Representing Diffusion MRI in 5D for Segmentation of White Matter Tracts with a Level Set Method.

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Abstract. We present a method for segmenting white matter tracts from high angular resolution diffusion MR images by representing the data in a 5 dimensional space of position and orientation. Whereas crossing fiber tracts cannot be separated in 3D position space, they clearly disentangle in 5D position-orientation space. The segmentation is done using a 5D level set method applied to hyper-surfaces evolving in 5D position-orientation space.

In this paper we present a methodology for constructing the position-orientation space. We then show how to implement the standard level set method in such a non-Euclidean high dimensional space. The level set theory is basically defined for N-dimensions but there are several practical implementation details to consider, such as mean curvature.

Finally, we will show results from a synthetic model and a few preliminary results on real data of a human brain acquired by high angular resolution diffusion MRI.

1 Introduction

Diffusion Weighted Magnetic Resonance Imaging is a modality that permits non-invasive quantification of the water diffusion in living tissues. The tissue structure will affect the Brownian motion of the water molecules which will lead to an anisotropic diffusion. Today, a diffusion tensor (DT) model is the most frequently used method to map the structural anisotropy. The tensor model, which basically only contains information about anisotropy and principal diffusion, has limited possibilities of resolving complex brain white matter architectures, particularly in regions with fiber crossings.

A recent approach first presented by Wedeen et al. in (1) is the Diffusion Spectrum Imaging (DSI) that provides a full 3D probability density function

(PDF) of the diffusion at each location. This PDF provides a detailed description of the diffusion and manages to resolve highly complex cytoarchitecture such as fiber crossings. For simplicity the PDF is normally reduced to an orientation density function (ODF) which is the radial projection of the PDF. Other approaches such as q-ball imaging (2) and persistent angular structure (PAS) (3) aim at directly obtaining the ODF without first measuring the PDF. All these methods are commonly referred to as high angular resolution diffusion (HARD) MRI. Currently, the HARD data is used to map cerebral connectivity through fiber tractography (4).

Jonasson et al. (5) presented a 3D geometric flow algorithm designed for segmenting fiber tracts from DT-MRI. The method was based on the assumption that adjacent voxels in a tract have similar properties of diffusion and we defined similarity measures between tensors to propagate the surface. Various problems can benefit from fiber tract segmentation, like quantitative investigation of the diffusion inside the chosen fiber tracts, white matter registration and surgical planning.

By diagonalizing the DT several practical representations can be computed such as direction of principal diffusion, anisotropy and comparisons between different compartments of diffusion. These simplifications are less straightforward for the ODF. Frank et al. (6) presented a way of determining the anisotropy from HARD data but only anisotropy is not sufficient for segmentation of white matter tracts and the problem of crossing fibers remain unsolved. By augmenting the dimensionality of our data many of these problems can be solved simultaneously. Instead of considering a 3D map of ODFs, we define a 5D position-orientation space (POS) as a combination of a spherical space of orientation and an Euclidean space of position. Two fiber tracts with different directions of diffusion that are crossing each other in the same voxel become separated in this 5D space and can be segmented separately without interference from one another. Another positive aspect of this 5D space is that it consists of only scalar values which allow us to adapt classical segmentation methods for grayscale images.

Firstly we will explain the underlying principles of POS and show how to define it from a 3D map of ODF. We will then show that it is possible to segment white matter structures from HARDI MRI data by propagating a hyper-surface in this non-Euclidean 5D space. The evolution of the interface is implemented using the level set method proposed by Osher and Sethian (7; 8; 9). The level set formalism is defined for N-dimensions and we will show how to practically apply it in 5D, with an emphasis on the computation of mean curvature in 5D.

2 Background Theory

2.1 Position Orientation Space

A HARDI experiment provides a 3D map of ODFs. Thus, for every position vector $\mathbf{x} = (x, y, z)$, in Euclidean 3D space, $\mathbb{R}^3$, there is an ODF measuring the intensity of diffusion in any direction, $\mathbf{u} = (\varphi, \theta)$ where $\mathbf{u}$ is a vector restricted to the unit sphere, S^2, with $(0 \le \theta < 2\pi, 0 \le \varphi \le \pi)$. The cartesian product of $\mathbb{R}^3$ and S^2 forms POS that we note Ω:

$$(\mathbf{x}, \mathbf{u}) \in \Omega = \mathbb{R}^3 \times S^2. \tag{1}$$

And its implied metric tensor allows us to determine the gradient operator as:

$$\nabla = \hat{\mathbf{x}}\frac{\partial}{\partial x} + \hat{\mathbf{y}}\frac{\partial}{\partial y} + \hat{\mathbf{z}}\frac{\partial}{\partial z} + \hat{\varphi}\frac{\partial}{\partial \varphi} + \frac{1}{\sin(\varphi)}\hat{\theta}\frac{\partial}{\partial \theta}. \tag{2}$$

To get some intuition about what POS is and why it is useful for fiber tract segmentation is it instructive to consider the case of a 2D map of ODF restricted to a plane. In Fig. 1a a 2D slice of ODFs is shown. The slice shows a crossing between two fiber tracts. The ODFs in the figure are restricted to the plane and can therefore be described through only one angle, θ. The intensity of the ODF varies with the angle. In the case where we only have one fiber there will be a peak in the intensity for the angle that corresponds to the direction of the fiber. In positions where two fiber tracts cross there will be two intensity peaks, one for the direction of each fiber. These two cases are illustrated in Fig.1b.

The third dimension represents the orientation of diffusion, hence the 2D ODF map is mapped as a 3D scalar field. This means that even though the two fiber tracts cross over in 2D, they will be separated in 3D and can therefore easily be segmented. Fig. 2 shows how the two fibers are segmented in 3D and then projected back to 2D.

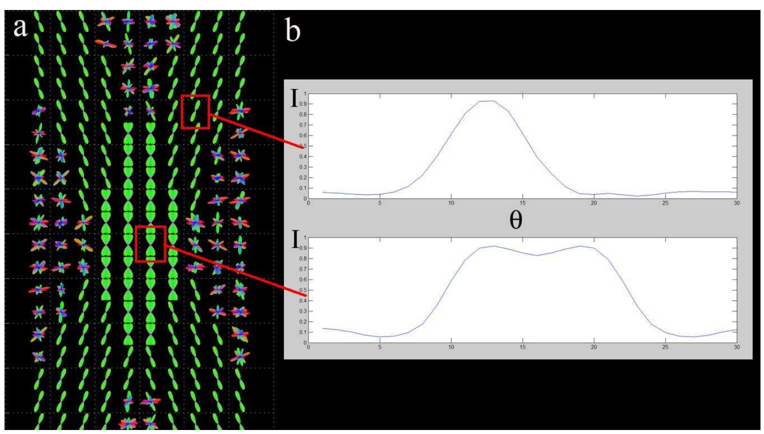

Fig. 1. Example of POS for a 2D slice of a volume of ODFs. The intensity is plotted for each angle.

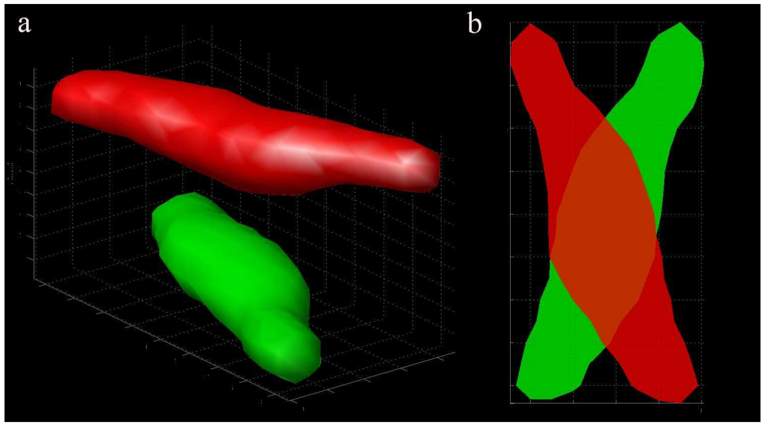

Fig. 2. Example of POS for a 2D slice of a volume of ODFs.

2.2 Level set evolution of N-dimensional interfaces.

Since the level set method was first introduced by Osher and Sethian (7; 8; 9) it is becoming a more and more popular numerical tool within image processing, fluid mechanics, graphics, computer vision etc. It is basically used for tracking moving fronts by considering the front as the zero level set of an embedding function, called the level set function, of the moving front. In image processing the level set method is most frequently used as a segmentation tool through propagation of a contour by using the properties of the image as well as properties of the contour itself, such as the mean curvature. It was originally used to detect edges in an image (10), but more recent applications detect textures, shapes, colors etc. The level set theory was initially used for two dimensional images but its general formulation makes it possible to use for N-dimensional images. The theoretical extension to three dimensions is commonly used and even though some of the properties of the 2D curves, such as the property of shrinking to a point under curvature flow, do not hold in the 3D case, the main part of the theory remains valid and works well for segmentation of 3D objects (11). The extension to even higher dimensions is straightforward.

Let the level set, $\phi(\mathbf{x}, t)$, be a smooth function where $\mathbf{x} \in$ POS and $t \in \mathbb{R}^+$. Then the hyper-surface in 5-dimensions is represented by the level set defined by $\{\mathbf{x} = (x, y, z, \varphi, \theta) \in POS : \phi(\mathbf{x}, t = 0)$.

The evolution of the hyper-surface embedded in the level set function is generally described through this equation:

$$\frac{\partial \phi}{\partial t} = F \mid \nabla \phi \mid, \tag{3}$$

where F is a speed function. For the particular case

$$F = -\nabla \cdot \left(\frac{\nabla \phi}{\mid \nabla \phi \mid} \right), \tag{4}$$

F is the mean curvature of level sets of ϕ and (3) becomes the 5-D mean curvature flow.

Chan and Vese presented in (12) a method for segmenting images without edge detection by using the weak formulation of the Mumford-Shah functional (13). The resulting equation for the interface evolution becomes (12):

$$\begin{cases} \frac{\partial \phi}{\partial t} = \delta_\epsilon(\phi) \left[\mu \nabla \cdot \left(\frac{\nabla \phi}{|\nabla \phi|} \right) - (u_0 - c_1)^2 + (u_0 - c_2)^2 \right] & \text{in } \Omega \\ \frac{\delta_\epsilon(\phi)}{|\nabla \phi|} \frac{\partial \phi}{\partial \vec{n}} = 0 & \text{on } \partial \Omega \end{cases} \tag{5}$$

where Ω is the image domain, in our case POS, and $\partial\Omega$ is the boundary of Ω. $\delta_\epsilon(\phi)$ is the ϵ-regularized Delta function (12) and $\mu > 0$ is a fixed parameter. u_0 is a given image which in our case is the ODF map represented as a scalar volume of intensity values in POS and c_1 and c_2 are defined as:

$$\begin{cases} c_1 = \frac{\int_\Omega H_\epsilon(\phi) u_0 dx}{\int_\Omega H_\epsilon(\phi)} \\ c_2 = \frac{\int_\Omega (1 - H_\epsilon(\phi)) u_0 dx}{\int_\Omega (1 - H_\epsilon(\phi))} \end{cases} \tag{6}$$

Here we have that $H_\epsilon(\phi)$ is the ϵ-regularized version of the Heaviside function and c_1 and c_2 are respectively the averages of the image u_0 on the region $\{\phi \geqslant 0\}$ and $\{\phi < 0\}$.

3 Method and implementation

3.1 Creating POS

We have constructed the 5D POS from a 3D map of ODF. The values of the ODF are placed on a 2D grid. Due to the symmetry of the diffusion data only a hemisphere is sampled so we have that:

$$(\varphi, \theta) \in \{0, \frac{\pi}{n}, ..., \pi - \frac{\pi}{n}\} \times \{0, \frac{\pi}{n} ..., \pi\}, \tag{7}$$

where n is the sampling step.

Due to the spherical geometry of the space there is a periodicity in the data. The two extremities along the θ-axis are neighbors. Due to the symmetry of the diffusion data this periodicity is also present along the φ-axis. If, due to the same symmetry, only a hemisphere is considered, the periodicity along the φ-axis can be disregarded. To cope with the periodicity of the data an exchange between the two ends of the level set along the θ-axis is made after every iteration.

3.2 Evolution of the hyper-surface.

The hyper-surface is evolved according to (5). Once the POS is defined we have a scalar image not too different from a classical gray scale image. The specific considerations except for the high number of dimensions are the periodicity and the computation of the gradients, see (2). Implementing a level set function in 5D is theoretically straightforward but practically difficult. One of the main problem is handling the storage of the huge amount of data that is treated. Optimizing the computation of the level set function and its re-initialization is crucial. There is however one important issue to consider theoretically: the computation of the curvature.

For evolving curves in 2D and surfaces in 3D the expression in (4) is already complicated. In the 2D case the expression of the mean curvature becomes:

$$\nabla \cdot \left(\frac{\nabla \phi}{\mid \nabla \phi \mid} \right) = \frac{\phi_{xx}\phi_y^2 - 2\phi_x\phi_y\phi_{xy} + \phi_{yy}\phi_y^2}{(\phi_x^2 + \phi_y^2)^{1/2}}. \tag{8}$$

Computing this equation for 5D, Mathematica gives a several pages long answer which is not satisfactory from a numerical point of view.

A lot of work has already been done for N-D mean curvature flows (14; 15). Hence, we propose to use the theory developed by Ambrosio and Soner (14) to determine the mean curvature in a 5D space.

Differential geometry decomposes the mean curvature, Γ, into its principal curvatures, κ_n, such as:

$$\Gamma = \frac{\kappa_1 + ... + \kappa_N}{N}. \tag{9}$$

The principal curvatures of a hyper-surface embedded in a level set function, ϕ, of codimension one are then given by the eigenvalues of the following $N \times N$ matrix:

$$\frac{1}{\mid \nabla \phi(x) \mid^2} P_{\nabla \phi(x)} \nabla^2 \phi(x) P_{\nabla \phi(x)}, \tag{10}$$

where P_p is a projection operator onto the space normal to the nonzero vector p:

$$P_p = I - \frac{p \otimes p}{\mid p \mid^2}, \tag{11}$$

where I is the identity matrix.

To test these theories we have evolved a 5D hyper-cube through a mean curvature flow and seen how it first turns into a hyper sphere and then finally shrink to a point, see Fig 3.

The level set function is re-initialized at every iteration using the fast marching method (16):

$$\mid \nabla \phi \mid = 1 \tag{12}$$

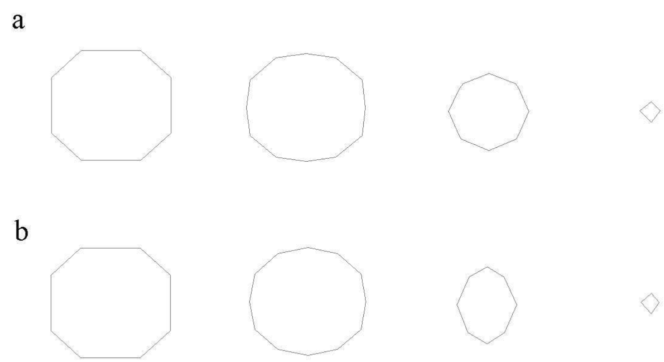

Fig. 3. A hyper-cube evolving under 5D mean curvature flow. a) x-z-plane, b) y-θ-plane.

4 Results

4.1 Synthetic data

To test the method we constructed a 3D volume of ODFs modelling two crossing fiber tracts, see left figure in Fig. 4. The ODFs are normalized by removing the minimum from each ODF. One surface was initialized by placing a small surface of a few voxels in each fiber tract. The hyper surface was evolved until convergence and then projected back into 3D Euclidean space. The result can be seen in Fig. 4. We see how each fiber tract is segmented completely without influence from the other crossing fiber.

4.2 Real data

Material The diffusion images were obtained on a healthy volunteer with a 3T Philipps Intera scanner. We used a diffusion weighted single shot EPI sequence with timing parameters: TR/TE/Δ/ δ =3000/154/47.6/35 ms, bmax = 12000mm2/s and a spatial resolution of 2x2x3mm3. The data were acquired by sampling q-space on a 3D grid with 515 diffusion encoded directions restricted to the interior of a sphere of radius 5. From this acquisition the ODF map is reconstructed according a standard DSI scheme (17).

Informed consent was obtained in accordance with institutional guidelines for all of the volunteers.

Results The ODFs are normalized by removing the minimum from each ODF. The small initial surfaces were placed inside brain region known to contain well

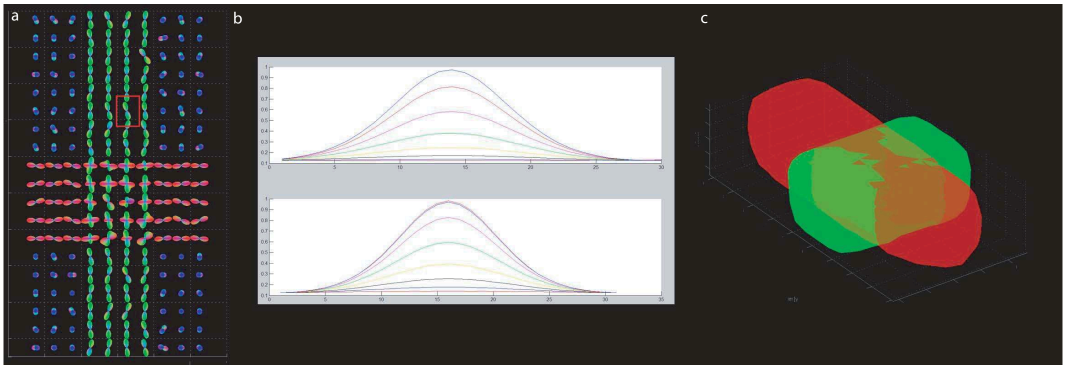

Fig. 4. a) Slice of the synthetic 3D volume of ODFs. b) The intensity of the different angles plotted against each other. c) The 3D projection of the 5D result.

known fiber tracts. The result are shown in Fig. 5 and display the core of important fiber tracts such as the corpus callosum (blue), the cortico spinal tract (red) and the arcuate fasciculus in green. These are early results but show proof of principle. The current problem is the handling of data storage and only smaller volumes can be treated at the moment.

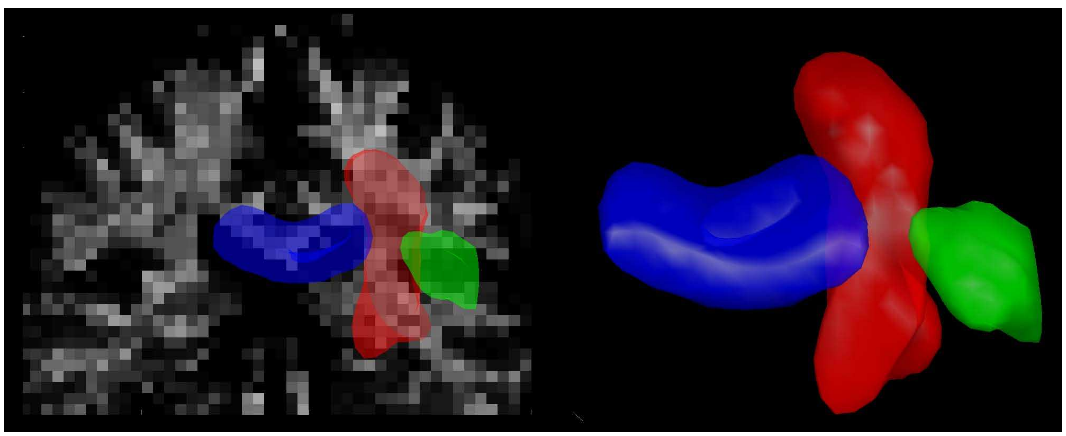

Fig. 5. Results from application on HARD MRI from a human brain. The red surface is a part of the cortico spinal tract. The blue surface is a segment of the corpus callosum and the green is the arcuate fasciculus.

5 Discussion and Conclusion

We have shown how extending the dimensionality of the segmentation space from 3D to 5D disentangles originally overlapping structures. We have seen from the result on synthetic data, that crossing fiber tracts in 3D are represented in 5D POS as separate objects characterized by intense diffusion. The results shown for brain HARD MRI data are the early results. Due to the huge 5D matrices only parts of the structures have been segmented. However, they clearly show the potential of this approach to clearly delimit structures of coherent diffusion. The problem of data handling will be solved with better computer power and a more efficient implementation and data storage.

Further, we have shown that it is possible to implement the level set method for evolving a hyper-surface in a non-Euclidean 5D space. To solve the problem of the implementation of the mean-curvature flow we have proposed to use the theory developed by Ambrosio and Soner (14).

Segmenting regions in HARD MRI is a new approach for interpreting data with a different objective than classical fiber tractography. Fiber tractography provides a map of the cerebral connectivity and aims at visualizing fiber tracts as a set of lines. Our approach treats one fiber tract as one single object characterized by intense and coherent diffusion. This representation gives a different view of the brain architecture that can be more appropriate for applications such quantitative investigation of the diffusion as well as for surgical planning and white matter registration.

Acknowledgements

This work is supported by NIH 1R01-MH64044 grant and the Swiss National Science Foundation grant number 2153-066943.01.

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