Axis-matching excitation pulses for CPMG-like sequences in inhomogeneous fields

Soumyajit Mandal, Van D.M. Koroleva, Troy W. Borneman, Yi-Qiao Song, Martin D. Hürlimann

Abstract

The performance of the standard CPMG sequence in inhomogeneous fields can be improved with the use of broadband excitation and refocusing pulses. Here we introduce a new class of excitation pulses, so-called axis-matching excitation pulses, that optimize the response for a given refocusing pulse. These new excitation pulses are tailored to the refocusing pulses and take their imperfections into account. Rather than generating purely transverse magnetization, these pulses are designed to generate magnetization pointing along the axis of the effective rotation of the refocusing cycle. This approach maximizes the CPMG component and minimizes the CP component of the signal. Replacing a standard 90° pulse with a new excitation pulse matched to the 180° refocusing pulse increases the signal bandwidth and improves the echo amplitudes by 30% in inhomogeneous fields in comparison to the standard CPMG sequence. Larger gains are obtained with more advanced refocusing pulses. Recent work demonstrated that it is possible to increase the signal to noise ratio (SNR) of individual echoes by more than a factor of 1.5 (in power units) without increasing the duration or amplitude of the refocusing pulses. This was achieved by replacing the standard 180° refocusing pulse by a short phase alternating pulse and the standard 90° excitation pulse by a broadband excitation pulse. We show here that with suitable axis-matching excitation pulses, the SNR further increases by over a factor of 2. We discuss the underlying theory and present several practical implementations of purely phase modulated axis-matching excitation pulses for a number of different refocusing pulses that were derived using methods of optimal control. To gain the full benefit of these new excitation pulses, it is essential to replace the standard phase cycling scheme based on 180° phase shifts by a new scheme involving phase inversion. We tested the new pulses experimentally and observe excellent agreement with the theoretical expectations. We also demonstrate that an additional benefit of axis-matching excitation pulses is the decrease of the transient that appears in the amplitudes of the first few echoes, thus enabling better measurements of short relaxation times.

Introduction

The Carr–Purcell–Meiboom–Gill (CPMG) [1,2] sequence plays a key role in many NMR applications ranging from quantum information processing [3–6], magnetometry [7–9] to applications in inhomogeneous fields that include stray-field NMR [10] and oilfield logging [11]. In these cases, the inhomogeneity of the static magnetic field B0 across the sample typically exceeds the strength of B1. As a consequence, T2 is very short and comparable to the pulse duration. To overcome this rapid signal decay, the CPMG sequence is used with a pulse spacing as short as possible. This generates the maximum number of echoes per unit time and can be used to improve the effective signal-to-noise ratio [12]. The short echo spacing also allows the monitoring of relaxation properties over a wide range of time scales.

The spin dynamics of the standard CPMG sequence in such grossly inhomogeneous fields is well understood [13–17]. With standard rectangular pulses and in a static magnetic field characterized by a gradient, the main contributions to the signal comes from frequency offsets within ±ω0Δν around the carrier frequency of the rf pulses. This range of frequency offsets can be increased with the use of composite, shaped, chirped or adiabatic pulses [18–27]. Much progress has been recently made in the development of broadband excitation and refocusing pulses that are also robust with respect to variation of the rf field strength and other constraints [25,28–31,26]. These developments took advantage of the availability of new algorithms for pulse sequence design based on methods of optimal control [32,33]. These algorithms make it feasible to find new sequences in an efficient manner in a high-dimensional parameter space.
The performance of the standard 180° refocusing pulse is improved by constructing a pulse with sophisticated phase- and/or amplitude modulation. Such pulses are more complex and typically much longer than the standard 180° pulse. This increase in pulse duration has the undesirable consequence that it entails an increase of the minimum echo spacing and an increase in the power consumption per refocusing pulse. This is of particular concern for mobile and field applications such as NMR well logging. For this reason, we investigated in [27] the potential of very short refocusing pulses. We searched for pulses under the constraint that the overall duration and maximum amplitude do not exceed those of the standard 180° refocusing pulse. We showed that it is possible to generate larger echoes by modulating the phase within a 180° refocusing pulse. The optimal refocusing pulse of duration \( t_{180} \) was found to be of the form \( \chi x \beta x \chi - x \) with \( \chi \approx \pm 27° \) and \( \beta \approx 126° \) [27]. This refocusing pulse is an example of a symmetric phase-alternating pulse, a class of pulses that was first described by Shaka et al. [34]. In the rest of this paper, we refer to the \( 27° \cdot x \cdot 126° \cdot x \cdot 27° \cdot x \) pulse as the SPA pulse.

In a gradient field, a modified CPMG sequence based on such SPA refocusing pulses and a perfect broadband excitation pulse generates echoes with a ratio of signal to noise power (SNR) that is 2.38 times larger compared to the standard CPMG sequence. With practical excitation pulses that are no longer than 20 times the duration of the refocusing pulses and without an increased \( B_0 \) amplitude, we demonstrated an improvement in SNR of 1.52 [27].

Here we show that it is possible to substantially improve the performance of the CPMG sequence in inhomogeneous fields by replacing the excitation pulse with a so-called axis matching excitation pulse, or AMEX pulse for short. This approach is also effective for more general CPMG-like sequences that contain broadband refocusing pulses (such as SPA pulses). The new excitation pulses take the limitations of the refocusing pulses explicitly into account and are specific for a given refocusing pulse and echo spacing. Rather than trying to generate transverse magnetization over the widest possible bandwidth, AMEX pulses generate magnetization that at each offset frequency aligns with the axis characterizing the refocusing cycle from echo to echo. We present practical AMEX pulses for a number of simple refocusing pulses that were obtained using methods of optimal control [33]. We show that this results in a significant increase of the SNR. Using AMEX pulses optimized for SPA refocusing pulses, we found experimentally an increase in SNR by over a factor of 3 compared to the standard CPMG sequence. Remarkably, this improvement substantially exceeds the theoretical limit achievable with a perfect broadband 90° excitation pulse and the same SPA refocusing pulse.

We first summarize the theory underlying the relevant spin dynamics and formulate the condition for the AMEX pulses. We also discuss the necessary modifications to the phase cycling. The search algorithm used to find the AMEX pulses is presented in Section 3. In Section 4, we present a number of AMEX pulses that were optimized for a number of different refocusing pulses, including the SPA pulse and several rectangular refocusing pulses. Experimental results are presented in Section 5. We finish with the conclusion and outlook for further work.

2. Theory

We start with a brief review of the relevant spin dynamics for a collection of uncoupled spins 1/2 placed in inhomogeneous \( B_0 \) and gradient fields. This problem has been studied extensively and further details can be found in the literature [13–15,24,31,17,35,27]. We consider a generalized CPMG-like sequence that consists of an initial excitation pulse followed by a long train of equally-spaced, identical refocusing pulses. The excitation and refocusing pulses can be simple rectangular pulses or complex composite pulses. We are considering the limit when the echo spacing, \( t_e \), is much shorter than the transverse relaxation time, \( T_2 \) and also short enough to make diffusion effects negligible. In this case, the propagator from echo to echo for any spin can be well approximated by an effective rotation \( R(n, \theta) \). The rotation is characterized by the axis \( \hat{n}(\omega_0, \omega_1) \) and nutation angle \( \theta(\omega_0, \omega_1) \). They depend on the offset frequency \( \omega_0 \), the strength of the rf field, \( \omega_1 \), the refocusing pulse, and the echo spacing \( t_e \). If we call the magnetization following the excitation pulse \( M(0^+) \), then the magnetization at the nominal center of the \( k \)th echo for a given value of \( \omega_0 \) and \( \omega_1 \) can be written as:

\[
\hat{M}_k = e^{-kt_e/2T_2} R(n, k\theta) \{ M(0^+) \}
\]

The effective relaxation time \( T_{2,eff} \) depends in general on both \( T_1 \) and \( T_2 \). In the limiting case of \( T_1 = T_2 = T_{2,eff} = T_2 \) [15]. The CPMG component can be identified as the component of the initial magnetization \( M(0^+) \) that is aligned with the axis \( \hat{n} \). At the nominal echo time of the \( k \)th echo, \( t_e = kT_2 \), this component is therefore invariant under the multiple application of the rotation \( R \) and becomes independent of the echo number \( k \) except for relaxation. In contrast, the component of \( M(0^+) \) that is perpendicular to \( \hat{n} \) evolves from echo to echo. This component gives rise to the oscillating CP part of the signal. For a sample in inhomogeneous fields, the CP components from different spins quickly dephase from each other and do not contribute to the detected signal after only a few echoes. The overall signal for the CPMG sequence in inhomogeneous fields shows therefore an initial transient with contributions from both the CPMG and CP components before it enters the asymptotic regime controlled solely by the CPMG component. In this asymptotic regime, the spectrum of the echo is given by the simple expression [15]:

\[
S_{asiy}(\omega_0, \omega_1) = \langle \hat{n} \cdot \hat{M}(0^+) \rangle \hat{n}.
\]

All the quantities on the right hand side depend on \( \omega_0 \) and \( \omega_1 \). Here \( \hat{n} = n_x + i n_y \) is the component of \( \hat{n} \) that is transverse to the applied magnetic field. In the time domain, the shape of the echo in the asymptotic limit is then given by

\[
S_{ain}(t) = \int d\omega_0 d\omega_1 f(\omega_0, \omega_1) e^{i\omega_0 t} \langle \hat{n} \cdot \hat{M}(0^+) \rangle \hat{n}.
\]

where \( f(\omega_0, \omega_1) \) describes the distribution of \( \omega_0 \) and \( \omega_1 \) over the sample.

In the practical implementation of the CPMG measurement, it is common practice to incorporate phase cycling of the initial excitation pulse. In its simplest implementation, the signals of two sets of CPMG measurements are subtracted from each other, where in the second measurement the phase of the excitation pulse is increased by \( \pi \). This procedure eliminates various detrimental effects that can interfere with the experiment, including pulse ringing from the refocusing pulses, dc offsets in the acquisition electronics, or contributions from undesired coherence pathways that originate from \( T_1 \) recovery during the train of the refocusing cycles. Standard phase cycling inverts the transverse component of \( M(0^+) \), while leaving the longitudinal component unaffected. The resulting signal after phase cycling can be written as:

\[
S_{asin}^{(DC)}(t) = \int d\omega_0 d\omega_1 f(\omega_0, \omega_1) e^{i\omega_0 t} \langle \hat{n}_L \cdot \hat{M}(0^+) \rangle \hat{n}_L.
\]
determine \( n \). An ideal excitation pulse generates \( M(0^+) = \hat{x} \) and ideal refocusing pulses generate \( n = \hat{x} \) over the whole range of offset frequencies \( \omega_n \). Various composite and shaped pulses [20,21,24,30,31,27] have been developed for the replacement of the standard 90° excitation and 180° refocusing pulses with the goal to increase the range of \( \omega_n \) over which a sizeable CPMG signal can be generated beyond the default range of \( 2\omega_0 \).

In general, there is a trade-off between the robustness with respect to offset frequency and the overall duration of the pulse. Here we focus on the limit of very short refocusing pulses, including the SPA refocusing pulse [27] mentioned earlier. This refocusing pulse of duration \( t_{180} \) was found to optimize the SNR in inhomogeneous fields. For even shorter refocusing pulses, phase modulation does not improve the performance and simple rectangular pulses were found to be the optimal solution [27].

2.1. Axis matching excitation pulse

In previous work, the initial excitation pulses were optimized for broadband performance, with the goal to transform the initial longitudinal magnetization \( \hat{z} \) into transverse magnetization \( \hat{x} \) over the widest possible range of offset frequencies \( \omega_n \), i.e. \( z = \hat{x} \). According to Eq. 4, this is the optimal choice for CPMG sequences with phase cycling as it optimizes \( (n_x \cdot M_i(0^+)) - n_z \).

However, inspection of the more general expression for the case without phase cycling in Eq. 3 shows that the asymptotic echo can be increased if the excitation pulse generates magnetization pointing in the direction of \( \hat{n} \). We call such excitation pulses that transform \( z \rightarrow \hat{n} \) ‘axis-matching excitation pulses’ (AMEX). AMEX pulses maximize \( (\hat{n} \cdot M(0^+)) \rightarrow 1 \) and generate asymptotic echoes proportional to \( n_z(\omega_n) \). Given that \( |\hat{n}_z| < 1 \), an ideal AMEX pulses will therefore generate a larger CPMG signal than a perfect 90° pulse. AMEX pulses take the imperfections of the refocusing pulses into account and compensate partially for its limitations.

The benefit of AMEX pulses is particularly significant for short refocusing pulses. Short refocusing pulses are generally less perfect refocusing pulses and \( \hat{n} \) can have sizeable longitudinal components, \( \hat{n}_z \). This is illustrated in Fig. 1 where the behavior of \( \hat{n} \) for four short refocusing pulses is displayed. The axis for the SPA pulse has large longitudinal components even close to resonance. But the benefit of AMEX pulses is not limited to the case of composite or shaped refocusing pulses (such as the SPA pulses). The approach also improves the performance of the CPMG sequence using simple rectangular refocusing pulses.

2.2. Generalized phase cycling for AMEX pulses

Before we identify practical AMEX pulses, we have to address the issue of phase cycling. Phase cycling is a standard ingredient in the practical implementation of the CPMG sequence with important benefits. It allows the selection of the desired coherence pathways: only magnetization that is tipped by the initial excitation pulse contributes to the measured echoes. Steady-state type contributions created by \( T_1 \) recovery during the sequence are filtered out. In addition, phase cycling makes the signal independent of voltage offsets that might exist in the acquisition electronics and it also eliminates effects due to pulse ringing from the refocusing pulses.

In standard phase cycling, only the transverse component of \( M(0^+) \) is inverted by the π phase shift. As a consequence it is only this component that contributes to the net signal. AMEX pulses deliberately create transverse and longitudinal magnetizations and it is essential to retain both components. A generalized phase cycling of AMEX pulses therefore requires a method to invert both the transverse and longitudinal components of \( M(0^+) \). In the general case, this requires two matched AMEX excitation pulses that transform \( \hat{z} \) magnetization onto \( \hat{n} \) and \( -\hat{n} \) respectively. For the special cases of refocusing pulses considered here, there is a simple approach to achieve this based on phase inversion of the AMEX pulse.

We first note that the refocusing pulses under consideration all have a simple symmetry. They are either single rectangular pulses of the form \( \theta_n \) or a symmetric phase alternating pulse of the form \( \theta_n(\theta_n^{i1}) \). It is straightforward to show that the effective axis of the refocusing cycle with such pulses has the following symmetries [34]:

\[
\begin{align*}
\hat{n}_x(-\omega_0, \omega_1) &= +n_z(\omega_0, \omega_1) \\
\hat{n}_y(-\omega_0, \omega_1) &= \pm n_z(\omega_0, \omega_1) = 0 \\
\hat{n}_z(-\omega_0, \omega_1) &= -n_z(\omega_0, \omega_1)
\end{align*}
\]

These symmetry properties are independent of the duration of the free precession intervals that proceed and follow the rf pulses as long as they are of equal length.

As a second ingredient of our approach, we take advantage of the general relationship between the propagator of a sequence of a set of rf pulses \( \{\theta_n, \theta_n^{i2}, \ldots, \theta_n^{iN}\} \) and that of the set with inverted phases, \( \{\theta_n, \theta_n^{i2}, \ldots, \theta_n^{iN}\} \). Following the analysis of Levitt [18], the propagator of a phase-inverted pulse at an offset frequency \( \omega_0 \), \( U^c(\omega_0) \), is related to the propagator of the original pulse at the offset frequency \( -\omega_0 \), \( U(\omega_0) \), by:

\[
U^c(\omega_0) = \exp(-\text{i} \omega_0 T_{2\text{arg}}(\hat{n}_z)) U(\omega_0) \exp(\text{i} \omega_0 T_{2\text{arg}}(\hat{n}_z)).
\]

This implies that the resulting magnetization of a set of rf pulses that is phase-inverted and is applied to an initial \( \hat{z} \) magnetization, \( M_0(\hat{z}) \), is related to the magnetization of the original set of rf pulses, \( M(\hat{z}) \), by:

\[
\begin{align*}
M_0(\hat{z})(\omega_0, \omega_1) &= -M(\hat{z})(-\omega_0, \omega_1) \\
M_0(\hat{z})(\omega_0, \omega_1) &= +M(\hat{z})(-\omega_0, \omega_1) \\
M_0(\hat{z})(\omega_0, \omega_1) &= +M(\hat{z})(-\omega_0, \omega_1)
\end{align*}
\]

Given the symmetries of Eqs. (5)–(10), the net signal \( \tilde{S}_{\text{net}} \) that results from the generalized phase cycling, i.e. the signal difference of the sequence run with the initial excitation pulse and that with the phase inverted excitation pulse, can be written as:

\[
\begin{align*}
2\tilde{S}_{\text{net}}(\omega_0, \omega_1) &= \left[ M(\hat{z}) \cdot \hat{n} - M_0(\hat{z}) \cdot \hat{n} \right] \\
&= \left[ (M_x(\hat{z}) + M_y(\hat{z}) + M_z(\hat{z})) n_z(\omega_0, \omega_1) \right] \\
&= S_{\text{net}}(\omega_0, \omega_1) + S_{\text{net}}(-\omega_0, \omega_1).
\end{align*}
\]
after the general phase cycling is predicted to show the exact symmetry. Given that $n_x = 0$, this implies that both in the frequency and time domain, the asymptotic echo in a gradient field is symmetric and has only in-phase components. The analysis above was based on the assumption that the refocusing pulses act along the $x$ direction. For refocusing pulses along the $y$ direction, the phase of the initial AMEX pulse has to be inverted, followed by a shift of $\pi$.

3. Search algorithm

To find suitable AMEX pulses, we take advantage of recent progress in optimal control methods and the development of powerful algorithms for NMR applications [33]. We began our search for AMEX pulses by using the GRAPE algorithm [32] to design an excitation pulse with 100 segments, each of length $0.1 \times t_{180}$, for the SPA refocusing pulse and an echo spacing $t_{E} = 7t_{180}$. The pulse segments were allowed to have variable amplitudes between 0 and $\omega_{1,\text{max}} = \pi/t_{180}$ and arbitrary phases. In the simulation, this pulse, which we refer to as AMEX$_{\text{SPA,0}}$, produced an asymptotic SNR that was 2.05 times larger than the standard CPMG sequence. We then discovered that the performance of this pulse was still fairly good (approximately 25% reduction in SNR) when the amplitude modulation was completely removed, i.e., the segment amplitudes were kept constant at $\omega_{1,\text{max}}$. We therefore decided to reduce the number of optimization variables by a factor of 2 by limiting ourselves to constant amplitude (purely phase modulated) pulses. Furthermore, we decided to use the phases of the AMEX$_{\text{SPA,0}}$ pulse as initial conditions for further pulse optimization. This strategy proved to be far more successful than repeatedly searching the entire optimization space with random initial conditions.

We used fmincon, Matlab’s constrained nonlinear minimization function, for further pulse optimization. Other optimization techniques were also tried, such as genetic algorithms and particle swarms. However, they proved to be significantly inferior to fmincon in terms of optimization speed and ability to find good solutions. The fmincon function is a gradient-based method that is designed for problems where both the objective and constraint functions are smooth, i.e., continuous with continuous first derivatives. As a result, their second-order derivatives (Hessians) are always defined. The fmincon function can use one of several optimization methods. We used either the active-set or interior-point method – there were no significant performance differences between them.

We minimized the following cost function, which is a weighted sum of the root-mean square (RMS) and integral of the asymptotic echo $S_{\text{asy}}(\omega_0)$:

$$
C = -\left[\sqrt{\int S_{\text{asy}}(\omega_0)^2 d\omega_0} + \lambda \int S_{\text{asy}}(\omega_0) d\omega_0\right].
$$

(12)

Here $\lambda$ is a real number that controls the strength of the second term in the cost function, and $S_{\text{asy}}(\omega_0)$ is purely real because $n_y = 0$ for SPA refocusing pulses. The first term in the cost function is proportional to the asymptotic SNR in voltage units. The second term is proportional to $S_{\text{asy}}(t = 0)$, the amplitude at the nominal center ($t = 0$) of the time-domain echo. This is because Fourier analysis shows that $S_{\text{asy}}(t = 0) = \int S_{\text{asy}}(\omega_0) d\omega_0$. This term biases the search towards symmetric time domain echo shapes that peak at $t = 0$, which are desirable for applying the generalized phase cycling procedure described in Section 2.2. In addition, we have found that this...
term also allows the optimizer to find better (higher SNR) solutions. We generally use $\dot{z} = 0.33$, which results in roughly equal weights being assigned to the two terms in the cost function. Finally, we assumed an acquisition window length of $T_{acq} = 4 \times t_{180}$ in all our simulations.

We found that the optimization landscape for our problem was highly non-convex, with many local minima, so initial conditions had to be chosen carefully. Using our procedure to optimize the phases of the AMEXSPA pulse produced a modified list of phases, which we refer to as the AMEXSPA$_{1}$ pulse. This pulse produces 2.74 times larger asymptotic SNR than the standard CPMG sequence, which is significantly larger than the original AMEXSPA$_{0}$ pulse.

We then searched for other excitation pulses that had different numbers of pulse segments, or different lengths for each segment. We began this search by perturbing the original optimized pulse by a small amount in the direction of the desired change. For example, if the goal was a pulse with fewer pulse segments, we dropped the last segment of the current pulse. This process produced a slightly sub-optimal list of phases, which were then re-optimized using the same algorithm. By repeating this process we were able to find a series of optimal pulses that gradually progressed towards the overall design goal. The gradual nature of this pulse modification process ensured that each perturbed solution remained a relatively good solution, i.e., near-optimal. This procedure prevented the optimizer from getting stuck in highly sub-optimal local minima, which is common in such high-dimensional search spaces with poor initial conditions.

We used a similar procedure to find excitation pulses matched to other refocusing pulses, such as rectangular pulses of different lengths. We began with the AMEXSPA$_{1}$ pulse, which is matched to the SPA refocusing pulse, and modified the latter by slightly shortening the lengths of its first and third segments (by 0.01 × $t_{180}$). We then re-optimized the excitation pulse for this modified SPA pulse. We repeated this process several times, allowing us to consistently find good excitation pulses while gradually converting the original SPA pulse into a rectangular 126$s_{x}$ pulse. It was then continued while gradually changing the length of the 126$s_{x}$ rectangular pulse, allowing us to find a series of excitation pulses matched to rectangular refocusing pulses of different flip angles.

### 4. Results: performance of CPMG sequence with AMEX pulses

Using the optimal control methods described in the previous section, we derived practical AMEX pulses for four different refocusing pulses, namely the rectangular pulses 124$s_{x}$, 135$s_{x}$, 180$s_{x}$, and the SPA pulse 27°.126$s_{x}$.27°. All optimized for $t_{E} = 7t_{180}$. Here we denote the rectangular pulses by their nutation angle on resonance. The 124$s_{x}$ refocusing pulse produced the highest SNR of all rectangular pulses with on-resonance nutation angles between 90° and 180°. The AMEX pulses were designed to be purely phase modulated with a fixed pulse amplitude of $\alpha_{1} = \pi/t_{180}$. Within the phase, the pulse was kept piecewise constant during intervals of 0.078$t_{180}$. This limits the maximum excitation bandwidth to approximately $\pm \alpha_{1} \times 0.078 = \pm 1.28 \alpha_{1}$. The main properties of these pulses are listed in Table 1. We list 6 different AMEX pulses for the SPA refocusing pulses. They were optimized for the same target function, but they have slightly different durations. The detailed description of the AMEX pulses of Table 1 is included in the Supplementary material.

The overall durations of the AMEX pulses listed in Table 1 are in the range of 8.6$t_{180}$ to 15.8$t_{180}$, which corresponds to 1.2$t_{E}$ to 2$t_{E}$. We were not able to find efficient AMEX pulses that were much shorter. This can be understood based on the properties of $\dot{n}$. The Table 1

<table>
<thead>
<tr>
<th>Excitation pulse</th>
<th>Refocusing pulses</th>
<th>AMEX pulse length</th>
<th>Relative SNR</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMEX$_{24}$</td>
<td>124$s_{x}$</td>
<td>8.580</td>
<td>1.77</td>
</tr>
<tr>
<td>AMEX$_{15}$</td>
<td>135$s_{x}$</td>
<td>8.580</td>
<td>1.75</td>
</tr>
<tr>
<td>AMEX$_{80}$</td>
<td>180$s_{x}$</td>
<td>8.580</td>
<td>1.59</td>
</tr>
<tr>
<td>AMEX$_{SPA,1}$</td>
<td>27°.126$s_{x}$.27°.</td>
<td>12.636</td>
<td>3.17</td>
</tr>
<tr>
<td>AMEX$_{SPA,2}$</td>
<td>27°.126$s_{x}$.27°.</td>
<td>15.756</td>
<td>3.16</td>
</tr>
<tr>
<td>AMEX$_{SPA,0}$</td>
<td>27°.126$s_{x}$.27°.</td>
<td>12.168</td>
<td>3.05</td>
</tr>
<tr>
<td>AMEX$_{SPA,1}$</td>
<td>27°.126$s_{x}$.27°.</td>
<td>11.232</td>
<td>3.01</td>
</tr>
<tr>
<td>AMEX$_{SPA,2}$</td>
<td>27°.126$s_{x}$.27°.</td>
<td>10.296</td>
<td>2.90</td>
</tr>
<tr>
<td>AMEX$_{SPA,0}$</td>
<td>27°.126$s_{x}$.27°.</td>
<td>8.580</td>
<td>2.81</td>
</tr>
</tbody>
</table>

The last column of Table 1 compares the calculated SNR of the asymptotic echoes for the CPMG sequence based on these AMEX pulses and the corresponding refocusing pulses, relative to that obtained with the standard CPMG sequence 90° – (180°)$^n$. For this analysis, we assume a constant gradient field and a uniform rf field. Following [27], the ratio of signal power to noise power (SNR) with matched filtering is given by:

$$\text{SNR} = \frac{\int d\mathbf{S}_{z}(t)_{27}^2}{N_{0}^2}.$$

where

$$t_{E} \approx 2k \frac{t_{F}}{t_{E}} \sqrt{1 - \frac{1}{4k^2 t_{F}^2}},$$

where $k = 1, 2, \ldots$. The high frequency modulation in $\dot{n}$ is controlled by $t_{E}$. The modulation frequency is approximately given by $\Delta \omega_{B} = 2n/2t_{E}$ for the transverse component $n_{t}$ and $\Delta \omega_{B} = 4n/2t_{E}$ for the longitudinal component $n_{l}$. The presence of this high frequency modulation explains why the durations of all the AMEX pulses in Table 1 are at least of the order of $t_{E}$. Shorter pulses cannot generate magnetization that follows adequately the rapid modulations of $\dot{n}$ with respect to $\omega_{B}$.

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$$\text{SNR} = \frac{\int d\mathbf{S}_{z}(t)_{27}^2}{N_{0}^2}.$$
the expression for the asymptotic signal in Eq. 11 and includes the effects of the generalized phase cycling. This quantity is generally close to 1 over a wide range of frequencies, but drops sharply at a set of distinct frequencies. These dips occur at the frequencies given in Eq. 13 where the refocusing pulses become ineffective and \( \vec{n} \) points in the longitudinal direction. At these frequencies, it is impossible to create any detectable asymptotic signal with these refocusing pulses, independent of the excitation pulse, and the direction of the initial magnetization is therefore irrelevant for the overall performance. Away from these special frequencies, the projection of the initial magnetization onto the effective axis is close to the ideal value of 1, especially in the vicinity of resonance. As the offset frequency increases, it drops off somewhat. This behavior could be further improved with AMEX pulses that use finer time steps than used in the present work (i.e. \( \Delta t < 0.078 t_{180} \)).

The spectra of the asymptotic echoes generated by the AMEX pulses combined with the corresponding refocusing pulses are shown in Fig. 3. They correspond to the convolution of \( S_{\text{asy}} \), given in the expressions (2) and (11), with the Fourier transform of the acquisition windows, assumed to be \( \pm 2 t_{180} \) around the nominal echo centers. Even though these relatively short AMEX pulses are not perfect, they generate asymptotic echoes that exceed the theoretical limit obtainable with perfect \( z \rightarrow x \) excitation pulses over much of the frequency range of \( \pm 10 \omega_1 \).

The AMEX pulses presented here were all optimized for an echo spacing \( t_e = 7 t_{180} \). If the echo spacing is varied, the frequency modulation of \( \vec{n} \) changes (see Fig. 1) and the current AMEX pulses are not matched to the new axis anymore. It is therefore essential to design the AMEX pulse for this particular value of \( t_e \). This effect is illustrated in Fig. 4. The calculated SNR of the asymptotic echo for the sequence AMEXSPA \( A \) shows a sharp maximum at \( t_e = 7 t_{180} \). When the echo spacing is varied by a small fraction of the pulse duration, \( t_{180} \), the SNR rapidly drops by about a factor of 2. This behavior using a sequence with an AMEX pulse is contrasted in Fig. 4 with the behavior using a broadband excitation pulse. In this case, the SNR is essentially independent of the echo spacing.

5. Experimental results

We have experimentally verified the performance of the new pulse sequences. We used a Bruker Avance-II spectrometer and a superconducting magnet (Oxford) operating at the proton frequency of 42.57 MHz. The spectrometer was equipped with an RF amplifier that can deliver 1 kW, and gradient amplifiers that can supply a maximum of 200 A. The sample was placed inside a cylindrical NMR tube with diameter of 5 mm and length of 15 cm, or a larger tube with diameter of 10 mm and length of 23 cm. The tube was centered within an imaging probe with inner diameter of 12 cm, with its long axis along the static field, i.e., parallel to the bore of the magnet. We can then create a uniform distribution of resonant offset frequencies within the sample by activating the z-gradient coil. The gradient coils can generate a maximum gradient strength of 40 G/cm, but we used a much smaller static gradient of \( g = 1 \) G/cm for most of our experiments. This minimizes diffusion effects. In addition, to probe the shapes of
orders of magnitudes larger than $\omega_1/(2\pi)$, and therefore not a limiting factor.

### 5.1. Echo shapes

We tested experimentally the performance of the new AMEX pulses listed in Table 2 on an extended sample of water in a constant-gradient field. We acquired the detailed shapes of 128 echoes, using an echo spacing $t_e = 7T_{180} = 3.5$ ms and incorporating the generalized phase cycling scheme based on phase inversion of the AMEX pulses. After the first few echoes, it was observed that the echo shapes quickly approached an asymptotic form for each sequence. The shapes of the first few echo differed slightly from those of the latter echoes. Fig. 5 displays the measured shapes of the first echo (left column) and the asymptotic echo (right column) for all the pulse sequences. The asymptotic echo shapes were obtained by averaging the shapes of the 50th to 128th echo and corrected for relaxation, using the measured relaxation time $T_2 = 1.99 \pm 0.06$ s. The top row shows the results for the standard CPMG sequence as a reference. All echo shapes were normalized with respect to the peak of the asymptotic echo for the standard CPMG sequence.

The results in Fig. 5 not only confirm the premise that AMEX pulses significantly increase the signal strengths of the generated echoes, but they also support the details of the underlying theory. The observed agreement between theory and experiment is excellent. The results demonstrate that sequences incorporating an AMEX pulse matched to the SPA refocusing pulses are able to generate echoes with a peak amplitude more than 4 times as large as those obtained with the standard CPMG sequence. Even with standard 180° refocusing pulses, the data shows that a well matched excitation pulse can more than double the echo peak compared to that generated with a standard 90° excitation pulse.

As predicted, the asymptotic echoes are in all cases symmetric in time and have only in-phase contributions. In contrast, the first echoes are slightly asymmetric with respect to time. This asymmetry is most noticeable at the edges of the acquisition window. It is caused by the contributions from the CP components that have not fully averaged out at the first echo.

### 5.2. Echo amplitudes and ratio of signal power to noise power

For a quantitative comparison of the resulting SNR, we extracted an amplitude from each echo using the asymptotic echo shape as a matched filter. Assuming that the noise is characterized by white, uncorrelated noise, this is the optimal procedure to process the data. The echo amplitude of the kth echo, $A_k$, was obtained from the measured magnetization $s_i(t)$ by integrating over the acquisition window using the filter $F(t) : A_k = \int_{T_{180}/2}^{T_{180}/2} d t F(t) s_i(t)$, where the filter was constructed from the asymptotic echo shape for the specific sequence: $F(t) = s_{asy}(t)/(\int_{T_{180}/2}^{T_{180}/2} d t ||s_{asy}(t)||^2)^{1/2}$. The resulting echo amplitudes for all sequences are shown in Fig. 6.

### Table 2

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Amplitude $A_0$</th>
<th>SNR (power)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Experiment</td>
<td>Theory</td>
</tr>
<tr>
<td>$90° - (180°)\alpha$</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>AMEX$_{124}$ - $(124)\alpha$</td>
<td>1.37</td>
<td>1.33</td>
</tr>
<tr>
<td>AMEX$_{135}$ - $(135)\alpha$</td>
<td>1.36</td>
<td>1.32</td>
</tr>
<tr>
<td>AMEX$_{180}$ - $(180)\alpha$</td>
<td>1.27</td>
<td>1.26</td>
</tr>
<tr>
<td>AMEX$_{SPA,A}$ - $(SPA)\alpha$</td>
<td>1.88</td>
<td>1.78</td>
</tr>
<tr>
<td>AMEX$_{SPA,C}$ - $(SPA)\alpha$</td>
<td>1.85</td>
<td>1.75</td>
</tr>
<tr>
<td>AMEX$_{SPA,L}$ - $(SPA)\alpha$</td>
<td>1.84</td>
<td>1.73</td>
</tr>
<tr>
<td>AMEX$_{SPA,R}$ - $(SPA)\alpha$</td>
<td>1.81</td>
<td>1.70</td>
</tr>
<tr>
<td>AMEX$_{SPA,F}$ - $(SPA)\alpha$</td>
<td>1.79</td>
<td>1.68</td>
</tr>
</tbody>
</table>
After the first few echoes, the echo amplitudes enter the asymptotic regime where they follow an exponential decay $A_{i}^{\text{asy}} = A_{0} \exp(-k \tau / T_{2})$ with a decay time of $T_{2} = 1.99 \pm 0.06$ s. For each sequence, the value of $A_{0}$, i.e. its amplitude extrapolated to $t = 0$, is marked by a red + sign. All amplitudes were normalized with respect to $A_{0}$ of the standard CPMG sequence. The values of $A_{0}$ for each sequence are listed in Table 2. We also list the square of $A_{0}$ which corresponds to the ratio of signal power to noise power (SNR) in the asymptotic regime, normalized by the SNR of the standard CPMG sequence. The theoretical predictions are given in the adjacent columns. The observed enhancements of SNR in the experimental results follow the predictions. In several cases, the experimental values are even slightly higher than the theoretical predictions. This is likely caused by inhomogeneities in the $B_{1}$ field and resulting difficulties in $B_{1}$ calibration that have a larger effect on the standard CPMG sequence than the new sequences.

The enhancements of the SNR with CPMG sequences based on AMEX pulses, listed in Table 2, are particularly significant when they are combined with SPA refocusing pulses. They are larger than those reported previously for sequences consisting of broadband excitation pulses and SPA refocusing pulses [27]. As a comparison, we reported in [27] enhancements in SNR with broadband excitation pulses [34,27,36] and SPA refocusing pulses of 1.52, using fixed pulse amplitudes. Even when the amplitude of the excitation pulse was allowed to increase 10-fold (resulting in a 100-fold increase in instantaneous RF power), the observed enhancement was only 2.14.

Even for CPMG sequences with standard rectangular refocusing pulses, the implementation of AMEX pulses can improve the performance significantly. When standard 180° refocusing pulses are used, replacing the standard 90° excitation pulse with an AMEX pulse results in a 60% enhancement in SNR. In contrast, a perfect broadband excitation pulse will improve the SNR by 1.27 in this case [27]. The enhancement is even larger when AMEX pulses are used with shorter rectangular refocusing pulses. We observed increases of about 86% with 124° and 135° refocusing pulses.

5.3. Transient

Analogous to the standard CPMG sequence, the modified CPMG sequences show a characteristic transient effect in the first few echoes.
echoes [14,15]. As discussed above, this is caused by imperfections of the AMEX pulses and the resulting presence of CP components in the initial magnetization \( M(0^+) \). These components are not invariant under the refocusing cycle and lead to an oscillating contribution in the echo amplitudes. In inhomogeneous fields, they average out quickly with increasing echo number and are therefore only noticeable at the first few echoes. An ideal AMEX pulse generates only the CPMG component, i.e. initial magnetization that is exactly co-linear with the axis of the effective rotation, \( \hat{n} \). In this ideal case, no transient occurs and the shapes of all echoes are identical. The presence of the transient is an indication that the current AMEX pulses are imperfect.

The transients for the current pulse sequences are more clearly seen in Fig. 7. It shows the deviations from the asymptotic behavior, i.e. the ratio of the measured echo amplitude to the exponential decay \( A_k/A_{(asy)}^k = A_k/(A_0 \exp (-kt/T_2)) \). In all cases, CPMG sequences with AMEX pulses display smaller transients compared to the standard CPMG sequence, as expected. In the case of rectangular refocusing pulses, the transient extends over four echo cycles, whereas for the SPA refocusing pulses, the transient is typically confined to the first two echoes. The AMEX_{SPA,B} pulse generates the smallest transient of all pulses studied.

6. Conclusion

We have shown that AMEX pulses greatly improve the performance of the CPMG sequence in inhomogeneous fields and lead to significantly larger echo amplitudes and a reduced transient. The AMEX pulses are designed to transform the magnetization, initially pointing in the longitudinal direction, to a direction pointing along the axis of the refocusing cycle. This can be considered to be the generalized CPMG condition. At any offset frequency, magnetization pointing along this axis is fully refocused and the resulting echo amplitudes decay with the intrinsic relaxation times. For a given refocusing pulse in a CPMG sequence, the use of the AMEX
pulse thus maximizes the resulting amplitudes of the echoes in the asymmetric regime and minimizes the CP component that gives rise to the transient in the initial echo amplitudes.

In this paper, we focused on applications of AMEX pulses with short refocusing pulses and in the presence of grossly inhomogeneous $B_0$ fields, i.e. where the range of offset frequencies is larger than the strength of the rf field. We have described AMEX pulses optimized for a constant distribution of resonant frequency offsets (constant static field gradient), and constant $\omega_0$. The same optimization procedure can be used to derive pulses optimized for more general $(\omega_0, \omega_r)$ distributions. The AMEX based approach is rather general and beneficial for other applications. This includes applications in more homogeneous fields and in cases where $B_1$ inhomogeneities are important [37]. Any CP component gives rise to an oscillating component in the echo amplitudes. In moderately homogeneous fields, these oscillations can extend over many echoes and complicate and often bias the extraction of relaxation times [38,39]. This is particularly important for short relaxation times. Since AMEX pulses minimize the CP components, they mitigate this problem.

There are a number of specific properties of AMEX pulses that distinguish them from standard broadband excitation pulses. AMEX pulses have to be designed for the specific refocusing cycle and depend on the details of the refocusing pulse and the echo spacing used in the experiments. Furthermore, the standard phase cycling of the excitation pulse cannot be used as this procedure effectively eliminates the critical longitudinal components of the magnetization generated by the excitation pulse. Instead, it is necessary to use a phase cycling scheme that inverts both the transverse and longitudinal components of the AMEX generated magnetization. For the simple refocusing pulses studied here that consist of phase-alternating pulses, we show that this can be achieved by simple phase inversion of the AMEX pulse. This scheme retains all the standard benefits of regular phase cycling and in addition, it symmetrizes the response with respect to the offset frequency.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jmr.2013.09.004.

References

[5] C.A. Ryan, J.S. Hodges, D.G. Cory, Robust decoupling techniques to extend coherence times in more homogeneous fields and in cases where $B_1$ inhomogeneities are important [37]. Any CP component gives rise to an oscillating component in the echo amplitudes. In moderately homogeneous fields, these oscillations can extend over many echoes and complicate and often bias the extraction of relaxation times [38,39]. This is particularly important for short relaxation times. Since AMEX pulses minimize the CP components, they mitigate this problem.

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