Software Tool to Generate Complex Structures for Validation of Fibre Tracking

T. G. Close[1,2], J-D. Tournier[1,3], F. Calamante[1,3], L. A. Johnston[2,4], I. Mareels[2,5], and A. Connelly[1,3]

[1]Brain Research Institute, Melbourne, Victoria, Australia, [2]National ICT Australia, Melbourne, Victoria, Australia, [3]Department of Medicine, University of Melbourne, Melbourne, Victoria, Australia, [4]Howard Florey Institute, Melbourne, Victoria, Australia, [5]Electrical Engineering, University of Melbourne, Melbourne, Victoria, Australia

Introduction

Despite important advances in fibre-tracking algorithms over the last few years, the field is currently limited by the lack of a 'gold standard' for validation and comparison of results. Much work has been done to validate these algorithms using comparisons with known anatomy and ex vivo measurements [e.g. 1,2], but these methods are both time-consuming and ultimately limited. In addition, manufacturing sufficiently complex physical phantoms is difficult due to the spatial scale at which diffusion-weighted (DW) MRI is sensitive. These impracticalities coupled with uncertainties in the true fibre positions has meant that tracking algorithms are often validated against simulated data, where the exact fibre configuration is known and the simulated conditions are easily altered. However, emulation of even basic characteristics of white matter (WM) fibres is a non-trivial task; relatively complex models have been constructed, but do not model the complex bending and crossing that have been shown to exist in WM in vivo [e.g. 3]. To address this problem, we have developed a fast flexible software tool that can generate random models of collections of WM bundles with a complexity comparable to that of WM. This provides an essential tool for current and future tracking algorithms to be robustly tested, and their limitations more thoroughly understood.

Methods

The proposed toolbox generates models consisting of a volume filled with 'strands', each modelled as a 3D curve with cross-sectional area specified by a nominal radius. The following criteria were deemed necessary for a sufficiently realistic model of WM fibres for DW-MRI simulation: the strands are appropriately space-filling; their volumes do not overlap; their cross-sectional area remains stable along their lengths; their curvature is limited; they are not overly circuitous; and they tend to run in large bundles. To achieve these characteristics, the algorithm starts from an arbitrary initial configuration and then adjusts the position of control points on the strands by minimising an appropriate cost function. The cost function includes terms to penalise the following properties: spatial overlap between different strands; curvature of individual strands; and length of individual strands. To ensure that strands ran in bundles, the optimisation is performed in two stages. First, the positions of a number of strands with large nominal radii (representing bundles) are optimised. These optimised strands are then sub-divided into a larger number of thinner strands. The positions of these new strands are then optimised again to reach the final configuration.

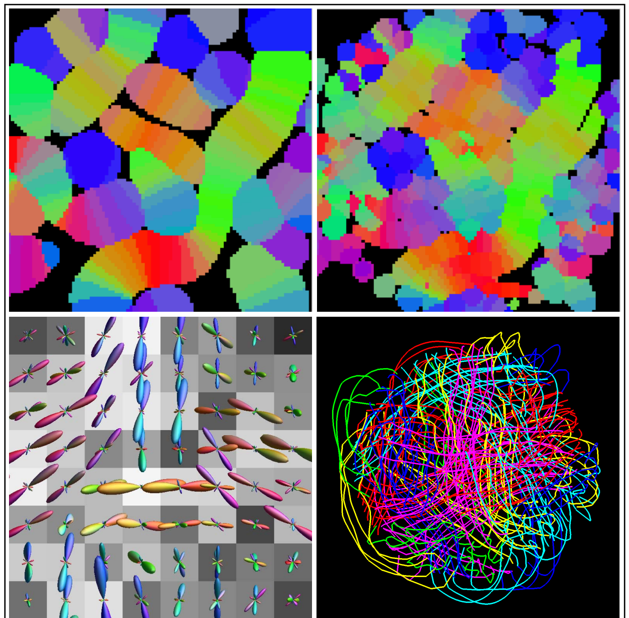

Figure 1: top: one slice from the 3D colour-coded direction map of initial bundles; left: after the first optimisation step; right: after the subdivision and final optimisation. Bottom left: fibre orientation distribution obtained using CSD over a representative region of interest from the final noisy DW data set. Bottom right: all 203 strands plotted as 3D curves, coloured according to their parent bundle.

The following procedure is then used to generate sample DW data sets. First, strand directions are mapped onto a high-resolution 3-dimensional grid. The appropriate DW signals are then computed in each grid element according to a suitable model; in this study, the standard diffusion tensor model was assumed (an isotropic tensor was assumed for grid elements not belonging to any strand). The signal within each simulated imaging voxel is then computed by summing the DW signal from its corresponding grid elements. Finally, quadrature noise of specified amplitude is added to the DW signals for each voxel.

As a simple illustration of the use of this toolbox, a sample simulated data set was generated using 35 initial strands with mean diameter = 4 mm (final configuration: 203 strands with mean diameter = 1.4 mm). The DW signal was computed by sampling on a 0.2 mm grid for a final imaging voxel size of 2 mm isotropic, assuming SNR(b=0) = 30 and a tensor model with ADC = 0.9×10^{-3} mm^2/s and FA = 0.8. The standard 'streamlines' fibre-tracking algorithm [4] was used to track a particular fibre bundle, using two different methods to estimate fibre orientations, the major eigenvector of the diffusion tensor (DT) [5] and the constrained spherical deconvolution (CSD) method [6].

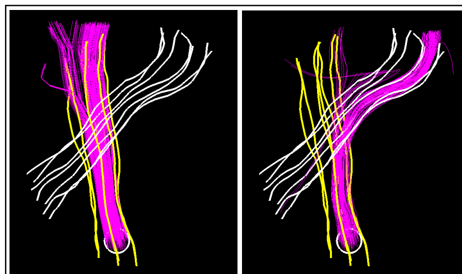

Figure 2: fibre-tracking results obtained using the simple streamlines algorithm, using fibre orientations obtained assuming the diffusion tensor model (left) and constrained spherical deconvolution (right). Tracking was initiated from the spherical seed region, in an attempt to track the yellow bundle. Only the two most relevant bundles from the set of 35 are shown to aid visualisation. Differences between the two sets of results are evident, and deviations from the true fibre paths can readily be appreciated.

Results

As can be seen in figure 1, the two-stage optimisation procedure produces configurations fulfilling all of the desired criteria. Notably, the strands fill almost all the available space, with very few grid elements not belonging to any strand. Also, the two-stage optimisation process does produce strands that run in large bundles. The configurations produced contain a high degree of complexity, as can be readily appreciated from the example in figure 1.

A simple example of how this toolbox might be used is shown in figure 2. The two different fibre-tracking methodologies can be seen to produce different results. Since the exact simulated strand configuration is known, it is possible to assess the reliability of each methodology objectively. Note that in this figure, only two of the 35 simulated bundles are displayed so that the results can be more easily visualised and understood.

Discussion

The toolbox described here is capable of generating configurations of strands that mimic features of white matter that are relevant for diffusion tractography, such as interfaces and 'interdigitation' between adjacent fibre bundles, giving rise to 'crossing fibre' voxels. The models generated have known configurations and levels of complexity appropriate for white matter, and can thus be used to formally assess the performance of current and future fibre-tracking methodologies. The level of complexity, diffusion model, and imaging parameters can all be adjusted, so that the 'operating range' of different methodologies can be objectively characterised. Finally, since each configuration is generated at random, a large number of models can be constructed with the same parameters, thus avoiding any bias due to the particular configuration of any one model. Although quantification of the tracking results is beyond the scope of this study, suitable measures of reliability can be devised that will allow objective assessment of tractography methodologies. This toolbox can therefore be used as a much-needed 'gold standard', and will be made freely available to provide researchers with a valuable tool with which to assess and compare their algorithms.

Acknowledgements: supported by National ICT Australia and the National Health & Medical Research Council of Australia.

References: [1] Dyrby *et al.*, Neuroimage 37: 1267-1277 (2007). [2] Pautler *et al.*, MRM 40: 740-748 (1998). [3] Behrens *et al.*, Neuroimage 34: 144-155 (2007). [4] Mori *et al.*, Ann Neurol 45: 265-269 (1999). [5] Basser *et al.*, Biophys J 66: 259-267 (1994). [6] Tournier *et al.*, Neuroimage 35: 1459-1472 (2007).