Towards minimizing tractography errors and quantifying fiber crossing ratios

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Target Audience: Imaging and clinical scientists interested in optimizing fiber tracking algorithms with an emphasis on identifying and quantifying complex intra-voxel fiber structures.

Purpose: High angular resolution diffusion techniques including diffusion spectrum imaging [1] and q-ball imaging [2] have been developed to resolve complex intra-voxel fiber structures. Thereby, the entire diffusion profile is captured in the so-called orientation distribution function (ODF). Various tracking algorithms have been proposed to reconstruct virtual nerve fiber bundles based on the ODF. A fundamental problem of these techniques is that a quantitative evaluation of the resulting fiber tracts is still error prone and dependent on the algorithm and anatomy of interest. Therefore, as a major drawback, it remains challenging to derive e.g. crossing ratios of two or more intersecting fiber populations in a robust and reproducible manner.
In this work, we present a method to minimize fiber tracking errors of any tracking algorithm to improve quantification of fiber crossing ratios. The method is validated using synthetic data of crossing fiber bundles and in-vivo data obtained in the human optic chiasm.

Methods: Fiber tracts resulting from any algorithm can be used to simulate a diffusion signal. To this end, the method described in [3] was extended to q-ball data. The error between the measured diffusion signal and the simulated fiber signal is computed by calculating the root-mean-square error of the difference of the normalized and the mean-subtracted diffusion signals and additionally by calculating the root-mean-square deviation of the mass-normalized ODFs reconstructed from the acquired diffusion data and the ODFs reconstructed from the simulated diffusion data (ODF reconstruction was performed according to [4]). Upon equidistant resampling of the fiber tracts [5], principle component analysis (PCA) is applied. In principle component space, the most important variables are randomly generated including the calculated covariance matrix and transformed back to fiber space. The distance of each new fiber to the original "population mean fiber" is calculated. Thereby, only fibers within a certain distance-threshold are accepted. The resulting fibers are combined with the existing fibers and a fiber subset is selected which minimizes the signal- and ODF-error.
Simulation data: A synthetic phantom of crossing fibers was generated according to [6] with a crossing angle of 70°, a crossing ratio of 0.4 and an SNR of 25. The synthetic phantom was up- and down-sampled by a factor of 5 to simulate partial volume effects. Fiber tracts were generated with the Diffusion Toolkit [7] using a modified FACT algorithm based on the ODF.
In-vivo data: Data were acquired on a Philips Achieva 3T system (Philips Healthcare, Best, the Netherlands) using a diffusion-weighted single-shot spin-echo EPI sequence with following parameters: FOV = 240 x 240 mm^2, acquisition matrix = 128 x 128, 12 contiguous slices (angulated in parallel with the optic system), slice thickness = 2 mm, SENSE factor = 3.5, TE = 62.4 ms. Diffusion-weighted images were acquired along 64 directions distributed uniformly on a half-sphere with a b-value of 3000 s/mm^2 in addition to a b = 0 s/mm^2 scan. The scan was repeated 3 times and averaged after motion correction to increase SNR. Fiber tracts were generated using an in-house developed deterministic algorithm with branching possibilities.

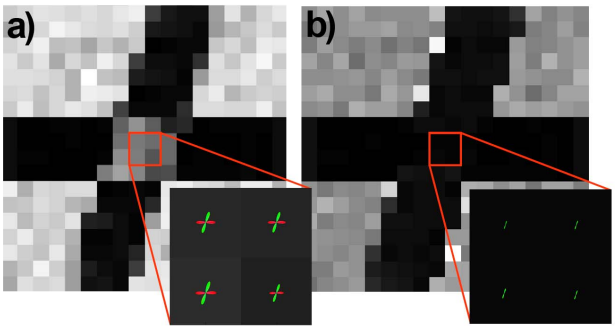

Figure 1: Mean ODF-error of the Diffusion Toolkit fibers in **1a** and after optimizing the fibers in **1b**

	crossing ratio	#horizontal fibers	#vertical fibers	ODF error
Diffusion Toolkit	0.487±0.0563	33.8±4.3	35.8±5.9	0.113±0.009
optimized	0.401±0.0248	57.4±2.7	93.6±3.8	0.0293±0.003

Table 1: Mean ODF-error of the Diffusion Toolkit in **a** and after optimization in **b**

Results: Figure 1a shows the mean ODF-error per voxel of the initial fiber tracts generated with the Diffusion Toolkit in the synthetic dataset, resulting in a crossing ratio of 0.48±0.0563 (ground truth ratio of the fiber branches was 0.4, with the vertical branch being denser). After generating new fibers with the PCA method and choosing the optimal fiber subset, a lower error was achieved resulting in a crossing-ratio of 0.4±0.0248, as depicted in figure 1b (5 simulations with different noise samplings were performed). In the close-ups of the crossing regions, the absolute error-ODFs are shown. Table 1 gives additional data of the optimization relative to the results obtained with the Diffusion Toolkit.
Figure 2 depicts the fiber tracts of the optic chiasm in a healthy volunteer. The resulting crossing ratio between contralateral and ipsilateral fiber populations changed from 0.38 before optimization to a ratio of 0.584 after optimization, which is in much better agreement with known anatomy [8].

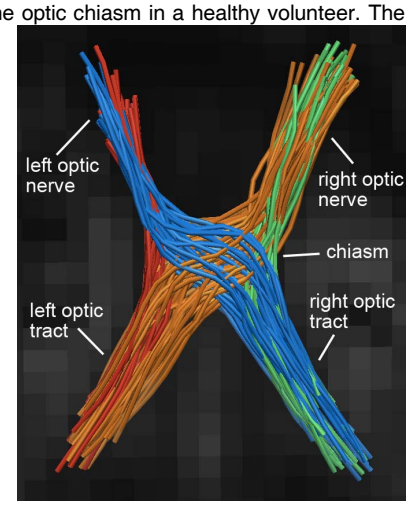

Figure 2: Resulting fibers of the optic chiasm

Discussion
It has been shown that the quality of fiber tracts can be examined in each voxel by calculating the error of the simulated diffusion signal according to the generated fibers. The presented method allows to generate new fiber tracts based on a given fiber population and by choosing an optimal subset of fibers. Thereby, the error between the simulated and the measured data is reduced.
In the synthetic data, a ratio very close to the ground truth could be reproduced and the resulting signal error could be minimized. Also in the in-vivo data, an anatomically feasible population ratio was quantified [8].
Different parameters, such as the response function and kernel width of the simulated fibers influence the absolute number of fibers. But relative measures between different populations should still be possible. Different axon size and myelination will also have an effect on population ratios, even though this effect should be smaller for larger b-values. Such effects should be negligible in the optic chiasm due to the similarity of the fiber populations, but need further investigation in the rest of the brain.

Conclusion This work has demonstrated a method which allows evaluating and optimizing tracking results based on measured data and the simulated diffusion signal. We showed that quantification of fiber crossing ratios has become feasible.

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