# Whole-brain track-density mapping as a tool for fiber tractography

**F. Calamante[1,2], J-D. Tournier[1,2], H. Pardoe[1,2], and A. Connelly[1,2]**

[1]Brain Research Institute, Florey Neuroscience Institutes (Austin), Melbourne, Victoria, Australia, [2]Department of Medicine, University of Melbourne, Melbourne, Victoria, Australia

**Introduction:** Important advances in fiber tractography have prompted numerous applications in clinical and research studies. Currently, the most commonly used tractography method is based on a multi-ROI approach (1), i.e. tracks of interest are isolated by constraining them to pass through 2 or more regions (e.g. a seed and a target). However, this approach relies on having good quality data (e.g. with good anatomical contrast, high spatial resolution and SNR, and with the same distortions as the diffusion data) to aid the user in the important step of precise ROI definitions. A further practical difficulty when comparing tractography results from multiple subjects is the presence of inter-subject differences. Several approaches have been proposed for data normalization, but they usually rely on low spatial resolution data (e.g. normalization based on *b*=0 images, FA maps, etc)(2-4). We propose the use of *whole-brain track-density* mapping as a tool to address these problems.

**Methods:** Track-density mapping (i.e. images based on the number of tracks traversing a given voxel or ROI) has been extensively used to estimate the probability of connection between regions, or as a tool to parcellate brain structures (5-7). It has also been used as a summary parameter to characterize fiber bundles (8). In our study, this approach is not used for a particular white matter structure (as in previous studies), but it is used to calculate *whole-brain* track-density maps. To this end, whole-brain probabilistic fiber tracking was performed as an initial step, and the total number of tracks present in each grid element was then calculated (note that the grid element can be *smaller* than the voxel size –see below). Fiber tracking was performed using the *MRtrix* package (http://www.brain.org.au/software/), based on the probabilistic streamlines method (6,7) and the constrained spherical deconvolution (CSD) technique (9) to model multiple fiber orientations. The relevant parameters were: step-size=0.1mm, maximum angle between steps=30º, CSD $l_{max}$ parameter=10. To illustrate the use of whole-brain track-density mapping as a tool to define ROIs for tractography, tracking was also performed on the fornix (a thin structure, hard to track consistently), by defining seed/target ROIs in the track-density map.

Diffusion-weighted (DW) data were acquired from 3 healthy volunteers on a 3T Siemens Trio system, using a twice-refocused SE-EPI sequence ($b$ = 3000 s/mm$^2$, 150 directions, 54 contiguous slices, voxel size 2.3×2.3×2.3 mm). A *b*=0 volume was acquired first, and repeated after every 10 DW volumes.

To illustrate the use of whole-brain track-density mapping in multi-study comparisons, the maps were nonlinearly co-registered to a custom template using SPM5. Default settings were used except for 4mm source image smoothing and 15mm nonlinear frequency cut-off. The inverse deformation was then applied to each track. The custom template was created by: (i) affine registration of maps to SPM5 white-matter priors; (ii) averaging and smoothing the registered maps using 4mm gaussian kernel (first-pass template); (iii) nonlinear co-registration of maps to first-pass template, followed by averaging and smoothing using 4mm kernel (custom template).

**Results:** Whole-brain track-density maps showed high contrast-to-noise ratio and good anatomical information, provided a sufficient number of tracks (relative to the final grid size of the map) are generated. For example, Fig. 1 shows an axial slice map generated with 100,000 tracks and 1mm isotropic grid (a), and with 350,000 tracks and 0.5mm isotropic grid (b). For comparison, (c) shows the FA map (interpolated to 1mm isotropic). Note that all maps in Fig. 1 were created using the *same* DWI data.

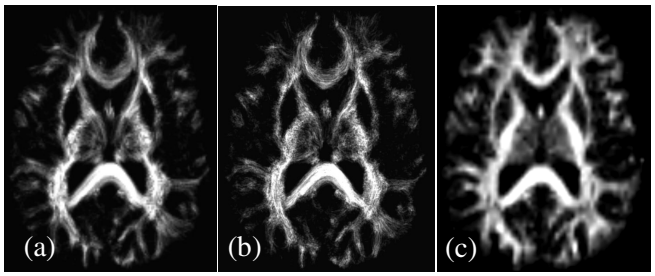


**Fig.1**: Whole-brain track-density maps generated with 100,000 tracks and 1mm isotropic grid (a), and with 350,000 tracks and 0.5mm isotropic grid (b). (c) FA map interpolated to 1mm isotropic.

Fig. 2 shows an example of these high quality maps to aid ROI definition for fiber tracking (e.g. see sharper delineation of the fimbria than the FA –yellow ellipsoid). This quality facilitates definition of seed and target ROIs, leading to an easier delineation of the fornix (see (c) for the tracking results).

As an illustration of their role in DWI normalization, Fig. 3 shows the fiber tracking results from 3 subjects (whole-brain tracking; 25,000 tracks/subject), after normalization to a custom template using the whole-brain track-density maps (generated from 100,000 tracks/subject and 1mm grid). The registration led to a good result (see superposition of common white matter structures, shown as regions in white).

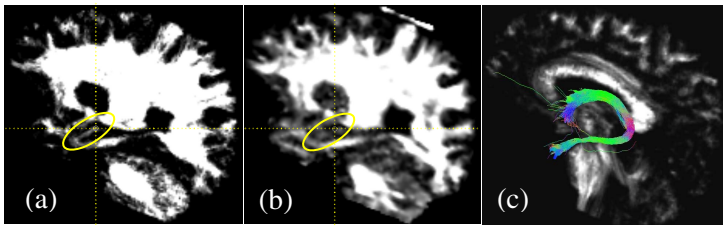


**Fig. 2:** (a) Sagittal whole-brain track-density map (100,000 tracks, 1mm isotropic). (b) FA map (interpolated to 1mm). The yellow ellipsoid highlights the fimbria. (c) Tractography results (1000 tracks) for the fornix, superimposed on a sagittal slice.

**Discussion:** While track-density maps from *partial* white matter structures have been previously used (e.g. (5-8)), this study has shown that *whole-brain* track-density mapping provides an important complementary tool for tractography. The maps have very good anatomical contrast and, importantly, since they are created from the tracks themselves, the maps are exactly in the same space (including distortions) as the diffusion data (cf. 3D $T_1$-weighted images). A further interesting property of these maps is that their spatial resolution and SNR can be tailored depending on the chosen grid size and the total number of tracks generated. For example, Fig.1 showed that high quality 0.5mm resolution maps can be generated from 2.3mm source DW data.

The whole-brain track-density maps can provide higher anatomical resolution than FA maps, since the latter suffer from a 'dilution' effect (given by the partial volume effect of the acquired DW voxel size). In contrast, the resolution of the track-density maps is determined by the track information in the whole neighborhood.

These maps should play an important role in clinical and research studies, not only as high resolution anatomical data but also, as shown in this study, to aid users in ROI definition for tractography (making that important step more robust) and for normalization of fiber tracks for inter-subject comparisons.

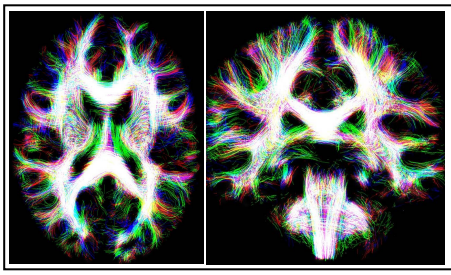

**Fig. 3**: Axial (left) and coronal (right) whole-brain fiber tracking results from 3 subjects (a 4mm slab is shown). Tracks were normalized to a custom template, and each subject displayed with one of the RGB color scheme. Areas in white indicate overlap of tracks from the 3 subjects.

**References:** (1) Mori S et al, *NMR Biomed* 2002;15:468. (2) Jones DK et al, *Neuroimage* 2002;17:592. (3) Park HJ et al, *Neuroimage* 2003;20:1995. (4) Hua K et al, *Neuroimage* 2008;39:336. (5) Johansen-Berg H et al, *Curr Op Neurol* 2006;19:379. (6) Behrens TEJ et al, *Nat Neurosci* 2003;6:750. (7) Parker GJM et al, *Phil Trans R Soc* B 2005;360:893. (8) Thomas B et al, *Brain* 2005;128:2562. (9) Tournier J-D et al, *NeuroImage* 2007;35:1459.