Modeling Molecular Diffusion in Brain Using Bayesian Probability Theory

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Abstract The diffusive motions of water molecules in biological tissue are influenced by μm-sized cellular structures. Over small volumes, such as within an MRI pixel, these structures often possess sufficient regularity that inferences may be made about their shapes from directionally-dependent diffusion measurements. In diffusion tensor imaging (DTI) this directional dependence, as measured by MRI, is modeled as a rank two tensor. The possibility exists that a more elaborate mathematical model would be more informative than DTI about the underlying tissue structure. In this study, Bayesian probability theory is used to analyze high signal-to-noise diffusion data from fixed whole baboon brain. A scheme for developing a parsimonious model of the data is described, and the resulting model is found to differ from the DTI analysis by the addition of a sub-population of molecules possessing diffusivities too small to measure. The size of this sub-population provides a new source of image contrast.

Introduction In a "standard" DTI analysis (1), the diffusion tensor is obtained by fitting the expression

$$S(\mathbf{G}) = exp\left(-k\sum_{i,j\le i} G_i G_j D_{ij}\right) \qquad [1]$$

to the MRI signal intensity, S, measured at varying gradient settings, specified by the vector $\mathbf{G}$. In this expression, D_{ij} are the diffusion tensor coefficients, k is a constant, and the indices i and j specify the gradient and tensor components. Recently, multiple methods have been published (2-4) for fitting diffusion data to more elaborate mathematical models to obtain additional information about tissue structure. Herein, we utilize Bayesian probability theory in the analysis of water diffusion data acquired from a formalin-fixed whole baboon brain.

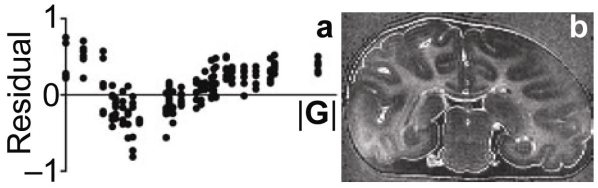

Figure 1. Systematic residuals result from fitting the diffusion data to Eq. 1. (**a**) $S(\mathbf{G})^{obs} - S(\mathbf{G})^{calc}$ is plotted for a single pixel. (**b**) Image of the standard deviations in the residuals.

Experimental A formalin-fixed baboon brain was placed within a 4.7 T imaging system. 161 diffusion-weighted images were acquired using randomized diffusion gradient strengths and directions, ranging from 0 to 40 G/cm. Each pixel corresponds to a 125 μL cubic volume, and has a signal-to-noise ratio of about 40:1.

Results and Discussion The standard DTI model was fit to the 161 $S(\mathbf{G})$ data values for each pixel in the image. In Figure 1a, a systematic deviation from the DTI model is observed in the plot of residuals versus $|\mathbf{G}|$ for a single pixel. Figure 1b shows an image of the standard deviation in the residuals, which indicates that the systematic deviation in the data from Eq. 1 persists throughout much of the brain. To characterize these trends, the $S(\mathbf{G})$ were modeled as an exponential distribution that contains the standard diffusion tensor model as a limiting case. Model selection was then used to determine which model best accommodated for the data. Such calculations, when applied to each pixel in the image, almost invariably resulted in a fitted distribution that is equivalent to the DTI model (given in Eq. 1) plus a constant offset. Figure 2 demonstrates the ability of the "DTI + constant" model to fit the data to the noise. The fitted offset indicates the presence of an immobile fraction of molecules. Evidence of "higher order" deviations from the DTI model was not observed. Notably, the magnitude of the constant offset provides a new source of image contrast, as shown in Figure 2.

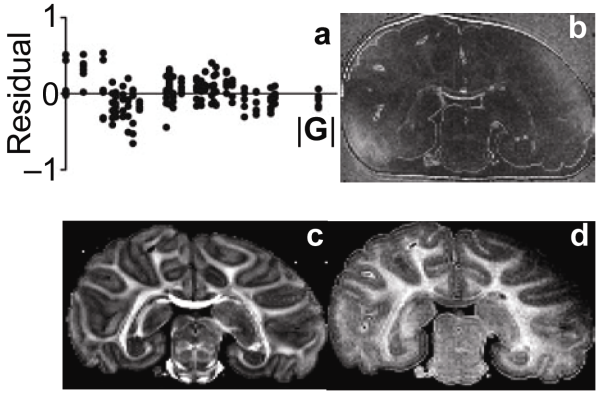

Figure 2. DTI + Constant results. (**a**) and (**b**) display residuals as in Figure 1. Residuals in (**a**) are from the same pixel as in Figure 1a. (**c**) is an image of diffusion anisotropy, expressed as A_σ (5), and (**d**) is an image of the constant.

Acknowledgement Supported by NIH grants F32 43010 and R01 37357. **References 1.** Basser, et al. *J. Magn. Reson, Ser. B* 103:247-254, 1994 **2.** Özarslan and Mereci, *Mag. Reson. Med.* 50:955-965, 2003 **3.** Alexander et al. *Mag. Reson. Med.* 48:331-340, 2002 **4.** Frank, *Mag. Reson. Med.* 47:1083-1099, 2002 **5.** Shimony et al. *Radiology* 212:770-784, 1999