Model Based Variational Smoothing and Segmentation

For Diffusion Tensor Imaging in the Brain

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ABSTRACT

This paper applies a unified approach to variational smoothing and segmentation to brain diffusion tensor image data along user-selected attributes derived from the tensor, with the aim of extracting detailed brain structure information. The application of this framework simultaneously segments and denoises to produce edges and smoothed regions within the white matter of the brain that are relatively homogeneous with respect to the diffusion tensor attributes of choice. The approach enables the visualization of a, smoothed, scale invariant representation of the tensor data field in a variety of diverse forms. In addition to known attributes such as fractional anisotropy, these representations include selected directional tensor components and, additionally associated continuous valued edge fields that may be used for further segmentation. A comparison is presented of the results of three different data model selections with respect to their ability to resolve white matter structure. The resulting images are integrated to provide better perspective of the model properties (edges, smoothed image, etc.) and their relationship to the underlying brain anatomy. The improvement in brain image quality is illustrated both qualitatively and quantitatively, and the robust performance of the algorithm in the presence of added noise is shown. Smoothing occurs without loss of edge features due to the simultaneous segmentation aspect of the variational approach, and the output enables better delineation of tensors representative of local and long range association, projection and commissural fiber systems.

Keywords: diffusion tensor imaging (DTI), magnetic resonance imaging (MRI), cerebral white matter, variational segmentation functional.

INTRODUCTION

Diffusion weighted and diffusion tensor magnetic resonance (MR) imaging has come into widespread use over the past few years. This is due, in large part, to the unique view diffusion imaging provides of the microstructural details within the cerebral white matter in health and disease. As it represents a relatively new class of image data, the processing required for visualization and analysis of tensor data provides numerous new challenges.

The history and general descriptions of the standard methods for diffusion imaging are discussed in detail in recent reviews of the field, see (Le Bihan et al., 2001; Mori & Barker, 1999; Parker, 2004). Diffusion imaging has been used in a host of clinical and research application areas (Hossmann, Fischer, Bockhorst, & Hoehn-Berlage, 1994; Meyer et al., 2000; Pierpaoli et al., 1993; Sorensen et al., 1996; Sorensen et al., 1999; Pfefferbaum et al., 2000; Lim et al., 1999; Klingberg et al., 2000; Wiegell, Larsson, & Wedeen, 2000). The ability to use diffusion tensor imaging (DTI) directionality and anisotropy to characterize the compact portion of discrete corticocortical association pathways in the cerebral white matter of living humans has been demonstrated and validated (Makris et al., 1997). Identification and visualization of specific fiber tracts (Basser, Pajevic, Pierpaoli, Duda, & Aldroubi, 2000; Conturo et al., 1999; Mori, Crain, Chacko, & van Zijl, 1999; Mori et al., 2002; Pierpaoli et al., 2001; Poupon et al., 1998; Poupon et al., 2001; Stieltjes et al., 2001; Zhang et al., 2000; Grimm et al, 2002) and exploration of the potential to elicit information about functional specificity (Darquie, Poline, Poupon, Saint-Jalmes, & Le Bihan, 2001) have also been carried out. The wide

variety of application areas, along with the fact that the novel *in vivo* data is obtainable in this fashion makes DTI a potentially powerful clinical tool.

Compared to conventional MR imaging, however, DTI image acquisition is quite slow, due to the need to encode multiple different directions of diffusion sensitivity. This leads to practical tradeoffs in the use of DTI between acquisition time, diffusion sampling method, spatial resolution and slice coverage. Partial volume effects are particularly problematic in DTI since competition of multiple different directional features within a voxel can render the resultant tensor not representative of the underlying anatomic structure. The development of methods that take optimal advantage of the diffusion data in light of potentially low signal to noise ratio is an important objective for making DTI more clinically relevant.

Prior work in regularizing or smoothing diffusion tensor fields include the work in (Poupon et al., 1998), where a Markovian model is proposed for the tracking of brain fiber bundles in the DTI data. Diffusion direction is applied to fiber tract mapping and smoothing in (Vermuri et al., 2001) where the total variation (TV) norm algorithm is applied to the raw data. Regularization of diffusion-based direction maps for the tracking of brain white matter fascicles is reported in (Poupon et al., 2001), where the emphasis is on the use of prior information in a Bayesian framework, and in (Parker et al., 2002), where the paths of anatomic connectivity are determined based on the directionality of the tensor. A continuous field approximation of discrete DT-MRI data has been applied in (Pajevic, Aldroubi & Basser, 2002) to extract microstructural and architectural features of brain tissue. Smoothing employing parametric patches has been applied in (Grimm et al., 2002) to three dimensional scattered data that describe anatomic structure.

In this paper, we present an algorithm for *simultaneous* smoothing or denoising and segmentation of diffusion tensor data. This algorithm smoothes the image field within homogeneous regions, while at the same time preserving edges of these regions at discontinuities by generating the associated edge fields based on user-selected tensor attributes. The smoothing and edge estimation is performed with respect to a user-selectable 'mapping', or models, of the input tensor data in order to emphasize specific properties of the tensor. Sample application of the algorithm is presented that demonstrates smoothing with respect to normalized tensor magnitude and principle eigenvector direction. In these examples, the identification of white matter anatomic structure is qualitatively enhanced and reduction of regional anisotropy variance is quantified. This reduction in variance is then shown to be robust in the presence of added noise. The source code for this tool is freely available.

While demonstrated with respect to specific data models, this simultaneous smoothing and segmentation framework is general, and opens a rich and versatile set of processing options to address the noisy, voxel-averaged sampling of DTI data. It also enables the selection of appropriate models of various physical characteristics of the diffusion tensor in cerebral white matter. Specific clinical objectives will dictate the optimal selection of "mapping" models and parameters for enhanced smoothing/ segmentation and will be the focus of future studies.

MATERIALS AND METHODS

Data Acquisition

The sample data used in this paper used the following protocol: Siemens 1.5 Tesla Sonata, 5 sets of interleaved axial slices to provide 2x2x2 mm contiguous coverage, single shot EPI with 6 directional diffusion encoding directions and a non-encoded baseline acquisition was performed with TR=8s, TE=96ms, averages=12, number of slices=12 per interleave, data matrix=256 (readout) x128 (phase encode), diffusion sensitivity b=568s/mm2. The total imaging time for the session was approximately 45 minutes. The subject provided informed consent and was a 35 year old, right-handed male normal control from a study of schizophrenia. The Institutional Review Board of the Massachusetts General Hospital approved the study protocol.

Computation of the Diffusion Tensor Attributes

Once the diffusion tensor, *g*, is sampled, the magnitude (or trace) can be calculated to express the total (no directionality) diffusivity at the voxel location. The directionality of the diffusion is assessed by an eigen decomposition of the diffusion tensor:

$$g = \sum_{i=1}^{3} \lambda_i s_i s_i^T$$

where $\lambda_i, s_i \quad i = 1,...3$ are the three eigenvalue - eigenvector pairs for the tensor with eigenvectors of unit magnitude. The largest eigenvalue and the associated eigenvector correspond to the major directionality of diffusion at that location. The fractional anisotropy *fa* (Basser & Pierpaoli, 1996) is a scalar measure that is often used to

characterize the degree to which the major axis of diffusion is significantly larger than the other orthogonal directions.

$$fa = \sqrt{\frac{3}{2}} \sqrt{\sum_i \left(\lambda_i - \frac{1}{3} \sum_j \lambda_j \right)^2 \Big/ \sum_i \lambda_i^2}$$

Specifically with respect to brain imaging, to the extent that white matter fiber systems have homogeneous directionality at the spatial scale of the voxel size, these fiber systems are expected to demonstrate significant anisotropy. More general eigenvalue/eigenvector based scalar as well as vector and tensor features can be used to capture the underlying structure in the diffusion tensor image.

We have developed a segmentation and smoothing approach that permits user selection amongst these (and other) features of the tensor image in order to capture the relevant underlying structural details.

The Approach

The core concept of the method is the simultaneous variational segmentation and smoothing formulation. Given an observed tensor field, g, the objective is to obtain two outputs: the smoothed tensor u, and edge field v. These outputs represent the simultaneous smoothing and segmentation, respectively, of the raw tensor data. The approach, shown schematically in Figure 1, makes use of the following:

- A specified data fidelity *model H(u, g)*,
- A continuity model, *F(u),* that forms a basis for adaptively determining the regions of continuity within which smoothing is to take place,

Energy Functional

In general, we may consider a region Ω of interest in a Euclidean space R^n. Let x designate the pixel position in Ω. Thus, for three-dimensional spatial data, we have n=3. Our results are based on the processing of a slice from a brain image, so n=2, and Ω is a two-dimensional region, and. the vector x is a two-dimensional position vector in, for instance, Cartesian coordinates. Over this region Ω, estimation of a field $u = u(x)$ is of interest, and measurements $g = g(x)$ are collected. The following energy functional (Ambrosio-Tortorelli, 1992) for scalar fields is based on the energy functional of (Mumford and Shah,1985,1989):

$$E(u,v) = \int_{\Omega} \left(\alpha (1-v)^2 Tr\left[f_x{}^T(u) f_x(u) \right] + \beta\ Tr\left((g-u)^T (g-u) \right) + \frac{\rho}{2} Tr\,(v_x^T v_x) + \frac{1}{2\rho} v^2 \right) dx \quad [1]$$

We generalize the above functional to vector field smoothing (introduction of tensor notation at this stage, while more cumbersome, provides no additional insight) with the introduction of the data fidelity and continuity functions $(h_1(u), h_2(g))$ and $f(u)$, respectively

$$E(u,v) = \int_{\Omega} \left(\alpha (1-v)^2 F(f_x(u)) + \beta\ H(h_1(u), h_2(g)) + \frac{\rho}{2} Tr\,(v_x^T v_x) + \frac{1}{2\rho} v^2 \right) dx \quad [2]$$

For a given data g and choices of functions $h_1(u), h_2(g)$ and $f(u)$, the energy functional is minimized with respect to u and v. Input data g and smoothed data u are *vector* fields (tensor processing can be recast as vector processing) of dimensions m and r respectively, whereas v is a *scalar* field that represents the edges of the smoothed vector field u. Further *g, u* and *v* are continuous n-dimensional fields and are *defined* for all *x in region* Ω in an n dimensional space R^n. The first term in the above functional represents

a smoothing penalty term that favors spatial smoothness of vector field *f(u)*, rather than of *u*, at all interior points of the region where edge field $v << 1$ with $0 \le v \le 1$ as explained later. It may be noted that the field *f* may be of a lower dimension than the field *u* and that the smoothing penalty is in terms of a metric $F(f_x(u))$ of $f_x(u)$, the Jacobian with respect to *x* of the smoothed continuity function *f(u(x)),* which we simply denote by *f(u)*. Note that since the edge field *v* is also simultaneously estimated, the spatial extent of smoothing is adaptive with the smoothing penalty tending to zero over parts of region Ω where edge strength *v* tends to 1.

The second term reflects data fidelity between the input data *g,* and smoothed field *u,* as given by the metric $H(h_1(u), h_2(g))$. We specify explicit forms for h_1, h_2, and *f* in the next section. The third and fourth terms represent prior models for the characteristics on the type of edge field dependent on just parameter ρ. The third term provides for smoothness of the edge field in terms of the 2-norm of its spatial gradient v_x, while the fourth term penalizes the excessive presence of edges. The constants α, β and ρ represent the chosen weights on the accompanying cost components and determine the nominal smoothing radius, the edge width as well as govern the value of edge function *v*. Specifically, the ratio α / β is related to the nominal smoothing radius, ρ to the edge width, and α governs the edge strength. Further details governing the choice of constants α, β and ρ is discussed in Shah, 1997. For more details on the segmentation approach, and on the results of the application of the functional for smoothing and segmentation of phantom, MR and fMRI scalar data as well as for the fusion of different modality data, see (Shah, 1997; Pien, Desai & Shah, 1997; Desai et al. , 2002; Kogan, Desai & Pien, 1999) and the references therein.

The edges are estimated based on continuity attributes $f(u)$ of the smoothed tensor field *u and the specified prior model on edge field*. The Euler Lagrange equations that are the necessary conditions associated with the minimization of the energy functional can be solved by the gradient descent method (e.g. Shah, 1996; Pien, Desai & Shah, 1997; Desai et al., 2002).

From the outputs *u* and *v*, additional relevant attributes associated with size, shape, and orientation of the diffusion ellipsoid may be distilled for further analysis. Example attributes include the trace (for diffusion magnitude), anisotropy measures (for diffusion 'shape'), and direction of eigenvectors (for diffusion orientation). *The ability to select functions f(u) and* $h_1(u), h_2(g)$ *to satisfy various continuity and data fidelity requirements, respectively, is an important advantage that enables the viewing of the same DTI data from different perspective.*

Application to DTI data

Depending on the objective, one can select the continuity functions $h_1(u), h_2(g)$ and fidelity function $f(u)$ to obtain an edge field v and an accompanying smoothed tensor field u with respect to specific features of the data. Differential smoothing concerns can thus be applied to different weighted eigenspace components of the tensor and more generally to any other sets of attributes of the tensor.

We next illustrate two different models that capture different characteristics of spatial similarity for the tensor data by selection of different forms of continuity function f (u) and the data fidelity function $h_2(g)$ while retaining the same form of function $h_1(u) = u$:

(A) normalized tensor smoothing: $f = u/\|u\|_2, h_2(g) = g$

(B) dominant directional tensor component smoothing: $f = u/\|u\|_2, h_2(g) = \lambda_1 s_1 s_1^T$

where λ_1 is the maximum of the three eigenvalues of the tensor g.

The first model represents a scale invariant continuity criterion for the tensor data *g*. By contrast, the second model assumes the same invariance continuity criterion as the first, but with respect to only the subspace of tensor g associated with its dominant eigenvector s_1. The objective of identifying regions of spatial continuity within the image, or equivalently, segmenting, motivates the choice of model. It may be noted that for dominant directional tensor smoothing in (B) above, we have chosen to work in the rank 1 dominant tensor space $s_1 s_1^T$ rather than the vector space of associated direction s_1.

For measures, we adopt the following choices for *F, H* of Eq. (2)

$$F(f_x(u)) = \|f_x(u)\|_2^2 = Tr\left[f_x(u)^T f_x(u)\right] \quad [3]$$

$$H(h_1(u), h_2(g)) = \|u - h_2(g)\|_2^2 = Tr\left[(u - h_2(g))^T (u - h_2(g))\right] \quad [4]$$

where *F* and *H* respectively represent the Euclidean norm of the gradient of $f(u)$ and the estimated error $u - h_2(g)$.

Assessment

In order to assess the results of the application of this processing to clinically relevant diffusion tensor imaging data, we selected a representative axial slice that included a comprehensive set of neuroanatomic white matter regions of interest. These anatomic regions include the corpus callosum, internal capsule, superior longitudinal fasciculus and cingulum bundle. First, we visually inspect the results of the smoothing modes on the appearance of fractional anisotropy (*fa*) maps as well as in visualization of

tensor orientation information. Second, we quantify these observations by evaluating the distribution of *fa* values over the anatomic regions listed above. Third, we evaluate the sensitivity of the proposed methodology by comparing using images the change in performance with traditional methods when noise is added to the raw data. We choose to add Gaussian noise at increasing level to the data, with negative values set to zero to remain within the physical constraint of non-negative intensity. In addition to comparing proposed method and the traditional approach using images, we also quantify the effect of noise on the performance of the proposed approach in terms of the coefficient of variation of the *fa* over each anatomic region of interest.

RESULTS

In this section, we demonstrate the operation of the algorithm in the context of two different smoothing models; characterize this processing in the context of anatomic information contained within the DTI data, and summarize some of the noise properties of the implementation. Figure 2 demonstrates a number of different views of the results of this smoothing procedure on an axial brain slice. This includes the raw (unsmoothed) data in the first column as well as the results of the two different smoothing models: normalized tensor in the second column, and in the third column, directional projection. The 'cuboid' and color representations (Pajevic & Pierpaoli, 2000) of the directional information contained in the resultant tensor fields are presented in the third and fourth rows, respectively.

From the edge field visualization in the first row, it is clear that the most details consistent with the anatomic structure emerge when smoothing is most selective within the edge field boundaries. Specifically, the edge map in the third column, which is based on the directional projection, displays more details than the edge map in the second column, which is based on the normalized tensor.

The second row of images indicates that the impact of edge preservation on the smoothing of the tensor field and its components can also be appreciated from the *fa* images for the smoothed tensor. The raw data's fractional anisotropy is shown in the first column for comparison.

It may be remarked that, by definition, the fractional anisotropy of the directional component in the raw data will be unity and of interest is the deviation from unity that arises from the spatial variation of the dominant direction component that is reflected in the smoothing. The quantitative impact of different modes of smoothing is presented in Table 1. This includes the mean and standard deviation of the functional anisotropy *fa* (as well as the coefficient of variation, CV) for five anatomically motivated and manually defined regions annotated in Figure 3. These regions were identified by a trained neuroanatomist using both tensor orientation and anisotropy information. For the case of normalized tensor smoothing, signal-to-noise ratio (SNR) or equivalently the reciprocal of the CV, is improved for all regions except for lateral ventricle whose edges with the adjacent region of internal capsule are not well delineated, resulting in loss of restricted regional smoothing at the border of that region. For the case of directional smoothing, SNR values are uniformly enhanced for all regions due to better regional edge details and attendant region limited smoothing. The CV is reduced by at least two and a half fold

when comparing directional smoothing to the original measures of anisotropy, indicating a concomitant increase in the resultant signal to noise ratio for these measures.

The ‘cuboid’ displays in the third row of Figure 2 can explain the superior performance of the directional projection method in the third column. These cuboid displays are better appreciated by looking at close up of particular regions, as is done in the second row of Figure 3. The close up region, a portion of the cerebral hemisphere, is indicated in the top image of the first row. In the third row of Figure 4, we added, for the sake of comparison, images displaying the dominant direction vectors for the raw data, the smoothed normalized tensor, and the smoothed directional projection. Again, we see that direction details are better kept using the smoothed directional projection. One example is the region above the thick arrows, where directional (curved corners) structure is preserved in the directional image, but smoothed over in the normalized tensor image. Comparison of other parts of the close up views leads to similar conclusion. It is this preservation of the higher dimensional directional characteristics of the tensor at the pixel level that is responsible for the superior image obtained from the directional projection method.

We now consider added noise, our third assessment criterion. The effect of added noise is evaluated to establish the robustness of the approach. In Figures 5 & 6 we compare the results of increasing noise levels added to the raw data. Levels of the additional noise range from 0 (no simulated noise added) to approximately 5 times the estimated sigma value. The sigma value was estimated from the raw data outside the brain. These images include: top row - raw data fractional anisotropy (fa); 2nd row - smoothed fractional anisotropy; 3rd row – our edge field v; bottom row - conventional

Sobel edge field of raw *fa*. Using anatomically based regions of interest (ROIs), Figure 6 illustrates, for the corpus collosum region, that the smoothed tensor based estimate of regional anisotropy *fa* in the second row of Figure 5 has a substantially lower coefficient of variation (bottom curve in Figure 6) than the original data (top curve in Figure 6); the reduction is by almost a factor of 10. Similar reductions were obtained for all other regions of Figure 4: cingulum bundle, superior longitudinal fasciculus, and internal capsule. Additionally, as Figure 5 indicates, comparison of edge fields from our approach on the third row with conventional Sobel edge field on the fourth row illustrates that, while added noise has a deleterious affect on the Sobel edge field, the new models introduced to the energy functional preserve details even as noise is added.

DISCUSSION

The above results demonstrate the *model based* variational segmentation functional approach's ability to provide a diverse collection of output images within a unified framework. The usefulness of the variational segmentation function approach has been demonstrated for other forms of brain imaging, such as structural (Pien, Desai, & Shah; 1997) and functional magnetic resonance imaging (fMRI) data (Desai, Mangoubi, Shah, Karl, Pien, Worth & Kennedy; 2002).

The versatility of these functionals, in their ability to produce a diverse collection of output images, is an important addition to the methods or tools available for image analysis. This innovation provides a *unified* framework for spatially selective smoothing of noisy brain image data along attributes of choice derived from the diffusion tensor whereby we can adaptively determine smoothed regions within the white matter that are

relatively homogeneous with respect to specific tensor properties of shape, size and orientation of associated diffusion ellipsoid. In addition to providing a demarcation of the regions with respect to user-specified attributes of homogeneity in the DT-MR data, the segmentation functional is amenable and flexible to using prior information on attributes of both the tensor and edge field with incorporation of additional penalty terms in the functional. Determining smoothed regions with specific tensor properties enhances the ability to characterize the morphometric properties of the compact portion, or 'stem', of the major white matter pathways in regions where partial volume problems and the validity of the tensor assumption are less problematic (Makris et al., 1997).

A comparison has been presented of attributes such as anisotropy and direction of diffusion for (a) the raw tensor itself without smoothing, (b) the smoothed normalized tensor, and (c) the smoothed tensor component associated with the dominant eigenvector. The underlying diffusion characteristics of the white matter in the brain motivate the choice of these mappings, while normalization provides scale invariance of salient features. It is therefore possible to visualize attributes of anisotropy and direction of the resultant tensor fields, and the associated edge field in various ways. In this fashion, the applicability of a unified and versatile image processing framework for smoothing and feature extraction in support of fiber pathway identification within the human brain is demonstrated.

Specifically, promise of the utility of the variational segmentation functional to improve the characteristics of tensor valued imaging data has been demonstrated. The result is an improvement of the overall signal that preserves the anatomic detail. Within the directional component smoothing case, regions of discrete directionality are

smoothed, but transitions between regions are well preserved. This can be particularly well seen as one traverses from the cortex towards the central portion of the images shown in Figure 4. The white matter contained within the gyral folds near the cortex remains nicely visualized and oriented 'out' of the gyri. Transitions of radially oriented white matter of the corona ratiata and U fibers with the perpendicularly oriented internal capsule and various associational pathways are clearly demarked. This level of detail is only retained in the directional smoothing case. Finally, it should be noted that visualization based upon the dominant direction color coding in Figure 2 is less sensitive to the underlying variations and noise structure, presumably due to the subtleties of the color variation of directional noise compared to the large color differences of the different fiber systems. For the images examined, directional smoothing thus seems appropriate due to the simple fact that it simultaneously smoothes while preserving directionality. This smoothing can act as a preprocessing step for virtually any subsequent processing of the diffusion data such as between group analyses of anisotropy data (Pfefferbaum, et al., 2000; Szeszko, et al., 2005), anatomic regional characterization (Makris, et al., 2005) and tractographic reconstruction (Johansen-Berg, et al 2005; Jones & Pierpaoli, 2005; Kang, et al. 2005).

Turning to results of Figure 5 and 6, we examine two aspects: the coefficient of variation over regions of interest, and the edges. First, as the graph demonstrates, the coefficient of variation of *fa* calculated over the anatomic region of the corpus callosum is dramatically reduced (improved) with simultaneous smoothing and segmentation, and that this substantial improvement holds even in the presence of the greatly reduced image quality at the maximum added noise.

Turning to edges in Figure 5, we observe that with incrementally increasing noise added to the raw data, the conventional (Sobel) edge field is seen to deteriorate more rapidly. By contrast, with our approach edges are maintained at the increased noise levels. This result is a direct consequence of working with a most dominant feature of the tensor, specifically, the dominant rank-1 tensor.

Limitations: A method that is generalizable in terms of the processing of image data and its dimensionality is presented. The application used to illustrate the processing, namely diffusion tensor imaging, is an important and new radiological tool for the clinical assessment of cerebral white matter. Processing can improve the resultant signal to noise ratio without penalizing the resultant spatial resolution and thus enhance the utility of these measurements. This improvement in signal to noise ratio can be used to shorten the potentially lengthy diffusion acquisition time. It is acknowledged that the tensor acquisition may not be optimal for observation of specific fiber tracts themselves, and that this acquisition optimization is an open research question. These processing tools, however, will extend to higher order (i.e. q-space and high angular resolution) diffusion acquisitions (Tuch et al., 2002; Jones et al., 2004), and can still play an important role in the processing and analysis of these classes of data acquisition. Indeed, the utility of submodel-based smoothing becomes even more important as the complexity of the input data increases. The flexibility of the methods we report here can easily be adapted for processing models defined in terms of any matrix decomposition of the acquired data, not just the eigen-decomposition typical in the six-direction tensor acquisitions. Also, there is a spatial resolution tradeoff between the need for high resolution to observe subtle white matter pathways and the acquisition time available for

the subjects. These processing tools will be helpful to extend the limits of SNR in the extraction of meaningful anatomic information. An additional area of potential impact for a tool such as this includes utilization of tensor information in solving for neural systems-based functional imaging (Buchel, 2004; McIntosh, 2004; Valdes-Sosa, 2004). It may be remarked that the focus of the reported work is the model based optimal extraction of information for a given SNR and DTI data acquisition parameters and future work remains necessary for optimization involving SNR and data acquisition parameters.

We note that simultaneous smoothing and segmentation process can change the nature of the error in the smoothed estimates and usage of smoothed estimates for further analysis such as for group analysis may need to employ alternate analysis approaches that are not necessarily based on a specific noise model assumption such as Gaussian noise. For example, for decision support, methods such as support vector machines can be employed

Additionally, the appeal of the method is in the flexibility to use various lower dimensional attributes of the higher dimensional data using functions F and H, and we demonstrate this strength here primarily in the context of 2D data. The method however can be readily applied to 3-D data. In the case of 3-D analysis, additional terms associated with gradients of the data and edge fields in the added third dimension arise in the energy functional E of (2). We therefore have edge surfaces in 3D that are smoother than those obtainable from edge boundaries produced by the 2D analysis

To conclude, we have presented a general framework for smoothing of diffusion tensor data and developed a freely available software tool to execute this processing. The preferred choice of the fidelity and continuity functions $h_1(u), h_2(g)$ and $f(u)$ generally

will depend on both the image and the objective of the image analysis task. There is no universal image model that outperforms all others in all situations. Moreover, different regions of the data domain require segmentations based on more than one model. An important objective in this study is therefore to identify for DTI data a small number of potent models that can be adapted for effective segmentation. Further, since no single model applies over the entire image due to variations in the underlying tissue and partial volume effects, *adaptive learning of relevant features at every voxel based on neighborhood characteristics* is another focus of ongoing research. The improved output data will enable a more refined analysis, including segmentation of white matter substructures using various manual and automated techniques.

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Information Sharing Statement: The software source code for this processing tool is available as Matlab code at www.cma.mgh.harvard.edu/HBP_RO1, the homepage for the supporting Human Brain Project grant. The sample data described here is available from the corresponding author.

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	(a) Raw Tensor fa	***(b) Smoothed normalized tensor fa***	***(c) Smoothed dominant directional tensor component fa***
Corpus Callosum			
Mean (m)	0.646	0.5806	0.9575
Std. dev. (σ)	0.117	0.1014	0.0493
CV ($100\sigma / m$)	18.1	17.46	5.14
Cingulum bundle			
Mean (m)	0.5524	0.4306	0.9238
Std. dev. (σ)	0.151	0.0953	0.0515
CV ($100\sigma / m$)	27.3	22.13	5.57
Internal capsule			
Mean (m)	0.3615	0.28	0.9308
Std. dev. (σ)	0.0768	0.0493	0.0620
CV ($100\sigma / m$)	21.24	17.61	6.67
Superior longitudinal fassicuclus			
Mean (m)	0.5676	0.4928	0.9496
Std. dev. (σ)	0.1078	0.0799	0.0598
CV ($100\sigma / m$)	18.99	16.21	6.30
Lateral ventricle			
Mean (m)	0.2647	0.2078	0.8103
Std. dev. (σ)	0.1136	0.1233	0.0883
CV ($100\sigma / m$)	42.92	59.34	10.90

Table 1: This table demonstrates the quantitative impact of different modes of smoothing and segmentation in terms of mean, standard deviation and coefficient of variation (CV) statistics of fractional anisotropy *fa* in five different regions of the brain for the particular 2-D slice of DTI data shown in Figure 4. The CV's in column (c) are lowest, an indication that directional smoothing yields effective segmentation of homogeneous regions.