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A Diffusion Tensor Imaging Tractography Algorithm Based on Navier-Stokes Fluid Mechanics

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Abstract

We introduce a fluid mechanics based tractography method for estimating the most likely connection paths between points in diffusion tensor imaging (DTI) volumes. We customize the Navier-Stokes equations to include information from the diffusion tensor and simulate an artificial fluid flow through the DTI image volume. We then estimate the most likely connection paths between points in the DTI volume using a metric derived from the fluid velocity vector field. We validate our algorithm using digital DTI phantoms based on a helical shape. Our method segmented the structure of the phantom with less distortion than was produced using implementations of heat-based partial differential equation (PDE) and streamline based methods. In addition, our method was able to successfully segment divergent and crossing fiber geometries, closely following the ideal path through a digital helical phantom in the presence of multiple crossing tracts. To assess the performance of our algorithm on anatomical data, we applied our method to DTI volumes from normal human subjects. Our method produced paths that were consistent with both known anatomy and directionally encoded color (DEC) images of the DTI dataset.

Index Terms

Tractography; DTI; white matter; fluid mechanics

I. Introduction

Diffusion tensor imaging (DTI) is a magnetic resonance imaging technique used to measure the *in vivo* self-diffusion of water within tissues [1]. In fibrous tissue, such as the white matter of the brain, the diffusion of water is anisotropic since water molecules move more easily parallel to the axis of the dominant local fiber tract orientation. Perpendicular to the fiber tract, the diffusion of water molecules is restricted primarily by the myelin sheaths and axonal membranes of neurons, which provide the greatest obstacle to diffusion [2]–[4].

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Previous work has established a link between anisotropic water diffusion in the brain and axonal integrity and orientation [5], [6]; DTI exploits this relationship to non-invasively investigate and quantify aspects of white matter architecture. A diffusion weighted magnetic resonance (MR) sequence is able to construct a probability density function (PDF) at each voxel that estimates the three dimensional displacement probability of water due to diffusion along the applied magnetic gradient. In the DTI reconstruction method developed by Basser *et al.*, diffusion weighted image (DWI) volumes from six or more non-collinear magnetic gradient directions are used to construct a diffusion tensor at each voxel by modeling the diffusion PDF as an anisotropic Gaussian function [1]. This diffusion tensor, D , is a symmetric 3×3 matrix that estimates the local directional dependence of anisotropic diffusion. Diagonalization of the diffusion tensor gives three eigenvectors and three eigenvalues that form a basis for the set of diffusion isoprobability ellipsoids and can be used to calculate rotationally invariant scalar measures of white matter integrity [7], such as the fractional anisotropy (FA), a measure of the voxel's deviation from purely isotropic diffusion, and the lattice index (LI), a measure of the local coherence of diffusion direction [7]. These scalar quantities are characteristically high in white matter and can provide a basis for white matter segmentation. However, they fail to provide information about regional connectivity. This has motivated the creation of DTI tractography methods that estimate the brain's regional connectivity based on the diffusion tensor field.

The earliest DTI tractography algorithms were streamline methods that generated paths by following the local major diffusion direction point by point through the image volume [8]–[12]. These streamline methods assume that there is a single mean fiber direction in each voxel that coincides with the local major eigenvector. Previous work has shown this assumption to be accurate in regions where local fiber bundle orientation is homogeneous and significant changes in major diffusion direction occur at least on the order of one voxel length [13], [14].

The errors in the results obtained using streamline methods arise primarily from two sources: noise and partial volume effects. Random noise in the image causes perturbations in the diffusion tensor, which can have significant effects on the reliability of these streamline methods [9], [15]. In particular, the integral path based approach of streamline methods accumulates noise as the tract evolves through the tensor field, causing a linear divergence of trajectories with path length. Previous work has demonstrated that the tracking error of these methods depends significantly on parameters such as the signal to noise ratio (SNR), image resolution, the magnitude of the local anisotropy, and the trajectory shape [14], [16]. Some methods have sought to make the streamline methods more robust in the presence of noise. A method by Lazar *et al.* reduced the dependence of the major eigenvector on noise by using the full diffusion tensor to deflect the incoming fiber trajectory [17]. Several methods filter the diffusion tensor to minimize the effect of noise by using, for example, a Kalman filter [18] or a stochastic labeling scheme [19]. Cheng *et al.* developed a streamline based method that iteratively generates tracts using the results of a previous 3D graph search algorithm; the approach was demonstrated to be more robust to noise and able to segment branching tract geometries better than conventional streamline methods [20]. Previous work has demonstrated that the tracking reliability of streamline methods is also significantly affected by partial volume effects [21], [22]. The low SNR of DTI forces the use of low image resolutions; typical voxel resolutions in DTI are approximately 1–3 mm. However, the typical axonal diameter is around 1 micron; this disparity leads to averaging of different fiber populations within the voxel. Some methods have tried to lessen partial volume effects in streamline methods by incorporating information from the full diffusion tensor [17].

Some existing methods use the uncertainty in the diffusion tensor field to compute measures of confidence for connection paths. Probabilistic tractography algorithms model the

uncertainty in fiber direction at each voxel as a PDF and use it to define a likelihood of anatomic connection between regions in the brain, commonly through a Monte Carlo based approach [23]–[25]. Further work by Parker *et al.* generated PDFs in regions containing fiber crossings by fitting a multi-Gaussian compartment model [26]. Probabilistic methods have been developed to attempt to resolve fiber crossings on the intravoxel level [27]. Friman *et al.* quantified the uncertainty using a Bayesian modeling framework [28]. Bootstrap methods estimate the uncertainty of fiber orientation in DTI without assuming a variance model and are based on repeated sampling of a set of diffusion-weighted (DW) images [29], [30]. Lazar *et al.* developed a bootstrap tractography method to estimate the dispersion of fiber tracking results [31].

Despite efforts to overcome their limitations, conventional streamline methods are restricted to producing a single path for each seed point and do not allow tracts to branch. This motivated the development of surface evolution methods based on the theory of level sets [32]. A comparison of tracking results of level sets based methods and streamline methods using a physical DTI phantom demonstrated that level sets based methods are more robust to noise and branching or crossing tract geometries than streamline methods [33]. Parker *et al.* pioneered this type of method, evolving a front based on the local major diffusion direction using fast marching methods (FMM) and finding the optimal path by a gradient descent method [34], [35]. The method considers only the major diffusion direction when computing the speed of the front, neglecting information in the other two minor eigen-vectors. Subsequent methods have been developed based on the original work of Parker *et al.* that use the full diffusion tensor to compute the speed of the evolving front [36], [37]. Evolving a discrete front results in discretization errors due to the limited number of possible propagation directions to neighboring voxels. To address this, Tournier *et al.* suggested an adaptive evolution grid [38]. Further work by Staempfli *et al.* proposed an advanced implementation of the FMM that incorporated the advantages of tensor deflection [17]; it uses the full diffusion tensor, limits discretization errors, and resolves crossing fibers [39]. Methods that focus on building tract sets have also been developed. One recent method uses a white matter atlas as a template for automatic segmentation of tracts, potentially resolving whole tracts systems [40].

Additional methods have been developed which use physical models as the basis for generating a connectivity metric. These algorithms model the dynamics of some artificial entity as it moves through the image volume. The physical laws that govern the dynamics of this substance are expressed as a set of partial differential equations (PDEs), which are solved numerically on the diffusion tensor field to produce a metric of connectivity. Early work in this area focused on developing methods modeled on the simple diffusion of heat or water through the image volume, whose dynamics is computed by solving the first order heat equation on the diffusion tensor field [41]–[43]. These methods have the advantages of level set and probabilistic methods and are based the same physical model used to construct the diffusion tensor field. Batchelor *et al.* generated connection-based probabilities using a metric based on time of arrival of the heat propagation front [42] and implemented an additional convection term in the heat equation [44]. O'Donnell *et al.* generated probability maps using a metric based on the total heat flow along a path in the heat flux vector field [41]. Using a closely related physical model, Hagmann *et al.* developed a random walk based algorithm modeled on the Brownian motion of water diffusing in a non-homogeneous medium [45]. Using physical models also allows the incorporation of diffusivity or anisotropy information into the model in a physically meaningful way. A method developed by Kang *et al.* uses the diffusivity to seed multiple successive anisotropic diffusion simulations to construct connection paths [46].

In this paper, we present a novel method modeled on the dynamics of a viscous fluid described by the second order non-linear Navier-Stokes equations, an extension of previous work by our group [47]. The Navier-Stokes equations govern flow for a viscous Newtonian fluid, a fluid whose internal stress forces are linearly related to its strain forces [48]. However, even though these equations are most commonly seen in the context of fluid mechanics, they have been shown to be successful in modeling a large number of diverse physical phenomena. Our second order nonlinear-based approach is an extension of previous linear PDE methods. We hypothesize that our method will have a better performance than competing tractography methods in the presence of noise and it will not require a white matter mask, commonly used by other PDE-based methods. This is because our model contains a viscous force not present in previous methods, represented as an additional convection term in the PDE. We model local viscosity of the fluid as a function of the local intervoxel and intravoxel anisotropy in the corresponding DTI image volume. The incorporation of this convection term in our flow field calculation allows us to closely couple the magnitude of the fluid velocity to the magnitude of the underlying anisotropy of the DTI tensor field, providing a dampening force in background areas, such as gray matter and CSF. This eliminates the need for the white matter mask used by other PDE-based methods to prevent the model from entering these areas. To compute an estimate of the most likely connection path between two regions in the brain, we simulate the flow of an artificial fluid between those two points through a volume whose dimensions, pressure, and local viscosity are derived from the underlying DTI data. We then numerically solve for the fluid velocity vector field. The estimated connection path is then computed by finding the optimal path through the fluid velocity that simultaneously maximizes both the fluid velocity and its gradient. We apply our method to DTI volumes from normal human subjects and to computer-generated DTI phantoms to validate our approach.

II. Methods

Our algorithm simulates the flow of an artificial fluid through a volume whose dimensions, viscosity, and flow of an artificial fluid pressure tensor field are derived from a DTI volume. Specific regions of interest are chosen as sources and/or sinks, and we simulate the flow of an artificial fluid governed by the Navier-Stokes equations. The most likely connection path is then estimated using a generalized gradient vector flow (GGVF) based approach to compute the trajectory through the fluid velocity vector field that simultaneously maximizes the magnitude of the fluid velocity and its gradient along the path. Our fluid model is valid only as a theoretical framework for generating a connectivity metric and does not try to model any aspect of the underlying diffusion process.

A. Fluid Model Construction

The Navier-Stokes equations describe the flow of a viscous Newtonian fluid through a pressure tensor field. In a generalized coordinate system, in the absence of external forces, and obeying the conservation of mass, the Navier-Stokes equations simplify to

$$\frac{\partial \rho v_i}{\partial t} + \nabla \cdot (\rho v_i \bar{\mathbf{v}}) = \nabla \cdot (\mu \nabla v_i) - [(\nabla \cdot \bar{\mathbf{P}})_i], \quad (1)$$

where $\bar{\mathbf{v}} = \{v_i\}$ in $\mathbb{R}^3$, μ is the viscosity, ρ is the fluid density, and $\bar{\mathbf{P}}$ is the pressure tensor.

These equations provide a way of solving for the velocity field of a fluid given its pressure and viscosity. Because we use the fluid velocity as a metric of connection strength, it is imperative that the pressure and viscosity of the fluid, which govern the flow dynamics in

our model, closely reflect the underlying diffusion process. We accomplish this by modeling these physical quantities using scalar measures derived from the diffusion tensor.

1) Viscosity—Our algorithm uses an artificial fluid whose viscosity at each point in the fluid volume is derived from measurements taken from the diffusion tensor image. Specifically, the local viscous force is modeled as the product of the local fractional anisotropy (FA), which describes the degree of directionality of the local diffusion, and the lattice index (LI), which describes the local similarity in diffusion direction:

$$\mu = k(1 - (FA \times LI)), \quad (2)$$

where the parameter k can be adjusted to control the strength of the viscous force. The viscous force therefore has the property of restricting fluid flow in areas of low anisotropy or coherence, such as gray matter and CSF. To demonstrate this relationship in well-known brain regions, consider Figure 1, which shows viscosity maps of 2D slices of DTI data from normal human subjects. Prominent white matter tracts, such as the anterior limb of the corpus callosum, marked by a star (★), have a highly organized architecture and therefore low viscosity. In contrast, the lateral ventricular space, marked by a delta (Δ), which contains CSF and has no architecture, is highly viscous.

2) Pressure—We derive the pressure field for our model by considering the diffusion tensor at each voxel as a pressure tensor over the volume of fluid in that voxel. This represents a direct mapping from diffusion space to pressure space,

$$\bar{\mathbf{D}} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix} \rightarrow \begin{pmatrix} p_{xx} & p_{xy} & p_{xz} \\ p_{yx} & p_{yy} & p_{yz} \\ p_{zx} & p_{zy} & p_{zz} \end{pmatrix} = \bar{\mathbf{P}}. \quad (3)$$

The elements of the pressure tensor are related to the corresponding elements of the diffusion tensor through a change of units ($\text{mm}^2/\text{s} \rightarrow \text{Pa (N/m}^2\text{)}$). Therefore, the local maximum pressure vector at any position is coincident with the major diffusion direction of the corresponding voxel. This has the effect of coupling the flow dynamics with the local diffusion profile. To demonstrate this relationship anatomically, consider Figure 2, which shows a pressure tensor image derived from a 2D axial slice of DTI data from a normal human subject taken at the level of the internal capsule. In this image, the pressure tensor at each voxel is represented by a tensor glyph, an ellipsoid whose axes are obtained through the diagonalization of the pressure tensor and whose color describes the dominant direction of the pressure force. In the enlarged view, the posterior limb of the corpus callosum, marked by a star (★), is characterized by coherent pressure along the y axis. In contrast, the neighboring ventricular space, marked by a delta (Δ), is characterized by an isotropic pressure force. This demonstrates that, in highly anisotropic areas, the major pressure force within each voxel is co-linear with the dominant diffusion direction.

B. Numerical Solution Using the Finite Volume Method

Once we define the pressure tensor field and viscosity scalar field based on the DTI dataset of interest, we use them to calculate the fluid velocity vector field between a fluid source and an arbitrary number of sinks as a time independent solution of the Navier-Stokes equations. Because an analytical solution to the Navier-Stokes equations is impossible with all but the most trivial models, we use a finite volume method to obtain an approximate numerical solution of the steady state, $\frac{\partial \rho v_i}{\partial t} = 0$. Dirichlet boundary conditions were imposed at the boundary of the brain volume, which was defined using a hand-drawn mask volume. The

flux of fluid across the boundary was set to zero to prevent loss of the artificial fluid outside the brain volume, leading to a non-conservative system.

$$\bar{v}(p)=0 \quad \forall p \in \partial\Omega \quad (4)$$

where $\bar{v}(p) = \{v_i\} \in \mathbb{R}^3$ at point p , an arbitrary point on the boundary of the brain volume, Ω

Each voxel is considered as a discrete control volume, V , and the Navier-Stokes momentum equations are integrated across it,

$$\int_V \nabla \cdot (\rho v_i \bar{v}) dV = \int_V \nabla \cdot (\mu \nabla v_i) - |(\nabla \cdot \bar{\mathbf{P}})_i| dV. \quad (5)$$

The derivatives in the Navier-Stokes equations are evaluated at the faces of each control volume using a hybrid differencing scheme. Our hybrid differencing scheme assumes an upwind differencing scheme between the control volume, α , and its neighbor, β , for cells which have a Peclet (Reynolds) number (the ratio of the relative strengths of convection to diffusion) greater than 2. Otherwise, the derivatives at the control volume faces are evaluated using a central differencing scheme.

Numerical integration yields a system of linear equations equal to the dimensions of the image volume. Because of the unique form of this large 3-D linear system, we use a variant tridiagonal matrix algorithm (TDMA) to solve for the fluid velocity vector field at the current time step [49]. We implemented the additive operator splitting (AOS) method described by Weickert *et al.*, which avoids any directional dependence in the obtained solution by eliminating the problem of multiplicative splitting [50]. This method is iteratively applied until a user-defined convergence criterion is reached. For all the experiments in this paper, we use a convergence criterion of $(V^i - V^{i-1}) < .05 V^{i-1}$, where V^i is the solution to the fluid velocity vector field at time, $t = i$.

C. Computing Probable Connections

Once we have a solution for the fluid velocity vector field, we estimate the most likely connection path between two seed regions by finding the optimal path that maximizes a weighted function of the magnitude of the fluid velocity and its gradient. Our approach is based on the generalized gradient vector flow (GGVF) method proposed by Xu *et al.* [51], [52]. The optimal path, expressed as a parameterized curve $r(s) = [x(s), y(s), z(s)]$ with $s \in [0, 1]$, minimizes the following energy functional,

$$E = \frac{1}{2} \int_0^1 [\alpha |r'(s)|^2 + \beta |r''(s)|^2] + (\Phi(r(s), t)) ds. \quad (6)$$

α and β are weighting factors, determining the influence of the curve's tension or rigidity, respectively. The choice of α and β can be made based on *a priori* information about the geometry of the tract of interest. In the experiments shown in this paper, we assume α and β are always equal to unity (1). $\Phi(r(s), t)$ is the GGVF field, $\Phi(r, t)$, restricted to the curve, r , parameterized by s .

To minimize E , $r(s)$ must satisfy the following Euler equation

$$\alpha|r''(s)|^2 + \beta|r'''(s)|^2 + (\nabla(\Phi(r(s), t))) = 0. \quad (7)$$

A solution to the above Euler equation is equivalent to the equilibrium solution of the following time-dependent partial differential equation,

$$\frac{\partial r(s, t)}{\partial t} = \alpha|r''(s, t)|^2 + \beta|r'''(s, t)|^2 + \nabla(\Phi(r(s), t)), \quad (8)$$

$(\Phi(r, t))$ is the GGVF field, defined as the solution to the following partial differential equation,

$$\frac{\partial \Phi(r, t)}{\partial t} = g(|\nabla f|) \nabla^2 \Phi(r, t) - h(|\nabla f|)(\Phi(r, t) - \nabla f). \quad (9)$$

f is calculated from the fluid velocity field, $v(x, y, z)$,

$$f(x, y, z) = w_1 |v(x, y, z)| + w_2 |\nabla v(x, y, z)|, \quad (10)$$

where w_1 and w_2 are weighting factors. This choice for f maximizes the weighted sum of the magnitude of the fluid velocity and the gradient.

The weighting functions, $g(|\nabla f|)$ and $h(|\nabla f|)$, are defined as

$$g(|\nabla f|) = e^{-(|\nabla f|/K)}, \quad (11)$$

$$h(|\nabla f|) = 1 - g(|\nabla f|), \quad (12)$$

where K is a constant.

To numerically solve the above time-dependent partial differential equations for $(\Phi(r, t))$ and E , we use an explicit finite differencing scheme with the following stability condition

$$\Delta t \leq \frac{(\Delta x)(\Delta y)(\Delta z)}{g_{max}}, \quad (13)$$

where Δt , Δx , Δy , Δz are the time and spatial sample intervals and g_{max} is the maximum value obtained by the function g .

D. Implementation of a Heat Equation Based DTI Tractography Method

To compare our method to the heat/diffusion PDE-based approaches, we implement a tractography method based on the anisotropic heat equation,

$$\frac{\partial u(x, y, z, t)}{\partial t} = \nabla \cdot \bar{\mathbf{D}} \nabla u(x, y, z, t), \quad (14)$$

where $|u(x, y, z, t)|$ is the amount of heat at position (x, y, z) at time t , and $\bar{\mathbf{D}}$ is the diffusion tensor at the corresponding voxel in the DTI image volume.

We follow an approach similar to that described by O'Donnell *et al.* [41] and solve for the steady state heat concentration ($\frac{\partial u}{\partial t}=0$) to generate the heat flow vector field. We use similar Dirichlet boundary conditions used for the fluid model, setting the value of the heat, $u(x,y,z)$ at the boundary to be equal to 0.

$$u(p)=0 \quad \forall p \in \partial\Omega \quad (15)$$

where $\nabla(p) = \{v_i\} \in \mathbb{R}^3$ at point p , an arbitrary point on the boundary of the brain volume, Ω . We numerically determine the solution to the heat flow vector field using a similar finite volume method used for the fluid model.

To generate probable connection paths through the heat flow vector field, $u(x, y, z)$, we modify the GGVF-based approach described above for calculating the optimal path through the fluid velocity vector field. Instead of the above definition for f , the GGVF field is calculated using the following definition,

$$f(x, y, z)=w_1|u(x, y, z)|+w_2|\nabla u(x, y, z)|, \quad (16)$$

where w_1 and w_2 are weighting factors. This choice for f maximizes the heat flow along the path rather than the fluid velocity.

E. Implementation of a Streamline DTI Tractography Method

In order to compare our method to streamline tractography approaches, we implement a tractography method based on the Fiber Assessment by Continuous Tracking (FACT) method [8]. To generate a probable connection path between any two ROIs in the DTI image volume, a seed point was chosen within one of those ROIs, designated the start ROI. From this seed point, we iteratively evolved the tract by stepping along the major diffusion direction at that point a user-defined step-size. In our experiments, we define the step-size to be one-tenth of the isotropic voxel length. Tractography was stopped when the tract reached the second ROI, the stop ROI. The tract was immediately terminated and the tract rejected if the FA ever dropped below 0.4 at any point in the tract or if the diffusion direction from voxel to voxel changed by more than 60 degrees. These termination criteria were based on values proposed by Mori *et al.* [8].

F. Calculation of the Average Fractional Anisotropy Along a Path

In the experiments that follow, we quantitatively validate our method by comparing its results with tracts generated by competing methods. Additionally, we assess the effect of noise on the performance of our method by comparing the results at different levels of noise intensity. To quantitatively validate our method in these ways, we require some metric of tract fidelity to the underlying ground truth. We chose to use the average fractional anisotropy along the tract, $\overline{FA}_p$, as one of our metrics of tract fidelity because its value is independent of the tractography method used. When used on tracts generated on the digital DTI phantoms below, where high FA voxel values are limited exclusively to the ground truth tract voxels, $\overline{FA}_p$ is a good metric of tract fidelity. $\overline{FA}_p$ is calculated by taking the average of the FA from a regular sample of points along the path, weighted by the normalized dot product of the major diffusion direction with the vector tangent to that point of the path,

$$\overline{FA}_p = \frac{1}{L} \int_s FA(s)(p(s) \cdot \mu_1(s)) ds, \quad (17)$$

where p is the tract parameterized by $s = [0, L]$, $\mu_1(s)$ is the major diffusion direction at the point s , and L is the total length of the tract. This gives a high value to tracts that run through high FA voxels parallel to their local major diffusion direction.

G. Algorithm Summary

We implemented our Navier-Stokes method in C++. Visualization of tractography results and tensor data was accomplished using an in-house customized version of BrainSuite [53]. The tractography algorithm implemented the above fluid-based model, numerically found a solution to the resulting fluid velocity vector field, and generated tracts using our GGVF based approach. It consists of the following steps:

1. Reconstruct the tensor volume from the signal DWI data using the approach given by Basser *et al.* [1].
2. Diagonalize the tensor volume to obtain the eigenvectors and eigenvalues for each voxel.
3. Compute the fractional anisotropy and lattice index at each voxel from the results obtained in 2
4. Compute the pressure volume from the results obtained in 2
5. Compute the viscosity volume from the results obtained in 3
6. Obtain an approximate solution for the fluid velocity vector field using the finite volume method described above. For the current step, $t = i$,
 - a. Use the above pressure and viscosity volumes to evaluate derivatives at the faces of each control volume.
 - b. Solve for the solution for the velocity vector field using the additive operator splitting method described by Weickert *et al.* [50].
 - c. Repeat steps a and b until the average difference of the solution between successive steps is less than 0.05 of the previous iteration's solution.
7. Find the most probable path connecting the ROIs using a GGVF based approach that maximizes the fluid velocity and the gradient of the velocity:
 - a. Compute f from the fluid velocity vector field and its gradient.
 - b. Use f to compute the GGVF field, $\Phi(r(s))$. Numerically solve the time-dependent partial differential equation for $\Phi(r(s))$ using an explicit finite differencing scheme.
 - c. Solve for the tract connecting the ROIs that minimizes a path through the energy field based on the GGVF field obtained in b.

We provided many parameters in this algorithm, both in computation of the velocity field and the probable connection paths, which we left for the user to define. The motivation was to allow the user to maximize the performance of this algorithm based on the form of the dataset, any *a priori* knowledge, and their available computational resources.

III. Results

We applied our method to both computer generated and human control DTI datasets. To assess the effect of noise on our method, we used a digital DTI phantom based on a helical pattern. Our method was able to correctly segment the structure of the phantom from computer generated DTI volumes with various levels of Rician noise. A comparison of our method with implementations of first order partial differential equation (PDE) and streamline methods using the same phantom showed that our algorithm is more robust in the presence of increasing levels of Rician noise. To assess the performance of our method in segmenting complex crossing fiber tract geometries, we used a phantom based on two intersecting helical patterns. Our method was able to correctly segment the most likely connection paths with a single set of ROIs, even when the anisotropy values of the tract voxels of the two helices were nearly identical. When applying our method to DTI volumes from a normal human subject, our method produced paths that were consistent with both known anatomy and directionally encoded color (DEC) images of the DTI dataset.

A. Comparative Validation of the Effect of Noise Using a Helical Digital DTI Phantom

The presence of noise within the diffusion tensor field adversely affects the fidelity of the paths generated by tractography algorithms to the underlying white matter. This is especially true of streamline methods where noise accumulates at each step as the tract evolves [8]. To assess the performance of our method in the presence of noise, we created a digital DTI phantom using a single helical tract pattern. We modeled the ground truth as an ideal tract with a single dominant diffusion direction at every voxel that is co-linear to the underlying helical shape. Diffusion at these voxels was assumed to have diffusion tensor eigenvalues, $\lambda_{1,2,3}$, consistent with cerebral white matter, $\lambda_{1,2,3} = \{1700, 200, 200\}$ [54], and the non-tract image voxels were assumed to have diffusion tensor eigenvalues, $\lambda_{1,2,3}$, consistent with cerebral gray matter, $\lambda_{1,2,3} = \{900, 700, 700\}$. Seven images were constructed using two b values ($b=0, 1000$) and six gradient directions. The images were acquired with image volume dimensions of $50 \times 50 \times 45$ with resolution $1 \times 1 \times 1 \text{ mm}^3$ and used to form the ideal signal image set. We added artificial noise to the images following a Rician distribution [55]. The level of noise added to the ideal signal image set was $\sigma(k) = kS_T$, where σ^2 represents the variance of the Rician distribution and where the signal is known to span the range $[0, S_T]$. We refer to k as the magnitude of the noise in the figures below.

Figure 3 shows 3D renderings of the probable paths generated by applying the three methods in our study to a digital phantom with noise magnitude of $k = .15$ ($\sigma_r = .15S_T$): our fluid mechanics based method, a heat-based PDE algorithm based on the work of O'Donnell *et al.* [41] and Batchelor *et al.* [42], and an implementation of a streamline method based on the FACT method [8]. ROIs were placed at either end of the helix, and these same ROIs were used for all three methods. The figure shows that our method accurately segments the original helical shape in the presence of noise. A visual comparison of the methods shows greater variability among the tracts produced by the two other algorithms. These variations do not correspond meaningfully with the underlying DEC and FA images.

We quantitatively compared the effect of various magnitudes of noise on the results generated by the three methods. Figure 4 shows a plot of the tract error (E_i) versus various magnitudes of noise, k , for tracts generated using the three methods. We use the tract error, E_i , as a metric to quantify the deviation of a tract from the ideal ground truth. It is defined for a tract, i , as

$$E_i = \frac{|L_i^{IH} - L^T|}{1 - \frac{L_i^{OH}}{L^T}}, \quad (18)$$

where L^T is the length of the ideal tract between the ROIs, L_i^{IH} is the length of the tract, i , that runs within voxels of the helical ground truth, and L_i^{OH} is the length of the tract, i , that runs outside the voxels of the helical ground truth. The tract error is proportional to the deviation of the length of the current tract from the ideal and is zero when length of the current tract and the ideal tract are identical. At each level of noise magnitude, k , we sampled tracts for each method. Figure 4 shows that our method generated paths with a smaller tract error than those generated with the other two methods at noise magnitudes less than $k = 0.6$. Above $k = 0.6$, the phantom becomes severely distorted, leading to significant errors in all three methods. We performed a one-way ANOVA on the average error of the tracts generated by each of the three methods for noise magnitudes $k < 0.6$. There were significant differences between each of the three methods ($p < 0.02$), confirmed by a post-hoc Tukey's test. At values of $k > 0.6$, the tract error for all three methods grows exponentially.

We also compared average FA along the path, $\overline{FA}_p$, for the tracts generated by each of the three methods. Since the diffusion at the tract voxels was fixed to be $\lambda_{1,2,3} = \{1700, 200, 200\}$, the ideal tract has $\overline{FA}_p = .9$. $\overline{FA}_p$ is an indicator of tract fidelity for this phantom since any deviation from the ideal tract will decrease the $\overline{FA}_p$. Figure 5 shows the $\overline{FA}_p$ for various magnitudes of noise. At each level of noise magnitude, k , we sampled tracts for each method. A comparison of the trends in $\overline{FA}_p$ for tracts generated by each of the three methods confirms the results in the previous figure. Our method generates paths with a greater $\overline{FA}_p$ than those generated with the other two competing methods at noise magnitudes less than $k = 0.6$. We performed a one-way ANOVA on the average $\overline{FA}_p$ of the tracts generated by each of the three methods for noise magnitudes $k < 0.5$. There were significant differences between each of the three methods ($p < 0.016$), confirmed by a post-hoc Tukey's test.

B. Validation of the Effect of Crossing Paths Using an Intersecting Helical Digital DTI Phantom

When multiple divergent paths can connect ROIs through the diffusion tensor field, it can be a challenge for some tractography approaches to pick the true best path. To demonstrate our method's performance in the presence of branching and crossing tracts, we created a digital diffusion tensor phantom using a double intersecting helical tract pattern. The pattern consists of one left-handed and one right-handed helix, existing in the same image volume with identical start and stop points. Each helix has a height of 35 mm, a width of 2 mm, a radius of 10 mm, a vertical loop separation of 10 mm, and an origin at a common point in the image volume. We modeled the ground truth of each helix as an ideal tract with a single dominant diffusion direction at every voxel that is co-linear to the tract. The diffusion direction at voxels where the two helices intersect was calculated as the average of the diffusion tensors of the two helices at that point, $\bar{D} = .5D_{LH} + .5D_{RH}$, where D_{LH} and D_{RH} are the diffusion tensor at that voxel of the left handed and right handed helix, respectively. The non-tract image voxels were assumed to have diffusion tensor eigenvalues consistent with cerebral gray matter, $\lambda_{1,2,3} = \{900, 700, 700\}$. Seven images were constructed using two b values ($b=0, 1000$) and six gradient directions with image volume dimensions of $50 \times 50 \times 45$ and resolution $1 \times 1 \times 1 \text{ mm}^3$ and used to form the ideal signal image set. We added noise following a Rician model [55]. The level of noise added to the ideal signal image set was $\sigma(k) = kS_T$, where σ^2 represents the combined variance of Rician distribution and where

the signal is known to span the range $[0, S_T]$. For all images in this experiment, $\sigma(k) = .015S_T$.

Three different phantoms (A, B, C) were created using the above protocol with varying diffusion values used to create each helix. For each phantom, the same ROIs were placed at the origin point of both helices and at the most distal intersection point, and probable connection paths were generated using our method. Three phantoms were constructed, each with the different diffusion tensor eigenvalues for the helices shown in Table 1.

Figure 6 shows the tracts generated for the three different phantoms described in Table 1, superimposed on surface models of the two helices. For phantoms A and B, voxels within the gold helix had a greater FA than the blue helix. Therefore, a path through the gold helix was the optimal tract connecting the ROIs. Our method successfully segmented these paths despite numerous local divergent crossing paths with the blue helix. For phantom C, voxels within the gold helix and blue helix had the same FA, and paths within both helices were equally likely to be the most probable connection between the ROIs. Therefore, our method accurately segmented tracts that traversed both the gold and blue helix with equal probability. Neither our heat-based PDE nor our streamline method was able to successfully segment the phantom (data not shown).

The histograms in Figure 7 shows the distribution of the average FA along the path, $\overline{FA}_p$, for tracts generated on each of the three phantoms described in Table 1. Tracts from phantoms A and B have an average $\overline{FA}_p$ close to the diffusion values of the gold helix used to create the phantom, which is the location of the ground truth path. However, the tracts from phantom C have an average $\overline{FA}_p$ close to the identical FA used to create both helices, and the location of the ground truth path is equally likely to be in either helix, as seen in Figure 7.

Table 2 shows the average $\overline{FA}_p$ and standard deviation for the tracts generated using each of the three phantoms described in Table 1. Table 2 confirms the results in Figure 7. All the tracts from each phantom have an average FA close to the diffusion values of the gold helix used to create the phantom, the location of the ground truth path. A one-way ANOVA showed significant differences between each of the three groups ($p = .00325$), confirmed by a post-hoc Tukey's test.

C. Anatomical Results

Diffusion tensor imaging data from normal human subjects were acquired using a 3T Siemens scanner with a standard quadrature head coil with the following scan parameters: image volume matrix size $192 \times 192 \times 55$ with resolution $1.25 \times 1.25 \times 2.5 \text{ mm}^3$, 64 gradient directions with uniform spherical sampling, and b values 0 and 1000 s/mm^2 . For each subject, the set of diffusion weighted images was skull-stripped using the Brain Surface Extraction (BSE) algorithm developed by Shattuck *et al.* [56], [57] and registered to the corresponding $b = 0$ image using a 12 parameter affine registration algorithm [58]. Diffusion tensor reconstruction was performed and lattice index and fractional anisotropy determined for each voxel in the image, according to [54].

1) Segmentation of Corticospinal Tracts—ROIs were drawn around the brainstem below the level of the pons and bilaterally within the corona radiata above the level of the corpus callosum. Figure 8D shows the approximate location of these ROIs, circled in white, superimposed upon the corresponding axial slice from the DEC volume. Figure 8A shows a 3D rendering of the likely paths produced by our method which connect these ROIs. These tracts cross the mid-sagittal plane at the level of the mid-pons before continuing downward

in the contralateral corticospinal tract (see white arrow, 8A), following a strong lateral diffusion profile characteristic of the mid-pontine crossing fibers, as seen in the corresponding directionally encoded color (DEC) image (Figure 8B, 8C). This is a well-known characteristic of the pyramidal tracts; fibers cross to the contralateral side of the brain at the mid-pons before descending to the appropriate spinal cord level [59].

2) Segmentation of Cerebellar Efferent Tracts—ROIs were drawn bilaterally around the location of the dentate nucleus and bilaterally around the thalamus and the red nucleus. Figure 9B shows the approximate location of the dentate ROIs, circled in white, superimposed on the the corresponding axial slice from the DEC volume. Figure 9A shows the 3D rendering of the likely paths produced by our method which connects all these ROIs together, superimposed upon surface models of the brainstem (gold) and ventricles (blue). This system provides a challenge for tractography algorithms because it crosses across the midline over multiple other tract systems and because it has multiple termination points in the midbrain. Our method was able to successfully segment the multiple tract systems and its multiple projections.

D. Computational Cost

The computational cost of this algorithm can vary widely, depending on the size of the data set and the algorithm parameters supplied by the user. We performed a timed simulation, generating 1000 probable connection paths on a control DTI dataset $192 \times 192 \times 55$ with resolution $1.25 \times 1.25 \times 2.5 \text{ mm}^3$, 64 gradient directions with uniform spherical sampling, and b values 0 and 1000 s/mm^2 , on a Dell Intel 3.8 GHz dual Xeon processor workstation with 4 GB RAM. The results were as follows:

- Computing velocity vector field for the entire brain: (310.86 minutes) 5 hours
- Probable connection path generation: (197.103 minutes) 3 hours

IV. Discussion

The *in vivo* study of white matter architecture in the human brain has been limited by the lack of non-invasive methods. Recent work establishing a link between anisotropic water diffusion in the brain and axonal integrity and orientation demonstrates the potential of DTI as a non-invasive *in vivo* tool for studying white matter [5], [6]. In particular, DTI tractography is used to explore important questions about how different regions of the brain are connected and how these connections change during development or the progression of disease. In this paper, we have introduced a method based on a Navier-Stokes fluid mechanics model that computes an estimate of the most likely path connecting regions in DTI volumes by simulating the flow of an artificial fluid through the volume. Our method is one of several PDE based approaches to DTI tractography. PDE based methods are advantageous because they use the full diffusion tensor to compute their connectivity metrics, and the diffusion or flow of artificial substances common to all PDE based methods can be made the basis of a quantitative statistical metric of connectivity in the brain [41], [42].

Early work using PDE based methods were focused on elliptical or parabolic models of heat flow or diffusion [41], [42]. Even though the Navier-Stokes equations were first developed for fluid mechanics, they have been shown to be successful in modeling a large number of diverse physical phenomena. As second order hyperbolic PDEs, they contain an additional convection term, not present in previous methods. We model this additional convection term as a local viscosity of the fluid, calculated from the local intervoxel and intravoxel anisotropy in the corresponding DTI image volume. This has an interesting effect. As demonstrated in Figure 1, the viscosity term dampens fluid flow in regions of low

anisotropy, such as gray matter and CSF. Our motivation for incorporating this viscosity term was that it would eliminate the need for the white matter mask common to previous PDE-based tractography methods. We represent the information in the diffusion tensor through the pressure tensor in the Navier-Stokes equations. Our model transforms the diffusion information obtained from the DTI dataset into a local pressure force acting on the artificial fluid in that voxel. The fluid flows in all directions within the voxel as determined by the value of the pressure tensor weighted by the local anisotropy. By modeling the regions of interest as source and sinks for this artificial fluid, we can numerically solve the Navier-Stokes equations on the DTI volume based on our viscosity and pressure values. We then obtain a fluid velocity vector field that can be used as a metric of connectivity since it reflects local anisotropy, similarity, and diffusion direction. By using the directional information in the diffusion tensor together with the local anisotropy and similarity information as a viscous force to model the fluid flow, we hypothesized that our model would have a superior performance in the presence of noise than previous PDE-based methods which only made use of the diffusion tensor. However, there are many parameters in this algorithm, both in computation of the velocity field and the probable connection paths, which we left for the user to define. The motivation was to allow the user to maximize the performance of this algorithm based on the form of the dataset, any *a priori* knowledge, and their available computational resources. This does put a burden on the user, and future work will focus on automating this process as much as possible to optimize the parameters for each dataset.

To quantitatively assess the performance of our method in the setting of noise and partial volume effects, we used computer generated DTI phantoms based on a helical tract pattern. Our method was able to correctly segment the underlying shape of the phantom in the presence of noise. Furthermore, a comparison of our method with an implementation of our heat-based PDE and streamline methods demonstrated that our method was more robust in the presence of increasing levels of Rician noise. Partial volume effects and crossing or branching fiber tract geometries are a primary source of error for tractography methods [21], [22]. To assess the performance of our method in segmenting crossing fiber tracts, we used a computer generated phantom based on two intersecting helical tracts. These tracts pose a challenge to traditional streamline methods since they cross repeatedly, diverging to reach their respective targets. Our fluid-based method was able to segment the most probable tracts with only a single set of ROIs. We also demonstrated the ability of our method to segment tracts accurately in human anatomical datasets. Using normal human brain DTI data, we used our algorithm to segment the corticospinal tracts. It is well known that the corticospinal tracts cross at the level of the pons to carry motor information to the spinal cord from the contralateral motor cortex [59]. Our results shown in Figure 8 confirm this, showing the most probable tracts crossing at the level of the mid-pons before descending in the contralateral tract. This result is further confirmed by inspection of the DEC volume (Figure 8B, 8C). Additionally, we segment the efferent cerebellar pathways in normal human brain DTI datasets. It is well known that the cerebellar efferents originate in the deep cerebellar nuclei, most notably the dentate nucleus, and terminate primarily in the contralateral red nucleus and contralateral thalamic nuclei [59]. Our results in Figure 9 confirm this by inspection of both the probable connections and the DEC volume.

Our results demonstrate an accurate and robust DTI tractography algorithm based on a fluid mechanics model. We compute a metric of connectivity from our artificial fluid velocity field calculated based on the underlying DTI dataset. One of the characteristics of diffusion MR is the lack of any specific direction in the diffusion signal. However, our choice of a directed fluid flow characteristic of the Navier-Stokes equations makes it so that fluid flow dynamics is not the same in both directions. Future work will focus on minimizing any possible complications that arise from this disparity. However, preliminary work has shown

that the direction-dependent differences in the velocity vector field have a predominantly local effect and do not significantly affect regional connectivity results. Further comparative validation will also be a focus of future work using both computer generated phantoms and anatomic datasets. In addition, we hope to extend this tractography method to data obtained using current high angular resolution diffusion imaging reconstruction methods [60]–[62].

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Fig. 1.

Viscosity maps derived from 2D slices of DTI data from human control subjects. Viscosity values were calculated from the corresponding diffusion tensor image ($\mu = k(1 - (FA \times LI))$) and are displayed according to the legend bar seen on the right side of the figure. A. Axial slice taken at the level of the internal capsule. The corpus callosum, marked with a star, ★, is a highly organized white matter tract and is therefore characterized by low viscosity. Conversely, the lateral ventricle, marked with a delta, Δ, contains CSF and is highly viscous. B. A mid-sagittal slice. As in A, the corpus callosum is marked with a star, ★ and is characterized by low viscosity. In contrast, the lateral ventricular space, marked with a delta, Δ, contains CSF and therefore has no architecture. Consequently, it is highly viscous.

Fig. 2.

Representations of the pressure tensor derived from 2D slices from human control subjects. At each voxel in the image, the pressure force is represented by a tensor glyph, an ellipsoid whose axis is obtained from a diagonalization of the corresponding pressure tensor. The color of the ellipsoid represents the dominant diffusion direction, according to the color coded axes in the figure with the superior-inferior z-axis (blue) coming out of the page, the anterior-posterior y-axis (green) vertical, and the left-right x-axis (red) horizontal. A. A 2D axial slice taken at the level of the internal capsule. The white box marks the enlarged area shown in B. B. Enlarged view from A. The posterior limb of the corpus callosum, marked with a star (★), is a highly organized white matter tract, and the pressure force acts on the artificial fluid co-linear with the fiber tract. In contrast, the lateral ventricular space, marked with a delta (Δ), contains little structure. Consequently, the pressure force is isotropic in that region.

Fig. 3.

Segmentation results of varying methods on a digital helical DTI phantom in the presence of Rician noise. ROIs were placed at either end of the helix and the same ROIs used for all methods. The same magnitude of Rician noise, $k = .15$ ($\sigma_r = .15S_T$), was added to all the signal images used to generate the phantom. The tracts are color-coded by the method used to generate them and are shown together with a surface model of the ground truth helix (white: 2nd order method; red: 1st order method; green: FACT method).

Fig. 4.

Line plot of the tract error for the segmentation results of our digital DTI phantom versus increasing noise magnitude, k . The magnitude of the noise, k , is given on the x-axis and is proportional to the amount of Rician noise added to the ideal signal image volumes generated from the phantom, $\sigma(k) = kS_7$, where σ^2 represents the combined variance of the Rician distribution and where the signal is known to span the range $[0, S_7]$. The tract error, E_t , is shown on the y-axis and is proportional to the difference in the length of the current tract and the ideal helical shape. At each k in the plot, the average tract error of the sampled tracts is given with error bars. The lines in the plot are color-coded based on the method used to generate them (black: 2nd order method; red: 1st order method; blue: FACT method). The plot shows that our method generated paths with a smaller tract error than those generated with the other two methods for noise magnitudes less than $k = 0.6$.

Fig. 5.

Line plot of average FA along the path, $\overline{FA}_p$, of the same tracts shown in Figure 4 versus increasing noise magnitude, k . $\overline{FA}_p$ is shown on the y-axis and is defined as the average of the dot product of the major diffusion direction with the tract, multiplied by the FA at that point. $\overline{FA}_p$ is an indicator of tract fidelity since any deviation from the ideal tract will decrease the $\overline{FA}_p$ for the tract. The magnitude of the noise, k , is given on the x-axis and is proportional to the amount of Rician noise added to the ideal signal image volumes generated from the phantom, $\sigma(k) = kS_T$, where σ^2 represents the combined variance of the Rician distribution and where the signal is known to span the range $[0, S_T]$. The lines in the plot are color-coded based on the method used to generate them (black = 2nd order method; red = 1st order method; blue = FACT method). The plot shows that our method generates paths with a greater $\overline{FA}_p$ than those generated with the other two competing methods at noise magnitudes less than $k = 0.6$.

Fig. 6.

Validation using a computer generated DTI phantom based on a double intersecting helical tract pattern. ROIs were placed at the origin point of both helices and at the most distal intersection point. Probable connection paths were generated for each phantom using our 2nd order method and color-coded to designate which diffusion values had been used to construct the corresponding phantom [white = phantom A; red = phantom B; green = phantom C] (see Table 1). For tracts generated from phantoms A (white) and B (red), our method correctly generated the paths within the gold helix, which had a greater FA at each voxel than the blue helix and was the most likely connection paths between the ROIs. For tracts generated from phantom C (green), the gold helix and blue helix had the same FA; paths within both helices were equally likely to be the most probable connection between the ROIs. Therefore, our method correctly generated tracts that traversed both the gold and blue helix with equal probability.

Fig. 7.

Histograms of average FA along the path, $\overline{FA}_p$, for tracts generated on each of the three phantoms described in Table 1 (A. = Phantom A; B. = Phantom B; C. = Phantom C). These plots confirm quantitatively the results seen visually in Figure 6. All the tracts in each group have an average FA close to the diffusion values of the gold helix used to create that particular phantom, the location of the ground truth path. Likely paths generated on phantoms A and B had an $\overline{FA}_p$ close to the anisotropy of the gold helix. Only the tracts generated from phantom C had an average $\overline{FA}_p$ that could have come from either helix.

Fig. 8.

Segmentation results of the corticospinal tracts using our method in human control DTI images. ROIs were placed within the brainstem below the level of the crossing pontine fibers and within the corona radiata above the level of the corpus callosum. Cross-sections of the approximate location of these ROIs are shown Figure 8D, drawn in white, superimposed on the corresponding axial DEC slices. Figure 8A shows the estimated connection paths between these ROIs generated by our method. An axial slice of the tensor glyphs at the level of the mid-brain is shown for spatial reference. The tracts show a prominent lateral course at the level of the mid-pons (Figure 8A: white arrow). This corresponds to a strong lateral diffusion component at that point as seen in the directionally encoded color (DEC) image of the axial slice at the mid-pontine level (Figure 8B, 8C: white arrow). The tensor glyphs and DEC image are color-coded by the axes shown in the figure.

Fig. 9.

Segmentation results of our method on the cerebellar efferent pathway through the superior cerebellar peduncle. The cerebellar efferents are known to originate in the deep cerebellar nuclei, most prominently the dentate nucleus. The two major projections of the cerebellar efferents are to the red nucleus and to the thalamus, where it synapses before projecting to the cortex. ROIs were drawn bilaterally around the location of the dentate nucleus. Figure 9B shows the approximate location of the ROI enclosing the dentate nucleus, circled in white, superimposed on the the corresponding axial slice from the DEC volume. Figure 9A shows the 3D rendering of the likely paths produced by our method, together with surface models of the brainstem (gold) and ventricles (blue). The tracts terminating in the red nucleus are shown in red. Those tracts terminating in the thalamus are shown in white.

TABLE I

Diffusivity values used to create each helix of the three intersecting double helical phantoms

Phantom	Diffusivity Values of Left-Handed (Gold) Helix ($\lambda_1 : \lambda_2 : \lambda_3$)	Diffusivity Values of Right-Handed (Blue) Helix ($\lambda_1 : \lambda_2 : \lambda_3$)
A	1900:100:100	1300:400:400
B	1600:250:250	1300:400:400
C	1300:400:400	1300:400:400

TABLE II

Average $\overline{FA}_p$ and standard deviation for tracts generated using the phantoms described in TABLE 1.

Phantom	Average $\overline{FA}_p$	Standard Deviation (s_{N-1})
A	.893	.0208
B	.809	.0299
C	.612	.0467