Probabilistic anatomical connectivity derived from the microscopic persistent angular structure of cerebral tissue

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Introduction Probabilistic methods for determining cerebral connectivity using DWI have recently been introduced. To date, probability density functions (PDFs) used in probabilistic methods have either been determined from the single diffusion tensor model, multi-tensor models or using diffusion spectrum imaging (DSI). The single tensor model of diffusion is a poor approximation where fibres cross, diverge, or have high curvature. Multi-tensor methods can identify more than one fibre population within a voxel but to date have not shown the capability to distinguish more than two fibre populations per voxel[1,2]. Unlike DSI, alternative q-space methods such as *q ball*[3] and *persistent angular structure* (PAS)-MRI[4], allow resolution of multiple fibre orientations using data from acquisition schemes common in clinical diffusion tensor MRI[5], thus creating the possibility for the extraction of multiple fibre populations with manageable data acquisitions. Both q ball and PAS-MRI compute functions of the sphere that reflect the angular structure of the particle displacement density and the peaks of these functions provide estimates of fibre orientations. Neither of these methods has been used in probabilistic tracking to date. Here we present a method for extracting probabilistic cerebral connectivity using PAS-MRI, which has been shown to have lower noise sensitivity than q ball[6], and demonstrate its utility in the examples of cerebral peduncle and precentral gyrus connectivity.

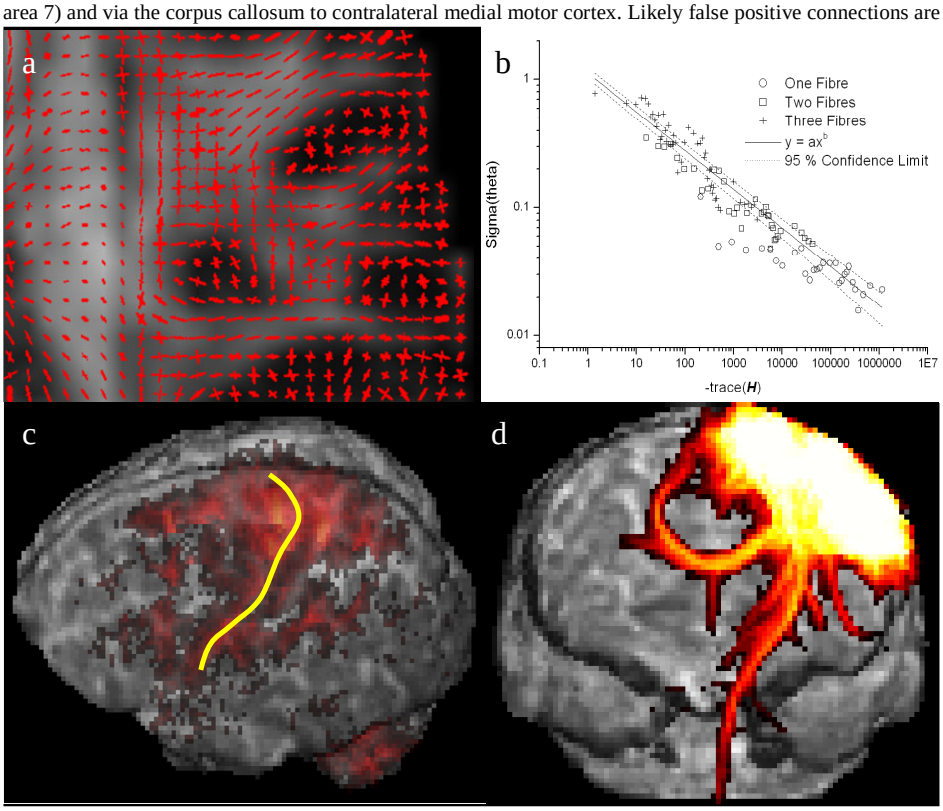
Data Single shot spin echo EPI diffusion weighted brain data were acquired on a GE Signa 1.5 T scanner at $2.3 \times 2.3 \times 2.3$ mm^3; TE = 95 ms; 54 gradient vectors with $|\mathbf{g}_i|$ = 22 mTm^{-1}; δ = 34 ms; Δ = 40 ms; b = 1156 smm^{-2} and a Philips 3T Achieva at $2.1 \times 2.1 \times 2.1$ mm^3; TE = 56 ms; 61 gradient vectors with $|\mathbf{g}_i|$ = 60 mTm^{-1}; δ = 14.12 ms; Δ = 27.77 ms; b = 1200 smm^{-2}.

Persistent angular structure The PAS is the function on the sphere, expressed as the product of waves on the sphere, that, when embedded in three-space on a sphere of radius r, has the Fourier transform that best fits the DWI measurements. The set of maxima of the PAS function that exceed a threshold provides the set of fibre-orientation estimates in a voxel. Figure (a) shows the PAS function in each voxel of a region from an axial section taken from a whole-brain data acquisition at 3T.

Noise-based fibre orientation uncertainty The effect of noise on the PAS function in the case of single, two, or three fibre populations is modelled using MR measurements synthesized from test functions derived from a mixture of tensors. To generate noisy measurements, we add random complex samples drawn from independent zero-mean Gaussian distributions of the real and imaginary parts to the Fourier transform of the test function at each $\mathbf{q}_i$ sampled in the acquisition. We repeat this process to obtain a population of noisy signal intensity estimates with which we estimate PDFs for probabilistic tracking. We model the distribution of the angle of deflection θ of the estimated fibre orientation with a zero-mean normal distribution. In the two and three fibre case, we assume that the estimates for each fibre are independent and identically distributed. We use the trace of the Hessian $\boldsymbol{H}$ of the PAS at the peak providing a fibre-orientation estimate to predict the standard deviation (σ_θ) of the normal distribution for that fibre-orientation estimate. To calibrate the mapping from trace($\boldsymbol{H}$) to σ_θ, we calculate $\boldsymbol{H}$ at each PAS peak recovered from the noisy synthetic data. Fig. (b) shows the relationship between trace($\boldsymbol{H}$) and σ_θ, which is close to linear on the log-log plot. Whilst the range of trace($\boldsymbol{H}$) and σ_θ varies according to the number of fibre directions, the plot for each configuration falls on the same line, to a good approximation.

Monte Carlo methods and connection probability We use the *PICo* probabilistic fibre tracking framework to generate maps of connection probability[2,7]. The method utilises a Monte Carlo streamline approach with 1000 iterations, sampling the PDFs at each voxel location encountered by a streamline on each iteration.

Experiments Two complementary experiments demonstrate the effectiveness of noise-based probabilistic tracking using PAS-MRI. In the first, the pattern of connection probability from a region of interest covering the cross section of the left cerebral peduncle is defined (Fig. (c)). Branches of relatively high connection probability are observed to the medial and lateral primary motor cortex, reaching the full extent of the primary motor strip (yellow line). Similar levels of connection probability are also seen to the premotor areas, other frontal lobe areas, sensory areas, and to the thalamus. In the second experiment, the pattern of connection probability from a region covering the extent of the left primary motor strip is defined (Fig. (d)). The highest probability connections include those via the corticospinal tract to the left pyramid, to the thalamus, possibly to the subthalamic nucleus, to the putamen, possibly to the globus pallidus, to the superior parietal regions (Brodmann area 7) and via the corpus callosum to contralateral medial motor cortex. Likely false positive connections are observed to Wernicke's area and to the fornix.



Discussion Probabilistic connectivity mapping benefits from the increased information content provided by PAS-MRI in comparison with diffusion tensor imaging, allowing more accurate definition of the routes and termini of connections. We have shown that the connections that pass via the cerebral peduncle may be reconstructed and that these, to a large degree, match what is expected from known anatomy. In particular, it is encouraging that the entire primary motor area is identified along the length of the precentral gyrus, showing marked lateral branching, as required to connect the mouth, face, eye, and finger cortical areas. Although faithful reconstruction of this, the largest fibre tract of the brain, seems a trivial requirement for diffusion imaging-based fibre tracking, it has been shown consistently until now that the lateral motor areas are 'invisible' to fibre tracking from the cerebral peduncles.

References

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