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## A machine learning based approach to fiber tractography

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**Purpose:** Current tractography pipelines incorporate several modelling assumptions about the nature of the underlying diffusion-weighted signal. In this work a purely data-driven and thus fundamentally new approach is presented that tracks fiber pathways by directly processing raw signal intensities. This approach has several advantages:

1. No assumptions about the diffusion propagator are made (e.g. Gaussianity).
2. The subtleties of the signal are not blurred by an abstracting modeling approach.
3. Artifacts are directly learned from data. Simplified noise models that are inadequate for modern coil configurations and acquisition methods become obsolete (e.g. Ricianity).
4. Fiber termination criteria are learned from data. Thresholds, such as on the FA, are obsolete.

**Methods:** The presented method is based on a random forest classification- and voting-process that guides each step of the streamline progression. Training: The classifier was trained on the output of a previously performed standard CSD streamline tractography [1]. Classifier input: To become independent of the gradient scheme, the signal is resampled to 100 directions equally distributed over the hemisphere using spherical harmonics. These samples are directly used as input features for the classifier. Additionally, the normalized previous streamline direction is used as classification feature. Classifier output: The classifier produces a fiber termination probability  $P_{stop}$  and a probability  $P(\mathbf{v}_i)$  for 100 different possible directions  $\mathbf{v}_i$  ( $1 \leq i \leq 100$ ).

Classifier voting: At each step of the streamline progression the signal is sampled at  $N$  random positions  $\mathbf{p}^j$  ( $1 \leq j \leq N$ ) within a distance  $r$  of the current streamline position  $\mathbf{p}$ . Classification is performed at each  $\mathbf{p}^j$  to infer the local proposal  $\mathbf{v}^j$ . The subsequent streamline direction  $\mathbf{v}$  is determined by voting of the proposals:  $\mathbf{v} = \sum_j \mathbf{v}^j$ . Two cases are distinguished in the determination of the proposal  $\mathbf{v}^j$ . Case 1 (termination unlikely): If  $P_{stop}^j \leq 0.5$ ,  $\mathbf{v}^j$  is determined based on the previous streamline direction  $\mathbf{v}_{old}$  and the probabilities  $P^j(\mathbf{v}_i)$  of each possible direction:  $\mathbf{v}^j = \sum_i w_i \mathbf{v}_i$ , with  $w_i = P^j(\mathbf{v}_i) \cdot \langle \mathbf{v}_i, \mathbf{v}_{old} \rangle$ . The dot product  $\langle \mathbf{v}_i, \mathbf{v}_{old} \rangle$  is a directional prior that enforces straight fibers. Additionally, a hard curvature threshold for the individual sampling directions  $\mathbf{v}_i^j$  is employed that, when exceeded, sets  $w_i = 0$ .

Case 2 (consider termination): If  $P_{stop}^j > 0.5$ , a potential tract boundary is identified and termination is considered. Now,  $\mathbf{p}^j$  is related to the direction  $\mathbf{v}_{old}$  in order to decide whether termination is preferable or should be avoided. A termination is considered much more likely if non-fiber regions lie straight ahead (i.e. in the current direction of streamline progression  $\mathbf{v}_{old}$ ). If the streamline progresses relatively parallel to the detected fiber bundle margin, a premature termination is rather avoided. This behavior is achieved by assessing the additional point

$$\hat{\mathbf{p}}^j = \begin{cases} \mathbf{p} - \mathbf{d} & \text{if } \langle \mathbf{v}_{old}, \bar{\mathbf{d}} \rangle \leq 0 \\ \mathbf{p} + (\bar{\mathbf{d}} - 2 \cdot \langle \mathbf{v}_{old}, \bar{\mathbf{d}} \rangle \cdot \mathbf{v}_{old}) \|\mathbf{d}\| & \text{if } \langle \mathbf{v}_{old}, \bar{\mathbf{d}} \rangle > 0 \end{cases} \quad \text{with } \mathbf{d} = \mathbf{p}^j - \mathbf{p} \quad \text{and} \\ \bar{\mathbf{d}} = \frac{\mathbf{d}}{\|\mathbf{d}\|}. \text{ If } P_{stop} \text{ at position } \hat{\mathbf{p}}^j \text{ is } > 0.5, \mathbf{v}^j \text{ is set to } (0,0,0) \text{ (vote for termination),}$$

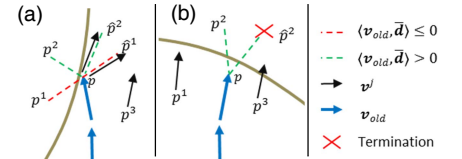
otherwise  $\mathbf{v}^j$  is set to  $\mathbf{v}^j = \hat{\mathbf{p}}^j - \mathbf{p}$  to guide the streamline along the non-fiber region (cf. Fig. 1). A streamline terminates if all sampling positions voted for termination.

Experiments: The classifier was trained with 30 trees and a maximum tree depth of 50. The approach was evaluated in comparison to 12 state of the art tractography methods using a simulated replication of the FiberCup phantom [2] and an *in vivo* dataset (81 gradient directions, b-value 3000 mm/s<sup>2</sup>, 2.5 mm isotropic voxels). Seeding was performed homogeneously within the brain mask (no white matter mask). Algorithms were run with their default parametrization. The presented method uses  $N = 50$  sampling points, a step size of  $0.5 \cdot f$  ( $f$  is the minimal voxel size),  $r = 0.25 \cdot f$  and a hard curvature threshold of 45° by default. Four metrics from the Tractometer evaluation protocol [3] and an additional measure for the local angular error were analyzed. The *in vivo* tractograms were qualitatively evaluated on basis of reconstructions of the corticospinal tract (CST) and the corpus callosum (CC) as well as by an analysis of the spatial distribution of fiber end points.

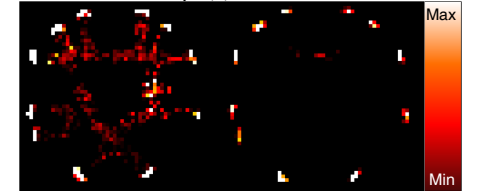
**Results and discussion:** Quantitatively, the presented approach performed best in four out of the five metrics (Tab. 1). Only 3% of the tracts terminated prematurely (cf. Tab. 1 and Fig. 2). Furthermore, the proposed approach yielded the highest percentage of valid connections (93%), the highest bundle coverage (94%) and one of the lowest local angular errors (4%). All 7 valid bundles in the phantom could be reconstructed successfully. Also, the percentage of invalid connections is with 4% close to the top score of 1% yielded by the deterministic CSD streamline tractography. *In vivo*, the approach successfully reconstructed crossing fiber regions such as the crossing between the CC, the CST and the superior longitudinal fasciculus (cf. Fig. 3). Our method was furthermore able to reconstruct parts of fiber bundles that other approaches often missed (cf. lateral projections of the CST in Fig. 3). In comparison to previous approaches like deterministic CSD tractography, most of the fibers reconstructed by the presented approach correctly terminated in the cortex (cf. Fig. 4).

**Conclusion:** The presented machine learning based approach to fiber tractography is the first of its kind and quantitative as well as qualitative phantom and *in vivo* experiments show promising performance compared to 12 established state of the art tractography pipelines.

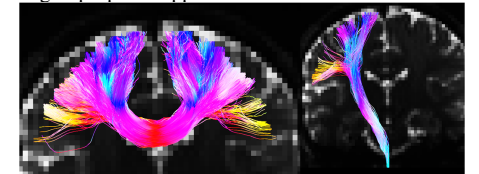
**References:** [1] Tournier et al. INT J IMAG SYST TECH 2012 [2] Neher et al. Magn Reson Med. 2014 [3] Côté et al. Med Image Anal. 2013



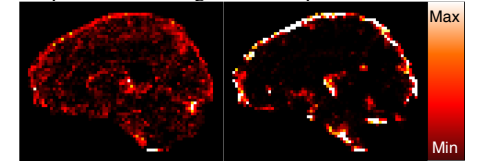
**Fig. 1:** Illustration of the voting process leading to a streamline reflection (a) and a termination after the next one or two steps (b).



**Fig. 2:** Voxel-wise number of fiber end points on the phantom dataset. Left: deterministic CSD. Right: proposed approach.



**Fig. 3:** Tracts obtained by proposed approach. Left: Corpus callosum. Right: Corticospinal tract.



**Fig. 4:** *In vivo* voxel-wise number of fiber end points. Left: deterministic CSD. Right: proposed approach.

| Model | Type     | No  | Valid      | Invalid | Bundle   | Angular |
|-------|----------|-----|------------|---------|----------|---------|
|       |          |     | Connection |         | Coverage | Error   |
| DT    | DET      | 60% | 25%        | 15%     | 21%      | 5°      |
| DT    | FACT     | 62% | 23%        | 14%     | 24%      | 6°      |
| DT    | TEND     | 84% | 8%         | 8%      | 21%      | 10°     |
| DT    | PROB     | 57% | 23%        | 20%     | 27%      | 8°      |
| DT    | Global   | 82% | 10%        | 8%      | 42%      | 12°     |
| CSA   | DET      | 24% | 67%        | 9%      | 70%      | 8°      |
| CSA   | PROB     | 91% | 5%         | 4%      | 83%      | 18°     |
| CSA   | Global   | 81% | 14%        | 5%      | 74%      | 13°     |
| DT-2  | DET      | 60% | 37%        | 3%      | 58%      | 6°      |
| CSD   | DET      | 21% | 78%        | 1%      | 86%      | 4°      |
| CSD   | PROB     | 66% | 28%        | 7%      | 93%      | 4°      |
| CSD   | Global   | 81% | 17%        | 2%      | 72%      | 12°     |
| -     | Proposed | 3%  | 93%        | 4%      | 94%      | 4°      |

**Tab. 1:** Quantitative results on the software phantom. The cells are colored relative to the best (green) and worst (red) result per metric.