the CH region in the  $^{13}\text{C}$  spectrum shown in Fig. 2, which illustrates the line narrowing achieved under RS-HEPT decoupling (A) compared to the CW decoupled spectrum (B). The measured linewidths in the two cases are 0.006 and 0.014 ppm, which correspond to 0.75 and 1.8 Hz, respectively (at 125 MHz  $^{13}\text{C}$  Larmor frequency).

and resolution is achieved compared to the CW decoupled spectrum. Specifically, a linewidth reduction from 0.014 to 0.006 ppm, that is, a narrowing by a factor of

more than two, was obtained, which appears to indicate that an even better narrowing is achievable in practice than predicted in theory, although the  $^1\text{H}$  chemical shift values used in simulation are close to the real ones. Most probably, this is due to the quite large difference between the rigid-molecule dipolar couplings used for computing the NMR signals in Fig. 1 and the motional averaged couplings in adamantane.

A big advantage of pulsed decoupling is represented by its reduced duty cycle, which allows long acquisition times to be employed without the risk of damaging the probe's coil. This is particularly relevant in the case of adamantane, a compound that is widely used in SS-NMR for calibration purposes. For instance, a better shimming can be obtained in the absence of artifacts caused by the FID truncation. In this way, much smaller effects of the  $B_0$  inhomogeneity upon the measured lineshape can be identified and corrected. In particular, by using an acquisition time  $t_{\text{acq}} \cong 1.3$  s under RS-HEPT decoupling, a substantial improvement in the lineshape and width could be obtained for the spectrum shown in Figs. 2 and 3 after the compensation currents in the shim coils have been further adjusted with respect to their previous values determined under CW decoupling, where a  $t_{\text{acq}}$  of about five times shorter was employed. Also, line-narrowing under RS-HEPT decoupling proves to be very sensitive to misadjustments in the tilt angle of the refocusing pulses. This enabled one a more accurate calibration of the  $rf$ -power attenuation level for a proton  $\pi$ -pulse compared to its direct estimation from  $^1\text{H}$  NMR spectra.

Finally, the decoupling efficiency of the RS-HEPT sequence under more realistic conditions with respect to  $^1\text{H}$  chemical shift interaction is investigated by numerical simulations performed on the same C-H8 spin-system, where chemical shielding parameters with values that are typical for the corresponding moieties in rigid organic solids are considered for the all eight protons in the system. The  $^{13}\text{C}$  NMR signals computed for  $\nu_{\text{R}} = 20, 40,$  and  $100$  kHz are drawn by continuous line in Fig. 4. Counting from the lower to the upper curve, they are ordered according to the increase in the spinning frequency. For reference, the CW and TPPM decoupled signals ( $\nu_{1\text{H}} = 100$  kHz,  $\nu_{\text{R}} = 10$  kHz) are also shown. Three distinct cases are illustrated in this figure, which differ from each other by the particular conditions employed with respect to the applied  $rf$  power. The computed signals shown in Fig. 4A correspond to decoupling under a RS-HEPT sequence which is composed of ideal  $\pi$ -pulses. It is obvious from a comparison with the results presented in Fig. 4B, where real  $\pi$ -pulses were considered, that a significant drop in the decoupling efficiency is caused by finite pulsewidth effects. Nevertheless, these effects can be almost entirely compensated (Fig. 4C) by using an extended decoupling block in the RS-HEPT sequence, and a TPPM-type of phase

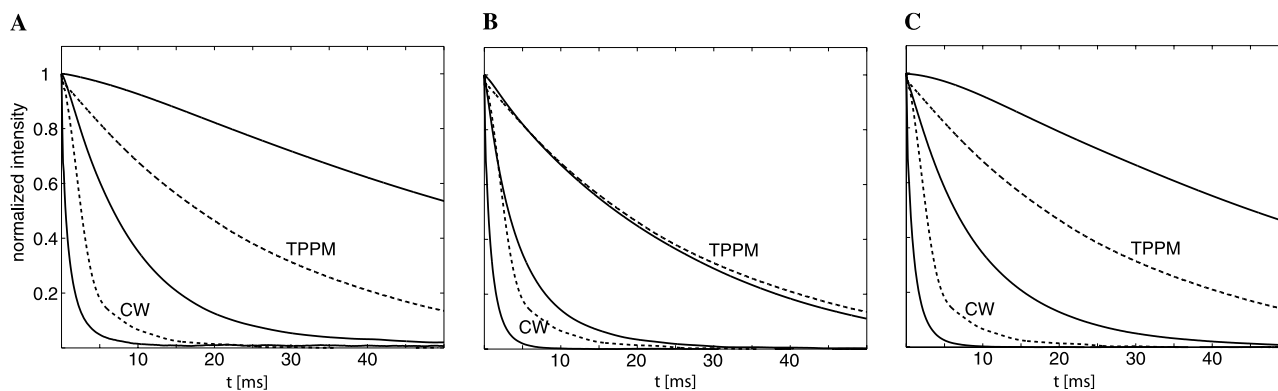


Fig. 4. Numerical simulations of the  $^{13}\text{C}$  FID acquired on resonance in a C-H8 spin system, of which structure is described in the text. Isotropic, and anisotropic, chemical shifts with values spanning a range of 8, and 10 ppm (at 500 MHz  $^1\text{H}$  Larmor frequency), are assigned to the eight protons in the system, according to the chemical moieties they belong to. Dotted lines correspond to CW and TPPM decoupling ( $\nu_{\text{1H}} = 100$  kHz,  $\nu_{\text{R}} = 10$  kHz), while the three curves drawn by continuous lines represent (counting from the lower to the upper curve) the RS-HEPT decoupled signals computed at  $\nu_{\text{R}} = 20, 40,$  and  $100$  kHz, respectively. For TPPM,  $\pi$ -pulses with a relative phase shift of  $\Delta\phi = 20^\circ$  were employed. The three illustrated cases correspond to: (A) ideal  $\pi$ -pulses; (B) real  $\pi$ -pulses with  $\nu_{\text{1H}} = 100$  kHz and  $\nu_{\text{1H}} = 200$  kHz (at  $\nu_{\text{R}} = 100$  kHz); (C) the same as in (B), except that the basic decoupling block extends over  $\tau = 4\tau_{\text{R}}$ , and thus contains two  $\pi$ -pulses. Their relative phases are shifted with respect to each other by an amount,  $\Delta\phi$ , whose value is optimized such that it maximizes the decoupling efficiency at a given spinning frequency. In particular, it was found that  $\Delta\phi = 70^\circ, 60^\circ,$  and  $30^\circ$  for  $\nu_{\text{R}} = 20, 40,$  and  $100$  kHz, respectively.

modulation scheme (see the figure caption for details). The results obtained here demonstrate that the refocusing mechanism is in principle feasible also in the case of larger  $^1\text{H}$  chemical shifts, but its efficient practical implementation through the RS-HEPT sequence would require spinning frequencies that are out of reach by the existing MAS equipment. Preliminary experimental investigations seem to confirm these findings, but to get more conclusive results further studies have to be undertaken under very fast MAS conditions (which are presently unavailable to us).

### 3. Conclusions

In this study, it was demonstrated that a simple Hahn-echo pulse sequence, which is known to completely refocus the heteronuclear dipolar interaction, can actually preserve most of its refocusing properties also in the presence of strong  $^1\text{H}$ - $^1\text{H}$  homonuclear dipolar couplings if used in a rotor-synchronized fashion under fast MAS. Applications to heteronuclear decoupling are however confined to compounds with small  $^1\text{H}$  chemical shielding parameters. For larger chemical shift values, typically encountered in rigid organic solids, an extremely fast spinning would be required to achieve better performances compared with conventional decoupling techniques, like CW or TPPM. A more detailed analysis of the refocusing mechanism that was briefly presented here is hoped to provide alternative solutions for compensating the detrimental effect of  $^1\text{H}$  chemical shift interaction at moderate spinning frequencies. Other potential practical applications can be also derived from such an analysis. For instance, if applied to  $^{13}\text{C}$  spins,

RS-HEPT proves insensitive to  $^1\text{H}$  chemical shift, which recommend it as a suitable decoupling method during those periods of a more complex NMR experiment when carbon chemical shift information is not needed. Research along these lines is under way in our laboratory, and the results will be reported in a forthcoming publication.

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