A generalized theoretical framework for the description of spin decoupling in solid-state MAS NMR: Offset effect on decoupling performance

Journal Article

Author(s):

Tan, Kong O.; Agarwal, Vipin; Meier, Beat H.; Ernst, Matthias

Publication date:

2016-09

Permanent link:

<https://doi.org/10.3929/ethz-b-000120064>

Rights / license:

[In Copyright - Non-Commercial Use Permitted](#)

Originally published in:

The Journal of Chemical Physics 145(9), <https://doi.org/10.1063/1.4961909>

A Generalized Theoretical Framework for the Description of Spin Decoupling in Solid-State MAS NMR: Offset Effect on Decoupling Performance

Kong Ooi Tan ^a, Vipin Agarwal ^{a,b}, Beat H. Meier ^{a,*}, and Matthias Ernst ^{a,*}

^a Physical Chemistry, ETH Zürich, Vladimir-Prelog-Weg 2, 8093 Zürich, Switzerland

^b TIFR Centre for Interdisciplinary Sciences, 21 Brundavan Colony, Narsinghi, Hyderabad 500 075, India

Corresponding Authors:

Matthias Ernst, maer@ethz.ch

Beat H. Meier, beme@ethz.ch

- Keywords: Solid-state NMR, heteronuclear spin decoupling, fast MAS, Floquet theory

Abstract

We present a generalized theoretical framework that allows the approximate but rapid analysis of residual couplings of arbitrary decoupling sequences in solid-state NMR under magic-angle spinning conditions. It is a generalization of the tri-modal Floquet analysis of TPPM decoupling (I. Scholz, et al., J. Chem. Phys. 130 (2009) 114510) where three characteristic frequencies are used to describe the pulse sequence. Such an approach can be used to describe arbitrary periodic decoupling sequences that differ only in the magnitude of the Fourier coefficients of the interaction-frame transformation. It allows a ~ 100 times faster calculation of second-order residual couplings as a function of pulse sequence parameters than full spin-dynamics simulations. By comparing the theoretical calculations with full numerical simulations, we show the potential of the new approach to examine the performance of decoupling sequences. We exemplify the usefulness of this framework by analyzing the performance of commonly-used high-power decoupling sequences and low-power decoupling sequences such as amplitude-modulated XiX (AM-XiX) and its super-cycled variant SC-AM-XiX. In addition, the effect of chemical-shift offset is examined for both high- and low-power decoupling sequences. The results show that the cross-terms between the dipolar couplings are the main contributions to the line broadening when offset is present. We also show that the SC-AM-XiX shows a better offset compensation.

1. Introduction

Efficient heteronuclear spin decoupling under magic-angle spinning (MAS)^{1–3} is one of the most important elements for high-resolution spectroscopy of organic and biological solids. Despite spectacular improvements during the past 25 years, there is still potential for further progress. A topic that has had limited attention is the offset dependence of decoupling performance^{2,4–8}. While this seems to be of limited interest in the case of high-power decoupling^{1,9–14} where the nutation frequency is much larger than the MAS frequency and the chemical-shift range of the protons ($\nu_1 \gg \nu_r, \Omega$), this issue is clearly important for low-power decoupling^{8,15–18}

where the nutation frequency of the decoupling field is smaller than the MAS frequency ($\nu_1 \ll \nu_r$) and in the same order of magnitude as the chemical-shift terms. With ever increasing maximum MAS frequencies over the past 20 years to nowadays 120 kHz^{19–22}, low-power decoupling has become a competitive alternative to high-power decoupling for MAS beyond 50 kHz with no or only a small compromise on the achievable line width^{1,15,23}. In general, but in particular for biological samples, low-power decoupling sequences are greatly preferred since the lower proton rf power reduces the sample heating and it improves overall probe stability by reducing the heating of the elements in the rf circuitry. However, the typical rf-field amplitude employed for the low-power decoupling sequence ($\nu_1 < \nu_r/4$) is in the same order of magnitude as the range of typical proton chemical shifts when using a high-field magnet. This situation might have detrimental effects on the performance of such decoupling sequences¹ because the optimum decoupling conditions can never be achieved simultaneously for all protons with different chemical shifts and, therefore, results in offset-dependent line broadening. To improve the offset dependence of low-power decoupling sequences, it is important to understand the mechanisms behind this effect in detail.

A theoretical understanding of offset effects in decoupling sequences is complicated by the complexity of the Hamiltonians required to describe the performance of such sequences. Typically, one has to calculate the interaction-frame Hamiltonians in a tilted frame of reference that includes the time-dependent radio-frequency Hamiltonians as well as the offset term and physical rotations of the sample. The theoretical treatment of Hamiltonians under several time dependencies, is best done using Floquet theory,^{24,25} which does not require that the characteristic frequencies appearing in the Hamiltonians are commensurate. Floquet theory results in a series expansion that can be used to calculate effective Hamiltonians to different orders as a function of the offset frequency. During decoupling under MAS, non-resonant first- and second-order terms typically determine the size of the residual coupling. In addition, resonance conditions can lead to a partial recoupling of heteronuclear terms leading to deterioration of the decoupling performance. However, not all resonance conditions are destructive and recoupling of the dipolar couplings between the protons can indeed improve the line width of the carbon resonances via the "self decoupling"^{3,26,27} mechanism.

The identification of characteristic frequencies contained in a pulse sequence is important because it defines the possible resonance conditions. The rf-irradiation part of all periodic pulse sequences can be characterized by a maximum of two characteristic frequencies,^{28–30} namely the modulation frequency ($\nu_m = 1/\tau_m$ where τ_m is the cycle time of a basic element) and the effective nutation frequency (ν_{eff}) of a decoupling sequence. In the case of MAS experiments, the physical spinning of the sample results in the modulation of the Hamiltonians by multiples of the spinning frequency ($\pm \nu_r$ and $\pm 2\nu_r$). Based on this universal feature, we have developed a

general Floquet framework that allows the calculation of non-resonant second-order terms for arbitrary decoupling sequences on three levels of approximation. On the lowest level, the formal effective Hamiltonian is always the same and can be written down without a detailed knowledge of the pulse sequence and the spin system involved (Fig. 1(a)). We obtain effective Hamiltonians that characterize the residual couplings that either arise from cross terms between heteronuclear dipolar couplings and CSA tensors or from cross terms between heteronuclear and homonuclear dipolar couplings. On a second level, the details of the pulse sequence become important since they determine the Fourier coefficients of the interaction-frame transformation. On this level, we can characterize the scaling factors of the various second-order cross terms without a detailed knowledge of the spin system. Finally, on the highest level, numerical effective Hamiltonians and residual couplings can be calculated based on spin-system parameters. Often, the last step is not required to compare the performance of different decoupling sequences. Such an approach to characterize the residual couplings is computationally much more efficient than full spin-dynamics simulations.

The versatility of the theoretical framework is demonstrated by theoretically calculating the residual couplings, i.e. the decoupling performance, as a function of pulse-sequence parameters for well-established heteronuclear decoupling sequences such as CW and TPPM decoupling in the high-power regime. We then compare the performance of the low-power amplitude-modulated XiX (AM-XiX) decoupling sequence and its super-cycled variant SC-AM-XiX.³¹ The theoretical analysis is verified by a comparison with exact numerical spin-dynamics simulations. The comparison between the two low-power decoupling sequences is extended to include chemical-shift offsets.

2. Theory

2.1 General Floquet Description of Decoupling Sequences

Let us consider a general spin system that is comprised of N I spins coupled to a single S spin. The Hamiltonian of the system is expressed in the usual rotating frame

$$\begin{aligned} \hat{\mathcal{H}}(t) = & \sum_{n=-2}^2 \omega_s^{(n)} e^{in\omega_s t} \hat{S}_z + \sum_{k=1}^N \sum_{n=-2}^2 \omega_k^{(n)} e^{in\omega_k t} \hat{I}_{kz} + \sum_{k=1}^N \sum_{n=-2}^2 \omega_{Sk}^{(n)} e^{in\omega_k t} 2\hat{S}_z \hat{I}_{kz} \\ & + \sum_{k < \ell} \sum_{\substack{n=-2 \\ n \neq 0}}^2 \omega_{k\ell}^{(n)} e^{in\omega_k t} \left(3\hat{I}_{kz} \hat{I}_{\ell z} - \hat{I}_k \cdot \hat{I}_\ell \right) + \hat{\mathcal{H}}_{\text{rf}}(t) \end{aligned} \quad (1)$$

where the symbols $\omega_s^{(n)}$ and $\omega_k^{(n)}$ represent the n -th spatial component of the chemical-shift tensors for the S and I spins respectively. Similarly, $\omega_{Sk}^{(n)}$ and $\omega_{k\ell}^{(n)}$ symbolize heteronuclear and homonuclear dipolar couplings accordingly. The rf Hamiltonian $\hat{\mathcal{H}}_{\text{rf}}(t)$ in Eq. (1) has, for a periodic irradiation, a general form of

$$\hat{\mathcal{H}}_{\text{rf}}(t) = \omega_1(t) \sum_{k=1}^N \left(\cos(\phi(t)) \hat{I}_{kx} + \sin(\phi(t)) \hat{I}_{ky} \right). \quad (2)$$

for an arbitrary decoupling sequence. We transform the Hamiltonian of Eq. (1) into an interaction frame with the rf-field Hamiltonian

$$\hat{\mathcal{H}}(t) = U_{\text{rf}}^{-1}(t) \hat{\mathcal{H}}(t) U_{\text{rf}}(t) \quad (3)$$

with the propagator

$$\hat{U}_{\text{rf}}(t) = \hat{T} \exp \left(-i \int_0^t \hat{\mathcal{H}}_{\text{rf}}(t_1) dt_1 \right). \quad (4)$$

Since only the I spins are involved in the rf Hamiltonian $\hat{\mathcal{H}}_{\text{rf}}(t)$ (Eq. (2)), the I -spin terms in $\hat{\mathcal{H}}(t)$ (Eq. (1)) will transform according to the following general equation

$$\hat{I}_z(t) = \hat{U}_{\text{rf}}^{-1}(t) \hat{I}_z \hat{U}_{\text{rf}}(t) = \sum_{\chi=x,y,z} a_{\chi}(t) \hat{I}_{\chi} = \sum_{k=-\infty}^{\infty} \sum_{\ell=-\infty}^{\infty} \sum_{\chi=x,y,z} a_{\chi}^{(k,\ell)} e^{ik\omega_m t} e^{i\ell\omega_{\text{eff}} t} \hat{I}_{\chi} \quad (5)$$

where k and ℓ are integer numbers, $a_{\chi}^{(k,\ell)}$ represents the Fourier coefficient characterizing the interaction-frame trajectory of the $\hat{I}_z$ operator (see Eq. (5)) under the rf Hamiltonian (Eq. (2)), $\omega_m = 2\pi / \tau_m$ is the modulation frequency resulting from the periodicity of the pulse sequence and ω_{eff} is the effective nutation frequency defined as

$$\omega_{\text{eff}} = \beta_{\text{eff}} / \tau_m, \quad (6)$$

where β_{eff} is the net flip angle^{28,29} that can be determined using Euler rotations or quaternions³² over the period of a basic cycle τ_m . This can be done because a series of consecutive rotations can be represented by a single rotation around an effective axis with a net flip angle, which is the fundamental theory of designing composite pulses.³³

The modulation frequency ω_m , the effective nutation frequency ω_{eff} , and the MAS frequency ω_r constitute the three basic frequencies that characterize the time-dependent interaction-frame Hamiltonian $\hat{\mathcal{H}}(t)$ that is given by

$$\hat{\mathcal{H}}(t) = \sum_{n=-\infty}^{\infty} \sum_{k=-\infty}^{\infty} \sum_{\ell=-\infty}^{\infty} e^{in\omega_r t} e^{ik\omega_m t} e^{i\ell\omega_{\text{eff}} t} \hat{\mathcal{H}}^{(n,k,\ell)}, \quad (7)$$

where $\hat{\mathcal{H}}^{(n,k,\ell)}$ are the Fourier coefficients of the time-dependent Hamiltonian in the interaction frame.

Possible resonance conditions are characterized by

$$n_0 \omega_r + k_0 \omega_m + \ell_0 \omega_{\text{eff}} = 0 \quad (8)$$

where (n_0, k_0, ℓ_0) are any set of integers that fulfill the resonance conditions of Eq. (8). The effective Hamiltonian on a resonance condition is then given by

$$\hat{\mathcal{H}} = \hat{\mathcal{H}}^{(1)} + \hat{\mathcal{H}}^{(2)} + \dots = \sum_{n_0, k_0, \ell_0} \hat{\mathcal{H}}^{(n_0, k_0, \ell_0)} + \sum_{n_0, k_0, \ell_0} \hat{\mathcal{H}}_{(2)}^{(n_0, k_0, \ell_0)} + \dots \quad (9)$$

where the first and second sum in Eq. (9) represents the first- and second-order effective Hamiltonian respectively.^{24,34} The full expressions for the Fourier components of the Hamiltonian $\hat{\mathcal{H}}^{(n_0, k_0, \ell_0)}$ and $\hat{\mathcal{H}}_{(2)}^{(n_0, k_0, \ell_0)}$ from Eq. (9) have already been derived in literature.²⁹ Since we are interested in the residual couplings under decoupling, we will focus now on the non-resonant terms

$$\hat{\mathcal{H}} = \hat{\mathcal{H}}^{(1)} + \hat{\mathcal{H}}^{(2)} + \dots = \hat{\mathcal{H}}^{(0,0,0)} + \hat{\mathcal{H}}_{(2)}^{(0,0,0)} + \dots = \hat{\mathcal{H}}^{(0,0,0)} - \frac{1}{2} \sum_{\nu, \kappa, \lambda} \frac{[\hat{\mathcal{H}}^{(-\nu, -\kappa, -\lambda)}, \hat{\mathcal{H}}^{(\nu, \kappa, \lambda)}]}{\nu \omega_r + \kappa \omega_m + \lambda \omega_{\text{eff}}} + \dots \quad (10)$$

where the second-order term often dominates the performance of decoupling sequences in rotating solids. We can decompose the non-resonant second-order term into six contributions

$$\hat{\mathcal{H}}^{(2)} = -\frac{1}{2} \sum_{\nu, \kappa, \lambda} \frac{[\hat{\mathcal{H}}^{(-\nu, -\kappa, -\lambda)}, \hat{\mathcal{H}}^{(\nu, \kappa, \lambda)}]}{\nu\omega_r + \kappa\omega_m + \lambda\omega_{\text{eff}}} = \hat{\mathcal{H}}_{\text{IS}\otimes\text{I}} + \hat{\mathcal{H}}_{\text{IS}\otimes\text{II}} + \hat{\mathcal{H}}_{\text{I}\otimes\text{II}} + \hat{\mathcal{H}}_{\text{II}\otimes\text{II}} + \hat{\mathcal{H}}_{\text{I}\otimes\text{I}} + \hat{\mathcal{H}}_{\text{IS}\otimes\text{IS}}. \quad (11)$$

The six second-order terms are given by

$$\hat{\mathcal{H}}_{\text{IS}\otimes\text{I}} = \sum_k \sum_{\nu=-2}^2 \sum_{\chi=x,y,z} i\hat{S}_z \hat{I}_{k\chi} q_{\chi}^{(\nu)} \left(\omega_{kS}^{(-\nu)} \omega_k^{(\nu)} + \omega_{kS}^{(\nu)} \omega_k^{(-\nu)} \right), \quad (12)$$

$$\hat{\mathcal{H}}_{\text{IS}\otimes\text{II}} = \sum_{k \neq \ell} \sum_{\nu=-2}^2 \sum_{\mu, \chi=x,y,z} -3i\hat{S}_z \hat{I}_{k\mu} \hat{I}_{\ell\chi} \left(q_{\mu\chi}^{(\nu)} \omega_{kS}^{(-\nu)} \omega_{\ell}^{(\nu)} - (q_{\mu\chi}^{(\nu)})^* \omega_{kS}^{(\nu)} \omega_{\ell}^{(-\nu)} \right). \quad (13)$$

$$\hat{\mathcal{H}}_{\text{I}\otimes\text{II}} = \sum_{k \neq \ell} \sum_{\nu=-2}^2 \sum_{\mu, \chi} -\frac{3i}{2} \hat{I}_{k\mu} \hat{I}_{\ell\chi} \left(q_{\mu\chi}^{(\nu)} \omega_k^{(-\nu)} \omega_{\ell}^{(\nu)} - (q_{\mu\chi}^{(\nu)})^* \omega_k^{(\nu)} \omega_{\ell}^{(-\nu)} \right) \quad (14)$$

$$\hat{\mathcal{H}}_{\text{II}\otimes\text{II}} = \sum_{k \neq \ell} \sum_{\chi} \sum_{\nu=-2}^2 \frac{9i}{8} \omega_{k\ell}^{(-\nu)} \omega_{k\ell}^{(\nu)} p_{\chi}^{(\nu)} \hat{I}_{k\chi} + \sum_{k \neq \ell \neq o} \sum_{\nu=-2}^2 \sum_{\mu, \chi, \xi} \frac{9i}{2} \hat{I}_{k\mu} \hat{I}_{\ell\chi} \hat{I}_{o\xi} \left(p_{\mu\chi\xi}^{(\nu)} \omega_{k\ell}^{(-\nu)} \omega_{o}^{(\nu)} - (p_{\mu\chi\xi}^{(\nu)})^* \omega_{k\ell}^{(\nu)} \omega_{o}^{(-\nu)} \right) \quad (15)$$

$$\hat{\mathcal{H}}_{\text{I}\otimes\text{I}} = \sum_k \sum_{\chi} \sum_{\nu=-2}^2 \frac{i}{2} q_{\chi}^{(\nu)} \hat{I}_{k\chi} \omega_k^{(-\nu)} \omega_k^{(\nu)} = \sum_k \sum_{\chi} \sum_{\nu=-2}^2 \frac{i}{2} q_{\chi}^{(\nu)} \hat{I}_{k\chi} |\omega_k^{(\nu)}|^2 \quad (16)$$

$$\hat{\mathcal{H}}_{\text{IS}\otimes\text{IS}} = \sum_k \sum_{\chi} \sum_{\nu=-2}^2 \frac{i}{2} q_{\chi}^{(\nu)} \hat{I}_{k\chi} \omega_{kS}^{(-\nu)} \omega_{kS}^{(\nu)} = \sum_k \sum_{\chi} \sum_{\nu=-2}^2 \frac{i}{2} q_{\chi}^{(\nu)} \hat{I}_{k\chi} |\omega_{kS}^{(\nu)}|^2 \quad (17)$$

Here, $q_{\chi}^{(\nu)}$, $q_{\mu\chi}^{(\nu)}$, $p_{\chi}^{(\nu)}$ and $p_{\mu\chi\xi}^{(\nu)}$ are the scaling factors for the corresponding cross terms and they are defined as

$$q_{\chi}^{(\nu)} = \sum_{\kappa} \sum_{\lambda=-1}^1 \frac{\varepsilon_{\chi\lambda j} a_j^{(-\kappa, -\lambda)} a_i^{(\kappa, \lambda)}}{\nu\omega_r + \kappa\omega_m + \lambda\omega_{\text{eff}}} \quad (18)$$

$$q_{\mu\chi}^{(\nu)} = \sum_{\kappa} \sum_{\lambda=-1}^1 \frac{\varepsilon_{\mu\lambda j} a_j^{(-\kappa, -\lambda)} a_{\chi i}^{(\kappa, \lambda)}}{\nu\omega_r + \kappa\omega_m + \lambda\omega_{\text{eff}}} \quad (19)$$

$$p_{\chi}^{(\nu)} = \sum_{\mu} \sum_{\kappa} \sum_{\lambda=-2}^2 \frac{\varepsilon_{\chi\lambda j} a_{\mu j}^{(-\kappa, -\lambda)} a_{\mu i}^{(\kappa, \lambda)}}{\nu\omega_r + \kappa\omega_m + \lambda\omega_{\text{eff}}} \quad (20)$$

$$p_{\mu\chi\xi}^{(\nu)} = \sum_{\kappa} \sum_{\lambda=-2}^2 \frac{\varepsilon_{\chi\lambda j} a_{\mu j}^{(-\kappa, -\lambda)} a_{\ell\xi}^{(\kappa, \lambda)}}{\nu\omega_r + \kappa\omega_m + \lambda\omega_{\text{eff}}} \quad (21)$$

where $\varepsilon_{\chi\lambda j}$ is the Levi-Civita symbol and $a_{\mu\chi}^{(\kappa, \lambda)}$ are the Fourier coefficients for the rank-two spin tensors that can be defined as the convolution of the rank-one Fourier coefficients $a_{\mu}^{(\kappa, \lambda)}$ (Eq. (5)):

$$a_{\mu\chi}^{(\kappa, \lambda)} = \sum_{k=-\infty}^{\infty} \sum_{\ell=-1}^1 a_{\mu}^{(k, \ell)} a_{\chi}^{(\kappa-k, \lambda-\ell)}. \quad (22)$$

Note that the scaling factors for the cross terms (Eqs.(18)-(21)) are comprised of pair of Fourier coefficients ($a_j^{(-\kappa, -\lambda)}$ and $a_i^{(\kappa, \lambda)}$ in Eq. (18)) such that the sum of the upper indices (κ and λ) are zero. This is obvious as we are considering only non-resonant Hamiltonians here.

Note that both sets of Fourier coefficients obey the relation $a_{\chi}^{(k,\ell)} = (a_{\chi}^{(-k,-\ell)})^*$ and $a_{\mu\chi}^{(k,\ell)} = (a_{\mu\chi}^{(-k,-\ell)})^*$. It is also important to emphasize that the scaling factors for the cross terms ($q_{\chi}^{(\nu)}, q_{\mu\chi}^{(\nu)}, p_{\chi}^{(\nu)}$ and $p_{\mu\chi}^{(\nu)}$) do not depend on the details of the spin system and the general expressions (Eqs. (12)-(17)) are the same for any periodic pulse sequence with non-zero values of the modulation frequency ω_m and an effective nutation frequency ω_{eff} . The details of the parameters of the decoupling sequences are encoded in the profile of the Fourier coefficients, $a_{\chi}^{(k,\ell)}$, which, in most cases, have to be calculated numerically.

The first two terms of Eq. (11), namely the cross term between the heteronuclear dipolar coupling and the I -spin CSA tensor ($\hat{\mathcal{H}}_{\text{IS}\otimes\text{I}}$, Eq. (12)) and the cross terms between heteronuclear and homonuclear dipolar couplings ($\hat{\mathcal{H}}_{\text{IS}\otimes\text{II}}$, Eq. (13)) are the only terms that lead to direct line broadening of the S-spin resonances. For simplicity, we will call the first term a CSA cross term and the second term a dipolar cross term. The other four cross terms ($\hat{\mathcal{H}}_{\text{II}\otimes\text{II}}, \hat{\mathcal{H}}_{\text{II}\otimes\text{I}}, \hat{\mathcal{H}}_{\text{IS}\otimes\text{I}}$, and $\hat{\mathcal{H}}_{\text{IS}\otimes\text{IS}}$) lead to expressions that contain only I -spin operators and do not impact the line width of the S spin directly. However, the first two terms can influence spin diffusion on the I spins since they contain two- and three-spin zero-quantum terms. The last two terms generate only fictitious fields which do not influence the residual line width directly but might lead to truncation effects in the Hamiltonian (vide infra). We will in the following focus on the effects of the first two cross terms as they are the only ones that have a direct impact on the observed residual line widths of the S spins.

Off-resonant irradiation: So far we have assumed on-resonance irradiation during decoupling and neglected the influence of proton chemical-shift offset terms. The simplest way of doing this is to include the offset of the radio-frequency irradiation into the interaction-frame transformation (Fig. 1(d)). The inclusion of a chemical-shift offset term into the radio frequency Hamiltonian leads to a modified propagator which now describes off-resonance irradiation

$$\hat{U}_{\text{rf}}^{(\Omega_{\text{off}})}(t) = \hat{T} \exp \left(-i \int_0^t \left(\hat{\mathcal{H}}_{\text{rf}}(t_1) + \Omega_{\text{off}} \sum_{k=1}^N \hat{I}_{kz} \right) dt_1 \right) \quad (23)$$

for the interaction-frame transformation (Eq. (5)) of the $\hat{I}_z$ operator:

$$\hat{I}_z(t) = \left(\hat{U}_{\text{rf}}^{(\Omega_{\text{off}})}(t) \right)^{-1} \hat{I}_z \hat{U}_{\text{rf}}^{(\Omega_{\text{off}})}(t) = \sum_{\chi=x,y,z} a_{\chi}(t) \hat{I}_{\chi} = \sum_{k=-\infty}^{\infty} \sum_{\ell=-\infty}^{\infty} \sum_{\chi=x,y,z} a_{\chi}^{(k,\ell)} e^{ik\omega_m t} e^{i\ell\omega_{\text{off}} t} \hat{I}_{\chi}. \quad (24)$$

Note that the inclusion of the offset term into the interaction-frame transformation will only change the effective nutation frequency $\omega_{\text{eff}}(\Omega_{\text{off}})$ and the Fourier coefficients $a_{\chi}^{(k,\ell)}$ as a function of the offset. The general expressions obtained for the effective Hamiltonians (Eqs. (11)-(17)) as well as the ones for the scaling factors (Eqs. (18)-(21)) are unchanged. A detailed calculation of the effective nutation frequency $\omega_{\text{eff}}(\Omega_{\text{off}})$ and the Fourier coefficients $a_{\chi}^{(k,\ell)}(\Omega_{\text{off}})$ as a function of the frequency offset is given in the Supplementary Information.

For a given sequence and offset frequency, the effective nutation frequency has to be calculated first and then the Fourier coefficients can be obtained. The numerical values can then be used together with the general expressions for the scaling factors (Eqs. (18)-(21)) to calculate the magnitude of the effective Hamiltonians as

a function of decoupling-sequence parameters (Fig. 1(a)). It is evident from Eqs. (12)-(17) that only the scaling factors of the effective Hamiltonians change and, therefore, it is sufficient to calculate only the scaling factor to gauge the performance of different decoupling sequences. The advantage in doing so is that one can follow the behavior of the second-order effective Hamiltonian without the need to specify a spin-system topology and geometry since the scaling factors are independent of these values. We consider a single chemical-shift offset for all spins in our theoretical framework and assume that the chemical-shift differences between the resonances are small and their effects are negligible for heteronuclear spin decoupling. The effect of chemical-shift differences can be significant in the context of homonuclear spin decoupling, and this effect can in principle be incorporated into the theoretical framework by using different interaction-frame transformations for different spins. The effects of a frequency offset on the decoupling performance are two-fold: (i) it deteriorates or improves the decoupling efficiency if the chosen parameters move closer to or further away from an offset-dependent resonance condition due to variations in $\omega_{\text{eff}}(\Omega_{\text{off}})$ or (ii) it can affect both the resonant and non-resonant parts of the effective Hamiltonians through changes in the values of the Fourier coefficients $a^{(k_0, \ell_0)}$.

2.2 Low-Power Amplitude-Modulated XiX Sequences

The amplitude and phases for low-power AM-XiX and SC-AM-XiX sequences³¹ are shown in Figs. 1(b) and 1(c), and their properties relevant for the Floquet calculations are summarized in Table 1. Analytical calculations of the effective nutation frequencies of these two decoupling sequences are straightforward in the case of on-resonance rf irradiation and given in Table 1. This can be achieved by either calculating the total propagator and then extracting the effective flip angle²⁹, or by using Euler rotations or quaternions³².

Table 1: Relevant parameters for AM-XiX and SC-AM-XiX decoupling sequences³¹.

	AM-XiX		SC-AM-XiX	
T	$\omega_1(t)$	$\phi(t)$	$\omega_1(t)$	$\phi(t)$
$0 \leq t < \tau_p$	$\omega_1^{\text{XiX}} + \omega_1^{\text{CW}}$	0	$\omega_1^{\text{XiX}} + \omega_1^{\text{CW}}$	0
$\tau_p \leq t < 2\tau_p$	$\omega_1^{\text{XiX}} - \omega_1^{\text{CW}}$	π	$\omega_1^{\text{XiX}} - \omega_1^{\text{CW}}$	π
$2\tau_p \leq t < 3\tau_p$	$\omega_1^{\text{XiX}} + \omega_1^{\text{CW}}$	0	$\omega_1^{\text{XiX}} + \omega_1^{\text{CW}}$	$\pi/2$
$3\tau_p \leq t < 4\tau_p$	$\omega_1^{\text{XiX}} - \omega_1^{\text{CW}}$	π	$\omega_1^{\text{XiX}} - \omega_1^{\text{CW}}$	$3\pi/2$
ω_{eff}	$\omega_1^{\text{CW}} \bmod \omega_m$		$2\omega_m \cos^{-1} \left(\cos^2 \left(\pi \omega_1^{\text{CW}} / (2\omega_m) \right) \right) / (2\pi)$	

In the case of off-resonance irradiation, the calculation of the effective field becomes more complex since the nutation axis is different for the two pulses in AM-XiX with the effective flip angles (β) and polar angles (θ) of the two pulses (see Fig. 1(d)) given by:

$$\begin{aligned}\beta_1 &= \tau_p \sqrt{(\omega_1^{\text{XiX}} + \omega_1^{\text{CW}})^2 + \Omega_{\text{off}}^2} \\ \beta_2 &= \tau_p \sqrt{(\omega_1^{\text{XiX}} - \omega_1^{\text{CW}})^2 + \Omega_{\text{off}}^2} \\ \theta_1 &= \tan^{-1}((\omega_1^{\text{XiX}} + \omega_1^{\text{CW}})/\Omega_{\text{off}}) \\ \theta_2 &= \tan^{-1}((\omega_1^{\text{XiX}} - \omega_1^{\text{CW}})/\Omega_{\text{off}})\end{aligned}\quad (25)$$

The effective nutation frequency of AM-XiX can be calculated as

$$\omega_{\text{eff}} = 2\omega_m \cos^{-1}(\cos(\beta_1/2)\cos(\beta_2/2) - \cos(\theta_1 + \theta_2)\sin(\beta_1/2)\sin(\beta_2/2))/(2\pi). \quad (26)$$

The same approach can be applied to SC-AM-XiX sequence. The flip angle (β) and the polar angle (θ) of the third and fourth pulse are the same as the ones of the first and second pulse $\theta_3 = \theta_1$, $\theta_4 = \theta_2$, $\beta_3 = \beta_1$ and $\beta_4 = \beta_2$ but the azimuthal angle of the last two pulses changes from 0 to $\pi/2$. The effective nutation frequency for SC-AM-XiX is then given by (see SI for the verification):

$$\begin{aligned}\omega_{\text{eff}} &= 2\omega_m \cos^{-1}\left(\left\{2\cos^2(\beta_1/2)(\cos^2(\beta_2/2) - \cos^2(\theta_2)\sin^2(\beta_2/2))\right.\right. \\ &\quad \left.+\sin(\beta_1)\sin(\beta_2)[\sin(\theta_1)\sin(\theta_2) - 2\cos(\theta_1)\cos(\theta_2)]\right. \\ &\quad \left.-\sin^2(\beta_1/2)[\cos(\beta_2) + \cos^2(\beta_2/2)\cos(2\theta_1) - \cos(2(\theta_1 + \theta_2))\sin^2(\beta_2/2)]\right\}/(4\pi)\end{aligned}\quad (27)$$

These equations were obtained by calculating the effective nutation over one cycle of the decoupling sequence using quaternions³² and extracting the flip angle from the total rotation matrix. The analytical expressions of Eqs. (26) and (27) for the effective nutation frequencies of the two decoupling sequences allow an efficient calculation of the Fourier coefficients of the interaction-frame trajectories.

3. Materials and Methods

The numerical simulations were performed in the spin-simulation environment GAMMA³⁵ using 200 powder orientations chosen using the ZCW scheme³⁶. The simulations were performed on either a CH₂ or C₂H₄ spin system with parameters similar to that of glycine ethylester. The details of the simulation parameters can be found in the Supplementary Information. All simulation data are normalized with respect to the line intensity under perfect decoupling. All experimental measurements were carried out on a sample of uniformly labeled 1,2-¹³C, ¹⁵N-glycine ethylester using a Bruker 1.3 mm triple-resonance MAS probe on a Bruker Avance-III 400 MHz spectrometer. The experimental data shown in Fig. 5 are normalized such that the line intensity for on-resonance decoupling was set to one. The experimental details are given in the Supplementary Information.

4. Results and Discussion

4.1 Predicting Decoupling Efficiency and Offset Effects in High-Power Sequences

In order to characterize the performance of CW and TPPM decoupling as a function of the pulse-sequence parameters, the scaling factors for the CSA cross term $q_{\chi}^{(v)}$ (Eq. (18)) and the dipolar cross term $q_{\mu\chi}^{(v)}$ (Eq. (19)) were calculated. We use the norm,²⁸ $\bar{q}_{\text{CSA}}^{(v)} = \sqrt{\sum_{\chi} |q_{\chi}^{(v)}|^2}$ for the CSA and $\bar{q}_{\text{DD}}^{(v)} = \sqrt{\sum_{\mu,\chi} |q_{\mu\chi}^{(v)}|^2}$ for the dipolar cross terms as a simple measures for the strength of these contributions. The norms for the cross terms are

calculated independently for the spatial rotating component $\nu=1$ and $\nu=2$ since they are weighted differently by the magnitude of the spatial components of the interactions in Eqs. (12)-(17). In principle, the two contributions can be combined but this requires full information about the magnitude and relative orientation of the tensors.

Figure 2 shows the calculated maps for the four coefficients $\bar{q}_{CSA}^{(\nu)}$ for the CSA (Figs. 2(a), 2(b), 2(e), and 2(f)) and $\bar{q}_{DD}^{(\nu)}$ ($\nu = 1$ or 2) for the dipolar cross terms (Figs. 2(c), 2(d), 2(g), and 2(h)) for CW decoupling as a function of the rf-field amplitude ν_1 and the frequency offset $\Delta\Omega$ for MAS frequencies of 15 kHz (Figs. 2(a)- 2(d)) and 60 kHz (Figs. 2(e)-2(h)). In general, we expect narrow lines and, therefore, high peak intensity if the magnitude of the cross terms is small, and on the contrary, low peak intensity and broad lines if the size of the cross terms is large. One can clearly see that for on-resonance decoupling only the CSA cross term contributes to the residual line width while the dipolar cross term is as expected very small³. However, with increasing frequency offset of the rf irradiation, the dipolar cross term becomes bigger leading to an increase in the residual splitting while the CSA cross term is mostly unchanged. Therefore, line broadening due to offset effects is mostly due to additional contributions from the dipolar cross terms.

Figure 3 shows the magnitude of the four coefficients $\bar{q}_{CSA}^{(\nu)}$ and $\bar{q}_{DD}^{(\nu)}$ for TPPM decoupling at 15 kHz MAS and 125 kHz rf-field amplitude as a function of the phase angle ϕ and the pulse length τ_p for the case of on-resonance decoupling (Figs. 3(a)- 3(d)) and for off-resonance decoupling with a frequency offset of 10 kHz (Figs. 3(e)- 3(h)). In the on-resonance case, the dipolar cross term (Figs. 3(c) and 3(d)) can be neglected as predicted in an earlier analysis of TPPM²⁹ while the CSA cross terms (Figs. 3(a) and 3(b)) show the expected areas of good decoupling at small phase angles and a flip angle of roughly 180°. In the off-resonance case (Figs. 3(e)- 3(h)), again the dipolar cross terms (Figs. 3(g) and 3(h)) become important and contribute to the residual line width while the CSA cross terms (Figs. 3(e) and 3(f)) are largely unchanged. These calculations show that in CW as well as in TPPM decoupling additional line broadening due to offset effects is mainly due to dipolar cross terms that are no longer (completely) averaged out as is the case for on-resonance irradiation.

4.2 Decoupling Efficiency of Low-Power Sequences

Figure 4 shows the calculated maps for the four coefficients $\bar{q}_{CSA}^{(\nu)}$ for the CSA (Figs. 4(a), 4(c), 4(e), and 4(g)) and $\bar{q}_{DD}^{(\nu)}$ for the dipolar cross terms (Figs. 4(b), 4(d), 4(f), and 4(h)) for the low-power decoupling sequences AM-XiX (Figs. 4(a), 4(b), 4(e), and 4(f)) and SC-AM-XiX (Figs. 4(c), 4(d), 4(g), and 4(h)), respectively. The line intensities obtained from full numerical simulations are shown in Figs. 4(i)- 4(l). Again, we expect narrow lines and, therefore, high peak intensity if the magnitude of the heteronuclear cross terms is small, and on the contrary, low peak intensity and broad lines if the size of the cross terms is large. These correlations can be verified by comparing the magnitude of the cross terms (Fig. 4(a)-(h)) with the line intensities obtained from the numerical simulations shown in Fig. 4(i)-(l). For instance, the size of the CSA cross term for AM-XiX is zero at $\nu_1^{CW} = 0$ (Figs. 4(a) and 4(e)), a fact that is known from the XiX sequence.¹¹ As the magnitude of the cross term increases with higher ν_1^{CW} field (Fig. 4(a)), the peak intensities fall (Fig. 4(i)). On the other hand, the size of the dipolar cross term is significant only at $\nu_1^{CW} = 0$ (Fig. 4 (b) and (f)) and at the resonance condition $\nu_1^{CW} = \nu_m$, which is indicated by black contours in Fig. 4(j). The fact that the CSA cross term is smaller for

lower ν_1^{CW} fields while the dipolar cross term is smaller at higher ν_1^{CW} fields, limits the area of good decoupling for the AM-XiX sequence. Hence, a compromise on the magnitude of the ν_1^{CW} field has to be chosen to minimize the total residual line broadening originating from both cross terms. The dipolar cross term can be neglected in all other regions because the symmetry of the Fourier coefficients originating from the CW part of the interaction-frame transformation imposes a cancellation of these terms except in areas close to the resonance conditions.

For the case of SC-AM-XiX, at $\nu_1^{\text{CW}} = 0$ (Figs. 4(c), 4(d), 4(g), and 4(h)) the two cross terms behave in a similar way compared to AM-XiX. However, for non-vanishing ν_1^{CW} amplitudes, the CSA cross term does not increase uniformly and linearly with respect to the ν_1^{CW} (Fig. 4(i)). It reaches a second minimum at $\nu_1^{\text{CW}} \approx 2\pi 5$ kHz (area marked with black contours in Fig. 4(k)) with a strong dependence on the modulation frequency (pulse length). In the same area, however, the dipolar cross terms are poorly averaged out (black contours at Figs. 4(k) and 4(l)) and, therefore, this area is not an overall good decoupling condition.

4.3 Offset Effects on Decoupling Efficiency of Low-Power Sequences

To investigate the sensitivity of the two low-power decoupling sequences to offset effects, a set of parameters was selected that resulted in good on-resonance ($\nu_{\text{off}} = 0$) decoupling performance, i.e., $\tau_p = 91.5 \mu\text{s}$, $\nu_1^{\text{XiX}} = 11.2$ kHz, $\nu_1^{\text{CW}} = 0.9$ kHz for AM-XiX and $\nu_1^{\text{CW}} = 2.1$ kHz for SC-AM-XiX. These decoupling conditions are labeled explicitly with black stars in Fig. 4(i) and 4(k). The dependence of the magnitude of the second-order cross terms on the offset is shown in Figs. 5(a) - 5(d) for both AM-XiX (blue) and SC-AM-XiX (red). For on-resonance decoupling the CSA cross terms dominate the residual line width while the dipolar cross terms are almost negligible (Figs. 5(a)- 5(d)). However, the CSA cross-terms do not change much up to ± 2 kHz variations in offset while the dipolar cross terms increase significantly over the same range of offset frequencies. The dipolar cross-term of AM-XiX increases almost twice as fast as the SC-AM-XiX term. Based on this behavior, one would expect that decreased decoupling efficiency as a function of offset effects are mostly originating from the dipolar cross term and that SC-AM-XiX shows better offset compensation.

This result can be confirmed by numerical simulations of the peak intensity as a function of the offset term as shown in Figure 5(e) and 5(f) for the CSA and dipolar cross terms, respectively. The maximum peak intensity drops to 26% (SC-AM-XiX) and 10% (AM-XiX) of their original values for an offset of 1 kHz. From this it is obvious that the dipolar cross term is the dominant contributions that leads to increased line broadening as a function of the offset frequency. The experimental results of Fig. 5(g) confirm our theoretical predictions and simulations that the SC-AM-XiX sequence has better decoupling performance than AM-XiX when an offset is present. Note that the experimental data appears to be broader because it is normalized with respect to the best experimental line intensity whereas the intensity in the simulations is normalized with respect to perfect decoupling. The numerical simulations are based on a three-spin CH_2 system to avoid complications arising from shifted resonance conditions due to fictitious-field terms and spin-diffusion effects that are due to cross terms involving only I spins (Eqs. (14)-(17)).

4.4 Full Numerical Simulations Based on the Analytical Equations

We have demonstrated that the performances of the decoupling sequences can be analyzed with the scaling factors (Eqs.(18)-(21)) and full numerical simulations are not required. However, to show the accuracy of the second-order analytical equations, we use the effective Hamiltonians ($\hat{\mathcal{H}}_{\text{IS}\otimes\text{I}}$, Eq. (12) and $\hat{\mathcal{H}}_{\text{IS}\otimes\text{II}}$, Eq. (13)) in combination with a spin system definition to simulate the spectra and compare them to full numerical simulations. Figure 6(a) shows on-resonance low-power AM-XiX decoupling where only the CSA cross term is required to get almost perfect agreement with full numerical simulations. In the case of off-resonance decoupling (Fig. 6(b)) the dipolar cross term alone does not result in a good agreement with the full numerical simulations but also the $\hat{\mathcal{H}}_{\text{IS}\otimes\text{IS}}$ (Eq. (17)) cross term needs to be included into the simulations. The cross term of the heteronuclear dipolar coupling with itself, also known as an auto-cross term,³⁷ leads to fictitious fields that truncate small terms in the effective Hamiltonian. Including both terms leads to a very good agreement of the simulated line shape with the full numerical simulation. The line shape obtained in the simulations of the residual coupling is different from what we expect for the experimental line shape. The reason for this difference is the additional narrowing of the lines by the "self decoupling"^{3,26,27} mechanism where proton spin flips lead to exchange phenomena between the two lines of the multiplet.

We can use this approach to estimate the achievable line widths with current decoupling sequences, e.g., for on-resonance decoupling using high-power TPPM or low-power AM-XiX decoupling, where only CSA cross terms will contribute in second order. For a two-spin C-H system with an assumed anisotropy of the CSA tensor of $\delta_{\text{CSA}} / (2\pi) = 3$ kHz and heteronuclear dipolar coupling of $\delta_{\text{D}} / (2\pi) = 46.6$ kHz, we find a second-order residual splitting of about 3 Hz for both sequences (AM-XiX: $\nu_r = 60.6$ kHz, $\nu_{\text{XiX}} = 11.2$ kHz, $\nu_{\text{ICW}} = 0.9$ kHz, $\tau_p = 91.5$ μs , TPPM: $\nu_r = 15$ kHz, $\nu_1 = 131$ kHz, $\phi = 17.6^\circ$, $\tau_p = 3.96$ μs). Also in these cases, the analytical calculations agree quite well with full numerical simulations. In a real molecule, cross terms to multiple protons and, in uniformly labeled molecules, cross terms between two heteronuclear dipolar couplings to the same proton will lead, typically, to a larger residual line width and we estimate the minimum achievable residual coupling under the above mentioned conditions to be in the order of 10-20 Hz. A further reduction in the residual couplings can be achieved either by spinning faster or by increasing the rf-field strength. There are also other factors that can affect the line width in actual experiments with real molecules, e.g., multiplet structure due to homonuclear J couplings, incomplete averaging of homonuclear S-spin dipolar couplings at lower MAS frequencies, or interference between spin dynamics and decoupling. In practical experiments, there can also be inhomogeneous line broadening due to the misalignment of the magic angle, RF and B_0 -field inhomogeneities, a distribution of isotropic chemical shifts due to sample inhomogeneity, or phase transients that might distort the pulse shape. These contributions will lead to additional broadening and typical experimental line width in rigid, well-ordered samples are in the order of 20-50 Hz.

5. Conclusions

In this study, we have introduced a generalized triple-mode Floquet framework to calculate the second-order effective Hamiltonians for arbitrary decoupling sequences under MAS. It builds on the fact that the interaction-

frame Hamiltonian of every periodic decoupling sequence can be characterized by three frequencies and the corresponding Fourier coefficients, namely the modulation frequency, the effective nutation frequency of the sequence, and the spinning frequency. The derived equations for the effective Hamiltonians are independent of the details of the decoupling sequence, which is manifested only through the values of the Fourier coefficients of the interaction-frame trajectory. These can be calculated numerically by evaluating the interaction-frame trajectory and determine the magnitude of scaling factors in the effective Hamiltonians. Based on the scaling factors, a systematic comparison of different decoupling sequences can be performed without the need to perform full numerical simulations.

We have illustrated the usefulness of such an approach by analyzing the decoupling performance of high-power and low-power decoupling sequences. The same formalism can also be used to analyze the influence of offset effects on the decoupling performance, which is especially significant for low-power decoupling sequences. In addition, it was shown that the theoretical framework is able to reproduce the line widths obtained from full numerical simulations. Such an analysis based on the Floquet treatment is computationally much more efficient than an analysis based on numerical simulations, whose performance depends on the details of the spin system. One of the main reasons that the Floquet calculations is much faster is that powder averaging is not required, and a preliminary analysis indicated a reduction in computation time by a factor of about 100. The high computational efficiency of the theoretical description can be used to screen large parameter spaces in order to optimize decoupling sequences as a function of pulse length, rf-field amplitude, or phase differences. In principle, this theoretical framework can be incorporated into numerical optimization strategies like optimal control theory³⁸ or genetic algorithm³⁹ to design better decoupling sequences.

Supplementary Material

Supplementary material with details of the parameters for the full numerical simulations as well as the experiments and a verification of Eqs. (26) and (27) is available at [INSERT LINK HERE](#).

Acknowledgements

We would like to thank Dr. P. K. Madhu, Dr. Anders Nielsen, and Dr. Johannes Wittmann for helpful discussions. This work has been supported by the Swiss National Science Foundation (Grants 200020_134681, 200020_159707 and 200020_146757) and the ETH Zürich (Grant No. ETH-04 09-3).

References

- ¹ P.K. Madhu, *Isr. J. Chem.* **54**, 25 (2014).
- ² P. Hodgkinson, *Prog. Nucl. Magn. Reson. Spectrosc.* **46**, 197 (2005).
- ³ M. Ernst, *J. Magn. Reson.* **162**, 1 (2003).
- ⁴ D.L. Vanderhart, W.L. Earl, and A. Garroway, *J. Magn. Reson.* **44**, 361 (1981).
- ⁵ A. Equbal, S. Paul, V.S. Mithu, P.K. Madhu, and N.C. Nielsen, *J. Magn. Reson.* **246**, 104 (2014).
- ⁶ M. Leskes, R.S. Thakur, P.K. Madhu, N.D. Kurur, and S. Vega, *J. Chem. Phys.* **127**, 024501 (2007).
- ⁷ R.S. Thakur, N.D. Kurur, and P.K. Madhu, *J. Magn. Reson.* **193**, 77 (2008).
- ⁸ V.S. Mithu, S. Paul, N.D. Kurur, and P.K. Madhu, *J. Magn. Reson.* **209**, 359 (2011).
- ⁹ R.S. Thakur, N.D. Kurur, and P.K. Madhu, *Chem. Phys. Lett.* **426**, 459 (2006).
- ¹⁰ M. Weingarth, P. Tekely, and G. Bodenhausen, *Chem. Phys. Lett.* **466**, 247 (2008).
- ¹¹ M. Ernst, H. Geen, and B.H. Meier, *Solid State Nucl. Magn. Reson.* **29**, 2 (2006).
- ¹² B.M. Fung, A.K. Khitrin, and K. Ermolaev, *J. Magn. Reson.* **142**, 97 (2000).
- ¹³ A.E. Bennett, C.M. Rienstra, M. Auger, K. V. Lakshmi, and R.G. Griffin, *J. Chem. Phys.* **103**, 6951 (1995).
- ¹⁴ P. Tekely, P. Palmas, and D. Canet, *J. Magn. Reson. Ser. A* **107**, 129 (1994).
- ¹⁵ M. Ernst, A. Samoson, and B.H. Meier, *J. Magn. Reson.* **163**, 332 (2003).
- ¹⁶ M. Kotecha, N.P. Wickramasinghe, and Y. Ishii, *Magn. Reson. Chem.* **45**, S221 (2007).
- ¹⁷ M. Weingarth, G. Bodenhausen, and P. Tekely, *J. Magn. Reson.* **199**, 238 (2009).
- ¹⁸ M. Weingarth, J. Trébosc, J.-P. Amoureux, G. Bodenhausen, and P. Tekely, *Solid State Nucl. Magn. Reson.* **40**, 21 (2011).
- ¹⁹ A. Böckmann, M. Ernst, and B.H. Meier, *J. Magn. Reson.* **253**, 71 (2015).
- ²⁰ Y. Nishiyama, Y. Endo, T. Nemoto, H. Utsumi, K. Yamauchi, K. Hioka, and T. Asakura, *J. Magn. Reson.* **208**, 44 (2011).
- ²¹ D. Wilhelm, A. Pürea, and F. Engelke, *J. Magn. Reson.* **257**, 51 (2015).
- ²² A. Samoson, T. Tuherm, J. Past, A. Reinhold, T. Anupöld, and I. Heinmaa, *Top. Curr. Chem.* **246**, 15 (2005).
- ²³ R.N. Purusottam, G. Bodenhausen, and P. Tekely, *Chem. Phys. Lett.* **614**, 220 (2014).
- ²⁴ M. Leskes, P.K. Madhu, and S. Vega, *Prog. Nucl. Magn. Reson. Spectrosc.* **57**, 345 (2010).
- ²⁵ I. Scholz, J.D. van Beek, and M. Ernst, *Solid State Nucl. Magn. Reson.* **37**, 39 (2010).
- ²⁶ G. Sinnig, M. Mehring, and A. Pines, *Chem. Phys. Lett.* **43**, 382 (1976).
- ²⁷ M. Mehring and G. Sinnig, *Phys. Rev. B* **15**, 2519 (1977).
- ²⁸ K.O. Tan, M. Rajeswari, P.K. Madhu, and M. Ernst, *J. Chem. Phys.* **142**, 065101 (2015).
- ²⁹ I. Scholz, P. Hodgkinson, B.H. Meier, and M. Ernst, *J. Chem. Phys.* **130**, 114510 (2009).
- ³⁰ K. Takeda, A. Wakisaka, and K. Takegoshi, *J. Chem. Phys.* **141**, 224202 (2014).
- ³¹ V. Agarwal, T. Tuherm, A. Reinhold, J. Past, A. Samoson, M. Ernst, and B.H. Meier, *Chem. Phys. Lett.* **583**, 1 (2013).
- ³² B. Blümich and H.W. Spiess, *J. Magn. Reson.* **61**, 356 (1985).
- ³³ C. Counsell, M. Levitt, and R. Ernst, *J. Magn. Reson.* **63**, 133 (1985).
- ³⁴ I. Scholz, B.H. Meier, and M. Ernst, *J. Chem. Phys.* **127**, 204504 (2007).
- ³⁵ S.A. Smith, T.O. Levante, B.H. Meier, and R.R. Ernst, *J. Magn. Reson. Ser. A* **106**, 75 (1994).
- ³⁶ V.B. Cheng, H.H.S. Jr., and M. Wolfsberg, *J. Chem. Phys.* **59**, 3992 (1973).
- ³⁷ G. De Paëpe, J.R. Lewandowski, A. Loquet, A. Böckmann, and R.G. Griffin, *J. Chem. Phys.* **129**, 245101 (2008).

- 36 N. Khaneja, T. Reiss, C. Kehlet, T. Schulte-Herbrüggen, and S.J. Glaser, J. Magn. Reson. **172**, 296 (2005).
- 39 M. Bechmann, J. Clark, and A. Sebald, J. Magn. Reson. **228**, 66 (2013).

ACCEPTED MANUSCRIPT

Figure Captions:

Figure 1:

Schematic diagram of a generalized theoretical framework for the description of heteronuclear spin decoupling. (a) shows the construction of general Hamiltonians for arbitrary decoupling sequences. The information of the decoupling sequences is encoded intrinsically in a set of Fourier coefficients $\{a_k\}$, which are calculated via interaction-frame trajectory, and then combined/substituted into the effective Hamiltonian in the later step. Two examples of low-power decoupling sequences: (b) AM-XiX and (c) SC-AM-XiX are shown here. The AM-XiX sequence has a modulation frequency of $\nu_m = 1/(2\tau_p)$ and effective nutation frequency $\omega_{\text{eff}} = \omega_1^{\text{CW}} \bmod \omega_m$ while SC-AM-XiX has $\nu_m = 1/(4\tau_p)$ and $\omega_{\text{eff}} = 2\omega_m \cos^{-1}(\cos^2(\pi\omega_1^{\text{CW}}/(2\omega_m)))/(2\pi)$ for on-resonance irradiation. (d) shows the effect of offset on the directions of the effective field for the first two pulses of AM-XiX and SC-AM-XiX.

Figure 2:

Simulated magnitude of the second-order cross terms for CW decoupling at MAS frequencies of 15 kHz ((a), (b), (c) and (d)) and 60 kHz ((e), (f), (g) and (h)) as a function of the rf-field amplitude ν_1 and the frequency offset $\Delta\Omega$. One can clearly see that in the on-resonance case ($\Delta\Omega = 0$) the dipolar cross term $\log_{10}(\bar{q}_{DD}^{(\nu)})$ ((c), (d), (g) and (h)) is very small ($< 10^{-8}$) and the CSA cross term $\log_{10}(\bar{q}_{CSA}^{(\nu)})$ ((a), (b), (e) and (f)) dominates the residual line with. With increasing frequency offset, the CSA cross terms vary only little, but the dipolar cross terms increase significantly leading to increased residual line width under CW decoupling.

Figure 3:

Simulated magnitude of the second-order cross terms for TPPM decoupling as a function of the phase difference between the two pulses ϕ and the pulse length τ_p at an rf-field amplitude of 125 kHz and a MAS frequency of 15 kHz. The top row ((a), (b), (c) and (d)) shows the case of on-resonance ($\Delta\Omega = 0$) decoupling while the lower row ((e), (f), (g) and (h)) shows the results for a frequency offset of $\Delta\Omega = 10$ kHz. The black lines indicate the possible resonance conditions in TPPM decoupling²⁹. One can clearly see the characteristic area of small CSA $\log_{10}(\bar{q}_{\text{CSA}}^{(\nu)})$ cross terms ((a), (b), (e) and (f)) where TPPM decoupling is known to achieve narrow lines. In the on-resonance case, the dipolar $\log_{10}(\bar{q}_{\text{DD}}^{(\nu)})$ cross terms ((c) and (d)) are negligible. In the case of off-resonance decoupling, the dipolar cross terms ((g) and (h)) increase significantly and start contributing to the residual line width.

Figure 4:

The size of the cross-term scaling factors $\log_{10}(\overline{q}_{CSA}^{(v)})$ ((a), (c), (e) and (g)) and $\log_{10}(\overline{q}_{DD}^{(v)})$ ((b), (d), (f) and (h)) with spatial component $v=1$ (a)-(d) and $v=2$ (e)-(h) for the decoupling sequence AM-XiX ((a), (b), (e), (f), (i) and (j)) and SC-AM-XiX ((c), (d), (g), (h), (k) and (l)) respectively. Simulated maximum line intensity of a CH_2 glycine spin system with ((i) and (k)) only CSA and no homonuclear dipolar coupling ((j) and (l)) only homonuclear dipolar coupling and no CSA. All data (a)-(l) were obtained at $\nu_1 = 60.6$ kHz, $\nu_1^{\text{XiX}} = 11.2$ kHz and 400 MHz. Note that the colour bars in ((i)-(l)) are inverted for easier comparison with the calculations, i.e. most intense peaks are in red while the least intense peaks are in blue.

Figure 5:

The effect of offset on the optimized decoupling conditions of the respective sequences. The size of the cross-term scaling factors $\bar{q}_{CSA}^{(\nu)}$ ((a) and (c)) and $\bar{q}_{DD}^{(\nu)}$ ((b) and (d)) for the spatial component $\nu=1$ ((a) and (b)) and $\nu=2$ ((c) and (d)) are shown here. Simulated maximum line intensity of a CH_2 glycine spin system with (e) only CSA and no homonuclear dipolar coupling (f) only homonuclear dipolar coupling and no CSA. The calculations and simulations in (a)-(f) were performed using $\tau_p = 91.5 \mu\text{s}$, $\nu_1^{\text{XiX}} = 11.2 \text{ kHz}$, $\nu_1^{\text{CW}} = 0.9 \text{ kHz}$ for AM-XiX (blue crosses) and $\nu_1^{\text{CW}} = 2.1 \text{ kHz}$ for SC-AM-XiX (red circles). Experimental data from reference ³¹ is shown in (g) for comparison. All data (a)-(g) were obtained at $\nu_r = 60.6 \text{ kHz}$ and at a proton resonance frequency of 400 MHz.

Figure 6:

Comparisons between calculated spectra with full analytical Hamiltonians inclusive of the details of a spin system and numerical simulations to elucidate the effect of (a) CSA cross terms and (b) dipolar cross terms are shown for the case of AM-XiX at MAS frequency of 60.6 kHz, $\tau_p = 91.5 \mu\text{s}$, $\nu_1^{\text{XiX}} = 11.2 \text{ kHz}$, $\nu_1^{\text{CW}} = 3 \text{ kHz}$, and offset $\Delta\Omega/2\pi$ of (a) 0 and (b) 800 Hz respectively. Both analytical (blue circle and black diamond) and numerical calculations (red cross) of the FIDs were performed up to a time evolution of $\sim 200 \text{ ms}$ for 5000 powder orientations, and processed with an exponential line broadening of 4 Hz. The relative orientations between the interactions are set to 0 for simplified calculations (see SI for more information).

(a) Floquet IS $\otimes$ I $\nu=1$

(b) Floquet IS $\otimes$ II $\nu=1$

(c) Floquet IS $\otimes$ I $\nu=1$

(d) Floquet IS $\otimes$ II $\nu=1$

(e) Floquet IS $\otimes$ I $\nu=2$

(f) Floquet IS $\otimes$ II $\nu=2$

(g) Floquet IS $\otimes$ I $\nu=2$

(h) Floquet IS $\otimes$ II $\nu=2$

(i) Sim IS $\otimes$ I

(j) Sim IS $\otimes$ II

(k) Sim IS $\otimes$ I

(l) Sim IS $\otimes$ II

— × — AM-XiX

— ○ — SC-AM-XiX

(a)

(b)