Brain tractography using Q-ball imaging and graph theory: Improved connectivities through fibre crossings via a model-based approach

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ABSTRACT

Brain tractography techniques utilize a set of diffusion-weighted magnetic resonance images to reconstruct white matter tracts, non-invasively and in-vivo. Streamline tracking techniques propagate curves from a seed to imply connectivity to distal voxels. Alternative approaches have been developed that attempt to quantify connection strength between all voxels and the seed. Tractography based on graph theory is amongst them. Despite its potential, graph-based tracking through complex fibre configurations has not been extensively studied and existing methods have inherent limitations. Anatomically unlikely connections may be identified in fibre crossing regions, by assigning relatively high connection strengths to all crossing populations. In this study, we discuss these limitations and present a new approach for robustly propagating through fibre crossings, as described by the orientation distribution functions (ODFs) derived from Q-ball imaging. Each image voxel is treated as a graph node and graph arcs connect neighbouring voxels. Weights representative of both structural and diffusivity features are assigned to each arc. To account for the existence of crossing fibre populations within a voxel, complex ODFs are decomposed into components representative of single-fibre populations and an image multigraph is created. The multigraph is searched exhaustively, but efficiently, to find the strongest paths and assign connectivity strengths between a seed and all the other image voxels. A comparison with the existing graph-based tractography as well as Q-ball driven front evolution tractography is performed on simulated data, and on human Q-ball imaging data acquired from five healthy volunteers. The new approach improves the connection strengths through fibre crossing regions, reducing the strengths of paths that are less anatomically plausible.

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Introduction

Diffusion-weighted (DW) MRI (Turner and Le Bihan, 1990) allows the reconstruction of brain white matter (WM) pathways non-invasively and in-vivo (Basser et al., 2000; Catani et al., 2002; Mori and van Zijl, 2002). DW images are utilized to estimate the underlying neuronal fibre orientations or orientation distribution functions (ODFs) (Alexander, 2006) in each image voxel, with an ODF reflecting the angular profile of the diffusion scatter pattern (Tuch, 2004). These estimates can then be used by tractography algorithms (Mori and van Zijl, 2002) to study brain anatomical connectivity (Hagmann et al., 2008).

Q-ball imaging (Tuch, 2004) is a model-free DW-MRI technique that allows reconstruction of the diffusion ODF. Due to the relatively high angular resolution of the acquisition protocol and the increased diffusion sensitization, it can capture subtle diffusion displacements of water molecules. In contrast to the single-peaked Gaussian ODF model used in diffusion tensor imaging (Basser et al., 1994), Q-ball imaging can reconstruct multi-peaked ODFs in cases of intra-voxel fibre crossings. In this study, we apply elements of graph theory on ODFs derived from Q-ball images to reconstruct WM tracts.

The simplest WM tracking approach, known as streamline tractography, propagates curves within the vector field of local fibre orientations (Basser et al., 2000; Mori et al., 1999; Tench et al., 2002). The streamline method provides deterministic connectivity information, which is not always adequate given the noisy nature of MRI images and the existence of partial volume (Jones, 2003). Probabilistic tractography methods (Behrens et al., 2003; Friman et al., 2006; Jones, 2008; Lazar and Alexander, 2005; Parker et al., 2003) deal with these problems by considering the uncertainty of orientation estimates in the curve propagation. Streamlines are repeatedly generated, but in each propagation step a fibre orientation sample is drawn randomly from the orientation distribution. A spatial distribution of curves is

then estimated from a seed voxel in a Monte Carlo fashion. The fraction of streamlines that pass through a specific voxel is defined as its index of connectivity to the seed. These techniques suffer from reduced connectivity values with distance from the seed. Moreover, generating many streamlines means long execution times, but is necessary to obtain converged connectivities.

Alternatives to streamline-based approaches have been developed. Methods that simulate the diffusion equation or directly solve Fick's second law in the image volume have been presented (Hageman et al., 2009; Hagmann et al., 2003; Kang et al., 2005; O'Donnell et al., 2002). In (O'Donnell et al., 2002), the diffusion equation is solved for a steady-state concentration of diffusing molecules using diffusion tensor estimates. A connectivity index is assigned to each path, reflecting the total flow along it. An extra viscosity term is employed in (Hageman et al., 2009) representing the anisotropy and spatial orientational coherence, slowing down propagation in isotropic regions. The solution of the diffusion equation has been used to evolve a front from a given seed in (Kang et al., 2005). Most likely paths to the seed are determined in a backward fashion, using both the front distance travelled and the fibre orientation of front voxels. All these methods tackle limitations of streamline tractography, such as fibre crossing and branching. However, solving a partial differential equation using a finite element approach is computationally expensive. Furthermore, it is not always straightforward to obtain a connectivity map across the whole brain (Hageman et al., 2009; Kang et al., 2005), and there might be a large number of model parameters to set.

Towards the calculation of distributed connectivity maps, front propagation approaches have been developed (Campbell et al., 2005; Fletcher et al., 2007; Jackowski et al., 2005; Parker et al., 2002; Staempfli et al., 2006; Tournier et al., 2003). Propagation speed values are calculated between neighbouring voxels using the fibre orientations (Parker et al., 2002), whole-tensor information (Staempfli et al., 2006), or Q-ball ODFs (Campbell et al., 2005). Based on these values, a surface is evolved using the isotropic fast marching algorithm (Sethian, 1996). The arrival times of the surface arrival can then be used to define paths back to the seed. Features of the path (the weakest link of the path for instance) can be used to assign a connectivity index to every image voxel. In (Jackowski et al., 2005) the anisotropic Lax–Friedrichs algorithm governs surface propagation, while an empirical front evolution method is presented in (Tournier et al., 2003). Front propagation seeded individually from two regions of interest (ROIs) is utilized in (Fletcher et al., 2007) to study the connectivity of the ROI pair.

In more recent tractography studies, a weighted graph representation of the image has been utilized (Iturria-Medina et al., 2007; Sotiropoulos et al., 2008b; Sotiropoulos et al., In press; Zalesky, 2008). Anatomical paths are identified by searching the image graph exhaustively, using either modified shortest-path algorithms (Iturria-Medina et al., 2007; Zalesky, 2008) or fuzzy connectedness (Sotiropoulos et al., 2008b, In press). These methods, as well as most of the front propagation methods, are inherently discrete in the orientation and spatial fields. However, compared to the streamline-based approaches and their probabilistic counterparts, they combine a) converged indices of connectivity to a seed for all image voxels (Iturria-Medina et al., 2007; Parker et al., 2002; Sotiropoulos et al., In press), b) connectivities that do not drop systematically with the distance from the seed (Iturria-Medina et al., 2007; Parker et al., 2002; Sotiropoulos et al., In press), c) inherent ability to incorporate information from other imaging modalities (Iturria-Medina et al., 2007), d) inherent ability to deal with fibre branching in a single-pass execution (Iturria-Medina et al., 2007; Parker et al., 2002; Sotiropoulos et al., 2008b) and e) relatively short execution times (Parker et al., 2002; Sotiropoulos et al., In press).

Despite the potential of such methods, only a few studies that utilize Q-ball imaging and non-streamline tractography exist (Campbell et al., 2005; Iturria-Medina et al., 2007). Propagation in each step is determined using the whole Q-ball ODF, and in crossing regions connections can be distributed equally towards all crossing directions, regardless of the path propagated so far. Therefore, anatomically unlikely connections may be identified. In this paper, we discuss this limitation and present a new graph-based tractography algorithm to deal more appropriately with crossing regions. The algorithm takes into account multiple fibre populations within a voxel, when partial volume exists, by treating the image as a multigraph. It is then possible to distribute the connectivities in a weighted manner, with the most appropriate fibre from the population obtaining the highest weight. Our aim is thus to reduce the connection strengths of paths from a seed that are less anatomically plausible, without using exclusion/inclusion ROIs that require some prior knowledge. We present results on simulated data as well as on a group of healthy human subjects and perform quantitative comparisons with both Q-ball based front evolution tractography (Campbell et al., 2005) and the recent graph-based tractography (Iturria-Medina et al., 2007). This work has been previously presented in a preliminary form (Sotiropoulos et al., 2009a, 2009b).

Methods

Brain tractography using graph theory

An image can be considered as a non-directed weighted graph $G = [V,A]$, with V being the set of graph nodes and A the set of graph arcs. Each voxel i in the image is a graph node and a neighbourhood system is chosen to define the set of neighbours F_i^{Neigh} of i. Arcs, a, exist between neighbouring voxels and weights, $w \in \Re$, are assigned to each arc reflecting both diffusivity and structural information of the connecting voxels. According to (Iturria-Medina et al., 2007) the weight of the arc between two neighbours i and j is symmetric and defined as:

$$w[a(i,j)] \equiv w_{ij} = w_{ji} = P_{\text{mat}}(i) \cdot P_{\text{mat}}(j) \cdot \left[P_{\text{Diff}}\left(i, \vec{r}_{ij}\right) + P_{\text{diff}}\left(j, \vec{r}_{ji}\right) \right]. \tag{1}$$

The term $P_{\text{mat}}(i)$ represents the probability of voxel i belonging to a specific tissue type. It can be computed by performing probabilistic tissue segmentation on structural images. $P_{\text{Diff}}\left(i, \vec{r}_{ij}\right)$ is a pseudo-probability term of observing diffusion from i along the direction $\vec{r}_{ij}$ that connects the centres of i and j. It can be computed by integrating the diffusion ODF over a solid angle ω around the vector $\vec{r}_{ij}$. The angle ω is determined by the neighbourhood system employed, i.e. the number of arcs arising from a node (for a $3 \times 3 \times 3$ neighbourhood, $\omega = 4\pi/26$). Then:

$$P_{\text{Diff}}\left(i, \vec{r}_{ij}\right) = \frac{1}{Z} \int_\omega \text{ODF}\left(i, \vec{r}\right) dS \approx \frac{1}{Z} \sum_{q=1}^{Q} \text{ODF}\left(i, \vec{r}_q\right) \cdot \Delta S_q, \tag{2}$$

where the integral is approximated by a sum of ODF terms evaluated at Q points $\vec{r}_q$ contained in the solid angle cone and obtained from an icosahedral tessellation. The normalization constant Z ensures that the maximum value of the set $\{P_{\text{Diff}}(i, \vec{r}_{ij}), j \in F_i^{\text{Neigh}}\}$ is 0.5. Using the above definitions the arc weights are $w \in [0,1]$. Note that in (Zalesky, 2008), the weights are defined by integrating the Bayesian posterior probability of fibre orientation.

Given the weights, paths can be defined in the image graph as chains of neighbouring voxels. The strength M of a path C that comprises of X nodes $i_1, i_2, \ldots i_X$ or equivalently of $X-1$ arcs $a(i_1,i_2)$, $a(i_2,i_3), \ldots a(i_{X-1},i_X)$ is given by:

$$M_C \equiv M_{i_1 \ldots i_X} = M_{i_X \ldots i_1} = w_{i_1 i_2} \cdot w_{i_2 i_3} \cdot \ldots \cdot w_{i_{X-1} i_X}. \tag{3}$$