# Resting State fMRI-Guided Fiber Clustering

Bao Ge[1], Lei Guo[1], Jinglei Lv[1], Xintao Hu[1], Junwei Han[1], Tuo Zhang[1,2], and Tianming Liu[2]

[1] School of Automation, Northwestern Polytechnical University, Xi'an, China
{oct.bob,guolei.npu,lvjinglei,xintao.hu,
junweihan2010,zhangtuo.npu}@gmail.com
[2] Department of Computer Science and Bioimaging Research Center,
University of Georgia, Athens, GA
tliu@cs.uga.edu

**Abstract.** Fiber clustering is a prerequisite step towards tract-based analysis of white mater integrity via diffusion tensor imaging (DTI) in various clinical neuroscience applications. Many methods reported in the literature used geometric or anatomic information for fiber clustering. This paper proposes a novel method that uses functional coherence as the criterion to guide the clustering of fibers derived from DTI tractography. Specifically, we represent the functional identity of a white matter fiber by two resting state fMRI (rsfMRI) time series extracted from the two gray matter voxels to which the fiber connects. Then, the functional coherence or similarity between two white matter fibers is defined as their rsfMRI time series' correlations, and the data-driven affinity propagation (AP) algorithm is used to cluster fibers into bundles. At current stage, we use the corpus callosum (CC) fibers that are the largest fiber bundle in the brain as an example. Experimental results show that the proposed fiber clustering method can achieve meaningful bundles that are reasonably consistent across different brains, and part of the clustered bundles was validated via the benchmark data provided by task-based fMRI data.

**Keywords:** Resting state fMRI, DTI, fiber clustering.

## 1 Introduction

Diffusion tensor imaging (DTI), as a powerful tool to image the axonal fibers in vivo, provides rich structural connectivity information that is believed to be closely related to brain function. In order to infer meaningful and comparable information from DTI data of different brains, the large number of fiber trajectories produced by DTI tractography need to be grouped into appropriate fiber bundles for tract-based analysis [4]. Many approaches reported in the literature used geometric, anatomical or structural features, e.g., fiber's Euclidean distances [3, 4], fiber shape information [11], or fiber's end point positions [10], to cluster fiber bundles. Though these methods have their own advantages in clustering meaningful bundles, the functional interpretation of the clustering results remains to be elucidated.

G. Fichtinger, A. Martel, and T. Peters (Eds.): MICCAI 2011, Part II, LNCS 6892, pp. 149–156, 2011.

Recently, resting state fMRI (rsfMRI) has been demonstrated to be an effective modality by which to explore the functional networks in the human brain, because similar low-frequency oscillations in rsfMRI time series between spatially distinct brain regions are indicative of correlated functional activity patterns in the brain [2]. In addition, a variety of recent studies demonstrated that structural connectivity derived from DTI data is closely correlated with the functional connectivity derived from rsfMRI data [8]. Inspired by these studies, we are motivated to apply the criterion of functional coherence to cluster white matter fibers. Our premise is that the clustered fibers within a bundle should have functional homogeneity or coherence. To achieve this goal, we represent a white matter fiber by two rsfMRI time series extracted from the two gray matter (GM) voxels that the fiber's two end points connect, and the functional coherence between white matter fibers is measured by the similarities of their rsfMRI time series. Then, the data-driven affinity propagation (AP) algorithm [7] is applied to cluster fibers into bundle tracts. We currently use the corpus callosum (CC) fibers, which are the largest fiber bundle in the brain, as an example for algorithm development and validation. Our experimental results in seven brains with multimodal rsfMRI and DTI datasets show that the proposed rsfMRI-guided fiber clustering method can achieve meaningful fiber bundles that are reasonably consistent across different brains, and part of the clustered bundles is validated by the benchmark data provided by task-based fMRI data.

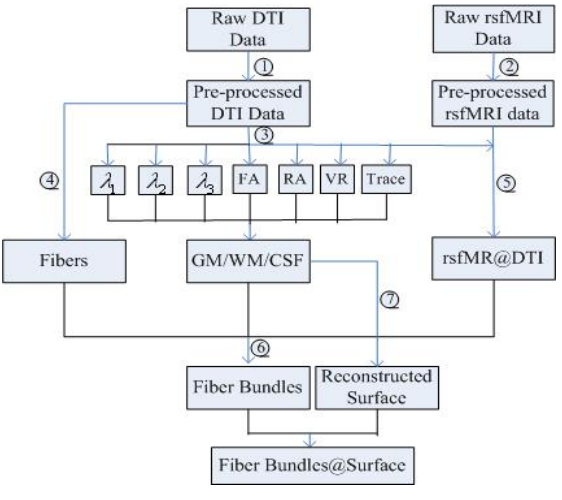



**Fig. 1.** The flowchart of our framework. (1) and (2): pre-processing steps; (3): segmentation of brain tissue using DTI data; (4): DTI tractography; (5): registration of rsfMRI to DTI images; (6): affinity propagation clustering guided by rsfMRI data; (7): WM (white matter)/GM (gray matter) cortical surface reconstruction from DTI data.

## 2 Materials and Methods

### 2.1 Overview

As summarized in Fig.1, our algorithmic pipeline includes the following steps. First, we pre-processed the raw DTI data, and then performed brain tissue segmentation and

fiber tracking based on DTI data. The tracked fiber trajectories were projected to the cortical surface via a similar method in [8] to facilitate the extraction of rsfMRI signals on the gray matter volume. Also, we registered the rsfMRI signals to the DTI space using FSL FLIRT. Then, we clustered fibers into bundles based on fibers' function coherences via the affinity propagation algorithm [7]. Finally, we identified consistent fiber bundles from seven subjects for evaluation and validation.

### 2.2 Multimodal Data Acquisition and Pre-processing

Seven volunteers were scanned using a 3T GE Signa MRI system. We acquired the rsfMRI data with dimensionality 128*128*60*100, space resolution 2mm*2mm*2mm, TR 5s, TE 25ms, and flip angle 90 degrees. DTI data was acquired using the same spatial resolution as the rsfMRI data; parameters were TR 15.5s and TE 89.5ms, with 30 DWI gradient directions and 3 B0 volumes acquired. For two out of the seven subjects, the working memory OSPAN tasks [12] was used for fMRI data acquisition with the parameters of 64×64 matrix, 4mm slice thickness, 220mm2 FOV, 30 slices, TR=1.5s, TE=25ms, ASSET=2. Pre-processing of the rsfMRI data included skull removal, motion correction, spatial smoothing, temporal pre-whitening, slice time correction, global drift removal, and band pass filtering (0.01Hz~0.1Hz). For the DTI data, pre-processing included skull removal, motion correction, and eddy current correction. After the pre-processing, fiber tracking was performed using MEDINRIA (FA threshold: 0.2; minimum fiber length: 20). Based on pre-processed DTI data, brain tissue segmentation was performed using the multi-channel fusion method akin to that in [5]. DTI space was used as the standard space from which to generate the tissue segmentation and exhibit the functional coherent fiber bundles. Since rsfMRI and DTI sequences are both EPI sequences, their distortions tend to be similar, and thus the misalignment between their images is much less than that between T1 and fMRI images [8]. DTI and fMRI images were registered via FSL FLIRT.

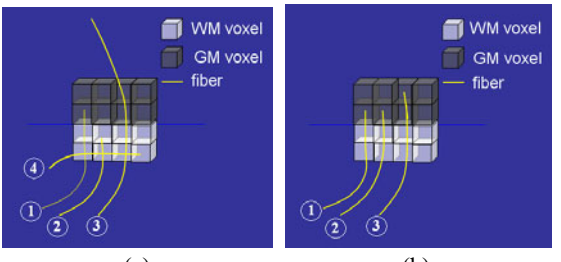
### 2.3 Fiber Clustering Based on Functional Coherence

**Extraction of rsfMRI Signals for a Fiber's Two Ends**

It should be noted that the blood supply to the white matter is significantly lower than that of the cortex (less than one fourth) [9], and the blood-oxygen-level dependence (BOLD) contribution of the white matter is relatively low. Hence, the investigation of gray matter rsfMRI signals is more reasonable. Therefore, before extracting rsfMRI signals from GM voxels for a fiber's two ends, we need to project some fibers onto the gray matter cortex in that the DTI-derived fiber trajectories are not necessarily located on the cortex due to two reasons. 1) DTI fiber tractography using the streamline approach has difficulty in tracking inside GM since the FA (fractional anisotropy) values around the boundaries of gray matter and white matter are relatively low. As a result, there are some fibers that cannot touch the GM. 2) There is discrepancy in brain tissue segmentation based on DTI data and the DTI tractography [5]. In this case, the fiber could be either outside the cortex if the gray matter (GM) is over-segmented, or inside the cortex if the GM is under-segmented.

In order to make use of the fiber connection information on the cortex, we projected the fibers onto the cortical surface guided by the tissue segmentaion map.

There are four types of fiber projections here. 1) If the end point of a fiber already lies on a GM voxel in the brain tissue map, no search is conducted, e.g., fiber #1 shown in Fig. 2(a); 2) If the end point of a fiber lies inside the cortex, e.g., the fiber #2 shown in Fig. 2(a), we search forward along the tangent direction until reaching the gray matter. 3) Otherwise, e.g., the fiber #3 shown in Fig. 2(a), we search backward along the tangent direction until reaching the gray matter. The search process stops either when the fiber arrives at a GM voxel or it exceeds a search threshold. 4) In very rare cases when a fiber cannot reach the surface, e.g., the fiber #4 shown in Fig. 2(a), we treat this fiber as an outlier and remove it from the data. Fig. 2(b) shows the positions that the fibers arrive at after the projection. The search was conducted iteratively until at least one GM voxel can be found in the 1-ring surface vertex neighborhood of the current seed point, or the number of iteration exceeds a given threshold. When multiple GM voxels exist, the closest one is used as the projected point. Finally, for each projected fiber, we extract the rsfMRI signals for two ends of the fiber.




(a) (b)

**Fig. 2.** Illustration of fiber projection. Gray matter and white matter voxels are represented by gray and white color boxes respectively. Fibers are represented by yellow curves. (a) The four situations before fiber projection; (b) The results of fiber projections for three situations.

**Measurement of Functional Coherence Among fibers**

As illustrated in Fig. 3, given any pair of fibers with four end points located in the gray matter, the functional coherence between these two fibers is defined as follows:

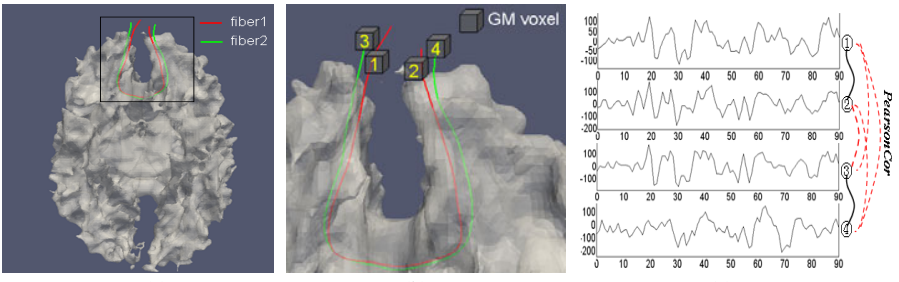
$$C=0.5*(max(C_{13},C_{14})+max(C_{23},C_{24})) \quad (1)$$

$$C_{13}=PsCor(v1,v3),\ C_{14}=PsCor(v1,v4),\ C_{23}=PsCor(v2,v3),\ C_{24}=PsCor(v2,v4)$$

where *vi* indexes the end points of two fibers, the function *PsCor* is the Pearson correlation coefficient of two end points' rsfMRI signals. Our premise here is that the fibers belonging to the same tract should have higher functional coherence, and those belonging to different tracts should have lower coherence.

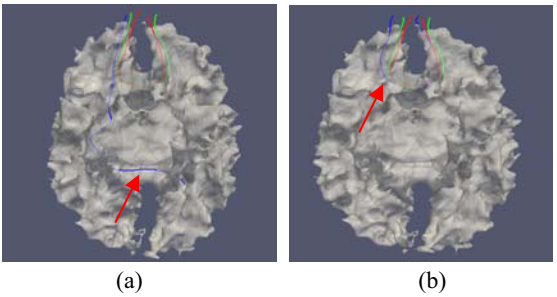
It should be noted that the crierion of functional coherence derived from rsfMRI data offers unique capability to cluster functionally coherent fibers into the same bundle and differentiate non-coherent fibers into different bundles. As an example, Fig. 4a shows three fibers that are functionally coherent, and thus they should be clustered into one bundle. However, if we use geometric or shape criteria [3, 4, 11], e.g., the Euclidean distances betweeen neighboring fibers, the blue fiber in Fig. 4a

(highlighted by a red arrow) is very likely to be separated from the bundle composed of the red and green ones. Another example is shown in Fig. 4b, in which the blue fiber (highlighted by a red arrow) has low functional coherence with the green and red ones and thus the blue one can be differentiated from other two fibers via rsfMRI data. However, geometry or shape based fiber clustering methods are likely to have difficulties in differentiating the blue fiber from other two fibers. Hence, the criterion of functional coherence is a powerful approach for fiber clustering.




(a) (b) (c)

**Fig. 3.** The calculation of fibers' functional coherence. (a) Two fibers overlaid on the reconstructed cortical surface (gray mesh); (b) The zoomed-in view of the black rectangle in (a); (c) The rsfMRI signals of the four end points. Their correlations are measured by Eq. (1).



(a) (b)

**Fig. 4.** (a). An example showing functional coherence can cluster fibers of different shapes or geometries into the same bundle. (b) An example showing functional difference can differentiate neighboring fibers into different bundles.

### Fiber Clustering via the Affinity Propagation Algorithm

The affinity propagation (AP) algorithm [7] has been widely used to identify data clusters automatically. In the AP clustering method, each cluster is represented by a data point called a cluster center, or an exemplar, and the method searches for cluster so as to maximize a goal function called net similarity [7]. In this paper, we applied the AP clustering method on the functional similarity matrix of all fibers in the corpus callosum, and achieved the clustered fiber bundles. In particular, each fiber cluster is represented by the fiber exemplar discovered during the AP clustering procedure.

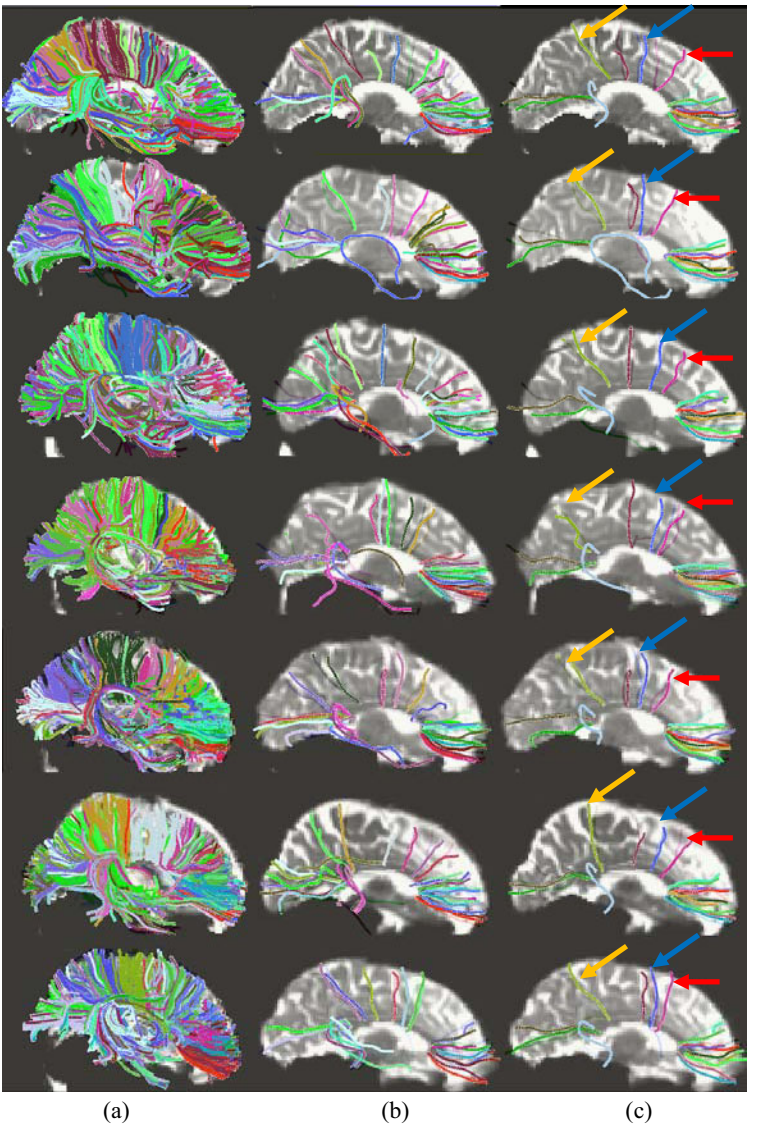



**Fig. 5.** The clustered fiber bundles for 7 subjects. (a) The fiber clusters with randomly set colors overlaid on the DTI B0 images; (b) The fiber exemplars of all clusters (c) The 16 most consistent fiber exemplars.

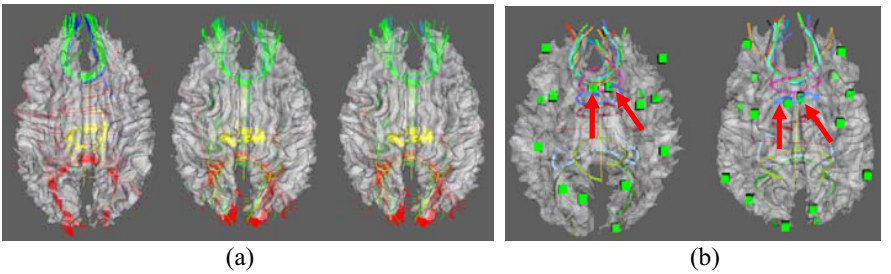
# 3 Experimental Results

## 3.1 Identification of Functionally Coherent Fiber Bundles

The fibers passing corpus callosum (CC) were clustered into aournd 30 bundles for 7 subjects separately, as shown in the 7 rows in Fig. 5(a). For the sake of visual differentiation, each fiber bundle was represented by the fiber exemplar obtained during the affinity propogation clustering procedure [7], as shown in Fig. 5(b). In order to identify the corresponding fiber bundles in different subjects, we computed the Hausdorff distances between the representative exemplars across subjects and picked out those exemplars that are closest to the representative exemplars in other subjects. We visually confirmed 16 most consistent and representative exemplar fibers in all fiber exemplars from 7 subjects and showed all of them in Fig. 5(c). Each corresponding fiber exemplar in Fig. 5(c) has the same color in different brains, and three of corresponding ones are highlighted by arrows of the same color. It is evident that the distributions of these 16 fiber exemplars are quite reasonable and consistent. As another exmple, Fig. 6(a) visualizes four corresponding bundles from 3 randomly selected subjects, showing that the clustered bundles are quite reasonable.

## 3.2 Validation by Task-Based fMRI Data

In addition to the qualitative visual evaluation of the clustered CC fiber bundles in Section 3.1, we used working memory task-based fMRI data [12] to examine the functional correspondence of the clustered fiber bundles in Section 3.1. Specifically, the working memory task-based fMRI data provided 16 consistently activated brain regions, as shown by green boxes in Fig. 6(b). These ROIs provide the benchmark data for comparison of functional correspondences of fiber bundles. It is striking that one fiber bundle (blue ones in Figs. 5(c) and Fig. 6(b)) clustered in Section 3.1 coincidently falls into the neighborhoods of two corresponding working memory ROIs of left and right paracingulate gyri (highlighted by yellow arrows) consistently in the testing subjects. These close vicinities indicate that the paracingulate gyri are consistently connected by the blue fiber bundle across individuals, suggesting that the rsfMRI-guided fiber clustering method grouped functionally coherent fibers into the same bundle. This result is considered as a validation of the rsfMRI-guided fiber clustering approach.



(a) (b)

**Fig. 6.** (a) Visualization of four corresponding fiber bundles from 3 randomly chosen subjects. They are labeled by the four different colors of blue, green, yellow, and red, respectively. (b) Joint visualization of 16 activated working memory ROIs (represented by green boxes) and clustered fiber bundles (represented by exemplars) for two subjects.

## 4 Conclusion

This paper presents a novel methodology of using rsfMRI data to guide fiber clustering. The underlying neuroscience basis is that axonal fibers within a bundle should have functional coherence, and our results have shown that functional coherence is a meaningful criterion for fiber clustering. In particular, part of the clustered bundles was validated via task-based fMRI data. Currently, only CC fibers were used for algorithm development and evaluation. In the future, we plan to apply the proposed method to other major fiber bundles such as cortico-cortical and cortical-subcortical pathways, and apply the methods for tract-based analysis of DTI datasets of brain diseases such as schizophrenia and Alzheimer's disease.

## References

1. Friston, K.: Modalities, modes, and models in functional neuroimaging. Science 326(5951), 399–403 (2009)
2. Fox, M.D., Raichle, M.E.: Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nat. Rev. Neurosci. 8, 700–711 (2007)
3. Maddah, M., Grimson, W., Warfield, S.: Statistical Modeling and EM Clustering of White Matter Fiber Tracts. In: ISBI, vol. 1, pp. 53–56 (2006)
4. Gerig, G., Gouttard, S., Corouge, I.: Analysis of Brain White Matter via Fiber Tract Modeling. IEEE EMBS 2, 4421–4424 (2004)
5. Liu, T., Li, H., Wong, K., Tarokh, A., Guo, L., Wong, S.: Brain Tissue Segmentation Based on DTI Data. NeuroImage 38(1), 114–123 (2007)
6. Liu, T., Nie, J., Tarokh, A., Guo, L., Wong, S.: Reconstruction of Central Cortical Surface from MRI Brain Images: Method and Application. NeuroImage 40(3), 991–1002 (2008)
7. Frey, B.J., Dueck, D.: Clustering by Passing Messages between Data Points. Science 315, 972–976 (2007)
8. Li, K., Guo, L., Li, G., Nie, J., Faraco, C., Zhao, Q., Miller, S., Liu, T.: Cortical surface based identification of brain networks using high spatial resolution resting state FMRI data. In: ISBI, pp. 657–659 (2010)
9. Mezer, A., Yovel, Y., Pasternak, O., Gorfine, T., Assaf, Y.: Cluster analysis of resting-state fMRI time series. NeuroImage 45(4), 1117–1125 (2009)
10. Ge, B., Guo, L., Li, K., Li, H., Faraco, C., Zhao, Q., Miller, S., Liu, T.: Automatic Clustering of White Matter Fibers via Symbolic Sequence Analysis. In: SPIE Medical Image, vol. 7623, pp. 762327.1–762327.8 (2010)
11. Zhang, T., Guo, L., Hu, X., Li, G., Nie, J., Jiang, X., Zhang, D., Liu, T.: Joint analysis of fiber shape and cortical folding patterns. In: ISBI, pp. 1165–1168 (2010)
12. Zhang, T., Guo, L., Hu, X., Li, K., Liu, T.: Predicting Functional Cortical ROIs based on Fiber Shape Models. In: Fichtinger, G., Martel, A., Peters, T. (eds.) MICCAI 2011, Part II. LNCS, vol. 6892, pp. 42–49. Springer, Heidelberg (2011)