Performance of cross-polarization experiment at conditions of radiofrequency field inhomogeneity and slow to ultrafast MAS

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Abstract

In this manuscript, we provide an analytical description of the performance of the cross-polarization experiment, including linear ~~ramp~~ramps and adiabatic tangential ~~sweep modifications~~sweeps, using effective Hamiltonians and simple rotations in 3D space. It is shown that radiofrequency field inhomogeneity induces a reduction of the transfer efficiency at increasing MAS frequencies for both the ramp and the adiabatic CP experiments. The effect depends on the ratio of the dipolar coupling constant and the sample rotation frequency. In particular, our simulations show that for small dipolar couplings (1 kHz) and ultrafast MAS (above 100 kHz) the transfer efficiency is below 40% when extended contact times up to 20 ms are used and relaxation losses are ignored. New recoupling and magnetization transfer techniques that are designed explicitly to account for inhomogeneous RF fields are needed.

1. Introduction

Cross polarization is a remarkable experiment with a very long history (Schaefer, 2007). In 1962, Hartmann and Hahn (Hartmann and Hahn, 1962) presented the theory of magnetization transfer in a two-spin system under conditions of double radiofrequency (RF) irradiation of a static sample. In 1973, Pines et al. (Pines et al., 1973) published their seminal work on proton-enhanced solid-state NMR of dilute spins such as ^{13}C and ^{15}N. While magic angle spinning (MAS) was introduced by Andrew et al. (ANDREW et al., 1958) and independently by Lowe (Lowe, 1959) already in 1958 and 1959, respectively, it was only in 1977 that cross polarization was successfully combined with sample rotation. The necessary modification of the Hartmann-Hahn conditions was described by Stejskal et al. (Stejskal et al., 1977). After that, many modifications with variable amplitude irradiations on one or both RF channels were developed. Among them, simple linear ramps (Metz et al., 1994) and adiabatic sweeps (Hediger et al., 1995) became most popular. Ramp-CP was originally introduced to broaden the Hartmann-Hahn (HH) matching condition and to obtain uniform signal amplitudes. In the original publication, low MAS frequencies (below ~10 kHz) were used and the sweep could cover several HH conditions. At the same time, it was realized that the largest enhancement in signal intensity is obtained when the sweep covers only one HH condition (Metz et al., 1994). The RF amplitude sweep implies a partially adiabatic inversion of the spins and compensates RF field inhomogeneities (Peersen et al., 1994; Hediger et al., 1995).

Until now, cross-polarization remains the main pulse sequence building block for magnetization transfers. At very high MAS frequencies, it becomes difficult to achieve HH zero-quantum matching where the difference of the two applied rf amplitudes is equal to the MAS frequency. Instead, the HH double-quantum matching condition must be used in which the sum of the RF amplitudes equals the MAS frequency. The spin dynamics remains the same with the exception that negative intensities are obtained ~(Meier, 1992). Cross-polarization is thus applied over an exceptionally wide range of conditions, from experiments using static samples to MAS experiments with rotation frequencies above 100 kHz.

Developments in NMR hardware and pulse sequences are largely driven by biomolecular applications. Due to difficulties in sample preparation, only limited amounts of material are available that do not allow to completely fill the MAS rotor. It has been noticed that restriction of the sample volume to 30% with aligning the sample in the center of the solenoidal coil does not lead to a substantial reduction in sensitivity in ^{15}N, ^{13}C correlation experiments. This volume-selective behavior of the cross-polarization experiment is due to the inhomogeneous radiofrequency (RF) field distribution generated by the solenoidal coil. Although the RF field is rather homogeneous in the central area of the rotor, it quickly decays towards the end of the coil and cross-polarization mediated polarization transfer is impaired due to mismatch of RF amplitudes. The limited availability of biological sample and the use of center-packed rotors are presumably the reason why the detrimental effects of RF field inhomogeneity were neglected in the development of new solid-state NMR experiments for so long. The rotors for ultrafast MAS, however, The most widespread coil design used by all vendors in most of the MAS solid-state NMR probes is a solenoid. Its simple design, large filling factor, high conversion ratio from RF power to RF field, and its possibility to be integrated into circuits tuned to multiple frequencies are among the major benefits. The main drawback is its

98 MAS are small and can be completely filled with sample. Under these conditions, RF inhomogeneity
99 comes up as a concern~~.~~ in its full range. With faster MAS and correspondingly smaller rotors that
100 contain less material, we are again facing ~~again~~ sensitivity issues. It is obviously desirable that the
101 whole sample contributes to the NMR signal. At this point, it appears that the inhomogeneity of the
102 RF field is the prevailing challenge for the development of new solid-state NMR methods.

103 In this tutorial article, we summarize the principles of the cross polarization (CP) experiment and focus
104 on the effect of RF field inhomogeneity. For demonstration purposes we limit our treatment to an
105 isolated heteronuclear pair of spin-1/2 nuclei that are coupled via the dipole-dipole interaction. We
106 assume that there is no chemical shift interaction. Using average Hamiltonian theory and simple 3D
107 rotations we explain the process of magnetization transfer assuming different amplitude swept CP
108 variants. We show that the total signal measured after the CP transfer decreases with increasing MAS
109 frequency. The effect is amplified for small dipolar couplings. We numerically optimize linear ramp and
110 adiabatic tangential sweep experiments to identify the conditions for the best performance as a
111 function of the dipolar coupling constant, contact time, and MAS frequency. Neither of these
112 techniques under any condition fully compensates for RF field inhomogeneities. The most striking
113 example of low efficiency is the CP transfer between a ^{15}N nucleus directly bonded to a ^{13}C atom
114 involving a dipolar coupling constant of about 1 kHz. With the forthcoming MAS technology in mind
115 that can reach MAS frequencies of up to 200 kHz, we predict that only 20% of the sample will

116 contribute to the NMR signal after a CP mixing time of 10 ms. It clearly calls for the development of
117 alternative magnetization transfer techniques that are suitable for ultrafast MAS NMR experiments.

118

2. Theory

120 A theoretical description of the cross polarization phenomenon can be found in many solid-state NMR
121 textbooks. Here, we revisit the relevant parts and focus on visualization of the magnetization transfer
122 process during variable-amplitude sequences, following the description presented by Rovnyak
123 (Rovnyak, 2008). In the following, we assume an isolated spin pair. A more general description that
124 considers the surrounding spins and homonuclear interactions within an $I_N S$ spin system can be found,
125 for example, in the work of Vega and coworkers (Marks and Vega, 1996; et al. (Ray et al., 1998). This
126 issue has been reviewed in the context of ultrafast MAS by Emsley and coworkers (Laage et al., 2009),
127 concluding that the perturbation effects of homonuclear interactions diminish with increasing spinning
128 rate. The authors infer that the behavior of the CP experiment at very fast spinning in a $I_N S$ spin system
129 is reminiscent of a ^{13}C-^{15}N spin pair, which we would like to analyze in the following in detail.

2.1. Hamiltonian decomposition into ZQ and DQ subspaces

131 We start with the Hamiltonian that contains the dipole-dipole interaction and the radiofrequency fields
132 with amplitudes ω_I and ω_S applied on resonance to spins I and S, respectively.

$$H = \omega_I I_x + \omega_S S_x + d_{IS}(t) 2 I_z S_z \qquad (1)$$

133 The dipolar term is time dependent due to magic angle spinning (angular frequency ω_R) and can be
134 expressed as

$$d_{IS}(t) = g_1 \cos(\omega_R t + \gamma) + g_2 \cos(2\omega_R t + 2\gamma) \qquad (2)$$

$$g_1 = -\frac{1}{\sqrt{2}} 2\pi b_{IS} \sin 2\beta \qquad (3)$$

$$g_2 = \frac{1}{2} 2\pi b_{IS} \sin^2 \beta \qquad (4)$$

135 where b_{IS} is the dipolar coupling constant ($b_{IS} = -\frac{\mu}{4\pi} \frac{\gamma_I \gamma_S}{r_{IS}^3} \frac{\gamma_I \gamma_S \hbar}{r_{IS}^3} \frac{1}{2\pi}$) in units of Hertz, and β, γ are the
136 Euler angles relating the orientation of the dipolar vector $\vec{r}_{IS}$ with the rotor axis (the α angle is
137 irrelevant as the dipolar coupling tensor has a vanishing asymmetry).

138 Subsequently, the reference frame is transformed into the tilted frame where the radiofrequency
139 fields are linear with I_z and S_z, while the dipolar term becomes transversal. This transformation is
140 represented by a $\pi/2$-rotation around $(I_y + S_y)$ and we obtain

$$H' = \omega_I I_z + \omega_S S_z + d_{IS}(t) 2 I_x S_x \qquad (5)$$

141 This form of the Hamiltonian allows decomposition of the spin dynamics problem into two separate
142 subspaces, the zero quantum (ZQ) and the double quantum (DQ) subspace. The ZQ and DQ subspaces
143 can be represented using fictitious spin-1/2 operators that are defined in Table 1.

144

Table 1. Fictitious spin-1/2 operators in zero quantum and double quantum subspaces.

Zero quantum	Double quantum
$$I_x^{ZQ} = I_x S_x + I_y S_y$$ $$I_y^{ZQ} = I_y S_x - I_x S_y$$ $$I_z^{ZQ} = \frac{1}{2}(I_z - S_z)$$	$$I_x^{DQ} = I_x S_x - I_y S_y$$ $$I_y^{DQ} = I_y S_x + I_x S_y$$ $$I_z^{DQ} = \frac{1}{2}(I_z + S_z)$$
Inverted relations	
$I_z = I_z^{DQ} + I_z^{ZQ}$ $\qquad S_z = I_z^{DQ} - I_z^{ZQ}$ $\qquad 2 I_x S_x = I_x^{DQ} + I_x^{ZQ}$	

146

147   The Hamiltonian can then be written as

$$H' = H^{ZQ} + H^{DQ} \tag{6}$$

$$H^{ZQ} = (\omega_I - \omega_S)I_z^{ZQ} + d_{IS}(t)I_x^{ZQ} \tag{7}$$

$$H^{DQ} = (\omega_I + \omega_S)I_z^{DQ} + d_{IS}(t)I_x^{DQ} \tag{8}$$

148

2.2. Magnetization transfer in static CP experiment

150   The magnetization transfer process in the tilted frame is described by a transition from I_z into S_z. The
151   action of RF pulses and the dipolar interaction on the spin state I_z in the tilted frame is evaluated
152   independently in the ZQ and DQ subspace, working with the initial spin states I_z^{ZQ} and I_z^{DQ},
153   respectively. If the sample is static, the zero-quantum Hartmann-Hahn condition is $\omega_I - \omega_S = 0$ and
154   the Hamiltonian in Eq. (7) reduces to $H^{ZQ} = d_{IS}I_x^{ZQ}$ (d_{IS} is time independent). The spin state
155   represented by the operator I_z^{ZQ} is rotated around the I_x^{ZQ} axis as a consequence of the dipolar
156   interaction. Simultaneously, the spin state I_z^{DQ} evolves in the DQ subspace. We can assume that $\omega_I +$
157   ω_S is much larger than d_{IS}. The effective rotation axis is thus oriented along I_z^{DQ}, see Eq. (8). As a result,
158   H^{DQ} has no effect on the I_z^{DQ} state. This is summarized in the following equations.

$$I_z^{ZQ} \xrightarrow{H^{ZQ}} I_z^{ZQ}\cos d_{IS}t - I_y^{ZQ}\sin d_{IS}t$$
$$= \frac{1}{2}(I_z - S_z)\cos d_{IS}t - \left(I_y S_x - I_x S_y\right)\sin d_{IS}t \tag{9}$$

$$I_z^{DQ} \xrightarrow{H^{DQ}} I_z^{DQ} = \frac{1}{2}(I_z + S_z) \tag{10}$$

$$I_z = I_z^{ZQ} + I_z^{DQ} \xrightarrow{H^{ZQ}+H^{DQ}} I_z\frac{1}{2}(\cos d_{IS}t + 1) + S_z\frac{1}{2}(1 - \cos d_{IS}t)$$
$$- \left(I_y S_x - I_x S_y\right)\sin d_{IS}t \tag{11}$$

159

160   The I_z spin state is transformed into S_z when $\cos d_{IS}t = -1$, resulting in a full inversion of the I_z^{ZQ}
161   operator.

162 For the double-quantum Hartmann-Hahn condition $\omega_I + \omega_S = 0$, the rotation occurs in the DQ
163 subspace. In analogy to the previous case, we assume $|\omega_I - \omega_S| \gg d_{IS}$. Under this precondition, the
164 ZQ spin state is not changed.

$$I_z^{ZQ} \xrightarrow{H^{ZQ}} I_z^{ZQ} = \frac{1}{2}(I_z - S_z) \tag{12}$$

$$
\begin{aligned}
I_z^{DQ} \xrightarrow{H^{DQ}} & I_z^{DQ} \cos d_{IS}t - I_y^{DQ} \sin d_{IS}t \\
& = \frac{1}{2}(I_z + S_z)\cos d_{IS}t - (I_y S_x + I_x S_y)\sin d_{IS}t
\end{aligned}
\tag{13}
$$

$$
\begin{aligned}
I_z = I_z^{ZQ} + I_z^{DQ} \xrightarrow{H^{ZQ}+H^{DQ}} & I_z \frac{1}{2}(\cos d_{IS}t + 1) - S_z \frac{1}{2}(1 - \cos d_{IS}t) \\
& - (I_y S_x + I_x S_y)\sin d_{IS}t
\end{aligned}
\tag{14}
$$

165 For $\cos d_{IS}t = -1$, the I_z^{DQ} operator is inverted resulting in generation of the operator $-S_z$. Note that
166 the double quantum Hartmann-Hahn condition yields negative signal intensity.

167 The dipolar coupling is an orientation dependent interaction. ~~The above derived results describe the~~
168 ~~matching conditions for a particular crystallite orientation.~~ To yield the magnetization transfer
169 dynamics for a powder sample, the ensemble of all possible crystallite orientations has to be accounted
170 for. The powder averaged inversion efficiency is lower since the condition of a complete transfer,
171 $\cos d_{IS}t = -1$, will hold only for a single orientation.

2.3. Magic angle spinning and average Hamiltonians

173 In case of MAS, the Hamiltonians become time dependent. The analysis is performed then using
174 average Hamiltonian theory (AHT) employing the Magnus expansion. A tutorial on AHT principles was
175 presented by Brinkmann (Brinkmann, 2016). To retain fast convergence of the Magnus series, the
176 Hamiltonian is expressed in an appropriate interaction frame. Eq. (2) implies four resonance conditions
177 upon transformation into a new rotating frame in which the periodic modulations of $d_{IS}(t)$ are
178 removed by application of RF fields. These resonance conditions are associated with the characteristic
179 frequencies $n\omega_R$ with $n = \pm 1, \pm 2$. We choose $n = +1$ and focus on the ZQ subspace. In general,
180 transformation to a new reference frame is described using a propagator $U_T(t)$. This propagator
181 transforms the Hamiltonian according to

$$H' = U_T^+(t)H U_T(t) - iU_T^+(t)\frac{d}{dt}U_T(t) \tag{15}$$

182 In this case, $U_T(t) = \exp(-i\omega_R t I_z^{ZQ})$. The transformation can be regarded as a rotation around I_z^{ZQ}
183 with a frequency $-\omega_R$. The second term in Eq. (15) is a Coriolis term which introduces the term
184 $-\omega_R I_z^{ZQ}$ into the transformed Hamiltonian.

$$H^{ZQ'} = (\omega_I - \omega_S - \omega_R)I_z^{ZQ} + d_{IS}(t)\left(I_x^{ZQ}\cos\omega_R t - I_y^{ZQ}\sin\omega_R t\right) \tag{16}$$

185 The first order Hamiltonian is the time average over the modulation period $\tau_R = 2\pi/\omega_R$,

$$\bar{H}^{ZQ} = \frac{1}{\tau_R}\int_0^{\tau_R} H^{ZQ'}dt \tag{17}$$

186   The integral over the time dependent parts in Eq. (16) is evaluated as follows (making use of
187   ~~goniometric~~trigonometric identities)

188    $$\frac{1}{\tau_R}\int_0^{\tau_R} [g_1 \cos(\omega_R t + \gamma) + g_2 \cos(2\omega_R t + 2\gamma)] \left(I_x^{ZQ} \cos \omega_R t - I_y^{ZQ} \sin \omega_R t \right) dt =$$

189    $$= \frac{1}{\tau_R}\int_0^{\tau_r} \left\{ g_1 \frac{1}{2}[\cos(2\omega_R t + \gamma) + \cos\gamma] + g_2 \frac{1}{2}[\cos(3\omega_R t + 2\gamma) + \cos(\omega_R t + 2\gamma)] \right\} dt \, I_x^{ZQ} +$$

190    $$- \frac{1}{\tau_R}\int_0^{\tau_r} \left\{ g_1 \frac{1}{2}[\sin(2\omega_R t + \gamma) - \sin\gamma] + g_2 \frac{1}{2}[\sin(3\omega_R t + 2\gamma) - \sin(\omega_R t + 2\gamma)] \right\} dt \, I_y^{ZQ} =$$

191    $$= \frac{1}{2} g_1 \cos\gamma \, I_x^{ZQ} + \frac{1}{2} g_1 \sin\gamma \, I_y^{ZQ}$$

192   We obtain the first order average Hamiltonian in the ZQ subspace thus as

$$\bar{H}^{ZQ} = (\omega_I - \omega_S - \omega_R) I_z^{ZQ} + \frac{1}{2} g_1 \left(\cos\gamma \, I_x^{ZQ} + \sin\gamma \, I_y^{ZQ} \right) \qquad (18)$$

193   The Hartmann-Hahn condition is corrected to account for the rotation of the sample and has the form
194    $\omega_I - \omega_S = \omega_R$. In this case, the component of $\bar{H}^{ZQ}$ along the I_z^{ZQ} axis is zero and the dipolar
195   interaction results in a rotation around an axis in the transversal plane, with a phase depending on γ.
196   For each crystallite, the spin state I_z^{ZQ} is flipped away from the z axis generating a transversal
197   component. These transversal components are equally distributed with respect to the γ angle and
198   average to zero in a powder sample. Only the projection on the I_z^{ZQ} axis is relevant, and we can
199   therefore arbitrarily set $\gamma = 0$.

200   The calculation can be repeated for other choices of n and the following zero-quantum average
201   Hamiltonians are obtained

$$\bar{H}^{ZQ} = (\omega_I - \omega_S - n\omega_R) I_z^{ZQ} + \frac{1}{2} g_n I_x^{ZQ} \qquad (19)$$

202   The fast convergence of the Magnus expansion is maintained and the proper description of spin
203   dynamics by an average Hamiltonian is valid in the vicinity of the Hartmann-Hahn condition ($\omega_I - \omega_S -$
204    $n\omega_R = 0$). The RF amplitudes ω_I and ω_S may become time dependent in case a linear ramp or an
205   adiabatic sweep is applied. In any case, we assume that RF changes are slow compared to the MAS
206   frequency to ensure validity of this treatment.

207   The analysis is completed by inspecting the spin dynamics in the DQ subspace. We apply the same
208   procedure as for the ZQ subspace, yielding

$$\bar{H}^{DQ} = (\omega_I + \omega_S - n\omega_R) I_z^{DQ} + \frac{1}{2} g_n I_x^{DQ} \qquad (20)$$

209   For the zero quantum condition, it is assumed that the I_z^{DQ} term dominates the average Hamiltonian
210    $\bar{H}^{DQ}$, i.e. $\omega_I + \omega_S - n\omega_R \gg d_{IS}$ for all $n = \pm 1, \pm 2$. Under these conditions, the initial state I_z^{DQ}

211   remains unchanged. However, these conditions might be violated for large RF amplitude sweeps or in
212   case of substantial RF field inhomogeneity.

2.4. CP matching profiles

214   For constant RF amplitudes, the magnetization transfer process can be analytically described to derive
215   the so-called CP matching profiles (sometimes dubbed Hartmann-Hahn fingers). This derivation was
216   previously published by Levitt (Levitt, 1991), and Wu and Zilm (Wu and Zilm, 1993). It is assumed that
217   both the ZQ and DQ Hartmann-Hahn conditions are independent. We reiterate the calculation for the
218   matching condition and focus first on the ZQ Hamiltonian given in Eq. (19). We proceed with the final
219   transformation into the effective field of the Hamiltonian. The Hamiltonian $\bar{H}^{ZQ}$ can be represented
220   as a vector in the xz plane. This vector has an angle ϕ with the x axis. The transformation into the
221   effective field is described by a rotation around I_y^{ZQ} by an angle $-\phi$, which is equivalent to the
222   application of the propagator $U_T = \exp(-i\phi I_y^{ZQ})$. It makes the x axis of the new frame to coincide
223   with the effective Hamiltonian vector. Note that the Coriolis term in Eq. (15) is zero because U_T is time
224   independent. The effective Hamiltonian can be written as

$$\bar{H}_{eff}^{ZQ} = \omega_{eff}^{ZQ,n} I_x^{eff} \tag{21}$$

$$\omega_{eff}^{ZQ,n} = \sqrt{(\omega_I - \omega_S - n\omega_R)^2 + \frac{1}{4}g_n^2} \tag{22}$$

$$\tan\phi = \frac{\omega_I - \omega_S - n\omega_R}{\frac{1}{2}g_n} \tag{23}$$

225   The initial spin state $\rho^{ZQ}(0) = I_z^{ZQ}$ transforms into $\rho^{eff}(0) = U_T^+ \rho^{ZQ}(0)U_T = \cos\phi\, I_z^{eff} +$
226    $\sin\phi\, I_x^{eff}$ in the effective field frame, and evolves with a frequency $\omega_{eff}^{ZQ,n}$ around the effective field
227   axis I_x^{eff}

$$\begin{aligned}
\rho^{eff}(t) &= \cos\phi\left(I_z^{eff}\cos\omega_{eff}^{ZQ,n}t - I_y^{eff}\sin\omega_{eff}^{ZQ,n}t\right) + \sin\phi\, I_x^{eff} \\
&= \sin\phi\, I_x^{eff} - \cos\phi\sin\omega_{eff}^{ZQ,n}t\, I_y^{eff} + \cos\phi\cos\omega_{eff}^{ZQ,n}t\, I_z^{eff}
\end{aligned} \tag{24}$$

228   The result is transformed back from the effective field frame into the ZQ subspace as $\rho^{ZQ}(t) =$
229    $U_T\rho^{eff}(t)U_T^+$. This yields

$$\begin{aligned}
\rho^{ZQ}(t) &= \sin\phi\left(I_x^{ZQ}\cos\phi + I_z^{ZQ}\sin\phi\right) - \cos\phi\sin\omega_{eff}^{ZQ,n}t\, I_y^{ZQ} \\
&\quad + \cos\phi\cos\omega_{eff}^{ZQ,n}t\left(I_z^{ZQ}\cos\phi - I_x^{ZQ}\sin\phi\right) \\
&= \sin\phi\cos\phi\left(1 - \cos\omega_{eff}^{ZQ,n}t\right)I_x^{ZQ} - \cos\phi\sin\omega_{eff}^{ZQ,n}t\, I_y^{ZQ} \\
&\quad + \left(\sin^2\phi + \cos^2\phi\cos\omega_{eff}^{ZQ,n}t\right)I_z^{ZQ}
\end{aligned} \tag{25}$$

230   Eq. (25) describes the trajectory of the I_z^{ZQ} operator in the ZQ subspace under the influence of the RF
231   pulses applied in the CP experiment. For evaluation of the magnetization transfer process, only the
232   projection on the I_z^{ZQ} axis is important. We assume that there is no evolution in the DQ subspace, i.e.
233    $\rho^{DQ}(t) = I_z^{DQ}$. The initial I_z operator thus evolves as (recall $I_z = I_z^{ZQ} + I_z^{DQ}$)

$$\rho^{ZQ}(t) + \rho^{DQ}(t) = \left(\sin^2\phi + \cos^2\phi \cos\omega_{eff}^{ZQ,n}t\right)\frac{1}{2}(I_z - S_z) + \frac{1}{2}(I_z + S_z) \qquad (26)$$

We obtain the CP transfer efficiency in the vicinity of the zero quantum condition (n) by collecting the terms in front of the S_z operator

$$\epsilon^{ZQ,n} = \frac{1}{2}\left(1 - \sin^2\phi - \cos^2\phi \cos\omega_{eff}^{ZQ,n}t\right) = \frac{1}{2}\left(\cos^2\phi - \cos^2\phi \cos\omega_{eff}^{ZQ,n}t\right)$$

$$= \frac{\cos^2\phi}{2}\left(1 - \cos\omega_{eff}^{ZQ,n}t\right)$$

$$\epsilon^{ZQ,n} = \frac{1}{2}\frac{\frac{1}{4}g_n^2}{(\omega_I - \omega_S - n\omega_R)^2 + \frac{1}{4}g_n^2}\left[1 - \cos\omega_{eff}^{ZQ,n}t\right] \qquad (27)$$

A similar calculation for the double quantum Hartmann-Hahn condition yields

$$\epsilon^{DQ,n} = -\frac{1}{2}\frac{\frac{1}{4}g_n^2}{(\omega_I + \omega_S - n\omega_R)^2 + \frac{1}{4}g_n^2}\left[1 - \cos\omega_{eff}^{DQ,n}t\right] \qquad (28)$$

$$\omega_{eff}^{DQ,n} = \sqrt{(\omega_I + \omega_S - n\omega_R)^2 + \frac{1}{4}g_n^2} \qquad (29)$$

Note the negative sign of the transferred magnetization for the double quantum Hartmann-Hahn transfer. Equations (27) and (28) are identical to the result of an alternative derivation presented by Marica and Snider (Marica and Snider, 2003). The CP MAS matching profile has the form of a Lorentzian function with a width that is dependent on the dipolar coupling b_{IS} and the crystallite orientation (Euler angle β), that are included in the g_n factors. In powders, a quantitative magnetization transfer is not possible as a consequence of the dependence of the size of the effective dipolar coupling on orientation. The magnetization transfer efficiency under MAS is independent of the γ angle. This property is referred to as γ-encoding. The powder average is obtained by evaluation of the integral

$$\langle\epsilon^{ZQ,n}\rangle_{powder} = \frac{1}{2}\int_0^\pi \epsilon^{ZQ,n}\sin\beta\, d\beta \qquad (30)$$

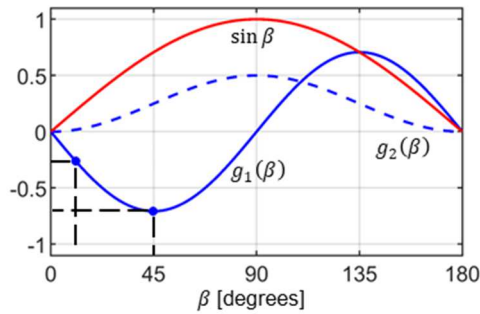



Figure 1. Dipolar coupling scaling factors $g_1(\beta)$ (solid blue line) and $g_2(\beta)$ (dashed blue line) defined in Eqs. (3), (4). The red curve represents the relative probability to find a specific orientation in a

249 powder sample. This weighting factor is employed for the calculation of the transfer efficiencies ϵ in
250 Eq. (30). β angles with β=15° and 45° are used for the visualization of the spin dynamics in the
251 Discussion.

252

2.5. Radiofrequency field inhomogeneity

254 Radiofrequency fields in MAS probes are realized using solenoid coils. However, a solenoid produces a
255 rather inhomogeneous distribution of magnetic fields across the sample (Tosner et al., 2017).
256 Moreover, as the sample rotates, individual spin packets travel along circles through a spatially
257 inhomogeneous RF field which is determined by the helical geometry of the solenoid coil. This RF
258 inhomogeneity introduces periodic modulations of both the RF amplitude and phase. For the special
259 case of the CP experiment, it was recently shown that these temporal modulations have a negligible
260 effect (Aebischer et al., 2021) and will be ignored in the present treatment. In addition, the distribution
261 of the RF fields depends on the frequency (Engelke, 2002), and can be influenced by different balancing
262 of the RF circuitry on different channels (Paulson et al., 2004). For simplicity, we assume the RF field
263 distributions to be equal for the I and S spins and disregard the radial dependency. The effect of RF
264 field inhomogeneity on the CP experiment was previously studied by Paulson et al. (Paulson et al.,
265 2004), and Gupta et al. (Gupta et al., 2015). An example of the distribution of the RF field along the
266 coil axis, denoted $\xi(z)$, is shown in Figure 2. As noted by Gupta et al., the profile deviates from a
267 Gaussian function and is well described by a power law dependence. In our study, we use the B_1 profile
268 calculated according to Engelke (Engelke, 2002).

269 The distribution of RF field amplitudes enters the formulas of the CP experiment using the substitution

$$\omega_I \xrightarrow{replace} \xi(z)\omega_I^{NOM}$$
$$\omega_S \xrightarrow{replace} \xi(z)\omega_S^{NOM}$$
(31)

270 where ω_I^{NOM}, ω_S^{NOM} refer to the nominal RF amplitudes realized in the center of the coil ($z = 0$ where
271 $\xi(0) = 1$). The overall experimental efficiency corresponds to the integral over the sample volume
272 weighted by the detection sensitivity of the coil. According to the reciprocity theorem (Hoult, 2000),
273 the sensitivity is proportional to the RF field. We assume that the sample extends over a length l, and
274 is placed symmetrically within the solenoid coil.

$$\langle \epsilon^{ZQ,n} \rangle_{powder}^{rf-inh} = \frac{1}{w} \int_{-l/2}^{+l/2} \langle \epsilon^{ZQ,n} \rangle_{powder} \, \xi(z) dz$$
(32)

275 The normalization factor w is given as

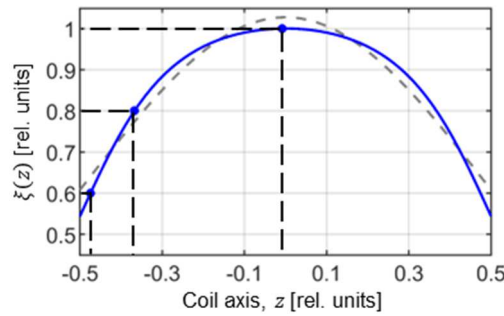
$$w = \int_{-l/2}^{+l/2} \xi(z) dz$$
(33)

276 It is not possible to match the Hartmann-Hahn conditions for the whole sample volume. Assuming that
277 the zero-quantum condition is fulfilled for the nominal rf amplitudes, i.e., $\omega_I^{NOM} - \omega_S^{NOM} = n\omega_R$, we
278 get

279
$$\omega_I - \omega_S - n\omega_R = \xi(z)\big(\omega_I^{NOM} - \omega_S^{NOM}\big) - n\omega_R = \xi(z)n\omega_R - n\omega_R = n\omega_R(\xi(z) - 1)$$

280 and

$$\overline{H}^{ZQ} = n\omega_R[\xi(z) - 1]I_z^{ZQ} + \frac{1}{2}g_n I_x^{ZQ} \tag{34}$$

281 Eq. (34) shows that in the case of an inhomogeneous RF field, the prevailing component along the I_z^{ZQ}
282 operator in the effective Hamiltonian $\overline{H}^{ZQ}$ is proportional to the MAS frequency ω_R, multiplied by the
283 order of the recoupling condition n. The effect of RF amplitude mismatch on spin dynamics is more
284 pronounced for small dipolar couplings, b_{IS}, which is reflected in the width of the CP MAS matching
285 profiles derived above. Thus, we could analytically derive a dependence of the performance of the CP
286 experiment on the MAS frequency.

287

288 **Figure 2**: RF field inhomogeneity profile along the axis of a solenoid coil. The profile is calculated
289 according to Engelke (Engelke, 2002) assuming a coil length of 7.9 mm, a diameter of 3.95 mm, and
290 assuming 7 turns (blue line). The grey dashed line represents a fit of the RF profile assuming a Gaussian
291 function suggested by Paulson et al. (Paulson et al., 2004). The power law relation introduced by Gupta
292 et al. (Gupta et al., 2015) yields a perfect fit of the theoretical behavior and exactly matches the blue
293 curve. Values ξ=0.6, 0.8, and 1.0 are used in the Discussion session to visualize spin dynamics.

294

2.6. Linear ramp and adiabatic sweep

296 The most popular way to overcome the limitations of the constant amplitude CP and the RF mismatch
297 at different positions of the sample is the use of a linear ramp or an adiabatic tangential sweep on one
298 of the RF channels. We can define

$$\omega_I^{NOM} = \omega_I^0 + f(t) \tag{35}$$

299 where the function $f(t)$ describes the sweep from $-\Delta/2$ to $+\Delta/2$ over time $t \in \langle 0, T \rangle$. The function
300 $f(t)$ can be defined for the linear ramp as

$$f(t) = \Delta\left(\frac{t}{T} - \frac{1}{2}\right) \tag{36}$$

301 and for tangential sweep as

$$f(t) = b \tan\left[\left(\frac{2t}{T} - 1\right)\arctan\frac{\Delta}{2b}\right] \tag{37}$$

302   where b parametrizes the curvature of the sweep. Values for b are typically in the range of $\frac{\Delta}{1000} < b <$

303   Δ. For $b = \frac{\Delta}{1000}$, $f(t)$ is almost constant except for the end points where the function rapidly changes

304   from/to $\mp\Delta/2$. For $b = \Delta$, $f(t)$ approaches the linear ramp. The influence of b on the shape is

305   illustrated in Figure 3. During a truly adiabatic transfer, the effective field is aligned with the initial

306   magnetization along the $+I_z^{ZQ}$ axis, and changes its orientation slowly towards $-I_z^{ZQ}$. The spin state is

307   locked along the effective field and is inverted as well (Hediger et al., 1995). The adiabaticity condition

308   is given as

$$\frac{d}{dt}\phi(t) \ll \omega_{eff} \tag{38}$$

309   where ω_{eff} is defined in Eq. (22), and the angle ϕ is given in Eq. (23). Adiabatic inversion pulses have

310   been an integral part of the NMR toolbox for a long time (Baum et al., 1985). There is, however, a

311   substantial difference between broadband inversion pulses and cross-polarization. Inversion pulses

312   allow to manipulate the effective field along both z and x directions, corresponding to offset and RF

313   amplitude, respectively. In the CP experiment, the x axis component of the effective Hamiltonian is

314   fixed and is determined by the dipolar coupling, see Eq. (19) and Eq. (20). In addition, perfect alignment

315   of the effective field with the initial state is difficult to achieve as the RF amplitudes are restricted to

316   the vicinity of the Hartmann-Hahn condition.

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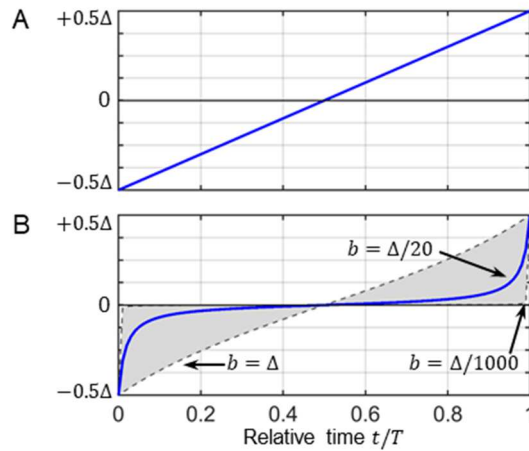
318

319   **Figure 3**: RF amplitude sweeps employed in cross-polarization experiments for (A) a linear ramp and

320   (B) an adiabatic tangential sweep. Eq. (36) and (37) mathematically describe the time dependent RF

321   amplitude. The parameter b determines the curvature of the adiabatic tangential shape.

322

2.7. RF amplitude sweeps and RF field inhomogeneity

324   In the following, we aim to include RF field inhomogeneity in the description of the RF amplitude sweep

325   of Eq. (35). We assume that the zero quantum Hartmann-Hahn matching conditions are fulfilled in the

326   middle of the sweep and in the center of the coil for the nominal RF field amplitudes, i.e. for $\omega_I^0 -$

327   $\omega_S^{NOM} = n\omega_R$. The I_z^{ZQ} component of the Hamiltonian $\bar{H}^{ZQ}$ then becomes

$$\omega_I - \omega_S - n\omega_R = \xi(z)\left[\omega_I^{NOM} - \omega_S^{NOM}\right] - n\omega_R$$
$$= \xi(z)\left[\omega_I^0 + f(t) - \omega_S^{NOM}\right] - n\omega_R = \xi(z)[f(t) + n\omega_R] - n\omega_R \qquad (39)$$
$$= \xi(z)f(t) + n\omega_R[\xi(z) - 1]$$

328   and

$$\bar{H}^{ZQ} = \{\xi(z)f(t) + n\omega_R[\xi(z) - 1]\}I_z^{ZQ} + \frac{1}{2}g_nI_x^{ZQ} \qquad (40)$$

329   Now, the sweep function $f(t)$ is scaled by the RF field inhomogeneity factor $\xi(z)$. At the same time,
330   the center of the sweep is shifted by an amount proportional to the MAS frequency ω_R. In Figure 4,
331   the sweep range is depicted in green as a function of position along the coil axis. Spins located in
332   volume elements towards the ends of the coil where the RF field is smaller experience RF amplitude
333   sweeps that do not cover the recoupling condition at all (e.g. for ξ=0.8 in Figure 4A). This is another
334   example of how increased MAS frequencies impact the cross-polarization experiment and cause a
335   decrease in performance.

336   When setting the numerical values of RF amplitudes ω_I^0, ω_S^{NOM}, and the sweep range Δ, it can happen
337   that double-quantum conditions are fulfilled in some places within the sample when the values are
338   scaled by the RF field inhomogeneity. The double quantum conditions are governed by the formula

$$\omega_I + \omega_S - n\omega_R = \xi(z)\left[\omega_I^{NOM} + \omega_S^{NOM}\right] - n\omega_R$$
$$= \xi(z)\left[\omega_I^0 + f(t) + \omega_S^{NOM}\right] - n\omega_R \qquad (41)$$
$$= \xi(z)f(t) + \xi(z)\left(\omega_I^0 + \omega_S^{NOM}\right) - n\omega_R$$

339   which is represented in red in Figure 4C. While the values ω_I^0, ω_S^{NOM} are satisfying the zero quantum
340   $n = +1$ condition around the center of the coil, at the same time, they satisfy the double quantum
341   $n = +2$ condition towards the ends of the coil (places where the red area crosses zero value). As a
342   result, there are parts of the sample that produce positive magnetization transfer and parts that
343   experience negative transfer. Thus, the overall efficiency of the experiment is decreased.

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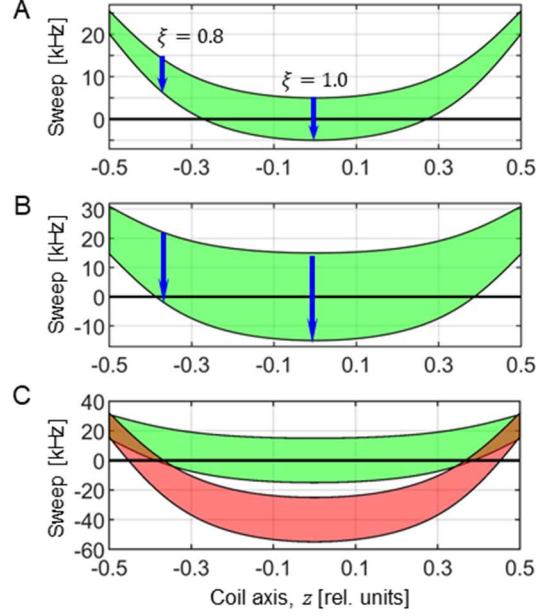
Figure 4: Visualization of the RF sweep ranges as a function of the position of a particular spin packet along the coil axis. The Hartmann-Hahn resonance condition is artificially defined for a sweep frequency 0 kHz. (A) The sweep range (green area) is evaluated according to Eq. (39) for $n = +1$ and assuming an MAS frequency of 50 kHz. The blue arrows indicate the direction of the sweep for an RF inhomogeneity factor of ξ=0.8 and 1.0. The sweep amplitude Δ corresponds to 10 kHz and 30 kHz in (A) and (B), respectively. (C) Overlay of the RF amplitude sweeps evaluated for the ZQ ($n = +1$) matching condition (Eq. (39), green) and DQ ($n = +2$) matching condition (Eq. (41), red) with nominal RF amplitudes $\omega_I^{NOM}/2\pi$=95 kHz and $\omega_S^{NOM}/2\pi$=45 kHz. These values were selected to demonstrate that the ZQ matching condition is satisfied in the center of the coil, and simultaneously a DQ is encountered for spin packets in regions of the sample where the RF amplitudes are scaled down by the RF field inhomogeneity.

3. Results and Discussion

3.1. CP matching profile

Experimentally, optimal cross polarization conditions are found in experiments in which the RF amplitude on one of the RF channels is systematically varied to yield the highest sensitivity. In case the Hartmann-Hahn recoupling condition is very narrow, this can be difficult as many repetitions with a small increment of the RF amplitude are required. In the Theory section, we derived analytical formulas for the CP matching profiles for constant RF amplitudes. We have found that for a homogeneous RF field distribution, the width at half height of the recoupling condition is governed by the size of the dipolar coupling and can be estimated as $0.468b_{IS}$ after powder averaging. Both the width and the maximal transfer efficiency are independent of the MAS frequency. Maximum transfer of 73% is achieved for mixing times satisfying the condition $tb_{IS} = 1.7$ for the $n = \pm1$ recoupling conditions. The same efficiency is obtained for the $n = \pm2$ conditions. However, due to the different spatial dependence and scaling factors in g_1 and g_2 terms (Eqs. (3) and (4)) the maximum is achieved there

371 for mixing times $tb_{IS} = 2.4$. These facts are well known and are presented graphically in Figure 5.

372 Figure 5A shows the CP matching profile calculated using Eq. (27) and (30) for $n = +1$ and assuming a

373 dipolar coupling constant b_{IS} of 1, 10, and 20 kHz, which are the characteristic values for ^{13}C-^{15}N, ^{1}H-

374 ^{15}N, and ^{1}H-^{13}C spin pairs, respectively. $\langle \epsilon^{ZQ,+1} \rangle_{powder}$ is represented as a function of the RF amplitude

375 mismatch $\delta_M/2\pi = \omega_I - \omega_S - \omega_R$ with respect to the exact Hartmann-Hahn.

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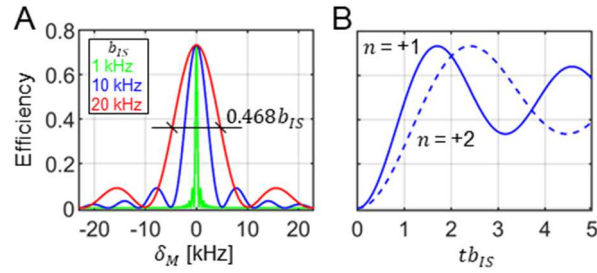
377

378 **Figure 5**: Properties of the constant amplitude CP experiment assuming homogeneous RF fields. (A)

379 The width of the CP matching profile around the zero-quantum (n=+1) Hartmann-Hahn matching

380 condition depends on the dipolar coupling strength b_{IS}. (B) Magnetization buildup of the transferred

381 magnetization for the n=+1 and n=+2 matching condition. Independently of the MAS frequency and

382 b_{IS}, the n=+2 condition reaches the same maximum, however, at longer mixing times. The curves were

383 calculated using Eqs. (27) and (30).

384

385 For inhomogeneous RF fields, the CP matching profile can be quantitatively described by inserting Eq.

386 (31) into Eq. (27) and taking the average in Eq. (32). Figure 6A shows the influence of inhomogeneous

387 RF fields and the induced asymmetric broadening of the matching profile $\langle \epsilon^{ZQ,+1} \rangle_{powder}^{rf-inh}$. Clearly, the

388 maximal transfer efficiency substantially decreases with increasing MAS frequency.

389 A closer inspection of the CP matching profiles in Figure 6A reveals that the maximum overall transfer

390 efficiency is not reached for the exact ZQ ($n = +1$) condition with $\omega_I^{NOM} - \omega_S^{NOM} = \omega_R$,

391 corresponding to δ_M= 0. In practice, it is advantageous to set ω_I^{NOM} little higher and thus shift the

392 volume element where the Hartmann-Hahn condition is matched away from the center of the coil.

393 This allows to partially compensate for the destructive effect of the RF field inhomogeneity. This

394 mismatch δ_M of the Hartmann-Hahn matching condition is naturally found during the experimental

395 setup when the RF fields are optimized to experimentally yield the best efficiency. However, the

396 mismatch is small (a few kHz at most) and generally decreases with decreasing MAS frequency (see

397 the dashed line in Figure 6A). Similarly, the RF field inhomogeneity has a subtle effect on the buildup

398 of the transferred magnetization. Figure 6B shows that maximum transfer occurs at shorter mixing

399 times for increased MAS frequencies.

400 Figure 6C shows how decreasing dipolar couplings result in a diminished Hartmann-Hahn transfer

401 efficiency. The calculations are carried out for three typical dipolar coupling values, and for MAS

402 frequencies in the range of 20 kHz to 200 kHz. Strikingly, for $\omega_R/2\pi$=200 kHz and b_{IS}=1 kHz, the

403 maximum transfer is only about 7%.

404   We used numerical simulations in SIMPSON (Bak et al., 2000; Tosner et al., 2014) to verify the
405   predictions of the analytical model. To implement an experiment, specific values of ω_I and ω_S need to
406   be selected. Consideration of RF field inhomogeneity increases the complexity of this selection process,
407   since certain values of ω_I, ω_S can lead to a situation in which ZQ and DQ recoupling conditions are
408   fulfilled simultaneously in different parts of the sample (Figure 4C). This phenomenon was explored
409   experimentally by Gupta et al. (Gupta et al., 2015). In case this situation is avoided, we find perfect
410   agreement between the analytical model and the numerical simulations (data not shown).

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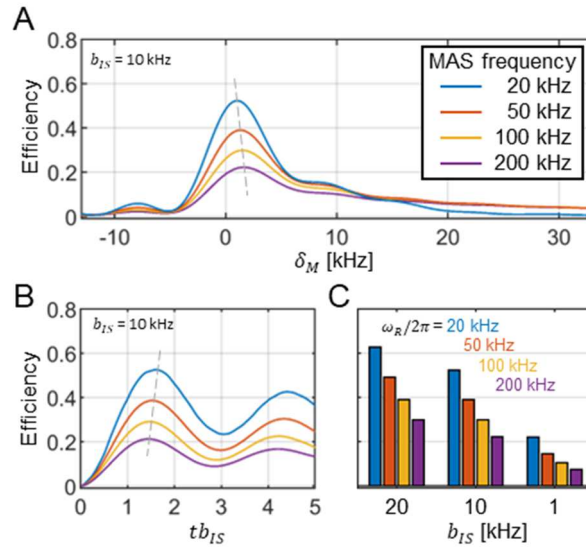
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413   **Figure 6**: Transfer efficiency of the constant amplitude CP experiment in the presence of RF field
414   inhomogeneity and assuming a dipolar coupling strength b_{IS} = 10 kHz. For the calculation, a rotor fully
415   packed with material is assumed. (A) The maximum of the CP matching profile decreases with
416   increasing MAS frequency for the zero-quantum (n=+1) condition. At the same time, the width
417   increases. A grey dashed line is used to indicate the position of the maximum. The maximum of the CP
418   matching profile shifts to higher mismatch values δ_M for increased MAS frequencies. (B) Magnetization
419   buildup curves for different MAS frequencies. The legend is indicated in panel (A). With increasing MAS
420   frequencies, magnetization reaches the maximum transfer at shorter mixing times. (C) Maximum
421   transfer efficiencies for the characteristic dipolar coupling values b_{IS} of 1, 10 and 20 kHz for different
422   MAS frequencies. Data were generated using Eqs. (27), (31) and (32).

423

424   ### 3.2. Visualization of the magnetization transfer trajectories

425   In the following, we aim to visualize the spin trajectory during the CP experiment in its basic form with
426   constant RF and with RF amplitude sweeps. We focus on the vicinity of the ZQ ($n = +1$) Hartmann-
427   Hahn condition and use the effective Hamiltonian $\overline{H}^{ZQ}$ given in Eq. (34) for the analysis. We consider
428   RF field inhomogeneity and assume nominal RF amplitudes that match the recoupling condition in the
429   center of the coil, $\omega_I^{NOM} - \omega_S^{NOM} = \omega_R$. Figure 7 shows the spin dynamics for two crystallite
430   orientations (β=15° and 45°), and three positions within the coil (ξ=0.6, 0.8, and 1.0). These conditions
431   are highlighted in Figure 1 and Figure 2. In the center of the coil where ξ=1.0, the Hamiltonian $\overline{H}^{ZQ}$

432 (blue vector) is aligned with the I_x^{ZQ} axis. The spin state vector $\rho^{ZQ}(t)$ (red vector) rotates in circles

433 within the yz plane with an angular velocity that depends on the crystallite orientation (Figure 7C,F).

434 This situation corresponds to the case without RF field inhomogeneity.

435 Depending on the position within the coil, a mismatch contribution in the effective Hamiltonian $\bar{H}^{ZQ}$

436 along the I_z^{ZQ} axis is obtained, which is according to Eq. (34) proportional to the MAS frequency. The

437 effective rotation axis is tilted away from the I_x^{ZQ} direction by an angle ϕ, Eq. (23). The effective

438 rotation frequency $\omega_{eff}^{ZQ,+1}$, Eq. (22), increases with increasing mismatch. Likewise, the I_x^{ZQ} component

439 of $\bar{H}^{ZQ}$ decreases with the decreasing effective dipolar coupling. This amplifies the effect of the RF

440 field inhomogeneity on the orientation of the effective Hamiltonian axis. The state vector rotates on

441 the surface of a cone (Figure 7AB,DE). As a consequence, the inversion becomes inefficient. Only the

442 central part of the sample yields a high transfer efficiency.

443

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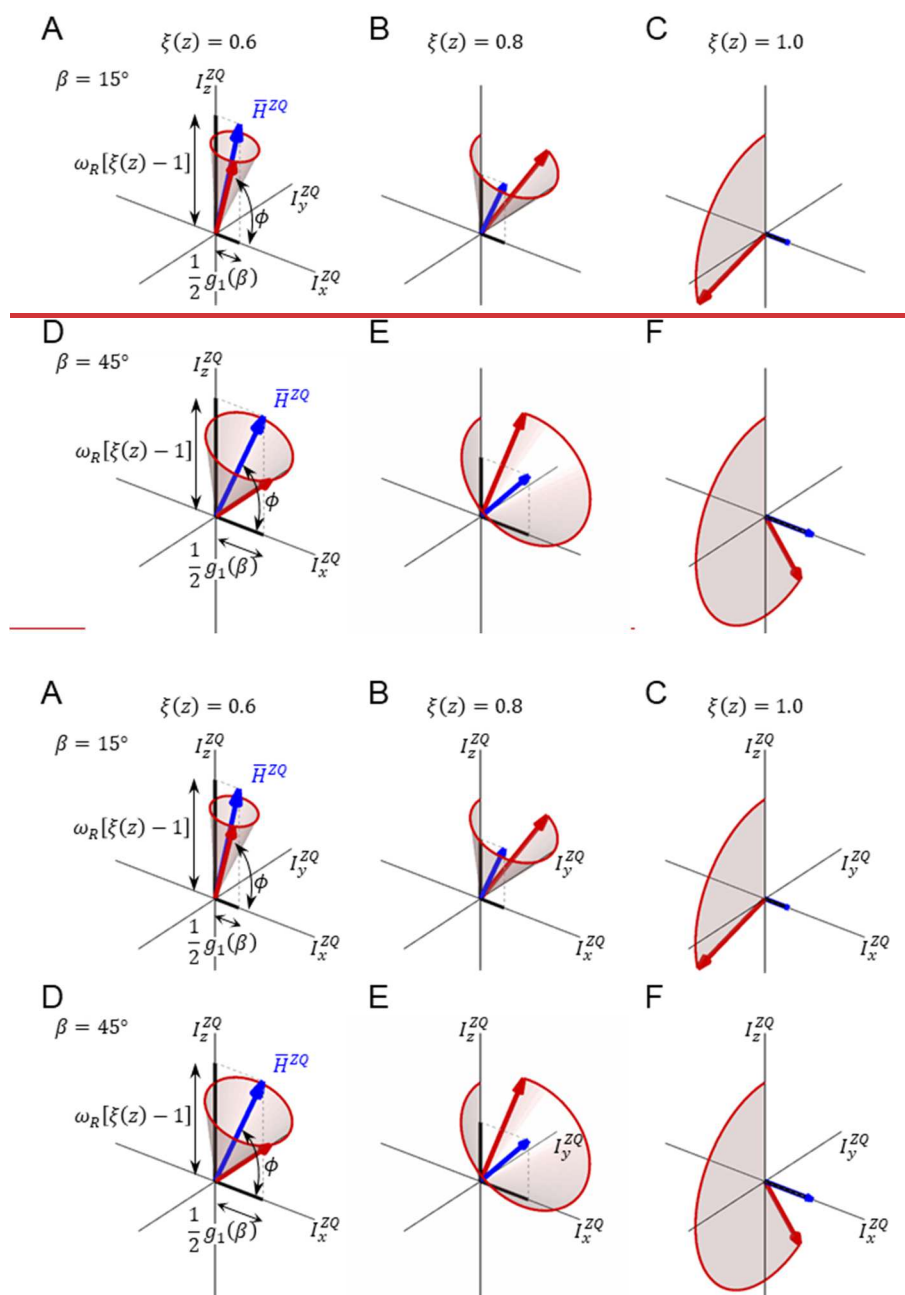
Figure 7. Visualization of the spin state trajectories for the constant amplitude cross-polarization experiment evaluated for two crystal orientations. (A-C) crystallite orientation β=15°, (D-F) β=45°. The calculations were carried out for 3 positions along the coil axis that correspond to RF field scaling values of $\xi(z)$=0.6 (panels A/D), 0.8 (panels B/E), and 1.0 (panels C/F). The state vector, ρ^{ZQ}, is represented by a red vector. The effective Hamiltonians are represented by blue vectors. ρ^{ZQ} rotates around $\bar{H}^{ZQ}$ on the surface of a cone (shaded area). In the simulation, an MAS frequency of 50 kHz and b_{IS}=10 kHz was assumed.

3.3. RF amplitude sweeps in the absence of RF field inhomogeneity

Continuous RF amplitude sweeps are used to improve the cross polarization efficiency. In this case, the effective Hamiltonian changes its orientation in the course of the pulse sequence. An adiabatic inversion is achieved if two conditions are fulfilled: (i) the initial state vector is aligned with the initial effective field vector and (ii) the effective field changes its orientation slowly. We focus on the zero quantum ($n = +1$) condition assuming a dipolar coupling constant b_{IS}= 10 kHz. In the following, spin state trajectories are calculated for two sweep amplitudes, Δ = 10 kHz and 30 kHz.

The spin state trajectories for the linear ramp are represented in Figure 8. The I_x^{ZQ} component of the effective Hamiltonian is fixed in time, and is given by the effective dipolar coupling at a given orientation (Eq. (40), assuming ξ=1.0). The maximal value of $\frac{1}{2}g_1(\beta)$ is reached for β=45° which together with the sweep amplitude of Δ=10 kHz and according to Eq. (23) results in a tilt angle of the effective field $\phi(t = 0, \beta = 45°)$=54.7° at the beginning of the pulse sequence (Figure 8B). Clearly, the initial state vector $\rho^{ZQ}(0) = I_z^{ZQ}$ is not aligned with the effective field of $\bar{H}^{ZQ}(t = 0)$. However, the inversion efficiency is high due to the slow change of the orientation of the effective field, $d\phi/dt$, such that the state vector can follow the effective field while it is rotating around it in rather large circles (see evaluation of the adiabaticity condition in Figure 8F). For a smaller effective dipolar coupling (for example, β=15° in Figure 8A), the angle ϕ is larger, close to 90°. During the linear ramp, the effective Hamiltonian amplitude $\omega_{eff}^{ZQ}(t)$ goes through a minimum in the middle of the sweep at $t = T/2$, where its value is solely determined by the effective dipolar coupling, see Eq. (22). At the same time, $d\phi/dt$ reaches its maximum (Figure 8E). Under these conditions, the state vector keeps track with the effective field (Figure 8A). When a larger sweep amplitude is employed, e.g. Δ=30 kHz, the orientation of the initial effective field is closer to the I_z^{ZQ} axis, $\phi(t = 0, \beta = 45°)$=76.7° (Figure 8D). At the same time, the amplitude of the effective Hamiltonian $\omega_{eff}^{ZQ}(t = 0)$ is increased as well. For the crystallite orientation β=15° (Figure 8C), however, we find that the adiabaticity condition is violated in the middle of the pulse sequence (Figure 8G). The state vector is not able to follow the effective field as $d\phi/dt$ becomes too high. As a consequence, the state vector keeps rotating near the equator (Figure 8C) and thus contributes little to the total transfer efficiency.
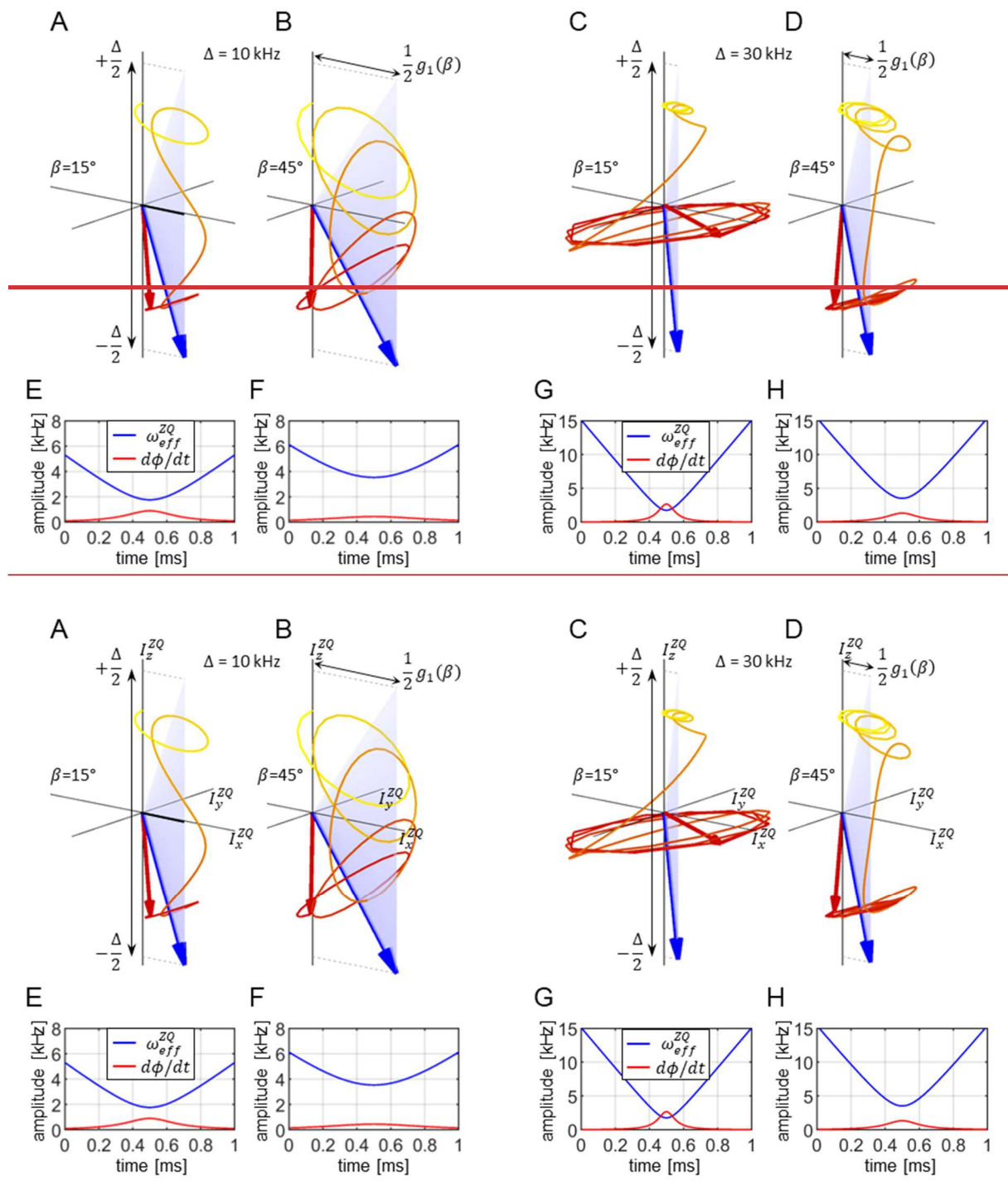
Figure 8. Visualization of the spin state trajectories for the linear ramp cross-polarization experiment assuming a homogeneous RF field distribution. For the simulation, a dipolar coupling b_{IS}=10 kHz was assumed. The CP contact time was set to T=1 ms. The calculation was carried out for two crystallite orientations (β=15° and 45°, panels A,C and B,D, respectively), and two sweep amplitudes (Δ=10 kHz and Δ=30 kHz, panels A,B and C,D, respectively). The blue-shaded areas represent the changing effective Hamiltonian. The blue arrow indicates the effective Hamiltonian at the end of the pulse sequence at $t = T$. The component along the I_z^{ZQ}-axis is time dependent, while the I_x^{ZQ}-axis component is fixed (see Eq. (40)). The beginning of the trajectory is depicted as a yellow line which gradually turns into red as the trajectory progresses. The final state of the spin state vector (initially

491 oriented along I_z^{ZQ}) is drawn as a red arrow. Panels E-H display $d\phi(t)/dt$ and $\omega_{eff}^{ZQ}(t)$. In C/G, the

492 adiabaticity condition $d\phi/dt<\omega_{eff}$ is violated during the sweep.

493

494 Spin state trajectories for the adiabatic variant of the CP experiment are shown in Figure 9. The

495 tangential sweep has been suggested to keep the rate of change $d\phi(t)/dt$ small compared to the

496 effective field amplitude at all times (Hediger et al., 1995). Initially, $\omega_{eff}(t)$ is large implicating that

497 $d\phi(t)/dt$ can be large. However, for small sweep amplitudes such as Δ=10 kHz the effective field

498 changes too rapidly for a portion of crystallites at the beginning and at the end of the sweep so that

499 the adiabaticity condition is violated (Figure 9E). Most of the dynamics takes place when the tangential

500 function goes through the central plateau, where the RF amplitudes do not change significantly over

501 an extended period of time. The state vector rotates in large circles around the effective Hamiltonian

502 that is oriented predominantly along the I_x^{ZQ} axis. When a larger sweep amplitude $\Delta = 30$ kHz is used,

503 the adiabatic regime is restored for most crystallite orientations and an improved transfer efficiency is

504 obtained.

505 Figure 10 compares the magnetization transfer during the RF sweep for the examples discussed above.

506 The transfer process is fast when the change of the effective field orientation is fast: in the middle of

507 the linear ramp, and at the beginning and at the end of the tangential sweep, provided the adiabaticity

508 condition is maintained (Figure 10AB). Figure 10CD shows the transfer efficiency as a function of

509 crystallite orientation. Note that the spin state inversion cannot be achieved for crystallite orientations

510 with an effective dipolar coupling that is vanishing, i.e., for β=0° and 90°. The portion of crystallites

511 yielding low transfer depends on the ratio of the sweep amplitude Δ and the dipolar coupling b_{IS}. For

512 the linear ramp Δ=10 kHz is preferable, while the tangential sweep using an amplitude $\Delta = 30$ kHz yields

513 high efficiency for most of the crystallites under the conditions investigated here. After powder

514 averaging, the magnetization transfer efficiency is on the order of 90% for the tangential sweep. We

515 would like to note that all predictions based on the ZQ average Hamiltonian agree well with exact

516 simulations using SIMPSON (data not shown).

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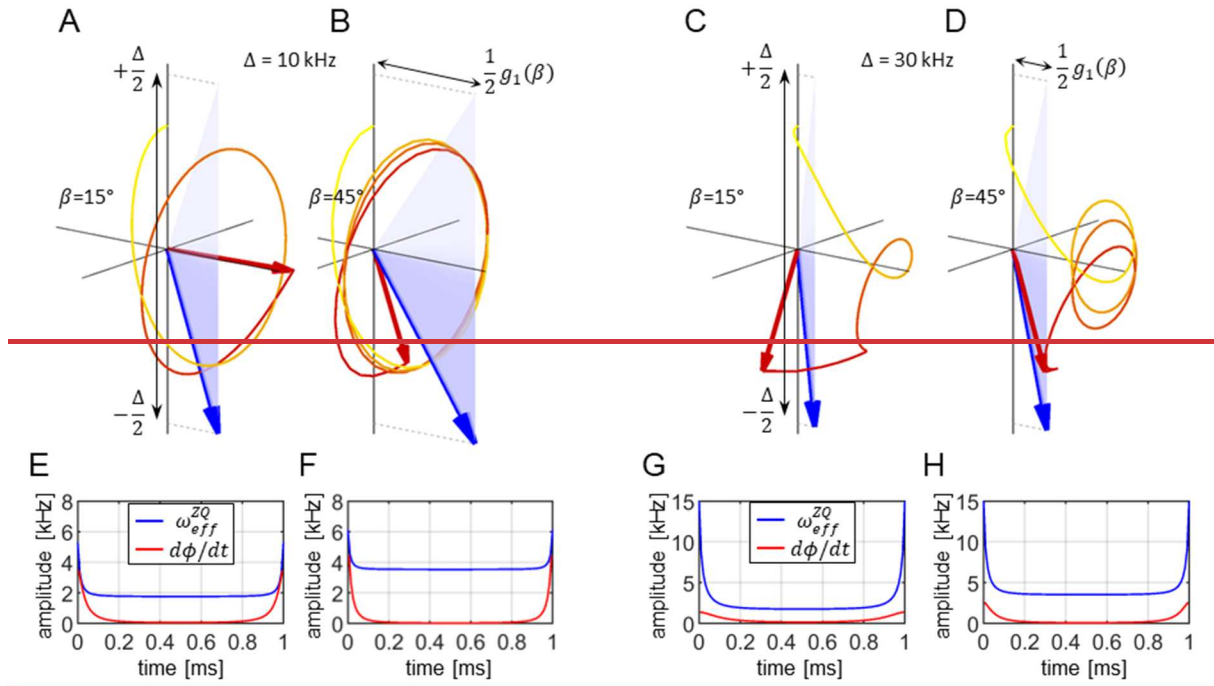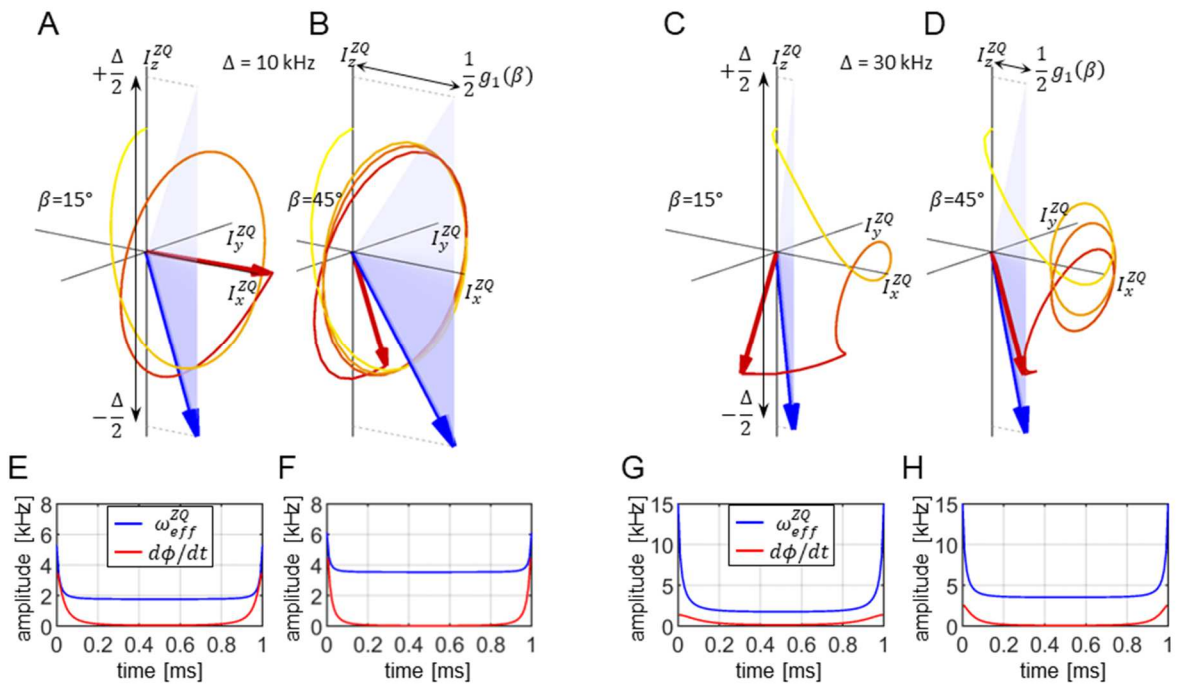
Figure 9: Visualization of the spin state trajectories for the adiabatic tangential sweep cross-polarization experiment assuming a homogeneous RF field distribution. For the simulation, a dipolar coupling b_{IS}=10 kHz was assumed. The CP contact time was set to T=1 ms. The calculation was carried out for two crystallite orientations (β=15° and 45°, panels A,C and B,D, respectively) and two sweep amplitudes (Δ=10 kHz and Δ=30 kHz, panels A,B and C,D, respectively, $b = \Delta/50$). The blue-shaded areas represent the changing effective Hamiltonian. The blue arrow indicates the effective Hamiltonian at the end of the pulse sequence at $t = T$. The component along the I_z^{ZQ}-axis is time dependent, while the I_x^{ZQ}-axis component is fixed (see Eq. (40)). The beginning of the trajectory is depicted as a yellow line which gradually turns into red as the trajectory progresses. The final state of the spin state vector

529   (initially oriented along I_z^{ZQ}) is drawn as a red arrow. Panels E-H display $d\phi(t)/dt$ and $\omega_{eff}^{ZQ}(t)$. In A/E

530   and B/F, the adiabaticity condition $d\phi/dt<\omega_{eff}$ is violated during the sweep.

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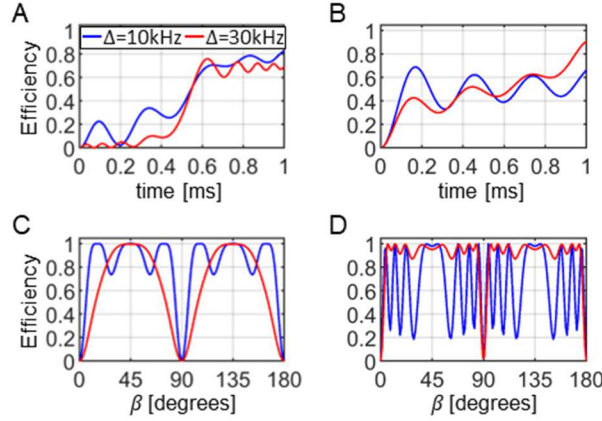
532

533   **Figure 10:** Powder averaged buildup of the transferred magnetization during the mixing time of the CP

534   experiment (A, B) and the final transfer efficiency as a function of crystallite orientation (C, D) for an

535   RF amplitude sweep using a linear ramp (A,C) and a tangential shape (B, D). The blue and red curves

536   correspond to sweep amplitudes of 10 and 30 kHz, respectively. In all simulations, a homogeneous RF

537   field distribution is assumed.

538

539   ### 3.4. RF amplitude sweeps in the presence of an inhomogeneous RF field

540   In the following paragraph, RF field inhomogeneities are included in the analysis. For simplicity, we

541   assume that the RF field varies along the solenoid coil axis as described in Figure 2 and the variation is

542   the same for both RF channels. We disregard time modulations induced by sample rotation in a

543   spatially inhomogeneous RF field. We assume that the Hartmann-Hahn condition is fulfilled for the

544   nominal RF amplitudes in the middle of the coil. The RF amplitude sweep is applied to the I channel.

545   We again examine the zero-quantum ($n = +1$) recoupling condition. The drive Hamiltonian $\overline{H}^{ZQ}$ is

546   given by Eq. (40). Sweeping the RF amplitude makes the I_z^{ZQ}-component of the effective Hamiltonian

547   time dependent. The range over which it varies depends on the position along the coil axis, and it is

548   visualized in Figure 4. The center of the sweep is shifted away from the exact matching condition

549   towards the ends of the coil by an amount that depends on the MAS frequency. As discussed above,

550   the evolution in the double-quantum subspace can be neglected, since $\overline{H}^{DQ}$ has a dominant

551   component along I_z^{DQ} axis which is much larger than the effective dipolar coupling. This can be

552   achieved by choosing a proper value for ω_S^{NOM}. At the same time, we have chosen conditions that

553   avoid simultaneous matching of different Hartmann-Hahn conditions within the sample volume.

554   The previous description of the RF amplitude modulated CP is valid in the center of the coil where

555   ξ=1.0. The situation is quite different in volume elements towards the ends of the coil. Figure 11

556   illustrates the spin state trajectories for the linear ramp CP experiment, assuming a crystallite angle

557   β=45°, a MAS frequency of $\omega_R/2\pi$=50 kHz, and a dipolar coupling constant of b_{IS}= 10 kHz. The scaling

558   factor ξ=0.8 is realized for $z = \pm0.36l$ (where l is the coil length) around the center of the coil. When

559 the sweep amplitude is Δ=10 kHz, the effective field does not get inverted during the sweep (Figure 4A
560 and Figure 11A) and therefore cannot invert the spin state, regardless of its adiabaticity (Figure 11E).
561 Increasing the sweep amplitude to Δ=30 kHz yields better results as the effective field approaches the
562 Hartmann-Hahn recoupling condition towards the end of the sweep period (Figure 4B and Figure 11C).
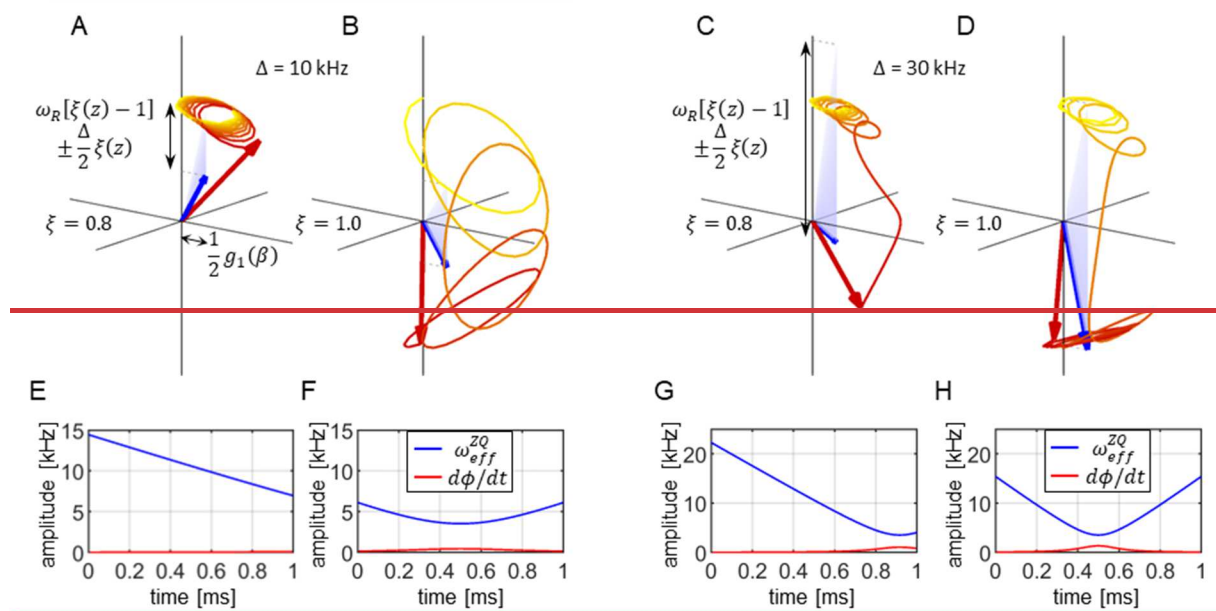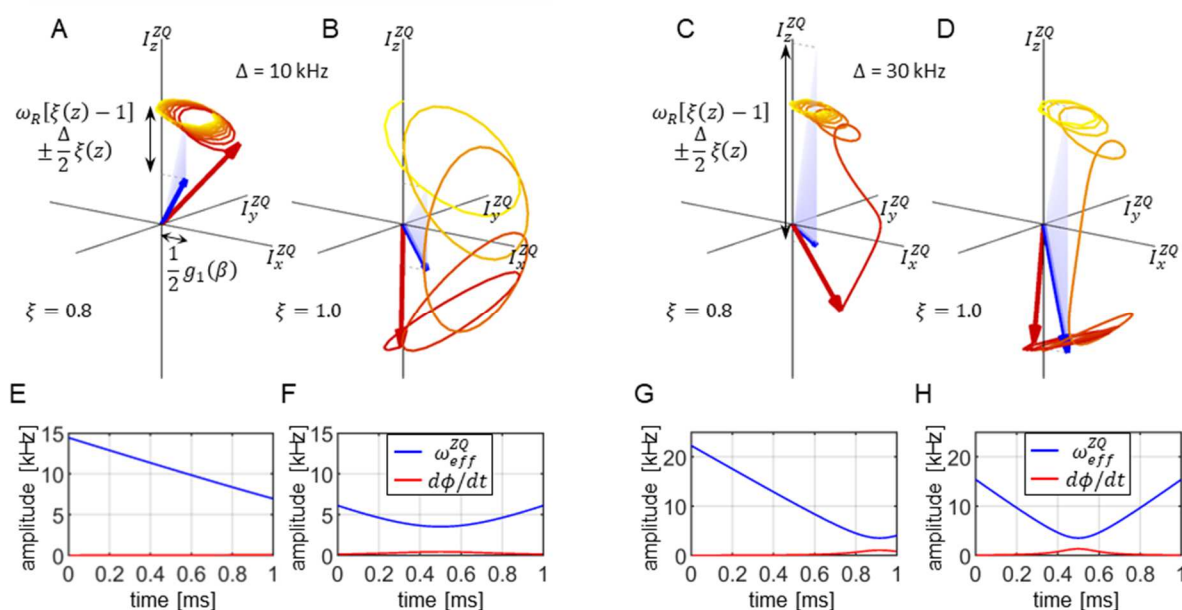
Figure 11: Visualization of the spin state trajectory for a linear ramp cross-polarization experiment
assuming an inhomogeneous RF field distribution. For the simulation, a dipolar coupling b_{IS}=10 kHz
was assumed. The CP contact time was set to T=1 ms. The calculation was carried out for one crystallite
orientation (β= 45°) and two positions along the coil axis with RF field scaling factors ξ=0.8 and 1.0
(panels A,C and B,D) and two sweep amplitudes Δ=10 kHz and Δ=30 kHz (panels A,B and C,D). The blue-
shaded areas represent the changing effective Hamiltonian. The blue arrow indicates the effective

Hamiltonian at the end of the pulse sequence at $t = T$. The component along the I_z^{ZQ}-axis is time dependent, while the I_x^{ZQ}-axis component is fixed (see Eq. (40)). The beginning of the trajectory is depicted as a yellow line which gradually turns into red as the trajectory progresses. The final state of the spin state vector (initially oriented along I_z^{ZQ}) is drawn as a red arrow. Panels E-H display $d\phi(t)/dt$ and $\omega_{eff}^{ZQ}(t)$ to appreciate whether the adiabaticity condition $d\phi/dt < \omega_{eff}$ is violated during the sweep.

For a tangential sweep, the spin state trajectories are depicted in Figure 12. Initially, and towards the end of the sweeping period, the RF amplitude changes rapidly and so does the effective field orientation. This can lead to a violation of the adiabaticity condition, as encountered for the calculation with a sweep amplitude of Δ=30 kHz (Figure 12C,G). Despite the fact that the Hartmann-Hahn matching condition is included within the sweep range, the state vector does not follow the effective field. These parts of the sample yield a low transfer efficiency.

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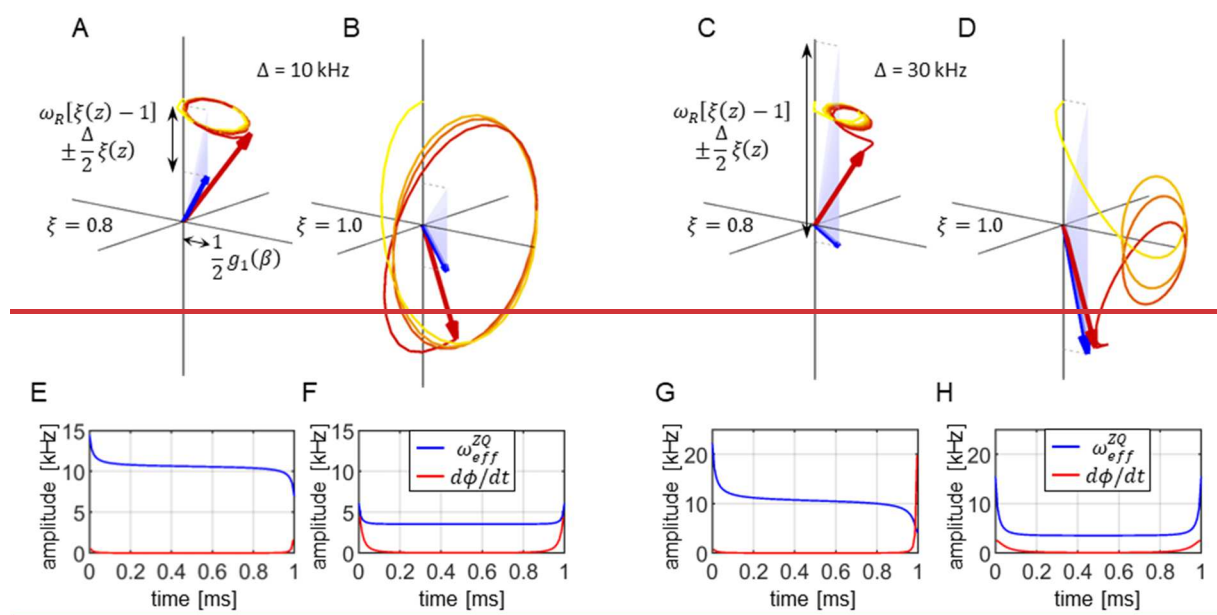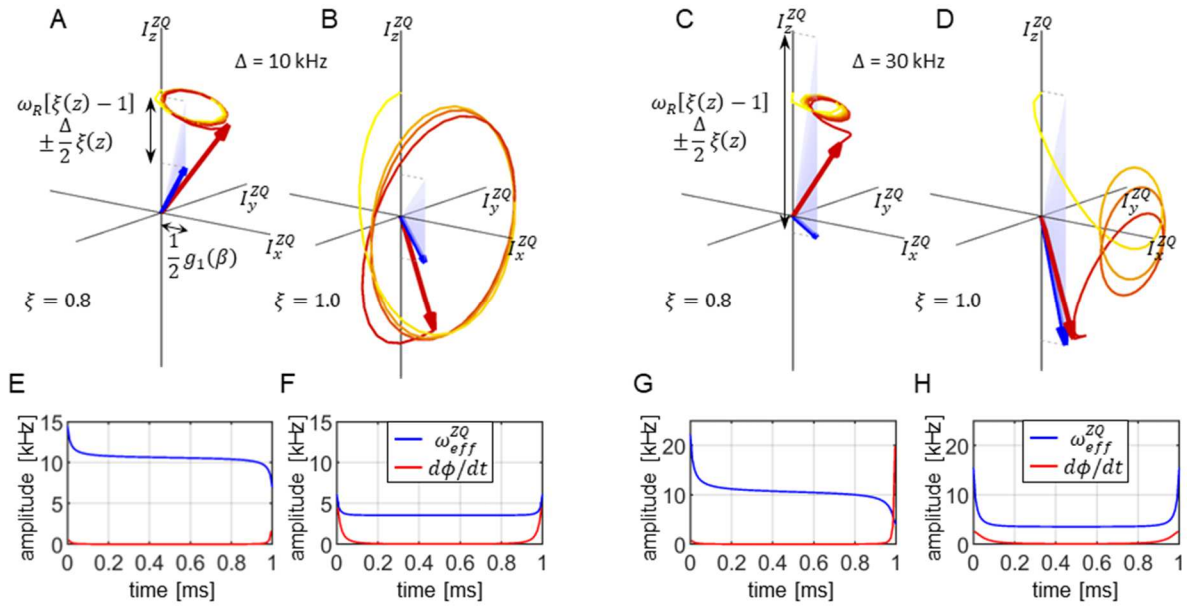
Figure 12: Visualization of the spin state trajectory for an adiabatic tangential sweep cross-polarization experiment assuming an inhomogeneous RF field. For the simulation, a dipolar coupling b_{IS}=10 kHz was assumed. The CP contact time was set to T=1 ms. The calculation was carried out for one crystallite orientation (β= 45°) and two positions along the coil axis with RF field scaling factors ξ=0.8 and 1.0 (panels A,C and B,D) and two sweep amplitudes Δ=10 kHz and Δ=30 kHz, assuming $b = \Delta/50$ (panels A,B and C,D). The blue-shaded areas represent the changing effective Hamiltonian. The blue arrow indicates the effective Hamiltonian at the end of the pulse sequence at $t = T$. The component along the I_z^{ZQ}-axis is time dependent, while the I_x^{ZQ}-axis component is fixed (see Eq. (40)). The beginning of the trajectory is depicted as a yellow line which gradually turns into red as the trajectory progresses. The final state of the spin state vector (initially oriented along I_z^{ZQ}) is drawn as a red arrow. Panels E-H display $d\phi(t)/dt$ and $\omega_{eff}^{ZQ}(t)$ to appreciate whether the adiabaticity condition $d\phi/dt<\omega_{eff}$ is violated during the sweep.

The buildup of the transferred magnetization integrated over the sample volume and detected by the NMR coil for both the linear ramp and the tangential sweep is presented in Figure 13A,B. It is not obvious which sweeping method will yield a higher total transfer efficiency. Of the four setups discussed so far, the linear ramp with Δ=30 kHz yields the best result. When comparing efficiency profiles along the coil axis (Figure 13C,D) we observe that tangential sweep is more efficient near the center of the coil but quickly loses efficiency when going towards the ends. However, linear ramp yields equal transfer over a larger sample volume.

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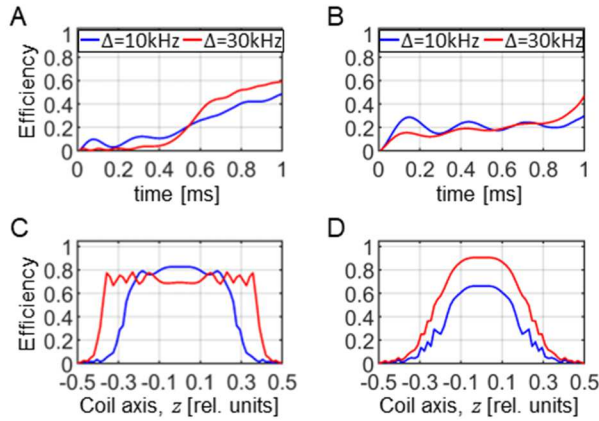


Figure 13: Powder averaged buildup of transferred magnetization during the mixing time of the CP experiment (A, B), and the final powder averaged transfer efficiency as a function of the position along the coil axis (C, D) for a linear ramp (A,C) and a tangential shape (B, D). The blue and red curves correspond to sweep amplitudes of Δ=10 kHz and Δ=30 kHz, respectively. In the calculation, an inhomogeneous RF field is assumed.

615

3.5. Numerical optimizations of linear and tangential sweeps

In this section, we discuss which parameters of a linear ramp and a tangential sweep yield the best transfer efficiency. We address this problem by a numerical optimization. The calculations are repeated for a range of dipolar couplings and MAS frequencies. In the case of the linear ramp, the sweep amplitude Δ and the offset δ_M from the exact Hartmann-Hahn condition are optimized. In case of the tangential sweep, the curvature parameter b is considered in addition (Figure 3). The offset parameter δ_M corresponds to the mismatch of the recoupling condition in the middle of the coil due to RF inhomogeneity and reflects the experimental optimization procedure where the amplitude ω_S^{NOM} is kept constant and the amplitude ω_I^0 is optimized around the expected recoupling condition. To ensure that not more than one matching condition is encountered during the sweep, the amplitude Δ was restricted to values within $\pm\omega_R/2$ (Hediger et al., 1995). The dynamics was evaluated using the effective Hamiltonian $\bar{H}^{ZQ}$ given in Eq. (40). The optimized parameters correspond to the best transfer efficiency obtained from 100 repetitions initiated by random guess. As expected, we obtain a different set of optimal parameters for each contact time, dipolar coupling, and MAS frequency.

The optimized transfer efficiencies are summarized in Figure 14. Remarkably, we have not found any significant differences in the performance of the linear ramp with respect to the tangential sweep. Both sweep methods yield the same total transfer efficiency, although they use different sweep parameters. An example of the best sweep shapes obtained for a dipolar coupling b_{IS}=10 kHz and an MAS frequency of 50 kHz is presented in Figure 15. The tangential sweeps tend to have a larger sweep amplitude Δ and a smaller offset values δ_M when compared to the linear ramp.

We observe that very long contact times are required to obtain high transfer efficiencies. For calculations involving different dipolar coupling strengths b_{IS} the same range of the reduced time parameter Tb_{IS} is used. In this way, longer mixing times T are maintained for smaller dipolar couplings b_{IS}. Better performance is obtained for cases with higher dipolar couplings which correlates with the

width of Hartmann-Hahn conditions in CP matching profiles. On the other hand, the transfer efficiency decreases at higher MAS frequencies due to increased volume selectivity. The most challenging are small dipolar couplings, on the order of 1 kHz and ultrafast MAS (>100 kHz) which are typical for [15]N-^{13}C spin pairs in proteins studied by proton-detected MAS solid-state NMR experiments. To more efficiently average proton dipolar interaction, MAS probe development aims at smaller diameter rotors to achieve higher MAS rotation frequencies. Currently, 0.4 mm MAS probes are in development that can reach MAS frequencies of up to 200 kHz. Our predictions suggest that only 20% of the sample will contribute to the detected NMR signal after a 10 ms [15]N-^{13}C CP mixing step at a MAS frequency of 200 kHz, i.e. up to 80% of the signal is lost in a single magnetization transfer step. The efficiency increases to ca. 40% when a 40 ms long mixing period is used, provided that there are no signal losses due to relaxation. However, note that the sensitivity in a pulse sequence with multiple CP transfer elements depends on all previous transfer steps. The first CP element pre-selects a volume that is maintained or further restricted in subsequent transfer elements.

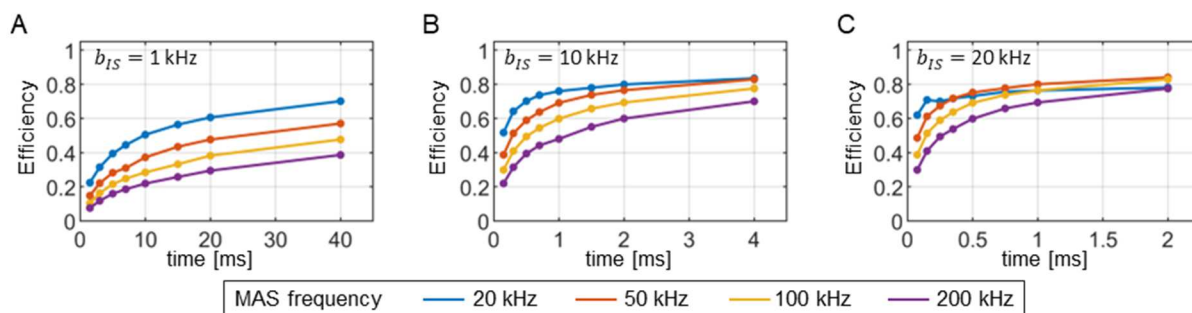



Figure 14. Maximum achievable transfer efficiencies in the cross-polarization experiment as a function of contact time and MAS frequency using numerical optimizations. Similar efficiencies are obtained for both the linear ramp and the tangential sweep, although different shape parameters have to be employed. Dipolar couplings of 1 kHz, 10 kHz and 20 kHz are used in the simulations for panels A, B, and C, respectively.

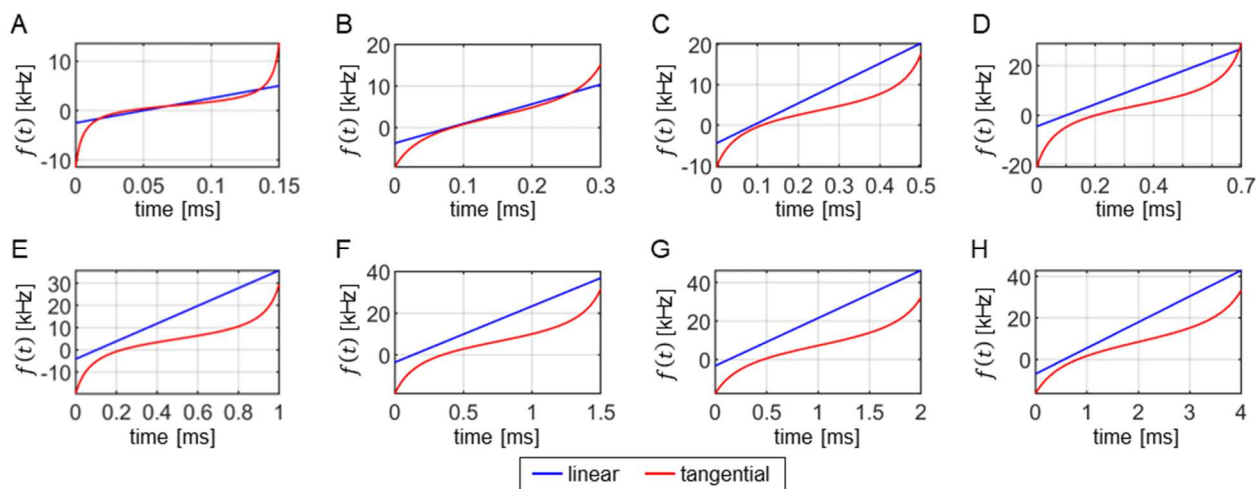
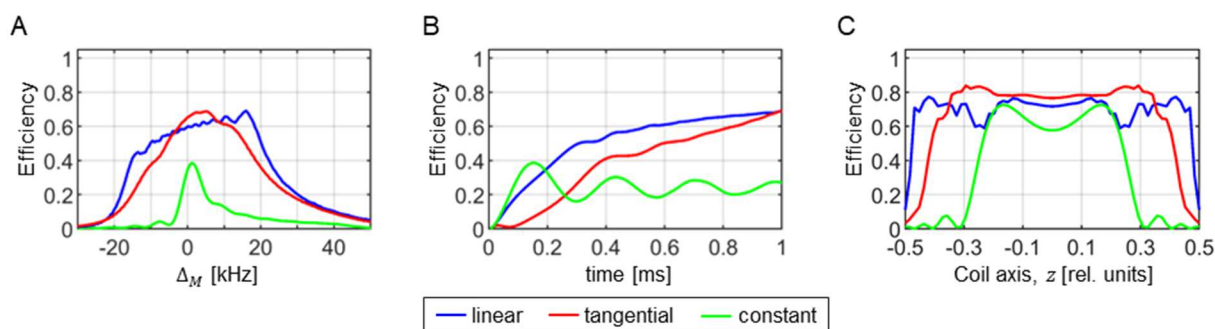



Figure 15: Comparison of optimal linear ramp (blue) and tangential sweep (red) shapes obtained by numerical optimizations at different contact times T=0.15, 0.3, 0.5, 0.7, 1.0, 1.5, 2.0, and 4.0 ms in

663 panels A-H, respectively. For the optimization, a dipolar coupling b_{IS}=10 kHz was assumed. The
664 calculations were performed assuming a MAS frequency of 50 kHz and a realistic RF inhomogeneity
665 distribution. Although the two shapes are different, they yield virtually identical total transfer
666 efficiencies.

667

668 We find that there is no difference between the linear ramp and the tangential shapes in terms of total
669 transfer efficiency. In Figure 16, we compare these two methods (together with a constant amplitude
670 CP) with respect to the width of the CP matching profile (panel A), the magnetization transfer buildup
671 (panel B), and the sample volume selectivity (panel C). As expected, the RF amplitude sweep
672 significantly improves the width and the height of the matching profile. The most important difference
673 is that the tangential sweep yields higher efficiency near the center of the coil and lower efficiency at
674 edges of the coil. Use of RF pulses and other recoupling elements can potentially result in a
675 preselection of a particular sample volume that cannot be utilized by the linear ramp for a further
676 transfer. Therefore, transfer elements should be optimized within the framework of the whole pulse
677 sequence to minimize a differential preselection of the sample volume during calibration experiments.

678

679 **Figure 16:** Comparison of the matching profiles (A), magnetization transfer buildups (B), and
680 contribution to the transfer efficiency of individual volume elements along the coil axis (C) for an
681 optimized linear ramp (blue), a tangential sweep (red), and a constant amplitude CP (green). For the
682 optimization, a dipolar coupling b_{IS}=10 kHz was assumed. The calculations were performed assuming
683 a MAS frequency of 50 kHz and a realistic RF inhomogeneity distribution. The CP contact time was set
684 to T=1 ms. In (A) and (C), the constant amplitude CP was evaluated after 160 μs when it reaches
685 maximum transfer efficiency.

686

687 The linear ramp and the adiabatic tangential sweeps were calculated for the ZQ ($n = +1$) condition.
688 However, the shapes are equally applicable to any other $n = \pm 1$ Hartmann-Hahn condition, as the
689 corresponding effective Hamiltonian has the same form. The $n = \pm 2$ Hartmann-Hahn conditions
690 suffer from increased RF field inhomogeneity (factor of 2 in Eq. 40) and have different powder
691 averaging properties implied by the $g_2(\beta)$ term. Thus, a decreased CP transfer efficiency for the $n =$
692 ± 2 matching condition is expected.

693

694 The transfer efficiencies of all pulse sequences were verified using numerical simulations in SIMPSON.
695 To avoid overlap of the different Hartmann-Hahn matching conditions, the zero quantum ($n = +1$)
696 condition with $\omega_S^{NOM}/2\pi$ = 60 kHz was selected using MAS frequencies of 20 and 50 kHz, while the
697 double quantum ($n = +1$) condition with $\omega_S/2\pi$ = 30 kHz was used for a MAS frequency of 100 kHz.
698 The agreement between SIMPSON and the effective Hamiltonian calculations is excellent except for a
699 simulation in which a dipolar coupling of 20 kHz and a MAS frequency of 20 kHz was assumed. In this
700 case, the numerically evaluated transfer efficiencies are about 10% lower. A plausible explanation is
701 that the first order average Hamiltonian approximation does not provide the full description of the
702 spin dynamics when the dipolar coupling and the MAS frequency are of similar value (in other cases it
703 holds $b_{IS} \ll \omega_R/2\pi$).

704

4. Conclusions

706 We have analyzed the magnetization transfer efficiency of the CP experiment as a function of the MAS
707 frequency in the presence of RF field inhomogeneity of a solenoid coil. We show that a sweep of the
708 RF amplitude through the Hartmann-Hahn matching conditions using either a linear ramp or a
709 tangential shape improves the performance in comparable way. We do not observe a difference in the
710 total transfer efficiency between these two methods. We find that magnetization transfer using a CP
711 recoupling element becomes inefficient in particular for small dipolar couplings for ultrafast MAS
712 experiments with rotation frequencies above 100 kHz. New recoupling methods that are designed
713 explicitly to account for inhomogeneous RF fields and ultrafast MAS conditions are needed to
714 overcome this issue in the future.

715

716 **Author contribution**

717 ZT and BR conceived the project. AŠ carried out numerical calculations. JB, AŠ, BR and ZT discussed the
718 results, sketched the plot of the paper, and collaborated on the final text. ZT wrote the paper.

719 **Competing interests**

720 At least one of the (co-)authors is a member of the editorial board of Magnetic Resonance.

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