NeuroImage 94 (2014) 312–336

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Track Orientation Density Imaging (TODI) and Track Orientation Distribution (TOD) based tractography

Thijs Dhollander [a,b,*], Louise Emsell [a,c,d,e], Wim Van Hecke [a], Frederik Maes [a,b], Stefan Sunaert [a,c,d,e], Paul Suetens [a,b,f]

[a] Medical Imaging Research Center (MIRC), KU Leuven, Leuven, Belgium
[b] Medical Image Computing (MIC), ESAT-PSI, Department of Electrical Engineering, KU Leuven, Leuven, Belgium
[c] Translational MRI, Department of Imaging & Pathology, KU Leuven, Leuven, Belgium
[d] Department of Radiology, UZ Leuven, Leuven, Belgium
[e] Leuven Research Institute for Neuroscience & Disease (LIND), KU Leuven, Leuven, Belgium
[f] iMinds - KU Leuven Future Health Department, Leuven, Belgium

ARTICLE INFO

Article history:
Accepted 23 December 2013
Available online 31 December 2013

Keywords:
Diffusion weighted imaging
Fiber tractography
Track-density imaging
Track orientation density imaging
Track-weighted imaging
Track orientation weighted imaging
Fiber orientation distribution
Track orientation distribution
Track-like local support

ABSTRACT

Ever since the introduction of the concept of fiber tractography, methods to generate better and more plausible tractograms have become available. Many modern methods can handle complex fiber architecture and take on a probabilistic approach to account for different sources of uncertainty. The resulting tractogram from any such method typically represents a finite random sample from a complex distribution of possible tracks. Generating a higher amount of tracks allows for a more accurate depiction of the underlying distribution. The recently proposed method of track-density imaging (TDI) allows to capture the spatial distribution of a tractogram. In this work, we propose an extension of TDI towards the 5D spatio-angular domain, which we name track orientation density imaging (TODI). The proposed method aims to capture the full track orientation distribution (TOD). Just as the TDI map, the TOD is amenable to spatial super-resolution (or even sub-resolution), but in addition also to angular super-resolution. Through experiments on *in vivo* human subject data, an *in silico* numerical phantom and a challenging tractography phantom, we found that the TOD presents an increased amount of regional spatio-angular consistency, as compared to the fiber orientation distribution (FOD) from constrained spherical deconvolution (CSD). Furthermore, we explain how the amplitude of the TOD of a short-tracks distribution (*i.e.* where the track length is limited) can be interpreted as a measure of track-like local support (TLS). This in turn motivated us to explore the idea of TOD-based fiber tractography. In such a setting, the short-tracks TOD is able to guide a track along directions that are more likely to correspond to continuous structure over a longer distance. This powerful concept is shown to greatly robustify targeted as well as whole-brain tractography. We conclude that the TOD is a versatile tool that can be cast in many different roles and scenarios in the expanding domain of fiber tractography based methods and their applications.

Abbreviations: ACT, anatomically-constrained tractography; AFD, apparent fiber density; APM, average pathlength map; ATI, angular track imaging; CB, cingulum bundle; CNR, contrast-to-noise ratio; CSD, constrained spherical deconvolution; DEC, directionally-encoded color; DIST, diffusion indices along streamline trajectories; DTI, diffusion tensor imaging; DWI, diffusion weighted imaging; FA, fractional anisotropy; fMRI, functional magnetic resonance imaging; FOD, fiber orientation distribution; GCC, genu of the corpus callosum; GM, gray matter; HARDI, high angular resolution diffusion imaging; IC, invalid connections; iFOD2, 2nd order integration over fiber orientation distributions; iTOD2, 2nd order integration over track orientation distributions; KDE, kernel density estimate; NC, no connections; PDF, probability density function; PET, positron emission tomography; PSF, point spread function; RGB, red-green-blue; RH, rotational harmonics; SCP, superior cerebellar peduncle; SH, spherical harmonics; SIFT, spherical-deconvolution informed filtering of tractograms; SNR, signal-to-noise ratio; TDI, track-density imaging; TFCE, threshold-free cluster enhancement; TLS, track-like local support; TODI, track orientation density imaging; TOD, track orientation distribution; TOWI, track orientation weighted imaging; TOWM, track orientation weighted mean; TOWT, track orientation weighted total; TRSE, twice-refocused spin-echo; TW-FC, track-weighted functional connectivity; TWI, track-weighted imaging; TWM, track-weighted mean; TW-PET, track-weighted positron emission tomography; TWT, track-weighted total; VC, valid connections; WM, white matter.

* Corresponding author.
E-mail address: thijs.dhollander@gmail.com (T. Dhollander).

http://dx.doi.org/10.1016/j.neuroimage.2013.12.047

1. Introduction

Since the advent of diffusion weighted imaging (DWI) in the mid-1980s, we have come a long way towards mapping the structural network of the (human) brain *in vivo* and non-invasively (Jones, 2010), leading to better insight in its complexity and eventually giving rise to a whole new field of connectomics (Hagmann, 2005; Hagmann et al., 2010; Sporns et al., 2005). A key development in achieving this has certainly been the introduction of the concept of fiber tractography at the end of the previous millenium (Basser, 1998; Basser et al., 2000; Conturo et al., 1999; Jones et al., 1999b; Lori et al., 1999; Mori et al., 1999; Poupon et al., 1999). Throughout the past decade, tractography has proven to be a powerful tool that comes with many advantages as well as important limitations (Jbabdi and Johansen-Berg, 2011). Current state-of-the-art algorithms, that can handle complex fiber architecture (*i.e.* so-called "crossing fibers") as well as take on a probabilistic approach to account for different sources of uncertainty, are now widespread and available for public use, *e.g.* Tournier et al. (2012); and were proven to be far superior to fundamentally limited techniques based on diffusion tensor imaging (DTI) for critical applications such as neurosurgical planning and navigation (Farquharson et al., 2013). Given the orientational information in each voxel (*e.g.* a fiber orientation distribution (FOD) from constrained spherical deconvolution (CSD), Tournier et al., 2007, 2008) and several constraining parameters (*e.g.* minimum and/or maximum track length, limited curvature, minimum FOD amplitude threshold, a mask, a seed region, …), a tractography algorithm yields a tractogram: a finite number of accepted tracks; a random sample from a distribution of possible tracks. The more tracks are generated, the more representative the tractogram becomes regarding this distribution.

Recently, track-density imaging (TDI) (Calamante et al., 2010, 2011) was proposed as a means to obtain super-resolution from DWI data by exploiting the continuous nature of dense tractograms consisting of a very large number (*e.g.* millions) of tracks. It does so by employing a strategy very similar to that of a common histogram: in each voxel of a (potentially high resolution) 3D grid, the number of tracks is simply counted. As the amount of tracks that can be generated is virtually unlimited, the underlying distribution can be approximated up to any detail, justifying the use of super-resolution. As such, TDI is an excellent tool to obtain a "classical" 3D image space representation of the spatial probability density function (PDF) of complex track distributions. In an attempt to capture and visualize some additional angular information, directionally-encoded color (DEC) TDI assigns to each track passing through a certain voxel a color based on the local orientation of the track (conforming to the color scheme widely used for DEC fractional anisotropy (FA) maps in DTI, *e.g.* red: mediolateral, green: anteroposterior, and blue: superoinferior). These colors (RGB values) are then summed in each voxel, resulting in the DEC TDI map. While the global pattern of colors does provide an additional visual cue for easier localization of known structures, it can on a local (voxel) level not distinguish between multiple fiber populations, nor describe other complex structure. This particular color scheme even lacks specificity in describing a *single* direction (*i.e.* even in DEC FA maps from DTI): in general, an RGB triplet can correspond to four different directions (when all R-, G- and B-values are nonzero). Therefore, the additional DEC in the context of TDI has no major use beyond being a practical visualization tool.

In this work, we introduce track orientation density imaging (TODI), a technique which aims to reconstruct a complete description of the track orientation distribution (TOD) in each voxel. We will describe the formalisms of TODI as a generalization of TDI to the entire 5D spatio-angular domain. To maintain full compatibility with the existing definition of TDI, the same mechanism is employed to map the tracks' spatial distribution: each track delivers a *unit* contribution to each voxel it intersects and thus the final weight of a voxel in the spatial distribution is proportional to its track count. Whereas this choice of using voxels as bins for a histogram-like approach in the 3D spatial domain is a straightforward one, it is less trivial to define such discrete bins in the 2D angular domain, *i.e.* on the sphere. A possible approach to discrete angular binning consists of generating a large set of uniformly distributed directions, *e.g.* by geodesation of an icosahedron or electrostatic repulsion (Jones et al., 1999a). A track could then locally contribute to the direction within the set that best approximates the track's (tangent) direction (Pannek et al., 2012). Such a strategy conceptually equals to defining a set of angular bins as resulting from the Voronoi tessellation (on the sphere) of the set of generated directions. Typically, most of these bins would be hexagonally shaped, though some would inevitably be pentagons (Saff and Kuijlaars, 1997), and using electrostatic repulsion might in practice even result in some heptagons. To simply avoid possible bias caused by any particular choice of angular bins, we rather choose to estimate the angular part of the distribution by use of a kernel density estimate (KDE). In TODI, we will represent the TOD in each voxel using a set of spherical harmonics (SH) basis functions and construct it by continuous integration of a spherical point spread function (PSF) along the intersecting part of each track: the resulting contribution of a track to a voxel is a full angular function. As for the PSF, we will first consider a SH delta function and further refine this choice to an apodized delta function (Raffelt et al., 2012a) to avoid the Gibbs truncation artifacts associated with the SH delta function's definition. More information on the construction of such apodized delta functions can be found in Appendix A. Based on the same principles as discussed in Calamante et al. (2010), TODI is also amenable to spatial super-resolution. Furthermore, we will discuss how these principles are inherently extended to the angular domain, effectively allowing for the complementary case of angular super-resolution. Even spatial *sub*-resolution could provide to be an interesting option in order to investigate the angular distribution of a tractogram over larger spatial volumes as a whole. The most extreme case of such spatial sub-resolution is to fully ignore all spatial information and only consider the angular distribution; *i.e.* as if the whole tractogram were encapsulated in a single spatial bin (*e.g.* a single large voxel).

Although TODI can be applied to *any* tractogram resulting from *any* fiber tractography algorithm, the results presented in this work are focused on its application to so called "short-tracks" tractograms. The short-tracks strategy was proposed in Calamante et al. (2012c) to mitigate the effect of the TDI map of a "regular" whole-brain tractogram featuring higher intensities in longer tracts[1], caused by those tracts containing more seed points. By imposing an upper limit on the track length, the short-tracks strategy distributes track densities more evenly over the brain. In our interest, this avoids dependence of TOD amplitudes on different relative tract lengths. Additionally, this renders the TOD in most voxels more comparable (qualitatively) to the FOD as resulting from CSD (Tournier et al., 2007, 2008), which is also independent of tract length. Even though the short-tracks TOD in each voxel certainly has, by definition and construction, a *completely different meaning* as compared to the FOD, it is of a similar qualitative nature in the sense that it also features sharp lobes along directions associated with white matter pathways. We will, however, explain how its amplitude can be interpreted as a measure of *track-like local support* (TLS). This consequently renders the short-tracks TOD itself a potentially interesting candidate to guide tractography using existing algorithms that were originally designed to perform FOD-based tractography. We reason that, in a tractography setting, the short-tracks TOD should be able to guide a track along directions that are more likely to correspond to continuous structure over a longer distance. We will explore the idea of such TOD-based tractography and compare it directly to FOD-based tractography. We also take this concept to the next level by employing TOD-based tractography itself to generate a new short-tracks tractogram that can be used to construct yet another TOD. The latter TOD can in its

[1] Throughout this article, the term "track" denotes a single streamline as obtained from a tractography algorithm, while "tract" refers to a full white matter bundle/structure (*e.g.* the corticospinal tract).