Studying white matter tractography reproducibility through connectivity matrices

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Introduction: Diffusion-weighted imaging (DWI) is often used as a starting point for *in vivo* white matter (wm) connectivity to reconstruct potential wm pathways between brain areas. In this study, we investigate the reproducibility of the connectivity matrix[1,2], resulting from different tractography parameters. We vary the number of streamlines used to construct the matrix in cortical to cortical connectivity and analyze its effects. We also compare the effect of probabilistic and deterministic local streamline tractography algorithms, seeding both from the wm and from wm-grey matter (gm) interface.

Methods: Diffusion-weighted images were acquired on a single volunteer along 64 uniformly distributed directions using a b-value of 1000 s/mm^2, a single-shot echo-planar imaging (EPI) sequence on a 1.5 Tesla SIEMENS Magnetom (128×128matrix, 2 mm isotropic resolution, TR/TE 11000/98 ms) and a GRAPPA factor of 2. An anatomical T1-weighted 1 mm isotropic MPRAGE (TR/TE 6.57/ 2.52 ms) image was also acquired. The whole sequence was repeated twice to obtain two distinct datasets (a1, a2). Additionally, subject 100408 of the Human Connectome Project[3] dataset was used.

Fiber Orientation Distribution Functions (fODFs) from spherical deconvolution[4] were used for tractography. Partial volume estimation maps from the T1-weighted image were obtained using FSL/Fast[5] and used in the tracking process[6]. Streamline tractography was done with and without particle filtering tractography[6] (PFT), seeding from both the wm mask and the wm-gm interface. Freesurfer[7] was used to obtain the cortical parcellation into 150 regions[8]. Each of the 150 gm regions were merged with their associated wm region to compute the connectivity between pairs of cortical regions[9].

Three millions streamlines connecting two regions together were generated with each tracking pipeline and dataset. One million of those streamlines were used to compute a pseudo ground truth connectivity matrix. The other two millions streamlines were used to compute the standard deviation and the average difference between a connectivity matrix computed with distinct subsets of streamlines (from 10,000 to 200,000 streamlines) and the pseudo ground truth matrix. All connectivity matrices **C** are normalized to sum to 1. The difference between two connectivity matrices is computed with: $\sum |C_1 - C_2|/2$. This can be interpreted as the fraction of streamlines that connect different regions in both matrices.

Results: Figure 1 shows the average difference with the pseudo ground truth matrix using streamlines subsets for the three datasets seeding from the wm-gm interface and deterministic tractography. Figure 2 shows the average difference with the pseudo ground truth matrix using streamlines subsets for the same dataset (a1) seeding from the interface using PFT, and from the wm mask using and not using PFT. Figure 3 shows the connectivity matrix in the lower triangular part and the standard deviation in the upper triangular part, using (a) 20,000 streamlines and (b) 200,000 streamlines.

Discussion and Conclusion: The reproducibility of the connectivity is surprisingly similar across tractography algorithms, seeding techniques and datasets, as shown in Figures 1 and 2. Within any given tested tractography pipeline and dataset, and using 100,000 streamlines to compute the connectivity matrix, 94% to 96% of connections were proportionally the same as the pseudo ground truth matrix. Those reproducible connections reduce rapidly using less than 20,000 streamlines as shown in Figures 1 and 2. This can be also observed in Figure 3 (a) where the standard deviation for most voxel is higher than in Figure 3 (b). Both the average and the maximum value of the standard deviation matrices are reduced as the number of streamlines increases (result not shown).

Even though the reproducibility is high, connectivity matrices are very different from each other, even among the same dataset. The fraction of seeds resulting in a streamline connecting pair of regions varied from 2.8% to 7.1% across tested tractography configuration and dataset. All streamlines not connecting two distinct pairs of regions of interest were discarded (e.g. streamlines connecting the sub cortical gm, the cerebellum or ending in the ventricles). Seeding from the wm-gm interface required 1.4 to 2.9 million seeds and seeding from the wm mask required 2.1 to 3.5 million seeds to obtain 100,000 connecting streamlines. In all cases, connectivity matrices tend to stabilize using more than 100,000 streamlines. However, which tractography pipeline is more characteristic of the underlying anatomical structure, and thus, which tractography pipeline is more reproducible across data acquisition for a single subject remains an open question. We found that the analysis of the reproducibility of the tractography through the connectivity matrix is a first step to address this question.
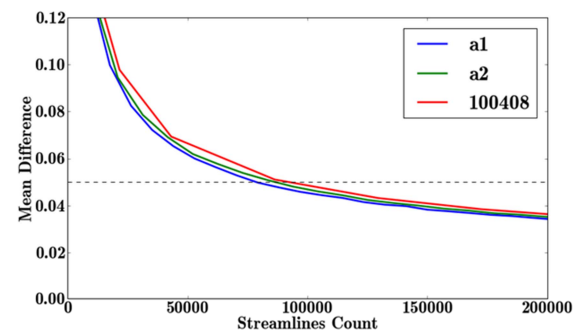

Figure 1. Difference with the pseudo ground truth matrices varying the number of input streamlines. Deterministic tractography seeding from the wm-gm interface on three datasets.
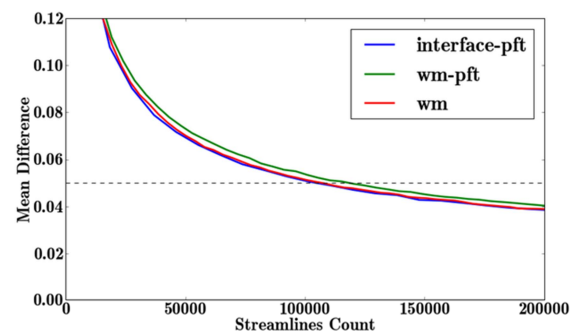

Figure 2: Difference with the pseudo ground truth matrices varying the number of input streamlines. Probabilistic tractography on dataset a1 seeding from the wm-gm interface and from the wm mask.
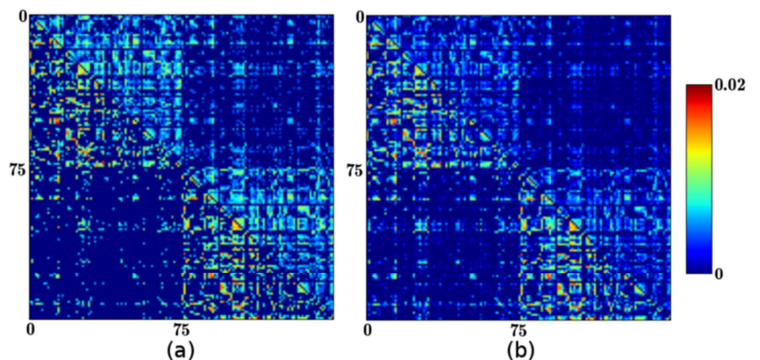

Figure 3: Logarithmic scale of connectivity matrices in the lower triangular part and the standard deviation in the upper triangular part. Computed with (a) 20 000 and (b) 200 000 streamlines.

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