Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

RECOVERY OF MULTIPLE FIBERS PER VOXEL BY ICA IN DTI TRACTOGRAPHY

Manbir Singh and Chi-Wah Wong
Departments of Radiology and Biomedical Engineering, University of Southern California, Los Angeles, CA, USA

ABSTRACT

Relying on a rank-2 tensor model for diffusion within a voxel, conventional streamline tractography utilizes principal component analysis (PCA) to detect the orientation of a single fiber within a voxel. When more than one fibers or tracts intersect within a voxel, the PCA estimated orientation lies somewhere in-between the multiple fiber directions and is obviously an incomplete and incorrect representation of the underlying fibers in the voxel. This paper investigates the applicability of Independent Component Analysis (ICA) to estimate individual tensors when multiple tensors corresponding to multiple intersecting fibers are present within a voxel. After establishing non-gaussianity of the Diffusion Tensor Imaging (DTI) signals, which is a pre-requisite for ICA, a Monte Carlo simulation study is conducted to show the accuracy of recovering the orientations of two or three tensors (fibers) mixed within a voxel. It is concluded that the principal eigen vectors but not the eigen values of multiple fibers are recoverable by conventional fast ICA.

1. INTRODUCTION

Detection of multiple fibers or tracts within a voxel remains a challenging problem in DTI tractography [1]. A rank-2 tensor (3×3 components) is commonly used to model the diffusion profile of a fiber and its eigen-values and eigen-vectors estimated through a PCA based approach are incorporated in tractography. When multiple fibers are located inside a voxel, a single tensor is an inadequate description of the mixture.

Several strategies have been reported in the literature to resolve individual fiber directions inside a voxel in tractography. This problem has also been called the "fiber crossing" problem and some of the key approaches used to address this problem previously are: 1) gaussian mixture model decomposition [2], including spatial regularization [3], where multiple diffusion tensors and their volume fractions are estimated under the assumption that the normalized diffusion signal magnitude is a mixture of gaussian diffusion distributions or known basis functions, 2) Probabilistic approaches [4,5] where a probability density function (PDF) is used to characterize different directions of diffusion within a voxel and Monte Carlo studies are conducted to obtain tracts including multiple tracts per voxel, and 3) HARDI (high angular resolution diffusion imaging) where high density samples of the diffusion field are acquired upon a spherical shell followed by model-based or preferably a model-free reconstruction [6]. HARDI approaches, however, require large number of gradient directions, usually >100, and a relatively long acquisition time (on the order of one hour), which have limited its practical application. Our motivation in this paper is to develop a methodology that could be used in routine clinical tractography where usually 6 - 25 gradient directions are used to acquire data in less than 10 minutes.

In a previous study [7], we proposed a novel ICA approach, called "modified mixture density ICA" which tuned its nonlinearity functions to minimize errors between the prefixed nonlinearity functions and the PDFs of intermediate sources. Even though this ICA was tested successfully with preliminary human data obtained from six gradient directions and four nonzero *b*-values, its application has been limited due to its computational complexity and slow convergence. Also, the previous ICA was designed to detect only two components inside a voxel without recovering their eigen-values and eigen-vectors, and it was not clear whether our previous ICA formulation would be applicable to the situation where more than two fibers were present in a voxel. We have now developed an approach based on a fast fixed-point ICA algorithm that is much faster and also obtained results with three fibers crossing within a voxel.

In addition, we present new work to answer the following key question: Is ICA applicable to the fiber-crossing problem?

ICA requires that the sources mixed within the detector be independent and non-gaussian. The sources in DTI correspond to the diffusion profiles of individual fibers that are mixed within a voxel. Thus the voxel becomes the sensor in the ICA framework and ICA would require that the diffusion profiles corresponding to individual fibers be independent and their PDFs be non-gaussian.

The diffusion of water molecules in the vicinity of one tract is not likely to be affected significantly by the diffusion of water molecules near another fiber. Thus it is reasonable to assume that the sources are independent. However, there is no *apriori* justification to assume that the sources are non-gaussian.

The formulation of the ICA approach is described briefly in Section 2. An investigation of the statistics of individual sources through experimental measurements is described in Section 3. The applicability of ICA to detect individual tensors within a mixture is investigated by

Monte Carlo simulation studies where we assumed a mixture of two and three fibers inside a voxel. These studies are described in Section 4. Finally based on the results of the simulation, we discuss in Section 5 the applicability of the ICA approach to solve the multiple-fiber crossing problem for incorporation in DTI tractography. The work reported here was based upon 25 gradient orientations ($b = 1000$), and one $b = 0$ acquisition, but would be applicable to other acquisition schemes.

2. THEORY

2.1. Formulation of ICA

In the statistical model of ICA, we obtain n measurements $x_1,...,x_n$ that are modeled as linear combinations of n sources [8]. In other words,

$$x_i = \sum_{j=1}^{n} a_{ij} s_j, \quad \text{for all } i = 1,...,n$$

where a_{ij} denotes the mixing fraction. In vector form

$$\mathbf{X} = AS$$

In the framework of ICA, S can be estimated from X by maximizing the non-gaussianity of $b^T X$ [8], where $b^T = A^{-1}$. In this paper, a consistent metric, negentropy is used to determine non-gaussianity of the signal, where the approximate negentropy J (y) is defined as follows [8]:

$$J(y) \propto [E\{G(y)\} - E\{G(v)\}] \ .$$

G can be any non-quadratic function and v is a Gaussian variable with the same mean and variance as y. Some examples of G are:

$$G_1(y) = \frac{1}{a_1} \log\cosh a_1 y$$

$$G_2(y) = -\exp(-y^2/2)$$

A fast fixed-point ICA algorithm based on negentropy was used in the work presented here. Symmetric orthogonalization was used under the assumption that all tensors carry equal weight and are estimated at the same time.

2.2. DTI Tractography

In diffusion tensor imaging, the signal M at a given value of b, where **b** is the gradient vector [1], can be written as follows:

$$\frac{M}{M_0} = \exp(-\mathbf{D}\mathbf{b}) = \frac{m(g,b)}{m(b=0)} = x_i$$

where M_0 is the signal at b=0 and **D** is a 1×6 vector derived from the tensor matrix. If g gradient directions are used, the **b** matrix would be $g \times 6$. Hence, for one voxel, we obtain a measurement x_i which is a 1×25 vector.

3. NON-GAUSSIANITY OF DTI SIGNAL

One requirement of ICA is that the source signals must be non-gaussian. In this section, clinical data from a 1.5 T MRI scanner with 55 gradient directions were used to investigate the statistics of the DTI signal. We used 55, instead of the typical 25 gradient directions used in clinical imaging, to improve the statistical power per voxel. Application of ICA was still evaluated with 25 gradient directions. Using conventional streamline tractography we extracted two fiber bundles, the genu and splenium of the corpus callosum to evaluate the non-gaussianity of individuals sources. These tracts, shown in Figure 1 as bold red lines, are likely to have only one fiber direction per voxel, and are thus a good representation of single sources in the ICA problem.

Figure 1: DTI Tractography results with Fractional Anisotropy $(FA) > 0.5$. The genu (top) and splenium (bottom) curved structures are clearly seen as thick red lines connecting the left and right brain.

After extracting voxels from each of the two major tracts, bootstrapping was used to obtain the statistics of the signal within each tract. In each voxel, there are signals from 55 gradient directions. In one iteration, 40 voxels were chosen at random and hence, $55 \times 40 = 2200$ data points were obtained. The negentropy and kurtosis were then computed for these points, and the process was repeated 100 times. Figure 2 show the statistics of one iteration for each of the tracts, and Table 1 shows a summary of the statistics of the bootstrapping experiment.

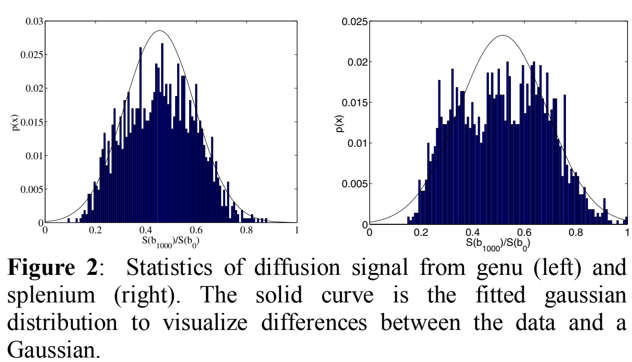

Figure 2: Statistics of diffusion signal from genu (left) and splenium (right). The solid curve is the fitted gaussian distribution to visualize differences between the data and a Gaussian.

Table 1: Summary of statistics using bootstrapping

	genu	splenium
Mean negentropy (zero for Gaussian)	2.7	2.6
Variance of negentropy	8e-5	1.74e-4
Mean kurtosis (zero for Gaussian)	-0.7045	-0.804
Variance of kurtosis	0.0046	0.0061

These studies suggest that the statistics or PDF of a single fiber, i.e., when a single source is contained within a voxel, conform to a sub-gaussian distribution. It is therefore concluded that the non-gaussianity requirement of ICA for individual sources within a mixture of sources is fulfilled when multiple fibers are present within a voxel.

4. SIMULATION FOR RESOLVING THREE FIBERS IN ONE VOXEL

In this section we synthesize data using a mixture model to investigate the applicability of ICA. The mixture is expressed as follows:

$$x_i = \sum_{i=1}^{n} k_i \exp(-\mathbf{D}_i \mathbf{b})$$

where k_i is the weighting of each tensor.

To implement ICA we need measurements corresponding to different mixtures of sources. To accomplish this, we consider neighbors of the "central" voxel under the assumption that fibers or sources would be mixed with different weights in these voxels. Figure 3 shows an example of the mixing configuration of two and three crossing fibers. The mixing ratios are generated from the contribution of individual fibers to each voxel. For example, in the 3-fiber case, the mixing ratios among the 8 neighbors shown are: [0.55 0.175 0.275;0.39 0.37 0.24;0.17 0.57 0.26;0.35 0.24 0.41;0.33 0.33 0.34;0.29 0.27 0.44;0.17 0.57 0.26;0.38 0.4 0.22;0.54 0.2 0.27].

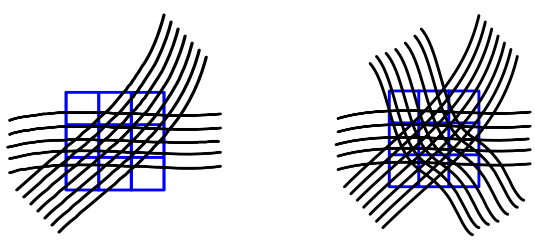

Figure 3: An example of two different configurations of crossing fibers.

For each measurement x_i, random complex noise was added with independent real and imaginary parts, each with distribution $N(0,\sigma^2)$ and $\sigma = 1/SNR$. The SNR for this work was chosen to be 25, which is a representative value obtained in 25-gradient measurements [9].

For each tensor in the mixing model, the eigen-values in this simulation study were set to be $\lambda_1 = 1.7\text{e-}9\ m^2s^{-1}$ and $\lambda_2 = \lambda_3 = 0.2\text{e-}9\ m^2s^{-1}$. The results obtained by a fixed point fast ICA to estimate the source tensors based on the above configuration are shown in Figure 4. It is observed that the error angles of the principle eigen-vectors between the original and estimated tensors are very small.

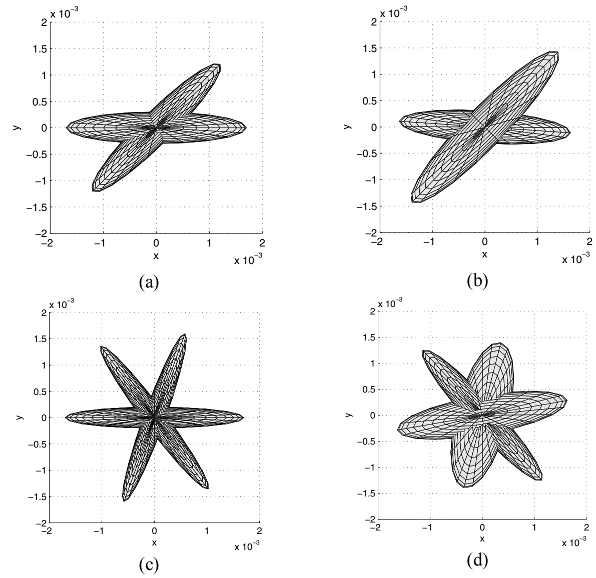

Figure 4: Result of tensor estimation of simulated DTI signals. (a) Synthetic tensors with two crossing fibers. (b) Estimated tensors from mixture data generated from (a). (c) Synthetic tensors with three crossing fibers. (d) Estimated tensors from mixture data generated from (c).

Next, a Monte Carlo simulation was conducted to investigate the accuracy of the ICA approach for a mixture of randomly oriented tensors. Six and ten neighbor configurations were used as shown in Figure 5. The two or three fibers were oriented at random angles in three-dimensions and ICA was applied to detect the individual fibers. The principle eigen vector was then computed for each tensor to estimate the angles between tensors.

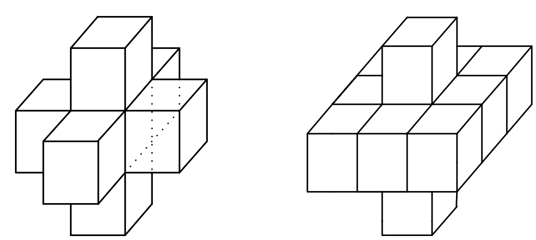

Figure 5: Six (left) and ten (right) neighbor configurations.

The absolute error angles between the principle eigen-vectors of the original and estimated tensors were calculated to evaluate the accuracy of recovering individual tensor orientations with ICA. The results for the two and three fibers cases are shown in Figures 6 and 7 respectively.

In Figure 6, it is observed that there is very little difference between the two neighbor configurations (left vs. right). More than 60% of the trials have less than 10 degrees error. In Figure 7, the 10-neighbor configuration (right) shows some improvement over the 6-neighbor configuration (left). In the 10-neighbor case, 58% of the trials have error less than 20 degrees. Also, as expected, the performance with three fibers is worse than the two fiber-crossing case. Figure 8 shows a sample of the synthetic data and the estimated components. It is observed that ICA could recover the "shape" of the components but not the variance of the components.

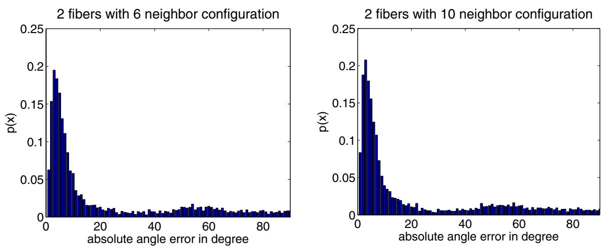

Figure 6: Results of the Monte Carlo simulation for 2 fibers.

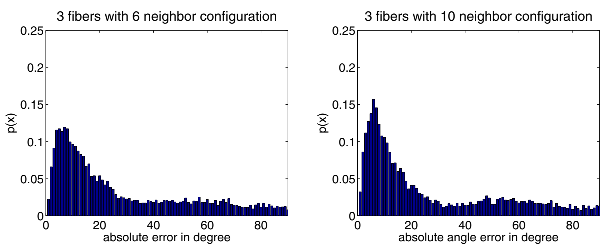

Figure 7: Results of the Monte Carlo simulation for 3 fibers.

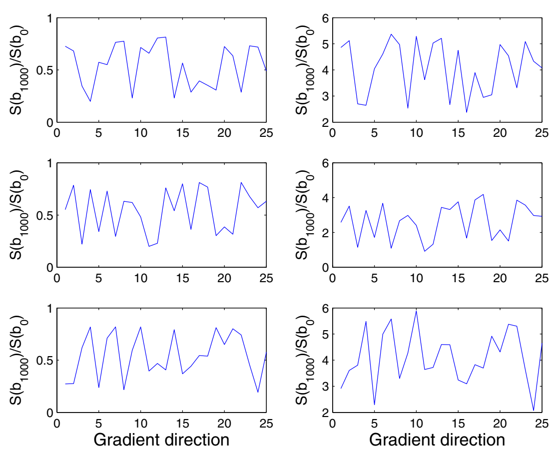

Figure 8: A sample of the original (left) and estimated (right) signals of individual tensors in the central voxel.

5. DISCUSSION

The simulation studies show that ICA could be used to detect orientations of individual fibers within voxels containing crossing fibers. The number of fibers per voxel that we have investigated in this paper is up to three.

One limitation of ICA is that the variance of the individual signals could not be recovered. This means that the eigen-values and hence the Fractional Anisotropy (FA) could not be recovered. Thus, further investigation is needed to recover the complete tensor information. However, knowledge of the orientation of individual tensors within voxels known to contain multiple fibers would provide very significant information to improve DTI tractography.

6. CONCLUSION

Simulation and experimental studies suggest that ICA is applicable to the multiple-fiber crossing problem and that the orientations of individual fibers are recoverable for up to three fibers per voxel.

ACKNOWLEDGMENT

This work was supported by grant NIA-NIH P50 AG05142. The code for fast ICA was obtained from http://www.cis.hut.fi/projects/ica/fastica.

REFERENCES

[1] S. Mori and P.C.M van Zijl, "Fiber tracking: principles and strategies- a technical review", *NMR Biomed*, 15:468-480, 2002.

[2] D.S. Tuch, T.G. Reese, M.R. Wiegell, N. Makris, J.W. Belliveau, and V.J. Wedeen, "High angular resolution diffusion imaging reveals intra-voxel white matter fiber heterogeneity", *Magnetic Resonance in Medicine*, 48: 577-582, 2002.

[3] A. Ramirez-Manzanares, M. Rivera, "Brain Nerve Bundles Estimation by Restoring and Filtering Intra-voxel Information In Diffusion Tensor MRI", *2nd IEEE workshop on Variational, Geometric and Level Sets methods in CV*, Nice, France, 2003.

[4] G.J.M. Parker and D. C. Alexander, "Probabilistic Monte Carlo based mapping of cerebral connections utilizing whole-brain crossing fibre information" C.J. Taylor and J.A. Noble (Eds.): *IPMI 2003*, LNCS 2732:684-695, 2003.

[5] G.J.M. Parker and D. C. Alexander, "Probabilistic anatomical connectivity derived from the microscopic persistent angular structure of cerebral tissue" *Phil. Trans.* R. Soc. B 360: 893-902, 2005.

[6] D.S. Tuch, "Q-ball imaging", *Magnetic Resonance in Medicine*, 52: 1358-1372, 2004.

[7] S.H Kim, J.W. Jeong, and M. Singh, "Estimation of multiple fiber orientations from diffusion tensor MRI using independent component analysis", *IEEE Trans. Nuclear Science*, 52(1), 266-273, 2005.

[8] Aapo Hyvarinen, Juha Karhunen, and Erkki Oja, "*Independent Component Analysis*", John Wiley & Sons, Inc., New York, 2001.

[9] D.C. Alexander, "Multiple-fibre reconstruction algorithms for diffusion MRI", *Annals of the New York Academy of Sciences*, 1064: 113-133, 2005.