Diffusion Tensor Based Global Tractography of Human Brain Fiber Bundles

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Abstract— **Tractography is a non-invasive process for reconstruction, modelling and visualization of neural fibers in the white matter (WM) of the human brain. It has emerged as a major breakthrough for neuroscience research due to its usefulness in clinical applications. In this research, we have investigated deterministic and probabilistic tractography approaches. We have evaluated the performance of different approaches on fiber bundle tracking using diffusion tensor imaging (DTI) data having multiple gradient directions. Experimental results show that global tractography is best for reconstruction of kissing and crossing fibers compared to deterministic tractography. We have also shown that DTI acquisition with a higher number of gradient directions provides better tracking results given limitations of acquisition and computation time.**

Index Terms— **Tractography, diffusion tensor imaging, white matter, gradient directions.**

I. INTRODUCTION

Diffusion tensor imaging (DTI) based tractography has been given much attention in recently due to its applications in several medical fields such as patients with acute stroke or brain tumors, neurodegenerative disorders including multiple sclerosis (hardening or thickening of tissue), epilepsy, Alzheimer disease, autism, and movement disorders [3]. DTI enables visualization and characterization of white matter fascicles in two and three dimensions. In general, it measures the displacement of water molecules on the micron scale and yields information about white matter (WM) fibers that pass within a voxel. Water molecules contain hydrogen nuclei (protons), which become aligned in a magnetic field. Motion or diffusion of water molecules is found to be much faster along the WM fibers than perpendicular to them [2]. The difference between the two motions (parallel and perpendicular to fibers, also termed diffusion anisotropy) is the basis of DTI.

DTI gradient directions are the list of vectors that describe the diffusion weighting directions for DTI acquisition on a MRI scanner. To observe the diffusion in all direction, many diffusion weighted images with diffusion weighting gradients are acquired in different directions. From these diffusion-weighted images, a 3D description of the direction for the diffusion of water within a voxel is inferred. Diffusion is anisotropic in nature and an ellipsoid is used to represent diffusion directions. These directions of water diffusion are tracked in DTI based tractography. Two different approaches to tractography [1] are considered in this research: deterministic and probabilistic. In deterministic tractography, the reconstruction of long neuronal pathways occurs in small successive steps by following the local direction of the fiber in a given voxel. This method is computationally efficient but minor errors in the determination of a local step may significantly affect the final path, making the method unstable. More recently, probabilistic approaches are predominant among tractography methods. Global tractography is a probabilistic approach. The global methods [8] try to reconstruct the fiber paths simultaneously while finding the configuration that minimizes the difference between the measured data and the reconstruction. This tracking is more stable in the presence of noise and imaging artifacts in the data.

In this research, we have compared the performances of deterministic and global tractography based on the simulation using various gradient directions data. We investigate the reconstruction performance considering crossing and kissing fibers and the effects of multi-gradient direction data. The background is discussed in section 2. Section 3 presents the description of the data sets. Methodology, experimental results, and the conclusion are discussed in sections 4, 5 and 6 respectively.

II. BACKGROUND

The development of magnetic resonance imaging (MRI) has led to the design of numerous imaging techniques. Among them DTI assesses white matter changes in the patients that are not normally seen on conventional MRI.

The relationship between the signal intensity of the diffusion weighted images S, diffusion sensitizing field gradient based on Stejeskal Tanner spin echo scheme and the signal value S_0 without the gradient is given in (1):

$$S = S_0 e^{-\gamma^2 G^2 \delta^2 (\Delta - \frac{\delta}{3}) D_{app}} \quad (1)$$

where γ is the gyromagnetic ratio of proton, δ and G represent the duration and the magnitude of the motion probing (or diffusion sensitizing field) gradient, Δ is the time between the centers of the pair of gradient pulses, and D_{app} is a scalar value called the apparent diffusion coefficient (ADC) which reflects molecular diffusivity under motion restriction such as fluid viscosity.

In DTI, the diffusion coefficient is a 3 ×3 symmetric positive semi-definite matrix as shown in (2).

$$\mathbf{D} = \begin{matrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{matrix} \quad (2)$$

The largest eigenvector of the diffusion tensor as shown in Fig. 1 is assumed to be oriented parallel to the local fiber

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tracts, which can be reconstructed in a brain dataset by following paths in the estimated eigenvector field.

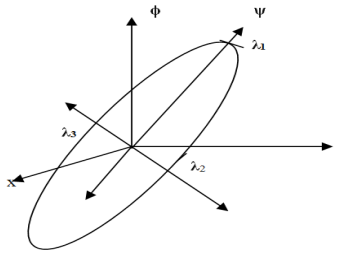


Fig. 1 Diffusion tensor represented by an ellipsoid ($\lambda_1 \geq \lambda_2 \geq \lambda_3$)

One of the most important factors in DTI acquisition is gradient direction. At least 6 gradient directions are required to calculate the diffusion tensor [4]. If gradient directions are increased, more diffusion weighted images are used to calculate the diffusion tensor, resulting in more accurate tensor estimation but much longer imaging time [7].

A long thin ellipsoid means very good diffusion for water along the long axis of that ellipsoid. The mean diffusivity (MD) and fractional anisotropy (FA) as shown in (3) and (4) respectively are the most widely used indices of DTI for representing the motional anisotropy of water molecules, being sensitive to the presence and integrity of WM fibers [11][12]. Color coded FA maps are the way to show the directional information embedded in DTI.

$$\text{MD} = \frac{\lambda_1+\lambda_2+\lambda_3}{3} \tag{3}$$

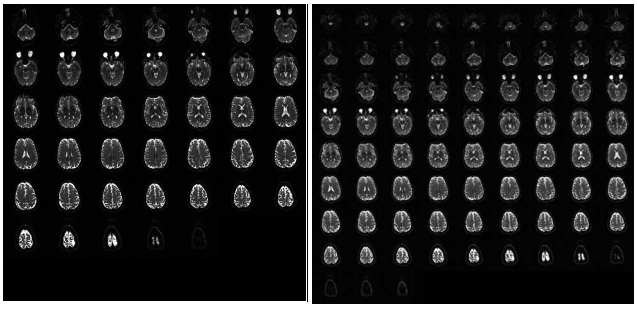
$$\text{FA} = \sqrt{\frac{3}{2}} * \sqrt{\frac{(\lambda_1-D)^2+(\lambda_2-D)^2+(\lambda_3-D)^2}{\lambda_1^2+\lambda_2^2+\lambda_3^2}} \tag{4}$$

These indices help to detect brain diseases. For example, in case of pediatric multiple sclerosis, the value D increases and FA decreases compare to their normal value [9] [10].

Deterministic tractography methods are primarily based upon streamline algorithms where the local tract direction is defined by the major eigenvector of the diffusion tensor [1]. Crossing and kissing white matter tracts create a significant challenge for reconstruction. These limitations can be solved using global tractography.

III. DATA SETS

Data provided by St Jude children's research hospital was used for this research. They have diffusion MRI scanners of 1.5 and 3 Teslas. Samples of the DTI data sets provided are shown in Fig. 2.



(a) (b)

Fig. 2 Example data (a) 12 directions (b) 20 directions

We have conducted research on four data sets: (1) 12 gradient directions, 4 averages (40 slices and each 3 mm thick) (2) 20 gradient directions, 3 averages (75 slices and each 2 mm thick) (3) 30 gradient directions, 2 averages (70 slices and each 2 mm thick), and (4) 64 gradient directions, 2 averages (96 slices and each 1.7 mm thick).

IV. METHODOLOGY OF TRACTOGRAPHY

We have done the simulation for both deterministic and probabilistic tractography. There are various deterministic and probabilistic tracking techniques such as connect the voxel [13], Fiber Assignment by Continuous Tracking (FACT) [11], path- integral method [14], Gibbs tracking [5], spin glass model [15]. FACT and Gibbs tracking techniques have been considered for our simulation. Camino [16] and DTI & fiber tools [16] are used for simulation. The simulation procedure is discussed step by step in the following sections.

A. Pre-processing

For both of the tractography techniques, the first step in processing the data is ordering and sorting. In this step artifacts and the quality of data [6] are controlled. At first, we have to change the raw image format because medical imaging supports some specific image format. After that the data was pre-processed using several tools. Pre-processing involved artifact removal, skull stripping and reformatting.

B. Diffusion Tensor Calculation

Voxel based single and multi diffusion tensor models for the orientation distribution function (ODF) were fit to the data by Camino. After calculating FA and MD, we obtained the orientation distribution function (ODF) as shown in Fig. 3. It is used to describe the directionality of multimodal diffusion in regions with complex fiber architecture present in the brain. The maximum diffusivity is normalized to voxel size. The color indicates the direction of maximum diffusivity i.e. red means left to right, green indicates anterior-posterior and blue for superior-inferior. This step is also performed in Gibbs tracking tensor calculation but is done only for those pixels having signal intensity above the threshold value 40 in the average image.

C. Deterministic Tractography

The tractography process was done in three steps: region of interest (ROI) selection, track, and visualization [6]. ROI was selected using the ITK snap tool [16]. Corpus callosum (CC) is the largest white matter structure in brain that connects the left and right cerebral hemispheres. So selecting CC as a ROI will give the maximum number of fiber connections. Using the ROI, Camino tracked the fiber connections and the visualization is done by the Paraview tool.

D. Global Tractography

Gibbs tracking is a powerful global tractography method. This method includes three main steps [5]: (1) Creation of a trial fiber configuration, (2) Calculation of the corresponding DW signal (simulated signal), and (3) Adjustment of the trial configuration with the experimentally measured signal to minimize the difference.

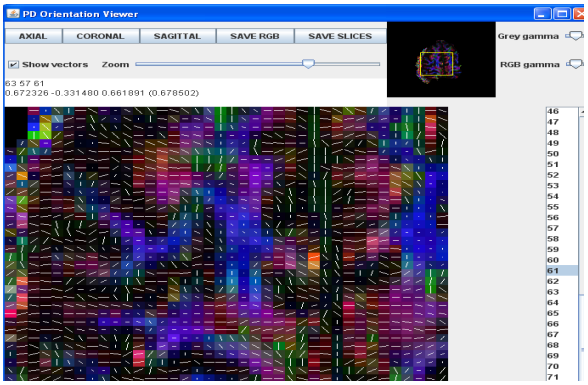


Fig. 3 Orientation distribution function of deterministic tractography.

The building elements of reconstructed fibers are small straight cylinders whose length, position and orientation can vary continuously. These cylinders are re-oriented through a process similar the distribution of states in the cooling of an ideal gas. The reconstruction begins at very high "temperature" where the cylinders are randomly distributed in the space occupied by the white matter as shown in Fig 4. The interaction between them results in building long fiber chains with decreasing temperatures. The neuronal fibers start and end on predefined surfaces, for example at the boundary with the grey matter. Each cylinder contributes a signal typical for parallel fibers to all voxels it crosses [5].

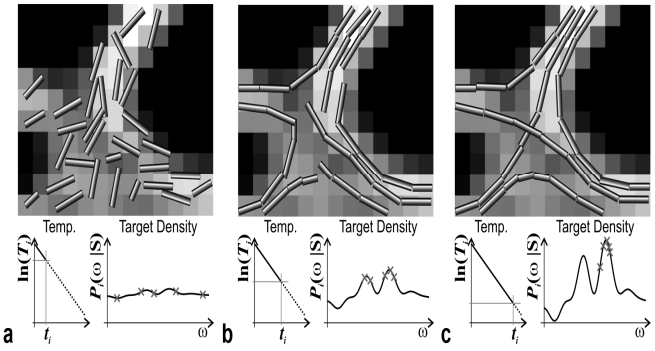


Fig. 4 Principle of Gibbs tracking method; (a) at high temperature (b) at lower temperature (c) temperatures close to zero. [5]

The sum of such contributions is the anisotropic part of the signal. This described method is known as the Gibbs Tracking [5], keeping in mind its close analogy to statistical physics. On the other hand, the described simulation can be considered as a Bayesian approach based on a spatial point processes. The interactions between the cylinders represent the a priori probability and the likelihood function represents the similarity of the measured signal and simulated signal.

Before the visualization step, the diffusion tensor images are provided with the tracking parameters. The tracking can be started by dense reconstruction that counts many fibers and takes in the range of 12-24 hours of computation or sparse reconstruction that shows fewer fibers and has reconstruction times around 1 hour.

After tracking completion, fibers are sent to a fiber viewer to show the fiber distribution of the whole brain, the spatial diffusion distribution, and the fiber distribution in a single slice.

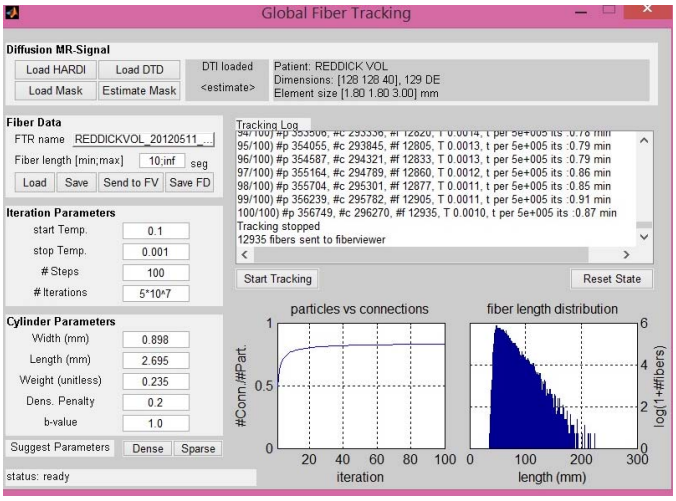


Fig. 5 Gibbs tracking of 12 D gradient directions using DTI & Fiber tools

V. EXPERIMENTAL RESULTS

We obtained the fiber trajectories after completing the deterministic and global tractography simulations. All the prepocessing and tensor calculation steps of simulation are run on an intel PC core i5, 1.8 GHz and 8 GB RAM with Windows 8™ as an operating system. Complete simulation of 12 directions data is possible on a laptop with the configuration as mentioned for prepocessing steps. Simulation of 20, 30 and 64 directions data sets are run on a high performance computing platform with 512 GB RAM.

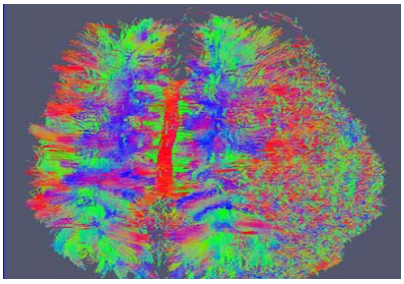


Fig. 6 Deterministic tractography

Visualization of fibers by deterministic tractography is shown in Fig. 6. A microscopic observation by an expert points out the limitation of this technique. The reconstruction does not work well where fiber crossing and kissing occur, though it takes only couple of hours for the simulation to execute. The tractography results for the Gibbs tracking method are shown in Fig. 7 and 8.

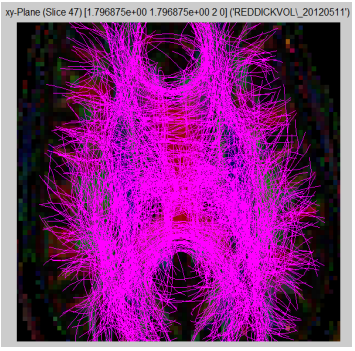
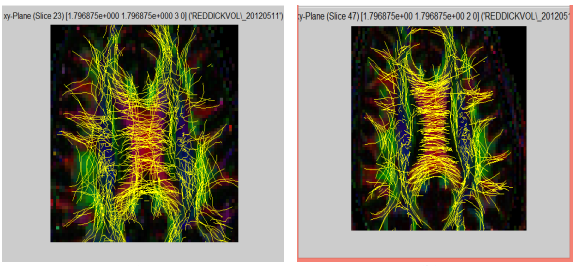


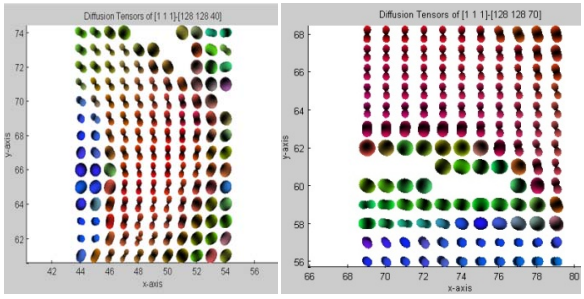
Fig. 7 Fiber tract for 20 D



(a) (b)

Fig. 8 Fiber cut (a) 12 D (b) 20 D

Fiber tract shows a projection of the complete actual fiber subset and fiber cut indicates the curve segments inside the actual slice of the current fiber structure subset. Spatial diffusion distribution represents diffusivity of the tensor in a particular position or region of interest as an ellipsoid as shown in Fig. 9. The maximal diffusivity is normalized to the voxel size. The color indicates the direction of diffusivity of the spatial distribution inside the current voxel.



(a) (b)

Fig. 9 Spatial distribution Red: left to right; Green: Anterior- posterior; Blue: Superior to inferior (a) 12 D (b) 30 D

For different positions or slices, we get different FA and MD values. The value of FA is normalized from 0 to 1. FA close to 0 indicates isotropic diffusion and anisotropic nature increases as FA values tend to 1. Here we have taken positions near to corpus callosum for different gradient directions and their corresponding FA and MD values are shown in Table 1.

TABLE I
COMPARISON OF FA AND MD VALUES FOR DIFFERENT GRADIENT DIRECTIONS

Gradient directions	Position	FA	MD
12 D	[67 68 23]	8.376×10^{-1}	6.730×10^{-4}
20 D	[66 70 47]	8.269×10^{-1}	6.686×10^{-4}
30 D	[67 69 43]	8.184×10^{-1}	6.604×10^{-4}
64 D	[67 64 47]	8.456×10^{-1}	6.292×10^{-4}

TABLE II
NUMBER OF FIBERS VS GRADIENT DIRECTIONS.

Gradient directions	Reconstruction process	Number of fibers	Time (Hours)
12 D	Sparse	12935	0:26
	Dense	80165	10:25
20 D	Sparse	13527	0.30
	Dense	83454	11:35
30 D	Sparse	13457	0:35
	Dense	88835	12:45
64 D	Sparse	14597	0:42
	Dense	99491	14:18

Tracking is started by selecting the required parameters like cylinder parameters, starting and ending temperature etc. An example of parameter sets for sparse reconstruction is provided in Fig. 5. In dense reconstruction, the weight of the cylinder was set to a low value e.g. 0.059. It can produce more fibers compared to the sparse process though it takes long computation time. Table 2 shows how the number fibers found are increased with an increase in gradient directions.

VI. CONCLUSION

Diffusion tensor imaging is a powerful tool for the visualization of white matter structures. Although deterministic approaches are computationally efficient, they have some limitations which can be overcome by global tractography. The characteristic features of the traced neural fiber networks, such as structure, topology, and connectivity, can serve as biomarkers for various dementias and brain diseases, and can be used in various clinical applications. It is shown that gradient directions have positive effect on tracking though the time requirement introduces artifacts in the data due to patient motion which limits the clinical application. There should be a trade off between the number of gradient directions and the specific clinical application. Developing a tractography algorithm to overcome difficulties associated with the current techniques is a topic of our future research.

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