## Diffusion Sensitization Direction Dependence of Biexponential Diffusion Decay Parameters in the Splenium

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Introduction: The non-monoexponetial nature of brain water diffusion decay curves as measured over extended but clinically accessible b-factors remains poorly understood and complex models (1-4) have been forwarded to describe the phenomenon. Herein we utilized biexponential functions to characterize diffusion decay curves from the splenium as a function of the angle  $\theta$  between axial in-plane diffusion sensitization directions and the primary left-to-right fiber direction in the splenium. The two-dimensional symmetry of this arrangement allows for straightforward examination of how the fractional amplitudes and fast and slow diffusion coefficients vary with  $\theta$ . An angular dependence of the form  $D_L \cos^2\theta + D_T \sin^2\theta$ , where  $D_L$  and  $D_T$  are considered diffusion coefficients along and perpendicular to the fibers respectively, characterizes the slow diffusion coefficient, consistent with a model proposed by Jespersen et al (1). A similar angular dependence is however, apparent for the fractional amplitudes and the fast diffusion coefficient, observations that remain unexplained by any current model.

Methods: Five volunteers (4 male, 1 female, age range 24 to 37 years) were scanned with a 1.5 T scanner (General Electric Medical Systems, Milwaukee, WI) with the approval of the local Institutional Review Board and with written informed consent. A line scan diffusion imaging (LSDI) sequence (4) was used to acquire data from an axial slice at the level of the splenium where fibers are oriented from left-to-right. Nominal voxel volumes were 0.11 cc, repetition and echo times were 2844 and 102 ms, respectively. Twelve b-factors from 50 to 4000 s/mm² were sampled along 11 in-plane diffusion gradient sensitization directions oriented at  $16.4^{\circ}$  intervals (-90° to  $74.6^{\circ}$ ) from the left-right direction. Normalized diffusion decay curves directions from ~ 0.5 cc regions-of-interest in splenium were fit to biexponential functions  $A\exp(-bD_A) + B\exp(-bD_B)$  to yield a fast component volume fraction A/(A+B) and fast and slow diffusion coefficients  $D_A$  and  $D_B$ . An LSDI 6-directional diffusion tensor sequence confirmed fiber orientation within the splenium.

Results: Plots of  $D_B$  (left), A/(A+B) (middle) and  $D_A$  (right) as functions of  $\theta$  are provided below. The solid line through the  $D_B$  data was generated with the equation  $D_L \cos^2\theta + D_T \sin^2\theta$  with  $D_L$  and  $D_T$  values of 0.45 and 0.05  $\mu m^2/ms$ , respectively. The fractional amplitude of the fast diffusion component A/(A+B) and its diffusion coefficient  $D_A$  demonstrated an angular dependence similar to that of  $D_B$ .

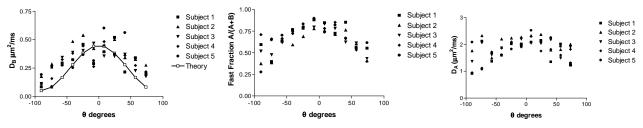


Figure:  $D_B$  (left), A/(A+B) (middle), and  $D_A$  (right) as functions of  $\theta$  within the splenium of five subjects.

Discussion: Assuming that the diffusion coefficient perpendicular to a fiber  $D_T$  is different than that along the fiber  $D_L$ , geometric considerations lead to a diffusion coefficient with an angular dependence of the form  $D(\theta) = D_L \cos^2 \theta + D_T \sin^2 \theta$  (1). We found that all three parameters of biexponential fits to splenium decay curves demonstrated such an angular dependence. A model in which the signal decays according to a fraction of spins f with an isotropic diffusion coefficient  $D_{eff}$ , and a fiber fraction spin component (1-f) with a diffusion coefficient  $D(\theta)$  would support a biexponential fit, though only the slow diffusion coefficient  $D(\theta)$  would be expected to demonstrate the experimentally observed angular dependencies shown above. Since assessing correct amplitudes and slopes of biexponential decay functions from experimental data is notoriously difficult (5), studies to determine whether the angular dependencies demonstrated by all three biexponential parameters is due to additional model complexity or is an artifact of the biexponential fitting process are warranted.

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