## **Characterization of Intravoxel Diffusion from HARD MRI**

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#### Introduction

The single Gaussian diffusion model is inappropriate for assessing multiple fiber orientations (1-4). Recently, a mixture of two Gaussian density functions was proposed to model the diffusion in the voxels where the single tensor model fits the data poorly (5,6). Such voxels were identified by using the spherical harmonics (SH) representation of ADC profiles, d (5), and the multiple max/min ratios of d (6). However, estimating tensor fields  $D_i$  or the field of their proportionality  $f_i$  in each isolated voxel presents a mathematically ill-posed problem. We propose a variational model to estimate  $D_i$  or  $f_i$  globally by simultaneous field smoothing and data fitting.

#### Methods

One of promising approaches for identifying voxels with fibers of multiple orientations is using SH representation of ADC profiles estimated from High Angular Resolution Diffusion-weighted (HARD) images (3,7). In our approach of determining fiber directions, the first step is to recover the ADC profiles from noisy HARD data by a simultaneous smoothing and estimation method (submitted to ISMRM 2004 separately). Under the assumption of two Gaussians, the diffusion is modeled by

$$e^{-bd(\mathbf{x},\theta,\phi)} = \sum_{i=1}^{2} f_i e^{-b\mathbf{u}^T D_i(\mathbf{x})\mathbf{u}}$$
(1.1)

where  $u^{T} = (\sin\theta\cos\phi, \sin\theta\sin\phi, \cos\theta)$ . Then,  $D_i$  and  $f_i$  can be determined by minimizing the following function:

$$\min_{L_{1},L_{2},f} \int_{\Omega} (\sum_{i=1}^{2} |\nabla L_{i}|^{P_{i}(\mathbf{x})} + |\nabla f|^{P_{f}(\mathbf{x})}) d\mathbf{x} + \lambda_{1} \int_{\Omega_{1}} (f-1)^{2} d\mathbf{x} + \lambda_{2} \int_{\Omega} \int_{0}^{2\pi} \int_{0}^{\pi} |\sum_{i=1}^{2} f_{i}e^{-b\mathbf{u}^{T}L_{i}L_{i}^{T}\mathbf{u}} - e^{-bd}|^{2} \sin\theta d\theta d\phi d\mathbf{x}$$
(1.2)

with the constraint  $L_{i}^{m,m} > 0$ . In (1.2) for  $i=1,2, \lambda_{i} > 0$  is a parameter,  $|\nabla L_{i}|^{p} = \sum_{1 \le m,n \le 3} |\nabla L_{i}^{m,n}|^{p}$ ,  $p_{i}(x) = 1 + \frac{1}{1+k |\nabla G_{\sigma} * \nabla L_{i}|^{2}}$ ,  $p_{f}(x) = 1 + \frac{1}{1+k |\nabla G_{\sigma} * \nabla L_{i}|^{2}}$  and  $L_{i} = 1 + \frac{1}{1+k |\nabla G_{\sigma} * \nabla L_{i}|^{2}}$ 

is a lower triangular matrix, such that  $D_i = L_i L_i^T$ . The Cholesky factorization is to achieve the positive definite constraint on  $D_i$ . Our model (1.2) presents four terms:

the first two terms regularize  $D_i$  and  $f_i$ , the third forces  $f \approx 1$  on  $\Omega_i$ , and the last is the non-linear data fidelity term based on 1.1. By the choice of  $p_i$  in a homogeneous region, if image gradients are close to zero and  $p_i(\mathbf{x}) \approx 2$ , the smoothed voxels are isotropic. Along the edges, image gradients make  $p_i(\mathbf{x}) \approx 1$ , the smoothing is the total variation based and only along the edge (similarly, for  $p_j$ ). At all other locations, the image gradient forces  $1 , and the diffusion is between isotropic and total variation based, and varies depending on the local properties of the image. Therefore, relevant features in these images can be well preserved after smoothing. Finally, the fiber orientations at each voxel are determined by the directions of the principle eigenvectors of <math>D_1$  and  $D_2$ . For the voxels where f (or 1 - f) is significantly large, we consider 1 - f (or f) as zero, and (1.1) reduces to the single tensor diffusion model.

Healthy human subjects (N = 12) were scanned using a 3.0 Tesla GE MRI system. The raw diffusion-weighted images were obtained using a single shot spinecho EPI sequence with TR/TE = 1000ms/85ms, FOV = 220mm<sup>2</sup>, matrix size = 128 x 128 (reconstructed to 256x256), NEX = 2 for reducing the overall time of the scanning. Diffusion-sensitizing gradients were applied in 55 directions (for HARD MRI acquisition) with b = 1000 sec/mm<sup>2</sup>. Twenty-four transversal slices of 3.8 mm thickness (1.2 mm gap) were selected covering the whole brain.

#### Results

We solved the minimization problem (1.2) using energy decent method with the information of  $f \approx 1$  on  $\Omega_l$  integrated into the selection of the initial f. By solving (1.2) we obtained the solutions  $L_i$  and f, and consequently,  $D_i$  (i = 1, 2). Fig. 1a represents the model solution  $f \approx 1$  on the dark red regions. The voxels in these regions are identified as isotropic or one-fiber diffusion. Figs. 1b and 1c are the color representation of  $D_1(\mathbf{x})$  and  $D_2(\mathbf{x})$  in a typical brain slice. The direction of the principle eigenvector is represented by its polar ( $\theta$ ) and azimuthal ( $\phi$ ) angles, which are uniquely determined on the color pie (8). The fiber orientation can be described by either ( $\theta, \phi$ ) or ( $\pi - \theta, \phi + \pi$ ). Fig. 2 shows the shapes of  $d(\mathbf{x}, \theta, \phi)$  together with the fiber directions at 4 particular voxels. The blue and red arrows indicate the orientations of the fibers determined from  $D_1$  and  $D_2$  respectively. The last shape corresponds to an isotropic diffusion. To examine the accuracy of our model in recovering fiber directions, we selected a region in the internal capsule known as one fiber orientation. For each voxel in this region we computed the direction in which d is maximized. This direction vector field is shown in Fig. 3a. Our model solution matches this result. The directions of the principle eigenvectors of  $D_1$  are shown in Fig. 3b. Comparing Figs. 3a and 3b, the vector field in Fig.3a is both well preserved and regularized due to the regularization terms in the model.

#### Discussion

Our approach differs from the existing methods in the following aspects. First, we recover  $D_i(\mathbf{x})$  or  $f_i(\mathbf{x})$  globally by simultaneous filed smoothing and data fitting, rather than estimating them from (1.1) in each isolated voxel. Second, we recover the ADC profile in SH representation from the noisy HARD data before estimating  $D_i(\mathbf{x})$  and  $f_i(\mathbf{x})$ . The recovered d and the voxel classification on diffusion anisotropy from d are incorporated into our energy function to enhance the accuracy of the estimation. Third, we applied the bi-Gaussian model to all the voxels in the field, rather than only the voxels where the single tensor model fits poorly. Since both the constraint of  $f \approx 1$  on the region of strong single fiber and multi-fiber diffusions can be separated automatically by the model solution. Thus, this approach will be less sensitive to the errors in the voxel classification.

### References

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