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Background gradient suppression in stimulated echo NMR diffusion studies using magic pulsed field gradient ratios

Petrik Galvosas,[1] Frank Stallmach,* and Jörg Kärger

Institut für Experimentelle Physik I, Fakultät für Physik und Geowissenschaften, Universität Leipzig Linnestrasse 5, 04105 Leipzig, Germany

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Abstract

By evaluating the spin echo attenuation for a generalized 13-interval PFG NMR sequence consisting of pulsed field gradients with four different effective intensities ($F^{p/r}$ and $G^{p/r}$), magic pulsed field gradient (MPFG) ratios for the prepare (G^p/F^p) and the read (G^r/F^r) interval are derived, which suppress the cross term between background field gradients and the pulsed field gradients even in the cases where the background field gradients may change during the *z*-store interval of the pulse sequence. These MPFG ratios depend only on the timing of the pulsed gradients in the pulse sequence and allow a convenient experimental approach to background gradient suppression in NMR diffusion studies with heterogeneous systems, where the local properties of the (internal) background gradients are often unknown. If the pulsed field gradients are centered in the τ-intervals between the π and $\pi/2$ rf pulses, these two MPFG ratios coincide to $\eta = G^{p/r}/F^{p/r} = 1 - 8/[1 + (1/3)(\delta/\tau)^2]$. Since the width of the pulsed field gradients (δ) is bounded by $0 \leqslant \delta \leqslant \tau$, η can only be in the range of $5 \leqslant -\eta \leqslant 7$. The predicted suppression of the unwanted cross terms is demonstrated experimentally using time-dependent external gradients which are controlled in the NMR experiment as well as spatially dependent internal background gradients generated by the magnetic properties of the sample itself. The theoretical and experimental results confirm and extend the approach of Sun et al. (J. Magn. Reson. 161 (2003) 168), who recently introduced a 13-interval type PFG NMR sequence with two asymmetric pulsed magnetic field gradients suitable to suppress unwanted cross terms with spatially dependent background field gradients.

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1. Introduction

Pulsed magnetic field gradient (PFG) NMR experiments are a very powerful tool for the investigation of molecular transport phenomena such as for example self-diffusion processes. The technique, which was introduced by Stejskal and Tanner [1], superimposes pairs of time-dependent inhomogeneous magnetic fields (the so-called pulsed field gradients) on to the static magnetic field B_0 of conventional NMR to encode and read the positions of the nuclear spins of the sample under investigation. Additional gradients of the magnetic field B_0 may originate from inhomogeneities of the magnet used or they are generated inside the sample due to internal susceptibility differences in heterogeneous materials (e.g., porous media). Diffusion measurements by PFG NMR may be disturbed by the interference of these background field gradients with the pulsed field gradients [2,3]. Experimentally, this interference may be reduced by applying alternating pulsed field gradients (APFG) in conjunction with π rf pulses. Karlicek and Lowe [2] introduced such an APFG sequence for the Hahn echo (CPMG) experiment and Cotts et al. [3] suggested extended versions of the stimulated echo sequence, the so called 9-, 13-, and 17-interval sequences. It has been shown theoretically that the unwanted cross

* Corresponding author. Fax: +49-341-9732549.
E-mail address: stallmac@physik.uni-leipzig.de (F. Stallmach).
[1] Present address: School of Chemical and Physical Sciences, Victoria University of Wellington, PO Box 600, Wellington, New Zealand.

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terms between the pulsed and the additional background field gradients in the spin echo attenuation, which—if not taken into account in the data analysis—are responsible for an erroneous determination of diffusion coefficients, are only canceled by the use of these APFG NMR sequences if the diffusing spins experience the same background field gradient in the prepare (encode) and read interval of the sequence.

Strictly speaking, this condition can only be fulfilled by a constant background gradient acting over the whole sample volume. However, many successful applications of the APFG NMR sequences for diffusion studies in heterogeneous (porous) systems show that the disturbing influences of space dependent internal background gradients, as generated by, e.g., internal susceptibility differences, are also reduced. This means that the above condition must be fulfilled on the length scale of the observed diffusion process, i.e., the diffusion length must be small compared to the length scale of internal susceptibility changes in the sample. In all other cases, i.e., if the diffusion length is comparable to or even larger than the length scale of susceptibility changes there is common belief that APFG sequences may still yield correct diffusivities, but due to inherent difficulties—no comprehensive theoretical treatment of such cases exist in the literature to date. Seland et al. [4] approached this problem by the simplified assumption that a disturbing constant background field gradient changes its sign for all spins due to diffusion during the time interval between the prepare and the read pulsed field gradients. In fact, the authors found a reintroduction of the cross term into the spin echo attenuation of their APFG (13-interval) sequence. As a consequence, in a previous paper [5] we showed theoretically and experimentally that the conventional stimulated spin echo PFG NMR experiment combined with a variation of the duration of the prepare interval (τ) is a suitable approach to measure true diffusivities in heterogeneous samples with unknown internal background field gradients.

By placing the pulsed gradients symmetrically about the π rf pulses, Sun et al. [6] modified the original 13-interval sequence [3] and showed that unwanted cross terms with spatially dependent background gradients are suppressed if the two pulsed gradients in the prepare and read interval are asymmetric with a fixed intensity ratio, which depends only on the time intervals in the pulse sequence. In contrast to Sørland et al. [7], who introduced asymmetric pulsed field gradients in order to remove unwanted coherences from the observed spin echo, and in contrast to the original 13-interval PFG NMR sequence, these asymmetric pulsed field gradients must be of equal polarity in the prepare and read interval, respectively.

With the present work, we extend this idea of Sun et al. [6] to the 13-interval PFG NMR sequence in which the pulsed field gradients are not symmetric to the π rf pulses, but have the same distance from the preceding rf pulse. We will show that the suppression of the cross terms with spatially dependent background gradients requires different ratios of the pulsed field gradient intensities for the prepare and read intervals. We shall call these ratios magic pulsed field gradient (MPFG) ratios, since they depend only on the time intervals in the pulse sequence and—under well-chosen experimental conditions—are limited to values between −5 and −7 for the effective pulsed gradients. The disturbing influence of the cross terms between the pulsed and the background gradients on the self-diffusion coefficients obtained experimentally is demonstrated for standard APFG NMR sequences with equal intensities of the pulsed field gradients. The cancellation of these cross terms by using the magic pulsed field gradient ratios is shown in a series of model experiments where a spatially dependent background gradient is simulated by a change of an externally applied constant gradient between the prepare and read intervals of the pulse sequence. Further on, by means of this MPFG approach for the first time the unwanted cross terms are suppressed also in those cases where the spatially dependent background gradients are generated by the magnetic properties of the sample itself.

2. Theory

In general, the attenuation of an NMR spin echo caused by a diffusion process (neglecting all relaxation processes) can be calculated via [8]

$$M(t_e) = M_0 \exp\left\{ -D\gamma^2 \int_0^{t_e} \mathrm{d}t' \times \left[\int_0^{t'} \mathrm{d}t''[G^*(t'') + g^*(t'')] \right]^2 \right\}, \quad (1)$$

where $M(t_e)$ and M_0 are the amplitude at the echo time (t_e) and immediately after the first rf pulse, respectively. γ is the gyromagnetic ratio, D is the diffusion coefficient, and $G^*(t) + g^*(t)$ denotes the sum of all pulsed and constant effective magnetic field gradients, as introduced by [2], respectively. If not stated otherwise, in this paper all gradients are introduced in the sense of effective gradients. However, for the sake of simplicity we omit the asterisk (*) in the following. In the presence of pulsed magnetic field gradients and background gradients the result of the integration of Eq. (1) can always be written as

$$\ln\frac{M(t_e)}{M_0} = -D\gamma^2(A_p + A_c + A_b), \quad (2)$$

with

$$A_{\mathrm{p}} = \int_0^{t_{\mathrm{e}}} \mathrm{d}t' \left[\int_0^{t'} G(t'')\,\mathrm{d}t'' \right]^2, \tag{2a}$$

$$A_{\mathrm{c}} = 2\int_0^{t_{\mathrm{e}}} \mathrm{d}t' \int_0^{t'} G(t'')\,\mathrm{d}t'' \int_0^{t'} g(t'')\,\mathrm{d}t'', \tag{2b}$$

$$A_{\mathrm{b}} = \int_0^{t_{\mathrm{e}}} \mathrm{d}t' \left[\int_0^{t'} g(t'')\,\mathrm{d}t'' \right]^2, \tag{2c}$$

where $A_{\mathrm{p}}, A_{\mathrm{c}}$, and A_{b} are the parts of the attenuation caused by the pulsed gradients, the cross term, and the background gradients, respectively.

2.1. Spin echo attenuation for a generalized 13-interval sequence

The values of the integrals (Eq. (2)) will be calculated for the generalized 13-interval sequence drawn in Fig. 1. This sequence consists of four pulsed field gradients of intensities $F^{\mathrm{p}}, G^{\mathrm{p}}, F^{\mathrm{r}}$ and G^{r} which are placed in the τ intervals between the $\pi/2$ and π rf pulses in the prepare (superscript p) and read (superscript r) intervals, respectively. All pulsed gradients have a width of δ and start at a fixed time interval δ_1 after the preceding rf pulse. Together with the time interval Δ, which denotes the time in which the magnetization is stored in longitudinal direction and which, generally, accounts for the major part of the diffusion time in the stimulated spin echo PFG NMR sequences, the three intervals τ, δ, and δ_1 completely define the timing of the pulse sequence. The time interval δ_2 given in Fig. 1 depends on the setting of τ, δ, and δ_1 and is calculated by $\delta_2 = \tau - \delta - \delta_1$. In order to observe a spin echo with this pulse sequence, the four pulsed gradients are not independent of each other. They must obey the echo condition, i.e., their time integrals over the prepare and read interval must be equal. For the rectangularly shaped gradient pulses drawn in Fig. 1, this condition is simply written as

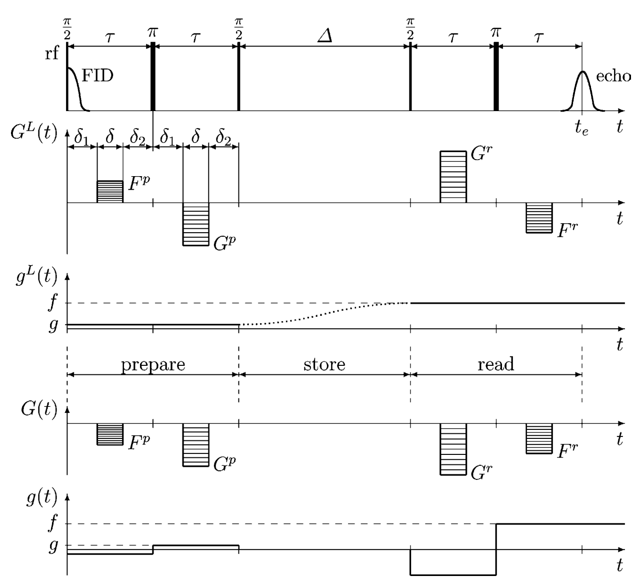

Fig. 1. Generalized 13-interval pulse sequence with four unequal pulsed field laboratory gradients with the intensities $F^{\mathrm{p,r}}$ and $G^{\mathrm{p,r}}$, respectively, starting at the time δ_1 after the preceding rf pulses and with two different background laboratory gradients with the amplitude g and f during the prepare and read interval. The lower part of the figure shows the same pulse sequence in terms of the effective gradients. *Note.* The polarities of the background gradients are arbitrary. The drawn situation is just one of four possibilities.

$$F^{\mathrm{p}} + G^{\mathrm{p}} = F^{\mathrm{r}} + G^{\mathrm{r}}. \tag{3}$$

Background field gradients can only affect the NMR signal during the τ intervals of the prepare and read periods. In order to explore the influence of a spatially dependent background gradient, which the molecules might experience due to diffusion in an internal inhomogeneous magnetic field of a heterogenous sample, different but constant intensities of the background gradient are assumed to act during the read (f) and prepare (g) intervals, respectively. Such an approach to treat the influence of a spatially dependent background gradient is an approximation which is justified if $\Delta \gg \tau$ in the pulse sequence and the mean diffusion path $\sqrt{2\tau D}$ is small compared to the length scale of significant changes of the internal background gradient.

Without any additional assumptions on the intensities and polarities of $F^{\mathrm{p,r}}$, $G^{\mathrm{p,r}}$, f or g, the evaluation of Eq. (2) is straightforward. Under the condition that the sign pattern of the effective pulsed gradients are the same in the prepare and read intervals of the sequence (condition I of Cotts et al. [3], as given in our Eq. (3) and Fig. 1), piecewise integration over successive time intervals in the pulse sequence, in an analogous way as introduced in [3], yields

$$\begin{aligned} A_{\mathrm{p}} = \delta^2 \Big\{ & (\Delta + \tau)(G^{\mathrm{r}} + F^{\mathrm{r}})^2 \\ & + \tau\Big[2(F^{\mathrm{r}})^2 - (F^{\mathrm{p}} + F^{\mathrm{r}})(G^{\mathrm{p}} - G^{\mathrm{r}})\Big] \\ & - \frac{1}{3}\delta\Big[(G^{\mathrm{p}})^2 + F^{\mathrm{p}}F^{\mathrm{r}} + G^{\mathrm{r}}(F^{\mathrm{p}} - F^{\mathrm{r}})\Big]\Big\}, \end{aligned} \tag{4a}$$

$$\begin{aligned} A_{\mathrm{c}} = \delta\big\{ & g\big[a(G^{\mathrm{p}} - F^{\mathrm{p}}) + 2\tau^2 F^{\mathrm{p}} + \tau(\delta_2 - \delta_1)G^{\mathrm{p}}\big] \\ & - f\big[a(G^{\mathrm{r}} - F^{\mathrm{r}}) + 2\tau^2 F^{\mathrm{r}} - \tau(\delta_2 - \delta_1)F^{\mathrm{r}}\big]\big\}, \end{aligned} \tag{4b}$$

$$A_{\mathrm{b}} = \frac{2}{3}\tau^3(f^2 + g^2), \tag{4c}$$

where we used Maple V Release 4 version 4.00c as tool for the tedious and lengthy mathematical calculations and transformations into the final form of Eqs. (4a)–(4c). The quantity a in Eq. (4b) depends on the timing of the pulsed field gradients in the τ intervals

$$a = \delta_1^2 + \delta_1\delta + \frac{1}{3}\delta^2, \tag{5}$$

and represents a convenient abbreviation used throughout this paper. The spin echo attenuation due to the cross term (Eq. (4b)) was written in such a way that its contributions originating from the the field gradients in the prepare ($F^{\mathrm{p}}, G^{\mathrm{p}}$, and g) and read ($F^{\mathrm{r}}, G^{\mathrm{r}}$, and f) intervals appear in separate lines.

2.2. Compatibility with previous results

Before we evaluate Eqs. (4a)–(4c) with respect to possible strategies of how to suppress the unwanted cross term by choosing certain pulsed field gradient patterns, we shall demonstrate that our generalized approach to treat stimulated echo APFG sequences (Eqs. (2–5)) yields spin echo attenuations consistent with previously published results.

Table 1 shows these consistency checks for four special cases each corresponding to one line in the table: (1) The pulse sequence and spin echo attenuations for the standard 9-interval sequence [3] are obtained by choosing $F = F^{\mathrm{r}} = F^{\mathrm{p}} = 0$ and $G = G^{\mathrm{r}} = G^{\mathrm{p}}$ in Fig. 1 and Eqs. (4a)–(4c). (2) The corresponding relations for the standard 13-interval sequence [3] follow by using four pulsed field gradients of equal intensity ($G = F^{\mathrm{p}} = G^{\mathrm{p}} = F^{\mathrm{r}} = G^{\mathrm{r}}$). (3) The 13-interval sequence with asymmetric pulsed field gradients for suppression of unwanted coherences suggested by Sørland et al. [7] is derived by choosing $F = F^{\mathrm{p}} = F^{\mathrm{r}}$ and $G = G^{\mathrm{p}} = G^{\mathrm{r}}$. In the original papers cited, these three sequences are treated with a constant background gradient. This is realized in our generalized approach by additionally setting $f = g$ in Eqs. (4a)–(4c). In agreement with the corresponding equation in the original papers, the last column in Table 1 shows that the unwanted cross terms disappear for these three sequences, if the pulsed gradients are centered in the τ intervals ($\delta_1 = \delta_2$). (4) However, under the same condition, the cross term in the 13-interval sequence does not cancel if the background gradients in the prepare and read intervals have equal intensity but opposite polarity ($f = -g$). This result was first obtained by Seland et al. [4]. Thus, in all four cases, the spin echo attenuations (A_{p}, A_{c}, and A_{b}) obtained via our generalized approach with Eqs. (4a)–(4c) exactly reproduce the known results. Therefore, they may be considered as special cases of our generalized 13-interval sequence (Fig. 1).

2.3. Background gradient suppression using magic pulsed field gradient ratios

For the generalized treatment of the 13-interval sequence, where we allow the background gradients to change during the store interval $\varDelta$ from g to f (see Fig. 1), the cross term with the pulsed field gradients generally do not cancel if their intensities are set as in the standard 13- and 9-interval sequence. This can easily be shown by introducing their specific pulsed field gradient pattern into Eq. (4b) as demonstrated in Section 2.2. However, the cross term can always be suppressed by choosing such pulsed field gradient patterns, which ensure that the terms in both square brackets in Eq. (4b) simultaneously become zero. The resulting conditions:

$$0 = a(G^{\mathrm{p}} - F^{\mathrm{p}}) + 2\tau^2 F^{\mathrm{p}} + \tau(\delta_2 - \delta_1)G^{\mathrm{p}}, \tag{6a}$$

$$0 = a(G^{\mathrm{r}} - F^{\mathrm{r}}) + 2\tau^2 F^{\mathrm{r}} - \tau(\delta_2 - \delta_1)F^{\mathrm{r}}, \tag{6b}$$

are fulfilled if the pulsed field gradient intensities in the prepare and read interval obey the two intensity ratios η^{p} and η^{r}:

$$\eta^{\mathrm{p}} \equiv \frac{G^{\mathrm{p}}}{F^{\mathrm{p}}} = \frac{a - 2\tau^2}{a + \tau(\delta_2 - \delta_1)}, \tag{7a}$$

$$\eta^{\mathrm{r}} \equiv \frac{G^{\mathrm{r}}}{F^{\mathrm{r}}} = 1 - \frac{2\tau^2 - \tau(\delta_2 - \delta_1)}{a}. \tag{7b}$$

Eqs. (7a) and (7b) represents the key result of our calculation. It means that regardless of the background gradients acting during the prepare and read intervals, it is always possible to suppress the unwanted cross terms if the above two intensity ratios of the pulsed field gradients are maintained in the generalized 13-interval sequence. The values of these intensity ratios depend only on the timing of the pulse sequence and not on any property of the system to be studied. In our opinion this is a very remarkable result which has the potential to revolutionize PFG NMR diffusion studies in heterogeneous systems, where magnetic susceptibility differences often lead to unknown internal field gradients. Therefore, we have coined the term MPFG ratios for pulsed field gradient intensity ratios, which cancel the cross terms with arbitrary background field gradients as long as they remain constant during the prepare and the read intervals. The two magic pulsed field gradient ratios

Table 1
Evaluation of Eqs. (4a)–(4c) for four known pulse sequences

Sequence type	f	F	δ_1	A_{p}/δ^2	$A_{\mathrm{c}}/\delta\tau g$
9-Interval [3]	g	0	δ_1	$(\varDelta + \tau - \frac{1}{3}\delta)G^2$	$(\delta_2 - \delta_1)G$
13-Interval [3]	g	G	δ_1	$(4\varDelta + 6\tau - \frac{2}{3}\delta)G^2$	$2(\delta_2 - \delta_1)G$
13-Interval [7]	g	F	δ_1	$(\varDelta + \tau)(G + F)^2 + 2\tau F^2 - \frac{1}{3}\delta(G^2 + F^2)$	$(\delta_2 - \delta_1)(F + G)$
13-Interval [4]	$-g$	G	δ_2	$(4\varDelta + 6\tau - \frac{2}{3}\delta)G^2$	$4\tau G$

By choosing the corresponding conditions for the pulsed and background field gradients, the spin echo attenuations (terms A_{p} and A_{c}) were calculated from Eqs. (4a)–(4c). The term A_{b} is the same for all four cases: $A_{\mathrm{b}} = (4/3)\tau^3 g^2$.

derived in Eqs. (7a) and (7b) and the echo condition (Eq. (3)) completely define the intensities of the four pulsed field gradients in the generalized 13-interval sequence. That means that changing one of the four pulsed field gradients requires corresponding changes to the three other pulsed gradients. Assuming that the first pulsed gradient in the prepare interval (F^p) is chosen as the independently varied gradient intensity to measure the spin echo attenuation, the intensity of the last pulsed gradient (F^r) in the read interval follows by combining Eqs. (3) and (7a) and (7b):

$$F^r = \frac{1+\eta^p}{1+\eta^r} F^p. \tag{8}$$

The required values for G^p and G^r are calculated by inserting F^p and F^r into Eqs. (7a) and (7b). Considering these interrelations between the four pulsed field gradients, the spin echo attenuation (Eq. 4a) becomes

$$A_p = (\delta F^p)^2 \left\{ (\Delta+\tau)(1+\eta^p)^2 + \tau \frac{2+\eta^p(2+\eta^p)+\eta^r(2+\eta^r)}{(1+\eta^r)^2} - \frac{1}{3}\delta\left[(\eta^p)^2 + \frac{1+\eta^p}{1+\eta^r}\left(1+\eta^r\frac{\eta^r-\eta^p}{1+\eta^r}\right)\right]\right\}. \tag{9}$$

Since the cross term is suppressed by choosing the magic pulsed field gradient ratios η^p and η^r according to Eqs. (7a) and (7b), Eq. (9) represents the only part of the spin echo attenuation which depends on the pulsed field gradients. Thus, the experimentally observed spin echo attenuations may be analyzed using Eq. (9) to yield the correct diffusion coefficient even in the presence of unknown, spatially dependent background field gradients.

In order to evaluate the proposed approach to background gradient suppression, the results represented in Eqs. (7–9) are considered for two special cases, which correspond to experimental situations often encountered in PFG NMR diffusion studies using the 13-interval sequence:

Case 1. *The pulsed field gradients follow the rf pulses immediately*, $\delta_1 = 0$ in Fig. 1. This case allows the longest delay between the end of the last pulsed field gradient (F^r) and the center of the spin echo, which might be important for the prevention of disturbing influences of eddy currents on the spin echo formation. Due to $\delta_1 = 0$, δ_2 is given by $\tau - \delta$ and a becomes equal to $(1/3)\delta$ (see Eq. (5)). Inserting these relations into Eqs. (7a) and (7b), the magic pulsed field gradient ratios simplify to:

$$\eta^p = \left(\frac{1}{3}\left(\frac{\delta}{\tau}\right)^2 - 2\right) \Big/ \left(\frac{1}{3}\left(\frac{\delta}{\tau}\right)^2 - \frac{\delta}{\tau} + 1\right), \tag{10a}$$

$$\eta^r = 1 - 3\frac{\tau}{\delta}\left(\frac{\tau}{\delta}+1\right). \tag{10b}$$

They depend only on the ratio between the width of the pulsed field gradients δ and the rf pulse distance τ. Fig. 2 shows the values of the magic pulsed field gradient ratios in dependence on δ/τ. Both ratios have a negative sign and their absolute values are larger than 1. Due to the definition of $F^{p/r}$ and $G^{p/r}$ as effective gradients (see Section 2.1 and Fig. 1), it follows that the corresponding laboratory gradients must always be of equal polarity to cancel the cross terms and the amplitude of the pulsed gradients $F^{p/r}$ must be smaller than the amplitude of the pulsed gradients $G^{p/r}$. The magic pulsed field gradient ratio for the read interval (η^r) diverges if δ/τ approaches zero (narrow pulsed field gradients). This, however, does not mean that G^r increases to very large values, which cannot be realized experimentally, since the echo condition simultaneously requires a value of F^r which—according to Eq. (8)—decreases in proportion to $1/(1+\eta^r)$. Using the magic pulsed field gradient ratios calculated via Eqs. (10a) and (10b), the A_p term of the spin echo attenuation of the generalized 13-interval sequence with $\delta_1 = 0$ becomes

$$A_p = \frac{(\delta F^p)^2}{(\delta^2 - 3\delta\tau + 3\tau^2)^2}\left\{(\Delta+\tau)(2\delta^2 - 3\delta\tau - 3\tau^2)^2 + \tau(2\delta^4 - 6\delta^3\tau + 15\delta^2\tau^2 - 18\delta\tau^3 + 9\tau^4) - \frac{1}{3}\delta(2\delta^4 - 6\delta^3\tau + 3\delta^2\tau^2 + 27\tau^4)\right\}. \tag{11}$$

Case 2. *Centering of pulsed field gradients*, $\delta_1 = \delta_2$ in Fig. 1. If the pulsed field gradients are centered in the τ intervals, the terms depending on $\delta_1 - \delta_2$ in the magic pulsed field gradient ratios (Eqs. (7a) and (7b)) vanish and both ratios coincide ($\eta = \eta^p = \eta^r$)

$$\eta = \frac{G^p}{F^p} = \frac{G^r}{F^r} = 1 - \frac{2\tau^2}{a}. \tag{12}$$

Since the echo condition (Eq. (3)) must be obeyed simultaneously, the G and F pulsed field gradients are required to be of equal intensity, i.e., $F \equiv F^p = F^r$ and $G \equiv G^p = G^r$. Using the definition of a (Eq. (5)) and applying the condition $\delta_1 = \delta_2$, this magic pulsed field gradient ratio (Eq. (12)) simplifies to

$$\eta = \frac{G}{F} = 1 - \left(8 \Big/ \left(1 + \frac{1}{3}\left(\frac{\delta}{\tau}\right)^2\right)\right). \tag{13}$$

A few important properties of this magic pulsed field gradient ratio are considered in more detail: (i) since the pulse sequence requires $0 \leqslant \delta \leqslant \tau$, the ratio between G and F must always be in the range $-7 \leqslant G/F \leqslant -5$ (see Fig. 2). Choosing such values should always be possible with modern NMR spectrometers. (ii) Due to (i) and the definition of F and G as effective gradients, it follows again that the laboratory gradients F^L and G^L must be

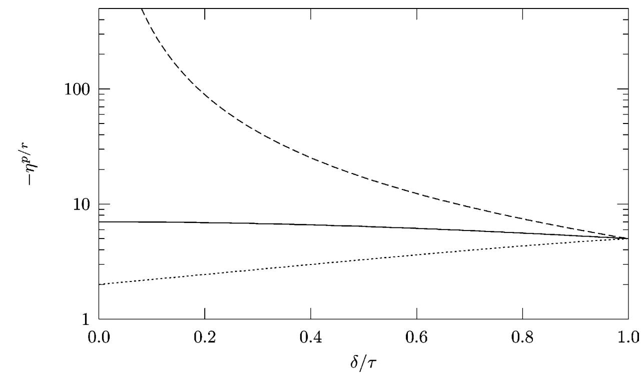

Fig. 2. Magic pulsed field gradient ratios for background gradient suppression as function of δ/τ for the generalized 13-interval sequence with $\delta_1 = 0$ (η^{p}, dotted line; η^{r}, dashed line) calculated via Eqs. (10a) and (10b) and with $\delta_1 = \delta_2$ ($\eta = \eta^{\mathrm{p}} = \eta^{\mathrm{r}}$, full line) calculated via Eq. (13).

of equal polarity and the amplitude of the pulsed gradient F must be smaller than the pulsed gradient G to cancel the cross terms. (iii) The penalty to be paid by choosing the magic pulsed field gradient ratio η according to the condition in Eq. (13) is a reduced sensitivity of the pulsed gradients, i.e., the term

$$A_{\mathrm{p}} = (\delta F)^2\left[(\Delta + \tau)(1+\eta)^2 + 2\tau - \frac{1}{3}\delta(1+\eta^2)\right], \qquad (14)$$

is much smaller compared to the A_{p}-term in the standard 13-interval sequence with $F = G$. However, with the increased availability of high-intensity pulsed field gradients [9–11] this reduced sensitivity may be compensated and should not present a serious limitation for the application of magic pulsed field gradient ratios for background gradient suppression.

The practical application of the pulsed gradient pattern obeying Eq. (13) is demonstrated in Section 3. It should be noted that the theoretical results of this special case were first published by Galvosas [12] in a Ph.D thesis and that this Case 2 corresponds to the experimental conditions used by Sun et al. [6], who modified the 13-interval sequence in a different way (see Fig. 3) and who first proposed asymmetric (magic) pulsed field gradients for suppression of background gradients, which may change during the store interval. However, in

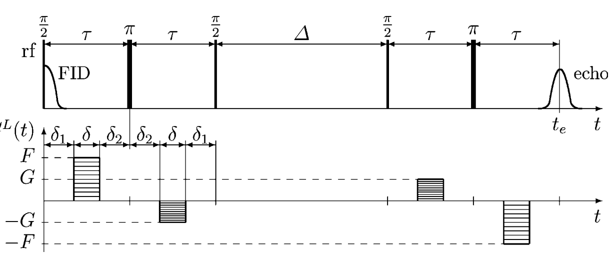

Fig. 3. 13-Interval pulse sequence for background gradient suppression with asymmetric pulsed field gradients G and F placed symmetrically about the π rf-pulses as introduced by Sun et al. [6]. The results for the magic pulsed field gradient ratio and the spin echo attenuation were recalculated and are given in Eqs. (15a)–(15c) and (16).

[6] the simplified equations for the magic pulsed field gradient ratio and the spin echo attenuation were not explicitly given.

2.4. Relation to paper of Sun et al.

In the above mentioned paper, Sun et al. [6] placed the pulsed field gradients symmetrically about the π rf pulses as drawn in Fig. 3. This definition of the time intervals δ_1 and δ_2 deviates from most common applications of the 13-interval sequence [3,4,7], where the pulsed field gradients start at the same distance from the preceding rf pulse as drawn in our Fig. 1. Applying the general presentation of the spin echo attenuation (Eq. (2)) to the definitions of the time intervals and pulsed gradients given in Fig. 3 and allowing the constant background gradients g and f to change during the store interval, one obtains

$$A_{\mathrm{p}} = \delta^2\left\{[\Delta + \tau - (\delta_2 - \delta_1)](G+F)^2 + 2(\tau + \delta_2 - \delta_1)F^2 - \frac{1}{3}\delta(G^2 + F^2)\right\}, \qquad (15a)$$

$$A_{\mathrm{c}} = \delta\left[a(G-F) + 2\tau^2 F\right](g - f), \qquad (15b)$$

$$A_{\mathrm{b}} = \frac{2}{3}\tau^3(f^2 + g^2), \qquad (15c)$$

which represents the equivalent to Eqs. (4a)–(4c) calculated for our generalized 13-interval sequence. Compared to Eq. (4b), the term proportional to $\delta_2 - \delta_1$ vanishes in the cross term A_{c} (Eq. (15b)), but it arises now in the part proportional to the squared pulsed gradients A_{p} (Eq. (15a)). While this may complicate the evaluation of the spin echo attenuation in respect to the diffusion coefficients, it has the advantage that for all possible settings of δ_1, there is only one magic pulsed gradient ratio necessary to cancel the cross terms with arbitrary background gradients g and f

$$\eta^{\mathrm{Sun}} = \frac{G}{F} = 1 - \frac{2\tau^2}{a} = 1 - \left(2\Big/\left(\left(\frac{\delta_1}{\tau}\right)^2 + \frac{\delta_1}{\tau}\frac{\delta}{\tau} + \frac{1}{3}\left(\frac{\delta}{\tau}\right)^2\right)\right), \qquad (16)$$

Eq. (16) is identical to Eq. (21) in [6], if $\tau = \delta_1 + \delta + \delta_2$ is substituted. Under the special condition that $\delta_1 = \delta_2$, i.e., that the pulsed gradients are centered in the τ intervals, Eqs. (4a)–(4c) and (15a)–(15c) yield the same result as presented in Case 2 of Section 2.3. This confirms the consistency between our approach and Sun et al. [6] to background gradient suppression.[2]

[2] Obviously, the term proportional to the squared pulsed gradients in Eq. (22) of [6] should correspond to our Eq. (15a), but the results differ. Because of the consistency in all our mathematical deviations, we assume a misprint or miscalculation occurring in Eq. (22) in [6].

If the background gradients are known, any type of APFG NMR experiment may be used to measure the correct diffusivities, by using the complete set of Eqs. (4a)–(4c) for data analysis. Unfortunately, in most applications the disturbing internal background gradients are unknown, preventing a correct evaluation of the spin echo attenuation. Thus, from a practical point of view, one chooses the 13-interval sequence according to Fig. 1 or Fig. 3 with a τ value as short as possible in order to ensure that the diffusing molecules remain in regions with constant internal background gradients during both the read interval and the prepare interval. By obeying the corresponding magic pulsed field gradient ratios, all cross terms are reduced to zero regardless of the actual intensities of the internal background gradients acting at the position of the molecules during the read and prepare intervals, which—due to $\Delta \gg \tau$—may have changed by diffusion during the z-store interval. Whenever possible, one may set $\delta_1 = \delta_2$, which simplifies the experimental set up and data analysis in both (Sun's and our) approaches to background gradient suppression.

3. Experimental

The astonishing result that the cross terms between the pulsed gradients and constant background field gradients, which may change during the z-store interval, cancel if the magic pulsed field gradient ratios (Eq. (13)) are maintained in the generalized 13-interval sequence has been confirmed experimentally. The pulsed gradients are generated in the usual way using an actively shielded anti-Helmholtz gradient coil (see [13]). Artificial background gradients of known but arbitrary intensities (g,f) which are additionally switched on during the prepare and read intervals of the pulse sequence can be produced using the same gradient coil. Thus, F and G as well as g and f are controlled via the NMR spectrometer hardware and software.

A suitable test sample for proving the complete cancelation of the cross terms with the above approach is water which has a known self-diffusion coefficient ($D = 2.3 \times 10^{-9}\,\mathrm{m^2/s}$ at 298 K, see [14]) and no internal background gradients. For our experiments it was slightly doped with $MnSO_4$ to shorten its longitudinal relaxation time to a value of $T_1 = 850\,\mathrm{ms}$. This allows sufficiently fast measurements with a repetition time of 4 s. All measurements with this sample were performed with a store period of $\Delta = 80\,\mathrm{ms}$, an rf pulse distance of $\tau = 10\,\mathrm{ms}$ and a pulsed field gradient width of $\delta = 1\,\mathrm{ms}$. The pulsed field gradients were always centered in the τ-intervals, thus $\delta_1 = \delta_2 = 4.5\,\mathrm{ms}$. The maximum intensity of the pulsed field gradients (either F or G gradient) was chosen to be 0.45 T/m. The ratio of the pulsed field gradient intensities was allowed to take each of the eight values $G/F = 3, 1, 0, -3, -5, -6.973, -9$, and -11, where $G/F = 1$ and 0 corresponds to the original 13-interval and 9-interval sequences, respectively, and $G/F = -6.973$ is exactly the value of the magic pulsed field gradient ratio (Eq. (13)) for the timing parameters chosen. $G/F = -1$ represents two equal Hahn echo PFG NMR sequences repeated after Δ. Since it behaves differently with respect to total intensity as well as diffusion time (independent of Δ!) it is not taken into account in the following considerations. The background gradient during the read period was always fixed at $f = 53 \times 10^{-3}$ T/m. The corresponding value in the prepare period (g) is variable, in order to simulate changing background gradients due to diffusion. g was changed in 11 equidistant steps from 53×10^{-3} T/m down to -53×10^{-3} T/m. Spin echo attenuations were measured for each g-value and each G/F ratio in dependence on the intensity of the pulsed gradients. Thus, the spin echo attenuation from which the diffusion coefficients are calculated are acquired in a 2D matrix, where g/f represents the influences of the background gradients and G/F the type of the PFG NMR sequence used to compensate for these unwanted influences.

In a second experiment, the proposed procedure to suppress background gradients by using the magic pulsed field gradient ratios is demonstrated for real field inhomogeneities, originating from the magnetic properties of the sample itself. The sample for this experiment consists of water ($T = 298\,\mathrm{K}$) and a piece of chromium ($d \approx 2\,\mathrm{mm}$) on the bottom of the NMR tube. Due to the magnetic properties of the chromium, a spatially depend local magnetic field arises from the presence of the external magnetic field $B_0 = 9.4\,\mathrm{T}$. Hence, different internal background magnetic field gradients g_i and f_i may act during the prepare and read intervals as a consequence of molecular displacement between the two intervals of time. In this second experiment we only compare the behavior of the original 13-interval sequence ($G/F = 1$) and the sequence satisfying Eq. (13) with $G/F = \eta$, where the external constant gradient is kept constant during the prepare and read intervals. For the 13-interval sequence with $G/F = 1$, the cross term (Eq. 4b) simplifies to

$$A'_c = 2\tau^2 G\delta(g_i - f_i), \tag{17}$$

under such conditions. Obviously, the sign of this term depends on the polarity of the pulsed magnetic field gradient G, while the internal, space depend background field gradients do not change their signs. Therefore, the apparent diffusion coefficient, measured with the 13-interval sequence under the condition $G/F = 1$, may be influenced by the polarity of the pulsed field gradient G. Since A'_c also depends on the rf-pulse distance τ we carried out experiments with variable τ-values ($\tau = 2, \ldots, 10\,\mathrm{ms}$) and both polarities of G. All other parameters have been chosen as in the first experiment described above. According to Eq. (17) the influence of the cross term should vanish for $\tau \rightarrow 0$ even for the 13-interval sequence with $G/F = 1$. In contrast, for the sequence satisfying our condition Eq. (13) with $G/F = -(6.973, \ldots, 6.385)$, we expect the measured diffusion coefficient to be independent of the polarity of G for arbitrary values of τ.

All experiments were carried out on the home-built NMR spectrometer *FEGRIS* 400 *NT* equipped with a MARAN Ultra console (Resonance Instruments, GB) and ultra-high intensity pulsed field gradient facilities as described in [11].

4. Results and discussion

The data analysis for the spin echo attenuations of the first experiment may follow two different routes. (i) Since the pulsed and the (simulated) background gradients are known, the complete set of Eqs. (4a)–(4c), including the cross terms Eq. (4b), can be used for data evaluation. The fit of the complete set of Eqs. (4a)–(4c) to the experimental data was very good yielding correlation coefficients of better than 0.9999 for each spin echo attenuation. The resulting individual self-diffusion coefficients have an uncertainty of less than 1% (95% confidence interval) and the absolute values are in agreement with the known value for water. The value averaged over all G/F- and g/f-ratios is $(2.28 \pm 0.01) \times 10^{-9}\,\mathrm{m^2/s}$ where the given uncertainty represents the maximum deviation from the averaged value. It was observed for the case $G/F = 1$, representing the 13-interval sequence, and $g/f = 0.2$. Thus, the set of Eqs. (4a)–(4c) correctly describe PFG NMR spin echo attenuations with known background gradients changing during the store interval, and with different ratios of pulsed field gradient intensities G/F.

(ii) The second way of data analysis assumes, that the background gradients are unknown, which is the case in most real applications of PFG NMR diffusion measurements in heterogeneous systems. Thus, the cross term (Eq. (4b)) between the pulsed and the background gradients can not be taken into account and evaluation of the diffusion coefficients from the spin echo attenuations is limited to the term containing only the pulsed gradients. Fig. 4 shows the dependence of the resulting apparent self-diffusion coefficients on the g/f- and G/F-ratios in a 2D-plot. As expected, if $g/f = 1$ which means if the background gradients are identical, the results for the apparent diffusivity are independent of G/F and yield the correct self-diffusion coefficient of the water. The same observation is true for $G/F = -6.973$, which yields for all values of g/f the correct diffusivity. For all other combinations of g/f and G/F the apparent self-diffusion coefficient clearly deviate from the value expected for water.

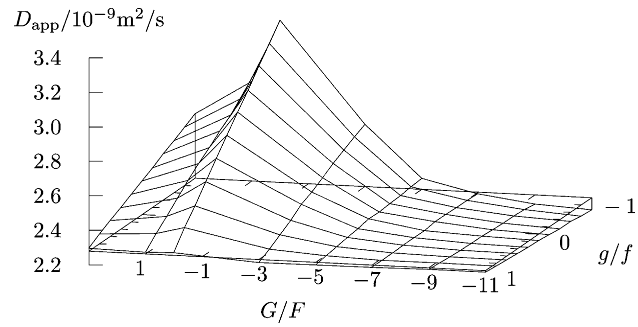

Fig. 4. Apparent self-diffusion coefficients of water calculated from spin echo attenuations measured in dependence on g/f and G/F. They result by neglecting the cross terms between G, F and g, f in the data analysis.

This is especially true for the 9-interval sequence ($G/F = 0$) and the 13-interval sequence ($G/F = 1$). Since this is a rather unexpected result, we redraw the 2D-plot for this two sequences in Fig. 5 in a 1D-graph and compare it with the corresponding results for the magic pulsed field gradient ratio $G/F = -6.973$. Only the latter results prove to be independent of the chosen setting of the background gradient g/f. Thus, these experimental results confirm the theoretical considerations which led us to the postulated complete cancelation of the unwanted cross terms for pulsed field gradients obeying the conditions of Eq. (13). Moreover, the hypothesis of Seland et al. [4] that the standard 13-interval sequence with $F = G$ does not cancel the cross terms for changing background gradients is confirmed experimentally for a set of g/f-ratios including their special case of $g/f = -1$.

For the pulse sequence according to Fig. 1 with $\delta_1 = \delta_2$ satisfying the magic pulsed field gradient ratio $\eta = G/F = -(6.973, \ldots, 6.385)$ (Eq. (13)), the data analysis of the second experiment (using the water sample with a piece of chromium) leads to apparent

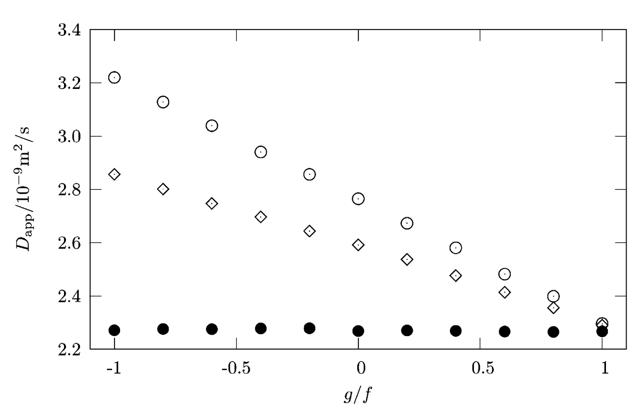

Fig. 5. Apparent self-diffusion coefficient of water in dependence on the ratio of the background gradient for $G/F = 0$ (○), $G/F = 1$ (◇), and $G/F = -6.973$ (●) calculated from the spin echo attenuation without taking into account the cross terms between G,F and g,f.

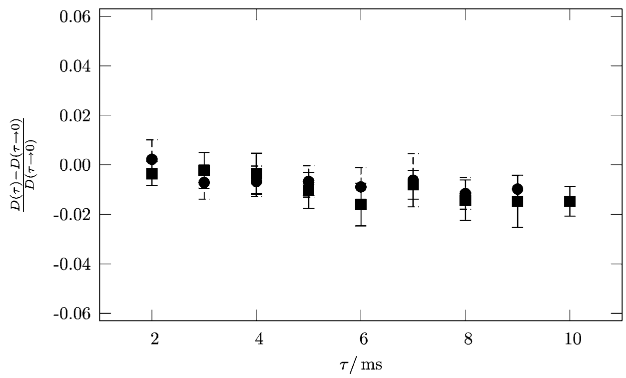

Fig. 6. Dependence of the normalized apparent diffusion coefficient on the rf-pulse distance τ for positive (●) and negative (■) pulsed field gradients G, respectively, measured with the pulse sequence according to Fig. 1 satisfying the magic pulsed field gradient ratio with $G/F = -(6.973, \ldots, 6.385)$ according to Eq. (13).

diffusion coefficients independent of the polarities of the pulsed field gradient G. As shown in Fig. 6, the self-diffusion coefficients are independent of the rf-pulse distance τ as well.

In contrast, the analysis for the 13-interval pulse sequence with $G/F = 1$, reveals the influence of the polarity of the pulsed field gradients G on the spin echo attenuations and thus the apparent diffusivities. Fig. 7 shows significant differences of the apparent diffusion coefficients for both polarities of the pulsed field gradients. As expected from Eq. (17), this difference decreases with the decreasing rf-pulse distance τ and vanishes for small values of τ.

The averaged difference in the internal background magnetic field gradients $\langle g_i - f_i \rangle$, which the water molecules experience in the sample with the piece of chromium, may be estimated from the difference of the apparent diffusion coefficients plotted in Fig. 7. For the experiment with $\tau = 10\,\text{ms}$, this difference is approximately $1 \times 10^{-10}\,\text{m}^2/\text{s}$. Using the two sets of parameters of the corresponding measurements with the opposite signs of the pulsed field gradients G and inserting them twice into Eq. (2), the difference $\langle g_i - f_i \rangle$ for the discussed experiment is calculated to be $(5 \ldots 10) \times 10^{-3}\,\text{T/m}$. It represents the averaged difference in the background gradients which a water molecule experiences during the diffusion time $2\tau + \Delta$. Thus, this value can be used to estimate the averaged second derivative of the magnetic field caused by the piece of chromium in the sample:

$$\frac{\Delta(\partial B/\partial z)}{\Delta z} = \frac{\langle g_i - f_i \rangle}{\sqrt{2D(2\tau + \Delta)}} \approx 300\,\text{T/m}^2. \tag{18}$$

Although the averaged difference in the background gradients is small compared to the constant external magnetic field gradient of $g = 53 \times 10^{-3}$ T/m and to the pulsed field gradient of up to $G = 200 \times 10^{-3}$ T/m, its influence becomes visible in Fig. 7 and can be suppressed by using the gradient scheme proposed with Eq. (13).

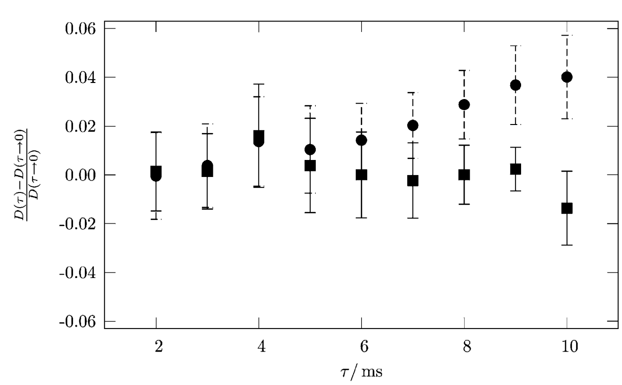

Fig. 7. Dependence of the normalized apparent diffusion coefficient on the rf-pulse distance τ for positive (●) and negative (■) pulsed field gradients G, respectively, measured with the 13-interval pulse sequence with $G/F = 1$ not obeying the magic pulsed field gradient ratio.

5. Conclusions

Measurements of diffusion coefficients in the presence of inhomogeneous samples by means of the PFG NMR spectroscopy may be influenced by local background magnetic field gradients. Via Eq. (2), it is in general possible to determine the three parts of the spin echo attenuation, arising from the pulsed and background field gradients, independent of the used pulse sequence. We proposed a generalized 13-interval sequence and calculated the spin echo attenuation for it under the special case of constant background magnetic field gradients which are however, allowed to arbitrarily change during the store interval Δ (see Eqs. (4a)–(4c)).

Our main result is that the unwanted cross term of such background gradients with the pulsed gradients, which may disturb the determination of the self-diffusion coefficients from the observed spin echo attenuation, may always be suppressed, if two MPFG ratios are maintained in the experiment. These two MPFG ratios (Eqs. (7a) and (7b)) coincide into one ratio given by Eq. (13), if the pulsed gradients are centered between the rf pulses. For this case, our results are shown to be con-

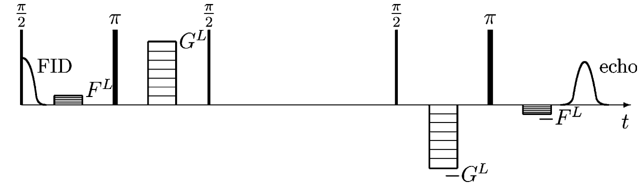

Fig. 8. Example for the pulsed gradient pattern in the generalized 13-interval sequence. The height ratio of the pulsed gradients (F^L and G^L) drawn and their polarities satisfy the magic pulsed field gradient ratio of Eq. (13) for $\delta_1 = \delta_2 = \delta$.

sistent with the recently published approach of Sun et al. [6], who first proposed asymmetric pulsed field gradients for suppression of unwanted cross terms with spatially dependent background gradients. The experimental results, presented in this work, confirm the validity of our theoretically obtained results for the echo attenuation in a generalized 13-interval sequence as well as for background gradient suppression using magic pulsed field gradient ratios.

For NMR diffusion studies in systems with unknown background gradients, we suggested the application of the generalized 13-interval sequence according to Fig. 1 with four unequal pulsed field gradients $F^{\mathrm{p,r}}$ and $G^{\mathrm{p,r}}$ obeying the magic pulsed gradient ratios of Eqs. (7a) and (7b). To simplify the experimental set up and the data analysis, one may center the pulsed gradients between the rf pulses and apply the magic pulsed field gradient ratio according to Eq. (13) to cancel unwanted cross terms. As an example for the realization of such experiments, Fig. 8 shows the intensities (on scale) and necessary polarities of the laboratory pulsed gradients G^{L} and F^{L}, which have to be maintained if one chooses $\delta_1 = \delta_2 = \delta$ (corresponding to $\tau = 3\delta$) requiring a MPFG intensity ratio of $F^{\mathrm{L}}/G^{\mathrm{L}} = 6.714$.

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