Inferring on connections: A Bayesian framework for global diffusion tractography

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Introduction. White matter fibre tractography algorithms often use local orientation information, provided by diffusion weighted MR imaging, to infer connectivity between distant regions of the brain. Here we take a novel approach to the tractography problem, which allows us to test the evidence for specific connections within the data. Instead of tracing connections using only local orientation information [1,2,3,4], we *propose* the existence of a connection between two remote regions. This allows the formal use of global information to resolve local uncertainty. We then use the Bayesian evidence to test whether the connection is supported in the data. This framework also formalises the connectivity-based segmentation problem, by allowing us to infer directly on the *location* of the connection within the candidate regions. Furthermore, the framework provides a natural basis for a formal fusion of functional connectivity information from FMRI or MEG/EEG with anatomical connectivity information from diffusion data.

Methods. Our model is composed of two sets of parameters. The local parameters model the diffusion data generation at the voxel scale by means of multiple compartments representing isotropic and anisotropic diffusion (see [5,6]). The set of global parameters is simply the set of all tracts connecting the candidate regions, and binary parameters representing the existence of a connection between each pair of regions. Inference on the model allows us to compute the posterior distribution of both local and global parameters at the same time giving, among others, posteriors on the local fibre directions, as well as the pathway trajectories. In order to test the existence of a connection, we can compare the model evidence between models where the priors on the connection parameters are: p(connection)=1 and p(connection)=0, for the connected and unconnected models. We use a Monte Carlo Markov Chain (MCMC) sampler to draw samples from the posterior distribution on the parameters, and we use cubic splines to represent the fibre tracts. The method allows us to compute posterior distribution on the extremities of the tracts, which is a natural candidate for segmentation of brain regions in terms of their global connections.

Results. We tested our global tractography on various known brain pathways with connection priors set to 1 to test whether we could recover known white matter trajectories. Fig. 1 shows some of the resulting pathways for the connections between (from top left to bottom right): the medial dorsal nucleus of the thalamus and the anterior frontal cortex (anterior thalamic radiation); the superior parietal and premotor cortices (SLFI); the anterior temporal and the lateral prefrontal cortex (Uncinate fasciculus); Broca's area and Wernicke's area (SLF3); lateral geniculate nucleus and the primary visual cortex. (optic radiations) Fig. 2 shows the posterior distributions of the local orientation parameters for the local (red) and global (blue) models, for a connection between the two hand areas of the primary motor cortex. The constraints change the posterior fibre directions in locations where the data contain high uncertainty (left sphere – note also the reduced variance in the global model) while the two posteriors are similar in regions with low uncertainty (right sphere). The mode of these distributions is represented by vectors on a coronal section.

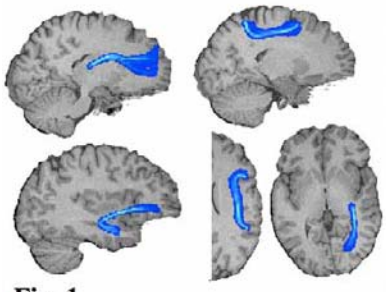

Fig. 1

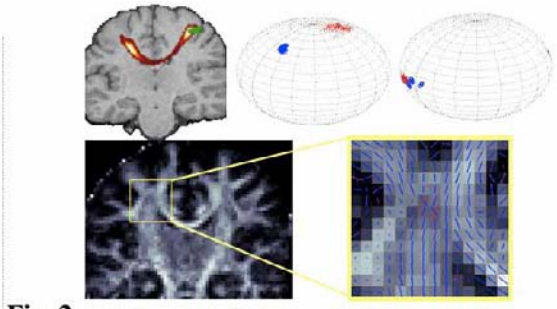

Fig. 2

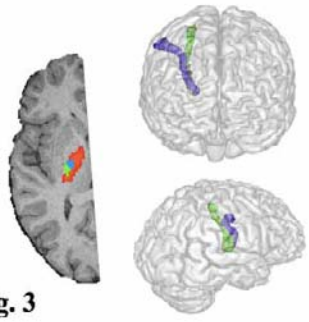

Fig. 3

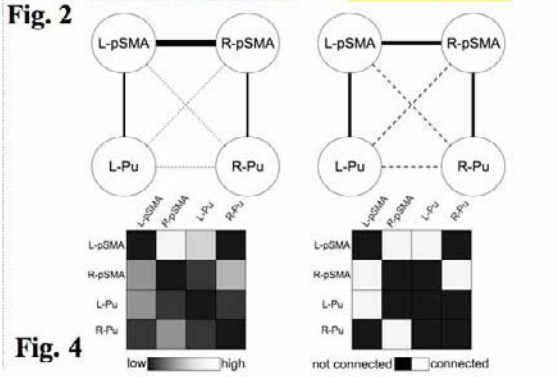

Fig. 4

Fig. 3 shows the result of a segmentation of the internal capsule with respect to connections to the primary motor cortex (hand area in green and face area in blue) – a particularly challenging segmentation for techniques that do not use global information. The segmentation is done on the basis of the posterior distribution on the extremities of the connections within the internal capsule. We see that these pathways twist from a medial-lateral to an anterior-posterior positioning throughout their descending trajectories toward the internal capsule. Finally, Fig. 4 shows The computation of the connection probability (left, using unconstrained probabilistic tractography) and the model evidence (right, continuous lines represent evidence for a connection) in a network composed of the bilateral pre-SMA and anterior putamen – Evidence for the known connection between putamen and preSMA is found despite the candidate regions being in grey matter (here the connections are tested independently).

Conclusions. Within the proposed framework, it is possible to propose the existence of a connection between two regions, formalise that proposal as a prior parameter and then test it by calculating the Bayesian evidence. This is a novel way of doing tractography that gives equivalent results to probabilistic tractography for known major anatomical tracts, but also allows tracing of tracts in which local tractography algorithms fail. It allows for inference on local directional parameters that is guided by large scale connections when local data are highly uncertain. This formalism naturally extends to various key questions in tractography studies. First, it naturally allows for the connectivity-based segmentation of brain areas, by inferring directly on the location of a connection. But more importantly, it allows inference on the existence of the connection via the Bayesian model evidence. This specific feature allows a natural extension toward a completely symmetrical fusion between diffusion data and functional data.

References. [1] Conturo et al (1999) PNAS 96:422–427; [2] Jones et al (1999) MRM 42:37–41; [3] Basser et al (2000) MRM 44:625–632; [4] Mori et al (2002) NMR Biomed 15:468–480; [5] Behrens et al (2003) MRM 50:1077–1088; [6] Hosey et al (2005) MRM 54:1480–1489