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Clustering method for estimating principal diffusion directions

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ABSTRACT

Diffusion tensor magnetic resonance imaging (DTMRI) is a non-invasive tool for the investigation of white matter structure within the brain. However, the traditional tensor model is unable to characterize anisotropies of orders higher than two in heterogeneous areas containing more than one fiber population. To resolve this issue, high angular resolution diffusion imaging (HARDI) with a large number of diffusion encoding gradients is used along with reconstruction methods such as Q-ball. Using HARDI data, the fiber orientation distribution function (ODF) on the unit sphere is calculated and used to extract the principal diffusion directions (PDDs). Fast and accurate estimation of PDDs is a prerequisite for tracking algorithms that deal with fiber crossings. In this paper, the PDDs are defined as the directions around which the ODF data is concentrated. Estimates of the PDDs based on this definition are less sensitive to noise in comparison with the previous approaches. A clustering approach to estimate the PDDs is proposed which is an extension of fuzzy c-means clustering developed for orientation of points on a sphere. MDL (Minimum description length) principle is proposed to estimate the number of PDDs. Using both simulated and real diffusion data, the proposed method has been evaluated and compared with some previous protocols. Experimental results show that the proposed clustering algorithm is more accurate, more resistant to noise, and faster than some of techniques currently being utilized.

Introduction

Diffusion of water molecules is conventionally investigated using diffusion tensor magnetic resonance imaging (DTMRI) that uses a symmetric positive definite matrix (tensor) to model the diffusion behavior. Under Gaussian diffusion condition, this model characterizes the diffusion behavior very well (Basser et al., 1994a, 1994b); however, it fails to model anisotropies of orders higher than two in the heterogeneous tissues containing more than one fiber population. Diffusion behavior can be evaluated more accurately if the probability density function (PDF) of the molecular displacement over diffusion time is determined from which desirable diffusion indices such as mean diffusivity, second order tensor (and related anisotropies), fourth order kurtosis, and even higher order statistics can be extracted. Estimation of the diffusion PDF conventionally involves diffusion spectrum imaging (DSI), a modified q-space imaging method that resolves intra-voxel diffusion heterogeneity by measuring diffusion spectra (Wedeen et al., 2000). This method is clinically impractical because it takes a long time to acquire the required data.

To address the time complexity, high angular resolution diffusion imaging (HARDI) and orientation distribution function (ODF) have been introduced as alternatives to DSI and diffusion PDF, respectively (Tuch et al., 2002). The ODF requires taking more than 50 measurements of HARDI, each corresponding to a specific gradient direction. The ODF maintains information about the orientation of the diffusivity by integrating over the radial component of the PDF in the spherical domain. The ODF may be estimated using the Funk–Radon transform, closely approaching the true ODF under certain conditions (Tuch, 2004). Descoteaux et al. estimated the ODF by a linear combination of the spherical harmonic coefficients that describe the diffusion signal within a voxel (Descoteaux et al., 2007).

In previous work (Jansons and Alexander, 2003; Tournier et al., 2004; Bloy and Verma, 2008; Ghosh et al., 2008), principal diffusion directions (PDDs) are defined as the directions of the ODF local maxima. Several methods have been proposed to find the PDDs from ODF based on this definition. Jansons and Alexander assumed a

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symmetry on the ODF with respect to the position vector x (Jansons and Alexander, 2003). That means the ODF peaks appear in equal and opposite pairs. In their method, for each spherical point s on the sphere S, the set M is defined as follows:

$$M = \left\{x \in S : ODF(x) = \max_{s \in T(x)} ODF(s)\right\} \quad (1)$$

$$T(x) = \{s \in S : |s - x| < \rho\} \cup \{s \in S : |s + x| < \rho\} \quad (2)$$

where ρ is a constant. The set M contains the candidate PDDs. Starting at each member of M, the estimates are refined by searching for local maxima using the Powell's method, a general method for estimation of the local minima without taking derivatives (Press et al., 2007). Finally, tiny ODF peaks smaller than the ODF mean are discarded. In Tournier et al. (2004) and Sakaie and Lowe (2007), the same strategies are adopted, except for the Powell's method which is replaced by spherical Newton's method and sequential quadratic programming (constraint spherical Newton's method) (Cottle et al., 2009), respectively. The problem of all these methods is the likelihood of getting trapped in small local maxima. In Descoteaux (2008), assuming that the PDDs are the local maxima of the normalized ODF projected on a tessellated sphere with a fine mesh, the finite difference method is applied to the sphere in order to obtain the PDDs. In this method, if the ODF value for a point is above all of its neighbors and above 0.5, the point will be reserved as a local maximum. Thresholding is required in order to diminish minor peaks. The method, subsequently, is dependent on the threshold value. Plus, this method is very sensitive to the mesh grid size. Frey et al. (2008) take derivative of the ODF smoothed by a Gaussian kernel to get the local maxima. Applying such kernel, which is used to diminish noise, may degrade the angular resolution of the PDDs. In Bloy and Verma (2008), the ODF is represented by a symmetric tensor constrained to the sphere resulting in a homogeneous polynomial representation. The idea takes advantage of such representation to take analytic derivatives and find the stationary points of the ODF instead of the maxima. These stationary points are then classified into primary maxima (PDDs), secondary maxima, minima and saddle points. In Ghosh et al. (2008), the stationary points are found by using Lagrange multipliers and applying the combination of subdivision methods and generalized normal form algorithms to the resulting polynomial system. The stationary points are then sorted and thresholded to extract the PDDs. In this paper, we refer to this technique Poly-Tensor method. One of the main problems of the Bloy's and Ghosh's methods is that classifying stationary points in order to get the PDDs may become erroneous in noisy data condition. In our previous work, we determined the first principal direction as the gradient direction in which the ODF is maximum and sorted the other gradient directions based on their angular distances from this principal direction (Nazem-Zadeh et al., 2011). We then estimated the envelope of the resulting 1D profile using a moving maximum filter whose output peaks are the remaining principal diffusion directions. This method is sensitive to noise. We refer to this technique as Angular-Distance method. Using finite difference method, Camino software package (Cook et al., 2006) locates local maxima by ascertaining all points at which the function is larger than all other points within a fixed search radius. It then removes duplicates and tiny peaks with function values smaller than a pre-specified threshold (Descoteaux et al., 2007). This procedure is both inaccurate and time-consuming. In addition, the number of PDDs is restricted to three for estimation and two for visualization. For DTI data with dimensions $128 \times 128 \times 56$, it takes almost a week to find up to three PDDs for each voxel, using a commonly used personal computer (Core 2Due CPU, E8400@ 3.00 GHz, 3.00 GHz, and 8 GB RAM).

All of the above methods define the PDDs as the directions in which the ODF data is locally maximal. The PDDs, based on this definition, are sensitive to noise. In addition, some of the methods post-process the results by discarding tiny ODF detected peaks. Depending on the kernel width, this may lead to discarding important diffusivity information. In this paper, the PDDs are defined as the directions around which the ODF data is concentrated (clustered). Estimates of the PDDs based on this definition are less sensitive to noise in comparison with the previous approaches. They may be related to clustering principles whereby a set of data points is considered as potential PDDs and examined to determine whether they properly represent the ODF data. In other words, they are examined to determine whether they minimize the overall distance of the data points from the cluster centers. Unfortunately, this approach involves an exhaustive search which is very time-consuming when there are more than two PDDs. To reduce the computational complexity, we propose an iterative algorithm based on fuzzy c-means clustering (Dunn, 1973; Bezdek, 1981) in which the cluster centers and memberships are iteratively updated. Our proposed algorithm benefits from good features of the fuzzy c-means algorithm and is sufficiently accurate for practical purposes. It transforms the original 3D cluster data into a 2D format and thus simplifies computation. The 2D data points contain co-latitudes and co-longitudes of the spherical angles.

The ODF can be considered as a convolution of complex fiber structure, denoted by fODF (fiber ODF), and the ODF response to a single fiber (ODF kernel). Therefore, fODF can be calculated by deconvolution of the ODF with the ODF kernel (Descoteaux et al., 2007; Tournier et al., 2004). The fODF has more distinct lobes and thus is more appropriate for locating the PDDs. Hence, we apply our algorithm to the fODF.

Starting with two cluster centers and using the spherical law of cosines, the proposed approach calculates the arc (geodesic) distances between points on the sphere and the cluster centers. The membership values and centers of the clusters are updated iteratively until convergence is achieved. To automatically determine the number of clusters, this number is increased by two and the resulting data representation is evaluated based on the minimum description length (MDL) criterion (Rissanen, 1989). Applications of the proposed method to simulated and clinical data show that our algorithm is more accurate, and easier to implement than current methods in the literature, especially when the signal-to-noise ratio (SNR) is low.

Materials and methods

Spherical deconvolution

Expansion of a function on a sphere using spherical harmonics is a generalization of Fourier series in the spherical coordinates (Mousa et al., 2006). The diffusion signal at any point of the unit sphere can be estimated using the spherical harmonic coefficients (SHCs) according to the equations:

$$S(\theta, \varphi) = \sum_{j=1}^{N} c_j Y_j(\theta, \varphi) \quad (3)$$

where S is the diffusion measurement, $\theta \in [0, \pi]$ and $\varphi \in [0, 2\pi]$ are co-latitude and co-longitude spherical angles, N is the total number of coefficients, c_j is the jth SHC, and the corresponding harmonic $Y_j(\theta, \varphi)$ is the non-singular separated solution for the Laplace equation on the surface of the sphere (see Appendix 1). In our previous work (Nazem-Zadeh et al., 2010), we investigated the characteristics of the SHC through simulations. The 8th order SHCs can represent diffusion profiles with a maximum of four major distinct peaks in each voxel (Descoteaux et al., 2006).

In Q-ball imaging, ODF data are computed from HARDI measurements distributed on a hemisphere using a Funk–Radon transform (FRT) (Descoteaux et al., 2007). Using the spherical harmonics,