# Obtaining representative core streamlines for white matter tractometry of the human brain

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Abstract. Diffusion MRI infers information about the micro-structural architecture of the brain by probing the diffusion of water molecules. The process of virtually reconstructing brain pathways based on these measurements is called tractography. Various metrics can be mapped onto pathways to study their micro-structural properties. Tractometry is an along-tract profiling technique that often requires the extraction of a representative streamline for a given bundle. This is traditionally computed by local averaging of the spatial coordinates of the vertices, and constructing a single streamline through those averages. However, the resulting streamline can end up being highly non-representative of the shape of the individual streamlines forming the bundle. In particular, this occurs when there is variation in the topology of streamlines within a bundle (e.g., differences in length, shape or branching). We propose an envelope-based method to compute a representative streamline that is robust to these individual differences. We demonstrate that this method produces a more representative core streamline, which in turn should lead to more reliable and interpretable tractometry analyses.

**Keywords:** Tractography, Tractometry, Bundle envelope, Core streamline, Diffusion MRI

## 1 Introduction

Tractography derived from diffusion MRI infers information about the structural architecture of the brain. In most studies, diffusion MRI metrics (e.g., fractional anisotropy (FA)) are often collapsed to a single scalar value per bundle [1]. Recently, a trend towards tract profiling [2,3] and direction-specific measurements within a voxel has emerged. Along-tract analysis is a technique that maps a given metric over the course of a bundle. The term *tractometry* was originally

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introduced by Bells et al. [4] and the technique has been refined over the years by various groups [2, 3, 5-7]. It can be used to characterise areas of the brain with abnormal properties in patients [8–10].

At the core of tractometry lies the concept of a *representative streamline* [11] which is used to project metrics along the course of a given bundle. This is typically done by resampling all streamlines forming the bundle to n points and by averaging their spatial coordinates in a point-wise fashion [2,3,11]. This technique will produce a reasonable estimate of the average trajectory when there is very little branching and dispersion between the streamlines forming the pathway (Figure 1, left). However, it is known that streamlines within a given bundle can vary in length and orientation, making it inappropriate to directly average their coordinates [11]. Indeed, if the underlying streamlines are even slightly dispersed from each other, the resulting representative streamline obtained by simply averaging the coordinates can end up running outside of the shape of the bundle (Figure 1, right). Not only does this representation become anatomically implausible, but also it can directly hamper further steps down the tractometry pipeline (e.g., when averaging metrics along different sections of the pathway). A common solution to overcome this problem is to perform tractometry only within the compact portion of the pathway by excluding data from the extremities, which tend to include fanning [2, 12]. This approach greatly helps to 1) quickly obtain a representative streamline and 2) mitigate variability between subjects since bundles are essentially reduced to a simpler representation. However, cutting both extremities inherently limits the benefits conferred by state-of-the-art tractography techniques that can recover faming and branching portions of white matter fasciculi. Here, we propose a technique to generate a representative streamline that is robust to multiple streamline lengths, arching configurations and orientations that naturally occur within a bundle.

## 2 Theory and Methods

### 2.1 Acquisition and processing

Multi-shell high angular resolution diffusion MRI data were acquired on a Siemens Prisma scanner (TR = 4500 ms, TE = 80 ms, with b-values of 1200, 3000, 5000 s/mm<sup>2</sup>, 60 diffusion directions per shell and 15 non diffusion weighted images at a voxel size of 1.5 mm isotropic). Correction for subject motion and distortions caused by eddy currents were performed using *FSL eddy* and *topup* [13]. Next, fibre orientation distributions functions (fODF) were computed using multishell multi-tissue constrained spherical deconvolution [14]. Tractography was performed using FiberNavigator [15], followed by manual bundle extraction of the corticospinal tract (CST), fornix (Fx), cingulum (Cg), arcuate fasciculus (AF) and inferior fronto-occipital fasciculus (iFOF). The main goal of the dissection plan was to preserve the characteristic anatomy, including fanning and branching, of each bundle [16]. tractography parameters were set as follows: min. fODF amplitude: 0.1, step size: 0.5 mm, max. angular threshold: 45°, min./max. streamline length: 30/200 mm with 1.5 million seeds covering the whole brain.





**Fig. 1.** Point-wise streamline averaging illustrated for two scenarios: pruned bundles (left) and fanning bundles (right). The mean streamline (purple) runs outside of the shape of the bundle when streamlines within a bundle slightly diverge from each other. Bundles: cingulum (Cg) and arcuate fasciculus (AF).

#### 2.2 Proposed representative streamline extraction algorithm

The proposed method starts by averaging the top 5% longest streamlines from a bundle of interest to get a coarse approximation of the bundle's core, defined by  $\mathbf{C} = \{p_i \in \mathbb{R}^3 | i = 1, \dots, n\}$  where  $p_i$  is a 3D point of the representative streamline. This core  $\mathbf{C}$  will serve as guidance for the propagation of a convex hull envelope along the entirety of the bundle. Next, we generate an orthogonal plane  $\mathbf{P}_i$  at each point  $p_i \in \mathbf{C}$  using the normal vector  $\mathbf{n}_i$  formed by  $p_i$  and  $p_{i+1}$ . Then, for each streamline from the bundle of interest, we find all line segments intersecting the current orthogonal plane  $\mathbf{P}_i$  up to a distance threshold of t mm (which is interactively-defined in our implementation). If multiple points from a streamline intersect a plane  $\mathbf{P}_i$  (e.g., a spurious streamline doubling back on itself), only the closest point to  $\mathbf{C}$  is preserved so that the actual shape of the bundle is represented by its 3D envelope. We then compute a 2D convex hull  $\mathbf{H}_i \subset \mathbf{P}_i$  for each group of points found in the previous step as illustrated in Figure 2. Finally, the centres of mass of each hull  $\mathbf{H}_i$  are linked together by fitting a  $4^{th}$  order b-spline curve comprising k knots, where k is a user-defined parameter. This step ensures that the representative streamline is located at the centre since there is no guarantee that this is the case using the initial approximation of C defined using the longest streamlines. The proposed framework is integrated within FiberNavigator, where all parameters are accessible to the user.



**Fig. 2.** Example of a cross-section generated along the core of a bundle from a normal plane  $(\mathbf{P}_i)$ . The black dots represent in-plane streamlines with their convex hull  $\mathbf{H}_i$  in dark blue. On the right, the representative streamline (light blue) is obtained by linking the centre of mass of each convex-hull (light blue dot).

#### 2.3 Label maps generation

We compared our technique with conventional point-based resampling (n = 50) computed using the mean distance flip algorithm, accounting for streamline direction [9]. Distance maps were then generated by computing the minimum Euclidean distance between each point of the bundle and the core representative streamline. A transfer function was used to visually map sections of the bundle assigned to respective locations along the core. A unique and smooth colour grading from one end of the bundle to the other indicates a correct assignment along **C**, which in turn reflects how the diffusion metrics are averaged locally.

## 3 Results

### 3.1 Bundles without branching and dispersion

Figure 3 shows results on tubular-shaped bundles (e.g., CST, Fx, iFOF) with little dispersion between the streamlines' starting and ending points. One can observe that the core streamline (i) has a length comparable to the rest of the streamlines within each bundle; (ii) lies inside the boundaries defined by all the streamlines. The colour grading also shows a gradual labelling of the streamlines' points along the core.

#### 3.2 Bundles with branching and dispersion

Figure 4 shows results on more complex bundles having different streamline lengths. In this example, the Cg consists of sub-components that connect the posterior cingulate cortex (PCC) to the medial prefrontal cortex (red streamlines) and the PCC to the parahippocampal gyrus (green streamlines). The complex configuration of the bundles inherently leads to an unrepresentative streamline when using the conventional point-based averaging (white arrows), as well as incorrect assignment of different sections along the bundle (indicated by the repeated green sections). The proposed cross-section method recovers an anatomically representative pathway which stays within the shape of the bundle.



Fig. 3. Label maps and representative streamlines illustrated for tubular-shaped bundles with little dispersion at the end points (e.g., directly connecting two brain regions) show agreement between the two methods (square: resampling method, circle: proposed method).

In the second example, the AF aggregates multiple sub-components with various arching streamlines that project to different areas of the lateral cortex. The representative streamline extracted from traditional averaging appears shorter than the full course of the bundle (white streamline). The inferior temporal aspect of the bundle (dark blue) is also incorrectly averaged and collapsed to the first point of the representative streamline. The last panel shows that the representative streamline traverses the full length of the bundle when using the proposed technique, which is also supported by the unique colour grading of the label map.

Figure 5 shows FA profiles computed along a tubular-shaped tract (Fx) and a fanning-shaped tract (AF). The Fx profiles appear similar in both resampling and cross-sections methods, except for a small shift induced by the larger anterior extent of the proposed method. The AF shows large differences between the two techniques in terms of profiling (red star), mostly due to the sub-optimality of the mean streamline as the representative streamline.



Fig. 4. Complex fanning bundles with dispersed end-points reveal an astray mean streamline when using a conventional resampling approach to compute the core C, as well as incorrect label mapping (white arrows).



**Fig. 5.** FA profiles illustrated for two representative streamline extraction algorithms. Left: Similar profiles are obtained for a tubular-shaped bundle (Fx). Right: Different profiles are obtained for a branching bundle (AF). The red star shows the location on the bundle where the maximum difference between the two methods occurs. Outlines of the bundles are shown for anatomical reference.

## 4 Discussion and Conclusion

We have shown that taking an average streamline as the representative pathway of a bundle can lead to non-representative results in the presence of tract branching and dispersion. To address this problem, we used orthogonal planes throughout the bundle to derive a representative core streamline that traverses its entire centre of mass and therefore, allowing for a more interpretable tractometry. Generating core streamlines based on convex-hulls has been applied previously in the creation of 3D meshes for visualisation [17], as well as for extracting skeleton streamlines for connectivity analysis using an atlas [18]. Here, we additionally show that this approach produces more representative core streamlines for tractometry analyses in various bundle shapes. A drawback to the current approach is that it requires that at least some streamlines run from one end of the bundle to the other. Otherwise, the cross-section propagation may halt prematurely and thus affect the computation of the representative streamline. In addition, we assume that the input bundles are already pruned from streamline loops and undesired false positives.

Since tract morphology varies between subjects, truncation and resampling streamlines based on a length criterion [3] or number of points [2,9] may inadvertently discard important information that is specific to the pathway of interest. This loss of information is inherent to the truncation approach and should be minimised when assigning diffusion metrics to a representative pathway to preserve the full extent of a bundle as much as possible [11]. We showed that this inevitably leads to discrepancies in tract profiling when assigning diffusion metrics to a representative streamline. An alternative approach to truncation and tract averaging could be to remove the need for a representative streamline by matching geometrical properties of streamlines between subjects [12,19]. Yet, the performance of those techniques still requires investigation for complex white matter configurations (e.g., fanning and branching). Nevertheless, truncation can also be useful to reduce potential issues associated with tractography and could still be applied in a post-processing step to our technique, once the representative streamline has been generated.

Finally, a potential improvement to the proposed method would be to recursively generate multiple convex hulls, allowing the algorithm to recover various sub-branches in fanning bundles. This could help in achieving a simplified - yet still anatomically accurate - representation of the core of a bundle, which is the centrepiece for the future design of tractometry pipelines.

# References

 Jones, D.K., Catani, M., Pierpaoli, C., Reeves, S.J., Shergill, S.S., O'Sullivan, M., Maguire, P., Horsfield, M.A., Simmons, A., Williams, S.C., Howard, R.J.: A diffusion tensor magnetic resonance imaging study of frontal cortex connections in very-late-onset schizophrenia-like psychosis. Am J Geriatr Psychiatry 13(12) (Dec 2005) 1092–1099

- Yeatman, J.D., Dougherty, R.F., Myall, N.J., Wandell, B.A., Feldman, H.M.: Tract profiles of white matter properties: automating fiber-tract quantification. PloS one 7(11) (2012) e49790
- Colby, J.B., Soderberg, L., Lebel, C., Dinov, I.D., Thompson, P.M., Sowell, E.R.: Along-tract statistics allow for enhanced tractography analysis. Neuroimage 59(4) (2012) 3227–3242
- Bells, S., Cercignani, M., Deoni, S., Assaf, Y., Pasternak, O., Evans, C., Leemans, A., Jones, D.: Tractometry–comprehensive multi-modal quantitative assessment of white matter along specific tracts. In: Proc. ISMRM. Volume 678. (2011)
- Jones, D.K., Travis, A.R., Eden, G., Pierpaoli, C., Basser, P.J.: PASTA: pointwise assessment of streamline tractography attributes. Magnetic Resonance in Medicine 53(6) (2005) 1462–1467
- Corouge, I., Fletcher, P.T., Joshi, S., Gouttard, S., Gerig, G.: Fiber tract-oriented statistics for quantitative diffusion tensor mri analysis. Medical image analysis 10(5) (2006) 786–798
- De Santis, S., Drakesmith, M., Bells, S., Assaf, Y., Jones, D.K.: Why diffusion tensor mri does well only some of the time: variance and covariance of white matter tissue microstructure attributes in the living human brain. Neuroimage 89 (2014) 35–44
- Dayan, M., Monohan, E., Pandya, S., Kuceyeski, A., Nguyen, T.D., Raj, A., Gauthier, S.A.: Profilometry: a new statistical framework for the characterization of white matter pathways, with application to multiple sclerosis. Human brain mapping 37(3) (2016) 989–1004
- Cousineau, M., Jodoin, P.M., Garyfallidis, E., Cote, M.A., Morency, F.C., Rozanski, V., GrandMaison, M., Bedell, B.J., Descoteaux, M.: A test-retest study on Parkinson's PPMI dataset yields statistically significant white matter fascicles. NeuroImage: Clinical 16 (2017) 222–233
- Groeschel, S., Tournier, J.D., Northam, G.B., Baldeweg, T., Wyatt, J., Vollmer, B., Connelly, A.: Identification and interpretation of microstructural abnormalities in motor pathways in adolescents born preterm. NeuroImage 87 (2014) 209–219
- O'Donnell, L.J., Westin, C.F., Golby, A.J.: Tract-based morphometry for white matter group analysis. Neuroimage 45(3) (2009) 832–844
- Glozman, T., Bruckert, L., Pestilli, F., Yecies, D.W., Guibas, L.J., Yeom, K.W.: Framework for shape analysis of white matter fiber bundles. Neuroimage 167 (Feb 2018) 466–477
- Andersson, J.L., Sotiropoulos, S.N.: An integrated approach to correction for offresonance effects and subject movement in diffusion mr imaging. Neuroimage 125 (2016) 1063–1078
- Jeurissen, B., Tournier, J.D., Dhollander, T., Connelly, A., Sijbers, J.: Multi-tissue constrained spherical deconvolution for improved analysis of multi-shell diffusion mri data. NeuroImage 103 (2014) 411–426
- Chamberland, M., Whittingstall, K., Fortin, D., Mathieu, D., Descoteaux, M.: Real-time multi-peak tractography for instantaneous connectivity display. Frontiers in neuroinformatics 8 (January 2014) 59
- Rojkova, K., Volle, E., Urbanski, M., Humbert, F., Dell'Acqua, F., Thiebaut de Schotten, M.: Atlasing the frontal lobe connections and their variability due to age and education: a spherical deconvolution tractography study. Brain Struct Funct 221(3) (Apr 2016) 1751–1766
- Enders, F., Sauber, N., Merhof, D., Hastreiter, P., Nimsky, C., Stamminger, M.: Visualization of White Matter Tracts with Wrapped Streamlines. In: IEEE Visualization 2005 - (VIS'05), IEEE (2005) 7–7

- Duda, J.T., McMillan, C., Grossman, M., Gee, J.C.: Relating structural and functional connectivity to performance in a communication task. International Conference on Medical Image Computing and Computer-Assisted Intervention (MICCAI) 13 (2010) 282–9
- Parker, G.D., Lloyd, D., Jones, D.K.: The best of both worlds: Combining the strengths of TBSS and tract-specific measurements for group-wise comparison of white matter microstructure. In: International Symposium on Magnetic Resonance in Medicine (Singapore). 2036 (2016)

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