Accounting for free and restricted diffusion processes in single- and double-PFG experiments using a novel bi-compartmental phantom

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Introduction

Studies of restricted diffusion have been conducted for decades using single pulsed field gradients (s-PFG) diffusion experiments[1]. In homogenous samples, the diffusion-diffraction oscillations arising from a single population of diffusing species has been observed, and the restricted diffusion profile was used to extract important microstructural features from the specimen[2]. However, systems that are more realistic such as biological tissue and porous media are characterized by compartmentation which may complicate the interpretation of structural features. In many cases, free diffusion and restricted diffusion coexist: for example, when cells are suspended in a medium, diffusion within the cell is restricted, but the medium is diffusing freely within the bulk. Partial volume contribution of cerebrospinal fluid (CSF) to white matter voxels can also be regarded as such a system. Moreover, in crossing fibers, diffusion in the direction parallel to one of the fibers is free, while for the perpendicular fiber it is restricted. The double-PFG (d-PFG) methodology has lately been gaining interest due to their ability to extract small compartmental dimensions even at low q values[3,4]. New theoretical studies offer a new general framework for restricted diffusion in multiple-PFG experiments, and especially for d-PFG[5,6]. Therefore, in this study, we characterized the superposition of restricted and free diffusion both experimentally and theoretically using a novel composite bi-compartmental phantom, in which the "ground-truth" is known *a-priori* using both single and double-PFG methodologies[7]. The findings were also applied to a crossing fibers phantom.

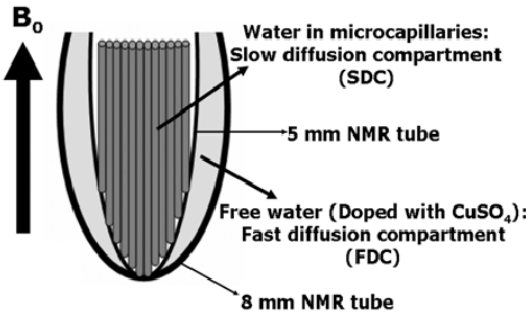

Figure 1. Bi-compartmental phantom

Methods

Figure 1 shows a cartoon of the bi-compartmental model used in this study. Freely diffusing water in the Fast-Diffusion-Compartment (FDC) undergoes Gaussian (free) diffusion while water in the microcapillaries experiences restricted diffusion forming the Slow-Diffusion-Compartment (SDC) of the bi-compartmental phantom. The nominal inner diameter (ID) of the microcapillaries is well defined, and was 10±1 or 19±1 μm in this study. All experiments were performed on an 8.4 T Bruker NMR spectrometer with a micro5 probe capable of producing up to 195 G/cm along the x- y- and z-directions. The effect of varying diffusion periods and varying volume fraction of free/restricted water was studied in both s- and d-PFG experiments. The d-PFG angular experiment[3-7] was also studied using the bi-compartmental phantom.

Results

Figure 2 shows the s-PFG experiment conducted with varying diffusion periods on the bi-compartmental model. Two phenomena can be seen in the different q-regimes. For high q-values, the diffraction patterns from water diffusing in the SDC can be gradually observed. At Δ>100 ms, the diffusion profile doesn't change at high q-values. However, at lower q-values, e.g., q<200 cm^{-1}, the diffusion curve changes dramatically for each value of Δ, and shows increased attenuation of the signal for every value of increasing Δ. The theoretical fitting to the experimental data yielded accurate compartmental dimensions with Δ as low as 50 ms, even prior to the appearance of diffusion-diffraction minima in the E(q) plots. Figures 3A and 3B show the angular d-PFG experiment in the bi-compartmental model at low and high q-values respectively. At the low-q regime, the angular dependence is lost, and the size of the compartment cannot be accurately extracted. However, at higher q-values, the angular dependence is retained, and the accurate size of the compartment is extracted with 0.2 μm sensitivity.

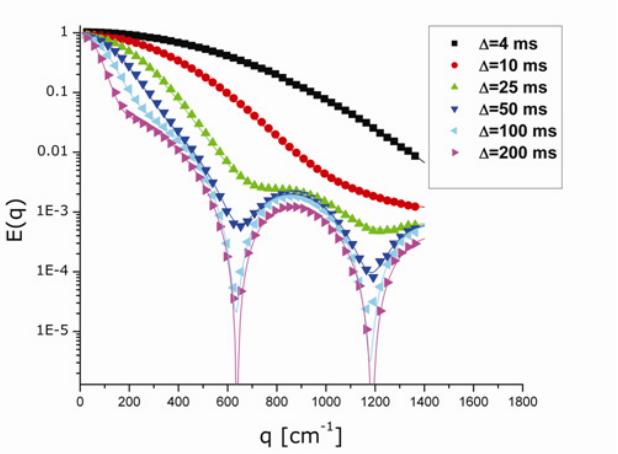

Figure 2. Varying diffusion periods in s-PFG experiments performed on a bi-compartmental phantom consisting of microcapillaries with inner diameter of 19 μm in the SDC and 80 μl of water in the FDC. The gradient duration was δ=2 ms and G_{max}=160 g/cm. Symbols represent experimental data, while the solid lines represent the theoretical fitting to the experimental data.

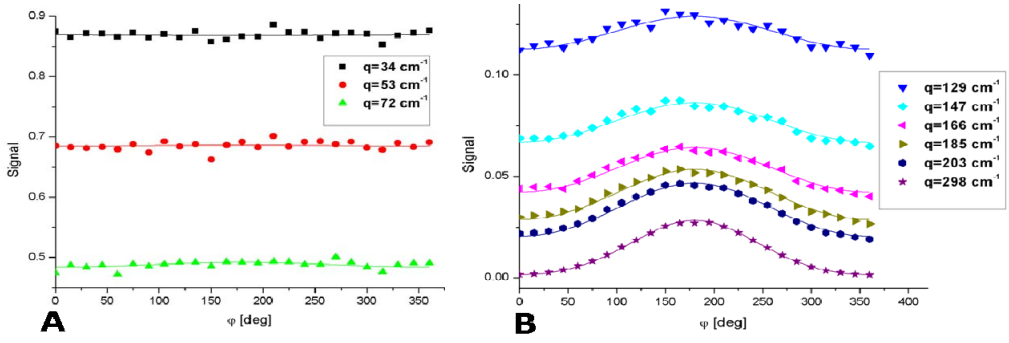

Figure 3. Angular d-PFG experiments performed on a bi-compartmental phantom consisting of microcapillaries with inner diameter of 19 μm in the SDC and 20 μl of water in the FDC. The diffusion periods were sufficiently long to probe the boundaries. Symbols represent experimental data, while the solid lines represent the theoretical fitting to the experimental data.

Conclusions

A phantom in which free diffusion coexists with restricted diffusion was studied using the s-PFG and d-PFG methodologies. We find that the free diffusion mode is prominent at low q-values, and that in this regime, free diffusion masks the microstructural information arising from the restricted compartment. Importantly, microstructural information could be retrieved at higher q-values where the restricted diffusion is accentuated, and the free diffusion is suppressed. This may be of importance both in biological tissues as well as in porous media.

References. [1]. E.O. Stejskal and J. E. Tanner, J. Chem. Phys. 42 (1965) 288-292. [2] P.T. Callaghan et al., Nature 351 (1991) 467-469. [3] E. Özarslan and P.J. Basser, J. Chem. Phys. 128 (2008) 154511. [4] N. Shemesh et al., J. Magn. Reson. 198 (2008) 15-23. [5] E. Özarslan et al., J. Chem. Phys. 130 (2009) 104702. [6] E. Özarslan, J. Magn. Reson. 199 (2009) 56-67. [7]. N. Shemesh et al., J. Magn. Reson. 200 (2009) 214-225.