

SIFT: Spherical-deconvolution Informed Filtering of Tractograms

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Introduction: There is increasing interest in the development of methods and models to analyse the structural connectivity of the entire human brain *in vivo* using diffusion MRI tractography. These analyses rely upon the reconstruction of the connectome being robust as well as biologically-accurate; unfortunately many methodological factors can influence this reconstruction (and hence any derived measures), even including the seeding strategy^[1]. This is in part due to the fact that in streamlines tractography, tracks are generated independently from one another, such that specific pathways in the brain may be over- or under-defined with respect to the underlying biology. Here we propose a post-processing filter of whole-brain fibre-tracking data to compensate for such methodological biases.

Method: Simulation results from Raffelt et al. ^[2] show that the amplitude of each peak in the Fibre Orientation Distribution (FOD) produced using spherical deconvolution is proportional to the intra-cellular volume fraction of the axons within the voxel that are aligned with that peak. Hence, if the results of whole-brain fibre-tracking were a perfect reconstruction of the underlying neuronal axon configuration, the track densities in high angular resolution space should correspond to the orientations and relative amplitudes of the FOD peaks. As such, we can construct a simple cost function:

$$f = \sum_{v \in WM} \sum_{p=1}^{P_v} (\mu \cdot TD_{v,p} - FOD_{v,p})^2 - \alpha \cdot \mu_0 \cdot TD_{v,p}$$

where $FOD_{v,p}$ is the amplitude of FOD peak number p within voxel v , $TD_{v,p}$ is the density of tracks traversing voxel v in the direction of peak p (taking into account the path length of each track through the voxel), P_v is the number of discrete peaks in voxel v , μ is an explicit numerical normalisation between track density and FOD peak amplitudes throughout the brain (μ_0 is the initial value of μ), and α is a regularisation parameter that biases toward retention of high track density. We consider only those voxels for which the diffusion signal originates predominantly from white matter: we perform EPI distortion correction using the method described by Holland et al. ^[3] (in addition to improving alignment with the corresponding T1 image, this also scales the diffusion signal according to local image compression / expansion), followed by rigid body registration to the subject's T1 image ^[4], segmentation of the T1 image into the three principal tissue types ^[5], and integration of the segmented tissues within the volume of each diffusion image voxel; we process only those voxels for which the grey matter fraction is below 0.1 and the CSF fraction is below 0.75. The peak FOD amplitudes are obtained through a simple gradient-ascent approach.

At the start of each iteration, the local gradient vector of the cost function given the prospective removal of each individual track is computed, which considers both changes in the track densities $TD_{v,p}$ of those peaks traversed by each track, and the corresponding change to the normalisation factor μ for all peaks. Tracks are then removed from the data set in order of greatest decrease to the cost function, until the gradient vector must be re-computed and the process repeated. Processing is completed when no track remains whose removal would cause a decrease in the cost function exceeding that of track density quantisation. Unlike the BlueMatter method ^[6], our technique can run on a desktop computer, and it requires fewer assumptions regarding the contribution of individual streamlines to the diffusion data.

Data acquisition: Diffusion-weighted images were acquired from a healthy volunteer on a 3T Siemens Tim Trio (2.5 mm isotropic / 60 directions / $b = 3,000 \text{ s.mm}^{-2}$), as well as a T1 anatomical contrast image using a 3D MPRAGE sequence with 0.9 mm isotropic resolution. FODs were estimated using Constrained Spherical Deconvolution ^[7], and ten million probabilistic streamlines generated using 2nd Order Integration over Fibre Orientation Distributions (iFOD2) ^[8]. Pre-processing and visualization was performed using the MRtrix software package ^[9] or in-house modifications thereof.

Results & Discussion: Figure 1 shows the white matter reconstruction before (Fig. 1.a) and after (Fig. 1.b-d) track filtering. In the original tractography results (Fig. 1.a), specific areas of the brain that are over-defined by this particular tractography algorithm include the inferior surface of the corpus callosum, and the cortico-spinal tracts just below the pons; these artefacts can be significantly reduced by filtering just 5% of the tracks (Fig. 1.b). However intensity variations still remain - one would expect the axonal density within the white matter to be homogeneous throughout the brain (based on the relative homogeneity of proton density and tissue relaxation rates), but the major white matter pathways are clearly over-defined in Fig. 1.b (likely due to the increased lengths of these bundles providing more volume for tractography to seed from), with reduced definition of the superficial white matter and projections within the gyral folds. With less regularisation (Fig. 1.c) this homogeneity is much improved, at the expense of overall track density. Running with no regularisation (Fig. 1.d) yields the most homogeneous white matter coverage, but with a 30-fold reduction in the number of tracks; hence the 'low SNR' appearance of the image.

In addition to improving the accuracy of the white matter reconstruction, this framework has the capability of evaluating different tractography algorithms & seeding strategies; better methods should yield a superior fit to the image data given the cost function, as well as provide a more accurate initial estimate of the connectome (and therefore require removal of fewer tracks to achieve convergence).

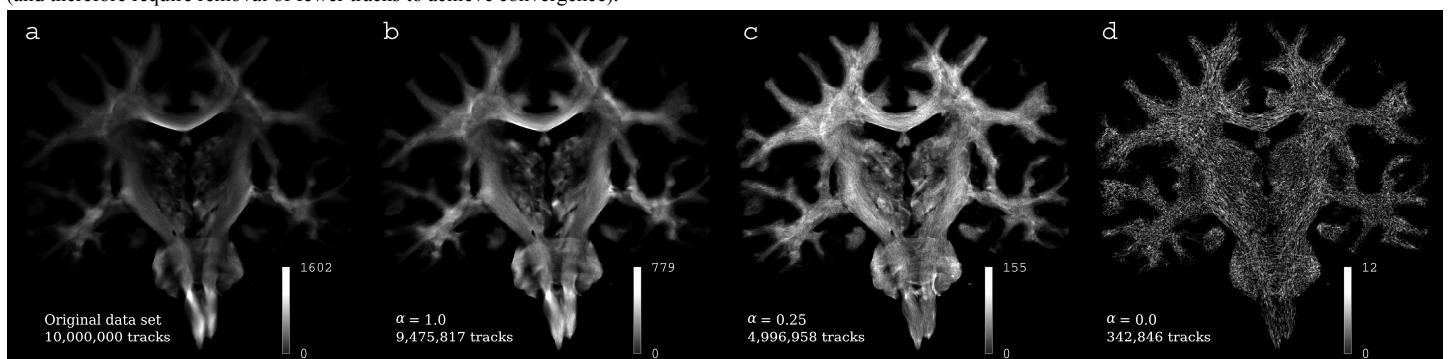


Figure 1: Super-resolution Track Density Images ^[10] – coronal 0.25mm slices. All images windowed linearly.

Conclusion: We have introduced a scalable mechanism for filtering the results of diffusion MRI whole-brain fibre-tracking to improve the homogeneity of white matter coverage and the accuracy of the whole-brain tractography reconstruction given the image data. Any analysis pipeline which depends upon a biologically-accurate reconstruction of the structural connections of the entire brain (e.g. network-based analyses ^[11]) should benefit from the reduction of biases associated with particular tractography algorithms or seeding strategies.

References: [1] Li et al., *HBM*; doi:10.1002/hbm.21332 [2] Raffelt et al., *NeuroImage*; doi:10.1016/j.neuroimage.2011.10.045 [3] Holland et al., *NeuroImage* **50**:175-183 (2010) [4] Ashburner and Friston, *Human Brain Function*, Academic Press, ch.2 (2003) [5] Smith et al., *NeuroImage* **23**:208-219 (2004) [6] Sherbondy et al., *In Proc. MICCAI* **12**:861-868 (2009) [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) [11] Knösche and Tittgemeyer, *Front. Syst. Neuro.* **5**:58 (2011)