Probabilistic Connectivity in Fibre Tractography

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INTRODUCTION: During the past decade there has been an increased interest in developing fibre tractography algorithms for the analysis of fibre pathways in the brain. Many approaches have been proposed to model the diffusion signal and to obtain reliable connectivity patterns. Nonetheless, the question of defining probabilistic connectivity indices which capture all the relevant information in the diffusion MRI signal remains open. To address this problem we employ a stochastic nonlinear differential equation to model the Brownian motion of water molecules in a medium. This model is fundamentally related to the physical processes underlying diffusion MRI. A local, parallelizable implementation allows for the incorporation of the local diffusion MRI data and its uncertainty, leading to probabilistic estimates of fibre tracts between two seed regions. We validate the approach with experimental results on a recent phantom introduced at the MICCAI 2009 Fibre Cup [3].

METHODS: The Fokker-Planck equation describing the Brownian motion of water using a 3D random walk has been introduced for fibre tractography in [1]:

$$\frac{\partial P}{\partial t} = -\sin\theta\cos\varphi\frac{\partial P}{\partial x} - \sin\theta\sin\varphi\frac{\partial P}{\partial y} - \cos\theta\frac{\partial P}{\partial z} + \frac{\sigma_\varphi^2}{2}\frac{\partial^2 P}{\partial \varphi^2} + \frac{\sigma_\theta^2}{2}\frac{\partial^2 P}{\partial \theta^2} - \frac{1}{\zeta}P. \qquad (1)$$

Here, $(x, y, z, \varphi, \theta)$ denotes a state (position and orientation in 3D) and P is the probability of reaching that state, when passing between a "source" and a "sink" region. Additionally, the parameters σ_φ and σ_θ control the degree of deviation of a particle following a random walk in 3D, described by Equation (1), and ζ specifies the particle's average lifetime. While the simple numerical method proposed in [1] is accurate enough to reconstruct simple fibre tracts, it becomes numerically unstable for more complicated fibre pathways with highly curving or twisting tracts. We propose a more accurate numerical method that is unconditionally stable, where we use the Crank-Nicholson scheme for the diffusion terms and a Lax-Wendroff scheme for the advection terms in Equation (1). This method eliminates the need for thresholds on maximum curvature or torsion values and it also allows information from the diffusion MRI data to be locally incorporated. To achieve this we use a bootstrap probabilistic deconvolution framework [2] to provide a non-parametric estimate of the underlying uncertainty in the data. The output of the bootstrap scheme is the average direction of maxima and their corresponding cones of uncertainty at each voxel, and these are used to compute a local σ_φ, σ_θ and a decay rate ζ for each state in the volume. This is done by finding the closest average fibre orientation distribution maximum to each (φ, θ) direction, computing the two angular differences between the given direction and the chosen maximum, and finally setting the corresponding σ_φ and σ_θ values equal to a scaled version of these differences. To set the decay rate, the current orientation is examined to see if it is within the cone of uncertainty around the chosen maxima. If so, the decay rate is increased linearly with the angle difference to support directions within the cone of uncertainty. If not, the decay rate is linearly decreased, causing the directions lying outside of the cone to be suppressed. In order to obtain the final reconstructed fibre pathway, two independent probability distributions are evolved based on the above Fokker-Planck equation. In the first, the particles are constrained to begin in one seed region to generate a "source" completion field. In the second the particles are constrained to end in the other seed region to generate a "sink" completion field. The final 3D completion field, which is a probabilistic representation of the connectivity pattern, is given by the multiplication of these two completion fields.

RESULTS: The proposed algorithm was tested on the MICCAI 2009 Fibre cup phantom [3], for which ground truth fibre tracts are available. Five different seed region pairs were explored (b-f), where the first four are associated with a true fibre tract while the last is not. A visual inspection of the reconstructed connectivity patterns can represent the confidence associated with each connection (in the sub-figures b-f below the probability of a state occurring is inversely proportion to the transparency of the associated orientation in red). However a quantitative measure of connectivity is typically more useful. In Table 1, we report a measure of connectivity, similar to the weakest link approach [4], which is obtained by first choosing the maximum probability value at each voxel and then selecting the lowest value among all the voxels required to observe the connection between the two seed regions. We also report the highest probability value along each inferred tract.

Exp.	Weakest Link	Strongest Link
(b)	0.1	0.82
(c)	0.2	0.87
(d)	0.2	0.98
(e)	0.05	0.57
(f)	0.008	0.37

Table 1

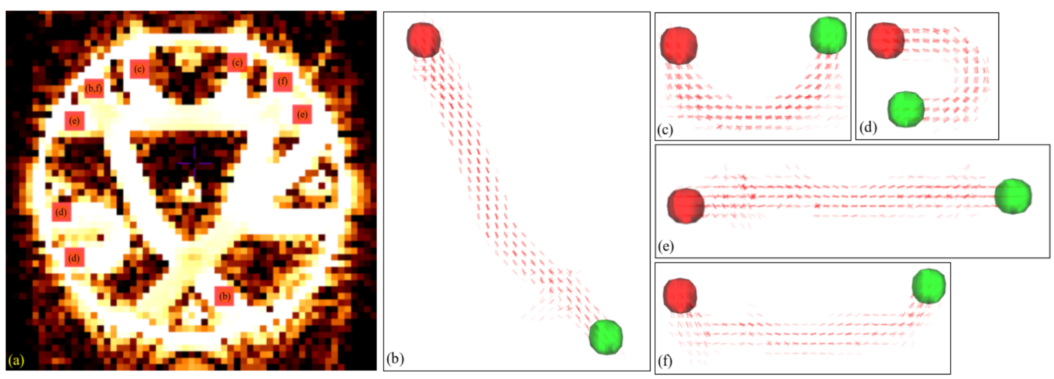

Figure (a) illustrates the mean diffusivity of the phantom data and the seed regions used in the experiments. Figures (b) through (f) show the results of the local parallel completion field algorithm for different source and sink pairs. The connectivity indices are summarized in Table 1.

DISCUSSION: We address the problem of fibre tractography and anatomical connectivity measurement by developing a computational model that characterizes the diffusion of water molecules. This leads to a probabilistic notion of fibre tracts, from which a justifiable connectivity measure can be computed. The results obtained on the phantom demonstrate the potential of the algorithm to reconstruct the most probable fibre pathways between two seed regions, along with a connectivity index. The two seed regions in the last experiment, between which a true fibre tract does not exist, result in the lowest connectivity index. The approach can also find highly curving fibre tracts (e.g. c, d) without the need to impose thresholds on maximum curvature or torsion. Furthermore, due to the probabilistic nature of the algorithm, there is no need to eliminate false positives, which is an issue that confounds many other tractography algorithms. Additional benefits of the algorithm are its low computational complexity (which is independent of the size of the seed regions) and the fact that the parameters are all derived automatically from the data, i.e., no further parameter tuning has been carried out. Given the probabilistic nature of the approach and the Markov property which underlies the random walk simulated by the Fokker Planck equation, the framework provides a basis for new theoretically driven measures of connectivity, which is a subject of ongoing work.

References: [1] Momayyez *et al.* MMBIA09: 178-185, 2009. [2] Momayyez *et al.* DMFC09: 81-92, 2009. [3] Poupon *et al*. MRM 60(6): 1276-83, 2008. [4] Lenglet *et al.* NeuroImage 45(1): S111-22, 2008.