Structurally-Informed Tractography: Improved Diffusion MRI Streamlines Tractography using Anatomical Information

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Introduction: An increasingly large variety of methods are available for assessing diffusion-weighted (DW) images of the brain using tractography. Although the individual pathways reconstructed by this process should ideally possess biological analogues, inadequacies in the methodology employed can lead to known false positive results; for instance, tracks crossing fluid-filled regions, which is not physically realistic. Here we propose a modular improvement to streamlines tractography which utilises the tissue information from an anatomical-contrast scan acquired during the same session. Unlike previous work in this field, where this image has been used to generate a propagation mask with greater accuracy than simple anisotropy thresholds [1], here we make more effective use of all of the information available from brain tissue segmentation to apply biologically realistic priors during tracking – we refer to this as "Structurally-Informed Tractography". We investigate the implications of these changes in the context of different models of diffusion, tractography algorithms and seeding strategies.

Method: To apply the information from an anatomical scan during tractography, it must be accurately aligned spatially with the corresponding DW images; use of an echo-planar readout during DW imaging results in susceptibility distortions in the phase-encode axis which cause mis-alignment with the (effectively) un-distorted anatomical scan. Superior image alignment is achieved by acquiring pairs of *b=0* images with reversed phase-encode acquisition direction, and estimating the main field inhomogeneity through the process described by Holland et al. [2]. This map is then used to unwarp the relevant distorted DW images, and a simple rigid body registration is used only to compensate for patient motion between scans [3]. Tissue probability maps are calculated using the FMRIB Software Library [4].

Anatomical priors are applied to each streamline as follows (*GM*, *WM* and *CSF* correspond to the local trilinear-interpolated partial volume fractions of grey matter, white matter and cerebro-spinal fluid respectively): • Tracks entering grey matter (defined as $WM < 0.2$ and $GM > CSF$) are considered to have terminated appropriately. • Tracks terminating due to low anisotropy (when tracking using the Diffusion Tensor [5]), low Fibre Orientation Distribution (FOD) amplitude (when using a spherical deconvolution-based approach), or high curvature, are rejected if $GM < 0.2$ or $GM < CSF$ (this permits terminations in sub-cortical grey matter, but not in deep white matter). • Tracks entering fluid-filled regions (defined as $CSF > 0.5$) are rejected. • The conventional minimum track length criterion is replaced by a threshold upon the path integral of the value of *WM* along the length of the track (this permits very short inter-gyral connections through the white matter, but U-fibres at the partial-volumed *GM*/*WM* interface must be longer). • If a track exits the field of view of either the diffusion or anatomical image, it is still deemed acceptable (necessary for tracking to the spinal column). • If a track is rejected due to a poor termination, and a probabilistic streamlines algorithm is being used, it may be truncated and re-traced in search of a better path – the extent of truncation is increased if further poor terminations are encountered. In addition, the effects of seeding strategy were investigated; uniform white matter seeding and bidirectional tracking was performed (using the segmented white matter mask), as well as random seeding from the isocontour where $WM = 0.2$ and $GM > CSF$ (effectively the grey matter – white matter boundary) with unidirectional tracking.

Data acquisition: Two diffusion-weighted image series were acquired from a healthy volunteer on a 3T Siemens Tim Trio (2 mm isotropic / 25 directions / b = 1,000 s.mm^{-2} and 2.5 mm isotropic / 60 directions / b = 3,000 s.mm^{-2}). For the b = 1,000 s.mm^{-2} data set, the local fibre orientation was taken as the principal eigenvector of the Diffusion Tensor [5], and one million deterministic streamlines generated using the FACT algorithm [6]; for the b = 3,000 s.mm^{-2} data set, fibre orientation distributions were estimated using Constrained Spherical Deconvolution [7], and one million probabilistic streamlines generated using 2nd Order Integration over Fibre Orientation Distributions (iFOD2) [8]. FA / FOD amplitude thresholds were 0.1, and minimum radius of curvature was 2.5 mm. All pre-processing and visualization was performed using the MRtrix software package [9] or in-house modifications thereof.

Results & Discussion: Figure 1 shows the reconstruction of the connectome using the two aforementioned tracking algorithms, using a conventional DWI-derived whole-brain mask (Fig. 1.a & d), a T1-derived white matter propagation mask (Fig. 1.b & e), and the anatomical priors proposed here (Fig. 1.c, f & g). Although the deterministic tensor tracking results may appear 'worse' with use of these anatomical priors (Fig. 1.c), this is in fact highlighting how a large number of tracks produced using this model were biologically unrealistic, with many streamlines artificially terminating inside the white matter (which are rejected when our priors are applied). For iFOD2 tracking, using the white matter segmentation as a tracking mask (Fig. 1.e) removes much of the partial volume effects (see for example the surface of the corpus callosum in Fig. 1.d & e) and spurious inter-gyral connections across the sulci, but incorrect track terminations remain in the deep white matter and at fluid interfaces; these are eliminated by applying our enhanced anatomical priors (Fig. 1.f & g).

It is generally accepted that uniform or random tractography seeding within a brain mask over-defines the major white matter structures of the brain, as they present a greater volume from which to seed. By instead seeding from the grey matter – white matter interface (Fig. 1.g), reconstruction of the superficial white matter projecting into the cortical folds is improved, along with the homogeneity of track termination coverage at the cortical surface.

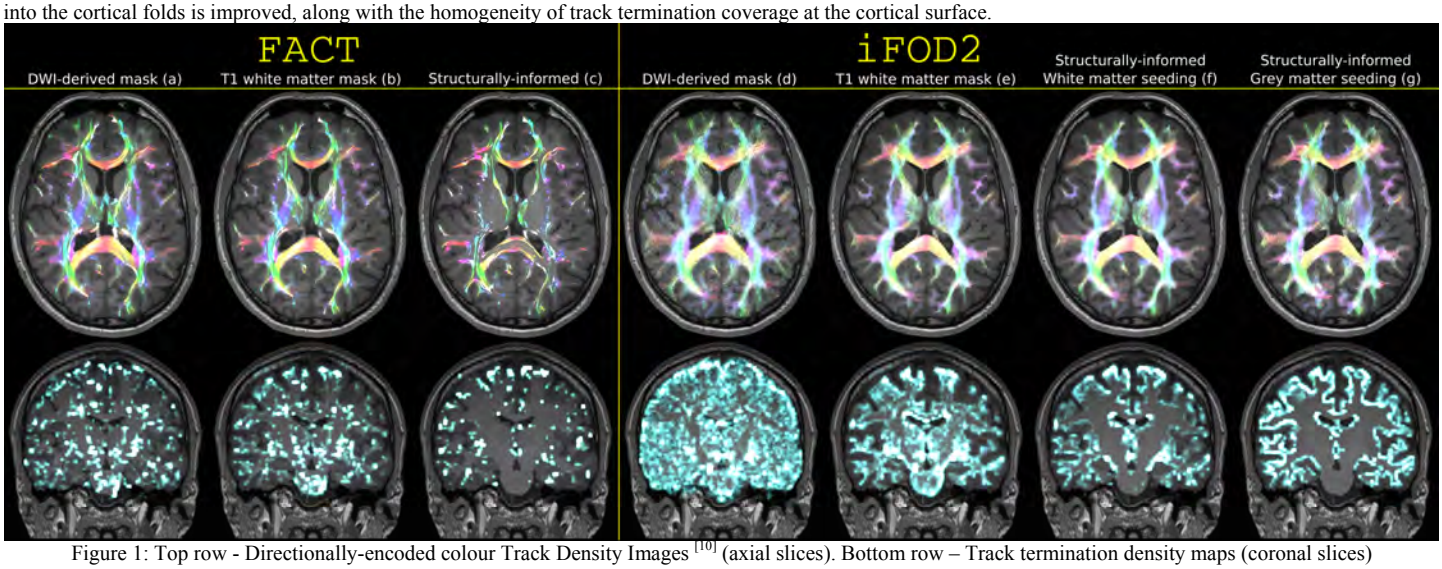

Figure 1: Top row - Directionally-encoded colour Track Density Images [10] (axial slices). Bottom row – Track termination density maps (coronal slices)

Conclusion: We have presented a modular addition to diffusion MRI streamlines tractography, which makes full use of the information available from a same-subject T1 anatomical contrast image. It improves the biological accuracy of tractography results when state-of-the-art methods are used, whilst highlighting the deficiencies in tensor-based methods. All analyses that utilise diffusion MRI fibre-tracking should benefit from the resulting improved reconstruction of the connectome.

References: [1] Guevara et al., *In Proc. ISMRM* **19**:2018 (2011) [2] Holland et al., *NeuroImage* **50**:175-183 (2010) [3] Ashburner and Friston, *Human Brain Function*, Academic Press, ch.2 (2003) [4] Smith et al., *NeuroImage* **23**:208-219 (2004) [5] Basser et al., *Biophys. Jour.* **66**:259-267 (1994) [6] Mori et al., *Ann. Neur.* **45**:265-269 (1999) [7] Tournier et al., *NeuroImage* **35**:1459-1472 (2007) [8] Tournier et al., *In Proc. ISMRM* **18**:1670 (2010) [9] MRtrix, www.brain.org.au/software [10] Calamante et al., *NeuroImage* **53**:1233-1243 (2010)