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Dictionary-based Fiber Orientation Estimation with Improved Spatial Consistency

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Abstract

Diffusion magnetic resonance imaging (dMRI) has enabled *in vivo* investigation of white matter tracts. *Fiber orientation* (FO) estimation is a key step in tract reconstruction and has been a popular research topic in dMRI analysis. In particular, the sparsity assumption has been used in conjunction with a dictionary-based framework to achieve reliable FO estimation with a reduced number of gradient directions. Because image noise can have a deleterious effect on the accuracy of FO estimation, previous works have incorporated spatial consistency of FOs in the dictionary-based framework to improve the estimation. However, because FOs are only indirectly determined from the mixture fractions of dictionary atoms and not modeled as variables in the objective function, these methods do not incorporate FO smoothness directly, and their ability to produce smooth FOs could be limited. In this work, we propose an improvement *Fiber Orientation Reconstruction using Neighborhood Information* (FORNI), which we call FORNI+; this method estimates FOs in a dictionary-based framework where FO smoothness is better enforced than in FORNI alone. We describe an objective function that explicitly models the actual FOs and the mixture fractions of dictionary atoms. Specifically, it consists of data fidelity between the observed signals and the signals represented by the dictionary, pairwise FO dissimilarity that encourages FO smoothness, and weighted ℓ_1 -norm terms that ensure the consistency between the actual FOs and the FO configuration suggested by the dictionary representation. The FOs and mixture fractions are then jointly estimated by minimizing the objective function using an iterative alternating optimization strategy. FORNI+ was evaluated on a simulation phantom, a physical phantom, and real brain dMRI data. In particular, in the real brain dMRI experiment, we have qualitatively and quantitatively evaluated the reproducibility of the proposed method. Results demonstrate that FORNI+ produces FOs with better quality compared with competing methods.

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Graphical abstract

Keywords

diffusion MRI; dictionary-based FO estimation; spatial consistency; pairwise FO dissimilarity

1. Introduction

Diffusion magnetic resonance imaging (dMRI) captures the anisotropic water diffusion in tissue and enables *in vivo* reconstruction of white matter tracts (Johansen-Berg and Behrens, 2013). *Diffusion tensor imaging* (DTI) (Basser et al., 1994) is a basic dMRI strategy that models the water diffusion using a Gaussian distribution, yet it fails to represent crossing fiber tracts. More advanced *high angular resolution diffusion imaging* (HARDI) (Tuch et al., 2002) and *diffusion spectrum imaging* (DSI) (Wedeen et al., 2005) have been proposed to resolve crossing fibers.

The reconstruction of fiber tracts using fiber tracking (Mori et al., 1999; Basser et al., 2000; Reisert et al., 2011) or volumetric tract segmentation (Bazin et al., 2011; Nazem-Zadeh et al., 2011; Yendiki et al., 2011; Ye et al., 2015b) has been applied to many studies on the human brain (Vishwas et al., 2010; Phillips et al., 2009; Catheline et al., 2010). Tract reconstruction requires estimation of *fiber orientations* (FOs) at each voxel. In fiber tracking, the FOs inform the geometry of streamlines that represent the nerve fibers; in volumetric tract segmentation, the FOs are important features that determine the labels of tracts assigned to each voxel. Therefore, the estimation of FOs has been an important research topic in dMRI analysis.

Voxelwise FO estimation algorithms which estimate FOs at each voxel independently were developed first (Behrens et al., 2007; Tournier et al., 2007; Ramirez-Manzanares et al., 2007; Merlet and Deriche, 2013). In particular, dictionary-based FO estimation algorithms (Ramirez-Manzanares et al., 2007; Aranda et al., 2015; Daducci et al., 2014; Landman et al., 2011; Ye et al., 2015a) have been proposed, where diffusion signals are represented by a

dictionary encoded by discretized basis FOs. These methods take advantage of the sparsity of FOs and formulate FO estimation as a sparse reconstruction problem, which could use a lower number of dMRI acquisitions to reconstruct FOs of good quality and thus reduce image acquisition time (Aranda et al., 2015).

Because noise can have a deleterious effect on the accuracy of FO estimation, especially in regions where fibers cross, spatial regularization of FOs has been used to improve FO estimation (Pasternak et al., 2008; Reisert and Kiselev, 2011; Michailovich et al., 2011; Rath et al., 2014; Auría et al., 2015; Ye et al., 2016). In Michailovich et al. (2011) and Rath et al. (2014), smoothness of *diffusion weighted images* (DWIs) is added to the spherical ridgelets model, which indirectly promotes FO smoothness. In Reisert and Kiselev (2011) FO continuity is introduced as regularization terms in the spherical harmonics framework. In Pasternak et al. (2008), smoothness of diffusion tensors has been incorporated in the energy function to be minimized. However, sparsity of FOs is not considered in these methods. Other approaches have combined spatial consistency of FOs with FO sparsity in the dictionary-based framework. For example, Auría et al. (2015) and Ye et al. (2016) use weighted l_1 -norm regularization to encourage both FO sparsity and spatial consistency. However, in these dictionary-based methods the variables to be estimated are the mixture fractions of dictionary atoms, and FOs are indirectly determined as the basis directions associated with nonzero mixture fractions. The smoothness of FOs is not explicitly incorporated in the objective functions of these methods, which could limit the ability of these methods to produce smooth FOs.

In this work, we reformulate the FO estimation problem so that the regularization of pairwise FO dissimilarity between neighbors can be incorporated into the dictionary-based framework to improve FO estimation. The proposed algorithm is named FORNI+, which stands for an improvement to *Fiber Orientation Reconstruction using Neighborhood Information* (FORNI) (developed in (Ye et al., 2016)). We model the diffusion signals by a set of fixed prolate basis tensors. Each basis tensor represents a possible discretized FO, and the dictionary is computed from these basis tensors and the imaging parameters. Instead of using the discretized FOs associated with nonzero mixture fractions of dictionary atoms as the final FO estimates as in previous works (Landman et al., 2012; Ye et al., 2016; Auría et al., 2015), we introduce the use of actual FOs. Then, the actual FOs and mixture fractions of dictionary atoms are explicitly modeled in the objective function, which consists of data fidelity, pairwise FO dissimilarity, and weighted l_1 -norm terms that ensure the consistency between the actual FOs and the FO configuration suggested by the mixture fractions. The FOs and mixture fractions are then jointly estimated by minimizing the objective function using an iterative alternating strategy. We applied FORNI+ to a simulation phantom, a physical phantom, and real brain dMRI data. In particular, in the real brain dMRI experiment, we have qualitatively and quantitatively evaluated the reproducibility of the proposed method on five subjects each having two successive scans (10 dMRI scans in total).

The rest of the paper is organized as follows. Section 2 introduces the proposed algorithm for FO estimation. In Section 3, experiments on the phantoms and real brain dMRI are

presented. In Section 4, discussion on the results and future work is given, and we summarize the paper in Section 5.

2. Methods

In this section, we first give background on dictionary-based FO estimation and how spatial consistency of FOs has been used to improve FO estimation. Then, we describe the proposed approach that better enforces FO smoothness in the dictionary-based framework, where the design of the objective function and the optimization strategy are presented.

2.1. Background: Dictionary-based FO Estimation

Diffusion signals can be modeled using a fixed tensor basis (Ramirez-Manzanares et al., 2007; Landman et al., 2012; Ye et al., 2016; Auría et al., 2015), which consists of N prolate tensors $\{\mathbf{D}_i\}_{i=1}^N$ whose primary eigenvectors (PEVs) $\{\mathbf{v}_i\}_{i=1}^N$ are approximately evenly distributed over the unit hemisphere and represent possible FOs. The number of the basis tensors can range from about 100 to 300, and in this work we select $N = 289$, which results from successive tessellation of an octahedron. The primary eigenvalues ($\lambda_1 \geq \lambda_2 \geq \lambda_3 > 0$) of $\mathbf{D}_i$ can be determined by examining the tensors in noncrossing tracts, and λ_2 and λ_3 are set equal (Landman et al., 2012).

Suppose the diffusion signal $S_{k,m}$ voxel m is associated with a gradient direction $\mathbf{g}_k$ and a b -value b_k ($k = 1, \dots, K$), and $S_{0,m}$ is the b_0 signal (where no diffusion gradients are applied) at m . By defining $\mathbf{y}_m = (S_{1,m}/S_{0,m}, \dots, S_{K,m}/S_{0,m})^T$, we have (Landman et al., 2012)

$$\mathbf{y}_m = \mathbf{G} \mathbf{f}_m + \boldsymbol{\eta}_m, \quad (1)$$

where $\mathbf{G} \in \mathbb{R}^{K \times N}$ is a dictionary matrix with $G_{ki} = e^{-b_k \mathbf{g}_k^T \mathbf{D}_i \mathbf{g}_k}$, $\mathbf{f}_m = (f_{m1}, \dots, f_{mN})^T$ consists of the unknown nonnegative mixture fractions of dictionary atoms, and $\boldsymbol{\eta}_m$ is a noise term.

Assuming the number of FOs at each voxel is small with respect to the number of gradient directions used in dMRI acquisition, the mixture fractions can be estimated by solving a sparse reconstruction problem (Ramirez-Manzanares et al., 2007; Landman et al., 2012)

$$\hat{\mathbf{f}}_m = \arg \min_{\mathbf{f}_m \geq 0} \|\mathbf{G} \mathbf{f}_m - \mathbf{y}_m\|_2^2 + \beta \|\mathbf{f}_m\|_1, \quad (2)$$

where β is a weighting constant. Then, basis directions with nonzero mixture fractions can be interpreted as FOs at voxel m . In practice, to account for the effect of noise, only basis directions associated with mixture fractions above a threshold f_{th} (Landman et al., 2012; Ye et al., 2016) are interpreted as FOs

$$\Omega_m = \{v_i | f_{mi} > f_{th}\}. \quad (3)$$

The choice of the threshold f_{th} has been investigated in Ye et al. (2016), and in this work we follow the suggestions given in Ye et al. (2016) and use $f_{th} = 0.1$.

The quality of FO estimation can be affected by image noise that is inherent in the acquisition, especially in regions with crossing fibers. Therefore, to prove the accuracy of the estimation, spatial consistency of FOs has been incorporated in the dictionary-based framework. Specifically, Ye et al. (2016) and Auría et al. (2015) replace the ℓ_1 -norm with weighted ℓ_1 -norm that encodes the interaction between neighbor voxels. For example, in Ye et al. (2016) the problem is formulated as

$$\{\hat{f}_m\}_{m=1}^M = \arg \min_{f_1, \dots, f_M \geq 0} \sum_{m=1}^M \|\mathbf{G} f_m - \mathbf{y}_m\|_2^2 + \beta \|\mathbf{C}_m f_m\|_1, \quad (4)$$

where M is the total number of voxels and $\mathbf{C}_m$ is a diagonal weighting matrix at m determined by the FOs (suggested by the mixture fractions) in the neighbors. $\mathbf{C}_m$ places small penalties on the mixture fractions associated with basis directions that are consistent with neighbor FOs so that spatial consistency is enforced. Since all the mixture fractions (and thus FOs) are to be estimated and coupled in the weighted ℓ_1 -norm, Eq. (4) is solved iteratively using a block coordinate descent strategy.

2.2. Incorporation of Pairwise FO Dissimilarity

Because in the objective functions of Ye et al. (2016) and Auría et al. (2015) the variables to be estimated are the mixture fractions of dictionary atoms, terms that explicitly represent the smoothness of FOs, such as pairwise dissimilarity of FOs, are not incorporated, and the ability to produce smooth FOs is limited. Note that the pairwise difference of mixture fractions only encourages identical FOs instead of smooth FOs (Ye et al., 2016) and is therefore not ideal for enforcing FO smoothness. In this work, we seek to improve FO estimation by making terms of FO smoothness compatible with the dictionary-based framework. To achieve this, instead of first estimating the mixture fractions of dictionary atoms and then determining FOs as basis directions associated with sufficiently large mixture fractions, we explicitly treat FOs as variables to be estimated. The details of our design are provided in the following sections. For readers' convenience, a list of the major symbols used in the proposed method is summarized in Table 1.

2.2.1. Objective Function Design—To relate the actual FOs with the dictionary-based framework, we assume that 1) there is a correspondence between the actual FOs and the discrete FOs suggested by the mixture fractions of basis directions; 2) the mixture fractions of the actual FOs can be approximated by the mixture fractions of the corresponding basis directions. Hereafter, we will refer to the actual FOs as FOs for simplicity. Suppose the FOs

and their mixture fractions at m are $\Omega_m = \{\omega_{mp}\}_{p=1}^{|\Omega_m|}$ and $\mathcal{H}_m = \{h_{mp}\}_{p=1}^{|\Omega_m|}$, respectively, where $|\Omega_m|$ is the cardinality of Ω_m . We choose to order h_{mp} ($p = 1, \dots, |\Omega_m|$) (and thus the corresponding ω_{mp}) in a descending order ($h_{m1} \dots h_{m|\Omega_m|}$), so that h_{mp} is the p -th largest element in $\mathbf{f}_m$ (note the correspondence between the actual FOs and dictionary representation). For convenience, we denote this simple mapping from $\mathbf{f}_m$ to h_{mp} by

$$h_{mp} = T_p(\mathbf{f}_m). \quad (5)$$

Note that the FOs are ordered simply for convenience of notation, and the choice of ordering does not affect our algorithm.

We want to ensure that the FOs are consistent with the mixture fractions of dictionary atoms (and thus their suggested discrete FOs) and that the FOs are spatially smooth. To achieve this, we use the following minimization problem

$$\begin{aligned} & \min_{\{\mathbf{f}_m\}_{m=1}^M, \{\Omega_m\}_{m=1}^M, \{\mathcal{H}_m\}_{m=1}^M, \{b_{mpnq}\}_{m=1}^M} \sum_{m=1}^M \left(\underbrace{\|\mathbf{G}\mathbf{f}_m - \mathbf{y}_m\|_2^2}_{E_1} \right. \\ & \quad + \underbrace{\beta \|\mathbf{C}_m \mathbf{f}_m\|_1}_{E_2} \\ & \quad \left. + \gamma \underbrace{\sum_{n \in \mathcal{N}_m} \sum_{p=1}^{|\Omega_m|} \sum_{q=1}^{|\Omega_n|} b_{mpnq} d^2(\omega_{mp}, \omega_{nq})}_{E_3} \right) \text{ s.t. } \mathbf{f}_m \geq \mathbf{0}, w_{mpnq} \geq 0, h_{mp} = T_p(\mathbf{f}_m), \sum_{q=1}^{|\Omega_n|} b_{mpnq} \\ & \quad = h_{mp}, \sum_{p=1}^{|\Omega_m|} b_{mpnq} = h_{nq}, \end{aligned} \quad (6)$$

where E_1 , E_2 , and E_3 enforce data fidelity, consistency between FOs and mixture fractions of dictionary atoms, and smoothness of FOs, respectively. β and γ are weights for E_2 and E_3 , respectively. The design of these terms is explained in the following paragraphs.

E_1 ensures the agreement between the observed signals and the reconstructed signals using the dictionary representation. When the *signal-to-noise ratio* (SNR) is sufficiently high (above 3:1), Rician image noise can be approximated by a Gaussian distribution (Gudbjartsson and Patz, 1995). Therefore, the squared difference (ℓ_2 -norm) in E_1 is commonly used to describe the disagreement between the observed and reconstructed diffusion signals (Landman et al., 2012; Daducci et al., 2014).

E_2 ensures the consistency between the FOs and mixture fractions of dictionary atoms using weighted ℓ_1 -norm regularization terms, where $\mathbf{C}_m$ is a diagonal matrix encoded by the FOs; the weighted ℓ_1 -norm can also promote the sparsity of the mixture fractions of dictionary atoms (Ye et al., 2016; Auría et al., 2015). Although E_2 seemingly resembles the use of weighted ℓ_1 -norm in Ye et al. (2016) and Auría et al. (2015), the purpose and actual design are quite different. In Ye et al. (2016) and Auría et al. (2015), the weighted ℓ_1 -norm enforces spatial consistency of FOs by encouraging consistent mixture fractions in the neighborhood; here, the weighted ℓ_1 -norm encourages the agreement between the FOs and the FO configurations suggested by the dictionary atoms, and the FOs need to be explicitly modeled.

In E_2 , the diagonal entries $C_{m,i}$ ($i = 1, \dots, N$) of $\mathbf{C}_m$ are designed as

$$C_{m,i} = 1 - \frac{\alpha}{|\tilde{\mathcal{N}}_m|} \sum_{n \in \tilde{\mathcal{N}}_m} \text{mind}_q(\omega_{nq}, \mathbf{v}_i) \leq \theta \left(1 - \frac{4}{\pi^2} \text{mind}_q^2(\omega_{nq}, \mathbf{v}_i) \right), \quad (7)$$

where $\tilde{\mathcal{N}}_m = \mathcal{N}_m \cup \{m\}$ is the union of m and its 6-connected neighborhood $\mathcal{N}_m$, $|\tilde{\mathcal{N}}_m|$ is the cardinality of $\tilde{\mathcal{N}}_m$, α is a constant controlling the interaction between the FOs and the mixture fractions of dictionary atoms, θ is a threshold, $\mathcal{A}(\cdot, \cdot) = |\arccos(\cdot, \cdot)| \in [0, \pi/2]$ measures the difference between two orientations, and $\text{mind}_q(\omega_{nq}, \mathbf{v}_i) \leq \theta$ is an indicator function

$$\text{mind}_q(\omega_{nq}, \mathbf{v}_i) \leq \theta = \begin{cases} 1, & \text{if } \text{mind}_q(\omega_{nq}, \mathbf{v}_i) \leq \theta \\ 0, & \text{if } \text{mind}_q(\omega_{nq}, \mathbf{v}_i) > \theta \end{cases}. \quad (8)$$

Because orientations that are too far away are not considered to have correspondence, it is desired that they have no influence on each other (Auría et al., 2015; Sigurdsson and Prince, 2014). Therefore, using the indicator function in Eq. (8), when the angle between $\mathbf{v}_i$ and its closest ω_{nq} in voxel n is greater than θ , no consistency between them is assumed in Eq. (7). If all FOs in $\tilde{\mathcal{N}}_m$ are more than θ away from $\mathbf{v}_i$, the weight is the same as that when no information in $\tilde{\mathcal{N}}_m$ is used. When the FOs in $\tilde{\mathcal{N}}_m$ are close to the basis direction $\mathbf{v}_i$, the weight for f_{mi} is small and f_{mi} is encouraged to be nonzero; in turn, the FOs that are inconsistent with the discrete FOs suggested by the mixture fractions are discouraged. In this way, the agreement between the FOs and the dictionary-based sparse representation is ensured. Note that the use of $\tilde{\mathcal{N}}_m$ allows consistency between the FOs and the dictionary representation not only at m but also in a neighborhood, which better takes advantage of the spatial information. We select $\theta = \pi/4$ (Sigurdsson and Prince, 2014) and let $\alpha \in [0, 1)$ so that $C_{m,i} \in (0, 1]$.

E_3 is designed to explicitly ensure FO smoothness according to Sigurdsson and Prince (2014). The dissimilarity between the FOs at voxel m and the FOs in the neighborhood of m is represented as a weighted sum of pairwise FO dissimilarities in Eq. (6), where b_{mpnq} is the (unknown) nonnegative weight of the interaction between two FOs ω_{mp} and ω_{nq} . Note

that the constraints $\sum_q b_{mpnq} = h_{mp}$ and $\sum_p b_{mpnq} = h_{nq}$ in Eq. (6) are used to reflect the fractional contributions of FOs. For example, suppose the mixture fraction of an FO is small; then the sum of the dissimilarity weights that involve this FO should also be small. For convenience, we denote the set of all b_{mpnq} as $\mathbf{B}$. Note that although the term E_3 is borrowed from Sigurdsson and Prince (2014), the optimization strategy in Sigurdsson and Prince (2014) cannot be trivially transferred into the proposed framework and some careful manipulation has to be made for the optimization, which will be seen later.

Algorithm 1 The Optimization Strategy of FORNI+

Input: Diffusion signals: $\{\mathbf{y}_m\}_{m=1}^M$; maximum number of iterations: $t_{\max}$; the initialization of FOs: $\{\Omega_m^0\}_{m=1}^M$; the iteration number starts from $t = 1$;

Output: FOs: $\{\Omega_m\}_{m=1}^M$; mixture fractions of FOs: $\{\mathcal{H}_m\}_{m=1}^M$; weights of similarity between neighboring FOs: $\mathbf{B}$; mixture fractions of dictionary atoms: $\{\mathbf{f}_m\}_{m=1}^M$

```

1:
    Initialize FOs:  $\{\Omega_m\}_{m=1}^M := \{\Omega_m^0\}_{m=1}^M$ 
2:   while  $t < t_{\max}$  do
3:     Fix  $\{\Omega_m\}_{m=1}^M$ ,  $\{\mathcal{H}_m\}_{m=1}^M$ , and  $\mathbf{B}$ , and solve for  $\{\mathbf{f}_m\}_{m=1}^M$  using Eq. (9)
4:     Apply Eq. (5) to compute  $\{\mathcal{H}_m\}_{m=1}^M$  and reinitialize  $\{\Omega_m\}_{m=1}^M$  using  $\{\mathbf{f}_m\}_{m=1}^M$ 
5:     Fix  $\{\mathbf{f}_m\}_{m=1}^M$ ,  $\{\mathcal{H}_m\}_{m=1}^M$ , and  $\{\Omega_m\}_{m=1}^M$ , and solve for  $\mathbf{B}$  using Eq. (12)
6:     Fix  $\{\mathbf{f}_m\}_{m=1}^M$ ,  $\{\mathcal{H}_m\}_{m=1}^M$ , and  $\mathbf{B}$ , and solve for  $\{\Omega_m\}_{m=1}^M$  using Eq. (13)
7:      $t = t + 1$  until convergence
8:   end while
9:   return  $\{\Omega_m\}_{m=1}^M$ ,  $\{\mathcal{H}_m\}_{m=1}^M$ ,  $\mathbf{B}$ , and  $\{\mathbf{f}_m\}_{m=1}^M$ 

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2.2.2. Optimization of the Objective Function—To solve Eq. (6), we use an iterative alternating optimization strategy as outlined in Algorithm 1. The FOs are initialized using the FORNI algorithm (Ye et al., 2016). At iteration t , we sequentially update the variables to be estimated as presented below.

First, we relax the constraint $h_{mp} = T_p(\mathbf{f}_m)$, fix $\{\Omega_m, \mathcal{H}_m\}_{m=1}^M$ and $\mathbf{B}$, and solve for $\{\mathbf{f}_m\}_{m=1}^M$. Because $\mathbf{C}_m$ is known when $\{\Omega_m\}_{m=1}^M$ is fixed, $\{\mathbf{f}_m\}_{m=1}^M$ can be estimated by solving a voxelwise weighted ℓ_1 -norm regularized least squares problem:

$$\mathbf{f}_m^t = \arg \min_{\mathbf{f}_m \geq 0} \|\mathbf{G} \mathbf{f}_m - \mathbf{y}_m\|_2^2 + \beta \|\mathbf{C}_m^{t-1} \mathbf{f}_m\|_1. \quad (9)$$

Here $\mathbf{C}_m^{t-1}$ is computed from the FOs $\{\Omega_m^{t-1}\}_{m=1}^M$ at iteration $t-1$ using Eq. (7). To solve Eq. (9), we follow a simple strategy proposed in Ye et al. (2015a), where a new variable $\mathbf{a}_m = \mathbf{C}_m^{t-1} \mathbf{f}_m$ is introduced. Since $\mathbf{C}_m^{t-1}$ is diagonal and $C_{m,i}^{t-1} > 0$, $\mathbf{C}_m$ is invertible. Therefore, we have

$$\hat{\mathbf{a}}_m = \arg \min_{\mathbf{a}_m \geq 0} \|\tilde{\mathbf{G}}_m \mathbf{a}_m - \mathbf{y}_m\|_2^2 + \beta \|\mathbf{a}_m\|_1, \quad (10)$$

where $\tilde{\mathbf{G}}_m = \mathbf{G}(\mathbf{C}_m^{t-1})^{-1}$. $\hat{\mathbf{a}}_m$ is computed using the optimization method in Kim et al. (2007) and $\mathbf{f}_m^t$ is then given as

$$\mathbf{f}_m^t = (\mathbf{C}_m^{t-1})^{-1} \hat{\mathbf{a}}_m. \quad (11)$$

Second, we fix $\{\mathbf{f}_m, \mathcal{H}_m, \Omega_m\}_{m=1}^M$, and solve for $\mathbf{B}$. We notice that with the updated $\mathbf{f}_m^t$, higher quality estimates of FOs and their mixture fractions $\mathcal{H}_m$ can be obtained. Therefore, we apply $h_{mp}^t = T_p(\mathbf{f}_m^t)$ for each m and p , and reinitialize $\{\Omega_m\}_{m=1}^M$ at iteration t as $\{\Omega_m^{t,0}\}_{m=1}^M$ ($\Omega_m^{t,0} = \{\omega_{mp}^{t,0}\}_{p=1}^{|\Omega_m^{t,0}|}$) using $\mathbf{f}_m^t$ and Eq. (3). This reinitialization also encourages the correspondence between the actual FOs and the dictionary representation. Then, we have

$$\underset{\mathcal{B}}{\text{minimize}} \sum_{p=1}^{|\Omega_m^{t,0}|} \sum_{q=1}^{|\Omega_n^{t,0}|} b_{mpnq} d^2(\omega_{mp}^{t,0}, \omega_{nq}^{t,0}) \text{ s.t. } b_{mpnq} \geq 0, \sum_{q=1}^{|\Omega_n^{t,0}|} b_{mpnq} = h_{mp}^t, \sum_{p=1}^{|\Omega_m^{t,0}|} b_{mpnq} = h_{nq}^t, \quad (12)$$

which can be solved using linear programming.

Third, we fix $\{\mathbf{f}_m, \mathcal{H}_m\}_{m=1}^M$ and $\mathbf{B}$, and solve for $\{\Omega_m\}_{m=1}^M$, which leads to

$$\{\Omega_m^t\}_{m=1}^M = \arg \min_{\{\Omega_m\}_{m=1}^M} \sum_{m=1}^M \beta \|\mathbf{C}_m \mathbf{f}_m^t\|_1 + \gamma \sum_{m=1}^M \sum_{n \in \mathcal{N}_m} \sum_{p=1}^{|\Omega_m^t|} \sum_{q=1}^{|\Omega_n^t|} b_{mpnq}^t d^2(\omega_{mp}^t, \omega_{nq}^t). \quad (13)$$

Whereas in Sigurdsson and Prince (2014) only the weighted sum of neighbor FO dissimilarities needs to be minimized, here we have additional terms involving the weighted ℓ_1 -norm due to the interaction between the FOs and mixture fractions of dictionary atoms in $\mathbf{C}_m$. Therefore, the optimization method in Sigurdsson and Prince (2014) cannot be directly used for the update of $\{\Omega_m\}_{m=1}^M$. To derive a minimization strategy, we rewrite the weighted ℓ_1 -norm using Eq. (7)

$$\|\mathbf{C}_m \mathbf{f}_m^t\|_1 = \sum_{i=1}^N \left(f_{mi}^t - \frac{\alpha f_{mi}^t}{|\tilde{\mathcal{N}}_m|} \sum_{n \in \tilde{\mathcal{N}}_m} \min_{q} d(\boldsymbol{\omega}_{nq}, \mathbf{v}_i) \leq \theta \left(1 - \frac{4}{\pi^2} \min_{q} d^2(\boldsymbol{\omega}_{nq}, \mathbf{v}_i) \right) \right). \quad (14)$$

Using the initialization $\{\Omega_m^{t,0}\}_{m=1}^M$ of FOs at iteration t , we can make approximations in Eq. (14) to allow us to solve a simpler problem. Specifically, letting $\tilde{q}_{ni} = \arg \min_q d^2(\boldsymbol{\omega}_{nq}^{t,0}, \mathbf{v}_i)$, where $\tilde{q}_{ni}$ represents the index of the current FO in voxel n that is closest to the basis direction $\mathbf{v}_i$, we use the approximation $\min_q d(\boldsymbol{\omega}_{nq}, \mathbf{v}_i) \leq \theta \approx d(\boldsymbol{\omega}_{n\tilde{q}_{ni}}^{t,0}, \mathbf{v}_i) \leq \theta$ and $\min_q d^2(\boldsymbol{\omega}_{nq}, \mathbf{v}_i) \approx d^2(\boldsymbol{\omega}_{n\tilde{q}_{ni}}^{t,0}, \mathbf{v}_i)$. Therefore, the interaction between $\mathbf{v}_i$ and the actual FOs in voxel n is considered only when the difference between $\mathbf{v}_i$ and the current estimate of $\mathbf{v}_i$'s closest FO in voxel n is no more than θ , and during optimization the difference between $\mathbf{v}_i$ and its closest FO in voxel n is approximated by the difference between $\mathbf{v}_i$ and the FO that is currently closest to $\mathbf{v}_i$. Then, we have

$$\{\Omega_m^t\}_{m=1}^M = \arg \min_{\{\Omega_m\}_{m=1}^M} \sum_{m=1}^M \sum_{i=1}^N \frac{4\alpha\beta f_{mi}^t}{\pi^2\gamma|\tilde{\mathcal{N}}_m|} \sum_{n \in \tilde{\mathcal{N}}_m} d(\boldsymbol{\omega}_{n\tilde{q}_{ni}}^{t,0}, \mathbf{v}_i) \leq \theta d^2(\boldsymbol{\omega}_{n\tilde{q}_{ni}}^{t,0}, \mathbf{v}_i) + \sum_{m=1}^M \sum_{n \in \tilde{\mathcal{N}}_m} \sum_{p=1}^{|\Omega_m|} \sum_{q=1}^{|\Omega_n|} b_{mpnq}^t d^2(\boldsymbol{\omega}_{mp}, \boldsymbol{\omega}_{nq}). \quad (15)$$

Eq. (15) minimizes the weighted sum of the differences 1) between FOs and their associated fixed discrete FOs suggested by the dictionary-based sparse representation and 2) between interacting neighbor FOs, which is better seen after rewriting it as

$$\{\Omega_m^t\}_{m=1}^M = \arg \min_{\{\Omega_m\}_{m=1}^M} \sum_{m=1}^M \sum_{p=1}^{|\Omega_m|} \left(\sum_{\tilde{p}=1}^{U_{mp}^t} \frac{4\alpha\beta g_{mp\tilde{p}}^t}{\pi^2\gamma|\tilde{\mathcal{N}}_m|} d^2(\boldsymbol{\omega}_{mp}, \mathbf{u}_{mp\tilde{p}}^t) + \sum_{\tilde{q}=1}^{V_{mp}^t} \tilde{b}_{mp\tilde{q}}^t d^2(\boldsymbol{\omega}_{mp}, \tilde{\boldsymbol{\omega}}_{mp\tilde{q}}^t) \right), \quad (16)$$

where

$$\mathcal{U}_{mp}^t = \{(g_{mp\tilde{p}}^t, \mathbf{u}_{mp\tilde{p}}^t)\}_{\tilde{p}=1}^{U_{mp}^t} = \{(f_{ni}^t, \mathbf{v}_i) | n \in \tilde{\mathcal{N}}_m, i=1, \dots, N, f_{ni}^t > f_{th}, p = \arg \min_{\tilde{p}} d(\boldsymbol{\omega}_{m\tilde{p}}^{t,0}, \mathbf{v}_i), d(\boldsymbol{\omega}_{mp}^{t,0}, \mathbf{v}_i) \leq \theta\}, \quad (17)$$

$$\mathcal{V}_{mp}^t = \{(\tilde{b}_{mp\tilde{q}}^t, \tilde{\omega}_{mp\tilde{q}})\}_{\tilde{q}=1}^{V_{mp}^t} = \{(b_{mpnq}^t, \omega_{nq}) | n \in \mathcal{N}_m, q=1, \dots, |\Omega_m|\}. \quad (18)$$

Here, $\mathbf{u}_{m\tilde{p}}^t$ represents a fixed FO currently suggested by the dictionary representation in m or m 's neighbor voxel, and among all the currently estimated actual FOs at m , the p -th actual FO is closest to and no more than θ away from this FO suggested by the dictionary representation. $g_{m\tilde{p}}^t$ is the mixture fraction of $\mathbf{u}_{m\tilde{p}}^t$. $\tilde{\omega}_{mp\tilde{q}}$ is just another way of writing all the unknown FOs ω_{nq} in the neighbors of m , and $\tilde{b}_{mp\tilde{q}}^t$ is the current estimate of the weight for the interaction between $\tilde{\omega}_{mp\tilde{q}}$ and ω_{mp} . $\mathcal{U}_{mp}^t$ and $\mathcal{V}_{mp}^t$ are used to conveniently represent the set of the pairs $(\mathbf{u}_{m\tilde{p}}^t, g_{m\tilde{p}}^t)$ and $(\tilde{\omega}_{mp\tilde{q}}, \tilde{b}_{mp\tilde{q}}^t)$, respectively, and U_{mp}^t and V_{mp}^t are the cardinality of $\mathcal{U}_{mp}^t$ and $\mathcal{V}_{mp}^t$, respectively.

Algorithm 2 Weighted Average of FOs

Input: FOs $\omega = \{\omega_r\}_{r=1}^R$ to average; weights $\gamma = \{\gamma_r\}_{r=1}^R$ of the FOs; the current FO ω_{mp}

Output: Averaged FO $\bar{\omega}$

```

1:  $\bar{\omega} \leftarrow \mathbf{0}$ 
2: for  $r = 1 : R$  do
3:   if  $\omega_r^T \omega_{mp} < 0$  then
4:      $\omega_r \leftarrow -\omega_r$ 
5:   end if
6:    $\bar{\omega} \leftarrow \bar{\omega} + \gamma_r \omega_r$ 
7: end for
8:    $\bar{\omega} \leftarrow \frac{\bar{\omega}}{\|\bar{\omega}\|_2}$ 
return

```

By analogy to Sigurdsson and Prince (2014), Eq. (16) can now be solved by iteratively updating each FO using the weighted sum of the neighbor FOs and the fixed basis directions. Note that unlike Sigurdsson and Prince (2014) where only the FOs in the neighborhood are involved, Eq. (18) also considers the agreement between the FOs and the FO configuration suggested by the dictionary representation. The update can be written as

$$\omega_{mp} \leftarrow \text{weightedAverage}(\omega, \gamma, \omega_{mp}), \quad (19)$$

where

$$\boldsymbol{\omega} = (\mathbf{u}_{mp1}^t, \dots, \mathbf{u}_{mpU_{mp}^t}^t, \boldsymbol{\omega}_{mp}, \tilde{\mathbf{w}}_{mp1}, \dots, \tilde{\mathbf{w}}_{mpV_{mp}^t}) \quad (20)$$

$$\boldsymbol{\gamma} = \frac{\left(\frac{4\alpha\beta g_{mp1}^t}{\pi^2 \gamma |\mathcal{N}_m|}, \dots, \frac{4\alpha\beta g_{mpU_{mp}^t}^t}{\pi^2 \gamma |\mathcal{N}_m|}, |\mathcal{N}_m| h_{mp}, \tilde{b}_{mp1}^t, \dots, \tilde{b}_{mpV_{mp}^t}^t \right)}{\sum_{\tilde{p}=1}^{U_{mp}^t} \frac{4\alpha\beta g_{mp\tilde{p}}^t}{\pi^2 \gamma |\mathcal{N}_m|} + 2|\mathcal{N}_m| h_{mp}}. \quad (21)$$

Here, $\boldsymbol{\omega}$ contains the vectors used in the weighted average and $\boldsymbol{\gamma}$ contains the weights of these vectors; $\text{weightedAverage}(\cdot, \cdot, \cdot)$ is a function for approximating weighted averages of FOs whose dissimilarity is defined by $\mathcal{d}(\cdot, \cdot)$ (Sigurdsson and Prince, 2014), and its definition is given in Algorithm 2.

3. Results

FORNI+ was evaluated on simulated data, a physical dMRI phantom, and real brain dMRI data both qualitatively and quantitatively. Because in Ye et al. (2016) a number of algorithms that perform voxelwise FO estimation (Landman et al., 2012; Merlet and Deriche, 2013; Tournier et al., 2007) or estimate FOs with the regularization of FO spatial consistency (Ye et al., 2016; Sigurdsson and Prince, 2014; Auría et al., 2015) have already been compared, in this work we selected two representative algorithms for comparison, which are CFARI (Landman et al., 2012) that estimates FOs in each voxel independently and FORNI (Ye et al., 2016) that incorporates spatial consistency of FOs in the estimation. In particular, in Ye et al. (2016) FORNI was found to have the best performance. CFARI, FORNI, and FORNI+ are implemented in the JIST software framework (Lucas et al., 2010).

3.1. Digital Crossing Phantom

A 3D digital simulation phantom was created to evaluate the proposed method. The geometry of the fiber tracts in the phantom is shown in Figure 1. The phantom contains regions that are occupied by a single tract, two crossing tracts, and three crossing tracts, respectively. One b_0 image and 30 gradient directions ($b = 1000 \text{ s/mm}^2$) were used for simulation. The diffusion signals were synthesized using a tensor model in noncrossing regions, and a two-tensor/three-tensor model in regions with two/three crossing tracts. The eigenvalues of each tensor are $\lambda_1 = 2.0 \times 10^{-3} \text{ mm}^2/\text{s}$ and $\lambda_2 = \lambda_3 = 0.5 \times 10^{-3} \text{ mm}^2/\text{s}$, leading to a *fractional anisotropy* (FA) of 0.71 and a *mean diffusivity* (MD) of $1.0 \times 10^{-3} \text{ mm}^2/\text{s}$ in single FO regions. The resolution is 1 mm isotropic.

Rician noise was added to the diffusion weighted signals. We first investigated the case where $\text{SNR} = 20$ on the b_0 image, because it has an SNR level similar to that of the real brain dMRI data tested in this work. The proposed method (with empirically determined parameters $(\alpha, \beta, \gamma) = (0.9, 0.3, 1.0)$) was then applied to this simulation phantom.

A qualitative evaluation is given in Figure 2, where cross-sectional views of ground truth FOs and the FOs estimated by CFARI, FORNI, and FORNI+ are shown and compared. Note that because the FOs in the vertical direction are not visible in the axial view, we also show a coronal view of the area highlighted in the axial view in Figure 2. We can see that the FORNI+ results resemble the ground truth, and that FORNI+ better resolves crossing FOs and produces smoother FOs than CFARI and FORNI.

We evaluated the proposed method quantitatively using the FO error measure in Ye et al. (2016), which measures the difference between the FO estimates and the ground truth. The boxplots of the FO errors over the entire phantom and in the subregions are shown in Figure 3, where the FORNI+ results are compared with those of CFARI (Landman et al., 2011) and FORNI (Ye et al., 2016). In all cases, FORNI+ produces more accurate FOs than CFARI and FORNI, and the improvement is most prominent in regions with three crossing tracts. Wilcoxon signed-rank tests were also performed for comparison, where the differences between FORNI+ and the competing algorithms are all highly significant ($p < 0.001$).

Fiber tracking was then performed using the estimated FOs. We used a streamlining strategy similar to Descoteaux et al. (2009) and Yeh et al. (2010). Specifically, starting from a seed voxel, the streamline is propagated by a fixed step size s in the propagation direction. The propagation direction at each location is computed from trilinear interpolation using the FOs at grid points. Because multiple FOs can exist at a grid point, the FO that is most aligned with the previous propagation direction is considered in the interpolation. Fiber tracking is terminated if FA in the current voxel is lower than a threshold t_{FA} or the angle between the current and previous propagation directions is larger than θ_t . In this work, we used $s = 1$ mm, $t_{FA} = 0.15$, and $\theta_t = 45^\circ$, which are common settings in fiber tracking (Clark et al., 2003; Ro et al., 2013). The tracking results are shown in Figure 4. The streamlines are color-coded by the orientation of each segment using the standard DTI color scheme (red: left-right; green: front-back; and blue: up-down) (Pajevic and Pierpaoli, 1999). Because of the symmetric tract geometry, we placed three seeds in the noncrossing regions of three tracts (see Figure 4). Consistent with the tract geometry shown in Figure 1, FORNI+ produces correct crossing fibers, and the streamlines are also smoother than the CFARI and FORNI results.

We also investigated how initialization affects FO estimation in FORNI+. We compared the results initialized by CFARI and FORNI, and the means and standard deviations of FO errors are shown in Table 2. The performances using the two initializations are similar and both better than CFARI or FORNI (see Figure 3). The initialization using the FORNI results gives slightly lower errors. These results indicate that FORNI+ can still perform well with a relatively worse initialization (CFARI), and also justify our use of FORNI for initialization.

Next, we studied the effect of the parameters α , β , and γ . Different combinations of $\alpha \in \{0.5, 0.7, 0.9, 0.99\}$, $\beta \in \{0.1, 0.3, 0.5\}$, and $\gamma \in \{0, 0.1, 1.0, 10.0\}$ were tested, and the average errors over the entire phantom are plotted in Figure 5. Note that when $\gamma = 0$, no regularization of pairwise FO difference is used. We observe that when $\gamma \neq 0$, the estimation error is greatly decreased compared with the cases where $\gamma = 0$, indicating the benefit of

introducing the constraint of pairwise FO dissimilarity. With nonzero γ , the errors are all close to about 3° , and the differences between these cases are small.

To investigate how noise levels affect the proposed method, we also tested FORNI+ on the simulation phantom with different SNR levels. Since the clinical dMRI data we use usually have an SNR about 20 on the b_0 image and high quality dMRI data may have better SNR, we included two additional noise levels, where $\text{SNR} = 25$ and $\text{SNR} = 30$ (computed on the b_0 image). The errors of FOs are evaluated and shown in Figure 6, where FORNI+ is compared with CFARI and FORNI. On these different noise levels, FORNI+ also has lower FO errors than CFARI and FORNI, and the differences are highly significant ($p < 0.001$) using Wilcoxon signed-rank tests.

3.2. The SPARC 2014 Physical Phantom

We performed FORNI+ on a physical phantom provided in the SPARC 2014 challenge (Ning et al., 2015). The physical phantom consists of two bundles of $15\ \mu\text{m}$ fibers filled with NaCl solution, and the two fiber bundles cross at about 45° (see the gold standard FOs in Figure 7 for reference). The dMRI scans of the phantom were acquired on a 3T Trio Siemens scanner. The in-plane resolution is 2 mm isotropic and the slice thickness is 7 mm. A small subregion of the central slice was released. Five b -values ($b = 1000, 2000, 3000, 4000, 5000\ \text{s/mm}^2$) were used. For each b -value, a separate acquisition with $\tilde{K} \in \{20, 30, 61, 81\}$ gradient directions was obtained. In particular, 10 repetitions were acquired for the dMRI scans with 81 gradient directions on all five shells. These repeated scans were averaged to provide a gold standard dMRI scan, which consists of five shells, each having 81 gradient directions. For more detailed description of the phantom, we refer the readers to Ning et al. (2015).

As suggested by the organizers of the SPARC 2014 challenge, gold standard FOs can be computed from the gold standard dMRI scan. With this high quality data, we assume that the voxelwise FO estimation method CFARI (Landman et al., 2012) is sufficient to provide gold standard FOs. This is supported qualitatively by the result shown in Figure 7, where the gold standard FOs were computed by CFARI and correctly represent the crossing FOs.

To evaluate our method, we selected the dMRI scan with 30 gradient directions on the shell $b = 1000\ \text{s/mm}^2$, because it has the number of gradient directions that is consistent with the simulation phantom in Section 3.1 and the real dMRI scans in Section 3.3. The FOs were then estimated by CFARI, FORNI, and FORNI+ (with $(\alpha, \beta, \gamma) = (0.9, 0.3, 1.0)$) on this dMRI scan, and the results are shown in Figure 7. Note that because both FORNI and FORNI+ require neighborhood information, yet the released scan has only one slice, we extrapolated the dMRI scan in the z -direction by repeating the slice. We can see that the FOs estimated by FORNI+ are consistent with the gold standard. FORNI+ better resolves the crossing FOs than CFARI and FORNI (see the highlighted region in Figure 7 for example). We have also computed the FO errors with respect to the gold standard using the FO error measure in Ye et al. (2016). The means and standard deviations of the errors in the scan are shown in Table 3, where FORNI+ is compared with CFARI and FORNI using Wilcoxon signed-rank tests. Results indicate that the FOs estimated by FORNI+ are significantly ($p < 0.01$) more accurate than those estimated by CFARI or FORNI.

3.3. In Vivo Brain dMRI

FORNI+ was next evaluated on real brain dMRI scans. We randomly selected five subjects from the Kirby21 data set (Landman et al., 2011) (<https://www.nitrc.org/projects/multimodal/>), which is a publicly available data set containing test-retest scans and has been widely used for reproducibility studies (Duda et al., 2014; Choe et al., 2015; Huo et al., 2017). For each subject, we applied FORNI+ to the two successive dMRI scans that were acquired with the same protocol on a 3T MR scanner (Achieva, Philips Healthcare, Best, Netherlands). Therefore, ten dMRI scans were processed in this experiment.

In the acquisition of each dMRI scan, one b_0 image and 32 gradient directions ($b = 700 \text{ s/mm}^2$) were used. Each dMRI scan has 65 axial slices, and the slice thickness is 2.2 mm. The original data matrix size is 96×96 . The scanner resampled the images, which leads to a data matrix size of 256×256 and an in-plane digital resolution of $0.828 \text{ mm} \times 0.828 \text{ mm}$. Details about the imaging protocol can be found in Landman et al. (2011). We resampled the DWIs to the original resolution of 2.2 mm isotropic. The second scan of each subject was rigidly registered to the first scan using the b_0 image. Note that the gradient table of the second scan was rotated accordingly.

FORNI+ (with $(\alpha, \beta, \gamma) = (0.9, 0.3, 1.0)$) was performed on the ten dMRI scans and compared with CFARI and FORNI. We focus our evaluation on *regions of interest* (ROIs) which contain the crossing of the *corpus callosum* (CC) and the *superior longitudinal fasciculus* (SLF). The results of FO estimation are shown (overlaid on the FA map) in Figures 8 and 9 for the five subjects. Compared with CFARI and FORNI, FORNI+ better constructs crossing FOs, and the estimation results of FORNI+ are more consistent between the two successive scans for each subject (see the highlighted regions for example). In addition, the FOs estimated by FORNI+ are more spatially consistent than those estimated by CFARI and FORNI.

To quantitatively evaluate the reproducibility, we placed ROIs in the SLF for each subject (see Figure 10 for example). Then, at each voxel in the ROI the differences of the FOs on the two successive scans were computed. Note that the computation of this difference can be achieved using the same way that computes the FO estimation error in Section 3.1, which measures the difference between estimates and ground truth. The FO differences for each subject are shown in Figure 11 using boxplots, where means are also indicated by the diamonds. In all cases, FORNI+ has the lowest means and medians of FO differences, which indicates that its results are more reproducible. In addition, we performed Wilcoxon signed-rank tests to compare the FO differences of FORNI+ with those of CFARI and FORNI, and the results are also indicated in Figure 11. Compared with CFARI, the FO differences of FORNI+ are significantly smaller for all subjects; compared with FORNI, the FO differences of FORNI+ are significantly smaller for all subjects except Subject 3. These results further demonstrate the better reproducibility of FORNI+ compared with the competing methods.

Next, we performed fiber tracking on the two scans of a representative subject to further demonstrate that the consistency of fiber streamlines is preserved with the proposed FO estimation. We placed seeding ROIs in the CC (see Figure 12). The seeding voxels were

located in several coronal slices close to the coronal slice shown in Figure 12; in each seeding voxel, eight seeds were placed uniformly in space. The tracking strategy and parameters in Section 3.1 were used. The streamlines tracked with the FOs estimated by CFARI, FORNI, and FORNI+ are shown and compared in Figure 12, and they are color-coded by the orientation of each segment using the standard DTI color scheme (red: left–right; green: front–back; and blue: up–down) (Pajevic and Pierpaoli, 1999). First, we can observe that both FORNI and FORNI+ better track the lateral CC than CFARI, and their results are reproducible on the two successive scans. In addition, the streamlines tracked with FORNI+ FOs are smoother than those tracked with FORNI FOs (see the circled regions where the color of the streamlines is more homogeneous in the FORNI+ results in Figure 12 for example).

4. Discussion

Although the regularization term $\|\mathbf{C}_m \mathbf{f}_m\|_1$ has a similar form to that in Ye et al. (2016), the actual design of $\mathbf{C}_m$ is different, thus leading to a different regularization term. Specifically, in this work $\|\mathbf{C}_m \mathbf{f}_m\|_1$ models the interaction between the actual FOs and the dictionary configuration and encourages the consistency between them, whereas the actual FOs are not modeled in the $\mathbf{C}_m$ in Ye et al. (2016). If the design of $\mathbf{C}_m$ in Ye et al. (2016) were directly used, then there would be no interaction between the actual FOs and the FO configuration suggested by the dictionary, and the regularization of pairwise FO dissimilarity would have no effect on the dictionary representation. In addition, our design of $\|\mathbf{C}_m \mathbf{f}_m\|_1$ enables the optimization of Ω_m to be a generalization of Sigurdsson and Prince (2014). The generalization is not apparent until nontrivial derivation in Eqs. (13)–(18). The resulting optimization of Ω_m involves data fidelity terms of orientations suggested by the dictionary in addition to the smoothness terms in Sigurdsson and Prince (2014) (see Eq. (16)).

In this work we have used a 6-connected neighborhood because we have observed empirically that use of 26 neighbors leads to very high errors on the simulated phantom (more than 20° in each subregion and the entire phantom), where quite a number of false FOs were produced. This is likely due to the use of too much irrelevant information in the neighbors. Although it is possible to weight the information in a 26-neighborhood to remove or suppress irrelevant information (like in Ye et al. (2016)), this introduces new parameters that must be selected or estimated. A simpler 6-connected neighborhood with three parameters (α , β , and γ) was therefore deemed to be preferable.

Because FORNI+ uses neighborhood information, the smallest angle that FORNI+ can resolve may be dependent on the spatial configuration of FOs. Therefore, it is difficult to claim a smallest crossing angle. However, we have observed that on the simulation phantom the proposed method has resolved crossing FOs with crossing angles of 60 degrees, and that on the physical phantom the proposed method resolves FOs with crossing angles of about 45 degrees.

In addition to giving deterministic estimates of FOs, it is useful to estimate the uncertainties of the FO estimates (Jones, 2003; Yap et al., 2014), which, for example, can be then used for probabilistic fiber tracking (Parker et al., 2003; Behrens et al., 2007; Jeurissen et al., 2011;

Jones, 2008). Since the proposed method formulates the FO estimation problem in a dictionary-based framework with sparsity assumption, it is possible to use the Lasso bootstrap strategy (Chatterjee and Lahiri, 2010, 2011) to estimate the distribution of diffusion signals (as described in Ye and Prince (2017)), from which the distribution of FOs can be computed using the proposed method.

In the current setting, we have used a single FO to represent each fiber population. In case of fiber dispersion, it is common to model the distribution of FOs for each fiber population using the Watson distribution (Zhang et al., 2011). Specifically, we can expand the dictionary so that each basis FO is associated with multiple columns, each corresponding to a different fixed discretized concentration parameter. The values of these columns can be computed using the signal model in Zhang et al. (2011). The distribution of each fiber population could then be determined by the FOs and their concentration parameters associated with nonzero mixture coefficients.

In this work we have used a fixed dictionary to represent diffusion signals. Methods that seek to use a learned dictionary to represent diffusion signals have been developed (Merlet et al., 2013; Bilgic et al., 2013; Cheng et al., 2013; Ye et al., 2012), and it is possible to incorporate such a strategy in the proposed framework. For example, the fixed dictionary can be replaced by a parametric dictionary that learns the eigenvalues and orientations of the basis tensors, and the smoothness of FOs can still be enforced as proposed in this work. By using such an adaptive dictionary, it is possible to reduce the errors caused by model inaccuracy and improve the estimation results.

Several algorithms have been proposed to estimate FOs in multiple types of tissue, which requires modeling of compartments of isotropic diffusion (Yap et al., 2016; Jeurissen et al., 2014). It is possible to include such diffusion components in the dictionary-based framework with spatial regularization. We can expand the dictionary to encode the isotropic diffusion. Since isotropic diffusion is not associated with any particular orientation, its spatial smoothness can be enforced by, for example, the TV-norm (Rudin et al., 1992) of the corresponding mixture coefficient (Zhou et al., 2014).

5. Conclusion

We have presented a dictionary-based FO estimation algorithm that incorporates FO dissimilarity regularization to improve estimation performance. We reformulate the problem so that FOs are explicitly included in the objective function, where pairwise FO dissimilarity regularization is added and consistency between the FOs and dictionary representation is ensured. The FOs and mixture fractions of dictionary atoms are jointly estimated using an iterative alternating optimization strategy. Results demonstrate that the proposed algorithm outperforms the competing methods.

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Highlights

- We estimate fiber orientations (FOs) in a dictionary-based framework
- Pairwise FO dissimilarity is explicitly modeled to improve FO spatial coherence
- Qualitative and quantitative validation was performed on phantom and real data
- Reproducibility was evaluated quantitatively on the Kirby21 dataset

Figure 1.
3D rendering of the simulation phantom.

Figure 2.

Cross-sectional views of the FOs on the simulation phantom. Note that because the FOs in the vertical direction are not visible in the axial view, we have shown a coronal view of the highlighted area in the axial view.

Figure 3. Boxplots of FO estimation errors of CFARI, FORNI, and FORNI+ over the entire simulation phantom and in each subregion (SNR=20). Mean errors are indicated by the diamonds. FORNI+ is compared with CFARI and FORNI using Wilcoxon signed-rank tests. *** $p < 0.001$.

Figure 4. Fiber tracking results on the simulation phantom. Streamlines are overlaid on the FA map. The seeds are indicated by the boxes.

Figure 5. FO errors over the entire simulation phantom with different combinations of parameters.

Figure 6. Boxplots of FO estimation errors of CFARI, FORNI, and FORNI+ with different noise levels on the simulation phantom. Mean errors are indicated by the diamonds. FORNI+ is compared with CFARI and FORNI using Wilcoxon signed-rank tests. *** $p < 0.001$.

Figure 7.
Gold standard FOs and FOs estimated by CFARI, FORNI, and FORNI+ on the SPARC 2014 physical phantom.

Figure 8. FO estimation results overlaid on the FA map in regions where CC and SLF cross (Subjects 1–3). Note the highlighted region for comparison.

Figure 9. FO estimation results overlaid on the FA map in regions where CC and SLF cross (Subjects 4–5). Note the highlighted region for comparison.

Figure 10.
An example of the ROI placed for the reproducibility study.

Figure 11.

Boxplots of the FO differences computed from the two successive dMRI scans of each subject in the selected ROIs. Mean differences are indicated by the diamonds. FORNI+ is compared with CFARI and FORNI using Wilcoxon signed-rank tests. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, and n.s. stands for not significant.

Figure 12.

Fiber tracking results on the two successive dMRI scans of a representative subject in the coronal view. Streamlines are overlaid on the FA map. Note the circled area for comparison.

Table 1
Major symbols used in FORNI+

Symbol	Definition
$\mathbf{v}_i$	Basis direction
i	Index for basis directions
N	Number of basis directions
$\mathbf{G}$	Dictionary matrix
m, n	Index for voxels
M	Number of voxels
$\mathcal{N}_m$	Neighborhood of m
$\hat{\mathcal{N}}_m$	Union of m and its neighborhood
y_m	Diffusion signal at m
$\mathbf{f}_m$	Mixture fraction of dictionary atoms at m
f_{mi}	i -th entry of $\mathbf{f}_m$
$\mathbf{C}_m$	Weighting matrix at m
$C_{m,i}$	i -th diagonal entry of $\mathbf{C}_m$
$\boldsymbol{\omega}_{mp}$	p -th FO at m
Ω_m	The set of all FOs at m
h_{mp}	Mixture fraction of the p -th FO at m
$\mathcal{H}_m$	The set of mixture fractions of FOs at m
p, q	Index for actual FOs
$d(\boldsymbol{\omega}_{mp}, \boldsymbol{\omega}_{nq})$	FO dissimilarity between the p -th FO at m and q -th FO at n
b_{mpnq}	Weight of the dissimilarity between $\boldsymbol{\omega}_{mp}$ and $\boldsymbol{\omega}_{nq}$
$\mathbf{B}$	The set of all weights b_{mpnq} in the image
α, β, γ	Parameters in FORNI+
θ	An angle threshold
t	Index for iterations

Table 2

Means and standard deviations of FO errors (°) of FORNI+ with different initializations.

Initialized by	Entire Phantom	Noncrossing	Two-tract Crossing	Three-tract Crossing
CFARI	3.01±1.97	2.88±1.87	3.16±1.63	5.96±4.85
FORNI	2.92±1.86	2.88±1.86	2.87±1.35	5.13±4.13

Table 3

Means and standard deviations of FO errors (°) of CFARI, FORNI, and FORNI+ on the SPARC 2014 physical phantom. Results of FORNI+ are compared with those of CFARI and FORNI using Wilcoxon signed-rank tests. Asterisks (**) indicate that the difference is significant ($p < 0.01$).

CFARI	FORNI	FORNI+
7.34±7.59**	7.20±6.57**	6.47±5.76