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A modified PGSE for measuring diffusion in the presence of static magnetic field gradients

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Abstract

With a proper timing of π pulses, it is possible to reduce the effect of the static internal magnetic field gradient on the measurement of diffusion with the pulsed gradient spin echo (PGSE). A pulse sequence that in the first order eliminates the effect of weak internal static gradients in a standard PGSE experiment is introduced. The method should be applied in the cases, where strong and short magnetic gradient pulses are used to investigate the motion of liquid in heterogeneous samples with large susceptibility differences such as porous media.

Keywords: Spin echo; Magnetic resonance; Gradient; Diffusion; Diffusion constant; Edge enhancement; Susceptibility; Internal gradient; Constant gradient; Porous media; Modulated gradient; Pulsed; CPMG; PGSE

1. Introduction

The pulsed gradient spin echo experiment is a powerful tool for investigation of molecular diffusion [1–5]. Static magnetic gradient influences the measurement and its effect can be reduced by the application of either π/2 (stimulated echo) or π (CPMG sequence) pulses [6–12]. Here a more efficient method is introduced.

The attenuation of spin echo $\beta = \ln(E_0/E)$ for isotropic diffusion can be written in the Gaussian approximation as [13–15]

$$\beta = \frac{1}{\pi}\int_0^{\infty} |\mathbf{F}(\omega)|^2 D(\omega)\mathrm{d}\omega. \quad (1)$$

E is the amplitude of the echo, E_0 is the amplitude of the free induction signal at the time of the echo 2τ,

$$\mathbf{F}(\omega) = \int_0^{2\tau} \mathbf{F}'(t)\mathrm{e}^{\mathrm{i}\omega t}\mathrm{d}t \quad (2)$$

is the frequency spectrum of the spin dephasing $\mathbf{F}'(t) = \gamma\int_0^t \mathbf{G}(t')\mathrm{d}t'$, and γ is the gyromagnetic ratio. In the effective magnetic field gradient $\mathbf{G}(t)$ the application of π pulses is accounted for and it can differ from the actual gradient $\mathbf{g}(t) : \mathbf{G}(t) = (-1)^{n_\pi(t)}\mathbf{g}(t)$; $n_\pi(t)$ is the number of π pulses applied up to the time t—the sign of the effective gradient changes upon every application of a π pulse. The diffusion spectrum tensor is the Fourier transform of the velocity correlation function and $D(\omega)$ is the component of the tensor along the direction of the gradient field

$$D(\omega) = \frac{1}{2}\int_{-\infty}^{\infty} \langle v(t)v(0)\rangle_c \mathrm{e}^{\mathrm{i}\omega t}\,\mathrm{d}t. \quad (3)$$

The subscript c denotes the second cumulant $\langle v(t)v(0)\rangle_c = \langle v(t)v(0)\rangle - \langle v\rangle\langle v\rangle$, where the average $\langle\cdots\rangle$ is taken over a suitable ensemble of spins [18] and v is the component of velocity along the direction of the magnetic field gradient. The value $D(\omega = 0)$ corresponds to the free diffusion constant. Using Parseval's theorem it is easy to show, that for free diffusion, the

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attenuation of Eq. (1) is transformed into the well-known expression given by Torrey [16]. The validity of the Gaussian approximation in the frequency domain approach is discussed in [17]. The approach is valid as long as the diffusion displacement ($2D\tau$) is short compared to the wavelength of the spin-dephasing grating ($1/\gamma G\delta$) and would in our case use gradients of the magnitude over kT/m.

Here, the gradient applied in a PGSE sequence is denoted as $\mathbf{G}_a$, the static gradient as $\mathbf{G}_s$ and their respective spin dephasings as $\mathbf{F}_a$ and $\mathbf{F}_s$. The attenuation of an echo in the combined field is

$$\beta = \frac{1}{\pi}\int_0^\infty |\mathbf{F}_a(\omega) + \mathbf{F}_s(\omega)|^2 D(\omega)\mathrm{d}\omega = \beta_a + \beta_s + \beta_{as}. \tag{4}$$

Here, β_a is the echo attenuation if $G_s = 0$. If the static gradient is much smaller than the applied gradient $G_s \ll G_a$, then we can in the first approximation neglect the echo attenuation of the static gradient $\beta_s = 1/\pi \int F_s^2(\omega)D(\omega)\mathrm{d}\omega$. The static gradient is observed only through the mixed term

$$\beta_{as} = \frac{1}{\pi}\int_0^\infty 2Re[\mathbf{F}_s^*(\omega)\cdot\mathbf{F}_a(\omega)]D(\omega)\mathrm{d}\omega, \tag{5}$$

where both gradient terms appear in a scalar product. In the cases, where the background gradient is not uniform, one should integrate the contributions over the sample to get the echo amplitude so in the case where the directional distribution of the background gradient is uniform the contribution from the mixed term will vanish.

Frequency spectra of spin dephasing for various gradient modulations usually have one or two dominant peaks. The peak of the dephasing spectrum for the spin echo in a static magnetic field gradient is centered around zero frequency. The dephasing spectrum of the modulated gradient has a peak at the modulation frequency and at zero; the amplitude of the latter depends on the average dephasing value. The product of overlapping peaks $F_s(\omega)$ and $F_a(\omega)$ is large and so is its contribution to the echo attenuation. It is possible to construct such a RF pulse sequence, that the peaks do not overlap and the mixed term will vanish.

In the following, the cases of PGSE and PGSE combined with two properly spaced additional π pulses will be analyzed for isotropic Brownian diffusion $D(\omega) = D$ in the static background gradient $\mathbf{G}_s$. D is the self-diffusion constant.

For a PGSE sequence of two gradient pulses δ long and Δ apart where the first gradient pulse is applied t_1 after excitation and the refocusing π pulse is applied at the time τ halfway between the gradient pulses (Fig. 1), the dephasing spectrum is

$$\mathbf{F}_a(\omega) = 4\gamma\mathbf{G}_a e^{i\omega\tau}\frac{\sin\frac{\omega\delta}{2}\sin\frac{\omega\Delta}{2}}{\omega^2}. \tag{6}$$

The dephasing spectrum of the static gradient (Fig. 2) is

$$\mathbf{F}_s(\omega) = 4\gamma\mathbf{G}_s e^{i\omega\tau}\frac{\sin^2\frac{\omega\tau}{2}}{\omega^2}. \tag{7}$$

Both spectra have a peak at zero frequency (Figs. 1C and 2C). The attenuation Eq. (4) is

$$\beta = \gamma^2 D\left[G_a^2\delta^2(\Delta - \delta/3) + \frac{2}{3}G_s^2\tau^3 - \frac{2}{3}\mathbf{G}_a\cdot\mathbf{G}_s\delta \times (\delta^2 + 3\delta t_1 + 3(t_1 - \tau)(t_1 + \tau))\right]. \tag{8}$$

For short gradient pulses $\delta \ll \tau$, with the first gradient pulse immediately after the excitation pulse $t_1 \ll \tau$, and for a weak static gradient $G_s \ll G_a$, the expression reduces to

$$\beta = \gamma^2 D\delta\Delta\mathbf{G}_a\cdot(\mathbf{G}_a\delta + \mathbf{G}_s\Delta/2). \tag{9}$$

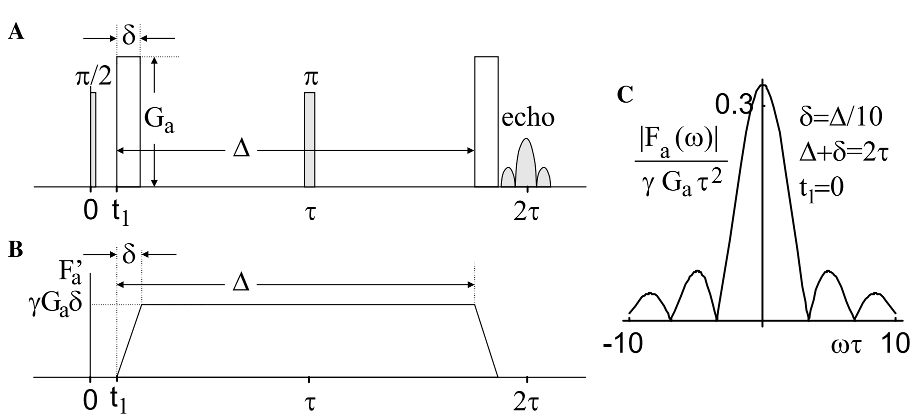

Fig. 1. (A) The PGSE sequence: gradient pulses G_a are δ long. The first gradient pulse is applied t_1 after excitation and the second pulse is applied Δ after the first one. The refocusing π pulse is in the middle between the gradient pulses, at time τ. The echo forms at time 2τ. (B) Spin dephasing $F_a'(t)$. The dephasing is constant in the interval between the pulses and should vanish if the echo is to form. Its Fourier transform—the dephasing spectra (C)—has a peak at zero frequency. The width of the peak is proportional to $1/\Delta$.

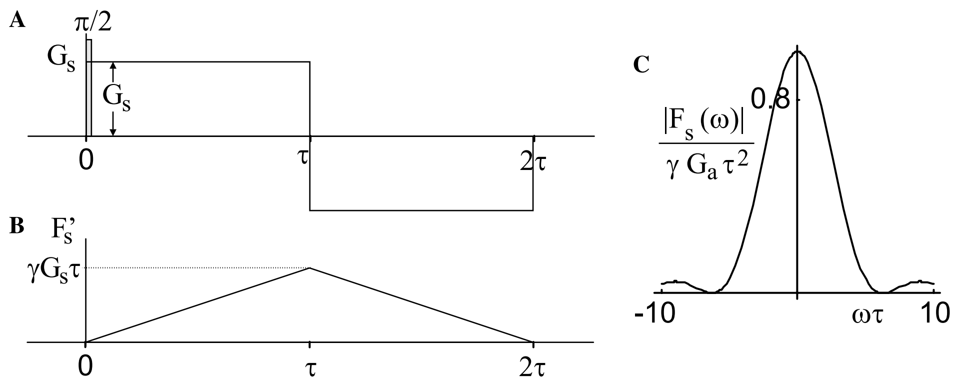

Fig. 2. (A) The effective static gradient. Although the gradient is constant in time, the π pulse at time τ, effectively changes its sign. (B) The spin dephasing for the static gradient $F_s'(t)$. The dephasing is zero at the time of the echo. (C) The dephasing spectra has a peak at zero frequency. The width of the peak is proportional to $1/\tau$.

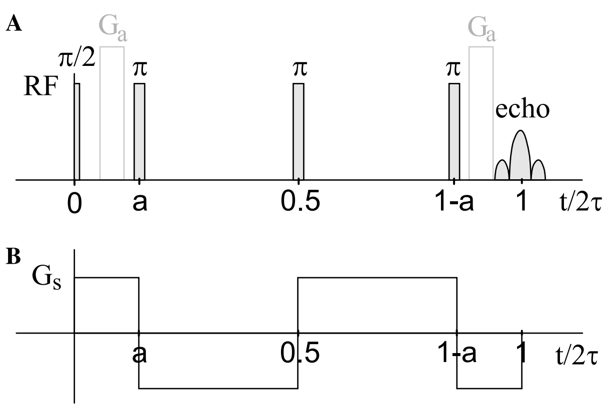

Fig. 3. (A) The PGSE sequence supplemented with two π pulses applied $a2\tau$ after excitation and $a2\tau$ before the echo. (B) The effective static gradient oscillates around zero.

When a PGSE sequence is combined with two additional π pulses applied symmetrically around the central π pulse as shown in Fig. 3, the dephasing of the applied gradient does not change. The time between the excitation and the first π pulse is denoted by $a2\tau$. The dephasing of the static gradient in this case differs from Eq. (7) and depends on the timing of additional π pulses (described by parameter a). The spectrum for a special case of a is shown in Fig. 4 and the spectrum for a general a is given by

$$\mathbf{F}_s(\omega) = 4\gamma \mathbf{G}_s e^{i\omega\tau} \frac{\left[\cos(\omega(1-2a)\tau) - \cos^2\frac{\omega\tau}{2}\right]}{\omega^2}. \quad (10)$$

This spectrum can have a lobe around zero frequency and a dominant peak centered off zero frequency. The echo attenuation for this sequence is

$$\beta = \gamma^2 D\left(G_a^2\delta^2(\Delta - \delta/3) + \frac{2}{3}G_s^2\tau^3[1 - 12(1-2a)^2 a]\right) + \beta_{as}. \quad (11)$$

The mixed term is

$$\beta_{as} = -\gamma^2 D \mathbf{G}_a \cdot \mathbf{G}_s \times \frac{2}{3}\delta\left[\delta^2 + 3\delta t_1 + 3(t_1^2 + (1 + 8(a-1)a)\tau^2)\right] \quad (12)$$

under the condition, that the π pulses are applied after the first gradient pulse $t_1(1-2a) < a(\delta + \Delta) - \delta$. The three π pulse sequence is equivalent to the standard PGSE in the case $a = \frac{1}{2}$.

In the case of short gradient pulses applied directly after excitation ($2\tau \doteq \Delta + \delta$), the mixed-term attenuation simplifies to

$$\beta_{as} = \frac{1}{2}\gamma^2 D \mathbf{G}_a \cdot \mathbf{G}_s \delta \Delta^2 (8(1-a)a - 1). \quad (13)$$

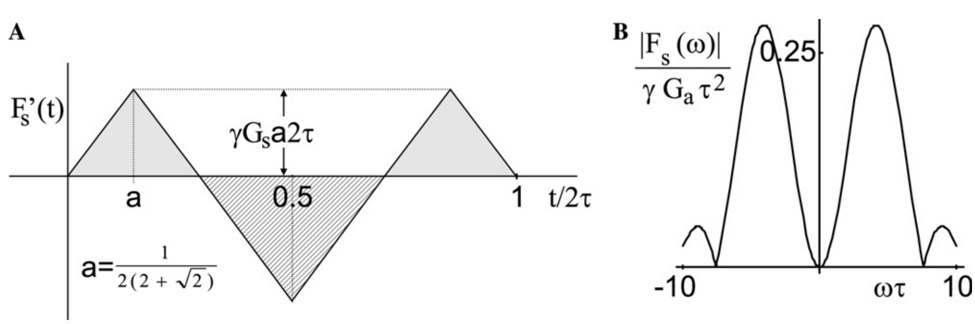

Fig. 4. (A) The dephasing of the static gradient oscillates, when two extra π pulses are applied. Shown is the case with $a = 1/(4 + 2\sqrt{2})$. (B) The dephasing spectrum for this a has a peak centered off zero frequency and no zero frequency lobe as opposed to the spectrum shown in Fig. 5 for $a = 1/6$.

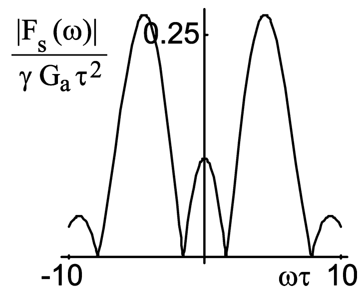

Fig. 5. The dephasing spectrum of the static gradient combined with the CPMG sequence of three π pulses: the time between the π pulses is twice the time between the π/2 and the first π pulse which corresponds to $a = 1/6$. The average dephasing in this case is not zero, so a finite lobe exists at zero frequency. The dominant peak is centered at $3\pi/2\tau$.

This term vanishes in the case $a = \frac{2-\sqrt{2}}{4} \approx 0.146$. In this case, the time integral of the dephasing $F'_s(t)$ is zero and there is no peak in $F_s(\omega)$ at zero frequency (Fig. 4B).

If the static gradient is large compared to the applied gradients, the term β_s prevails over β_{as}. The term β_s is minimal for $a = 1/6$ which corresponds to the CPMG timing, so in the case of strong internal gradients the CPMG timing of π pulses is a better solution. When the PGSE is combined with three CPMG timed π pulses (Fig. 4A for the case of $a = 1/6$), the dephasing spectrum of the static gradient is

$$\mathbf{F}_s(\omega) = 4\gamma\mathbf{G}_s e^{i\omega\tau} \frac{\sin^2\frac{\omega\tau}{6}\left[2\cos\frac{2\omega\tau}{3} - 1\right]}{\omega^2}. \qquad (14)$$

The dominant peak of the spectrum is centered at frequency $\omega = 3\pi/2\tau$ (Fig. 5) and the attenuation is

$$\beta = \gamma^2 D\left(G_a^2\delta^2(\Delta - \delta/3) + \frac{2}{27}G_s^2\tau^3\right) - \frac{2}{3}\gamma^2 D\mathbf{G}_a \cdot \mathbf{G}_s\delta\left[\delta^2 + 3\delta t_1 + 3(t_1^2 - \tau^2/9)\right]. \qquad (15)$$

The condition $4t_1 < \Delta - 5\delta$ must hold so it is possible to implement the CPMG timing.

In the case $2\tau \approx \Delta$ the attenuation term is

$$\beta = \gamma^2\mathbf{G}_a D\delta\Delta \cdot (\mathbf{G}_a\delta + \mathbf{G}_s\Delta/18) + \gamma^2 D G_s^2\Delta^3/108. \qquad (16)$$

The first term in the brackets is the short PGSE attenuation in the zero background gradient approximation. The second term is the contribution of the mixed term and is nine times smaller then the term of the PGSE sequence without extra π pulses.

The reason why the three π pulse CPMG timing is not suited for strong gradient pulses is that although its spectrum peak is shifted off zero frequency, a finite lobe at zero frequency still remains. This lobe, combined with the zero frequency lobe of the PGSE dephasing, gives the mixed term. To get rid of it, the first and the third π pulse in the CPMG timed sequence have to be slightly shifted so the gray area under the dephasing curve in Fig. 4A is the same as the hatched area, with other words: the average of the dephasing must be zero. The mixed term is zero in this case.

2. Experiment

The experiment was performed on a 5 mm i.d. water-filled tube at room temperature in a 0.7 T magnetic field of a 10 cm bore electromagnet equipped with microimaging gradient coils and a 10 mm i.d. detection coil. In the standard PGSE sequence, the pulses with $\delta = 1.7$ ms, $\Delta = 100$ ms, $\tau = 54$ ms, and $t_1 = 5.1$ ms were employed. The applied gradient was stepped from 0 to 0.37 T/m. The effective gradient was modulated with 10 μs block π pulses: one such pulse for PGSE and three pulses for PGSE combined with CPMG and modified PGSE (denoted here MCPMG). An average of eight echoes, acquired with 3 s repetition time, was recorded for every gradient step. The sequences were tested with uniform background gradient set by the shimming coils. By measuring T_2^* and T_2 the order of background gradient mag-

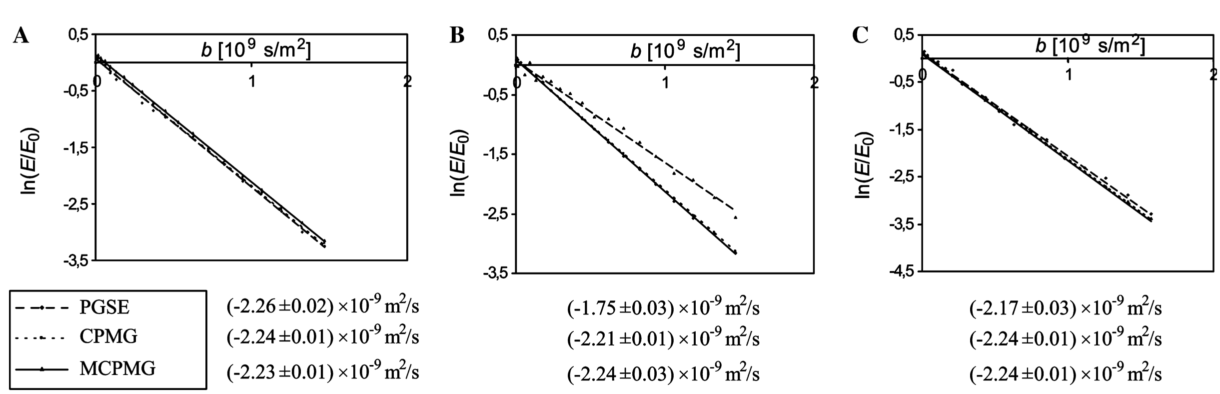

Fig. 6. Stejskal–Tanner plots of PGSE, CPMG and MCPMG sequences measured on water with: (A) no background gradient, (B) applied gradient in the direction of background gradient, and (C) applied gradient perpendicular to background gradient. The results for the diffusion constant agree in the cases (A) and (C) but in the case (B) the PGSE sequence returns significantly different result than the background gradient compensated sequences.

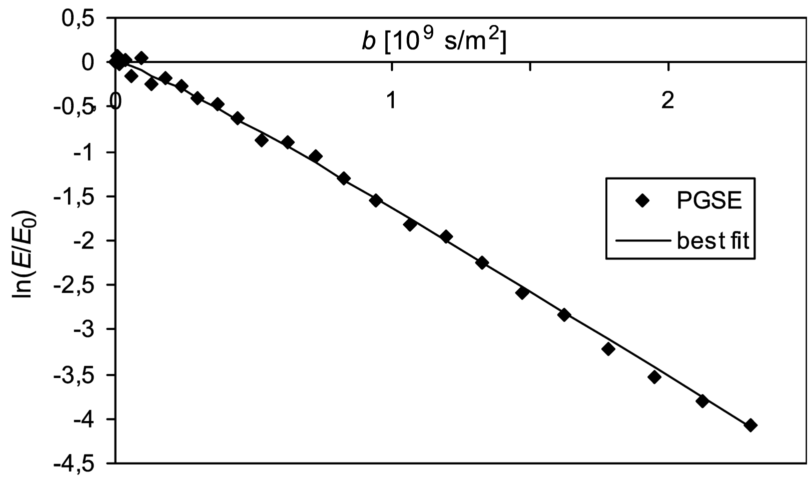

Fig. 7. Plot of attenuation in PGSE vs. b. The fitting curve is given by $\ln(E/E_0) = -bD(365\frac{G_s^2}{G_a^2} + 30\frac{G_s}{G_a})$, and the best fit parameters are $D = 2.1 \times 10^{-9}$ m/s^2 and $G_s = -2.0 \times 10^{-3}$ T/m.

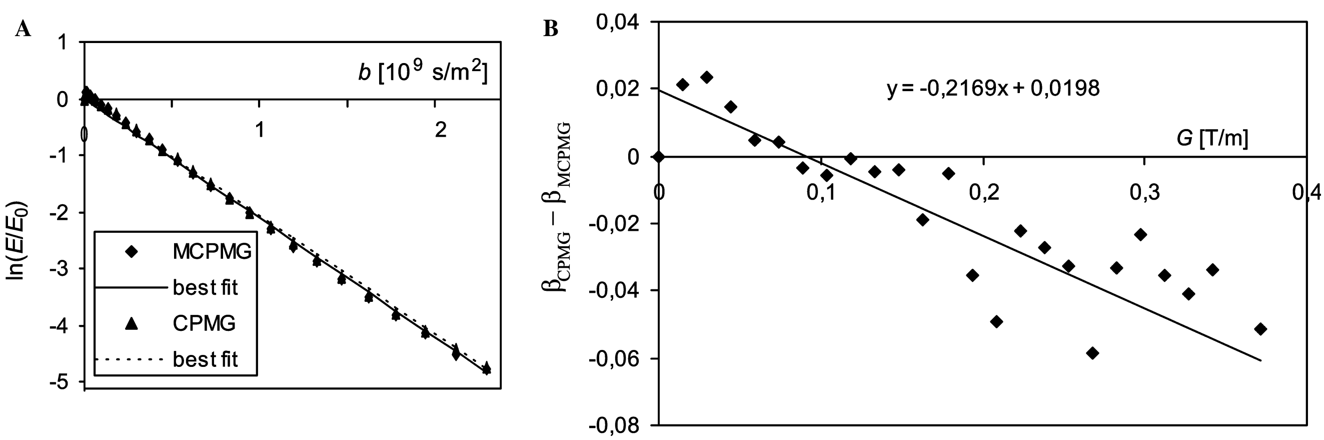

Fig. 8. (A) Plot of attenuation in CPMG and MCPMG vs. b. The fitting curves are given by Eq. (17) and the reported best fit parameters. The curves appear identical. In (B) the difference $\beta_{\mathrm{CPMG}} - \beta_{\mathrm{MCPMG}}$ is shown. It is proportional to the applied gradient according to Eq. (18).

nitude is estimated to mT/m. The results for PGSE, PGSE combined with CPMG, and MCPMG are shown in a Stejskal–Tanner plots in Fig. 6, where $\ln E/E_0$ is plotted against the b factor: $b = \gamma^2\delta^2(\Delta - \delta/3)G_a^2$.

The slope of the plot is the diffusion constant in the case with no background gradient. With the background gradient the plot is not a straight line but follows the curve given by

$$\beta = bD\left(1 + c_s\frac{G_s^2}{G_a^2} + c_{as}\cos\theta\frac{G_s}{G_a}\right), \tag{17}$$

where θ is the angle between the background and the applied gradient. The parameters for the sequence used were

	c_s	c_{as}
PGSE	$\frac{2\tau^3}{\delta^2(3\Delta-\delta)} = 365$	$\frac{3\Delta^2}{2\delta(3\Delta-\delta)} = 30$
CPMG	$\frac{2\tau^3}{9\delta^2(3\Delta-\delta)} = 41$	$\frac{\Delta^2}{6\delta(3\Delta-\delta)} = 3.3$
MCPMG	$\frac{(3\sqrt{2}-4)\tau^3}{\delta^2(3\Delta-\delta)} = 44$	0

It is clear that the sensitivity of CPMG and MCPMG on the static gradient is an order smaller then the sensitivity of the PGSE.

The results of PGSE measurement shown in Stejskal–Tanner plot in Fig. 6B are presented in Fig. 7. Here the fit is modeled by Eq. (17) and the non-linear regression analysis returns the best fit values $D = (2.1 \pm 0.1) \times 10^{-9}$ m/s^2 for the diffusion constant and $G_s = -(2.0 \pm 0.1) \times 10^{-3}$ T/m for the background gradient. The background gradient was anti-parallel to the applied gradient.

The results of CPMG and MCPMG shown in Fig. 8A appear identical on the same scale but the difference of the attenuations is proportional to the applied gradient with the slope given by the background gradient

$$\beta_{\mathrm{CPMG}} - \beta_{\mathrm{MCPMG}} = \gamma^2 D\left(\frac{(-3\sqrt{2}-34)\tau^3}{27}G_s^2 + \frac{\Delta^2\delta}{18}G_sG_a\right). \tag{18}$$

This residue is shown in Fig. 8B and the best fit of the slope gives the same value of background gradient as the fit of the PGSE measurement.

3. Conclusion

To remove the influence of a weak static magnetic field gradient (whatever its origin might be) in a PGSE measurement of diffusion, two additional π pulses should be used, one $\tau(2-\sqrt{2})/2$ and the other $\tau(2+\sqrt{2})/2$ after the π/2 pulse. The gradient pulse length δ must not exceed the time between the excitation and the first π pulse. One should be careful about the phases of the RF pulses to reduce the incomplete refocusation so the phase cycle for the first four echoes $xyyy$, $-xyyy$, $x{-}y{-}y{-}y$, $-x{-}y{-}y{-}y$ was used in the presented study. The first symbol denotes the polarization of the π/2 pulse and the last three are the polarizations of the π pulses. It is possible to find the best timing of the pulses for general conditions but it may not be possible to reduce the effect to zero. In that case, more RF pulses should be used. In the case of a strong signal or short transverse relaxation time the alternative is to use stimulated echo as described in [9]. For instance, in the condition II 13-interval pulse sequence the parameters describing the influence of the background gradient are $c_s = 6.2$ and $c_{as} = 0.5$ making this sequence even less sensitive to the background gradient.

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