DT-MRI ESTIMATION, REGULARIZATION AND FIBER TRACTOGRAPHY

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ABSTRACT

Diffusion tensor MRI probes and quantifies the anisotropic diffusion of water molecules in biological tissues, making it possible to non-invasively infer the architecture of the underlying structures. In this article, we present a set of new techniques for the estimation and regularization of diffusion tensors MRI datasets as well as a novel approach to the cerebral white matter connectivity mapping. Numerical experimentations conducted on real diffusion weighted MRI will exhibit promising results.

1. INTRODUCTION

Diffusion imaging is a magnetic resonance imaging technique introduced in the mid 1980s [8] which provides a very sensitive probe of biological tissues architecture. Diffusion shows, at a broader scale, how molecules tend to move from low concentration areas to high concentration areas over distances of about 10 to 15 μm during typical times of 50 to 100 ms. The key concept that is of primary importance for diffusion imaging is that diffusion in biological tissues reflects their structure and their architecture at a microscopic scale. For instance, Brownian motion is highly influenced in tissues such as cerebral white matter or the *annulus fibrosus* of inter-vertebral discs. Measuring, at each voxel, that very same motion along a number of sampling directions (at least 6, up to several hundreds) provides an exquisite insight into the local orientation of fibers and is known as diffusion-weighted imaging. Shortly after the first acquisitions of images characterizing the anisotropic diffusion of water molecules *in vivo*, Basser et al. [2] proposed in 1994 the model, now widely used, of the diffusion tensor featuring an analytic means to precisely describe the three-dimensional nature of anisotropy in tissues.
Numerous works have already addressed the problem of the estimation and regularization of the diffusion tensor fields. References can be found in [25], [24], [4], [11], [17]. We will tackle these two tasks within a common variational framework respectively in section 2 and 3.

Most normal brain functions require that specific cortical regions communicate with each other through fiber pathways. Until very recently, there was no non-invasive imaging method capable of resolving the white matter connections between those regions while functional MRI or positron emission tomography give us crucial information on the spatial localization of cerebral activation when a given task is performed. Reliable estimation of the anatomical connectivity is thus fundamental if we want to better understand cerebral processes and will be discussed in section 4 where we will propose a novel approach relying on a better modelization of the stochastic processes describing the motion of water molecules and that are highly dependent on the white matter geometry.

2. ESTIMATION OF DIFFUSION TENSORS

2.1. Data acquisition

Our dataset consists of 30 diffusion weighted images $S_k : \Omega \rightarrow \mathbb{R},\ k = 1, ..., 30$ as well as 1 image S_0 corresponding to the signal intensity in the absence of a diffusion-sensitizing field gradient (ie. $b = 0$ in equation 1). They were obtained on a GE 1.5 T Signa Echospeed with standard 22 mT/m gradient field. The echoplanar images were acquired on 56 evenly spaced axial planes with a 128×128 pixels in each slice. Voxel size is 1.875 $mm \times 1.875$ $mm \times 2.8$ mm. 6 gradient directions $\mathbf{g}_k$, each with 5 different b-factors and 4 repetitions were used. Imaging parameters were: b values between 0 and 1000 $s.mm^{-2}$, $TR = 2.5$ s, $TE = 84.4$ ms and a square field of view of 24 cm [16]. Those data are courtesy of CEA-SHFJ/Orsay, France[1].

2.2. Linear estimation

We recall that the estimation of a field of 3×3 symmetric positive definite tensors $\mathbf{T}$ is done by using the Stejskal-Tanner equation [19] for anisotropic diffusion 1 at each voxel x.

$$S_k(x) = S_0(x) e^{-b \mathbf{g}_k^T \mathbf{T}(x) \mathbf{g}_k} \quad \forall x \in \Omega \tag{1}$$

where $\mathbf{g}_k$ are the normalized non-colinear sensitizing gradient and b the diffusion weighting factor. Many approaches have been derived to estimate the tensor $\mathbf{T}$.
If we effectively restrict ourselves to 6 gradient orientations, Westin et al. derived in [25] a compact analytical solution to equation 1 and, by doing so, eliminated the need to solve it for every single data point. The idea relies on the introduction of a dual tensor basis $\tilde{\mathbf{G}}_k$, computed from the tensor basis $\mathbf{G}_k = \mathbf{g}_k\ \mathbf{g}_k^T$, and which can be used to decompose any given tensor $\mathbf{T}(x)$. We then end up with the closed form

$$\mathbf{T} = \sum_{k=1}^{6} \frac{1}{b} \ln(S_0/S_k)\ \tilde{\mathbf{G}}_k \tag{2}$$

This method turns out to be highly sensitive to noise and easily influenced by potential outliers. This is due to the low number of measurements intrinsically used by this approach and by the

[1]The authors would like to thank J.F. Mangin and J.B Poline for providing us with the data

choice of the minimization function (see [11] where the Geman-McLure M-estimator is used in order to reduce outlier-related artefacts). Moreover resulting tensors may not be positive definite, which requires a subsequent reprojection step.

2.3. Variational estimation

In order to deal with a more complete estimation approach, we propose to incorporate some important priors such as tensor positivity and regularity into a variational formulation of the estimation problem by minimizing the following energy on the manifold of positive definite tensors $P(3)$

$$\underset{\mathbf{T}\in P(3)}{\operatorname{Arg\,min}} \int_\Omega \sum_{k=1}^{n} \psi(\|\ln(S_0/S_k) - b\mathbf{g}_k^T \mathbf{T}\mathbf{g}_k\|) + \alpha\rho(\|\nabla\mathbf{T}\|)d\Omega \tag{3}$$

where ψ controls the robust estimation and the Lagrange multiplier α together with the scalar function ρ drive the anisotropic regularity of the solution. Note that if $\psi(u) = u^2$ and $\alpha = 0$, the criterion reduces to a simple multilinear regression by least square that generalizes the linear estimation method of Westin et al [25] and provides a positive definite solution since the minimization is done on the constrained space $\in P(3)$ of the positive definite tensors. This variational method converges to a much more consistent solution thanks to its global behavior. We refer the interested readers to the article [21], where we give more details and adress the problem of carefully designing numerical schemes, based on manifold integration, to ensure that the estimate stays on $P(3)$ at each step of the gradient descent used to solve the associated Euler-Lagrange equations.

3. REGULARIZATION OF DT-MRI DATASETS

The variational estimation method naturally brings some spatial coherency and smoothness into the generated tensor field. However, the fundamental properties of diffusion tensors, like diffusivities and principal orientations, are contained in their spectral features. It can then be interesting to regularize the tensor field with regard to those spectral elements. This will bring more coherence into the tensor structural information and thus improve the tracking of neural fibers.

3.1. On some non-spectral methods and their limitations

Non-spectral methods are based on a direct anisotropic smoothing of the diffusion weighted data S_k [23] or consider each tensor as 6 independent scalar components $\mathbf{T}_{ij}$ (by symmetry) with possible coupling. We thus evolve each $\mathbf{T}_{ij}$ by minimizing the following quantity:

$$\underset{\mathbf{T}\in P(3)}{\operatorname{Arg\,min}} \int_\Omega \frac{\alpha}{2}\|\mathbf{T} - \mathbf{T}_0\|^2 + \rho(\|\nabla\mathbf{T}\|)d\Omega \tag{4}$$

where $\mathbf{T}_0$ designates the initial noisy tensor field and the field gradient norm $\|\nabla\mathbf{T}\|$ behaves as a coupling term between the tensors components. However, eigenvalues tend to diffuse faster than eigenvectors, resulting in a *swelling* effect on the tensors.

Spectral methods separately consider the eigen-elements of the tensors. Eigenvalues smoothing is typically perfomed by a vector-valued anisotropic PDE ([18] and references therein) satisfying the maximum principle in order to preserve the positiveness. The three orthonormal eigenvectors define a matrix of $O(3)$ which can be regularized by acting only on the principal eigenvector $\mathbf{u}^1$ and then reconstructing the associated tensor [6]. The field of orthonormal matrices can also be evolved ([20]) under a scheme preserving the eigenvectors norms and angles. This boils down to solving a system of coupled and constrained PDEs. However, all these approaches require a time-consuming step of eigenvectors realignment since a given vector and its opposite are both solution of the same singular value decomposition and thus yield artificially discontinuous vectors fields.

3.2. A fast isospectral method

In [4], we proposed a versatile and efficient alternative to the previous spectral techniques which do not require any spectral decomposition by building flows acting on a given submanifold $\mathcal{M}$ of the linear space of matrix-valued function and preserving some constraints. We showed that this amounts to characterize the velocity of the flows (ie. the tangent space of $\mathcal{M}$) at each point of $\mathcal{M}$. Actually the contraints of interests here (orthogonality, eigenvalues conservation ...) can be expressed in term of Lie groups and homogeneous spaces. For example, an isospectral flow acts on a field of real symmetric matrices and preserves their eigenvalues. Moreover its velocity is directly derived from the matrix gradient, hence no need for realignment. If $[A, B]$ denotes the Lie bracket, the general form for our isospectral flow is given by:

$$\frac{\partial\mathbf{T}}{\partial t} = [\mathbf{T}, [\mathbf{T}, (\mathbf{H} + \mathbf{H}^T)]] \tag{5}$$

where $\mathbf{H} = (H_{ij})$ prescribes the desired regularization process, such as

$$H_{ij} = \operatorname{div}(\rho'(\|\nabla\mathbf{T}\|)\nabla T_{ij}/\|\nabla\mathbf{T}\|) \tag{6}$$

where ρ denotes the same scalar function as in section 2.3 and preserves important structures of the tensor field. A specific numerical scheme based on the exponential map was also proposed for the actual implementation of the PDE 5. Results of non-spectral smoothing and isospectral flow on diffusion tensors estimated in the genu of the corpus callosum are presented on figure 1.

4. WHITE MATTER FIBERS TRACTOGRAPHY

4.1. Introduction

The main idea on which rely most classical algorithms for brain connectivity mapping ([12], [13], [15] and references therein) is that, despite the potentially multi-directional environment within a voxel, water diffusion in many regions of the white matter is highly anisotropic and thus, within the limits imposed by the Gaussianity assumption, the orientation of the major eigenvector aligns with the predominant axonal direction. It is then safe to say that we should be able to identify macroscopical three-dimensional architectures of the white matter by using simple line propagation techniques. These local approaches provide fast algorithms to estimate 3D curves, more or less accurately, by integration of the major eigenvector field. Euler or higher-order Runge-Kutta schemes are typically used with intravoxel interpolation of the diffusion tensor field to achieve subvoxel accuracy and reconstruct smooth and more precise curves. By taking into account the anisotropy information in the interpolation process, dynamicaly adjusting the time

step (in high curvature regions for example) or constraining the angle between successive steps, various studies have shown coherent results for known anatomical regions.
All these approaches however fails to recover fibers bundles whenever they enter a region of low anisotropy. The estimate of the curve tangent becomes highly unreliable and Lazar et al. [7] proposed a method based on advection-diffusion equations and making use of the whole diffusion tensor in order to propagate in the most coherent fashion without getting stopped by locally isotropic regions (see figure 2 where we reconstructed about 8000 fibers in less than 5min on a 1Ghz PC. Well known structures such as the corpus callosum, the external capsule or cortico-spinal tracts can easily be identified). These algorithms have been augmented to incorporate some natural constraints such as regularity, stochastic behavior or local non-Gaussianity ([1], [3], [14]).
To better describe the complexity of the diffusion profile, high angular resolution DWI [22] or q-space and Diffusion Spectrum Imaging [10] have been proposed but still yield long acquisition times. Finally more global algorithms ([5]) have been introduced to better handle situations of false planar or spherical tensors (with underlying fibers crossings) or fascicles junctions [17] using some a priori knowledge of the low curvature of most of the fascicles.

4.2. White matter as a Riemannian manifold

In this section, we propose to use stochastic processes and differential geometry to derive a physically motivated distance function in the white matter seen as a 3-manifold M and thus show how to estimate fibers bundles by geodesics computation. The outline of this work, detailled in [9], is as follows: A Brownian motion in linear homogeneous space is entirely determined by its initial distribution μ and a transition mechanism which is either a probability density function p or an infinitesimal generator $\mathcal{L}$. By Fick's law and conservation of mass for a linear anisotropic homogeneous medium, p is actually the fundamental solution (the gaussian kernel) of

$$\frac{\partial C}{\partial t} = \nabla.(\mathbf{D}\nabla C) = \mathcal{L}C \tag{7}$$

However, the solution of equation 7 in the case of a nonlinear anisotropic inhomogeneous (as white matter is) medium is nontrivial. But we actually do not need the explicit solution of this problem since the differential operator $\mathcal{L}$, which is nothing but the Laplace-Beltrami operator, will give us everything we need to characterize the geometry of the manifold supporting the diffusion process, ie. the white matter. Indeed, it can be shown that the inverse of the diffusion tensor $\mathbf{D}^{-1}$ is the metric $\mathbf{G} = (g_{ij})$ of that manifold. Thus, the sole knowledge of the diffusion tensor shall enable us to compute the intrinsic distance *in the space of the brain white matter* to any voxel x_0. It can be shown that the distance function ϕ is Lipschitz on all M and verifies

$$|\text{grad}\phi|^2 = \frac{\partial \phi}{\partial x_i}\frac{\partial \phi}{\partial x_j} g^{ij} = 1$$

with $(g^{ij}) = \mathbf{G}^{-1}$ denoting the metric of the cotangent space. In [9], we propose a level-set formulation and the associated numerical scheme to solve the intrinsic eikonal equation on (M, g). Finally, numerical schemes were proposed to estimate the geodesics on M converging towards x_0. Estimation of the integral curves of the intrinsic distance function are classicaly obtained by back-propagating in its gradient directions $\mathbf{G}^{-1}d\phi$ or by solving the actual geodesic equation. This last approach is efficiently implemented by computing the Christoffel symbols and using the exponential map, which yields accurate schemes for the estimation of geodesics. Computation of neural fibers as geodesics in the region of the splenium of the corpus callosum yields the results presented on figure 3. As we can notice, the main advantage of this method over line propagation techniques is that it is not at all influenced by localized isotropic areas (as we can see on the figure, the red areas do not affect the shape of the recovered fibers).

5. CONCLUSION

Diffusion MRI gives a direct insight into the microstructure of biological tissues through the observation of random molecular motion. This challenging project requires various sophisticated computational techniques before beeing able to actually infer any conclusion on the anatomical connectivity. In this paper, we have presented some major trends for the estimation and the regularization of the diffusion tensor fields as well as adressed the problem of white matter connectivity mapping. Our ongoing efforts are in validating all these techniques on a larger set of real data.

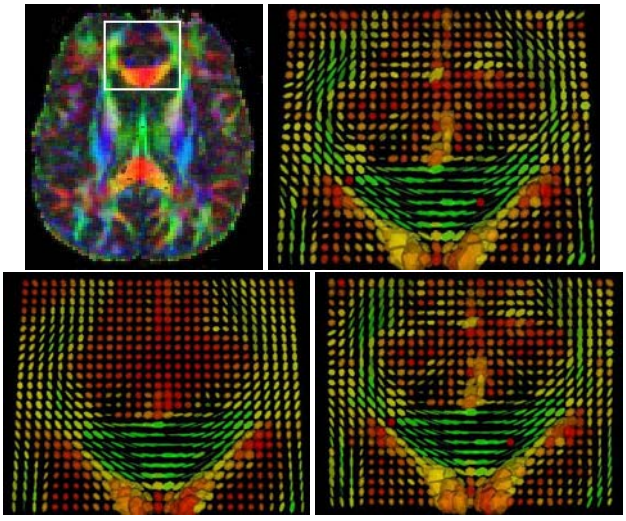

Fig. 1. Left to right: (a) RGB mapping of the major eigenvector weigthed by FA and ROI (b) Raw tensors in the genu of the corpus callosum and regularized fields by (c) a non-spectral method, (d) an isospectral flow

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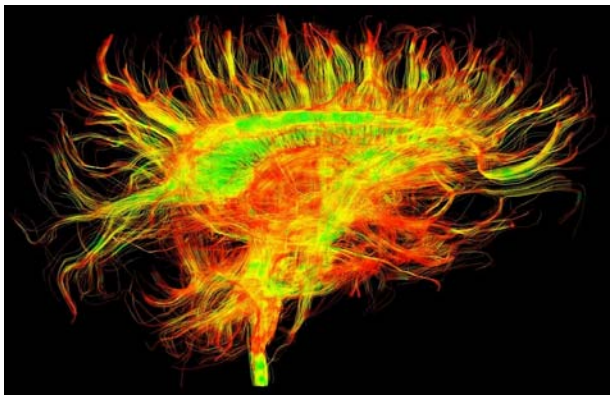

Fig. 2. Whole brain tractography by advection-diffusion based line propagation

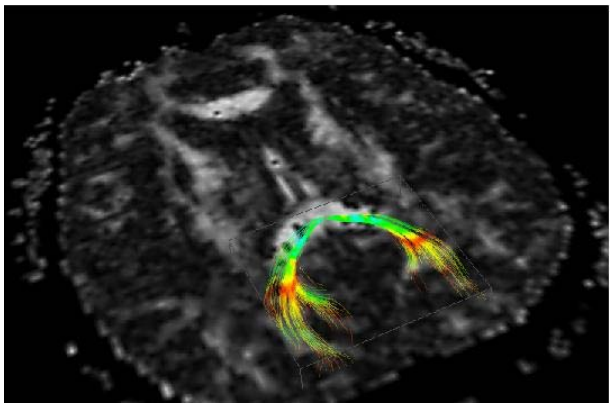

Fig. 3. Inferred geodesics in the splenium of the corpus callosum (red: low anisotropy - blue: high anisotropy)

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