A NEW METHOD FOR FIBER TRACTOGRAPHY IN DIFFUSION TENSOR MAGNETIC RESONANCE IMAGES

L. M. San-José-Revuelta, M. Martín-Fernández, C. Alberola-López
Dept. de Teoría de la Señal y Comunicaciones e I.T.
University of Valladolid, 47011 Valladolid, SPAIN
Phone: +34 983 423660, Fax: +34 983 423667
{lsanjose,marcma,carallb}@tel.uva.es

ABSTRACT
This paper deals with the development of a new fiber tracking algorithm to be used with high resolution diffusion tensor fields acquired via magnetic resonance imaging. The tracking of white matter fibers in the human brain will improve the diagnosis and treatment of many neuronal diseases. The algorithm here proposed is based on a mixture of geometrical and probabilistic criteria. The method performs satisfactorily in regions with branching and crossing fibers and offers the capability of reporting a probability value for the computed tracts. This certainty figure takes into account both the anisotropy and the information provided by all the eigenvectors and eigenvalues of the diffusion matrix at each voxel.

KEY WORDS
Diffusion Tensor MRI, fiber tracking, synthetic images

1. Introduction

During the last decade the development of Magnetic Resonance Imaging (MRI) has led to the design of numerous imaging techniques. One of these is Diffusion Tensor MRI (DT-MRI), which measures the diffusion of hydrogen atoms within water molecules in the 3D space. Since in cerebral white matter most random motion of water molecules are restricted by axonal membranes and myelin sheets, diffusion anisotropy allows depiction of directional anisotropy within neural fiber structures [1]. The DT-MRI technique has raised great interest in the neuro-science community for a better understanding of the fiber tract anatomy of the human brain. Several methods have already been reported to use DT-MRI data for tracking nerve fibers and derive connectivity between different parts of the brain. Though this field of search is still in its infancy, its development is growing very fast [2].

There exist many possible and important applications for white matter tractography, and more will appear in the near future as DT-MRI and fiber tracking are becoming standard clinical procedures. Among their most important applications we can find: brain surgery (knowing the extension of the fiber bundles could minimize the functional damage to the patient), white matter visualization using fiber traces (for a better understanding of brain anatomy) and inference of connectivity between different parts of the brain (useful for functional and morphological research of the brain).

Apart from a very few approaches for direct volume rendering [3], the great majority of DTI visualization techniques focus on the integration of sample points along fiber trajectories and their three-dimensional representation [4]. These streamline-based approaches are called fiber tracking and they usually make use only of the principal eigenvector of the diffusion ellipsoid as an estimate of the predominant direction of water diffusion in a voxel [1]. The in vivo visualization of fiber tracts opens up completely new perspectives for neurological research.

Nevertheless and due to some deficiencies in these tracking algorithms and several shortcomings inherent in datasets (noise, artefacts, partial voluming, etc.), they may be illusive by depicting fiber tracts which do not exist in reality or by missing to visualize important connectivity features, e.g. branching structures. In order to avoid misinterpretations, the viewer of the visualizations must be provided with some information on the uncertainty of a depicted fiber and of its presence in a certain location. In this paper we propose an estimation algorithm which takes into account the whole information provided by the diffusion matrix, i.e., it does not only consider the principal eigenvector direction but the complete 3D information about the certainty or likelihood of continuing the path through every possible future direction (voxel hypotheses on possible next paths).

Since we present an initial version of our work, numerical simulations have been performed only on DT-MRI synthetic images, where the primary results here discussed have shown the efficiency of the proposed tracking algorithm. Future work will study the performance on real DT-MR white matter images.

2. Review of Previous Related Approaches

DT-MRI fiber-tracking algorithms commonly use the principal eigenvectors as estimates of the fiber orientation and the linear diffusion anisotropy values at each voxel in order to guide the tracking process. Several seed points are selected within a region of interest at voxels where a predetermined anisotropy
threshold is reached. For each seed point a fiber is tracked in both directions by following the local vector orientation. If we step from voxel to voxel using the discrete vector at each voxel, the tracked line will increasingly differ from the ideal line with each further step. Thus, a more continuous approach is required [1]. The general solution for the vector field integration is the Runge-Kutta approach [5], which allows estimation of the next sample on the line by computing a weighted average of vector orientations. In [6], Mori et al. proposed a method which traces the line on a subvoxel level, linearly interpolating the principal eigenvectors as well as the anisotropy values from the neighboring voxels. In order to avoid non-realistic connections, the angle between the vector orientation of the sample and a pre-defined angle is compared. However, even the selection of high thresholds cannot ensure the production of absolutely correct results [7]. Coulon et al. [8, 9] proposed a field regularization technique for principal eigenvector diffusion fields. On the other hand, Poupon et al. [10] base their regularization technique on a low curvature hypothesis for fascicles. More recently, Pasternak et al. [11] proposed to use a multiple diffusion tensor approach, where the regularization algorithm results in multiple orientation describing each voxel. Other approaches include the tensorline approach [12] and the exhaustive search approach [13, 14]. The former uses the incoming vector from the last tracking step as an estimate and reflects it according to the tensor shape in the current voxel. The exhaustive search approach by Conturo et al. [13], initiates tracking using all brain voxels as seed candidates, thus generating a great number of fiber lines. Afterwards, only those fibers which penetrate the branching region of interest are kept. Recently, a similar approach with seeds that are evenly distributed over the volume was proposed by Vilanova et al. [14].

3. Algorithm Description

The tracking algorithm proposed in this paper uses both geometrical and probabilistic criteria and iterates over several points in the analyzed volume. Specifically, these points are voxels given by the highest probability in the previous iteration. The algorithm starts in a seed voxel, $V_0$, which is specified by the user.

At every iteration, the method evaluates a set of parameters related to the central voxel of a cubic structure similar to that shown in Figure 1. The central point, $V_c$, (No. 14 in the figure) represents the last point of the tract being analyzed. In the first iteration $V_i = V_0$. There exist 26 possible directions to take for the next iteration (in order to select the next point of the tract). Once $V_c$ is selected, the previous point and all those points exceeding the limits of the MR volume are also removed from the list of possible destination points (valid points).

![Figure 1](image.png)

**Figure 1.** Cubic structure used and reference criteria for the axes indexes ($x$, $y$, $z$) and ($m$, $n$, $p$). Central point is $V_c$ (No. 14).

### 3.1 Local Probability

Once a list of valid points is available, a measure $P_i$, i.e. [valid points], is evaluated for each of them based on a probability value of going from voxel $V_i$ to voxel $V_c$. This probability takes into account the eigenvalues and eigenvectors available at point $V_c$ from the DT-MR image diffusion matrix. In order to calculate this probability, the information shown in Table 1 is used.

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<td>$18^\circ$</td>
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Table 1. Modifications of indexes ($m$, $n$, $p$) when moving from $V_c$ to the neighboring voxel $V_i$, $1 \leq i \leq 27$, $i \neq 14$.

This table shows, for each of the 26 voxels shown in Figure 1, the changes that must occur in indexes ($m$, $n$, $p$), when a tract goes from voxel $V_c$ to voxel $V_i$. For instance: when going from point No. 14 ($V_{14}$) to point No. 6, coordinate $m$ reduces by 1, $n$ remains the same, and $p$ increases by 1. This is represented in Table 1 with “(- 0 +)”. With the information of Table 1 the probability of each possible destination $V_i$ can be calculated taking into account the projection of each of the eigenvectors to each of the directions defined in the triplet “(- - -), (- - 0), ... (+ + +)”. Besides, each projection is weighted by the corresponding eigenvalue. Thus, in the previous example, $P_i$ should be calculated as

$$P_i = V_{14} \lambda_1 + V_{24} \lambda_2 + V_{34} \lambda_3 + ... + V_{15} \lambda_1 + V_{25} \lambda_2 + V_{35} \lambda_3 \quad (1)$$
Where $V_{x}$ represents the $x$-component of eigenvector $j$, $1 \leq j \leq 3$ (assuming that $\lambda_{1} > \lambda_{2} > \lambda_{3}$), and so on. The axes reference criterion for the $(x, y, z)$ vector components is also shown in Figure 1. Note that, for this calculus, the sign “−” in the triplet is equivalent to sign “+”. In order to properly weight and calculate Equation (1), $P_{i}$ must be weighted by 0.33 if there are no zeros in triplet $i$, and by 0.5 if there is one zero.

### 3.2 Anisotropy

Both of the following anisotropy indexes can be used in the algorithm:

$$fa = \sqrt{\left(\lambda_{1} - \lambda_{2}\right)^{2} + \left(\lambda_{2} - \lambda_{3}\right)^{2} + \left(\lambda_{3} - \lambda_{1}\right)^{2}}$$

$$\Delta_{12} = \frac{\lambda_{1} - \lambda_{2}}{\lambda_{3} + \lambda_{2} + \lambda_{3}}$$

If both $fa(V_{c})$ and $fa(V_{i})$ (or $\Delta_{12}$) do not exceed a certain threshold (0.2), then point $V_{i}$ is eliminated as a possible destination point.

### 3.3 Local and path probabilities

Taking into account both the probability given by Equation (1) and the anisotropy given by Equation (2) or Equation (3) we find the local probability of voxel $i$, $i \in \{\text{valid points}\}$, as

$$P_{i}' = a \cdot \mu_{1} \cdot fa(V_{i}) + (1-a) \cdot \mu_{2} \cdot P_{i}$$

where parameter $a$ allows the user to give a higher relative weight to either the anisotropy or to the local probability, and $\mu_{1}$ and $\mu_{2}$ are scaling factors (normally, 1 and 1000, respectively).

The probability $P_{i}'$ of each voxel can be recursively accumulated, yielding the probability of the path generated by the successive values of $V_{c}$,

$$P_{p}(k) = P_{p}^{n} \cdot P_{p}(k-1)$$

with $k$ being the iteration number, and $P_{p}^{n}$ the value of $P_{p}$ normalized to its highest value.

### 3.4 Eigenvectors and direction considerations

Besides the considerations referred in the previous subsections, the final probability of voxel $i$ makes also use of the so-called smoothness parameters (described in [15]) which judge the coherence of fiber directions among the trajectories passing through voxel $V_{c}$.

$$sp_{1} = \hat{v}(V_{c}(k)) \cdot \hat{v}(V_{c}(k-1))$$

$$sp_{2} = \hat{v}(V_{c}(k)) \cdot \mathbf{v}_{\text{max}}(V_{c})$$

$$sp_{3} = \hat{v}(V_{c}(k)) \cdot \mathbf{v}_{\text{max}}(V_{i})$$

$$sp_{4} = [\mathbf{v}_{\text{max}}(V_{c}(k)) \cdot \mathbf{v}_{\text{max}}(V_{i})]$$

where $\hat{v}(V_{c}(k))$ and $\hat{v}(V_{c}(k-1))$ are normalized vectors, $\mathbf{v}_{\text{max}}(V_{c}(k)) / \mathbf{v}_{\text{max}}(V_{c})$, $\mathbf{v}_{\text{max}}(V_{c}(k-1)) / \mathbf{v}_{\text{max}}(V_{c}(k-1))$, $V_{c}(k-1)$ denotes the preceding voxel of $V_{c}$, and $\mathbf{v}_{\text{max}}(V_{c}(k-1))$ is the vector pointing from $V_{c}(k-1)$ towards $V_{c}$ (see Figure 2).

![Figure 2. Votexs and vectors involved in the calculus of the smoothness parameters.](image)

$v_{\text{max}}(V_{c}(k))$ and $\mathbf{v}_{\text{max}}(V_{i})$ are the principal eigenvectors (corresponding to the largest eigenvalue of the diffusion tensor) at the voxels $V_{c}$ and $V_{i}$, respectively. Note that parameters $sp_{1}, \ldots, sp_{4}$ measure the angles between the orientations of these vectors. As shown in Figure 2, Equations (6)-(9) imply that $sp_{1} \in [-1, 1]$, and $sp_{2}, sp_{3}, sp_{4} \in [0, 1]$. The thresholds for $sp_{2}, sp_{3}$ and $sp_{4}$ are chosen to be the same value. These three parameters are used to maintain the local directional coherence of the estimated tract and bend the trajectory following unlikely pathways [15]. The threshold for $sp_{1}$ is set to be a value between 0.6 and 0.9 such that the tracking direction could be moved forward consistently and smoothly, preventing the computed path from sharp transitions.

With the four smoothness parameters, the following parameter is calculated for all those points in the structure of Figure 1 that are valid points, and whose smoothness parameters satisfy the four threshold conditions,

$$P_{z}(i) = b (\xi_{1} sp_{1} + \xi_{2} sp_{2} + \xi_{3} sp_{3} + \xi_{4} sp_{4}) +$$

$$+ \left(1-b\right) \mu_{1} \cdot fa(V_{i})$$

where, $\xi_{1}, \xi_{2}, \xi_{3}$ and $\xi_{4}$ are the corresponding weights of the smoothness parameters (normally, 0.25), and $b$ is a weighting factor.

### 3.5 Final criterion

Taking into account both criteria given by Equations (5) and (10), the follow metric is calculated and used for selecting the best $s$ voxels:
\[ P(i) = 0.5 \left( \frac{P_p(i)}{\max_j P_p(i)} + \frac{P_g(i)}{\max_j P_g(i)} \right) \] (11)

A pool of voxels is formed by selecting at the end of each iteration the \( s \) best voxels according to Equation (11). The first voxel of the pool becomes the central voxel \( V_c \) at the beginning of the next iteration (afterwards, it is removed from the pool) expanding this way the current pathway. Obviously, before adding the \( s \) surviving voxels to the pool, it must be checked that they do not belong to: (i) previous points of the current path, and (ii) already existing points in the pool. In our simulations \( 1 \leq s \leq 5 \).

4. Numerical Results

In order to evaluate the tracking properties of the proposed algorithm, we have generated three different synthetic DT-MRI data in a 50x50x50 grid, where the true path of the fiber tract is known. To make the simulated field more realistic, Rician noise [16] was added in the diffusion weighted images which were calculated from the Stejskal-Tanner equation using the gradient sequence in [17] and a \( b \)-value of 1000. The three test images considered are shown in Figure 3.

Figure 3. Synthetic DT-MRI images used for testing the proposed algorithm: “cross” (left), “earth” (center) and “log” (right).

The desired noisy synthetic diffusion tensor data was obtained using an analytic solution to the Stejskal-Tanner equation. The eigenvectors in the isotropic areas were \( \lambda_1 = \lambda_2 = \lambda_3 \), while in the remaining voxels of the image \( \lambda_1 = 7, \lambda_2 = 2, \lambda_3 = 1 \). In the study of robustness the SNR varies from 0 to 30 dB.

As an example, Figure 4 shows the cross test volume with SNR = 10 (left) and with SNR = 30 dB (right).

Figure 4. Representation of the cross synthetic image with SNR = 10 (left) and SNR = 30 dB (right).

Figure 5 shows the tracing results for the cross-like test image (Fig. 3, left), for different selections of the initial seed \( V_0 \). The two parts of the cross are located as follows: one of them is parallel to the \( x \) axis, with \( 20 \leq n,p \leq 30 \), and the other is parallel to the \( y \) axis, with \( 20 \leq m,p \leq 30 \). It can be seen how the algorithm can be designed in order to pass through isotropic zones where different fiber bundles cross (\( 20 \leq m,n,p \leq 30 \)). It is also appreciated how the algorithm differentiates between the totally isotropic zones extrinsic to the tracts and the fiber bundles themselves.

Figure 5. Tracking results for the cross-like image in the absence of noise. Green: seed point. Blue: fiber path voxels. Red: extrinsic voxels.

The differentiation between intrinsic and extrinsic voxels, i.e., voxels belonging to a fiber or to a very isotropic area, respectively, is attained by mapping the path probabilities given by Equation (5) into a color scale and classifying them according to some fixed thresholds. Three different seeds \( (S_1, S_2, S_3) \) are shown in Figure 5. \( S_1 \) and \( S_2 \) belong to the intrinsic volume (voxels with a very high anisotropy) and the algorithm moves through the most probable direction following the main direction of the cross in each situation. On the other hand, when an extrinsic point as \( S_3 \) is selected as seed, the algorithm explores in the neighboring voxels until it finds a voxel \( V_i \) with a high anisotropy value (point \( P_1 \) in Figure 5). Once \( P_1 \) is found, the tracking algorithm proceeds as in the case of \( S_1 \) and \( S_2 \).

Results for the second image (“earth”, Fig. 3 center) are shown in Figure 6. In this case, the fibers are like geographical parallels of different spheres with the same center and different radius, situated on plane \( x-y \) and with a totally isotropic cylindrical volume in the center, parallel to the \( z \) axis (Figure 3 center).

Again, the results show a satisfactory performance under the conditions considered. The same comments for the seed points \( S_1, S_2 \) and \( S_3 \) are valid in this case. Note that the extrinsic point \( S_3 \) is located in the inner cylinder parallel to the \( z \) axis.
The third case to be analyzed is that of a synthetic volumetric image consisting of logarithmic curves symmetrically distributed around the y axis as shown in Figure 3 (right). This scenario constitutes the most complicated situation since the diffusion field experiments variations with the three coordinate axes. Results are shown in Figure 7.

Figure 7 shows that the algorithm finds again the proper fiber path whatever (extrinsic or intrinsic) seed voxel is chosen. In this case, the extrinsic seed $S_3$ is located far away from the fiber bundles region, thus making the algorithm explore a wider range of points before reaching the point $P_1$ that belongs to an existing logarithmic path.

Finally, the robustness of the tracking algorithm is evaluated by studying the convergence performance for different values of the SNR. Results are shown in Table 2.

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<th>20</th>
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<tr>
<td>Log</td>
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<td>82.1</td>
<td>86.1</td>
<td>96.0</td>
<td>98</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Convergence performance for different SNRs values in the three different test images considered. Cell values represent percentage of right convergence.

It can be seen how the algorithm converges properly within a very wide range of SNRs. The percentages obtained for the “cross” and the “earth” test images are very close, while for the “log” case the algorithm exhibits a slightly lower convergence.

5. Summary and Conclusions

An algorithm for fiber tracking has been developed and tested with several synthetic DT-MRI data. The novelty of the algorithm comes from the fact that it combines both the probability of advancing in a specific direction based on the projection of all the eigenvectors components into the corresponding directions (and, hence, making use of more information than merely the principal eigenvector of the diffusion ellipsoid) and four smoothness criteria based on the relation between the voxels and eigenvectors’ orientations. Three different synthetic tensor data were generated to validate the algorithm. Numerical results showed the satisfactory tracking capability of the proposed method as well as its convergence robustness. In the immediate future the algorithm will be slightly improved through a fine tuning of the parameters and applied to real white matter DT-MRI (if in time, results will be included in the final version of this paper).

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