A High Throughput and Efficient Visualization Method for Diffusion Tensor Imaging of Human Brain White Matter Employing Diffusion-Map Space

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Abstract—**Diffusion tensor imaging (DTI) possesses high dimension and complex structure, so that detecting available pattern information and its analysis based on conventional linear statistics and classification methods become inefficient. In order to facilitate classification, segmentation, compression or visualization of the data, dimension reduction is far-reaching. There have been many approaches proposed for this purpose, which mostly rely on complex low dimensional manifold embedding of the high-dimensional space. Dimension reduction is commonly applicable through linear algorithms, such as principal component analysis and multi-dimensional scaling; however, they are not able to deal with complex and high dimensional data. In this light, nonlinear algorithms with the capability to preserve the distance of high dimensional data have been developed. The purpose of this paper is to propose a new method for meaningful visualization of brain white matter using diffusion tensor data to map the 6-dimensional tensor to a three dimensional space employing Markov random walk and diffusion distance algorithms, leading to a new distance-preserving map for the DTI data with lower dimension and higher throughput information.**

Keywords- human brain white matter; nonlinear dimensionality reduction; Diffusion Map; distance-preserving mapping; diffusion tensor magnetic resonance imaging (DTMRI)

I. INTRODUCTION

To gain a better insight through disease effects on brain anatomy and physiology, a systematic pattern of anatomy must be detected in anatomical imaging of the brain. diffusion tensor imaging (DTI) is a promising method, which yields fundamental information of the brain tissue microstructure and composition by means of magnetic resonance imaging (MRI)-based measurement of local diffusion tensor (DT) of water molecules in human brain [1]. In particular, DTI is used to characterize and to map the 3-dimensional (3D) diffusion of water as a function of spatial location and a 3D image like mean-diffusivity (MD) or fractional-anisotropy (FA), which can be measured from the main orientation of water diffusion for each voxel in the image. Due to the lack of constraining process of diffusion by axons present in myelinated fiber tracts, brain regions, like cortical and subcortical gray matter and cerebrospinal fluid, have a vast isotropic diffusivity [2]. The diffusion tensor can be utilized for characterizing magnitude, degree of anisotropy and orientation of directional diffusion. Therefore, mapping diffusion anisotropy and principal diffusion directions is one of the best ways to estimate white matter connectivity patterns in the brain obtained from white matter tractography. This could result in voxel-wise and tensor-wise analysis of diffusivity and anisotropic change in the white matter, which enables neuroscientists to chart the complex network of neural fiber tracts in the human brain.

DTI possesses high dimension and complex structure, so that detecting available pattern information and its analysis based on conventional linear statistics and classification methods become inefficient. In order to facilitate such classification, segmentation, compression or visualization of the data, derogating the undesirable properties of high-dimensional spaces, i.e. dimensionality reduction is far-reaching. Dimensionality reduction is based on finding valid structures and geometric characterization of high dimensional data, to be realized with several techniques, which are categorized into linear and nonlinear methods. Linear methods are based on classic approaches, such as principal component analysis (PCA) and multi-dimensional scaling (MDS) [3]. Although they guarantee acquisition of real data structures lying on or near a linear subspace of high dimensional input space, they cannot deal with complex nonlinear data. This has led to development of nonlinear methods, such as Kernel PCA [4], iso-map and diffusion-map (DM) techniques for biological data with highly nonlinear manifolds [3, 5-10].

This paper seeks to address a technique for multiple valued DTI data visualization, based on images with pixels sampled from underlying manifold, e.g. every single pixel may consist of a high dimensional vector as the positive semi-definite tensor in a DT-MRI acquisition. Diffusion map (DM) represents a dataset via a weighted graph of corresponding points to vertices and edges, in which the spectral properties of the graph Laplacian would be used to map 6-dimensional data to a 3D representation. Diffusion distance is applied by using a specific value, which is obtained for the closeness of each data point, performing the random walk for a number of time steps. Thus, pairwise diffusion distances in the low-dimensional representation of the data is maintained [11, 12]. Differences between DT-MRI pixels are mainly evaluated using a diffusion distance metric with regard to rank 3, second-order positive semi-

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definite DTs, while the difference between DT pixels is approximated by DM. In this article, we evaluated case studies of high-dimensional phantom data as well as normal clinical brain DT-MRI.

II. METHOD

A. Theory

To represent the best reflection of the underlying DTI data, high dimensional DT-MRI data are used. As long as the pixel dimensionality is greater than 3D space, dimensionality reduction must be employed in order to represent the low dimensional image pixels. To achieve this intention, pixel dissimilarities must be measured and pixels must be mapped to perceptually meaningful colors [13]. The principal manifold, which is obtained with distance metric, is sampled to return high dimensional pixel values. Manifold learning techniques are used to learn the manifolds (e.g. DM), derived analytically or by approximation. Diffusion distance between two corresponding points on the manifold are the measured differences between any two high dimensional pixels. Similarities between DT pixels are evaluated by diffusion metric that scales the rank 3 manifold of DT pixels. DTs are symmetric 3×3 matrices, or second-order rank 3 diffusion tensors. They contain 6 unique elements. Furthermore, DTs must be positive semi-definite (PSD), in that 6 unique elements are defined in Diffusion tensors which are symmetric 3×3 matrices, i.e. $f(\mathrm{y}) : \mathrm{y} \in \mathrm{R}^3 \rightarrow \mathrm{R}^6$. An example of data distribution of a real data is shown in Fig. 1.

Measuring dissimilarities between observations is an important step in handling high dimensional data. As far as the DT-MRI goes, estimation of DM and dissimilarity metrics are needed for the manifold learning structures, assuming $y^{(1)}, y^{(2)}, \ldots, y^{(k)} \in M$, M is the manifold embedded in R^n.

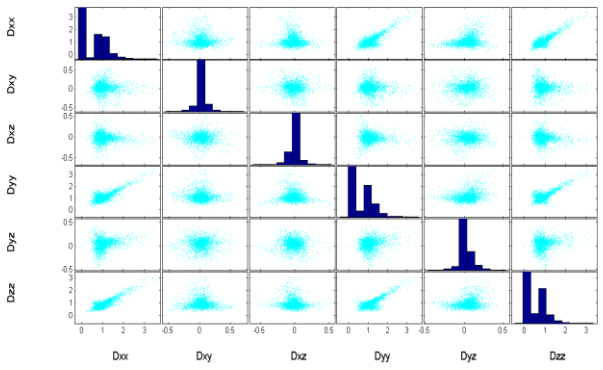

Figure 1. Distribution of multi-dimensional DT-MRI data

B. Implementation of Diffusion Map Algorithm in DT-MRI

The implemented algorithm proposed for DT-MRI of human brain is outlined in six steps as follows:

1. Constructing the similarity matrix, W, of the graph; the entries of W are the weights along the edges connecting corresponding nodes i and j, to be determined by the heat kernel as follows [11]:

$$W_{ij} = \exp\left(-\frac{\| \mathrm{y}_i - \mathrm{y}_j \|^2}{\varepsilon}\right) \quad (1)$$

in which W is PSD and $\|.\|$ is the Euclidean norm. One should note that $W \epsilon R^{k \times k}$ is a symmetric matrix. In the DM algorithm, the choice of the parameter ε is very important. Lafon in [10] chose ε *to* be in the order of the average smallest non-zero value of $\| \mathrm{y}_i - \mathrm{y}_j \|^2$, that is:

$$\varepsilon = \frac{1}{k}\sum_{i=1}^{k} \min \| y_i - y_j \|^2 \;;\; y_j \neq y_i \quad (1)$$

2. Formulating $k \times k$ normalization matrix of D; diagonal entries of D are row or column sum of W [14]:

$$D_{ii} = \sum_{j=1}^{n} W_{ij},\ i \in 1 \ldots n \quad (3)$$

The W matrix is then normalized as

$$P = D^{-1} W \quad (2)$$

Since DMs adopted from the theory of dynamical systems, matrix P is considered as a Markov matrix, defining the forward transition probability matrix of a data point.

3. Find the eigenvalues of P; the conjugate matrix of P is calculated as below:

$$\tilde{P} = D^{-\frac{1}{2}} W D^{\frac{1}{2}} \quad (3)$$

This so-called normalized graph Laplacian preserves the eigenvalues.

4. Singular value decomposition (SVD) of $\tilde{P}$; to be calculated by:

$$\tilde{P} = U \Lambda U^* \quad (4)$$

yielding the eigenvalues $\Lambda = \mathrm{diag}([\lambda_1, \lambda_2, \ldots, \lambda_n])$ and eigenvectors in matrix $U = [u_1, u_2, \ldots, u_n]$ [12].

5. Computing eigenvectors of P; one notes that eigenvalues of P and $\tilde{P}$ stay the same [12]:

$$V = D^{-\frac{1}{2}} U \quad (5)$$

6. Creating low-dimensional coordinates in the embedded space ψ using Λ and V, as follows:

$$\Psi = V \Lambda \quad (6)$$

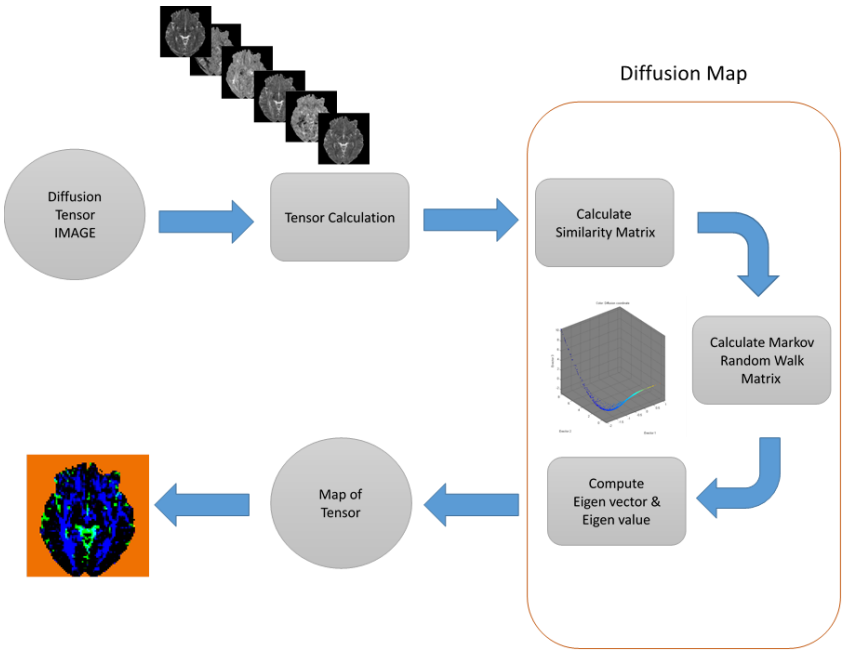

Figure 2. Overview of the proposed method

Now, for each n-dimensional point x_i, there is a corresponding d-dimensional coordinate, where $d < n$. The coordinates for a single point can be expressed as:

$$\Psi_d : y_i \rightarrow [\lambda_2 \upsilon_2(y_i), \lambda_3 \upsilon_3(y_i), \ldots, \lambda_{d+1} \upsilon_{d+1}(y_i)] \quad (7)$$

An overview of all these steps is shown in Fig. 2.

III. MR Data

The simulated MR images used for this work are adopted from [15].

The real MR acquisition was carried out on four normal subjects on a 1.5T clinical Siemens scanner (MAGNETOM Avanto, Erlangen, Germany). The maximum gradient strength was 40 mT/m and the slew rate equaled 200 mT/m/s. DT images were acquired using a single-shot echo-planar pulse sequence with the following specifications: *TR/TE* = 8500/97 *ms*, *b*-value = 1000 s/mm^2, *FOV* = 171 *mm*, matrix size = 76×76, slice thickness = 2.5 *mm*, voxel size = 2.3×2.3×2.5 mm^3, number of directions = 30, and NEX = 1.

IV. Results

A. Results on simulated MR images

In these simulated data, the implemented DM method was compared with other methods, such as fractional anisotropy (FA) map, PCA, MDS and ISO-MAP (as shown in Fig. 3). Since the amount of the Entropy of a color in the color image represents the amount of information, here, we evaluated the image entropy resulting from each method, which is indicated in Table I. As it can be inferred from Fig. 3 and Table I, DM technique extracts more information in a DT-MR image.

B. Results on real MR images

Fig.4 indicated the results of applying the proposed DM technique on the real data, in comparison with the corresponding FA map. It is apparent that DM map contains more information than both T2-weighted image and FA map. This suggests that DM could be successfully employed for further statistical analysis of human brain.

V. Discussion And Conclusion

This study set out to propose a method for visualization of DT-MRI as a robust method to noise, preserving distance in nonlinear data, while keeping low-dimensional space. The proposed analysis suggests that the DM dimensionality reduction improves white matter segmentation and visualization, particularly in the low-SNR regime of DT-MRI, while it stays an active research problem. As DT-MRI has found wide applications in research and clinics, the proposed method could open new insights about how pathologies and treatments could affect the DTI measurements.

Manifold learning problems involve vector bundle on graphs providing the demand for vector diffusion mapping. Since vector diffusion mapping is an extension form of diffusion

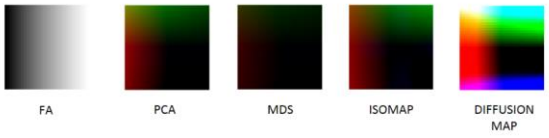

Figure 3. Simulated data obtained using different methods

mapping, their properties and convergence behavior are similar. Besides, because the idea of vector diffusion mapping is a natural extension form of graph Laplacian operator combined with diffusion mapping on graphs, in the future, we are going to investigate the issues of smoothing and interpolation, as well as clustering of components of DTI datasets, leading to successful fiber clustering.

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TABLE I. THE ENTROPY OF THE COLOR IMAGES EMPLOYING EACH TECHNIQUE

Method	PCA	MDS	ISOMAP	DM
Entropy	53.05	50.17	58.87	803.05

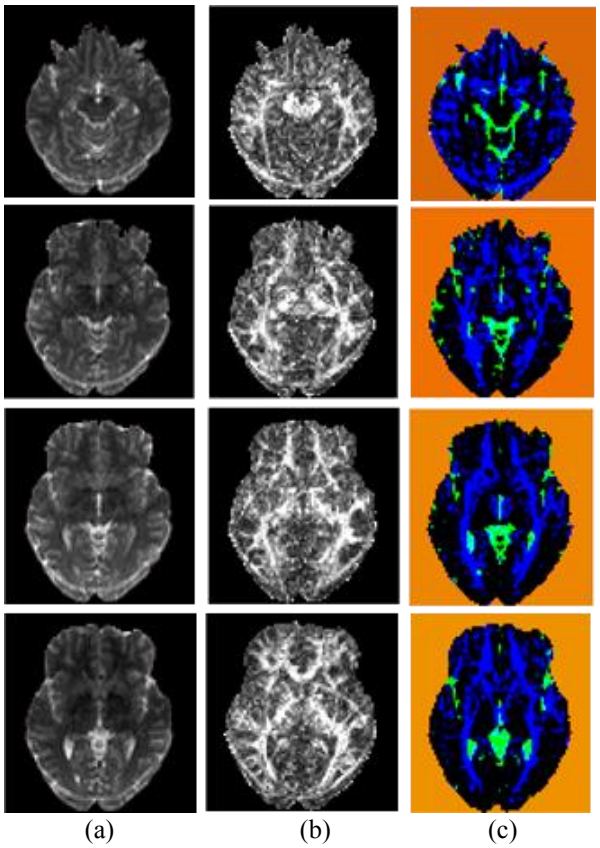

Figure 4. Real data (a) T_2-weighted images (b) fractional anisptropy (FA) maps (c) proposed diffusion map (DM) method