Modeling White-matter Fiber-orientation Uncertainty for Improved Probabilistic Tractography

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Abstract: Tractography uses fiber-orientation estimates to trace the likely paths of white-matter tracts through the brain, in order to map brain connectivity non-invasively. In this paper, we propose a novel probabilistic framework for modeling fiber-orientation uncertainty and improve probabilistic tractography. The main innovation in the present formulation consists in coupling a particle filtering process with a clustered-mixture model approach to model directional data. Mixtures of von Mises-Fisher (vMF) distributions are used to support the probabilistic estimation of intravoxel fiber directions. The fitted parameters of the clustered vMF mixture at each voxel are then used to estimate white-matter pathways using particle filtering techniques. The technique is validated on simulated as well as on real human brain data experiments.

1 INTRODUCTION

White matter fiber tracking or "tractography" uses fiber-orientation estimates to trace the likely paths of white-matter tracts through the brain. Tractography techniques are powerful tools to capture white matter (WM) connectivity non-invasively. Before applying tractography techniques, diffusion Magnetic Resonance Imaging (MRI) measurements are applied to probe the dispersion of water molecules within tissue over a time. A probability distribution on the displacement of water molecules describes the scatter pattern of molecules during the diffusion time. Since white matter axons are tiny compared to typical MRI voxels, voxels contain hundreds of thousands of axon fibers, which can adopt a wide range of complex configurations. The simpler and most commonly used method, Diffusion Tensor Imaging (DTI) uses a Gaussian distribution to model the dispersion. DTI assumes that the diffusion scatter pattern exhibits a single directional pattern, and is therefore unable to model multiple-directional fiber pathways within a voxel. Other model-based approaches, such as the multi-tensor model (Tuch et al., 2002), or multi-compartment models (Behrens et al., 2007; Assaf and Basser, 2005) have been devised to account for distinct groups of "populations" of fibers. However, model-based techniques recover but a few number of dominant fiber-orientations, and have difficulty in discriminating common anatomical fiber configurations (Seunarine and Alexander, 2009). To resolve complex orientations, model-free methods and High Angular Resolution Diffusion Imaging (HARDI) protocols have been developed. For instance, Q-ball imaging (QBI) (Tuch, 2004) is one popular HARDI-based method used to resolve fiber crossings. It reconstructs the angular profile of the diffusion propagator, commonly known as the (diffusion) orientation distribution function (ODF). The ODF exhibits multiple local maxima in crossing regions, which are used as fiber orientation estimates. Two more recent model-free models are the Diffusion Spectrum Imaging (DSI) (Wedeen et al., 2005), and the Generalized q-Sampling Imaging (GQI) (Yeh et al., 2010) methods. These methods perform non-parametric reconstructions that resolve multiple peaks in each voxel, without requiring prior knowledge of the number of fiber populations. Similarly to other methods for ODF reconstruction, DSI and GQI use shell or grid sampling schemes to extract information about the extent of diffusion anisotropy, and map vector fields that represent the fiber orientations at each voxel. In contrast to QBI, DSI and GQI are not limited to a single spherical shell and a single diffusion gradient coefficient (b-value) to characterize diffusion anisotropy.

As pointed out by (Seunarine et al., 2007; Seunarine and Alexander, 2009), most tractography algorithms still use the basic DTI single-fiber recon-

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struction and it is not clear how to generalize them to exploit the extra information that multiple fiber reconstructions provide. Even when probabilistic tractography is used to estimate the uncertainty of fiber-orientations, the information used to track through fiber configurations is limited to the principal diffusion directions. For instance, in (Parker and Alexander, 2003) fiber-orientations are detected by a Monte Carlo streamline approach, and the sharpness of the peaks are used as indicators of uncertainty. In (Seunarine et al., 2007), the authors have shown that the peaks of multiple-fiber reconstructions provide useful information that can be used to improve tractography results. They used the Bingham distribution to model the peak uncertainty in fiber-orientation estimates obtained from the ODF. Hence, better peak shape uncertainty estimates provided improved tractography results. The main drawback of the above technique is that it requires a costly and complicated calibration. The calibration procedure constructs a mapping from two Hessian (or second derivative) eigenvalues to Bingham parameters, using simulations on two-tensor mixture models with known peak directions (Seunarine et al., 2007).

The above considerations motivated us to devise a probabilistic framework for modeling fiber-orientation uncertainty and improve probabilistic tractography. Two key ideas govern the present development and implementation. First, we model fiber-orientation uncertainty by using directional data clustering to estimate white matter fiber orientations. A clustered-mixture-model approach to model directional ODF data based on von Mises-Fisher (vMF) distributions is used, in order to support the probabilistic estimation of intravoxel fiber directions. The generalized fractional anisotropy (GFA) (Tuch, 2004) is applied to the reconstructed ODF in order to threshold the population of acquisition directions before clustering.

In this "clustered-vMFs" approach, each estimated voxel fiber direction is associated with a component of the fitted mixture of vMF distributions. Hence, each voxel fiber principal direction may be specified by the summary statistics of the estimated vMF component in the mixture. It is worth noting that, in opposition to (Seunarine et al., 2007), no calibration is required. Fitting the mixture of von Mises-Fisher (vMF) distributions to the clustered data, automatically defines the parameters defining the statistical properties of the main peak directions. Moreover, the number of fitted clusters automatically define the pattern of fibers in a voxel.

The second key idea consists in using the fitted parameters of the clustered-vMFs approach at each voxel to guide probabilistic fiber tracking using particle filtering. Several probabilistic techniques have been proposed in the literature to cope with directional uncertainty, partial volume effects, and errors in fiber orientation estimates (Parker and Alexander, 2003; Zhang et al., 2009). Probabilistic methods generate multiple trajectories based on a distribution of fiber bundles at a given seed point, in order to map the connection between the seed voxel and other voxels of the brain. In these techniques, Markov Chain Monte Carlo (MCMC) methods are used to sample from fiber orientation distributions. In order to make the sampling stage more effective, several authors (Zhang et al., 2009; Pontabry et al., 2013; Rowe et al., 2013) have proposed to apply particle filtering to recursively estimate the posterior distribution of fibers at each propagation step. In a similar vein, in this work we have used the Sequential Monte Carlo (SMC) framework (Doucet et al., 2000) to model fiber trajectories. The SMC algorithm propagates for each seed a cloud of particles representing the density probability of the fiber path passing through the seed voxel. The main innovation in the present formulation consists in coupling the particle filtering process with the clustered-vMFs estimate outlined above.

The paper is organized as follows. Section 2 presents the underlying methodology supporting the proposed approach, namely the particle filtering strategy and the clustered-vMFs model. In Section 3 we report on experiments applied to simulated as well as to real brain data. The results of the proposed methodology are compared to those from standard streamline approaches. Section 4 draws some conclusions and points to future working directions.

2 METHODS

2.1 Fiber Tracking Model

In a particle filtering context, fiber tracking is formulated as a non-Gaussian state space model (Doucet and Johansen, 2011). In this model, given the prior probability distribution that characterize the uncertainty of local fiber orientations, a posterior distribution of the target fiber is estimated. Given that both the prior and the posterior distribution are non-Gaussian, particle filtering techniques are well suited to estimate the complex geometry of the fiber paths, and account for directional uncertainties. In contrast, linear filtering methods such as Kalman filtering are often inappropriate to track complex configurations.

In a volume $\Omega \subset \mathbb{R}^3$, a fiber trajectory can be modeled as a sequence of n displacement vectors u_k with

$k = 1,\ldots,n$. From a given starting point u_0, at each time step k, each streamline is propagated one step from its previous location $u_{k-1}^{(i)}$ with a direction vector $v_k^{(i)}$ sampled from the importance density by a step size λ, such that $u_k^{(i)} = u_{k-1}^{(i)} + \lambda v_k^{(i)}$. The state of a particle at time step k, $x_k^{(i)}$, is defined by its location $u_k^{(i)}$ and direction vector $v_k^{(i)}$.

As detailed in (Doucet and Johansen, 2011), particle filtering algorithms can be interpreted as instances of a single generic SMC algorithm. Earlier particle filtering algorithms, such as the popular Sequential Importance Sampling (SIS), suffered from a degeneracy problem as simulation time increased: variance of the estimates increased with time k. Degeneracy is a key factor conditioning the application of SIS algorithms. However, by introducing a re-sampling step degeneracy can be greatly mitigated. Modern SMC methods are a combination of SIS and resampling. SMC methods sample sequentially from a sequence of target probability densities $\pi_k(x_k)$.

As outlined in Algorithm 1, by a sequence of prediction, weighting and selection steps, the particle filter provides a discrete approximation of a posterior distribution $p(x_k|y_{0:k})$ on a time-varying parameter x_k at time step k, given the observations $y_{0:k}$ for time steps $0,1,2,...,k$, and the initial state distribution $p(x_0)$. At each time step k, N particles are propagated by sampling from an importance distribution $\pi(x_k^{(i)} \mid x_{0:k-1}^{(i)}, y_{0:k})$. In the weighting stage, importance weights $w_k^{*(i)}$ are assigned in accordance to the likelihood $p(y_k|x_k^{(i)})$. The discrete approximation to the posterior distribution $p(x_k \mid y_{0:k})$, denoted by $\tilde{w}_k^{(i)}$, is computed by normalizing the importance weights $w_k^{*(i)}$. Finally, a resampling step is used to remove particles with low weights and proliferate those with high weights. Resampling may be applied at each time step, or alternatively, it may be applied only when the variance of the normalized weights is superior to a pre-specified threshold. The threshold, designated ε_{ESS} in Algorithm 1, is often specified in terms of the Effective Sample Size (ESS) criterion (Liu, 2001), which assesses the variability of the weights by,

$$ESS = \left(\sum_{i=1}^{N} (\tilde{w}_k^{(i)})^2 \right)^{(-1)}. \quad (1)$$

In Algorithm 1, the importance distribution $\pi(x_k \mid x_{0:k-1}^{(i)}, y_{0:k})$ is a vMF distribution. The initial state distribution $p(x_0)$, is the vMF distribution parameterized by one of the components of the clustered-vMFs estimate for the current voxel, as detailed in Section 2.2. The likelihood $p(y_k|x_k^{(i)}) = (v_k \cdot \mathcal{V}(u_k))$, is defined by a vMF distribution parameterized by the parameters of the most likely vMF cluster component, for direction v_k, at each point location u_k.

Input :
$\mathcal{V}$ Voxels' cluster statistics
N Number of particles
ε_{ESS} Resampling threshold

for *particle* $i = 1$ **to** N **do**
  $x_0 \sim p(x_0)$
  $w_0^{*(i)} = \frac{1}{N}$
end
for *times* $k = 1$ **to** K **do**
  for *particle* $i = 1$ **to** N **do**
    $x_k^{(i)} \sim \pi(x_k \mid x_{0:k-1}^{(i)}, y_{0:k})$
    $w_k^{*(i)} = w_{k-1}^{*(i)} p(y_k \mid x_k^{(i)})$
    $\tilde{w}_k^{(i)} = \frac{w_k^{*(i)}}{\sum_{j=1}^{N} w_k^{*(i)}}$
  end
  $ESS = \left(\sum_{i=1}^{N} (\tilde{w}_k^{(i)})^2 \right)^{(-1)}$
  if $ESS < \varepsilon_{ESS}$ **then**
    Resample $\{\tilde{w}_k^{(i)}, x_k^{(i)}\}$ according to importance weights
  end
end

Algorithm 1: Sequential Monte Carlo.

In the resampling stage, the usual practice is to attribute equal importance weights to the newly introduced particles (Doucet and Johansen, 2011). The use of equal weights helps maintaining the diversity of the population of particles at intermediate tracking stages, which favors the exploration of new trajectories emerging from the current state. However, this particle filtering setting may be too rich for the resolution of the diffusion directions estimated at each voxel. White matter axon radii are in the range $[0.1, 10]$ μm, whereas MRI voxels typically have sides in the range $[1,5]$ mm. Voxels therefore contain hundreds of thousands of axon fibers (Seunarine and Alexander, 2009), but the estimated principal diffusion directions are typically reduced to 2 or 3 per voxel, originating the so-called "partial volume effects" (Alexander et al., 2001). These effects introduce uncertainties in anisotropy measurements at each voxel, which influence ODF reconstruction accuracy and the anatomic validity of fiber track estimates. An alternative procedure, is to attribute new importance weights according to the weights already evolved for the population of particles. This procedure helps maintaining the selection pressure over low

weighted particles and reduces trajectory irregularities, driving the sequence of distributions to a maximum a-posterior path, at the cost of particle diversity. The result is a more conservative set of estimated directions, and a reduced capability of the algorithm for exploring very long pathways. Nonetheless, it may still confer realistic fiber track estimates for brain tractography.

2.2 Clustered-vMFs Model

The fiber tracking model outlined in Section 2.1 uses vMF distributions as sampling distributions of interest. A d-dimensional unit random vector $\boldsymbol{x} \in \mathbb{S}^{d-1}$ is said to have d-variate vMF distribution if its probability density function is given by

$$f(\boldsymbol{x}|\boldsymbol{\mu},\boldsymbol{\kappa}) = c_d(\boldsymbol{\kappa})e^{\boldsymbol{\kappa}\boldsymbol{\mu}^T\boldsymbol{x}}, \quad (2)$$

where $\|\boldsymbol{\mu}\| = 1, \boldsymbol{\kappa} \geq 0$ and $d \geq 2$. The normalizing constant $c_d(\boldsymbol{\kappa})$ is given by

$$c_d(\boldsymbol{\kappa}) = \frac{\boldsymbol{\kappa}^{d/2-1}}{(2\pi)^{d/2} I_{d/2-1}(\boldsymbol{\kappa})}, \quad (3)$$

where $I_r(.)$ represents the modified Bessel function of the first kind and order r. The density $f(\boldsymbol{x}|\boldsymbol{\mu},\boldsymbol{\kappa})$ is parameterized by the mean direction $\boldsymbol{\mu}$, and the concentration parameter $\boldsymbol{\kappa}$. The $\boldsymbol{\kappa}$ parameter characterizes how strongly the unit vectors drawn according to $f(\boldsymbol{x}|\boldsymbol{\mu},\boldsymbol{\kappa})$ are concentrated about the mean direction $\boldsymbol{\mu}$. Larger values of $\boldsymbol{\kappa}$ imply stronger concentration about the mean direction ((Mardia and Jupp, 2000)). The vMF distribution is unimodal for $\boldsymbol{\kappa} > 0$, and is uniform on the sphere for $\boldsymbol{\kappa} = 0$.

For directional clustering estimation, we consider a mixture of k vMF distributions (Banerjee et al., 2005) that serves as a model for directional ODF profile data, corresponding to multiple fiber orientations. A mixture of k vMF distributions has a density given by

$$f(\boldsymbol{x}|\boldsymbol{\Theta}) = \sum_{h=1}^{k} \alpha_h f_h(\boldsymbol{x}|\boldsymbol{\theta}_h), \quad (4)$$

where $f_h(\boldsymbol{x}|\boldsymbol{\theta}_h)$ denotes a vMF distribution with parameter $\boldsymbol{\theta}_h = (\boldsymbol{\mu}_h, \boldsymbol{\kappa}_h)$ for $1 \leq h \leq k$, $\boldsymbol{\Theta} = \{\alpha_1, \ldots, \alpha_k, \boldsymbol{\theta_1}, \ldots, \boldsymbol{\theta_k}\}$, and the α_h are non-negative and sum to 1. The Expectation Maximization (EM) framework is used for estimating the mean and concentration parameters of the mixture. The clustering algorithms proposed by (Banerjee et al., 2005) and implemented in (Hornik and Grün, 2012) were used to fit the vMF mixture. The principal ODF profile statistics are extracted directly from the estimated clusters. The number of fibers in each voxel is automatically estimated from the reconstructed ODF profile by the vMF approach using the Bayesian Information Criterion (BIC) criterion (Schwartz, 1979). In other words, "BIC" is used to decide on the number of components to select. All relevant statistical information about the ODF orientation and multiple fiber components may then be extracted from this fitting process.

The preceding description specifies a clustered mixture-model approach to model directional ODF data based on von Mises-Fisher (vMF) distributions. In this "clustered-vMFs" approach, each estimated voxel fiber direction is associated with a component of the fitted mixture of vMF distributions. Hence, each voxel fiber principal direction may be specified by the summary statistics of the estimated vMF component in the mixture. Based on voxel ODF reconstructions, our method estimates intravoxel fiber directions by clustering mixtures of von Mises-Fischer distributions fitted to probabilistic distributions.

As opposed to other approaches where mixture of vMF distributions are used to represent diffusion, e.g., (Rathi et al., 2009), our method works directly with the sampled ODF distributions. Moreover, the proposed clustered-vMFs statistical procedure does not care for ODF reconstruction. The process of ODF reconstruction is kept independent from the process of statistical cluster estimation. The objective of the clustered-vMFs model is to gather statistical information in order to support robust probabilistic tractographic algorithms (Ferreira da Silva, 2012). Therefore, multiple ODF reconstruction approaches can be easily integrated in the proposed framework by a simple "plug-in" technique.

Before applying the clustered-vMFs approach we need to obtain the ODF profiles at each voxel. As pointed out in the Introduction, model-free methods and HARDI protocols are more adequate than current model-based methods for resolving complex orientations. Any of the model-free methods mentioned in the Introduction, (e.g., QBI, GQI, DSI), could be used for reconstructing ODF profiles. Starting with the raw HARDI signal acquired on a grid of q-space, the ODF profile is estimated at each voxel, considering a sampling density of unit vectors on a unit $\mathbb{S}^2$ grid or shell. To summarize anisotropic properties of the ODF and infer the underlying crossing patterns of the fibers we use the GFA metric (Tuch, 2004),

$$GFA = \sqrt{\frac{n\sum_{i=1}^{n}(\psi(\boldsymbol{u}_i) - \langle\psi\rangle)^2}{(n-1)\sum_{i=1}^{n}\psi(\boldsymbol{u}_i)^2}}, \quad (5)$$

where $\langle\psi\rangle = (1/n)\sum_{i=1}^{n}\psi(\boldsymbol{u}_i) = (1/n)$ is the mean of the ODF, $\langle\boldsymbol{u}\rangle$ is the mean diffusion direction, and $\langle.\rangle$ denotes the average over ψ. The GFA metric proposed in (Tuch, 2004), is an extension for HARDI protocols of the fractional anisotropy (FA) metric

commonly used in diffusion tensor imaging (DTI). When a threshold is applied to the estimated GFAs at each voxel, the non-thresholded unit vectors provide directional statistics information about the estimated ODF profile.

This directional clustering procedure has several advantages compared to traditional approaches for orientation mapping. In fact, current best practices perform multiple maxima extraction based on procedures which are very sensitive to the local modes that appear in the reconstructed ODFs. Signal noise and low sampling resolution yield deformed ODF reconstruction profiles, thus affecting accuracy and precision in multiple orientation evaluations. In contrast, estimating orientations from clustered directional data is much less sensitive to local modes in the reconstructed ODF profile. Moreover, the procedure is more robust to noise since it estimates orientations statistically from sampled data.

3 EXPERIMENTAL RESULTS

3.1 Fiber Bundle Simulation

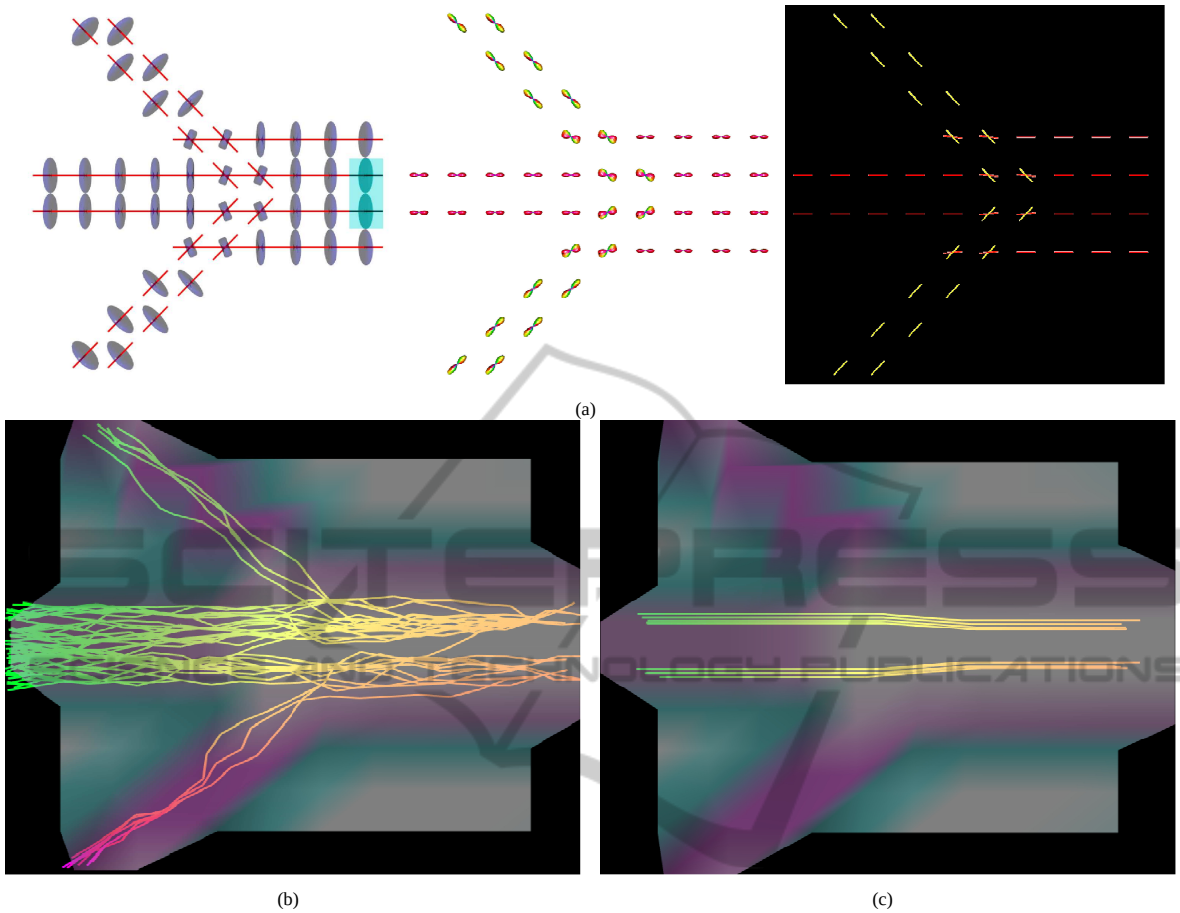
To validate the fiber tracking model described in Section 2 we performed simulations with synthetic fields of diffusion profiles. Firstly, we simulated diffusion profiles at each voxel by generating diffusion-weighted signals for single and multiple fibers simulations, using the method detailed in (Ferreira da Silva, 2013). Secondly, we estimated ODF profiles by applying the model-free GQI method to extract information about the extent of diffusion anisotropy, and map vector fields that represent the fiber orientations at each voxel. Thirdly, the clustered-vMFs approach was used to obtain summary statistics of the vMF components in the mixture of von Mises-Fisher distributions. Finally, the SMC algorithm was applied to guide probabilistic fiber tracking. The parameters of the clustered-vMFs approach at each voxel were used to propagate a cloud of particles, according to the fitted density probability for the fiber bundle trajectory being tracked. Based on the resampling strategy outlined in Section 2.1 for path tracking, we derive a map of fiber pathways for the simulated field of diffusion profiles.

Figure 1(a) shows an example of a simulated diffusion field of crossing bundles, the field of reconstructed ODF profiles, and the field of estimated principal directions. We specified two voxels as seed voxels (see the left panel of Figure 1(a)) and applied the probabilistic SMC algorithm to obtain the tracks represented in Figure 1(b). The SMC algorithm was applied with 100 particles and 5 fibers per seed voxel. For comparison purposes we have also applied a standard deterministic streamline tracking procedure to the same simulation. The streamline procedure follows the tractographic approach outlined in Mori and van Zijl (Mori and van Zijl, 2002) to map fiber tracts. As seen in Figure 1(c), the streamline algorithm is unable to resolve regions of crossing fiber configurations. Typically a single directional path is selected in these regions. In contrast, the probabilistic method is able to map multiple fiber pathways in crossing fiber regions.

3.2 Human Brain Data Experiments

In this Section we report on experiments using a DICOM data set provided by the "Advanced Biomedical MRI Lab, National Taiwan University Hospital". Specifically, we have used the data set "DSI 203-point 2mm" publicly available from `http://dsi-studio.labsolver.org/download-images`. This data set is from a normal 24-year-old male volunteer, and has been provided as a demonstration data set in connection with the "DSI Studio" software for diffusion MR images analysis (Yeh et al., 2010). The data set was obtained with an echo planar imaging diffusion sequence with twice-refocused echo, dimension $96 \times 96 \times 60$, and slice thickness 1.9 mm. Further details on the data set specification are available from the internet address mentioned above. We have tested our model with the two *b*-tables that accompanies the data set. One is a *b*-table for a $\mathbb{S}^2$-like grid denoted by "dsi203_bmax4000.txt". The other is the *b*-table for the 3D-DSI sampling scheme used in the DICOM data acquisition. This *b*-table has 203 points uniformly distributed on a 3D grid limited to the volume of the unit sphere. In both tables, the *b*-values range from 0 to 4000. The ODF reconstructions were performed with 321 points uniformly distributed on the unit S^2 hemisphere.

As for the simulation procedure outlined in Section 3.1, we obtained estimates of the voxels' ODF profiles using GQI basis functions. To summarize anisotropic properties of the ODF and infer the underlying crossing patterns of the fibers we used the GFA metric. A GFA threshold of 0.3 was applied on the normalized ODFs, prior to vMF clustering estimation. The SMC algorithm was then applied to estimate fiber paths. The following is a summary of tractography results applied to two Regions Of Interest (ROIs). For the first ROI, 43 seeds were placed along the Corpus Callosum (CC) region in sagittal view, as illustrated in Figure 2(a). We then applied the clustered-vMFs method followed by SMC to track the



(a)

(b) (c)

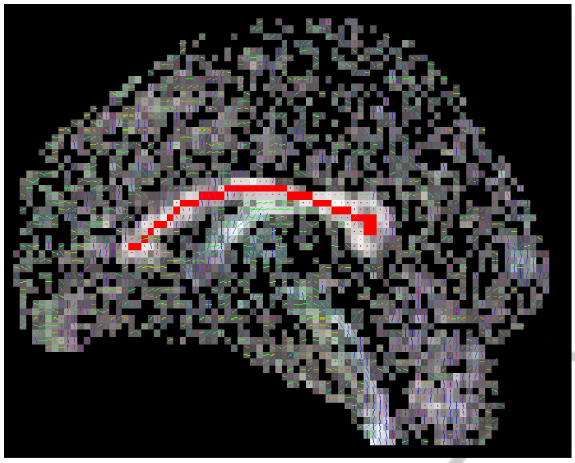
Figure 1: (a) Simulated diffusion field with seeds marked in light-blue rectangle (left panel), field of reconstructed ODF profiles (middle panel), and field of estimated principal directions (right panel); (b) Fiber pathways mapped using the proposed probabilistic approach; (c) Fiber pathways mapped using a standard streamline approach.

fiber paths from each seed by propagating 150 particles, for a maximum of 300 steps. Five starting fibers were randomly placed within each voxel for tracking initiation. All selected principal diffusion directions estimated for the seed voxel were tracked. Figure 2(b) shows tractography results of the corpus callosum for sagittal slice 48. For comparison purposes, the same ROI and seeds were used to drive a standard deterministic streamline algorithm. Similarly, 5 starting fibers were randomly placed within each voxel for tracking initiation. The results are shown in Figure 2(c).

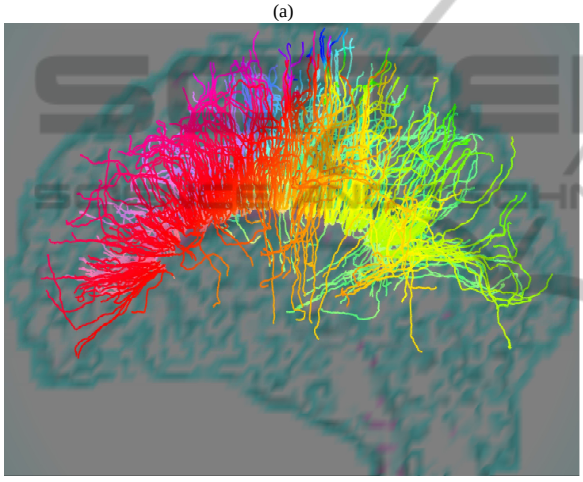
The second ROI used for testing was the corticospinal tract (CST), which connects the spinal cord to the cerebral motor cortex. Tractography of the CST is a challenging task. On the one hand, in some regions of the brain other fascicles may cross with the CST. On the other hand, the CST itself is made of several bifurcating sub-fascicles to ensure connections with the whole motor cortex. Unsurprisingly, standard deterministic streamline algorithms fail to map the CST accurately, because they are unable to cope with the complexity of bifurcating pathways. Five seeds used placed on each side of the CST-ROI bundle for coronal slice 53 as illustrated in Figure 3(a). This figure visualizes the location of the chosen seeds, by overlaying the GFA image with the first two main fiber directions at each voxel for coronal slice 53. Figure 3(b) shows tractography results of the CST for coronal slice 53 using the proposed approach. Figure 3(c) shows similar tractography results for the deterministic streamline algorithm.

4 CONCLUSIONS

We have presented a methodology to support improved probabilistic tractography in comparison with currently used approaches. The methodology builds statistical inferences at each voxel based on clusters of vMF distributions to drive sequential Monte Carlo



(a)



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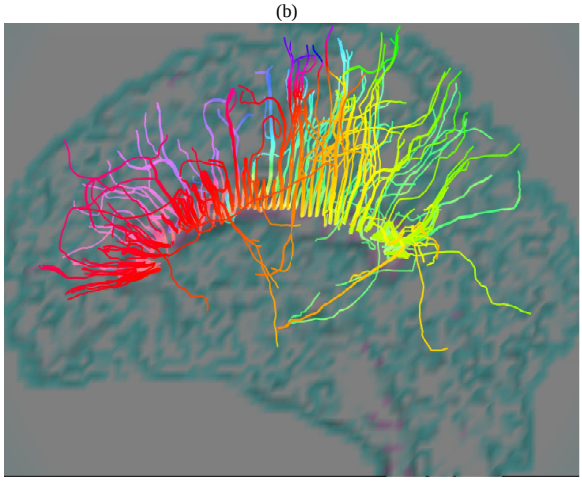
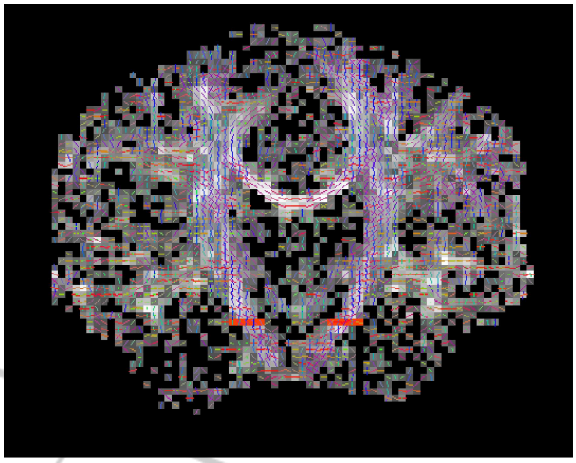
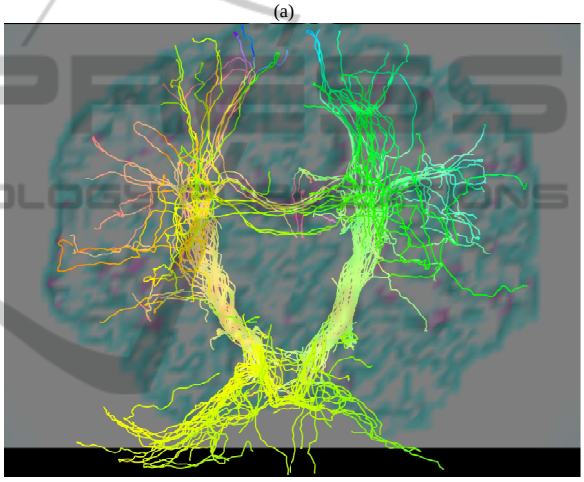


(c)

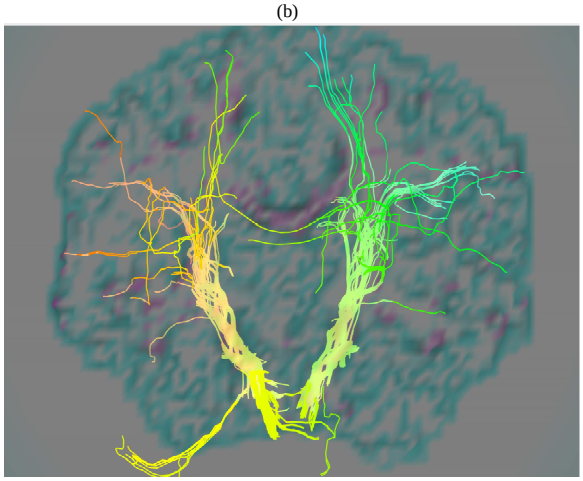
Figure 2: Corpus Callosum tractography: a) GFA image with seeds' locations in red; b) Probabilistic tractography using the proposed approach; c) Tractography using a standard streamline algorithm.



(a)



(b)



(c)

Figure 3: CST tractography: a) GFA image with seeds' locations in red; b) Probabilistic tractography using the proposed approach; c) Tractography using a standard streamline algorithm.

path estimates. We have shown how the improvement of fiber directional estimates can benefit the particle filtering tracking process. Moreover, by decoupling the two stages, statistical directional estimation and probabilistic fiber tracking, the proposed methodology is well-suited to support a wide range of methods for ODF reconstruction. The methodology provides a better account of white matter pathways in regions with complex fiber configuration than streamline-oriented approaches. However, comparing results of in vivo fiber tracking is a difficult task in general. In the future, we intend to test the proposed methodology for performing human brain connectivity analysis. Connectivity networks may provide alternative validation tools for quantitative comparisons.

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