Fuzzy Nonparametric DTI Segmentation for Robust Cingulum-Tract Extraction

Suyash P. Awate, Hui Zhang, and James C. Gee

Department of Radiology, University of Pennsylvania, Philadelphia, PA 19104, USA
{awate,gee}@mail.med.upenn.edu, huiz@seas.upenn.edu

Abstract. This paper presents a novel segmentation-based approach for fiber-tract extraction in diffusion-tensor (DT) images. Typical tractography methods, incorporating thresholds on fractional anisotropy and fiber curvature to terminate tracking, can face serious problems arising from partial voluming and noise. For these reasons, tractography often fails to extract thin tracts with sharp changes in orientation, e.g. the *cingulum*. Unlike tractography—which disregards the information in the tensors that were previously tracked—the proposed method extracts the cingulum by exploiting the statistical coherence of tensors in the entire structure. Moreover, the proposed segmentation-based method allows *fuzzy* class memberships to optimally extract information within partial-volumed voxels. Unlike typical fuzzy-segmentation schemes employing Gaussian models that are biased towards ellipsoidal clusters, the proposed method *models the manifolds* underlying the classes by incorporating nonparametric data-driven statistical models. Furthermore, it exploits the nonparametric model to capture the *spatial continuity and structure* of the fiber bundle. The results on real DT images demonstrate that the proposed method extracts the cingulum bundle significantly more accurately as compared to tractography.

1 Introduction

Diffusion tensor (DT) magnetic resonance (MR) imaging allows us to differentiate the cerebral white/gray-matter structures such as the corpus callosum, thalamic nuclei, cingulum, etc. Extraction of these structures is of key interest in clinical studies concerning schizophrenia, Parkinson’s disease, and Alzheimer’s disease [1,2,3,4,5]. The driving clinical application for this paper is to investigate whether there are changes in the anterior cingulum in cocaine users that are associated with decreased gray-matter concentration in the same region [6].

The efficacy of tract-extraction methods on DT images can be severely limited by noise and partial-voluming artifacts. For instance, tractography methods often fails to extract the cingulum [3,4]—a thin tract that undergoes sharp changes in orientation and severe partial-volume contamination from the highly-anisotropic corpus callosum and the highly-isotropic ventricles lying adjacent to it (Figure 1). Tractography methods, which incorporate thresholds on the fractional anisotropy (FA) and fiber curvature to terminate tracking, can also consistently underestimate the size of fiber bundles [7].

Alternative approaches for extracting structures from DT images rely on segmentation approaches. Unlike tractography that disregards the information in the tensors that were previously tracked, segmentation approaches exploit the coherence of tensors in the entire structure of interest. Moreover, segmentation methods that allow fuzzy class memberships optimally extract information within partial-volumed voxels—crisp segmentations incorrectly account for this information towards the representation of a single class. In these ways, segmentation schemes can be more robust to DT-image artifacts.

Previous work in DTI segmentation employs Gaussian models that may not effectively model the tensor statistics because they are inherently biased towards ellipsoidal clusters. Fundamental anatomical characteristics of fiber bundles make fibers change their orientation *significantly*, e.g. cingulum (Figure 1), as they connect different structures. Thus, tensors in fiber bundles inherently lie on *manifolds* that do not conform to Gaussian models that are characterized by the mean. For instance, tensors in U-shaped/C-shaped bundles, that include tensors which start and end at similar orientations, must lie on a closed manifold.

This paper makes several contributions. It proposes a novel scheme based on fuzzy segmentation for extracting fiber bundles, e.g. cingulum, relying on a *non-parametric* statistical framework. The proposed method does not impose strong parametric tensor models, but adapts its models to arbitrary tensor probability density functions (PDFs), and the underlying manifolds, in data-driven ways. It extends the nonparametric model to capture the *spatial continuity and structure* of the fiber bundle. The *fuzzy* framework optimally extracts information from partial-volumed voxels. Results on real DT images show that the proposed method extracts the cingulum significantly more accurately than tractography.

2 Related Work

Typical methods for crisp and fuzzy segmentation [8,9,10] rely on representing each class by *only a single point* in the feature space (the class mean) and measure class membership based on the Euclidean/Mahalanobis distance to the class mean. Such approaches, however, (a) bias the segmentation towards ellipsoidal clusters in feature space and (b) do *not* yield themselves easily in capturing the spatial structure of the fiber bundle in the image. Nonparametric modeling approaches for crisp structural-MR segmentation [11,12] address the concern in (a), but not in (b). The proposed method: (i) generalizes class representation in fuzzy methods to the manifold underlying the class, (ii) extends a data-driven nonparametric scheme to adaptively infer the spatial structure of the fiber bundle in the image, and (iii) extracts information from partial-volumed tensors in a principled manner by incorporating fuzzy class memberships.

Segmentation methods entail quantifying distances between tensors that respect the group structure of the Riemannian DT space [13,14,1,15]. Lenglet *et al.* [1] use an affine-invariant Riemannian metric and model each class by a single Gaussian. Wang and Vemuri [2] use a piecewise-smooth Mumford-Shah framework to capture the spatial variations in tensors across a bundle. In contrast,

the proposed method relies on nonparametric models and optimally extracts information from partial-volumed voxels using fuzzy class memberships.

The extraction of the cingulum tract, a key component of the limbic system that is relevant to memory and emotion, holds significance in many clinical studies relating to schizophrenia. Gong *et al.* [4] employ tractography to extract the cingulum bundle to study the left-right asymmetry in the structure. Their tractography results, however, clearly shows fibers “leaking” out of the cingulum. Concha *et al.* [3], acknowledging the impracticality of tractography for cingulum extraction, *divide* the cingulum into 3 parts (anterior, superior, descending) and perform tractography *independently* in each of these parts. In each part, they include tracts that pass through manually-selected regions-of-interest in the start, middle, and end of the part. The proposed method, on the other hand, extracts the cingulum in a simple, systematic, and optimal manner.

3 Nonparametric Statistical Diffusion-Tensor Modeling

This section describes the statistical formulation underlying the proposed nonparametric modeling technique. It starts by describing a generic kernel-based modeling scheme, that is independent of the particular metric associated with the Riemannian space. It then presents an appropriate tensor metric to considerably simplify the scheme, from a practical viewpoint, while maintaining the mathematical soundness of the framework.

We use kernel-based nonparametric PDF estimation based on a Parzen-window scheme in Riemannian space. For DT data, the kernel functions are smooth functions of the Riemannian geodesic distance on the tensor manifold. The mathematical expression for the Parzen-window tensor-PDF estimate is consistent with the expression of the usual (Euclidean) PDF estimate—it also relies on the intuitive notion of a kernel function having the largest value at the datum and monotonically-decreasing values with increasing distance from the datum. In the Riemannian case, each datum is the intrinsic mean of the associated kernel for sufficiently small bandwidths. We now describe this scheme.

Let $\mathcal{M}$ be a compact Riemannian manifold without boundary, of dimension D , with an associated metric-tensor g . The metric tensor induces an inner product on the manifold that generates the geodesic distance function $d_g(\cdot, \cdot)$ between two entities on $\mathcal{M}$. Let Z be a random variable on the probability space $(\Omega, \mathcal{A}, P)$ that takes values in $\mathcal{M}$. Let $\{z_1, z_2, \dots, z_n\}$, where each $z_i \in \mathcal{M}$, be an independently-drawn and identically-distributed random sample derived from the PDF $P(Z)$. Let $K(Z)$ be a nonnegative and sufficiently-smooth kernel function. Then, the *consistent* nonparametric PDF estimate is [16]:

$$\hat{P}(z) = \frac{1}{N} \sum_{i=1}^N \frac{1}{\theta_{z_i}(z)} \frac{1}{\sigma^D} K\left(\frac{d_g(z, z_i)}{\sigma}\right), \quad (1)$$

where σ is the bandwidth associated with the kernel and $\theta_a(b)$ is the quotient of the canonical measure of the Riemannian metric $\exp_a^*g$ on $T_a(\mathcal{M})$ by the

Lebesgue measure of the Euclidean structure g_a on $T_a(\mathcal{M})$. We choose $K(\cdot)$ as the standard-Normal PDF: $K(\beta) = (1/(2\pi)^{D/2}) \exp(-\beta^2/2)$.

To evaluate the probability at any one point z we need to, in general, compute $\theta_{z_i}(z)$ separately for all the points z_i in the Parzen-window sample. This can become cumbersome, depending on the particular Riemannian tensor metric employed. The recently-proposed Log-Euclidean metric [14], in contrast to the affine-invariant Riemannian metric [13,1,15], induces a Riemannian space having zero curvature by mapping the DT space of 3×3 symmetric positive-definite matrices in an isomorphic, diffeomorphic, and *isometric* manner to the associated *Euclidean* vector space of 3×3 symmetric matrices. This mapping is precisely the matrix logarithm (denoted $\log_M$), i.e. $d_g(z, z_i) = \|\log_M(z) - \log_M(z_i)\|_{\text{Frobenius}}$ and $\theta_{z_i}(z) = 1$. The Parzen-window PDF estimate then simplifies to $\hat{P}(z) = (1/N) \sum_{i=1}^N G(z; z_i, \sigma)$, where $G(z; z_i, \sigma)$ is a multidimensional isotropic Gaussian (mean z_i and variance along each dimension σ^2) in the Riemannian space with $d_g(\cdot, \cdot)$ as the geodesic distance measure. Essentially, this scheme maps the diffusion tensors, using the matrix logarithm, to a Euclidean space and, in turn, computes probabilities using standard Parzen-window estimation in that space.

4 Fuzzy Segmentation with Manifold-Based Models

This section proposes a fuzzy-segmentation framework for fiber-tract extraction. It extracts tracts by iteratively optimizing an information-theoretic objective function and relying on nonparametric class models.

Our goal is to segment the image into $\mathcal{C}$ different classes ($c = 1, 2, \dots, \mathcal{C}$). For extracting a single fiber bundle, $\mathcal{C} = 2$. These classes are distinguished by their respective PDFs $\{P_c(\cdot)\}_{c \in \mathcal{C}}$. The segmentation problem is, in a way, equivalent to that of deducing these PDFs.

Voxels in a fuzzy-segmentation framework can be *members* of more than one class—a standard notion in fuzzy set theory that does *not* constrain entities to belong to one set alone. We incorporate this notion using the fuzzy-membership functions that we define next. Consider $\mathcal{C}$ random variables $\{F_c : \mathcal{M} \rightarrow \mathbb{R}\}_{c \in \mathcal{C}}$ that give a class-membership value for each element $\mathbf{z} \in \mathcal{M}$ belonging to class c . For all voxels t and all classes c , we want $0 \leq F_c(\mathbf{z}_t) \leq 1$ and $\sum_{c=1}^{\mathcal{C}} F_c(\mathbf{z}_t) = 1$. Under these constraints, we define the optimal fuzzy segmentation as:

$$\operatorname{argmax}_{\{F_c(\cdot)\}_{c=1}^{\mathcal{C}}} \sum_{c=1}^{\mathcal{C}} \left(\int_{\mathcal{M}} F_c(\mathbf{z}) P_c(\mathbf{z}) \log P_c(\mathbf{z}) d\mathbf{z} - \alpha \int_{\mathcal{M}} F_c(\mathbf{z}) \log F_c(\mathbf{z}) d\mathbf{z} \right). \quad (2)$$

The first term of the energy in (2) is a *modified* Shannon's entropy that allows each observation $\mathbf{z} \in \mathcal{M}$ to contribute some amount to the entropy of every class c that is proportional to its membership in class c —partial-volumed voxels would contribute to the descriptions of multiple classes. α is a user-controlled parameter that controls the degree of fuzziness/softness imposed on the segmentation.

The method of Lagrange multipliers—and the short-hand terms F_{ct} and P_{ct} for $F_c(\mathbf{z}_t)$ and $P_c(\mathbf{z}_t)$, respectively—gives the objective function as:

$$\mathcal{J} = \sum_{c=1}^C \sum_{t \in \mathcal{T}} \left[F_{ct} \log P_{ct} - \alpha F_{ct} \log F_{ct} \right] + \sum_{t \in \mathcal{T}} \lambda_t \left[\sum_{c=1}^C F_{ct} - 1 \right], \quad (3)$$

where $\{\lambda_t\}_{t \in \mathcal{T}}$ is the set of Lagrange multipliers.

The proposed method modifies the nonparametric statistical model in [16] so as to exploit the prior information that the tract is a *spatially-continuous* entity in the image-coordinate space and, subsequently, to infer the *spatial structure* of the tract. We do this by augmenting the tensor-valued feature space by the 3D-coordinate space of the voxels. To include spatial information, we define the probabilities by P_{ct} as: $P_{ct} = (1/|\mathcal{S}_c|) \sum_{s \in \mathcal{S}_c} G(\mathbf{z}_t; \mu_{cs}, \sigma_c) G(t; \nu_{cs}, \rho_c)$, where the tensors $\{\mu_{cs}\}_{s \in \mathcal{S}_c}$, voxel locations $\{\nu_{cs}\}_{s \in \mathcal{S}_c}$, and bandwidths σ_c and ρ_c together model the PDF for class c in the *augmented feature space* $\langle \mathcal{M}, \mathcal{T} \rangle$. This PDF captures: the manifold(s) underlying the tensor data in the tract, the variability of the tensors around the manifold(s), and the spatial continuity of the tract. For all classes, σ_c is a penalized maximum-likelihood estimate for the Parzen-window PDF of the entire image $\mathbf{z}_{t \in \mathcal{T}}$ [17]. We use $\rho_c = 1$.

We need to maximize $\mathcal{J}$ with respect to F_{ct} , μ_{cs} , ν_{cs} , and λ_t . Solving the Karush-Kuhn-Tucker (KKT) necessary conditions for optimality gives the update for the fuzzy memberships $F_{ct} (\forall s \in \mathcal{S}_c, \forall c = 1, 2, \dots, C)$ as:

$$F_{ct} = \frac{(P_{ct})^{1/\alpha}}{\sum_{c=1}^C (P_{ct})^{1/\alpha}}. \quad (4)$$

Observe that, as expected, a large probability P_{ct} for voxel t to be in class c produces a correspondingly larger membership value F_{ct} of that voxel in class c . $\alpha \rightarrow \infty$ implies $F_{ct} \rightarrow 1/|C|$; a completely fuzzy segmentation. For $\alpha \rightarrow 0$, $F_{ct} \rightarrow 1$ if class c with the largest P_{ct} ; otherwise $F_{ct} \rightarrow 0$.

The updates for the class parameter $\mu_{cs} (\forall s \in \mathcal{S}_c, \forall c = 1, 2, \dots, C)$ are:

$$\mu_{cs} = \frac{\sum_{t \in \mathcal{T}} F_{ct} \frac{G(\mathbf{z}_t; \mu_{cs}, \sigma_c) G(t; \nu_{cs}, \rho_c)}{P_{ct}} \mathbf{z}_t}{\sum_{t \in \mathcal{T}} F_{ct} \frac{G(\mathbf{z}_t; \mu_{cs}, \sigma_c) G(t; \nu_{cs}, \rho_c)}{P_{ct}}}; \nu_{cs} = \frac{\sum_{t \in \mathcal{T}} F_{ct} \frac{G(\mathbf{z}_t; \mu_{cs}, \sigma_c) G(t; \nu_{cs}, \rho_c)}{P_{ct}} t}{\sum_{t \in \mathcal{T}} F_{ct} \frac{G(\mathbf{z}_t; \mu_{cs}, \sigma_c) G(t; \nu_{cs}, \rho_c)}{P_{ct}}}$$

where the updated parameters μ_{cs} and ν_{cs} are weighted averages of the tensors $\mathbf{z}_t$ and voxel locations t , respectively. Observe that the weights take values between 0 and 1. The implementation is numerically stable because by construction, $0 \leq F_{ct} \leq 1$ and $0 \leq G(\mathbf{z}_t; \mu_{cs}, \sigma_c) G(t; \nu_{cs}, \rho_c) / P_{ct} \leq 1$. For the application in this paper, the iterative optimization method took about 4 iterations to converge; each iteration taking about 5 minutes using unoptimized Matlab code.

5 Results, Validation, and Discussion

We obtain real DT images: $128 \times 128 \times 40$ voxels; voxel size $1.7 \times 1.7 \times 3$ mm; single-shot spin-echo diffusion-weighted echo-planar imaging; 12 images per subject; 12 isotropically-distributed diffusion-encoding directions ($b=1000$ s/mm²).

Fig. 1. The extracted cingulum, seen as the white background in the glyph-based color-coded DT visualization (sagittal slices), using: (a1)-(c1) tractography, and (a2)-(c2) proposed fuzzy-segmentation-based approach (white $\Rightarrow$ fuzzy membership value $F_{ct} = 1$, black $\Rightarrow F_{ct} = 0$, gray $\Rightarrow 0 < F_{ct} < 1$). (d) A manual segmentation (crisp) for the slice in (b1) or (b2) superimposed on the DT image. (e) An initialization (1 slice only; slice in (b1) or (b2)) for the segmentation superimposed on the DT image.

For extracting each cingulum in the brain, we obtained an initial (crisp) segmentation, on just a *single sagittal slice* of the cingulum, by thresholding tensors that: (i) have high FA (to separate white matter from the rest of the brain) and (ii) are orientated along anterior-posterior or inferior-superior directions. We manually remove voxels in the initialization (one slice) that clearly belonged to other far-off tracts, e.g. the fornix lying inferior to the corpus callosum [3].

Figure 1(a)–(c) shows the results of a standard tractography technique for the tract extraction using two regions-of-interest in the superior part of the cingulum. It is clear that tractography fails to extract the cingulum—a thin tract with sharp changes in orientation. On the other hand, Figure 1(d)–(f) shows that the proposed fuzzy segmentation approach—that exploits the statistical coherence of tensors in the entire structure—performs significantly better. Figure 2 shows the result, on another real DT image. For validation and quantitative comparison, we obtain two manual (crisp) segmentations by using interactive software to delineate color-coded scalar FA images—the color at each voxel is derived from the orientation of the tensor at that voxel. The Dice overlap metrics (averaged

Fig. 2. The extracted cingulum in axial slices (inferior $\rightarrow$ superior) using: (a), (c) tractography, and (b), (d) proposed fuzzy-segmentation-based approach

Fig. 3. Effect of partial voluming on tractography: (a)-(e) show regions near the cingulum/corpus-callosum interface in consecutive axial slices (inferior $\rightarrow$ superior)

over the two manual segmentations) for these two DT images were: (i) 0.63 and 0.60 for the proposed method (after thresholding the fuzzy membership values F_{ct} with a value of 0.5) and (ii) 0.32 and 0.33 for tractography.

Figure 3 shows enlarged axial views of the tractography result near the interface of the corpus callosum (red) and the cingulum (green). Significant partial voluming in this region, worsened by the low inter-axial-slice resolution, leads to a change in the orientation of the cingulum tensors. Thus, many cingulum tensors are no longer aligned with the direction of the cingulum tract, but rather have deviated orientations (brown) towards the orientation of the corpus callosum. Such phenomena cause fiber tracking, which uses thresholds on FA and curvature, to either: (i) wander far away from the desired cingulum tract, e.g. Figure 2(a)-(b), (loose thresholds) or (ii) terminate prematurely (conservative thresholds). In addition to this inherent trade-off, tractography suffers because it relies *solely* on the orientation of the current tensor and ignores the information in the tensors that were previously tracked. The proposed method—by optimally exploiting the information contained in *all* the tensor values, locations, and partial-volumed voxels in a unified framework—extracts the cingulum with significantly higher accuracy. Future work includes better quantification of the improvements obtained with the proposed method.

Acknowledgments

The authors gratefully acknowledge NIH support of this work via grants HD042974, HD046159, NS045839, and EB06266.

References

1. Lenglet, C., Rousson, M., Deriche, R., Faugeras, O., Lehericy, S., Ugurbil, K.: A Riemannian approach to diffusion tensor image segmentation. In: Proc. Info. Proc. Med. Imag, pp. 591–602 (2005)
2. Wang, Z., Vemuri, B.: DTI segmentation using an information theoretic tensor dissimilarity measure. *IEEE Trans. Med. Imag.* 24(10), 1267–1277 (2005)
3. Concha, L., Gross, D., Beulieu, C.: Diffusion tensor tractography of the limbic system. *Amer. J. Neuroradiology* 26, 2267–2274 (2005)
4. Jiang, G., Zang, Z., Xie, W., Guo, X.: Asymmetry analysis of cingulum based on scale-invariant parameterization by diffusion tensor imaging. *Human Brain Map* 24, 92–98 (2005)
5. Ziyen, U., Tuch, D., Westin, C.F.: Segmentation of thalamic nuclei from DTI using spectral clustering. In: Proc. Med. Image Comput. and Comp. Assisted Intervention, pp. 807–814 (2006)
6. Franklin, T., Acton, P., Maldjian, J., Gray, J., Croft, J., Dackis, C., O'Brien, C., Childress, A.: Decreased gray matter concentration in the insular, orbitofrontal, cingulate, and temporal cortices of cocaine patients. *Biol. Psychiatry* 51(2), 134–142 (2002)
7. Kinoshita, M., Yamada, K., Hashimoto, N., Kato, A., Izumoto, S., Baba, T., Maruno, M., Nishimura, T., Yoshimine, T.: Fiber tracking does not accurately estimate size of fiber bundles in pathological conditions: initial neurosurgical experience using neuronavigation and subcortical white matter stimulation. *NeuroImage* 25(2), 424–429 (2005)
8. Zhuang, X., Huang, Y., Palaniappan, K., Zhao, Y.: Gaussian mixture density modeling, decomposition, and applications. *IEEE Trans. Image Proc.* 5(9), 1293–1302 (1996)
9. Leemput, K.V., Maes, F., Vandermeulen, D., Seutens, P.: Automated model-based tissue classification of MR images of the brain. *IEEE Tr. Med. Imaging* 18, 897–908 (1999)
10. Pham, D., Prince, J.: An adaptive fuzzy segmentation algorithm for three-dimensional magnetic resonance images. In: Proc. Info. Proc. Med. Imag, 140–153 (1999)
11. Kim, J., Fisher, J.W., Yezzi, A.J., Cetin, M., Willsky, A.S.: A nonparametric statistical method for image segmentation using information theory and curve evolution. *IEEE Trans. Image Processing* 14(10), 1486–1502 (2005)
12. Awate, S.P., Tasdizen, T., Foster, N.L., Whitaker, R.T.: Adaptive, nonparametric Markov modeling for unsupervised, MRI brain-tissue classification. *Medical Image Analysis* 10(5), 726–739 (2006)
13. Fletcher, P.T., Joshi, S.C.: Principal geodesic analysis on symmetric spaces: Statistics of diffusion tensors. In: ECCV Workshops CVAMIA and MMBIA, pp. 87–98 (2004)
14. Arsigny, V., Fillard, P., Pennec, X., Ayache, N.: Geometric means in a novel vector space structure on symmetric positive-definite matrices. *SIAM J. Matrix Analysis and Applications* (in press)
15. Pennec, X., Fillard, P., Ayache, N.: A Riemannian framework for tensor computing. *Int. J. Comput. Vision* 66(1), 41–66 (2006)
16. Awate, S.P., Gee, J.C.: A fuzzy, nonparametric segmentation framework for DTI and MRI analysis. In: Proc. Info. Proc. in Med. Imag (IPMI) (to appear, 2007)
17. Chow, Y., Geman, S., Wu, L.: Consistent cross-validated density estimation. *Annals of Statistics* 11(1), 25–38 (1983)