

MR characterization of compartment shape anisotropy (CSA)

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INTRODUCTION

The orientational dependence of the diffusion-weighted MR signal intensity has been exploited to characterize the integrity and orientation of white-matter pathways in the brain. Anisotropy observed in traditional single pulsed field gradient (single-PFG) acquisitions is primarily a product of the interaction between cellular membranes and diffusing water molecules suggesting the restricting character of the membranes [1]. Thus, such anisotropy is observed when the cells have an elongated structure. Moreover, any incoherence in the orientation of cells leads to a decrease in the observed anisotropy. Consequently, the measured anisotropy in single-PFG scans emerges from the interplay between the anisotropy of the cells (hereafter referred to as compartment shape anisotropy, CSA) and the coherence in the population of cells (hereafter referred to as ensemble anisotropy, EA).

There is yet another mechanism of anisotropy at a sub-compartmental length scale, which is induced by the restricting barriers [2], called microscopic anisotropy (μA). Figure 1 illustrates when these different mechanisms of anisotropy may be encountered. When the cells are spherical, only μA can be observed. A randomly oriented population of anisotropic cells will in addition exhibit CSA. Finally, if the anisotropic cells have any orientational preference in their alignment, all three mechanisms of diffusion anisotropy coexist.

It was shown recently that μA and EA can be probed simultaneously and differentiated using the double-PFG pulse sequences [2], a realization of which is depicted in Figure 2. Such a development led to the inference of an apparent compartment size using the double-PFG experiment with arbitrary timing parameters and small gradient strengths. In this study, we extend the theory of restricted diffusion to account for CSA as well.

THEORY

To incorporate the effects of CSA, we consider capped cylinders of length L and radius r . The symmetry axis of the cylinder is oriented along the unit vector \mathbf{u} . The two gradients of the double-PFG experiment, \mathbf{G}_1 and \mathbf{G}_2 , can be applied along any two directions; the angle between them is denoted by ψ . Unlike in [2], this geometry necessitates the inclusion of higher order terms in a Taylor series representation of the MR signal intensity because for highly anisotropic structures, it may not be possible to simultaneously meet the conditions $2\pi|\mathbf{q}_1|r \ll 1$ and $2\pi|\mathbf{q}_2|r \ll 1$, where $2\pi\mathbf{q}_i = \gamma\delta_i\mathbf{G}_i$. Therefore, the signal attenuation expression for completely arbitrary parameters of the double-PFG experiment, $S(\mathbf{G}_1, \mathbf{G}_2, \delta_1, \delta_2, \Delta_1, \Delta_2, t_m; \mathbf{u}, r, L)/S_0$ was derived. For brevity, we shall denote this quantity by $E(\mathbf{q}_1, \mathbf{q}_2; \mathbf{u}, r, L)$. When the cells are not perfectly coherent, one can associate an orientation distribution function, $f(\mathbf{u})$, to the ensemble. It is convenient to express this function in the spherical harmonic basis, i.e.,

$$f(\mathbf{u}) = \sum_{l=0}^{\infty} \sum_{m=-l}^l a_{lm} Y_l^m(\mathbf{u}). \text{ Then the overall signal from the ensemble is: } E(\mathbf{q}_1, \mathbf{q}_2; r, L) = \sum_{l=0}^{\infty} \sum_{m=-l}^l a_{lm} \int E(\mathbf{q}_1, \mathbf{q}_2; \mathbf{u}, r, L) Y_l^m(\mathbf{u}) d\mathbf{u}.$$

The coefficients a_{lm} characterize a true fiber orientation distribution and hence EA. Of particular interest in this expansion is the $l=m=0$ term, which yields the 'isotropic' part of the signal that is free of EA. As was done in [2] for differentiating μA from EA, the $l=m=0$ term can be used to differentiate CSA from EA allowing the characterization of compartment shape anisotropy (related to cell eccentricity) as a true indicator of anisotropy at the cellular level.

RESULTS

To investigate the predicted anisotropy, an isotropic distribution of capped cylinders with $r=4\mu\text{m}$, $L=20\mu\text{m}$, free space diffusion coefficient $D_0=2 \times 10^{-3} \text{mm}^2/\text{s}$ are simulated. First, it was confirmed that the developed methodology accurately reproduces the previously reported results such as the small- q behavior [2], and the diffraction-like zero-crossings of the MR signal [3], which was recently validated experimentally [4]. Although a direct quantitative comparison is not possible because of the differences in the geometry considered, the results were found to be qualitatively in agreement with those in [5-7] as well.

Some of the simulation results depicting the dependence of the MR signal attenuation on the angle between the two gradients are illustrated in Fig. 4. On the left panel, the sensitivity of the observed anisotropy on the mixing time, t_m , is depicted. When t_m is short, the motions occurring within the respective encodings of the double-PFG acquisition are correlated, and a bell-shaped curve is observed, which is a signature of μA . As t_m gets longer, the shape of the curve changes gradually, and eventually the effect of μA disappears, and the anisotropy is a function of CSA only. On the right panel of Fig. 4, the dependence of anisotropy on the q -value is shown when t_m is long. As predicted in [5,2], when the q -value is very small, CSA cannot be observed. However, increasing the q -value makes the CSA-related anisotropy visible. Note that when this happens, the signal values are still relatively high, supporting the view that CSA can be observed in relatively low signal-to-noise ratio (SNR) conditions.

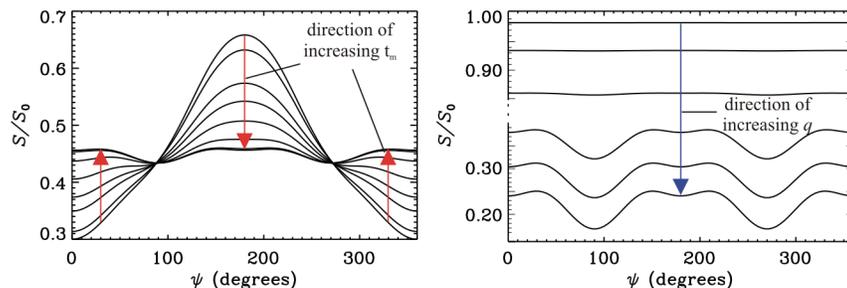


Fig. 4: The simulation parameters are: $\delta_1=\delta_2=0.1\text{ms}$, $\Delta_1=\Delta_2=500\text{ms}$. Left panel: $q_1=q_2=28\text{mm}^{-1}$, t_m between 0.1 and 500 ms. Right panel: $t_m=500\text{ms}$, $q_1=q_2$ between 4 and 40mm^{-1} .

[6] Y. Cheng, D. G. Cory, J Am Chem Soc, 121, 7935-6 (1999). [7] M. A. Koch, J. Finsterbusch, Proc Intl Soc Mag Reson Med, 14, 1631 (2006).

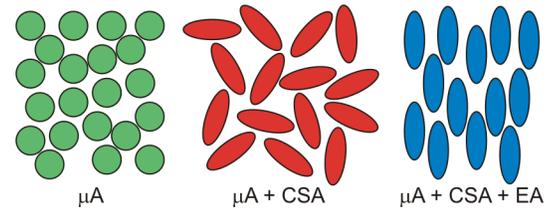


Fig. 1: Different scenarios for diffusion anisotropy.

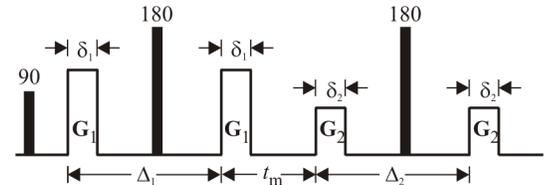


Fig. 2: The spin echo version of the double-PFG experiment.

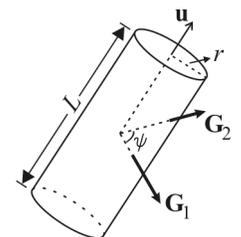


Fig. 3: The geometry considered in this study.

CONCLUSION: For the first time, we presented a method that accounts for all experimental parameters of the double-PFG experiment and exploits its sensitivity to anisotropy that is prevalent at different length scales of a heterogeneous medium such as biological tissue. The results of this study are expected to be useful in noninvasively measuring cell size and eccentricity while simultaneously inferring fiber orientation distributions from such specimens. The technique demands low-to-moderate gradient strengths and it is not too stringent on SNR, hence may be clinically applicable.

References: [1] C. Beaulieu, P.S. Allen, Magn Reson Med, 31, 394-400 (1994). [2] E. Ozarslan, P.J. Basser, J Chem Phys, 128, 154511 (2008). [3] E. Ozarslan, P.J. Basser, J Magn Reson, 188, 285-94 (2007). [4] N. Shemesh, Y. Cohen, J Magn Reson, 195, 153-61 (2008). [5] P. P. Mitra, Phys Rev B, 51, 15074 (1995).