Surface-based and Shape-informed U-fiber Atlasing for Robust Superficial White Matter Connectivity Analysis

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Abstract. Superficial white matter (SWM) U-fibers contain considerable structural connectivity in the human brain; however, related studies are not well-developed compared to the well-studied deep white matter (DWM). Conventionally, SWM U-fiber is obtained through DWM tracking, which is inaccurate on the cortical surface. The significant variability in the cortical folding patterns of the human brain renders a conventional template-based atlas unsuitable for accurately mapping U-fibers within the thin layer of SWM beneath the cortical surface. Recently, new surface-based tracking methods have been developed to reconstruct more complete and reliable U-fibers. To leverage surface-based U-fiber tracking methods, we propose to create a surface-based U-fiber dictionary using high-resolution diffusion MRI (dMRI) data from the Human Connectome Project (HCP). We first identify the major U-fiber bundles and then build a dictionary containing subjects with high groupwise consistency of major U-fiber bundles. Finally, we propose a shape-informed U-fiber atlasing method for robust SWM connectivity analysis. Through experiments, we demonstrate that our shape-informed atlasing method can obtain anatomically more accurate U-fiber representations than state-of-the-art atlas. Additionally, our method is capable of restoring incomplete U-fibers in low-resolution dMRI, thus helping better characterize SWM connectivity in clinical studies such as the Alzheimer's Disease Neuroimaging Initiative (ADNI).

Keywords: U-fiber · Surface-based · Shape-informed.

1 Introduction

Superficial white matter (SWM) U-fibers play an essential role in analyzing the structural connectivity in the human brain [3, 11]. Compared to well-studied deep white matter (DWM), however, there are much fewer studies focusing on SWM due to their anatomical variability in the complicated cortical folding patterns [9]. Many previous works on SWM rely on conventional volume-based fiber tracking methods [21, 20] and utilize the well-known methods and tools [1, 7]

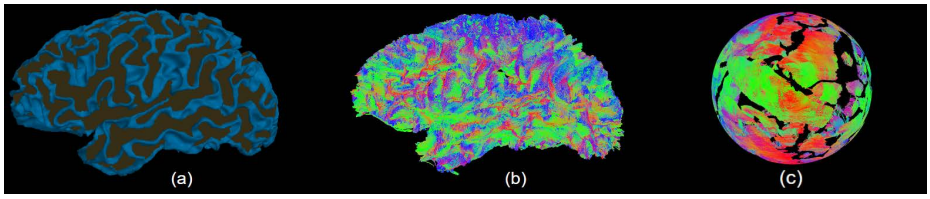

Fig. 1. An illustration of surface-based U-fiber tracking and their spherical representation for an HCP subject (Subj ID: 100206). (a) White matter cortical surface and sulcal patches. (b) Whole-brain U-fiber tractography generated by surface-based tracking. (c) The registered spherical representation of U-fibers of the left hemisphere.

from DWM studies. Recently, surface-based tracking methods [18, 14] have been proposed that allow us to reconstruct U-fibers with higher fidelity to cortical anatomy. Building upon novel surface-based tracking methods, we propose in this work a novel shape-informed atlasing method of U-fibers that can advance the analysis of U-fiber connectivity in clinical diffusion MRI.

There have been a lot of efforts in building a compact and reliable SWM atlas and utilizing such atlas to enhance our understanding of SWM in the past few years. Roman et al. [17] proposed an automatic method for the representative SWM bundles for the whole brain. They report that their atlas outperforms their previous atlas in [15], as well as the atlas [10] and the SWM bundles in Zhang et al.'s atlas [25]. Roman et al. found that certain SWM bundles' dMRI measures are correlated with the cognitive impairment for Alzheimer's Disease [16]. Xue et al. [24] utilized Zhang et al.'s atlas and proposed a deep learning method for the consistent SWM parcellation task. These works employ volume-based tracking methods, which may not be suitable for accurately capturing the complicated cortical folding patterns and U-fiber connections. Conventional atlasing methods usually represent the average U-fibers across subjects and do not account for individual variability in cortical folding patterns. A more personalized strategy could help accurately describe the cortical-cortical U-fiber connections.

In this work, we propose a novel surface-based and shape-informed U-fiber atlasing method for robust SWM connectivity analysis. We use the surface-based tracking method [14] and the spherical representation of U-fibers to build our dictionary and method. We first identify 77 major U-fiber bundles on a cohort of HCP subjects with high groupwise consistency to form the dictionary. After that, we draw shape-informed references from the dictionary to develop our atlasing method that can generate high-quality U-fiber representations on new subjects. We compare our atlasing approach with a previous SWM atlas [17] and demonstrate the effectiveness of our proposed method in terms of anatomical accuracy and integrity of U-fibers. Through experiments, we show that our shape similarity indeed captures the geometric information of the cortical surface, and our shape-informed atlasing method outperforms the conventional volume-based method. The application of our atlasing method in low-resolution dMRI data

from ADNI further demonstrates that our method can more successfully detect SWM connectivity changes in Alzheimer's disease.

2 Method

In this section, we first present the method for U-fiber dictionary construction using surface-based fiber tracking on high-resolution HCP data. After that, we propose our shape-informed approach for personalized atlasing of U-fiber bundles that can be applied to low-resolution dMRI data in clinical studies.

2.1 Surface-based U-fiber dictionary construction

Major U-fiber bundles identification: We use the surface-based tracking [14] and spherical registration method [6] to compute the registered spherical representation of U-fibers [12] as shown in Fig. 1. To identify the major U-fibers, we use the Desikan atlas [5] to set up a list of valid regions of interest (ROIs). For a tract, it connects to either two ROIs or different parts within a single ROI. We can assign labels for every subject's U-fibers by recording the cortical labels of triangles corresponding to a tract's start point and end point. QuickBundle [8] is used to cluster the tracts and discard small clusters in the same pair of ROIs for every subject. We use an adaptive way to grid search proper QuickBundle thresholds for different ROIs. Fig. 2 (a-c) shows an example of results based on the threshold from grid search as compared to those from an overly small and large threshold. After this intra-subject clustering, we obtain the cluster centroids of each pair of ROIs for every subject. Then, we choose the pair of ROIs, which defines the U-fiber bundle, that has valid connections in more than half of the total subjects as identified major U-fiber bundles.

Dictionary of major U-fiber bundles with groupwise consistency: We aim to build a dictionary of U-fiber bundles with groupwise consistency across a cohort of HCP subjects for robust connectivity analysis. We retain the major U-fiber bundles at the subject level as identified in the previous section and perform another layer of QuickBundle clustering on the remaining cluster centroids. Unlike the previous intra-subject clustering, we believe that most of the centroids represent a number of valid tracts at the subject level. Here, we aim to find the most consistent centroids at the group level. A hierarchical density-based clustering method [2] is used to first identify the disconnected components of the centroids and then choose a proper QuickBundle threshold. After this inter-subject clustering, we discard small clusters as shown in Fig. 2 (d-f) and define the U-fiber's groupwise consistency as $\sum_{n=1}^{M}(Mcr/Mct)$, where M is the number of major bundles we identified, M_{cr} is the remaining centroids of major bundle and M_{ct} is the total centroids of major bundle. We can then rank all subjects based on the groupwise consistency of their U-fiber bundles and choose a subset of high groupwise consistency to form our dictionary of high-quality surface-based U-fiber bundles.

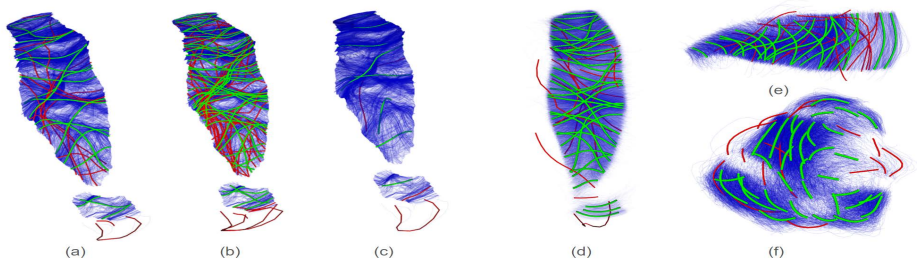

Fig. 2. Intra-subject and inter-subject clustering of U-fibers. For intra-subject clustering, results based on threshold from grid search, an overly small and large threshold are shown in (a), (b), and (c), respectively. In (a)-(c), blue: curves to be clustered; green: cluster centroids to keep; red: cluster centroids to remove. We show results for inter-subject clustering on (d) motor sensory U-fiber, (e) middle temporal to superior temporal U-fiber, and (f) U-fiber within the lateral occipital region. In (d)-(f), blue: centroids from clustering results for all HCP subjects; green: centroids with high inter-subject consistency; red: centroids with low inter-subject consistency.

2.2 Shape-informed atlasing of U-fibers from dictionary

Building upon the dictionary of U-fiber bundles, we develop a personalized approach to maximize the match of the geometric information of the cortical folding patterns. We use the patch-based matching methods in [26] to rank the shape similarity between sulcal patches of the subjects in the dictionary and a given test subject. Following the gyral/sulcal segmentation in [19], a sulcal patch can be defined as the set of vertices segmented as the sulcal area in a certain cortical ROI. The shape similarity score (SS) between patch i and j is defined as $-(0.5 * D_{\chi^2}(H_i^{dt}, H_j^{dt}) + 0.5 * D_{\chi^2}(H_i^{si}, H_j^{si}))$,

where D_{χ^2} is the chi^2 distance, H_i^{dt} and H_i^{si} are histograms of distance transform(dt) [26] and shape index(si) of patch i. We can then choose a subset of subjects within the dictionary with the most similar cortical patches and compare their U-fiber bundles (BUAN score from [4]) with the corresponding U-fiber bundle of the test subject.

Next, we develop a shape-informed atlasing process to identify and project U-fiber bundles from the dictionary onto a given surface patch of a new subject. First, the new subject's cortical surface is mapped and registered to the spherical template of FreeSurfer. Second, dictionary subjects with the closest SS scores are identified together with their U-fiber bundles in matched sulcal patches. Third, we pull-back the identified U-fiber bundles from dictionary subjects back to the sulcal patch of the new subject using the composition of their spherical mapping and registration to the template space. This will generate the atlasing U-fibers in the original 3D image space of the cortical surface.

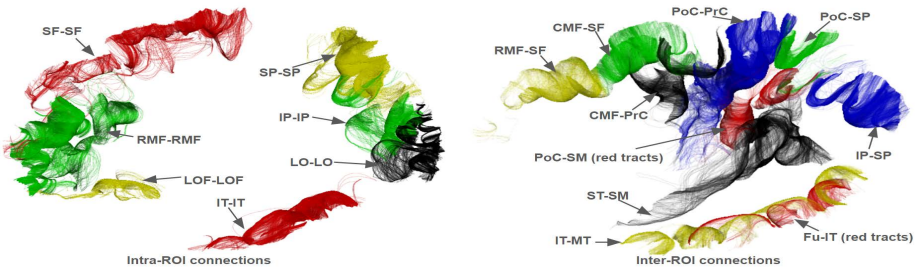

Fig. 3. Visualization of intra-ROI and inter-ROI U-fiber bundles of a HCP subject (subject ID: 133928) in our dictionary.

3 Experiment and evaluation

3.1 Dataset

Two publicly available datasets were used in this study. Human Connectome Project (HCP) dataset [23] with T1-weighted MRI images (isotropic 0.7 mm) and multi-shell dMRI images (isotropic 1.25 mm, b values = 1000, 2000, 3000 s/mm^2) was used to build the dictionary. Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset [13] with T1-weighted MRI images (isotropic 1.0 mm) and single-shell dMRI images (isotropic 2.0 mm, b value = 1000 s/mm^2) was used to evaluate our shape-informed atlasing method.

3.2 Dictionary creation

755 HCP subjects were used in this study to build our dictionary. The fiber orientation distribution (FOD) reconstruction was computed using method [22]. The tractography was generated using surface-based probabilistic tracking method [14]. For this tracking method, we randomly sampled 30 times at each triangle within the sulcal patch of the white matter triangular meshes. We set the step size to be 0.1mm with a maximum angular threshold of 10 degrees between steps. Our U-fiber tracking results contain approximately 60000 tracts per hemisphere for every HCP subject. In total, we identified 77 stable U-fiber bundles for intra- and inter-ROI connections. A complete list of these 77 U-fiber bundles is in table 1. After evaluating inter-subject groupwise consistency, we rank all HCP subjects and choose the top 300 subjects and their U-fiber bundles as our dictionary. As an illustration, representative major U-fiber bundles of one HCP subject in our dictionary are plotted in Fig. 3. We will release this dictionary publicly to the research community together with our shape-informed atlasing method.

3.3 Shape-informed U-fiber atlasing evaluation and application

Comparison with previous atlas: To compare with the state-of-the-art SWM atlas R from [17], we first show qualitative results. Atlas R's whole brain U-fibers

Table 1. We have 23 intra-ROI and 54 inter-ROI bundles in our dictionary. Abbreviation for this table: Bankssts (Ba), Caudal middle frontal (CMF), Cuneus (Cu), Entorhinal (En), Fusiform (Fu), Inferior parietal (IP), Inferior temporal (IT), Lateral occipital (LO), Lateral orbitofrontal (LOF), Lingual (Li), Medial orbitofrontal (MOF), Middle temporal (MT), Parahippocampal (PH), Paracentral (PC), Pars opercularis (POp), Pars orbitalis (POr), Pars triangularis (PTr), Postcentral (PoC), Precentral (PrC), Precuneus (PrCu), Rostral middle frontal (RMF), Superior frontal (SF), Superior parietal (SP), Superior temporal (ST), Supramarginal (SM), Transverse temporal (TT), Insula (In). LH and RH in the bracket indicate that this major U-fiber only occurs in one hemisphere.

Intra	**Intra**	**Inter**	**Inter**	**Inter**	**Inter**
Ba - Ba	PeCa - PeCa	Ba - IP	Fu - Li	Li - PeCa	PoC - SP
CMF - CMF	PoC - PoC	Ba - MT	Fu - PH	Li - PrCu(LH)	PoC - ST(LH)
Cu - Cu	PrC - PrC	Ba - ST	IP - LO	MOF - SF	PoC - SM
Fu - Fu	PrCu - PrCu	CMF - POp	IP - MT	MT - ST	PrC - SF
IP - IP	RMF - RMF	CMF - PrC	IP - SP	MT - SM(LH)	PrC - In
IT - IT	SF - SF	CMF - RMF	IP - SM	PC - PrCu	PrCu - SP
LO - LO	SP - SP	CMF - SF	IT - LO	PC - SF	RMF - SF
LOF - LOF	ST - ST	Cu - LO	IT - MT	POp - PTr	SP - SM
Li - Li	SM - SM	Cu - Li(LH)	LO - Li	POp - PrC	ST - SM
MOF - MOF		Cu - PrCu	LO - MT	POp - RMF	ST - TT
MT - MT		Cu - SP	LO - SP	POp - In	ST - In
PC - PC		En - PH(LH)	LOF - POr	POr - PTr	SM - TT
POp - POp		Fu - IT	LOF - In(RH)	PTr - RMF	
PTr - PTr		Fu - LO	Li - PH	PoC - PrC	

is a collection of U-fibers from HCP subjects in a Montreal Neurological Institute (MNI) space. To use atlas R, one must register a new subject into MNI space or warp altas R into individual space. Fig. 4 (a, b) shows a clear mismatch of the cortical surface with the warped motor-sensory U-fibers from atlas R. On the other hand, our shape-informed atlasing method can generate U-fibers aligned very well with the subject's cortical surface mesh (Fig. 4 (d)) almost to the same degree as those generated directly from surface-based tracking (Fig. 4 (c)). For the quantitative comparison, U-ratio [14] (the Euclidean distance between the start and end point of a tract divided by tract length) is computed to measure the shape of U-fibers. The mean U-ratio for whole brain U-fibers of the atlas R is 0.56, while the mean U-ratio of tracts in our proposed dictionary is 0.34, which suggests our dictionary provides more plausible U-shaped fibers.

Advantage of our shape-informed U-fiber atlasing method: In Fig. 5(a), the patch with high shape similarity is indeed more similar than the patch with low shape similarity visually. To demonstrate the advantage of our method, we use 80 HCP subjects with valid U-fibers as the test set, and we use the dictionary set as the template set. For simplicity, we only use left motor-sensory U-fibers for next experiments. We first rank the shape similarity of motor-sensory patches between the template set and test set. For one test subject, we obtain the most similar 3 and least similar 3 template subjects based on shape similarity and com-

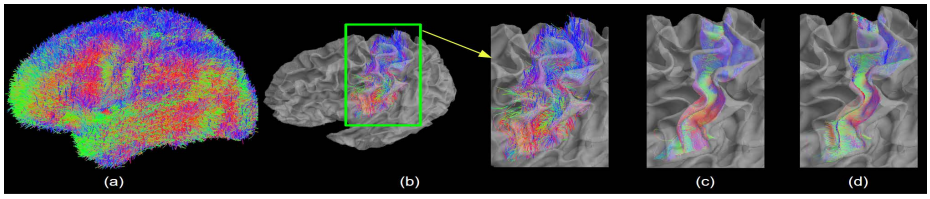

Fig. 4. Comparison of U-fibers from different atlasing methods. (a) Whole brain U-fibers in the atlas R. (b) Overlay of the warped motor-sensory U-fibers from atlas R with the white matter cortical surface of a test HCP subject (subject ID: 172938). (c) U-fiber generated by surface-based tracking using the FOD of the same subject. (d) U-fibers were obtained from our shape-informed atlasing method.

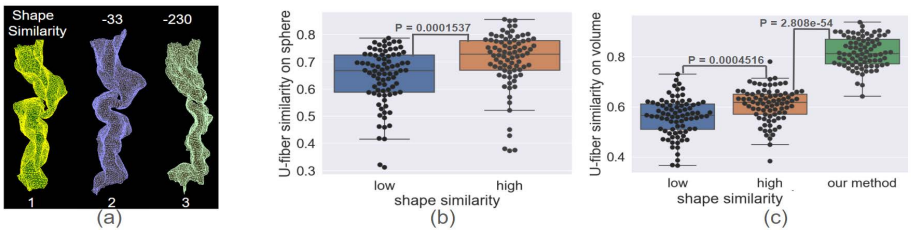

Fig. 5. Quantitative demonstration of the advantage of our shape-informed atlasing method for motor-sensory patches. (a) The SS scores displayed over patches 2 and 3 match well with their geometric similarity to patch 1 from the test HCP subject (subject ID: 172938). Patch 2 is more similar to patch 1, hence it has a higher SS score than patch 3. (b) U-fiber similarity from reference U-fibers with lowest and highest shape similarity as measured on the sphere. (c) The first two box plots show the same U-fiber similarity measured after warping all U-fibers to the MNI space. The right-most box shows the U-fiber similarity measured after we pull-back reference U-fibers with the highest shape similarity to the cortex of the test subject using our atlasing method.

pute the corresponding U-fiber similarity on the sphere. As shown in Fig. 5(b), there is a group difference in U-fiber similarity on the sphere between patches with the most and least similar shapes. The same procedure is applied to U-fibers on volume in MNI space between the template set and the test set. For comparison, We calculated the U-fiber similarity in volume between U-fiber from our method and U-fibers from test subjects. The group difference of U-fiber similarity in volume between most and least shape similar shows that patch similarity positively correlates with U-fiber similarity in volume in Fig. 5(c). Additionally, U-fibers from our atlasing show higher similarity to the test subject than volume-based registered U-fibers, demonstrating the advantage of our method.

Robust SWM connectivity analysis in low-resolution ADNI data: For ADNI dMRI data with much lower resolution than HCP, it is often challenging to generate reliable and robust whole brain SWM tractography even with surface-based fiber tracking. To quantitatively describe the poor performance of U-fiber in ADNI data, we compute a cortical surface coverage measure by divid-

ing the number of triangles touched by U-fibers by the total number of triangles in a given cortical region. As shown in Fig. 6 (a, b), our dictionary subjects from HCP have much higher coverage than ADNI subjects in both precentral and postcentral cortical regions. With our shape-informed atlasing method, we can obtain a more complete representation of the U-fibers as shown in Fig. 6 (c, d).

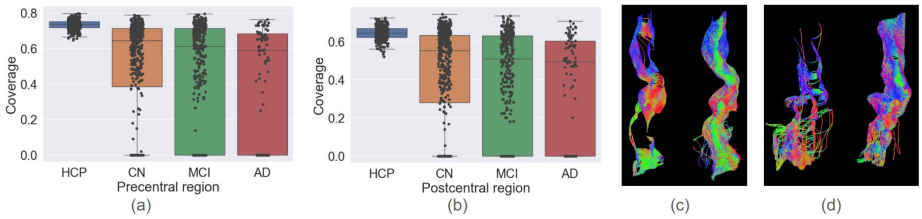

Fig. 6. Shape-informed atlasing provides a more complete representation of U-fibers in subjects with incomplete U-fibers. (a) and (b) show the coverage of our dictionary subjects from HCP in the precentral and postcentral cortical region as compared to those from ADNI (CN, MCI, and AD subjects). (c,d) are examples from ADNI with incomplete U-fibers on the left and U-fibers from our method on the right. (c) is a CN subject (subject ID: 003_S_4441), (d) is an AD subject (subject ID: 011_S_6303).

Table 2. P-values for comparing motor-sensory SWM connectivity: CN vs AD.

CN vs AD : subjects with incomplete U-fibers	FA	MD	RD
U-fibers from tractography	0.4002	0.7788	0.8778
U-fibers from our atlasing method	0.3629	0.01861	0.01712
CN vs AD: all subjects	FA	MD	RD
U-fibers from tractography	0.5240	0.07622	0.2162
U-fibers from our atlasing method	0.006397	4.062e-05	0.01293

We compute common micro-structural measures including fractional anisotropy (FA), mean diffusivity (MD) and radial diffusivity (RD) to compare the SWM connectivity between the CN (n = 495) and AD (n=79) group in the ADNI dataset. We first identified 134 CN subjects and 20 AD subjects with less than 2000 tracts in motor-sensory U-fiber from surface-based tracking, which we consider incomplete. As shown in Table 2, the micro-structural measures on the reconstructed U-fibers are statistically insignificant between AD and CN subjects. After applying our shape-informed atlasing method, statistically significant differences can be observed for the MD and RD measures between the CN and AD groups. Furthermore, we applied our atlasing method to the entire cohort to generate their U-fiber representation in the motor-sensory cortex. As shown in Table 2, U-fibers from our atlasing method outperform the original u-fibers

from tracking for the detection of group differences in SWM connectivity. These results demonstrate that our method can provide more reliable and robust SWM connectivity analysis for low-resolution dMRI data in clinical studies.

4 Conclusion

In this paper, we propose a novel surface-based and shape-informed SWM atlasing framework for robust SWM analysis. We use surface-based U-fiber tracking to build a dictionary containing HCP subjects with high groupwise consistency of major U-fibers. The shape-informed atlasing method allows more reliable brain connectivity analysis of SWM in clinical studies with low-resolution diffusion MRI.

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Disclosure of Interests. The authors have no competing interests to declare that are relevant to the content of this article.

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