Influence of Microscopic Background Gradients on the Diffusion Parameters observed in a Fiber Model System

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Introduction

Measurements of diffusion parameters can yield important information on tissue, as diffusion is restricted or hindered by cell membranes, and may even allow to estimate integrity and course of fiber tracts in the living brain. To validate these methods, model systems with known fiber orientations are commonly used. However, systematic errors due to microscopic background gradients caused by susceptibility differences within the sample can compromise the accurate measurement of diffusion properties. The most prominent of these is the cross-term with diffusion gradients that can be addressed with compensation methods. Cotts *et al* developed a corresponding modification of the stimulated echo diffusion preparation by introducing refocusing RF excitations. However, this approach fails if the background gradients experienced by a diffusing molecule differ between beginning and end of the diffusion weighting. Sun *et al* [2] suggested an extension that considers changes in background gradients during the middle interval of the stimulated echo preparation and involves the so-called "magic" gradient amplitude ratio. In the present study, the effect of microscopic background gradients on the observed diffusion properties in a fiber model system is demonstrated and the efficiency of the two compensation methods is investigated.

Methods

A 3 T whole-body MR system (Siemens Magnetom Trio) with a wrist coil was used for the measurements. A phantom was built from parallel sections of a cylindrical, water-filled capillary, consisting of polytetrafluorethylene (Cole-Parmer, Illinois, USA), and positioned in a water-filled plastic bottle. The capillary had outer and inner diameters of 356 µm and 51 µm, respectively, yielding a mean time required for diffusion across the capillary lumen of τ_D = 640 ms according to Einstein's equation.

The diffusion-weighted signal was measured using spin-echo and echo-planar imaging for two different *b*-values (1000 s mm^{-2} and 2000 s mm^{-2}) and for 60 different gradient directions derived from a truncated icosahedron. A slice of 10 mm thickness perpendicular to the static field direction was acquired with a field-of-view of 128 mm × 80 mm and an in-plane resolution of 2 mm. The time-dependent apparent diffusion coefficient for the capillaries oriented perpendicular to the static magnetic field was investigated by varying the separation of the diffusion gradient pulses in five equal steps from Δ = 90 ms to 1890 ms. A stimulated echo preparation was employed to attain long diffusion times with moderate signal loss and sensitivity to background gradients. The methods of Cotts *et al* and Sun *et al* to suppress cross-terms of background gradients were compared to the standard (STE) preparation that does not take background gradients into account.

Results and Conclusions

The diffusion coefficients (*D*) along and perpendicular to the capillaries observed with the three preparation methods are presented in Fig. 1. The measured *D* in freely diffusing water is independent of Δ and corresponds to the value expected from the literature ($D = 2.2{\cdot}10^{-3}$ s mm^{-2}) for all three preparation methods.

In the capillary packing, the STE preparation yields *D* values that are already reduced for short Δ, even in the direction of the capillaries (upper graph) where water diffusion is expected to be unhindered. These values further decrease with increasing diffusion time. The fractional anisotropy reveals even for diffusion times as short as 115 ms, i. e. well below τ_D, a pronounced diffusion anisotropy that surprisingly *de*creases with increasing diffusion time (Fig. 2).

With the preparation of Cotts, the observed diffusion coefficients are higher, and the coefficient along the fiber better agrees with the free diffusion value (upper graph). The improvement is even more pronounced for the preparation of Sun. Here, diffusion coefficients for short diffusion times are closest to that of free water, and the diffusion coefficient along the fiber has the lowest deviation from that of free water. In addition, the fractional anisotropy for Sun's preparation shows an increase with diffusion time (data not shown).

In conclusion, neglecting microscopic background gradients may lead to erroneous measurements of diffusion properties. The best compensation of background gradient cross-terms is achieved with the preparation of Sun indicating that the diffusing spins do not experience a constant background gradient.

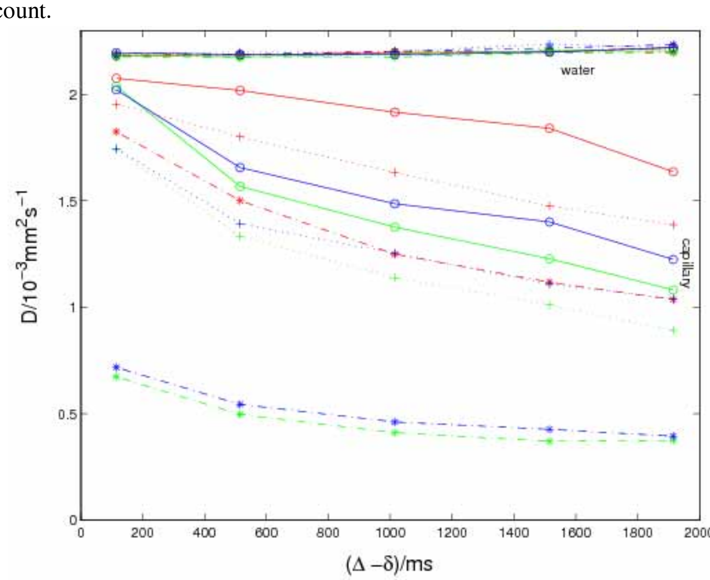

Figure 1: *D* versus Δ − δ (δ = 25 ms gradient pulse duration), in water and in the capillary packing, for the STE preparation (*) and the modifications of Cotts (+) and Sun (o). D_{xx} in red, D_{yy} in green, and D_{zz} in blue.

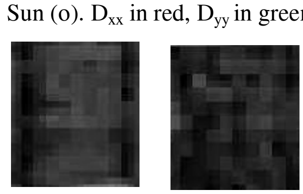

Figure 2: Maps of fractional anisotropy obtained within the capillary packing with STE preparation and Δ of 115 ms (left) and 1915 ms (right). The averaged anisotropy decreases with diffusion time.

References

[1] R. M. Cotts et al, J. Magn. Reson. 83, 252-266 (1989)

[2] P. Z. Sun et al, J. Magn. Reson. 161, 168-173 (2003)