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Optimal DSI reconstruction parameter recommendations: Better ODFs and better connectivity

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ABSTRACT

Diffusion Spectrum Imaging (DSI) has been used for tractography in several publicly available software and a number of recent high impact publications. However, there are several important theoretical, numerical and practical considerations that are often ignored. We revisit the theoretical and state-of-the-art processing steps necessary to go from the DSI signal to the diffusion orientation distribution function (dODF) used by tractography. We show that the parameters in the reconstruction have huge impact on the reconstruction quality and that, while there is no consensus about what they should be, the parameters we most often see in the literature are *not optimal*. We provide applicable recommendations that improve the accuracy of extracted local orientations and improve accuracy of global connectivity as measured by the *Tractometer*, a tractography online evaluation system. These recommendations come for "free" as they are applicable to all existing DSI data and do not require a significant increase in computation time. Hence, this paper highlights the *do's and dont's* of DSI reconstruction.

Introduction

In recent years, Diffusion Spectrum Imaging (DSI) has often been referred to as the gold standard technique to reconstruct the diffusion orientation distribution function (dODF). Although requiring a long acquisition scheme, it was successfully used in recent high impact and pioneer connectomics works (Hagmann et al., 2008; Honey et al., 2009). It was also at the center of Wedeen et al.'s Science publication (Wedeen et al., 2012), which was followed by a debate with Catani et al. (Catani et al., 2012; Wedeen et al., 2012). Furthermore, DSI is one of the protocols used in the MGH-UCLA Human Connectome Project (HCP)[1] (Wedeen et al., 2008). This has led to an increased use of the diffusion orientation distribution function (dODF) computed from DSI. However, DSI, as described in Wedeen et al. (2005) and Hagmann et al. (2007), has several important theoretical, numerical and practical considerations that have mostly been overlooked. In particular, we show that DSI as it is implemented in most available reconstruction software (Diffusion Toolkit[2] (Wang et al., 2007) and DSI Studio[3]) is *not optimal*. In the past, advances in diffusion MRI local reconstruction methods, such as Diffusion Tensor Imaging (DTI) (Basser et al., 1994), Q-Ball Imaging (QBI) (Aganj et al., 2010; Descoteaux et al., 2007; Tuch, 2004) or Constrained Spherical Deconvolution (CSD) (Descoteaux et al., 2009; Tournier et al., 2007, 2004), have been focused on i) validating the soundness of the models (Tournier et al., 2008), ii) mathematically constraining them to better represent physical limitations (Arsigny et al., 2006; Pennec et al., 2006; Tournier et al., 2007) and iii) cornering their pitfalls (Jones and Cercignani, 2010; Parker et al., 2013). However, DSI seems to have slipped through this thorough evaluation process. One could argue that the lack of freely available DSI data until recently[1] combined with the lengthy acquisition protocol may have led to this status.

This work highlights the *do's and dont's of DSI* by addressing the DSI limitations and revisiting the theoretical and state-of-the-art processing steps of the DSI reconstruction. The paper proposes a list of recommendations to perform better DSI, which produces dODFs that better represent the underlying white matter structure to increase tractography accuracy and thus increase global connectivity accuracy. The contributions are three-fold: 1) revisiting the theoretical foundations of DSI, 2) investigating the steps used to go from the DSI signal to the dODF and 3) giving recommendations for DSI processing to produce better dODFs without significant computation time increase. The suggested improved DSI reconstruction has the advantage of being applicable to all existing DSI data and future DSI data using the same MRI protocol.

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[1] http://www.humanconnectomeproject.org/.
[2] http://trackvis.org/dtk/.
[3] http://dsi-studio.labsolver.org/.

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Theory

Diffusion-weighted (DW) imaging is a technique that aims to non-invasively recover information about the diffusion of the water molecules in biological tissues (LeBihan et al., 1986). We can quantify the water diffusion by estimating the displacement of the particles using the pulsed gradient spin-echo (PGSE) sequence (Stejskal and Tanner, 1965). The relationship between the diffusion signal attenuation, $E(\mathbf{q})$, in q-space and the diffusion propagator, $P(\mathbf{R})$, in real space, is given by a Fourier transform (FT) relationship[4] (Callaghan, 1991; Ozarslan et al., 2009) such that

$$\text{EAP}:=P(\mathbf{R}) = \int_{\mathbf{q}\in\mathbb{R}^3} E(\mathbf{q}) e^{2\pi i \mathbf{q}\cdot\mathbf{R}}\, \mathrm{d}\mathbf{q}, \tag{1}$$

where $E(\mathbf{q}) = S(\mathbf{q})/S_0$, where $S(\mathbf{q})$ is the diffusion signal measured at position $\mathbf{q}$ in q-space, and S_0 is the baseline image acquired without any diffusion sensitization ($\mathbf{q} = \vec{0}$). We denote $q = |\mathbf{q}|$ and $\mathbf{q} = q\mathbf{u}$, $r = |\mathbf{R}|$ and $\mathbf{R} = r\mathbf{v}$, where $\mathbf{u}$ and $\mathbf{v}$ are 3D unit vectors. The wave vector $\mathbf{q}$ is $\mathbf{q} = \gamma\delta\mathbf{G}/2\pi$, with γ the nuclear gyromagnetic ratio of the hydrogen nucleus and $\mathbf{G} = g\mathbf{u}$ the applied diffusion gradient vector, assuming a rectangular gradient pulse. The norm of the wave vector, $\mathbf{q}$, is related to the diffusion weighting factor (the b-value), $b = 4\pi^2 q^2 \tau$, where $\tau = \Delta - \delta/3$ is the effective diffusion time with δ the time of the applied diffusion sensitizing gradients and Δ the time between the two pulses for the PGSE sequence. We can measure the approximation of the diffusion propagator by taking the ensemble average over the imaging voxel, hence the name Ensemble Average Propagator (EAP). The EAP is the full 3D displacement probability function of water molecules, which faithfully characterizes the water diffusion phenomenon. Note that the Fourier relationship between the EAP and the diffusion signal of Eq. (1) is strictly valid only if the narrow pulse condition is met, which is rarely the case for in vivo 3D q-space MRI. However, the violation of this condition induces a convolution over a range of diffusion times in the measurements, preserving the large-scale structure and orientation of the inferred propagator (Alexander et al., 2002).

Many recent techniques have been proposed to recover the EAP. These can be generally separated between signal modelling (Assemlal et al., 2009; Cheng et al., 2010; Descoteaux et al., 2011; Ghosh and Deriche, 2012; Hosseinbor et al., 2013; Jian et al., 2007; Özarslan et al., 2009, 2006) and model-free techniques (Gramfort et al., 2014; Lin et al., 2003; Menzel et al., 2011; Paquette et al., 2014; Vemuri et al., 2012; Wedeen et al., 2005; Wu and Alexander, 2007; Ye et al., 2012). The generic approach of signal modelling is to fit one or a sum of continuous functions to the diffusion signal and then solve Eq. (1) analytically to obtain the EAP. That EAP will be represented by a linear transform of coefficients of the signal. For model-free techniques, Eq. (1) has to be discretely approximated in some way and the resulting EAP will be discrete. Even for these advanced techniques recovering the full diffusion propagator, the diffusion orientation distribution function (dODF) remains an object of high interest for its use in tractography since its maxima correlate well with the orientation of the underlying structure. The dODF is obtained by integrating the EAP over the radius in spherical coordinates (Eq. (2)):

$$\text{dODF}:=\Psi(\phi,\theta) = \int_0^\infty P(\phi,\theta,r) r^2\, \mathrm{d}r \tag{2}$$

[4] There is a widespread error in the DSI literature, where the Fourier transform between EAP and signal is given with a negative sign in the exponent. This is possibly originating from some of the more fundamental works on diffusion MRI. For a detailed description of this issue with a discussion on its consequences, see (Ozarslan et al., 2009).

Diffusion Spectrum Imaging (DSI) (Wedeen et al., 2005) is part of the model-free category, the EAP $P(\mathbf{R})$ is obtained directly by taking the inverse discrete Fourier transform (iDFT) of $E(\mathbf{q})$. In order to do so, the q-space has to be sampled in a grid-like manner. This Cartesian discretization of q-space naturally leads to artefacts when dealing with the phenomenon of water diffusion which has strong angular features. Fig. 1 shows the non-uniform angular coverage of the DSI scheme when projected on the sphere. In comparison, recent techniques (Caruyer et al., 2013) can be used to assure uniform angular coverage for multiple b-value shell acquisitions.

Diffusion Spectrum Imaging (DSI) revisited

The classical DSI acquisition scheme (DSI515) (Wedeen et al., 2005) is comprised of q-space points of a cubic lattice within the sphere of five lattice units in radius, leading to 515 diffusion measurements (Fig. 1). This is the default DSI grid resulting in a DSI signal living on an 11 × 11 × 11 Cartesian grid.

In theory, we only need to take the inverse Fourier transform of the signal to obtain the EAP and then do a radial integration to obtain the dODF (discretization of Eqs. (1) and (2)). However, in practice, to compute an dODF from the 11 × 11 × 11 Cartesian grid DSI signal, more steps are involved. Unfortunately, these steps are rarely studied in DSI publications (Hagmann et al., 2007; Lin et al., 2003; Wedeen et al., 2005) and have been mostly overlooked. They are however very important to obtain an accurate dODF for tractography.

Numerical DSI reconstruction steps

The DSI reconstruction steps include *numerical discretization*, *q-space truncation*, *low-pass filtering*, *interpolation*, *zero-padding* and *real space radial truncation*. These steps are detailed in Eqs. (3a), (3b), (3c), (3d) and (3e). One can appreciate how these steps heavily deviate from the continuous q-space formula of Eqs. (1) and (2). These numerical implementation steps cannot be ignored as mere discretization related operations and lead to well-known Fourier theory artefacts, as detailed here:

1) Replace Eq. (1) in Eq. (2)

$$\Psi(\phi,\theta) = \int_{r\in\mathbb{R}} r^2 \left[\int_{\mathbf{q}\in\mathbb{R}^3} E(\mathbf{q}) e^{2\pi i \mathbf{q}\cdot\mathbf{R}}\, \mathrm{d}\mathbf{q} \right] \mathrm{d}r \tag{3a}$$

2) q-space truncation at $q_{\max}$:

$$\Psi(\phi,\theta) \approx \int_{r\in\mathbb{R}} r^2 \int_{|\mathbf{q}|\le q_{\max}} |E(\mathbf{q})| e^{2\pi i \mathbf{q}\cdot\mathbf{R}}\, \mathrm{d}\mathbf{q}\, \mathrm{d}r \tag{3b}$$

3) Apply low-pass filter (K(β)) and zero-pad the grid to size L × L × L ($Z_L\{.\}$) before inverse Fourier transform (iFFT):

$$\Psi(\phi,\theta) \approx \int_{r\in\mathbb{R}} r^2\, \text{iFFT}[Z_L\{|E_{DSI}(\mathbf{q})| \cdot K(\beta)\}]\, \mathrm{d}r \tag{3c}$$

4) Interpolation of the EAP grid onto a spherical grid ($I_{\phi,\theta,\Delta r}\{.\}$) and discretization of the radial sum inside the grid ($[0, \lfloor L/2 \rfloor]$):

$$\Psi(\phi,\theta) \approx \sum_{r\in[0,\lfloor L/2\rfloor],\Delta r} r^2\, I_{\phi,\theta,\Delta r}\{\text{iFFT}[Z_L\{|E_{DSI}(\mathbf{q})| \cdot K(\beta)\}]\} \tag{3d}$$