Blurred streamlines: a new concept to improve tractography accuracy by spatially blurring signal contributions

Alessandro Daducci[1], Francesco Gobbi[1], Nicola Febbrari[1], Matteo Battocchio[1], and Simona Schiavi[1]
[1]*University of Verona, Verona, Italy*

Synopsis

Tractography is a powerful tool to study brain connectivity but it suffers from an intrinsic sensitivity/specificity trade-off. The former can be increased by constructing more streamlines, while filtering methods can be used to improve the latter. However, creating too many streamlines may introduce redundancy in the tractograms and negatively affect the performances of filtering methods, especially those based on linear optimization. Here, we introduce the "blurred streamlines", a novel concept based on a combination of streamline clustering and spatial blurring of their signal contributions. Preliminary results show the potential of this formulation and open new perspectives for improving tractography accuracy.

Introduction

Tractography represents an invaluable tool in neuroscience as it allows studying brain connectivity in vivo. However, to achieve high sensitivity a large number of streamlines is required which also introduces many false positives[1]. To address this problem, microstructure informed tractography methods have been proposed[2-7]. They combine the tractogram with signal forward-models to infer the individual contributions of each streamline and filter out those not supported by the data. The Convex Optimization Modeling for Microstructure Informed Tractography (COMMIT)[6] achieves this by solving a linear system:

$$\text{argmin} \ \ ||\boldsymbol{Ax}-\boldsymbol{y}||_2^2 \ \text{ s.t. } \boldsymbol{x} \geq 0$$

where the signal contributions of the streamlines are encoded as separate columns of $\boldsymbol{A}$ (Fig.1). Consequently, if some streamlines follow similar trajectories, they become redundant for explaining the acquired data and the corresponding columns tend to become linearly dependent, making it difficult to interpret the estimated contributions $\boldsymbol{x}$. To prevent the onset of this collinearity[8] problem, we introduce the novel concept of "blurred streamlines".

Methods

The proposed method is shown in Fig.2. Given a tractogram, we first cluster its streamlines to minimize the redundancy between them, and then we spatially blur the signal contributions of the resulting centroids to guarantee coverage of all voxels. A streamline usually contributes to the signal only in those voxels it passes through (Fig.3A,left); with the terms *blurred streamlines* and *blurred signal contributions* we mean that a streamline can instead contribute also to adjacent voxels (Fig.3A,right) in order to capture the intrinsic uncertainty of fiber trajectories estimated through tractography.
The procedure to achieve this is illustrated in Fig.3B-C and is based on the Frenet-Serret frames[9,10]. For each centroid streamline C we create replicas of C by sweeping a series of N circles with radii $r \in \{r_1, \dots, r_N\}$ along its path (Fig.3B). All circles lie on a plane that is always orthogonal to C throughout the sweep and are subdivided into M sectors separated by an angle $\alpha = 2\pi/M$. Thus, each circle defines exactly M copies of C, one per sector, which are obtained by radially displacing all points of C from their initial position to a distance r and rotating them by an angle $k\alpha$, with $k \in \{1, \dots, M\}$, about the center. The signal contributions of a replica of C are computed as usual, i.e., considering only the traversed voxels, and the total signal contributions corresponding to a centroid are obtained by summing those of all its replicas. However, the signal contributions of all replicas at radius r are scaled, as function of r, according to a Gaussian distribution centered on C with standard deviation σ (Fig.3C). Therefore, the blurred signal contributions of a centroid C_i, which form the i-th column of $\boldsymbol{A}$ are defined as:

$$\boldsymbol{A}_i = \sum_{j=1}^{N} w(r_j) \sum_{k=1}^{M} S(C_i, r_j, \alpha_k)$$

where $\alpha_k = 2\pi k/M$ and $S(C_i, r_j, \alpha_k)$ are the signal contributions of the replica of C_i at radius r_j and sector α_k, which are then scaled by the factor $w(r_j) = \exp(-0.5\, r_j^2/\sigma^2)$.
We evaluated the efficacy of blurred streamlines on a well-known synthetic phantom as in[7] which consists of 27 bundles between 53 gray-matter regions mimicking realistic fiber configurations of the brain (Fig.4A). We generated 1 million streamlines using both deterministic and probabilistic algorithms of MRtrix3[11], discarding those ending prematurely in white matter. Finally, we used QuickBundles[12] with the Average of Pointwise Euclidean Metric to cluster the streamlines.

Results and Discussion

Fig.4 analyzes the behavior of our new formulation when varying the extent of clustering and blurring; plots correspond to deterministic tracking, which contained 273 invalid bundles (IB), but similar results were obtained for probabilistic. Standard COMMIT (i.e., no clustering) reduced the IB by ≈17% (273→226) without losing valid bundles (VB), but *a much higher percentage of IB can be removed with blurred streamlines* (≈71%, 273→80). As the blur radius increases more IB are filtered out, but an excessive blur may lead to losing VB, although only marginally (Fig.4B). Fig.4C shows that increasing the blur requires more computation time (6'→1h20') and RAM (377MB→6.5GB). Nonetheless, the clustering step can reduce significantly the size of the tractogram (Fig.4C,left) thus alleviating the computational demands on our method. Fig.5 visually compares the connectomes estimated in both deterministic and probabilistic cases using COMMIT with and without blurred streamlines, using the same amount of computational resources.
It is worth noting that a direct approach to reducing the redundancy by removing linearly dependent columns from $\boldsymbol{A}$ would be impractical due to the size of the data, i.e., millions of streamlines and thousands of voxels with multiple dMRI measurements. Our preliminary results clearly show the *effectiveness of our heuristic solution*, which also helps to improve the accuracy of reconstructions. Future work will be necessary to

confirm its validity in the case of real brain data. Finally, we investigated the effects of blurred streamlines using COMMIT; however, since other filtering procedures[3-7] might suffer from redundancy in the tractograms, blurred streamlines may have positive effects also for such methods.

Conclusions

We called attention to the presence of redundancy in tractography and the possible ramifications it may have on the accuracy of the reconstructions when using filtering techniques based on linear formulations. To mitigate this problem, we introduced a *novel way to define how streamlines contribute to the signal*. Our results suggest that this new formulation represents an effective solution towards more accurate tractography reconstructions.

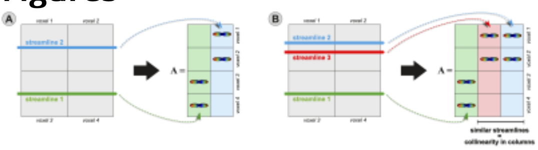
Acknowledgements

Alessandro Daducci was supported by the Rita Levi Montalcini Programme for young researchers of the Italian Ministry of Education, University and Research. The authors would like to thank Filippo Baccaglini and Valentina Nale (M.Sc. students at the University of Verona) for their help during the initial stages of the project.

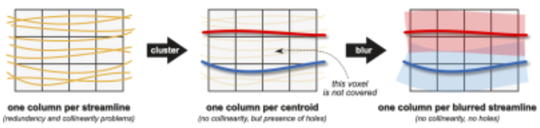
References

1. K. Maier-Hein et al., “The challenge of mapping the human connectome based on diffusion tractography,” Nat Commun, vol. 8, pp. 1349, 2017
2. A. Daducci, A. Dal Palú, M. Descoteaux, J.-P. Thiran, “Microstructure informed tractography: Pitfalls and open challenges,” Front Neurosci, vol. 10, pp. 247, 2016
3. R. Smith, J.-D. Tournier, F. Calamante, A. Connelly, “SIFT: spherical-deconvolution informed filtering of tractograms,” Neuroimage, pp. 298–312, 2013
4. R. Smith, J.-D. Tournier, F. Calamante, A. Connelly, “SIFT2: Enabling dense quantitative assessment of brain white matter connectivity using streamlines tractography,” NeuroImage, vol. 119, pp. 338–51, 2015
5. F. Pestilli, J. Yeatman, A. Rokem, K. Kay, B. Wandell, “Evaluation and statistical inference for human connectomes,” Nat Methods, pp. 1058–63, 2014
6. A. Daducci, A. Dal Palù, A. Lemkaddem, J.-P. Thiran, "COMMIT: Convex Optimization Modeling for Microstructure Informed Tractography," IEEE Trans Med Imaging, vol. 34, no. 1, pp. 246-57, 2015
7. S. Schiavi, M. Ocampo-Pineda, M. Barakovic, L. Petit, M. Descoteaux, J.-P. Thiran, A. Daducci, "A new method for accurate in vivo mapping of human brain connections using microstructural and anatomical information," Sci Adv, vol. 6, no. 31, pp. eaba8245, 2020
8. D. A. Belsley, E. Kuh, R.E.Welsch, Regression diagnostics: identifying influential data and sources of collinearity, New York (N.Y.) : Wiley, 1980
9. J. A. Serret, "Sur quelques formules relatives à la théorie des courbes à double courbure," J Math Pures Appl, pp. 193-207, 1851
10. J. F. Frenet, "Sur les courbes à double courbure," J Math Pures Appl, pp. 437-47, 1852
11. J.-D. Tournier, R. Smith, D. Raffelt, R. Tabbara, T. Dhollander, M. Pietsch, D. Christiaens, B. Jeurissen, C.-H. Yeh, A. Connelly, "MRtrix3: A fast, flexible and open software framework for medical image processing and visualisation," Neuroimage, vol. 202, pp. 116-37, 2019
12. E. Garyfallidis, M. Brett, M. Correia, G. Williams, I. Nimmo-Smith, "Quickbundles, a method for tractography simplification," Front Neurosci, vol. 6, pp. 175, 2012

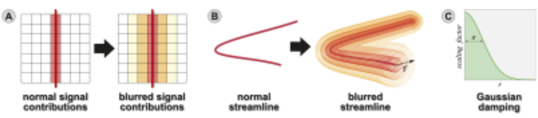
Figures



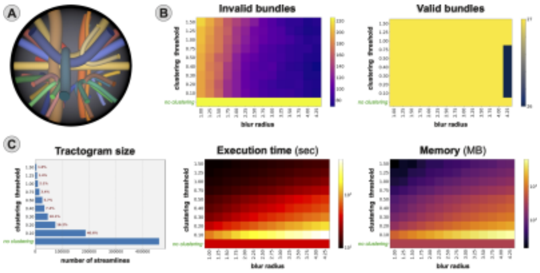
The problem addressed in this work. When streamlines follow similar trajectories, the corresponding columns in matrix ***A*** tend to become linearly dependent, posing serious concerns for the interpretation of the estimated coefficients.



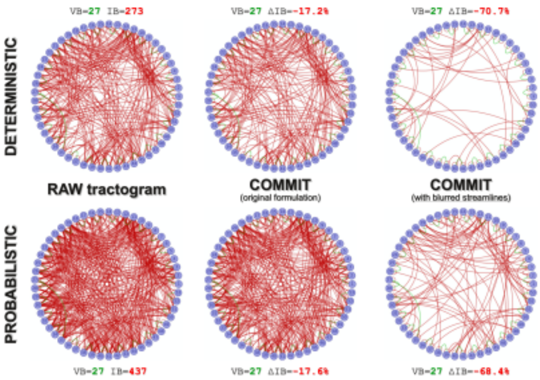
Our solution consists of two steps. First, we cluster the input streamlines (left, yellow) to minimize the redundancy between them. The resulting centroids (middle, red and blue streamlines) are, by construction, sufficiently dissimilar and likely generate non-collinear columns in ***A***. However, the simplified tractogram with only these centroids may not cover properly all voxels. Thus, we spatially blur their signal contributions (right, transparent areas) to guarantee proper coverage.



Blurred streamlines. A streamline contributes to the signal only in those voxels it passes through, whereas a blurred streamline can contribute also to adjacent voxels. The signal contributions decrease as function of the distance *r* and according to a Gaussian distribution with standard deviation σ centered on the streamline itself.



Characterization of the behavior of the blurred streamlines formulation when varying the extent of the clustering (clustering threshold) as well as of the blur (blur radius). In simulated data with known ground truth, we evaluated the number of valid bundles (VB) and invalid bundles (IB), the size of the clustered tractogram as well as the required computational resources (execution time and RAM). Plots correspond to deterministic tractography.



Quantitative comparison of the performance of COMMIT without and with blurred streamlines. ΔIB is the reduction (in percentage) of the IB with respect to the raw tractogram. Green and red arcs represent the reconstructed VB and IB between the 53 gray-matter regions (blue nodes). For both deterministic and probabilistic cases, the standard COMMIT can reduce the number of IB by ≈17%, whereas the introduction of blurred streamlines enables a much higher percentage of reduction (≈70%).