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Diffusion configuration of water molecules in diffusion weighted imaging

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ABSTRACT

In the studying of fibers microstructure of brain white matter, many reconstruction methods have been proposed to interpret the diffusion-weighted signal. Those methods can be categorized into model-based and model-free methods. In this paper, the diffusion configuration of water molecules are discussed, and two questions are put forward to analyze the performance of the current algorithms about diffusion configuration. The first question is what the diffusion profile looks like in voxel? The second question is what is the location of fibers in a voxel? As a result, firstly, most of model-based algorithms ignore much information coming from the isotropic diffusion, which will lead to an inaccurate estimation. Secondly, model-free algorithms just provide direction information of fibers, ignore or cannot provide location information of fibers. So unfortunately, neither model-based methods nor model-free methods can resolve those two questions very well. How to resolve those questions is still an open problem, and it may be an interesting direction in the future research.

1. Introduction

In the past two decades, diffusion magnetic resonance imaging (MRI) has proven to be a unique tool for investigating the microstructure of biological tissue *in vivo* [1,2]. It allows the mapping of the diffusion process of water molecules in biological tissues, *in vivo* and non-invasively. The diffusion process of molecules is caused by Brownian motion of molecules due to their thermal energy. This motion can be described as a random walk of each individual molecule. Molecular diffusion in tissues is not free, reflecting interactions of molecules with many obstacles, such as macromolecules, fibers, and membranes. When the diffusion is concentrated to a preferred direction it is referred to as anisotropic diffusion. In contrast, water diffuses in a spherical pattern in tissues since the restriction is identical in every direction, and this is referred to as isotropic diffusion. The effect of diffusion anisotropy or isotropy can be detected in diffusion weighted imaging (DWI) by observing variations in the diffusion measurements when the direction of the gradient pulses is changed.

In diffusion weighted MRI, it is now generally accepted that microscopic boundaries of diffusion in the brain coincide with the local orientations of white matter (WM) fiber tracts. The diffusion MRI as a tool for modeling intravoxel diffusion has inspired a number of promising applications in which white matter connectivity can be evaluated in both health and disease [3]. The diffusion MRI is now widely used to characterize regional anisotropy and orientation of WM throughout the brain, and the fiber pathways can be 3D delineated by tractography algorithms. In the diffusion weighted MRI, images are acquired using the Stejskal–Tanner pulsed gradient spin-echo method [4]. It describes measured signal intensity $S(\mathbf{g}_i)$ in the presence of a diffusion sensitizing gradient in direction $\mathbf{g}_i$ as a function of unweighted intensity $S(0)$, the apparent diffusion coefficient (ADC) $D(\mathbf{g}_i)$, and an acquisition constant b:

$$S(\mathbf{g}_i) = S(0)\exp(-b \cdot D(\mathbf{g}_i)), \tag{1}$$

where $b = \gamma^2 G^2 \delta^2(\Delta t - \delta/3)$ is b-value. γ is the gyromagnetic ratio, δ is the duration of the diffusion gradient pulses, and G is the strength of the diffusion gradient. The apparent diffusion coefficient $D(\mathbf{g}_i) = \mathbf{g}_i^T \mathrm{D} g_i$, $\mathbf{D}$ is diffusion tensor.

In diffusion tensor imaging (DTI) images, diffusion tensor is used to describe the diffusion profile of water molecules [5]. Diffusion tensors can be modeled as ellipsoids with the eigenvectors describing the major and minor axes of the ellipsoid and the associated eigenvalues scaling these axes. Isotropic diffusion profiles result in spherical tensors while anisotropic diffusion profiles produce linear

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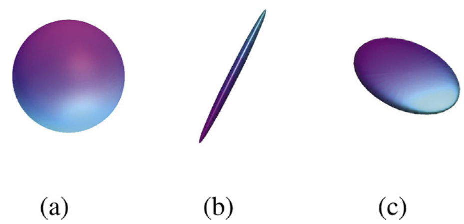

Fig. 1. Diffusion ellipsoids of water molecules according to diffusion tensor imaging. (a) Spherical case, (b) linear case and (c) planar case.

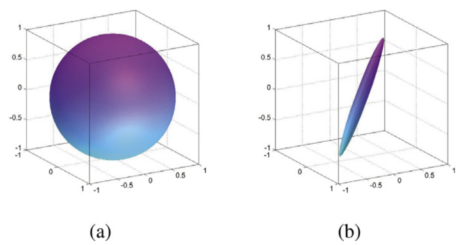

Fig. 2. Diffusion profiles in a voxel according to diffusion tensor imaging.

tensors (ellipsoid). The parameters which describe these tensors are obtained from DWI images. Fig. 1 shows the diffusion profiles of water molecules according to diffusion tensor imaging: (a) is spherical case, (b) and (c) are linear case and planar case, respectively.

The diffusion ellipsoids of water molecules are accepted widely, especially in diffusion tensor imaging. Fig. 2 shows the diffusion profiles in a voxel. Assuming the box in Fig. 2 denotes a voxel, the diffusion profile of water molecules is a sphere if no any nerve fibers in this voxel, which is shown in Fig. 2(a). If there is one fiber or a bundle of fibers in a voxel, the diffusion profile of water molecules is a narrow ellipsoid (linear case), which is shown in Fig. 2(b). One tensor DTI model can only map a single orientation inside a voxel, so it is limited to characterize the complexity of white matter structure within a voxel. That is to say, one tensor DTI algorithms are in principle not able to resolve more than one orientation of fibers per voxel.

In voxel, the ellipsoid tensor may not corresponds only to one fiber, it may describes more than one fiber, which is shown as Fig. 3. The reason is that fibers usually appear as bundles, and we can not measure each fibers separately by now.

To overcome the limitation of DTI, several reconstruction methods have been proposed to interpret the diffusion-weighted signal in the studying of fibers microstructure. Those methods can be categorized into model-based and model-free approaches [6,7]. One of the simplest model-based method is diffusion tensor imaging, which describes a Gaussian estimate of the diffusion orientation and strength at each voxel. To handle more complex diffusion patterns, several model-based methods have been introduced, such as

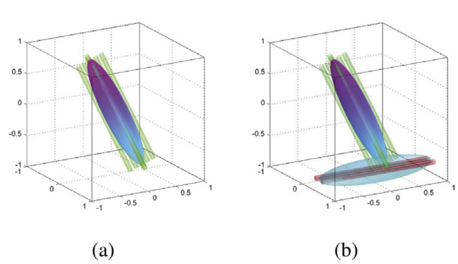

Fig. 3. Ellipsoid tensor may corresponds to a fiber or a bundle of fibers. (a) One orientation of fiber bundle and (b) two orientations of fiber bundles.

higher-order tensors [8,9], two tensors or multi-tensors tractography [10,11].

The model-free approaches, or called *q*-space imaging methods, often provide more information about the diffusion pattern. Those methods are based on the Fourier relation between the diffusion MR signals and the underlying diffusion propagator. Instead of estimating fibers as in parametric models, model-free techniques estimate an diffusion orientation distribution function (ODF) describing an arbitrary configuration of fibers. High angular resolution diffusion imaging (HARDI) measures diffusion along many uniformly distributed directions on a sphere and can characterize more complex fiber geometries [12]. Diffusion spectrum imaging (DSI) is a variant of diffusion-weighted imaging that is sensitive to intra-voxel heterogeneities in diffusion directions caused by crossing fiber tracts and thus allows more accurate mapping of axonal trajectories [13]. Tuch introduced Q-ball imaging (QBI) to numerically compute the ODF using the Funk–Radon transform [14]. The model-free ODF is the angular profile of the diffusion PDF of water molecules and can be approximated using different sets of basis functions such as spherical harmonics (SH) [15,16]. A multiple-shell scheme and a grid scheme, also known as the Cartesian sampling scheme used by diffusion spectrum imaging are also proposed [17]. To further extend the applicability of *q*-space imaging methods, generalized q-sampling imaging (GQI) is proposed, which could be applied to balanced sampling schemes such as single-shell, multi-shell, and grid sampling schemes, with accuracy comparable to QBI and DSI [18]. Spherical deconvolution approach is proposed to estimate fiber orientation density function from diffusion-weighted MRI data directly [19].

In this paper, we will put forward two questions to analyzes the performance of the current algorithms about diffusion configuration. The first question is about the diffusion profile of water molecules. The second question is about the location of fibers in voxel. The remainder of this paper is organized as follows: Section 2 analyzes the the diffusion profiles in voxel. In Section 3, the location of fibers is discussed. Finally, Section 4 concludes the paper.

2. What the diffusion profile looks like in voxel?

In diffusion tensor imaging, the Gaussian diffusion profiles in voxel are widely accepted, which is shown in Fig. 2. Many reconstruction methods are designed and realized based on this model. The diffusion profile of water molecules is a sphere if there are no any nerve fibers in this voxel. If there is one fiber or a bundle of fibers in a voxel, the diffusion profile of water molecules is a narrow ellipsoid.

However, this model is probably inaccurate. For example, Fig. 2(b) is precise only when no any other isotropic diffusion water molecules, or other anisotropic diffusion water molecules in the voxel simultaneously. Considering the size of voxel and the radius of water molecules diffusion, this situation is almost imposable.

Actually there usually have many isotropic and anisotropic diffusion water molecules in a voxel simultaneously. The diffusion profile of each isotropic diffusion water molecules is a sphere, and the diffusion profile of each anisotropic diffusion water molecules is a narrow ellipsoid. The size of spheres and narrow ellipsoids may be different to each other, which depends on many factors of diffusion. And the spheres and narrow ellipsoids may even overlap. Fig. 4 shows the voxel with many water molecules. Fig. 4(a) is the situation of no fibers, there are many small spheres in voxel, which correspond to many diffusion profiles of isotropic water molecules. Fig. 4(b) shows a voxel with a fiber or a bundle of fibers (narrow ellipsoid) and many isotropic diffusion water molecules (spheres).