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The anomalous effect of surface diffusion on the nuclear magnetic resonance signal in restricted geometry

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Abstract

Anisotropy of diffusion properties in a specimen plays a key role in numerous applications of nuclear magnetic resonance (NMR) imaging, like non-invasive tracking of fibers in the central nervous system. We suggest that contrasting fiber structures with certain diameters could be improved if second-order effects are taken into account. We introduce a procedure consisting of two standard diffusion NMR experiments differing in their gradient pulse characteristics. These two echo signals will be called the background and principal signals. We show that the difference obtained by subtracting one echo signal from the other has either typical or anomalous properties. In the typical case, as the duration of the gradient pulse in the second experiment is set to smaller and smaller values, the difference from the background echo signal tends toward its maximum. In contrast, in the anomalous case the difference between the background and the principal signals has a maximum at a certain nonzero duration of the pulse in the second experiment. This critical duration is determined by different characteristics, including the diameters of fibers. For this anomalous effect to take place the fast surface diffusion channel coupled to the surrounding media is required. The diffusion of magnetic molecules along the surface of restricted media and the coupling of the surface and the bulk translational motions can strongly modify the echo attenuation NMR signal. The origin of this strong anomalous effect is the change of the symmetry of the lowest diffusion eigenmode of the system. We illustrate the effect of surface diffusion for a cylindrically symmetric system and describe the experimental conditions under which the anomalous behavior of the echo signals can be observed.

1. Introduction

In the last few decades nuclear magnetic resonance (NMR) [1] has been a topic of extensive research, having broad applications in physics, chemistry, neuroscience and medicine. NMR measurement provides a very effective method to study the spin properties of a system and extract information about spin distribution and interactions in the system. There are two main applications of NMR: magnetic resonance spectroscopy and magnetic resonance imaging (MRI) [2]. Magnetic resonance imaging allows one to determine the nuclear spin distribution (usually hydrogen atom distribution) and spin relaxation in the spin systems. The imaging is based on the attenuation echo signal upon application of a special magnetic field pulse sequence to the spin system. Depending on the systems and the parameters which are studied, there are different types of MRI. Namely, functional MRI [3], which is used to measure brain activity, diffusive MRI [4], which addresses spin diffusion; and others.

In the present paper we address the problem of spin diffusion in NMR imaging. We consider the case of restricted diffusion with molecular motion in a restricted geometry. Experimentally restricted diffusion is studied by a special method, the magnetic resonance pulsed-gradient method [4], which is based on measurements of a magnetic resonance echo attenuation signal for a special Stejskal–Tanner sequence of magnetic field gradient pulses [5]. There are two mechanisms of suppression of the echo signal in these measurements. The first mechanism is related to spin relaxation processes, and the second mechanism is related to molecular diffusion, which results in dephasing of spins and correspondingly to suppression in the signal. From the strength of the attenuation signal the parameters of molecular diffusion and the geometry of restricted media can be extracted [6–9]. Diffusion MRI and especially its modification, diffusion tensor imaging, in which the diffusion coefficients in different directions are measured, becomes now a very powerful method to produce images of biological tissues, non-invasive animal anatomy studies [10, 11], fiber tracking [7, 12, 13], timely detection of changes of apparent diffusion during such pathologies as stroke [14], and estimation of the response to treatment in brain cancer patients [15]. Magnetic resonance imaging is also widely used to study the properties of nanocrystalline systems, e.g. nanocrystalline ion conductors, where a slow diffusion of Li ions in grain regions and a fast diffusion of ions in interfacial regions affect the Li solid-state NMR signal [16].

The problem of diffusion in heterogeneous biological systems has been extensively studied in the literature in relation to the effective diffusive characteristics of the media, which manifest themselves in the diffusive MRI measurements [17–20]. Different analytical and numerical methods have been employed to find an effective diffusion coefficient of the disordered heterogeneous media consisting of different homogeneous phases. It was shown that the effective diffusion coefficient depends on the microscopic diffusion coefficients, on the volume fractions of the different phases and their permeability. In the present paper we study not the effective diffusion properties of the media, but the manifestation of the intrinsic heterogeneous structure of the system in the diffusive MRI signal. Namely, we show below that the echo signal in the pulsed-gradient measurements can be strongly affected by *molecular surface diffusion* along the boundaries of restricted media. The presence of a surface channel can modify the signal not only quantitatively but also qualitatively. The origin of this modification is the following. The echo signal from diffusive media can be analytically expressed in terms of eigenmodes of the diffusive operator [21]. Such a signal usually depends on the lowest eigenmodes [21, 22]. An interesting property of restricted media with surface diffusion is that the surface diffusion along the boundary of the system can rearrange the order of the eigenvalues of the diffusion operator. This rearrangement can change the symmetry of the second lowest eigenmode, which produces new qualitative features of the echo signal. Such a property of the surface diffusion can be used to extract from the echo signal the parameters of the surface channel, such as a surface diffusion coefficient. Below we define the surface channel as a narrow layer near the boundary surface of the diffusive medium. The diffusion coefficient within the narrow surface layer is different from the diffusion coefficient in the volume.

In the present paper we consider a cylindrically symmetric restricted geometry with spin diffusion both inside the medium and along the boundary surface of the medium. The restricted medium in the shape of a cylinder is the simplest structure for which the anomalous effects of surface diffusion can be observed and, to some extent, analytical analysis of the system can be done. The similar anomalous effects should also be expected for spherically symmetric media and for restricted media of other shapes. The restricted medium

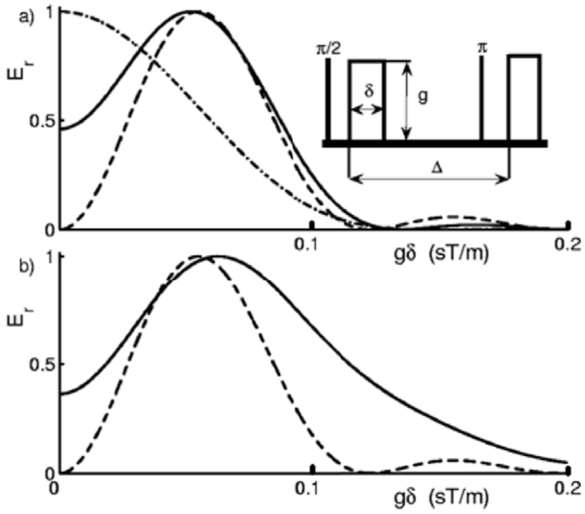

Figure 1. (a) The residual echo signal as a function of $g\delta$ is shown for $\alpha_R = 200$, $\alpha_\Delta = 0.667$ and different values of α_D: 1.2 (dashed line), 9 (solid line) and 20 (dashed–dotted line). These values correspond to $D_s = 1 \times 10^{-7}$ m^2 s^{-1} (dashed–dotted line), $D_s = 4.5 \times 10^{-8}$ m^2 s^{-1} (solid line) and $D_s = 6 \times 10^{-9}$ m^2 s^{-1} (dashed line) and $D_v = 5 \times 10^{-9}$ m^2 s^{-1}, $\delta = 0.1$ ms, $\Delta = 30$ ms, $R = 10$ μm. Inset: schematic illustration of Stejskal–Tanner gradient pulse sequence. (b) The residual echo signal as a function of $g\delta$ is shown for $\alpha_R = 200$ and different values of α_Δ: 0.667 (dashed line) and 20 (solid line). These values correspond to $D_s = 6 \times 10^{-9}$ m^2 s^{-1}, $D_v = 5 \times 10^{-9}$ m^2 s^{-1}, $\delta = 0.1$ ms, $R = 10$ μm and $\tau_v = \tau_s = 0.1$ ms.

with cylindrical symmetry could be considered as a model of fibers in biological systems: for example, axons in the white matter of the live lamprey spinal cord [11]. This model can also be applied to solid-state systems, e.g. nanocrystalline ion conductors [16]. In all these cases our model consists of two regions: (i) the region in the bulk of the restricted media, inside the cylinder, and (ii) the boundary surface layer. We introduce the diffusion of the molecules in both of the regions, i.e. volume and surface diffusions with different diffusion coefficients. We also consider the coupling between these regions through the exchange of molecules between two regions. This system can be described by the model (1)–(10) (section 2). Our analysis shows a novel anomalous effect described in section 3.

2. Main system of equations

Diffusion NMR measurements are based on the Stejskal–Tanner pulse sequence [5], which is shown schematically in the inset in figure 1(a). It consists of $\pi/2$ and π radio-frequency pulses, and two rectangular magnetic gradient pulses of duration δ and magnitude g. The time interval between the gradient pulses is Δ. The echo signal after these pulses is measured. There are different approximations used to find the expression for the echo signal. One of them, which is explored in the present paper, is based on the narrow-gradient pulse approximation [4, 23–26]. Within this approximation we assume that the gradient pulses are so narrow, i.e. δ is so small, that there is no diffusion of molecules during time δ. In this case the echo signal can be expressed in the following form:

$$E(q,\Delta)=\int\int \mathrm{d}\vec{r}\,\mathrm{d}\vec{r}_1\,\rho(\vec{r})P(\vec{r},\vec{r}_1,\Delta)\mathrm{e}^{\mathrm{i}2\pi\vec{q}(\vec{r}-\vec{r}_1)}, \quad (1)$$

where $\rho(\vec{r})$ is the initial molecular density distribution, $\vec{q}=\gamma\vec{g}\delta/2\pi$, γ is the nuclear gyromagnetic ratio, the echo signal is normalized, $E(0,\Delta)=1$, and

$$P(\vec{r},\vec{r}_1,\Delta)=\sum_n \psi_n(\vec{r})\psi_n(\vec{r}_1)\mathrm{e}^{-\lambda_n\Delta} \quad (2)$$

is a conditional probability that a molecule diffuses from point $\vec{r}$ to point $\vec{r}_1$ over the time interval Δ. Here $\psi_n(\vec{r})$ and λ_n are the nth eigenfunction and eigenvalue of the diffusion operator within the restricted media. The conditional probability describes the property of the diffusive media only and does not depend on the presence of a magnetic field and the magnetic gradient pulses. In expression (1) the information about the gradient pulses is introduced through the exponent $\exp[\mathrm{i}2\pi\vec{q}(\vec{r}-\vec{r}_1)]$. From equations (1) and (2) we can see that, at a small time interval between the gradient pulses, Δ, the main contribution to the echo signal comes from the eigenmode with the lowest eigenvalue.

The surface diffusion channel can strongly modify the symmetry and other properties of the lowest eigenfunctions. The change in the symmetry of the eigenmodes can modify the echo response from the restricted media. To illustrate the effect of surface diffusion on the echo signal in pulsed-gradient experiments we consider a cylindrically symmetric system, e.g. cylindrical pore or cylindrical fiber. The radius of the cylinder is R. We assume that there is a surface diffusion channel at the surface of the cylinder. In general the surface diffusion coefficient in the surface channel is different from the volume diffusion coefficient.

The molecular diffusion in the system with the surface diffusion channel is described by the Torrey–Bloch-type equations [27] combined with surface–bulk coupling equations [28]

$$\frac{\partial c(\vec{r},t)}{\partial t}=D_V\Delta_r c(\vec{r},t) \quad (3)$$

$$\left.\frac{\partial u(\vec{r},t)}{\partial t}\right|_{r=R}=[D_S\Delta_s u(\vec{r},t)-D_V\nabla_n c(\vec{r},t)]|_{r=R} \quad (4)$$

$$-D_V\nabla_n c(\vec{r},t)|_{r=R}=\left.\left[\frac{ac(\vec{r},t)}{\tau_v}-\frac{u(\vec{r},t)}{\tau_s}\right]\right|_{r=R}, \quad (5)$$

where $c(\vec{r},t)$ and $u(\vec{r},t)$ are the volume and surface densities of the molecules (magnetic moments), D_V and D_S are the volume and surface diffusion coefficients, Δ_s is the surface Laplacian and ∇_n is the gradient along the normal to the boundary. The second term on the rhs of equation (4) is a standard diffusion term, while the first term plays the role of a source in the surface diffusion equation. This source is due to diffusion of the molecules from the volume to the surface. Equation (5) describes a microscopic coupling of the volume and surface diffusion processes. This coupling occurs through a narrow transition region of width a [28]. The width of the transition region is of the order of an elementary diffusion hopping length, i.e. free path across the surface channel. Within the transition region the molecules in the volume are absorbed by the surface at a rate of $1/\tau_v$, while the molecules at the surface are leaving the surface at a rate of $1/\tau_s$. Therefore equation (5) is a detailed balance equation within the transition region.

The eigenmodes of the system of equations (3)–(5) have the following form: $c(\vec{r},t)=\mathrm{e}^{-\lambda_m^2 t}\mathrm{e}^{\mathrm{i}m\phi}c_0(\rho)$ and $u=\mathrm{e}^{-\lambda_m^2 t}\mathrm{e}^{\mathrm{i}m\phi}u_0$. Here m is an integer (angular momentum), ρ and ϕ are polar coordinates, λ_m^2 is a corresponding eigenvalue and u_0 is a constant. Upon substituting these expressions in equations (3)–(5) we derive the equation for eigenvalues of the diffusion problem:

$$\beta_m J_{m-1}(\beta_m)-[m-A_m(\beta_m)]J_m(\beta_m)=0, \quad (6)$$

where J_m is a Bessel function of the mth order, $\beta_m=\lambda_m R/\sqrt{D_V}$ and A_m is given by the expression

$$A_m(\beta)=\frac{\alpha_R}{1-\frac{\alpha_R(a/R)}{\alpha_\tau(\beta^2-m^2\alpha_D)}}. \quad (7)$$

Here we introduce the following dimensionless parameters:

$$\alpha_R=\frac{R^2}{\tau_v D_V},\qquad \alpha_\tau=\frac{\tau_s}{\tau_v},\qquad \alpha_D=\frac{D_S}{D_V}. \quad (8)$$

These parameters characterize the system and determine the properties of the echo signal. For each value of m, equation (6) has an infinite number of solutions, i.e. eigenvalues, which can be labeled by index k. The corresponding eigenfunctions are Bessel functions, $J_m(\beta_{m,k}\rho/R)$. With the known set of eigenvalues and eigenfunctions of diffusion problem (3)–(5) we can find the echo signal from equation (1). The final result has the form [26]

$$E(Q,\Delta)=\sum_{m,k}\mathrm{e}^{(-\beta_{mk}^2/\alpha_\Delta)}\frac{(1+\delta_{m,0})\beta_{mk}^2}{[A_m(\beta_{mk})]^2+\beta_{mk}^2-m^2}\times\frac{\left[Q\frac{\mathrm{d}J_m(Q)}{\mathrm{d}Q}+A_m(\beta_{mk})J_m(Q)\right]^2}{(Q^2-\beta_{mk}^2)^2}, \quad (9)$$

where $\alpha_\Delta=\frac{R^2}{D_V\Delta}$ and $Q=qR$.

We can see from equation (9) that contributions of different eigenfunctions are determined by exponential activation factors $\mathrm{e}^{(-\beta_{mk}^2/\alpha_\Delta)}$. At small α_Δ, i.e. at large Δ, the main contribution to an echo signal comes from the eigenfunction with the smallest eigenvalue. Usually the lowest eigenfunction has the highest symmetry. In the present problem the highest symmetry means that the function has $m=0$. From equation (6) we can see that the lowest eigenvalue is always $\beta=0$, which is realized at $m=0$. The corresponding eigenfunction is constant over the whole restricted region and is not affected by the presence of the surface diffusion channel. Then the contribution of the lowest eigenmode ($\beta=0$) forms the background echo signal, which is proportional to $[J_1(Q)/Q]^2$. In dimensionless units, $Q=qR$, the background signal does not depend on parameters of the restricted media. Therefore we can subtract the background value from the echo signal (9) and obtain the residual signal, $E_r(Q)=E(Q)-E_{\beta=0}(Q)$, which has information about the structure and parameters of restricted media with the surface diffusion channel. Therefore, for the residual signal we obtain the following expression:

$$E_r(Q,\Delta) = \sum_{m,k,\beta_{m,k}\neq 0} e^{(-\beta_{mk}^2/\alpha_\Delta)} \frac{(1+\delta_{m,0})\beta_{mk}^2}{[A_m(\beta_{mk})]^2+\beta_{mk}^2-m^2} \times \frac{[Q\frac{dJ_m(Q)}{dQ}+A_m(\beta_{mk})J_m(Q)]^2}{(Q^2-\beta_{mk}^2)^2}. \quad (10)$$

Below we present the analysis of the residual echo signal, E_r, and show that the surface diffusion channel can modify this signal qualitatively. This is due to the fact that surface diffusion can rearrange the relative contributions into the residual echo signal of the eigenmodes with $m = 0$ and 1.

3. Results and discussion

As we can see from expression (10) the term with $m = 0$ is proportional to the Bessel function of zeroth order, while all other terms, i.e. $m \neq 0$, are proportional to higher-order Bessel functions. This fact determines a special dependence of these terms on parameter Q. Namely, the $m = 0$ term in equation (10) has its maximum at $Q = 0$, while all other terms have their maximum at $Q > 0$ and they are zero at $Q = 0$. This property can be used to determine experimentally if the lowest eigenfunction has $m = 0$ or $m > 0$ (in the residual signal we do not need to consider the eigenfunction with $\beta = 0$, which always has $m = 0$).

The order of eigenvalues depends on the values of parameters α_R, α_τ and α_D, and strongly affects the residual echo signal. To study the echo signal in the present system we calculate numerically the eigenvalues and corresponding eigenfunctions from equation (6) for different values of parameters of the system and then calculate the residual echo signal, $E_r(Q)$, at various values of α_Δ. Below we assume that the parameter α_τ equals 1, i.e. $\tau_s = \tau_v$. Then the property of the system depends only on two dimensionless parameters, α_R and α_D. Depending on the values of these parameters there are two different types of behavior of $E_r(Q)$. (i) In the first type (type (T)) the lowest eigenvalue corresponds to $m = 0$. The residual echo signal as a function of Q has maximum at $Q = 0$ and then decreases with some oscillations. This is a typical dependence observed in many restricted diffusion experiments. (ii) In the second type (type (A)) the lowest eigenvalue corresponds to $m = 1$. The residual echo signal has zero value at $Q = 0$, then increases and reaches the maximum at some finite value of Q. These dependences can be observed only at small values of α_Δ, when only the function with the lowest eigenvalue contributes to the echo signal. At higher values of α_Δ there is a mixture of different contributions to the echo signal. Therefore, type T behavior is observed when $\beta_{0,2} < \beta_{1,1}$, while type A behavior is observed if $\beta_{0,2} > \beta_{1,1}$.

In figure 1(a) we present the results of calculations, which illustrate the characteristic dependences of the residual echo signal in the system with surface diffusion. The results are shown for fixed values of $\alpha_R = 200$ and $\alpha_\Delta = 0.667$, and different values of $\alpha_D = 1.2$, 9 and 20. With increasing α_D we observe the transition from anomalous regime A to typical regime T. Due to a finite value of α_Δ in the intermediate region we have a mixture of two dependences A and T.

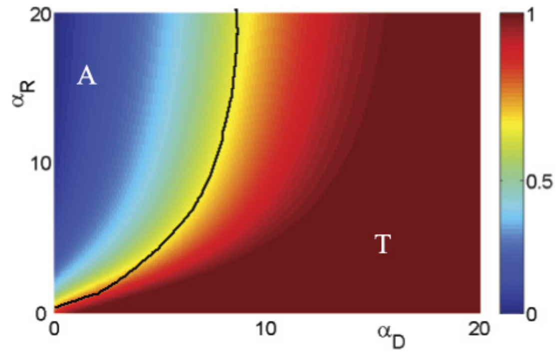

Figure 2. A normalized value of a residual echo signal at $Q = 0$, i.e. the ratio $E_r(0)/E_{r,max}$, is shown by different colors in the α_R–α_D plane. The parameter α_Δ is 3. The boundary between two different domains, A and T, is shown by a solid line. Domains A and T are determined by the condition: $\beta_{0,2} < \beta_{1,1}$ (domain A) and $\beta_{0,2} > \beta_{1,1}$ (domain T).

(This figure is in colour only in the electronic version)

The results, shown in figure 1(b), illustrate the transformation of the anomalous signal with the increasing parameter α_Δ. The parameters $\alpha_R = 200$ and $\alpha_D = 1.2$ in figure 1(b) correspond to anomalous regime A. Therefore at small $\alpha_\Delta = 0.667$ we have a behavior corresponding to the eigenmode with $m = 1$, i.e. the residual echo signal is zero at $Q = 0$ and has a maximum at some finite value of Q. With α_Δ increasing ($\alpha_\Delta = 20$), there is a mixture of terms corresponding to eigenmodes with higher eigenvalues. Such a mixture results in behavior similar to case T, when the echo signal has a finite value at $Q = 0$ and its maximum value is reached near $Q = 0$.

The domains of parameters within which we have type T or type A behavior are determined from the solution of equation (6). In domain T we have $\beta_{0,2} < \beta_{1,1}$, while domain A is characterized by a relation $\beta_{0,2} > \beta_{1,1}$. In figure 2 the boundary between two domains in a plane α_R–α_D is shown by a solid line. We can see from this figure that anomalous behavior, i.e. A behavior, can be observed only at relatively slow surface diffusion, i.e. at small values of α_D. At a large value of parameter α_R domain A is determined by an asymptotic relation $\alpha_D \lesssim 9$, i.e. $D_S \lesssim 9D_V$.

The parameter α_Δ in equation (10) can be considered as an effective 'temperature', which controls the mixture of terms, corresponding to different eigenmodes. Therefore at large values of α_Δ the echo signal is determined by the mixture of the contributions of a few modes with the lowest eigenvalues. The anomalous dependence of the signal on parameter Q can be described by the ratio of $E_r(Q = 0)$ and the maximal value of $E_r(Q)$: $\phi = E_r(0)/E_{r,max}$. At a very small α_Δ this ratio is 0 in domain A and 1 in domain T. At a finite value of α_Δ there is a smooth transition from $\phi = 0$ to 1. This property is illustrated in figure 2, in which the ratio ϕ is shown at $\alpha_\Delta = 3.0$.

The anomalous behavior can be achieved only under favorable coupling between volume and surface diffusions, $\alpha_\tau \sim 1$. Under this condition there is a dependence of the

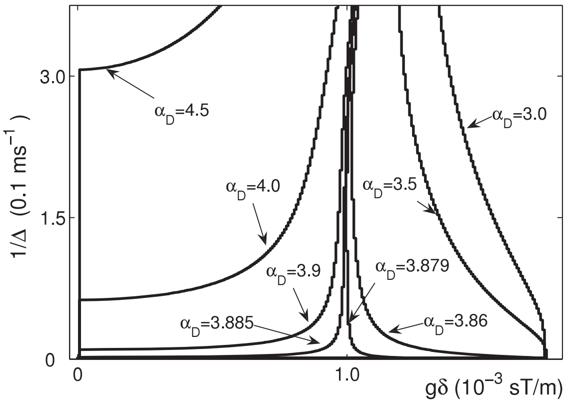

Figure 3. The position of the maxima of the echo signal, $E_{\mathrm{r,max}}$, is shown in the $1/\Delta$–$g\delta$ plane for different values of α_D. Here $\alpha_R = 2$ and $\alpha_\tau = 1$.

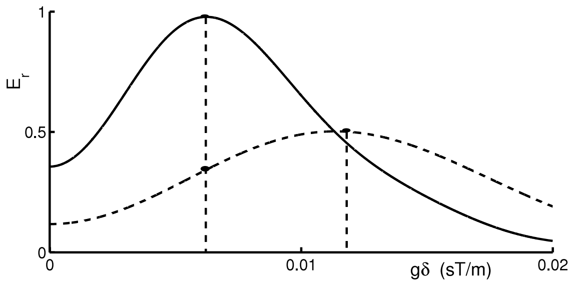

Figure 4. The residual echo signal is shown for two cylinders with radii $R = 5\ \mu$m (dashed line) and $R = 10\ \mu$m (solid line). Here $D_{\mathrm{V}} = 5 \times 10^{-9}$ m^2 s^{-1} and $D_{\mathrm{S}} = 6 \times 10^{-9}$ m^2 s^{-1}, $\tau_{\mathrm{v}} = \tau_{\mathrm{s}} = 0.1$ ms and $\Delta = 1$ ms.

coefficient $A_m(\beta)$ on the parameter m, which results in the possibility of reordering the eigenvalues. If $\alpha_\tau \gg 1$, i.e. $\tau_{\mathrm{s}} \gg \tau_{\mathrm{v}}$, then we have only absorption of the molecules by the surface. In this case the coefficient $A_m(\beta)$ has a weak dependence on m which leads to T-type behavior only. In the case of surface absorption the boundary conditions take the form $D_{\mathrm{V}}\nabla_{\mathrm{n}}c = \rho c$, where ρ is the surface relaxivity [26]. The system with just the surface absorption has been studied extensively in the literature [26, 29–31].

We can also characterize the anomalous behavior of the echo signal by the value of Q at which the residual echo signal, E_{r}, has a maximum, $E_{\mathrm{r,max}} = E_{\mathrm{r}}(Q = Q_{\mathrm{max}})$. To illustrate the appearance of anomalous dependence in realistic systems, in figure 3 we show the position of the maxima, Q_{max}, in a $g\delta$–$(1/\Delta)$ plane for different values of parameter α_D and for a fixed value of $\alpha_R = 2$. For typical dependence the maximum is at $g\delta = 0$, while for anomalous dependence the maximum is at $g\delta > 0$. We clearly see the transition from T dependence at small α_D to A dependence at large α_D. Here the critical value of $\alpha_D \approx 3.88$ determines the boundary between these two dependences.

One of the applications of the above results would be the possibility of tuning the residual echo signal by varying the magnitude of the gradient pulse, g. Under the optimal value of g the residual echo signal has a maximum value. The value of optimal g depends on the size of the restricted media. The effect of the tuning of the echo signal by varying the gradient

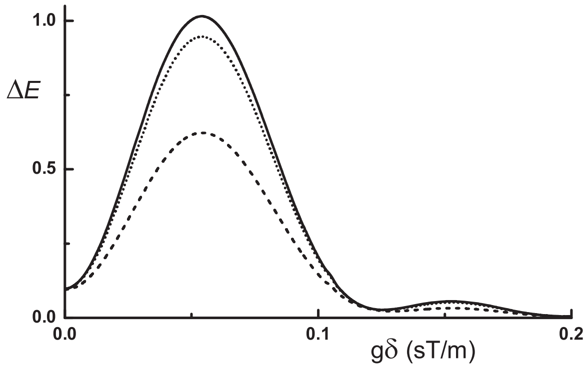

Figure 5. The difference $\Delta E(Q, \Delta_1, \Delta_2)$ (see equations (11) and (12)) is shown as a function of $g\delta$ at $\alpha_{\Delta_1} = 2.0$ and different values of α_{Δ_2}: $\alpha_{\Delta_2} = 0.0$ (solid line), $\alpha_{\Delta_2} = 0.5$ (dotted line) and $\alpha_{\Delta_2} = 1.0$ (dashed line). The other parameters are $D_{\mathrm{s}} = 6 \times 10^{-9}$ m^2 s^{-1}, $D_{\mathrm{v}} = 5 \times 10^{-9}$ m^2 s^{-1}, $R = 10\ \mu$m and $\tau_{\mathrm{v}} = \tau_{\mathrm{s}} = 0.1$ ms. At $\alpha_{\Delta_2} = 0.0$ the difference $\Delta E(Q, \Delta_1, \Delta_2)$ is equal to the residual echo signal.

pulse, g, is illustrated in figure 4 for a system of two cylinders with radii of 5 and 10 μm. We can see from the figure that, if the gradient $g\delta \approx 0.012$ s T m^{-1} is applied to a system, then only the residual echo signal from the cylinder of radius 5 μm is at maximum. If we tune the gradient pulse and apply $g\delta \approx 0.007$ s T m^{-1} then we can increase the residual echo signal from the cylinder of radius 10 μm by almost twice as much.

The residual echo signal discussed above is obtained by subtracting the background value from the original echo signal. The background contribution to the echo signal corresponds to $\beta = 0$ and therefore it does not depend on the values of Δ, i.e. α_Δ. This fact can used to realize experimentally the subtraction of the background contribution from the echo signal. Namely, the residual echo signal can be obtained experimentally as the difference between two echo signals with different values of α_Δ. From equation (9) we obtain that the difference

$$\Delta E(Q) = E(Q, \Delta_1) - E(Q, \Delta_2) \tag{11}$$

has the following form:

$$\Delta E(Q, \Delta_1, \Delta_2) = \sum_{m,k,\beta_{m,k}\neq 0} [\mathrm{e}^{(-\beta_{mk}^2/\alpha_{\Delta_1})} - \mathrm{e}^{(-\beta_{mk}^2/\alpha_{\Delta_2})}] \times \frac{(1+\delta_{m,0})\beta_{mk}^2}{[A_m(\beta_{mk})]^2 + \beta_{mk}^2 - m^2} \times \frac{[Q\frac{\mathrm{d}J_m(Q)}{\mathrm{d}Q} + A_m(\beta_{mk})J_m(Q)]^2}{(Q^2 - \beta_{mk}^2)^2}. \tag{12}$$

If the parameter α_{Δ_2} is zero then the difference $\Delta E(Q, \Delta_1, \Delta_2)$ is exactly equal to the residual echo signal, i.e. $\Delta E(Q, \Delta_1, \Delta_2) = E_{\mathrm{r}}(Q, \Delta_1)$. Under finite but small values of α_{Δ_2} the difference is a good approximation to the residual echo signal. In figure 5 we show the difference $\Delta E(Q, \Delta_1, \Delta_2)$ at fixed $\alpha_{\Delta_1} = 0.2$ and different values of $\alpha_{\Delta_2} = 0$, 0.5 and 1. As we mentioned above, at $\alpha_{\Delta_2} = 0$ the difference $\Delta E(Q, \Delta_1, \Delta_2)$ is equal to the residual echo signal, $E_{\mathrm{r}}(Q, \Delta_1)$. At finite values of α_{Δ_2} we can see a deviation from E_{r}. The deviation is less than 6% at $\alpha_{\Delta_2} = 0.5$ and increases with increasing the parameter α_{Δ_2}. Therefore, if α_{Δ_2} is small then the difference

ΔE can be considered as a good approximation of the residual echo signal.

In the above approach we did not take into account the bulk and surface spin relaxation, which enter into the standard Torrey–Bloch equations through the term of the form $-\mu c$. This term introduces an additional suppression of the echo signal by a factor of $\exp(-t\mu)$. Then the condition in which the diffusive attenuation of the echo signal can be observed is that the time Δ should be less than μ^{-1}. If $\mu^{-1} < \Delta$ then the echo signal is suppressed, but the anomalous effect can still be observed. The condition of suppression of the anomalous effect is that the relaxation time μ^{-1} should be greater than the typical diffusion time, $R^2/D \sim 0.01$ s.

The analysis of the MRI echo signal was based on a narrow pulse approximation, i.e. the duration, δ, of the gradient pulse is assumed to be so small that diffusion does not occur during time δ. For a cylindrical sample of radius R this condition means that $\delta \ll R^2/D_v$. For example, if $R = 10\ \mu$m and $D_v \sim 10^{-8}\ \mathrm{m^2\ s^{-1}}$ then $\delta \ll 0.01$ s. In terms of the amplitude, g, of the gradient pulse this condition means $g \gg 0.1\ \mathrm{T\ cm^{-1}}$. Such conditions can be achieved in experimental systems, for example, in [11], where the pulse duration is 6 ms.

It is a challenge to measure the ratio of surface and volume diffusion coefficients in leaving tissues directly. What has been measured in the diffusion MRI is an average diffusion coefficient, but not individual coefficients of surface and volume diffusions. The approach described here can also be used to estimate this ratio by comparing positions of the experimentally obtained maximum of the anomalous signal to the numerically obtained one (figure 3).

In conclusion, we have shown a strong qualitative effect of the surface diffusion channel on the echo attenuation signal from restricted geometry. In some range of parameters of the system the residual echo signal, which is obtained by subtracting the background value, can have anomalous behavior, which means that the echo signal has a maximum value at some finite value of the magnitude, g, of the gradient pulses. This fact can be used to enhance the accuracy of the measurements by studying the echo signal around the maximum value. Also, the method allows one to enhance the contrast of the MRI image of the fibers with a particular diameter. The anomalous dependence can also be used to extract the information about the surface diffusion channel. We have discussed only the case of the media consisting of parallel cylindrical fibers, e.g. white matter of the brain [11]. The same qualitative results are also valid for media consisting of spheres. The effect described here could be used for tuning MRI measurements to trace fibers with particular characteristic diameters or for timely detection of changes in the diffusion coefficients and fiber diameters.

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