DIAMOND: a novel biophysical diffusion model that characterizes the distribution of anisotropic micro-structural environments with DWI.

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Purpose. To develop a novel biophysical model to characterize the distribution of three dimensional microstructural environments in each voxel with diffusion-weighted imaging (DWI).

Theory. We propose a novel biophysical model of the diffusion signal. Inspired by the ADC approach of [1], we consider measurements of the signal arising from a large number of individual homogeneous spin packets within a voxel. However, in contrast to the 1D model of [1], we model the 3-D Gaussian diffusion of each homogeneous spin packet with a full diffusion tensor $\mathbf{D}$, capturing the 3-D structure of the local restriction to diffusion. Furthermore, we consider that each voxel is composed of N_c large scale microstructural environments (LSME) (or compartments) (Fig 1a), and that each compartment has in turn some degree of heterogeneity (Fig 1b) and is therefore described by a continuous distribution of homogeneous spin packets. More precisely, each LSME composition is described with a matrix-variate Gamma distribution of spin packets, which is a peak-shaped probability distribution defined over the space of tensors. This leads to the following description of the signal formation:

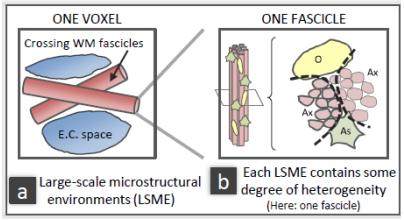

Fig 1. We consider that each voxel contains multiple large scale microstructural environments (a), and that each LSME contains some degree of heterogeneity. For example, Fig. (b) illustrates a fascicle composed of axons with various radiuses and myelination degree and glial cells.

$$S_k = S_0 \sum_{j=0}^{N_c} f_j \int_{\mathbf{D}\in\mathcal{S}_3^+} P_{\kappa^j,\mathbf{\Sigma}^j}(\mathbf{D}) \exp\left(-b_k \mathbf{g}_k^T \mathbf{D} \mathbf{g}_k\right) d\mathbf{D} \quad . \tag{1}$$

$\mathcal{S}_3^+$: set of 3×3 symmetric positive-definite (SPD) matrices, $f_j \in [0,1]$: fractions of occupancy, $P_{\kappa^j,\mathbf{\Sigma}^j}(\mathbf{D})$: matrix-variate Gamma distribution of shape and scale parameters κ^j and $\mathbf{\Sigma}^j$

Equation (1) corresponds to a sum of Laplace transforms and has a closed form solution [2]:

$$S_k = S_0 \sum_{j=0}^{N_c} f_j \left(1 + \frac{b_k \mathbf{g}_k^T \mathbf{D}_0^j \mathbf{g}_k}{\kappa_j}\right)^{-\kappa_j} = S_0 \sum_{j=0}^{N_c} f_j \exp\left(-\kappa_j \log\left(1 + \frac{b_k \mathbf{g}_k^T \mathbf{D}_0^j \mathbf{g}_k}{\kappa_j}\right)\right) . \tag{2}$$

Our model captures the DIstribution of Anisotropic MicrOstructural eNvironments from DWI (DIAMOND) [2]. The parameters of (2) provide novel indicators of the tissue microstructure. The statistical expectation of $P_{\kappa^j,\mathbf{\Sigma}^j}(\mathbf{D})$ is a tensor $\mathbf{D}_0^j = \kappa_j \mathbf{\Sigma}_j$ that describes the average 3-D diffusivity of the compartment j. The shape parameter κ_j determines the concentration of the distribution (the density becoming more concentrated about $\mathbf{D}_0^j$ as κ_j increases) and describes the compartment homogeneity. Specifically, a distribution with a sharp peak indicates a compartment with a highly homogeneous microstructure; a distribution with a broad peak indicates a highly heterogeneous compartment described by a heterogeneous family of spin packets.

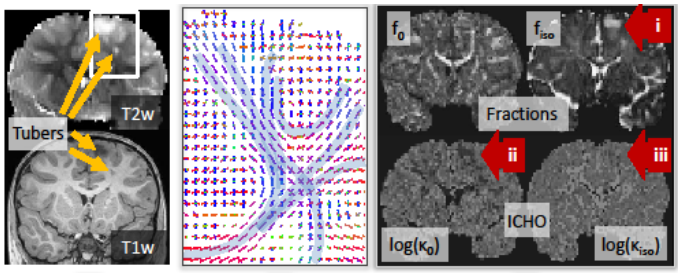

Fig 2. CUSP65 imaging and DIAMOND reconstruction of the brain of a TSC patient. (a): T1w and T2w acquisitions, in which cortical tubers are characterized by an hypo-intensity on T1w and an hyper-intensity on T2w. (b): The estimated fascicle orientations successfully matches the known anatomy, while only 65 directions (CUSP65) was acquired. (c): Estimated fractions of occupancy (top row) and concentration parameter κ_j (bottom row) for the unrestricted diffusion (fiso; κiso) and for the fascicle of larger fraction of occupancy (f0; κ0).

Methods. Estimation of the parameters of the DIAMOND model requires imaging with multiple b-values. This was achieved by a CUSP65 gradient encoding scheme [3] (~12min acquisition time) which provides high SNR and a large number of different b-values. We imaged a patient with Tuberous Sclerosis Complex (TSC), a genetic disorder characterized by the presence of benign tumors in the brain called cortical tubers. At each voxel, we considered one isotropic compartment to model unrestricted diffusion and $N_c - 1$ anisotropic compartments to represent WM fascicles. The number of fascicles at each voxel was estimated with a novel approach based on the minimization of the generalization error [4].

Results. Firstly, we found that in the region of the tuber, the estimated fraction of unrestricted diffusion is increased (Fig 2c.i). This might reflect an increased extra-cellular space, the presence of perivascular spaces, or the presence of giant cells typically observed in TSC brain specimens. Secondly, we observed a reduction in the concentration parameter for the fascicle located in the tuber (Fig 3c.ii), indicating an increased anisotropic heterogeneity *consistent* with the orientation of the fascicle. In contrast, there was no significant heterogeneity consistent with unrestricted diffusion (Fig 3c.iii). We speculate that this may reflect heterogeneous myelination or heterogeneous mixture of glial cells as observed in mice models of TSC.

Conclusion. We proposed a novel biophysical model of the diffusion signal that characterizes the distribution of microstructural environments in each voxel. DIAMOND may lead to novel biomarker and novel investigations of the white-matter microstructure, in both normal development and in disease and injury.

Bibliography & References Cited

1. Yablonskiy, D.A., G.L. Bretthorst, and J.J. Ackerman, *Statistical model for diffusion attenuated MR signal.* Magn Reson Med, 2003. **50**(4): p. 664-9.
2. Scherrer, B., et al., *Characterizing the DIstribution of Anisotropic MicrO-structural eNvironments with Diffusion-weighted imaging (DIAMOND).* Med Image Comput Comput Assist Interv., 2013. **16**: p. to appear.
3. Scherrer, B. and S.K. Warfield, *Parametric representation of multiple white matter fascicles from cube and sphere diffusion MRI.* PLoS One, 2012. **7**(11).
4. Scherrer, B., M. Taquet, and S.K. Warfield, *Reliable Selection of the Number of Fascicles in Diffusion Images by Estimation of the Generalization Error.* Inf Process Med Imaging, 2013. **23**(7917): p. 742--753.