# Probabilistic connectivity using Kullback-Leibler distance

# J. Lee<sup>1</sup>, M. K. Chung<sup>2</sup>, D. Hsu<sup>3</sup>, and A. L. Alexander<sup>4</sup>

<sup>1</sup>Waisman Center, University of Wisconsin-Madison, Madison, WI, United States, <sup>2</sup>Statistics, University of Wisconsin-Madison, MI, United States, <sup>3</sup>Neurology, University of Wisconsin-Madison, Madison, WI, United States, <sup>4</sup>University of Wisconsin-Madison

# Introduction

White matter tractography (WMT) is a promising method for estimating the white matter pathways that connect different brain regions. The probabilistic WMT is one approach to describe the white matter connectivity. Propagated diffusion profiles based on the measured diffusion tensor from diffusion tensor imaging may be used for the probabilistic WMT. In this study we extend the work by Morris et al [1] using continuous propagators with isotropic Gaussian kernel smoothing and anisotropic Gaussian kernel smoothing [2]. This study aims to show that the Kullback-Leibler (KL) distance with isotropic Gaussian kernel smoothing and measured diffusion tensor based anisotropic Gaussian kernel smoothing produces more robust probabilistic connectivity maps.

The KL distance is a statistical metric for measuring the dissimilarity between two probability distributions, p and q: p is a distribution of interest and q usually

represents a null distribution in the KL distance formula  $KL(\bar{r}) = \sum_{\bar{s}} p(\bar{s}) \cdot \log(\frac{p(\bar{s})}{q(\bar{s})})$ , where  $\bar{r}$  is the position vector, and  $\bar{s}$  is a dummy position index to calculate the

summation within a discrete window in the formula. The distribution p may be generated using the anisotropic Gaussian kernel that is based on tensor  $\overline{D}$  in DTI WMT.

The anisotropic Gaussian kernel is a formulated as  $K_{t,Anisotropic}(r) = \frac{\exp(-r\overline{D}^{-1}r/4t)}{(4\pi)^{n/2}(\det\overline{D})^{1/2}}$ , where  $\overline{D}$  is diffusion tensor and t is a parameter that governs the extent of the

diffusion, i.e. smoothing [2]. The anisotropic Gaussian kernel is convoluted with a volume of matrix that has a seeding point (intensity 1) to generate the distribution of the interest (p). The null distribution q is obtained using the isotropic Gaussian diffusion propagation. The isotropic Gaussian kernel may be formulated

as  $K_{t,isotropic}(\vec{r}) = \frac{\exp(-\vec{r}^2/4t)}{(4\pi)^{n/2}}$ . This isotropic kernel is formed simply by inserting the identity matrix for the  $\overline{D}$  in the anisotropic Gaussian kernel above.

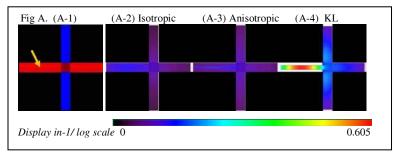
# Methods

<u>Simulations</u>: A simple three-dimensional numerical phantom (the matrix size, 100x100x100) shown in the Fig A-1 was constructed. The phantom consisted of two perpendicular synthetic fiber bundles with high anisotropy (FA value of the horizontal bar shaded in red: 0.82, FA value of the vertical bar shaded in blue: 0.87) crossing each other with surroundings filled with very low anisotropy tensors (FA<0.02). Major eigenvectors of the diffusion tensors in the horizontal branch were assigned to be directed parallel to the horizontal direction, and the vertical direction for the vertical bar. A seed was placed in the left side (arrow in yellow) of the horizontal branch. Anisotropic Gaussian kernel diffusion propagations were performed. After 600 iterated convolution with Gaussian kernels with a seeded matrix, the KL distance was calculated. The size of the summation window was 5 x 5 x 5 for the KL distance formula above.

<u>Human brain data</u>: A single-shot spin echo EPI sequence with diffusion-tensor encoding (12 directions, b=1000s/mm<sup>2</sup>), was used to get a DTI data from a subject (identical slice locations, voxels =  $0.84 \times 0.84 \times 1.8$ mm, 52 slices, acquisition matrix  $128 \times 128$ , 10 NEX, 23 cm FOV). For the distribution *p*, anisotropic diffusion was propagated using the anisotropic Gaussian kernel that was constructed as described in [2] with a seed point at midline of the splenium (Fig B) and internal capsule (Fig C). The corresponding null distribution was acquired using isotropic Gaussian kernel smoothing. A stopping criterion for those two propagations was set by the time of arrival when the diffused intensity in a voxel situated far from the seeding region was no longer zero. All propagation was restricted for the region where FA is greater than 0.3.

#### Results

In the numerical phantom simulation, the KL distance demonstrated branching into both the vertical and horizontal pathways which was not obvious in either Fig A-2 (isotropic diffusion) or Fig A-3 (anisotropic diffusion) maps. Regions that were parallel to the tensor shape in the horizontal branch were highlighted around a seed point. In the case of human brain data, both the isotropic diffusion propagation (B-2) and anisotropic propagation (B-3) starting from the midline of splenium reached the frontal lobe area, but the KL distance measurements did not propagate to the anterior part of the brain. An example of internal capsule was depicted in Fig C. The left lateral side that was diffused with Gaussian kernels (Fig C-2 and C-3) did no longer exist in the KL distance map. The KL distance map shows dominant connectivity patterns along the cortico-spinal tract



### **Discussion and Conclusions**

In general, the KL distance map showed a wider dynamic range than diffusion profiles that Gaussian kernel convolution smoothing generated. Probabilistic tractography based on anisotropic Gaussian kernel smoothing was visualized according to the measured diffusion tensor and also smoothed the pathway at the same time. Therefore it may be suitable for a group comparison study providing a higher SNR.

#### Reference

[1] Morris et al., Proc.intl. Soc. Mag. Reson. Med., 2006. [2] Lee et al., Proc. Intl. Soc. Mag. Reson. Med 2005

