## 'Dynamic' seeding: Informed placement of streamline seeds in whole-brain fibre-tracking

Robert Elton Smith<sup>1</sup>, J-Donald Tournier<sup>2,3</sup>, Fernando Calamante<sup>1,4</sup>, and Alan Connelly<sup>1,4</sup>

Imaging division, The Florey Institute of Neuroscience and Mental Health, Heidelberg, Victoria, Australia, 2Centre for the Developing Brain, King's College London, London, United Kingdom, <sup>3</sup>Department of Biomedical Engineering, King's College London, London, United Kingdom, <sup>4</sup>Department of Medicine, The University of Melbourne, Heidelberg, Victoria, Australia

Target audience: Researchers interested in the quantitative assessment of brain white matter connectivity using diffusion MRI tractography.

Purpose: Methods for reconstruction of whole-brain structural connectivity using diffusion MRI tractography typically fall into one of two categories: either 'local' (e.g. streamlines-based) or 'global'[1]. While local approaches are computationally efficient and very dense reconstructions may be produced, they fail to provide an adequate explanation of the diffusion data, making such reconstructions non-quantitative<sup>[2]</sup>; on the other hand, global approaches may satisfy this requirement, but are highly computationally expensive, and may not possess an adequate number of trajectories for subsequent analyses to be robust. More recently, a class of 'hybrid' methods has emerged that imbue an initial whole-brain tractography reconstruction with quantitative properties, by perturbing the reconstruction in such a manner that correspondence with the diffusion image data is achieved. This may be done through selection of an appropriate subset of streamlines<sup>[3,4,5]</sup>, determining appropriate weights for streamlines [6,7,8], or indeed through perturbation of the streamline trajectories themselves [8]. Here we propose a novel method within this class of hybrid approaches, which operates during tractogram generation rather than subsequent to it: the total streamlines density in each fibre orientation is monitored as streamlines are generated, and the relative differences between fibre densities (as estimated by the diffusion model) and reconstructed streamlines densities are used to dynamically alter the placement of subsequent streamline seeds. We demonstrate the effectiveness of this approach by comparing it to typical naïve homogeneous streamline

seeding, both throughout the white matter and from the interface between grey and white matter.

Method: We use the model as defined in the Spherical-deconvolution Informed Filtering of Tractograms (SIFT) method<sup>[5]</sup> for comparing fibre densities to reconstructed streamlines densities. After each generated streamline is written to the output file on disk, it is subjected to a streamline mapping process, which determines the subset of Fibre Orientation Distribution (FOD) lobes traversed by the streamline, as well as its length through each voxel. This information is used to update the streamlines density currently attributed to each FOD lobe, as well as the total reconstructed streamlines density (which directly influences the proportionality coefficient  $\mu$  within the SIFT model<sup>[5]</sup>). Appropriate seed locations for new streamlines are determined using a rejection sampling framework: all FOD lobes begin with a uniform initial seeding probability (e.g. 0.001); whenever a lobe is selected at random for sampling, the seeding probability for that lobe is updated by comparing its current attributed streamlines density to its fibre density as estimated from the FOD, i.e. if an inadequate number of those streamlines generated thus far pass through that lobe, its seeding probability is increased, and vice-versa. The algorithm therefore forms a closed loop system, where generated streamlines influence the placement of subsequent streamline seeds; moreover, it is independent of the particular streamlines algorithm used (Fig. 1).

Data acquisition & pre-processing: Image data were acquired from a healthy male volunteer on a 3T Siemens Tim Trio system (Erlangen, Germany). The DWI protocol was as follows: 60 diffusionsensitisation directions at b=3,000s.mm<sup>-2</sup>, 7 b=0 volumes, 60 slices, 2.5mm isotropic voxels. An

Streamlines (N threads) Streamline seeding Streamlines mapping (N threads) eamlines density mage update (1 thread) coefficient µ Figure 1: Flow chart for proposed dynamic seeding

framework. Rectangles: processes; parallelograms: data.

anatomical T1-weighted image was acquired using an MPRAGE sequence (TE/TI/TR = 2.6/900/1900ms, 9° flip, 0.9mm isotropic voxels). Diffusion images were corrected for subject motion, susceptibility-induced distortions<sup>[9]</sup> and B<sub>1</sub> bias field<sup>[10]</sup>. FODs were estimated using Constrained Spherical Deconvolution (CSD)<sup>[11]</sup>. Tractograms of 10 million streamlines each were generated using the iFOD2 probabilistic streamlines algorithm<sup>[12]</sup>, incorporating the Anatomically-Constrained Tractography framework<sup>[13]</sup>. Seeding was performed using one of three mechanisms: randomly throughout the white matter ('WM'), randomly placed at the grey matter – white matter interface ('GMWMI')<sup>[13]</sup>, and using the proposed dynamic seeding framework ('Dynamic'). Results were compared quantitatively by comparing the cost function value (quality of fit of streamlines reconstruction to diffusion image data within the SIFT model) before and during application of the SIFT method. Results: Time required to generate 10 million streamlines on Core i7 system: WM = 101 minutes; GMWMI = 65 minutes; Dynamic = 87 minutes.

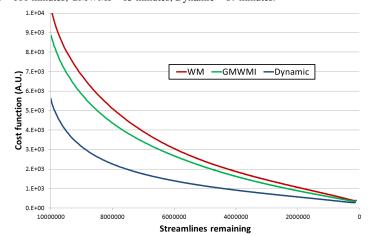


Figure 2: Target voxel-wise fibre densities as provided by spherical deconvolution, and differences between target fibre densities and reconstructed streamlines densities

Figure 3: Value of cost function within SIFT as a function of the number of remaining streamlines

Discussion: The proposed dynamic seeding framework incorporates global reconstruction information into otherwise locally-informed streamlines tractography, providing a superior fit to the acquired image data than naïve homogeneous seeding (Fig. 2), with negligible impact on execution time. However, it cannot provide perfect reconstruction densities without further processing, as it can only compensate for a subset of reconstruction biases present in streamlines tractography. It is therefore ideal for use in conjunction with other methods within the class of hybrid approaches that perturb a tractogram toward the image data (e.g. [3-8]), as it provides tractograms with better initial distributions of reconstructed streamlines density that will require less modification in order to provide an adequate fit (Fig. 3).

References: [1] Tournier et al., MRM 2011:65 ;1532-56 [2] Jones et al., NeuroImage 2013:73;239-254 [3] Sherbondy et al., MICCAI 2009: 861-868 [4] Sherbondy et al., MICCAI 2010:183-190 [5] Smith et al., NeuroImage 2013:67;298-312 [6] Smith et al., ISMRM 2014:0278 [7] Daducci et al., IEEE TMI 2014:99 [8] Lemkaddem et al., doi:10.3389/fneur.2014.00232 [9] Andersson et al., NeuroImage 2003:20;870-888 [10] Tustison et al., IEEE TMI 2010:29;1310-1320 [11] Tournier et al., NeuroImage 2007:35;1459-1472 [12] Tournier et al., ISMRM 2010:1670 [13] Smith et al., NeuroImage 2012:62;1924-1938