Mapping Tractography Across Subjects

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Abstract. Diffusion magnetic resonance imaging (dMRI) and tractography provide means to study the anatomical structures within the white matter of the brain. When studying tractography data across subjects, it is usually necessary to align, i.e. to register, tractographies together. This registration step is most often performed by applying the transformation resulting from the registration of other volumetric images (T1, FA). In contrast with registration methods that *transform* tractographies, in this work, we try to find which streamline in one tractography correspond to which streamline in the other tractography, without any transformation. In other words, we try to find a *mapping* between the tractographies. We propose a graph-based solution for the tractography mapping problem and we explain similarities and differences with the related well-known graph matching problem. Specifically, we define a loss function based on the pairwise streamline distance and reformulate the mapping problem as combinatorial optimization of that loss function. We show preliminary promising results where we compare the proposed method, implemented with simulated annealing, against a standard registration techniques in a task of segmentation of the corticospinal tract.

1 Introduction

Diffusion magnetic resonance imaging (dMRI) [1] is a modality that provides non-invasive images of the brain white matter. It captures the diffusion process of the water molecules in each voxel which represents structural information of neuronal axons. From dMRI data, tracking algorithms [9, 14] allow to reconstruct the $3D$ pathways of axons within the white matter of the brain as a set of streamlines, called tractography. A *streamline* is a 3D polyline representing thousands of neuronal axons in that region of the brain, and a *tractography* is a large set streamlines, usually $\approx 3 \times 10^5$.

Current neuroscientific analyses of white matter tractography data are limited to qualitative intra-subject comparisons. Thus, it is quite difficult to use the information for direct inter-subject comparisons [5, 2]. This leads to the need of initial alignment, or registration, of tractographies via some methods before doing further study. Registration is most often performed by applying the transformation resulting from the registration of other images, such as $T1$ or fractional anisotropy (FA), to tractography [6, 5, 12]. Recently, [10] proposed group-wise registration using the trajectory data of the streamlines. The idea to work on deterministic tractography rather than other images is quite innovative.

And, it may be advantageous to directly align the streamlines because the result would be closely related to the final goal of registration.

Similar to [10], in this work, we explore the idea of working on deterministic tractography rather than other images. However, in contrast to all current tractography registration methods, which are based on rigid or non-rigid shape transformation of one tractography into another, our approach tries to find which streamline of one tractography corresponds to which streamline in the other tractography, without transformations. This correspondence is a *mapping* from one tractography to the other.

In this work we propose to solve the problem of finding the mapping between two tractographies through a graph-based approach similar to that of the well-known graph matching problem [3, 13]. In the graph matching problem the aim is to find which node of one graph corresponds to which node of another graph, under the assumption that graphs have the same number of nodes and that the correspondence is one-to-one.

Given a tractography of N streamlines $T = \{s_1, \ldots, s_N\}$ and a distance function d between streamlines, we can create an undirected weighted graph by considering each streamline as a vertex and the edge connecting vertex s_i and s_j as the distance between the two streamlines, $d(s_i, s_j)$. Then, intuitively, the problem of tractography mapping becomes very similar to that of graph matching, but with some key differences. Firstly, the size of the two tractographies/graphs is in general not the same. Global differences in the anatomy of the brains, e.g. different volume, motivates this difference. Secondly, in general there is not a one-to-one correspondence between the streamlines/nodes but a many-to-one correspondence. This is anatomically likely if we consider that a given anatomical structure (*tract*), e.g. the cortico-spinal tract (CST), whose streamlines should have direct correspondence across subjects, may have different number of streamlines. In this case, for example, multiple streamlines of one CST would correspond to a single streamline in the other CST. Because of these differences, it is generally not possible to directly apply efficient graph matching algorithms to the problem of mapping tractographies.

In the following we formally describe the tractography mapping problem starting from the graph matching problem and define the details of the optimization problem to solve. We provide a preliminary algorithmic solution, based on simulated annealing, to minimize the proposed loss function. Then, we apply our proposed solution to a tractography segmentation task in order to compare a standard registration-based method to our proposed method on a fair ground. We conclude the paper with a brief discussion of the preliminary encouraging results.

2 Methods

An undirected weighted graph $G = (V, E)$ of size N is a finite set of vertices $V = \{1, \ldots, N\}$ and edges $E \subset V \times V$. The graph matching problem can be described as follows. Given two graphs G_A to G_B with the *same* number of

vertices N, the problem of matching G_A and G_B is to find the correspondence between vertices of G_A and vertices of G_B, which allows to align, or register, G_A and G_B in some optimal way. The correspondence between vertices of G_A and of G_B is defined as a *permutation* P of the N vertices, i.e. there a one-to-one correspondence between the two set of vertices. P is usually represented as a binary $N \times N$ matrix where P_{ij} is equal to 1, if the ith vertex of G_A is matched to the jth vertex of G_B, otherwise 0. Given A and B, i.e. the $N \times N$ adjacency matrices of the two graphs, the quality of the matching is assessed by the discrepancy, or loss, between the graphs after matching as:

$$L(P) = \|A - PBP^\top\|_2 \tag{1}$$

where $\|A\|_2 = \sqrt{\sum_{ij}^{N} A_{ij}^2}$ is the Frobenius norm. Therefore, the graph matching problem becomes the problem of finding P^* that minimize L over the set of permutation matrices $\mathcal{P}$:

$$P^* = \underset{P \in \mathcal{P}}{\operatorname{argmin}} \|A - PBP^\top\|_2 \tag{2}$$

which is a combinatorial optimization problem. The exact solution to this problem has extremely high complexity and only approximate solutions are available in practical cases [3, 13].

Let $T_A = \{s_1^A, \ldots, s_N^A\}$ and $T_B = \{s_1^B, \ldots, s_M^B\}$, where $s = \{x_1, \ldots, x_{n_s}\}$ is a streamline and $x \in \mathbb{R}^3$, be the tractographies of two subjects. Let d be a distance function between streamlines. We define two graphs G_A and G_B with adjacency matrix $A \in \mathbb{R}^{N \times N}$ and $B \in \mathbb{R}^{M \times M}$ where $A_{ij} = d(s_i^A, s_j^A)$ and $B_{ij} = d(s_i^B, s_j^B)$. Our current choice of d is discussed in Section 3, however any common streamline distance from the literature can be used.

The loss function of a *mapping* Q from T_A to T_B is then:

$$L(Q) = \|A - QBQ^\top\|_2 \tag{3}$$

where the mapping Q is a binary $N \times M$ matrix and Q_{ij} is equal to 1, if s_i^A of T_A is mapped to s_j^B of T_B and 0 otherwise. Note that, in general, Q is not a permutation matrix. In order to find the optimal mapping Q^*, we minimize L so that T_B is most similar to T_A:

$$Q^* = \underset{Q \in \mathcal{Q}}{\operatorname{argmin}} \|A - QBQ^\top\|_2 \tag{4}$$

where $\mathcal{Q}$ is the set of all possible mappings. Because in general $N \neq M$ and because Q is a mapping and not just a permutation, the tractography mapping problem is more general than the graph matching problem, i.e. the size of the search space $\mathcal{Q}$, i.e. M^N, is much larger than $\mathcal{P}$. As a consequence, the efficient solutions available in the literature of graph matching, e.g. [13], are not applicable, because they heavily rely on the assumptions that we violate here. In Section 3 we implemented a simple preliminary solution to the combinatorial optimization problem by means of the Simulated Annealing meta-heuristic [8].

2.1 Comparison

In order to compare the proposed method against a standard registration procedure on a fair ground, we cannot rely on the value of the loss function L, because it is defined only in the case of mapping. For this reason, we compared the two approaches on the practical task of automatic tractography segmentation, i.e. finding a given tract of interest in T_B given its segmentation in T_A. Our hypothesis is that reducing L leads to better overlap between tractographies, which is important for practical applications like segmentation. In Section 3 we describe an experiment to test this hypothesis and provide the necessary details. Here we introduce the metric that we use for comparing registration and mapping. As proposed in [5], we compare the set of voxels crossed by the streamlines of each tractography after mapping or after registration. As measure of the overlap between T_A and $Q(T_B)$[1], we adopt the Jaccard index:

$$J(T_A, T_B|Q) = \frac{|T_A \cap Q(T_B)|}{\min\{|T_A|, |Q(T_B)|\}} \tag{5}$$

Note that in the above equation, $|T|$ is the volume computed as number of voxels that any streamline $s \in T$ goes through, and $|T_A \cap Q(T_B)|$ indicates the number of voxels in common between T_A and $Q(T_B)$.

3 Experiments

We designed an experiment to provide empirical evidence that reducing the loss in Equation 3 is related to an increase of the Jaccard index, i.e. of the overlap between tractographies.

The dataset used for the experiment is based on dMRI data recorded with a $3T$ scanner at Utah Brain Institute, 65 gradients ($64 + b0$); b-value = 1000; anatomical scan ($2 \times 2 \times 2mm^3$). The tractography was reconstructed with the EuDX algorithm [4] using the dipy[2] toolbox. We considered 4 healthy subjects and focused the analysis on the corticospinal tract (CST). CST is a set of streamlines projecting from the lateral medial cortex associated with the motor homunculus. This tract is of main interest for the characterization of neurodegenerative diseases, like the amyotrophic lateral sclerosis (ALS). The CST tracts were segmented by the expert neuroanatomists using a toolbox [11] that supports an interactive selection of streamlines. The size of the segmented tracts is reported in Table 1 (see column *size*).

The reference method, against which we compared mapping, is the affine registration of the tractographies in a common MNI space using the voxel-based FLIRT method [7]. The registration is defined as follows: First, FA images were registered to the MNI-FMRIB-58 FA template, then the affine transformation was applied to the tractographies. The Jaccard index computed between the CST_A and CST_B in common space is reported in Table 1 (see column FLIRT).

[1] For sake of brevity we denote as $Q(T_B)$ the result of applying mapping Q to T_B.

[2] http://www.dipy.org

We then used mapping to compute the same quantity. The first step was encoding the tractographies as graphs, which required to define a distance between streamlines. We refer to the commonly used Mean Average Minimum distance (MAM) [14], based on the Hausdorff distance:

$$d_{MAM}(s, s') = \frac{1}{2}(D(s, s') + D(s', s)) \tag{6}$$

where $D(s, s') = \frac{1}{n_s} \sum_{i=1}^{n_s} d(x_i, s')$, and $d(x, s') = \min_{j=1,\ldots,n_{s'}} ||x - x'_j||_2$.

Mapping a tract such as CST, which usually comprises 10^2 streamlines, to an entire tractography T_B, which usually consist of 10^7 streamlines, is computationally extremely expensive because the space of all possible mappings $\mathcal{Q}$ has size $|T_B|^{|CST|}$. For this reason, we introduced a heuristic to retain some of the streamlines in T_B. The intuitive idea was to define a superset of streamlines of the CST for subject B, denoted CST_B^+. The heuristic is in two steps: first, we computed the medoid s_m of CST_B, and the radius $r = \max\{d(s_m, s_i), \forall s_i \in CST_B\}$. Second, we filtered the streamlines in T_B such that $CST_B^+ = \{s_j \in T_B | d(s_m, s_j) \leq \alpha \cdot r\}$, where $\alpha = 3$. See Table 1, column CST_B, for the actual sizes of the supersets.

Computing the optimal mapping Q^* requires to solve, even in an approximate way, the minimization problem of Equation 4. As a preliminary strategy to approximate the optimal mapping Q^*, we implemented the simulated annealing (SA) [8] meta-heuristic, a reference method for combinatorial optimization. SA requires the definition of a function to move from the current state, i.e. the current mapping Q, to a (potentially better) neighbouring one. As transition function we used a stochastic greedy one where, given the current mapping Q, one streamline of CST_A is selected at random and then it is greedily remapped to the streamline in CST_B^+ providing the greatest reduction in the loss. As starting point of the annealing process, we used the 1-nearest neighbour of CST_A with respect to CST_B^+ after the registration of T_A and T_B. We ran the simulated annealing for 1000 iterations, which required a few minutes on a standard computer[3].

The results reported in Figure 1 show the behaviour of the loss during the optimization process for the mapping of CST_A (subject ID 205), with respect to the tractography of three other subjects (subject IDs 204, 206 and 212). In all cases, as the number of iterations increases, the value of loss function decreases.

In Table 1 are reported the results of the comparison between registration and mapping methods, measured by the Jaccard index. The overlap between CST_A and CST_B provided by FLIRT registration is generally quite poor. This is partly expected because even after the registration of T_A and T_B, CST_A and CST_B may have a systematic displacement due to the variability of anatomy across subjects. The results of mapping at different iterations of the optimization

[3] We are aware that this method of combinatorial optimization can be significantly improved, but we claim that the it was sufficient to do a preliminary investigation of the relation between the loss L and the overlap between tractographies, by means of the Jaccard index.

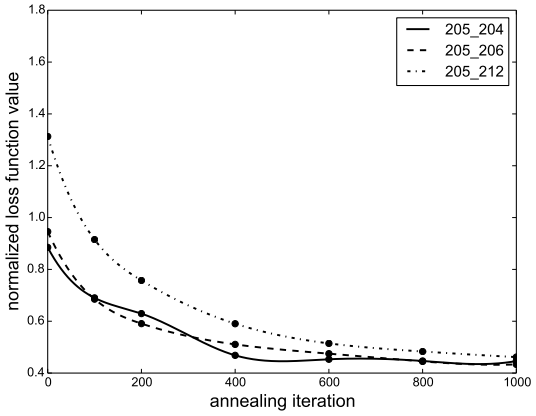

Fig. 1. Plots of the normalized loss ($L_{norm} = \frac{L}{|CST_A|}$) as a function of number of iterations with simulated annealing, when mapping the CST of subject 205 to those of subjects 204, 206 and 212.

A	B	size			Jaccard index			
subject ID	subject ID	$\|CST_A\|$	$\|CST_B\|$	$\|CST_B^+\|$	*FLIRT*	*SA-0*	*SA-100*	*SA-1000*
205	204	60	124	682	0.18	0.55	0.52	**0.59**
	206	60	100	550	0.15	0.77	0.81	**0.82**
	212	60	68	374	0.10	0.74	0.77	**0.90**

Table 1. Comparison of registration vs. mapping. The subject IDs of CST_A and CST_B are reported in the first two columns. Their sizes together with that of CST_B^+ are in columns three to five. The last four columns report the overlap between CST_A and CST_B in terms of Jaccard index (higher is better), for FLIRT registration (6th column) and for mapping with simulated annealing (SA-0, SA-100, SA-1000 columns).

process shows a remarkable global increase in the Jaccard index and a general trend of improved alignment when more iterations are computed.

4 Discussion and Conclusion

In this work we addressed the challenge of finding an alignment between the tractographies of two subjects. We recast the question as a problem of mapping between two sets of streamlines and we provided the formulation of the corresponding minimization problem. Preliminary results show that this approach is promising despite some limitations. The computational complexity represents a major issue that may prevent to scale up to whole tractography.

References

1. Basser, P.J., Mattiello, J., LeBihan, D.: MR diffusion tensor spectroscopy and imaging. Biophysical journal 66(1), 259–267 (Jan 1994), http://dx.doi.org/10.1016/s0006-3495(94)80775-1
2. Bazin, P.L.L., Ye, C., Bogovic, J.A., Shiee, N., Reich, D.S., Prince, J.L., Pham, D.L.: Direct segmentation of the major white matter tracts in diffusion tensor images. NeuroImage 58(2), 458–468 (Sep 2011), http://dx.doi.org/10.1016/j.neuroimage.2011.06.020
3. Conte, D., Foggia, P., Sansone, C., Vento, M.: Thirty years of graph matching in pattern recognition. Int. J. Patt. Recogn. Artif. Intell. 18(03), 265–298 (May 2004), http://dx.doi.org/10.1142/s0218001404003228
4. Garyfallidis, E.: Towards an accurate brain tractography. Ph.D. thesis, University of Cambridge (2012)
5. Golding, D., Tittgemeyer, M., Anwander, A., Douglas, T.: A comparison of methods for the registration of tractographic fibre images. In: Robinson, P., Nel, A. (eds.) Proceedings of the Twenty-Second Annual Symposium of the Pattern Recognition Association of South Africa. pp. 55–59 (2011)
6. Goodlett, C.B., Fletcher, P.T., Gilmore, J.H., Gerig, G.: Group analysis of DTI fiber tract statistics with application to neurodevelopment. NeuroImage 45(1 Suppl) (Mar 2009), http://dx.doi.org/10.1016/j.neuroimage.2008.10.060
7. Jenkinson, M., Smith, S.: A global optimisation method for robust affine registration of brain images. Medical image analysis 5(2), 143–156 (Jun 2001), http://view.ncbi.nlm.nih.gov/pubmed/11516708
8. Laarhoven, P.J.M., Aarts, E.H.L. (eds.): Simulated Annealing: Theory and Applications. Kluwer Academic Publishers, Norwell, MA, USA (1987), http://portal.acm.org/citation.cfm?id=59580
9. Mori, S., van Zijl, P.C.M.: Fiber tracking: principles and strategies, a technical review. NMR Biomed. 15(7-8), 468–480 (Nov 2002), http://dx.doi.org/10.1002/nbm.781
10. O'Donnell, L.J., Wells, W.M., Golby, A.J., Westin, C.F.F.: Unbiased groupwise registration of white matter tractography. Medical image computing and computer-assisted intervention : MICCAI ... International Conference on Medical Image Computing and Computer-Assisted Intervention 15(Pt 3), 123–130 (2012), http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3638882/
11. Olivetti, E., Nguyen, T.B., Avesani, P.: Fast Clustering for Interactive Tractography Segmentation. the 3rd IEEE Intl Workshop on Pattern Recognition in NeuroImaging (2013), http://dx.doi.org/10.1109/PRNI.2013.20
12. Wang, Y., Gupta, A., Liu, Z., Zhang, H., Escolar, M.L., Gilmore, J.H., Gouttard, S., Fillard, P., Maltbie, E., Gerig, G., Styner, M.: DTI registration in atlas based fiber analysis of infantile Krabbe disease. NeuroImage 55(4), 1577–1586 (Apr 2011), http://dx.doi.org/10.1016/j.neuroimage.2011.01.038
13. Zaslavskiy, M., Bach, F., Vert, J.P.: A Path Following Algorithm for the Graph Matching Problem. IEEE Transactions on Pattern Analysis and Machine Intelligence 31(12), 2227–2242 (Oct 2008), http://dx.doi.org/10.1109/tpami.2008.245
14. Zhang, S., Correia, S., Laidlaw, D.H.: Identifying White-Matter Fiber Bundles in DTI Data Using an Automated Proximity-Based Fiber-Clustering Method. IEEE Transactions on Visualization and Computer Graphics 14(5), 1044–1053 (Sep 2008), http://dx.doi.org/10.1109/tvcg.2008.52