Model-based neuroanatomy: Tractography validation, white-matter connections and geometrical organization

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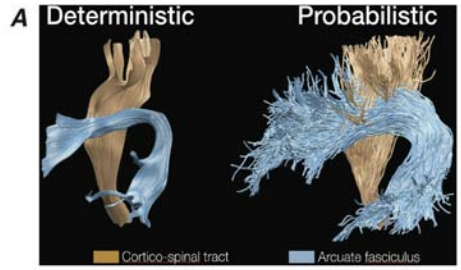
Target audience. Investigators using diffusion-weighted MRI (DWI) data and fiber-tractography algorithms.



B

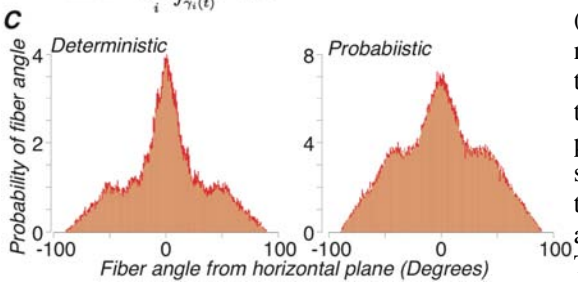
$$\mathcal{E}(\{w_i(t)\}) := \mathcal{E}_{\text{data}} + \alpha\mathcal{E}_{\text{smooth}}$$

$\gamma_i(t) =$ fascicle i

$w_i(t) =$ weights along fascicle i

$$\mathcal{E}_{\text{data}} = \sum_{\text{voxels}} (\text{predicted} - \text{measured})^2$$

$$\mathcal{E}_{\text{smooth}} = \sum_i \int_{\gamma_i(t)} (w_i'(t))^2\, dt$$



Purpose. Diffusion-weighted MRI (DWI) coupled with fiber tractography allows for non-invasive measurement of the organization of white-matter fascicles in the living human brain. Investigators can choose between many possible DWI measurements and tractography algorithms to estimate a full set of white-matter fascicles; the connectome. Each algorithm, creates connectomes based on different principles, such differences make connectome measurements dependent not only on the brain biology but also on tractography (e.g., Fig 1A; Fascicles identified with two different tractography algorithms). Hereafter, we propose a method for validating connectomes based on both their geometric consistency and their quality in predicting the diffusion signal. We apply this method to study the geometric structure of white-matter fibers.

Methods. We acquired DWI data with 96 diffusion-weighting directions (b = 2000) at 3T. We generated whole-brain human connectomes by applying different tractography methods, including constrained spherical deconvolution and tensor-based tractography with probabilistic and deterministic approaches (1). Using the fascicles generated by a given algorithm, we associated with each node on a fascicle a nonnegative weight describing its localized contribution to the diffusion measurements. These weights were optimized numerically by trading off between two terms, one measuring how well the diffusion signal is predicated by the set of locally-weighted fascicles and another optimizing for smoothness in the variation of the weights along fascicle curves (Fig. 1B). We then discarded fascicle with small weight from further consideration (validation), and based subsequent analyses of connectome properties on the retained parts. The accuracy of this procedure was evaluated by cross-validating against an independent data set from the same subject (2); this cross-validation showed which tractography algorithms generate the most useful fascicles after weighting. We also studied the geometry of the white-matter fascicles (distributions of fiber lengths, angles and connectivity) after our weighting procedure, which reduced the dependence of such measurements on the choice of tractography techniques.

Results. The predicted geometric organization of the white-matter varies considerably depending on the tractography algorithm utilized. Fig. 1C shows the distribution of fiber angles generated by different tractography algorithms. Our optimized weights, however, help identify tractography algorithms that generate connectomes best representing the measured diffusion signal. We show that the optimal algorithms from this point of view are probabilistic tractography algorithms based on constrained-spherical deconvolution. These algorithms produce connectomes with wider distributions of fiber angles. Algorithms exhibiting the best cross-validation performance produce fibers with wider distributions of angles, suggesting that a range of fibers angles is necessary for best predicting the measured diffusion signal.

Discussion. We present a validation method for generating weights associated with points along white-matter fascicles derived from diffusion-weighted data and fiber tractography. These weights describe the contribution of the local piece-wise contribution of the fascicles to the diffusions signal and thus are correlated with the likelihood of their presence in the brain. In addition, the weights reflect the assumption that a fascicle's contribution to the diffusion signal is a physical quantity that should vary smoothly along its length. Fascicles with uniformly small weights are deleted because they have a highly inconsistent contribution to the diffusion signal. Fascicles retained provide an accurate representation of the measured diffusion signal.

Conclusion. Evaluating the predictions made by different tractography algorithms enables analysis of the geometric structure of white-matter connectomes and establishes a principle to reduce the dependence of the tractography results on the choice of tracking algorithm. Probabilistic tractography predicts diffusion data most reliably by generating fascicles that exhibit a wider set of fiber orientations. These findings are a fundamental advancement in the understanding of the geometric structure of the white-matter.

References. (1) Tournier JD. J-Tournier JD. Calamante F. Connelly A. Robust determination of the fibre orientation distribution in diffusion MRI: Non-negativity constrained super-resolved spherical deconvolution. Neuroimage 35 (2007) 1459–1472 4. (2) Pestilli, F., Yeatman, J., Rokem, A., Kay, K., and Wandell, B. Evaluating the accuracy of white-matter connectomes. ISMRM, Salt Lake City, UT (2013).