

# NMR molecular diffusion in the presence of distant dipolar field interactions

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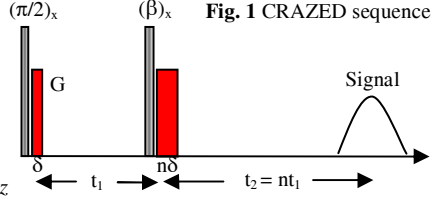
**Introduction:** Intermolecular multiple quantum coherences are made observable by the action of distant dipolar fields (DDF) and have found application in medical imaging [1, 2]. However, some aspects of the signal attenuation are poorly understood when both self-diffusion and DDF interactions occur [3, 4, 5, 6]. Employing an iterative perturbation procedure, the Bloch-Torrey equations modified to include the DDF can be solved in terms of a power-series expansion where the diffusion and dipolar field terms are treated as integral operators. The results are compared to the complete solution obtained by numerical methods [7] revealing that previously reported calculations [5, 6] for the first order solution can be extended to a broader range of validity. The method allows for experimentally controlling and testing this new range.

**Methods:** In the rotating frame the Bloch-Torrey equations modified to include the distant dipolar field are given by:  $(\frac{\pi}{2})_x$   $(\beta)_x$  **Fig. 1** CRAZED sequence

$$(1) \frac{\partial}{\partial t} M_z(r, t) = D \nabla^2 M_z \quad \text{and} \quad \frac{\partial}{\partial t} M^+(r, t) = D \nabla^2 M^+ + i\gamma B_{dc}(r, t) M(r, t)^+, \quad \text{with} \quad M^+ = M_x + iM_y$$

Following the pulse sequence of Fig. 1 and initially neglecting the effect of the DDF the solution of Eq.(1) with G along  $B_0z$  for  $t > t_1$  yields:

$$(2) M_0^+(r, t) = M_0^+(r, t_1) \left[ \sin^2 \frac{\beta}{2} e^{-(n-1)^2 D k^2 t} e^{-i(n-1)kz} - \cos^2 \frac{\beta}{2} e^{-(n+1)^2 D k^2 t} e^{-i(n+1)kz} \right] \quad \text{and} \quad M_z(r, t) = -M_0 \sin \beta e^{-Dk^2 t} \cos kz$$



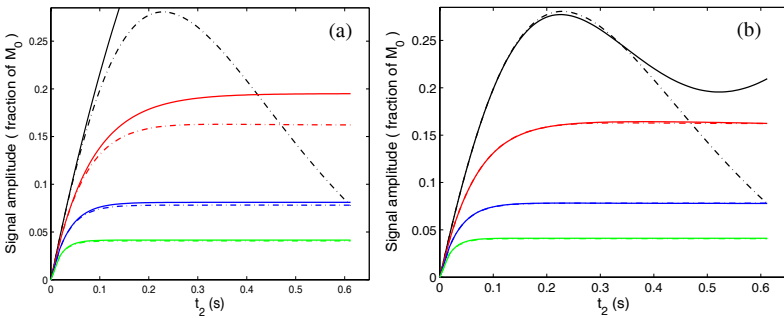
The parameter  $k = \gamma G \delta$  denotes the wave vector of spatial modulation magnetization caused by the magnetic field gradient, where  $\gamma$  is the gyromagnetic ratio, G is the gradient amplitude with duration  $\delta$  (Effects of relaxation are ignored in this analysis, but can be included without difficulty). Eq.(1) can be recast in the following form

$$(3) M^+(r, t) = M^+(r, 0) + [\mathbf{S} + \mathbf{T}] M^+(r, t), \quad \text{where} \quad \mathbf{S} M^+(r, t) = D \int_0^t \nabla^2 M^+(r, t') dt' \quad \text{and} \quad \mathbf{T} M^+(r, t) = i\gamma \int_0^t B_{dc}(r, t') M^+(r, t') dt'$$

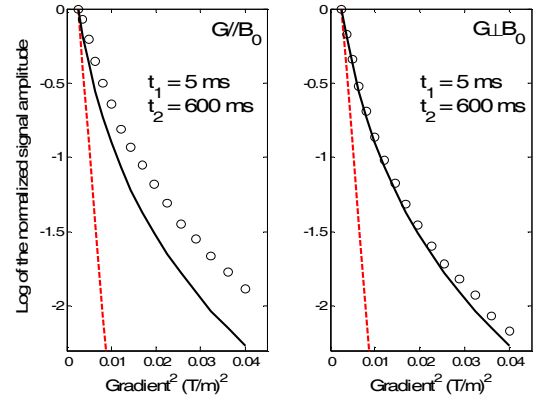
In a regime where  $kL \gg 1$  (L is the characteristic distance of the sample), the DDF immediately after the  $\beta$  pulse is  $B_{dc}(r, t) = \mu_0 M_z(r, t) = -\mu_0 M_0 e^{-Dk^2 t} \sin \beta \cos kz$ . The results in Eq.(2) considering only diffusion will be used as a "seed", i.e., an initial tentative solution for  $M^+(r, t)$  in the right side of Eq.(3). The new solution, now including the dipolar term, is again reinserted into the right side of Eq.(3) producing a series expansion. This iteration process produces the following sequence:

$$\begin{aligned} M_1^+(r, t) &= M_0^+(r, 0) + [\mathbf{S} + \mathbf{T}] M_0^+(r, t) = [\mathbf{I} + \mathbf{T}] M_0^+(r, t); \\ M_2^+(r, t) &= M_1^+(r, 0) + [\mathbf{S} + \mathbf{T}] M_1^+(r, t) = [\mathbf{I} + \mathbf{T} + \mathbf{S}\mathbf{T} + \mathbf{T}^2] M_0^+(r, t); \\ &\vdots \\ M_\infty^+(r, t) &= [\mathbf{I} + \underbrace{(\dots + \mathbf{S}^2\mathbf{T} + \mathbf{S}\mathbf{T}) + \mathbf{T}}_{1^{\text{st}} \text{ order in } \mathbf{T}} + \underbrace{(\dots + (\mathbf{S}^2\mathbf{T}^2 + \mathbf{S}\mathbf{T}\mathbf{S}\mathbf{T} + \mathbf{T}\mathbf{S}^2\mathbf{T}) + (\mathbf{S}\mathbf{T}^2 + \mathbf{T}\mathbf{S}\mathbf{T}) + \mathbf{T}^2)}_{2^{\text{nd}} \text{ order in } \mathbf{T}} + \dots] M_0^+(r, t). \end{aligned}$$

**Results and discussion:** Fig. 2(a) shows that as  $1/Dk^2$  decreases the first order solution reproduces quite well the results of the complete numerical solution. The first order solution turns out to be a good approximation for  $\tau_d Dk^2 < 1$  where  $\tau_d = 1/\gamma\mu_0 M_0$  is the characteristic dipolar time. This is a much less demanding restriction for the use of this solution [5, 6]. Also important to mention is the remarkable signal insensitivity to diffusion observed for long  $t_2$  [8, 9]. In addition, for  $t_2 < \tau_d$ , which is the usual regime for in vivo applications, the first order solution shows good agreement with the numerical solution irrespective of the diffusion attenuation. Fig. 2(b) shows the result of considering higher order terms in the expansion. Fig. 3 shows that the first order solution range of validity can be controlled by, e.g., changing the orientation of the correlation gradients. The curves also show that the NMR signal in the presence of the DDF (interval  $t_2$ ) is in fact less sensitive than that obtained by the conventional pulsed-gradient spin-echo (PGSE) method.



**Fig.2** DDF signal as a function of acquisition time  $t_2$  for several gradient amplitudes. From top to bottom:  $1/Dk^2 = 647, 161, 72$  and  $40$  ms ( $\beta = 90^\circ, T_1 \approx T_2 \rightarrow \infty, \tau_d \approx 98$  ms). The dashed lines are obtained from the numerical solution of Eq.1 and the solid lines are analytical solutions extracted from the iterative method. On the left, (a), the solid lines are first order approximate solution and on the right, (b), the solution includes a few terms of the next order contribution. The discrepancy in the first curve (black solid line) in (b) indicates that for longer intervals more terms are necessary to improve the fitting. For more realistic relaxation times, this approximation is sufficient to reproduce all results.



**Fig.3** Experiments (circles) conducted at 9.4T where the DDF signal (echo peaks) obtained from doped water is recorded as a function of gradient intensity for two gradient orientations. Solid (black) lines represent the first order solution. The dashed (red) lines show PGSE curves for  $\Delta \approx t_2$ .

**References:** [1] W.S. Warren et al., Science **281**, 247 (1998); [2] A. Schäfer et al., Magn. Reson. Medicine **53**, 1402 (2005); [3] P. Robyr and R. Bowtell, J. Magn. Reson. A **121**, 206 (1996); [4] I. Ardelean and R. Kimmich, J. Chem. Phys. **112**, 5275 (2000); [5] C. Ramanathan and R. Bowtell, J. Chem. Phys. **114**, 10854 (2001); [6] M. Engelsberg and W. Barros, J. Chem. Phys. **122**, 034501 (2005); [7] J. Jeener, Concepts of Magn. Reson. **14**, 79 (2002); [8] W. Barros, J. C. Gore, and D. F. Gochberg, J. Magn. Res. **178**, 164 (2006); [9] W. Barros and D. F. Gochberg, Chem. Phys. Lett. **431**, 174 (2006).