Probabilistic Monte Carlo Based Mapping of Cerebral Connections Utilising Crossing Fibre Information

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Synopsis A methodology is presented for estimation of a probability distribution function (PDF) of voxel fibre orientations when one or two fibres are present in a voxel. The method models water diffusion in a single fibre by a Gaussian density function and in multiple fibres by a mixture of Gaussian densities. Monte Carlo streamline methods are used to establish probabilities of connection between brain regions using these PDFs.

Introduction Probabilistic methods for determining the connectivity between brain regions have recently been introduced[1-5]. Each of these approaches utilises Monte Carlo methods to sample PDFs defined at each point within the brain to describe the local uncertainty in fibre orientation. Each PDF is intended to interpret the information available from a diffusion imaging acquisition in terms of the likely underlying fibre structure. Given an accurate PDF it should therefore be possible to define the probability of connection between any two points within the brain using a Monte Carlo approach based on, for example, streamlines. To date all PDFs used in these methods have been defined in terms of the diffusion tensor model. This assumes that diffusive water molecule displacements are Gaussian distributed, which is a poor approximation where fibres cross. This leads to either inaccurate PDFs, which may assign unwarranted confidence in a particular fibre orientation, or overly conservative PDFs that reflect the fact that the tensor provides ambiguous fibre orientation information in these regions. Here, we use a mixture of Gaussian densities, which enables us to define PDFs with decreased uncertainty in regions containing crossing fibres.

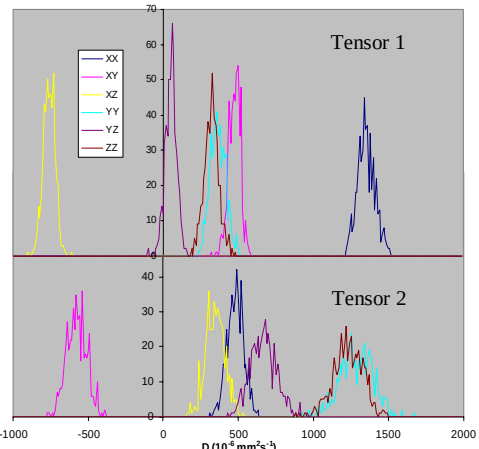

Fig. 1. *Distributions in tensor elements obtained by adding noise to a simulated data set representing the best estimate of two Gaussian densities. 1000 iterations performed.*

Data Acquisition Single-shot EPI diffusion weighted brain data were acquired using a GE Signa 1.5 tesla scanner with: standard quadrature head coil; cardiac gating (TR = 20 RR ~ 20 s); 42 axial slices; TE = 95 ms; 60 non-collinear diffusion-weighting directions with a *b*-factor of 1156 smm^{-2}; δ = 32 ms; Δ = 40 ms; 3 acquisitions with a *b*-factor ~ 0 smm^{-2} [6,7]; 96 × 96 acquisition matrix, zero-filled to 128 × 128; 240 mm field of view, 2.5 × 2.5 × 2.5 mm^3 voxels as acquired, reconstructed to 1.875 × 1.875 × 2.5 mm^3. Eddy current induced distortions were removed using an affine multi-scale two-dimensional registration[8].

Model Fitting We use the algorithm of Alexander *et al*[9] to determine voxels where the tensor model of diffusion is inadequate and in these cases fit a mixture of two Gaussian densities; otherwise the tensor model is applied. The principal directions of the two diffusion tensors in the mixture model provide estimates of the orientations of the crossing fibres. We assume that we cannot resolve the directions of more than two fibres with the number of diffusion-weighted measurements acquired.

PDF Definition The effect of noise on the fitting process is modelled using a simulated complex MR measurement. A realistic amount of zero-mean random Gaussian-distributed noise is repeatedly added to define a PDF describing the effects of noise on apparent fibre direction. For the single tensor model, it is apparent that the addition of noise generates an approximately normal distribution of the principal direction of diffusion, allowing an easily parameterised PDF that depends on tensor anisotropy and the noise level. For the mixture model no straightforward parameterisation exists to describe the resultant distributions of the underlying fibre directions. We use a voxel-by-voxel lookup table generated from the noise addition process to define the PDF. The distribution of each tensor element appears approximately normal (Fig. 1), with the variance defined by the relative diffusivities, orientations, and proportions of fibres present.

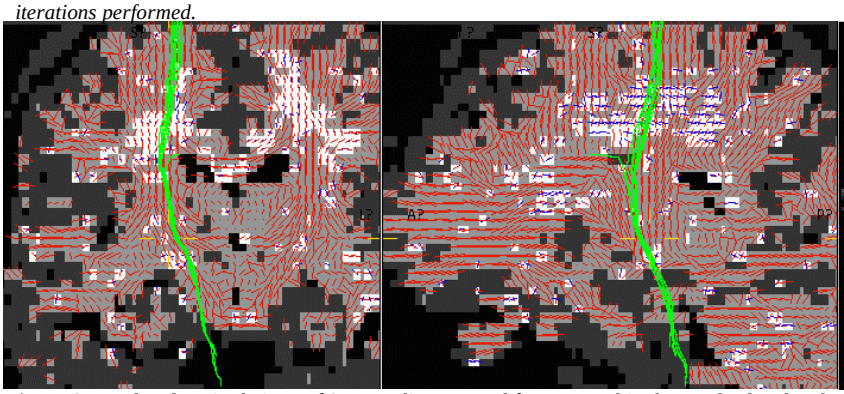

Fig. 2. *Coronal and sagittal views of 8 streamlines started from a voxel in the cerebral peduncle. Dark grey voxels: grey matter; light grey voxels: n = 1; white voxels: n = 2.*

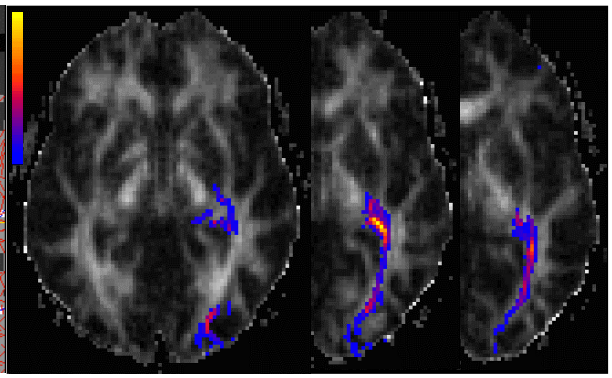

Fig. 3. *Connection probability from a voxel in the lateral geniculate nucleus. Colour scale represents a probability scale of 0 – 1.*

Probabilistic tracking The PICo framework is utilised to enable probabilistic fibre tracking[4,5], allowing maps of connection probability to be generated. The method utilises a Monte Carlo streamline approach, sampling the PDFs within each voxel on each iteration. An example of a single iteration of fibre tracking through regions of one or two crossing fibres in the region where the corona radiata meets the superior longitudinal fasciculus is shown in Fig. 2. Figure 3 shows a map of connection probability to a voxel in the lateral geniculate nucleus.

Conclusion The use of the Gaussian mixture model allows the orientation of many crossing fibres within the brain to be distinguished. By simulating the effects of data noise we are able to generate PDFs representing the possible fibre orientations within a voxel. In combination with the PICo tracking method this allows us to generate probabilistic maps of connection. The resultant probabilities therefore reflect the influence of noise on the diffusion measurement and allow a confidence of connection to be established.

References 1. Behrens, T.E.J., *et al., Proc. Int. Soc. Magn. Reson. Med.*, 1142, 2002. **2.** Koch, M.A., *et al., NeuroImage*, 16, 241, 2002. **3.** Lazar, M. and Alexander, A.L., *Proc. Int. Soc. Magn. Reson. Med.*, 539, 2002. **4.** Parker, G.J.M., *et al., Proc. Int. Soc. Magn. Reson. Med.*, 1165, 2002. **5.** Parker, G.J.M., *et al., ISMRM Workshop on Diffusion MRI (Biophysical Issues), Saint-Malo, France*, 245, 2002. **6.** Jones, D.K., *et al., Magn. Reson. Med.*, 42, 515, 1999. **7.** Wheeler-Kingshott, C.A.M., *et al., Proc. Int. Soc. Magn. Reson. Med.*, 1118, 2002. **8.** Symms, M.R., *et al., Proc. Int. Soc. Magn. Reson. Med.*, 1723, 1997. **9.** Alexander, D.C., *et al., Magn. Reson. Med.*, 48, 331, 2002.

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