Detection of microscopic anisotropy in gray matter using d-PGSE

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Introduction: Brain gray matter is a complex tissue having multiple cell types such as soma, randomly oriented axons, dendritic fibers, and oligodendrocytes. Although DT-MRI[1] is sensitive enough to detect *macroscopic* anisotropy in white matter fasciculi, no non-invasive *in vivo* MR method can characterize *microscopic* anisotropic domains at the scale of the dendritic network in gray matter. To assess whether displacement MR experiments can provide such information, we propose using the Double Pulsed Gradient Spin Echo (d-PGSE) sequence[2,3], an established technique in material sciences used to observe anisotropic diffusion of molecules in materials, whose principal axes are randomly (isotropically) distributed over a macroscopic length scale. A long-term goal of this work is to detect subtle architectonic differences within different cortical gray matter regions, such as features of the dendric branching pattern, fraction of neuropil, etc.

Materials: A microscopically anisotropic, macroscopically isotropic phantom was constructed, consisting of 0.5 mm long glass tubes of 20 µm inner diameter (ID) and 90 µm outer diameter (OD). The tubes were filled with water and randomly dispersed in deuterated dichloro-benzene. Fixed cortical gray matter tissue from a Rhesus monkey was also used.

Methods: The d-PGSE sequence (fig. 1) consists of two consecutive PGSE blocks. Diffusion gradients can be applied along the same or orthogonal directions in different blocks. The resulting echo attenuation depends on the molecules' diffusion history, hence on the materials' microscopic topology, and the applied diffusion gradients. The echo attenuation of a microscopically isotropic sample, e.g., a PDMS polymer solution (fig. 2 a), will not depend on the direction of the diffusion gradients applied in each block, while the echo attenuation of a microscopically anisotropic sample will. The shape, degree and difference of the two types of attenuation profiles depend on molecular displacements during and between the two PGSE blocks.

Results and Discussion: All experimental (nine) curves in the isotropic PDMS sample (fig 2 a) overlap, indicating microscopic isotropy with no observable software or hardware artifacts. The phantom results (fig 2 b) clearly show microscopic anisotropic diffusion of water inside the tubes, despite their random orientation. Fig. 2 d shows the echo attenuation of a single PGSE experiment of the Rhesus monkey cortical tissue, which appears isotropic, but exhibits restriction in the high q regime. The d-PGSE experiment (fig 2 c), performed on the same monkey tissue sample shows anisotropy both in the low and high q regimes. This finding is surprising in light of Cory et al., who detected microscopic anisotropy only in the high-q regime. While information extracted from the high q regime is invaluable to specify fine structural features of network architecture, our data indicates that microscopic anisotropy in macroscopically isotropic gray matter could also be detectable at a much lower q value, using smaller gradient strengths and at a high signal to noise ratio. This suggests the feasibility of biological and clinical applications of the d-PGSE.

References:

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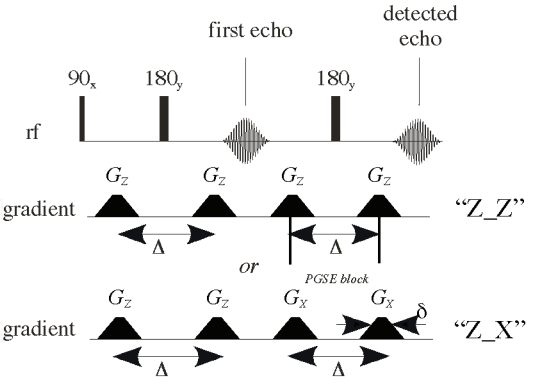

Figure 1:Double PGSE pulse sequence

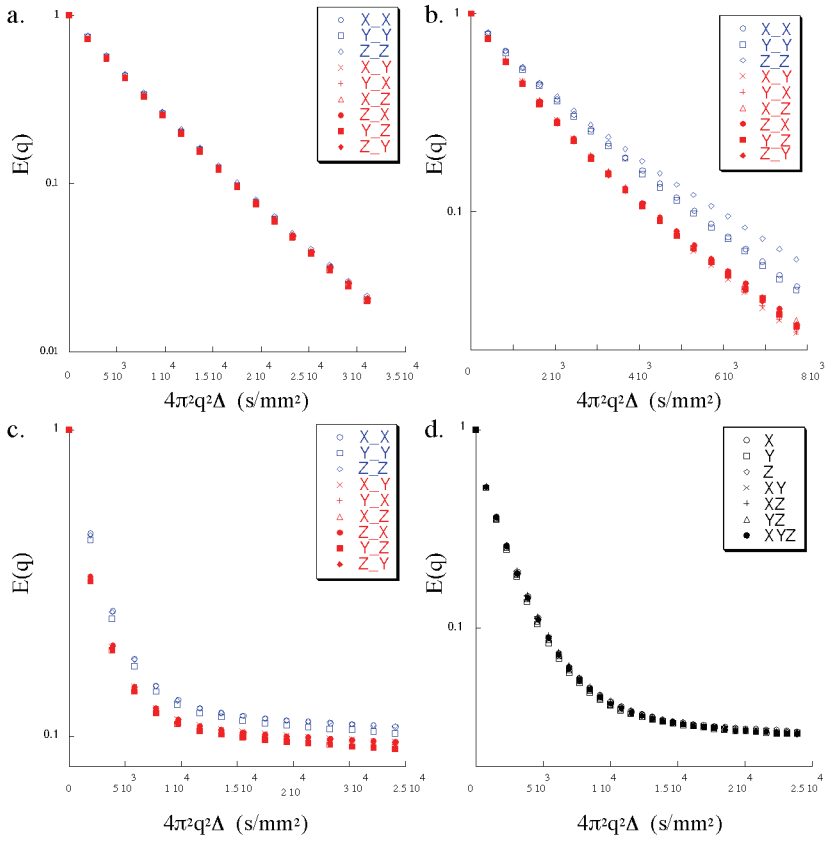

Figure 2:double-PGSE echo attenuation *vs.* $q=(1/2\pi)\gamma\delta G$ for: a. 5 centistokes PDMS. G=400 mTm^{-1}, Δ=75 ms and δ=6 ms. b. phantom. G=300 mTm^{-1}, Δ=110 ms and δ=3 ms. c. Rhesus monkey cortical tissue. G=400 mTm^{-1}, Δ=75 ms and δ=6 ms. and d. single PGSE echo attenuation for Rhesus monkey cortical tissue. G=400 mTm^{-1} Δ=60 ms and δ=6ms.