Registration of High Angular Resolution Diffusion MRI Images Using 4^{th} Order Tensors*

Angelos Barmpoutis, Baba C. Vemuri, and John R. Forder

University of Florida, Gainesville FL 32611, USA
{abarmpou,vemuri}@cise.ufl.edu, jforder@mbi.ufl.edu

Abstract. Registration of Diffusion Weighted (DW)-MRI datasets has been commonly achieved to date in literature by using either scalar or 2^{nd}-order tensorial information. However, scalar or 2^{nd}-order tensors fail to capture complex local tissue structures, such as fiber crossings, and therefore, datasets containing fiber-crossings cannot be registered accurately by using these techniques. In this paper we present a novel method for non-rigidly registering DW-MRI datasets that are represented by a field of 4^{th}-order tensors. We use the Hellinger distance between the normalized 4^{th}-order tensors represented as distributions, in order to achieve this registration. Hellinger distance is easy to compute, is scale and rotation invariant and hence allows for comparison of the true shape of distributions. Furthermore, we propose a novel 4^{th}-order tensor re-transformation operator, which plays an essential role in the registration procedure and shows significantly better performance compared to the re-orientation operator used in literature for DTI registration. We validate and compare our technique with other existing scalar image and DTI registration methods using simulated diffusion MR data and real HARDI datasets.

1 Introduction

In medical imaging, during the last decade, it has become possible to collect magnetic resonance image (MRI) data that measures the apparent diffusivity of water in tissue *in vivo*. A 2^{nd} order tensor has commonly been used to approximate the diffusivity profile at each image lattice point in a DW-MRI [4]. The approximated diffusivity function is given by

$$d(\mathbf{g}) = \mathbf{g}^T \mathbf{D} \mathbf{g} \tag{1}$$

where $\mathbf{g} = [g_1 \; g_2 \; g_3]^T$ is the magnetic field gradient direction and $\mathbf{D}$ is the estimated 2^{nd}-order tensor.

Registration of DW-MRI datasets by using 2^{nd}-order tensors has been proposed by Alexander et al. [2]. In this work a tensor re-orientation operation was

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proposed as a significant part of the diffusion tensor field transformation procedure. A framework for non-rigid registration of multi-modal medical images was proposed in [12]. This technique performs registration based on extraction of highly structured features from the datasets and it was applied to tensor fields. Registration of DTI using quantities which are invariant to rigid transformations and computed from the diffusion tensors was proposed in [7]. By registering the rigid-tranformation invariant maps, one avoids the re-orientation step and thus can reduce the time complexity. The locally affine multi-resolution scalar image registration proposed in [8] was extended to DTI images in [17]. In this method the image domain of the image being registered is subdivided (using a multi-resolution framework) into smaller regions, and each region is registered using affine transformation. The affine transformation is parametrized using a transformation vector, a rotation, and an SPD matrix. By using this parametrization one can avoid the polar decomposition step which is required in order to extract the rotation component for re-orientation purposes.

All the above methods perform registration of DW-MRI datasets based on scalar images or 2^{nd}-order tensorial approximations of the local diffusivity. This approximation fails to represent complex local tissue structures, such as fiber crossings, and therefore DTI registration of dataset containing such crossings leads to inaccurate transformations of the local tissue structures.

In this paper we present a novel registration method for DW-MRI datasets represented by a field of 4^{th}-order tensors. We propose to use the Hellinger distance measure between 4^{th}-order tensors represented by angular distributions (corresponding to the normalized coefficients of these tensors), and employ it in the registration procedure. Hellinger distance is very commonly used in communication networks and also in density estimation techniques as it is quite robust and has attractive asymptotics [5]. From our point of view, this distance is easy to compute and is scale and rotation invariant, thus allowing for true shape comparison [9]. Another key contribution of our work is the higher-order tensor re-transformation operation, which is applied in our registration algorithm. We validate our framework and compare it with existing techniques using simulated MR and real datasets.

2 Registration of 4^{th}-Order Tensor Fields

This section is organized as follows: First, in 2.1 we briefly review the formulation of 4^{th}-order tensors in DW-MRI. Then, in section 2.2 we define the Hellinger distance between 4^{th}-order tensors represented by angular distributions, which will be employed in section 2.3 for registration of 4^{th}-order tensor fields.

2.1 4^{th}-Order Symmetric Positive Tensors from DW-MRI

The diffusivity function can be modeled by Eq. 1 using a 2^{nd}-order tensor. Studies have shown that this approximation fails to model complex local diffusivity profiles in real tissues [14,10,11,1] and a higher-order approximation must be employed instead. Several higher-order approximations have been proposed in literature and among them, spherical harmonics [14,6], cartesian tensors [10] etc. have been popular. A 4^{th}-order tensor can be employed in the following diffusivity function

$$d(\mathbf{g}) = \sum_{i+j+k=4} D_{i,j,k} g_1^i g_2^j g_3^k \quad (2)$$

where $\mathbf{g} = [g_1\ g_2\ g_3]^T$ is the magnetic field gradient direction. It should be noted that in the case of 4^{th}-order symmetric tensors there are 15 unique coefficients $D_{i,j,k}$, while in the case of 2^{nd}-order tensors we only have 6.

A positive definite 4^{th}-order tensor field can be estimated from a DW-MRI dataset using the parametrization proposed in [3]. In this parametrization, a 4^{th}-order symmetric positive definite tensor is expressed as a sum of squares of three quadratic forms as $d(\mathbf{g}) = (\mathbf{v}^T\mathbf{q}_1)^2 + (\mathbf{v}^T\mathbf{q}_2)^2 + (\mathbf{v}^T\mathbf{q}_3)^2 = \mathbf{v}^T\mathbf{Q}\mathbf{Q}^T\mathbf{v} = \mathbf{v}^T\mathbf{G}\mathbf{v}$ where $\mathbf{v}$ is a properly chosen vector of monomials, (e.g. $[g_1^2\ g_2^2\ g_3^2\ g_1g_2\ g_1g_3\ g_2g_3]^T$), $\mathbf{Q} = [\mathbf{q}_1|\mathbf{q}_2|\mathbf{q}_3]$ is a 6×3 matrix obtained by stacking the 6 coefficient vectors $\mathbf{q}_i$ and $\mathbf{G} = \mathbf{Q}\mathbf{Q}^T$ is the so called *Gram matrix*. Gram matrix $\mathbf{G}$ is symmetric positive semi-definite and has rank=3. By using this parametrization and following the algorithm presented in [3], a Gram matrix $\mathbf{G}$ is estimated at each voxel of a DW-MRI dataset. Then, one can uniquely compute the tensor coefficients $D_{i,j,k}$ from the coefficients of $\mathbf{G}$.

Given two different DW-MRI datasets depicting the same or different subjects, one can register them by using the information provided by the coefficients $D_{i,j,k}$ of the corresponding 4^{th}-order tensor fields. For this purpose, we need to define the appropriate metric between higher-order tensors, which will be later employed by the registration algorithm.

2.2 Distance Measure

In this section we define a distance measure between symmetric positive definite 4^{th}-order tensors using their corresponding normalized representations which are angular distributions. A family of angular distributions for modeling antipodal symmetric directional data is the angular central Gaussian distribution family, which has a simple formula and a number of properties discussed in [16].

The family of angular central Gaussian distributions on the q-dimensional sphere S_q with radius one is given by $p(\mathbf{g}) = \frac{1}{Z_q(\mathbf{T})}(\mathbf{g}^T\mathbf{T}^{-1}\mathbf{g})^{-\frac{q+1}{2}}$ where $\mathbf{g}$ is a $(q+1)$-dimensional unit vector, $\mathbf{T}$ is a symmetric positive-definite matrix and $Z_q(\mathbf{T})$ is a normalizing factor. In the S_2 case, $\mathbf{g}$ is a 3 dimensional unit vector, $Z_2(\mathbf{T}) = 4\pi\sqrt{|\mathbf{T}|}$, and $\mathbf{T}$ is a 3×3 symmetric positive-definite matrix similar to the 2^{nd}-order tensor used in DTI. A generalization of this distribution family for the case of higher-order tensors should involve an appropriate generalized normalizing factor as a function of higher-order tensors and a generalization of the tensor inversion operation, which may not lead to a closed-form expression. In order to get closed-form expressions we define a new higher-order angular distribution as

$$p(\mathbf{g}) = \frac{1}{\int_{S_2} d(\mathbf{g})^2} d(\mathbf{g})^2 \tag{3}$$

where in the case of 4^{th}-order tensors $d(\mathbf{g})$ is given by Eq. (2) and the integral is over S_2 (i.e. over all unit vectors $\mathbf{g}$). The integral in Eq. (3) can be analytically computed and it can be written in a sum-of-squares form [3].

Given two angular distributions we need to define a scale and rotation invariant metric in order to make true shape (obtained after removing scale and orientation) comparison between them. This can be efficiently done by the Hellinger distance between 4^{th}-order tensors $\mathbf{D}_1$ and $\mathbf{D}_2$:

$$dist^2(\mathbf{D}_1, \mathbf{D}_2) = \int_{S_2} (\sqrt{p_1(\mathbf{g})} - \sqrt{p_2(\mathbf{g})})^2 = \int_{S_2} (\frac{d_1(\mathbf{g})}{\sqrt{\int_{S_2} (d_1(\mathbf{g}))^2}} - \frac{d_2(\mathbf{g})}{\sqrt{\int_{S_2} (d_2(\mathbf{g}))^2}})^2 \tag{4}$$

Here we use the notation $\mathbf{D}$ to denote the 15-dimensional vector consisting of the unique coefficients $D_{i,j,k}$ of a 4^{th}-order tensor. Eq. 4 can also be analytically expressed in a sum-of-squares form and it is invariant to scale and rotations of the 3D space, i.e. the distance between $p_1(\mathbf{g})$ and $p_2(\mathbf{g})$ is equal to the distance between $p_1(s\mathbf{R}\mathbf{g})$ and $p_2(s\mathbf{R}\mathbf{g})$, where $\mathbf{R}$ is a 3×3 rotation matrix and s is a scale parameter.

In the following section we use the above distance measure for registering a pair of misaligned 4^{th}-order tensor fields.

2.3 Registration

In this section we present an algorithm for 4^{th}-order tensor field registration. Given two 4^{th}-order tensor fields $I_1(\mathbf{x})$ and $I_2(\mathbf{x})$, where $\mathbf{x}$ is the 3D lattice index, we need to estimate the unknown transformation $F(\mathbf{x})$, which transforms the dataset $I_1(F(\mathbf{x}))$ in order to better match $I_2(\mathbf{x})$. In the case of an affine transformation we have $F(\mathbf{x}) = \mathbf{A}\mathbf{x} + \mathbf{T}$, where $\mathbf{A}$ is a 3×3 transformation matrix and $\mathbf{T}$ is the translational component of the transformation.

The estimation of the unknown transformation parameters can be done by minimizing the following energy function

$$E(\mathbf{A}, \mathbf{T}) = \int_{\Re^3} dist^2(I_1(\mathbf{A}\mathbf{x} + \mathbf{T}), \mathbf{A}^{-1} \times I_2(\mathbf{x}))d\mathbf{x} \tag{5}$$

where $dist(.,.)$ is the distance measuere between 4^{th}-order tensors defined in section 2.2, and the integral is over the 3D image domain. $\mathbf{A}^{-1} \times I_2(\mathbf{x})$ denotes some higher-order tensor re-transformation operation. This operation applies the inverse transformation to the tensors of the dataset I_2 in order to compare them with the corresponding tensors of the transformed image I_1.

In the case of registering 2^{nd}-order tensor fields, it has been shown that the unknown transformation parameters can be successfully estimated by applying only the rotation component of the transformation to the dataset I_2 [2]. This happens because of the fact that 2^{nd}-order tensors can approximate only single fiber distributions, whose principal direction transformation can be adequately performed by applying rotations only to the tensors.

In the case of 4^{th}-order tensors, multiple fiber distributions can be resolved by a single tensor, whose relative orientations can also be affected by the deformation part of the applied transformation. Therefore, tensor re-orientation is not meaningful for higher-order tensors and in this case a tensor re-transformation operation must be performed instead, using the full affine matrix $\mathbf{A}$, which is defined in section 2.4. Affine transformation has been also used in DTI; for more details and justification of the scheme, the reader is referred to [15].

Equation (5) can be extended for non-rigid registration of 4^{th}-order tensor fields by dividing the domain of image I_1 into N smaller regions and then registering each smaller region by using affine transformations. Similar method has been used for scalar image registration [8] and DTI registration [17]. The unknown transformation parameters can be estimated by minimizing

$$E(\mathbf{A}_1, \mathbf{T}_1, \ldots, \mathbf{A}_N, \mathbf{T}_N) = \sum_{r=1}^{N} \int_{\Re^3} dist^2(I_{1,r}(\mathbf{A}_r\mathbf{x} + \mathbf{T_r}), \mathbf{A}_r^{-1} \times I_2(\mathbf{x}))d\mathbf{x} \quad (6)$$

Eq. 6 can be efficiently minimized by a conjugate gradient algorithm used in a multi-resolution framework, similar to that used in [8] and [17].

2.4 3D Affine Transformation of 4^{th}-Order Tensors

Assume that we have vectorized the coefficients $D_{i,j,k}$ into a 1×15 vector $\mathbf{D}$ in some specific order $D_n = D_{i_n,j_n,k_n}$, (e.g. $D_1 = D_{4,0,0}$, $D_2 = D_{2,2,0}$, etc.). By using this vector, Eq. 2 can be written as $\sum_{n=1}^{15} D_n {g_1}^{i_n} {g_2}^{j_n} {g_3}^{k_n}$. If we apply an affine transformation defined by the 3×3 matrix $\mathbf{A}$ to the 3D space, the previous equation becomes $\sum_{n=1}^{15} D_n (\mathbf{a}_1\mathbf{g})^{i_n} (\mathbf{a}_2\mathbf{g})^{j_n} (\mathbf{a}_3\mathbf{g})^{k_n}$,where $(\mathbf{a}_1\mathbf{g})^{i_n} (\mathbf{a}_2\mathbf{g})^{j_n} (\mathbf{a}_3\mathbf{g})^{k_n}$ is a polynomial of order 4 in 3 variables g_1, g_2, g_3, and a_i is the i^{th} raw of $\mathbf{A}$. In this summation there are 15 such polynomials and each of them can be expanded as $\sum_{m=1}^{15} C_{m,n} {g_1}^{i_m} {g_2}^{j_m} {g_3}^{k_m}$, by computing the corresponding coefficients $C_{m,n}$ as functions of matrix $\mathbf{A}$. For example if we use the same vectorization as we did in the previous example, we have $C_{1,1} = (A_{1,1})^4$, $C_{1,2} = (A_{1,1})^2(A_{2,1})^2$, etc. Therefore, we can construct the 15×15 matrix $\mathbf{C}$, whose elements $C_{m,n}$ are simple functions of $\mathbf{A}$, and use it to define the operation of transforming a 4^{th}-order tensor $\mathbf{D}$ by a 3D affine transformation $\mathbf{A}$ as

$$\mathbf{A} \times \mathbf{D} = \mathbf{C}(A) \cdot D \quad (7)$$

3 Experimental Results

In the experiments presented in this section, we tested the performance of our method using simulated diffusion-weighted MR data and real HARDI data sets. The figures in this section are depicting probability profiles estimated from the 4^{th}-order tensors [11]. The synthetic data were generated by simulating the MR signal from single fibers and fiber crossings using the simulation model in [13]. A

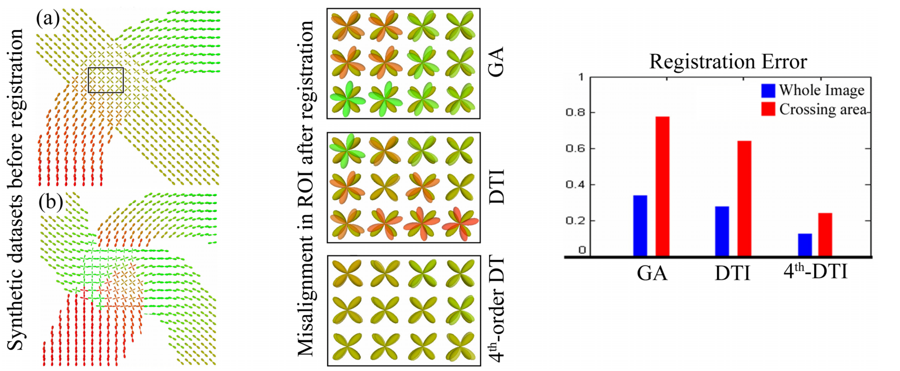

Fig. 1. Left: a) Synthetically generated dataset by simulating the MR signal [13]. b) Dataset generated by applying a non-rigid transformation to (a). Center: Crossing misalignment in ROI after registering datasets (a) and (b) using various methods. Right: Quantitative comparison of the registration errors. The errors were measured by Eq. 4 for the whole field.

dataset of size 128×128 was generated by simulating two fiber bundles crossing each other (Fig. 1a). Then, a non-rigid deformation was randomly generated as a b-spline displacement field and then applied to the original dataset. The obtained dataset is shown in Fig. 1b.

In order to compare the accuracy of our 4^{th}-order tensor field registration method with other methods that perform DTI regitration or registration of scalar quantities computed from tensors (e.g. GA), we registered the dataset of Fig. 1a with that of Fig. 1b by performing: a) General Anisotropy (GA) map registration using the method in [8], b) DTI registration using the algorithm in [17] and c) 4^{th}-order tensor registration using our proposed method. Fig. 1 (center) shows a comparison of the registration results in the region of interest (ROI) shown in the box of Fig. 1a. Each plate in this column shows the misalignment of the fiber crossing profiles after registering using the above methods. By observing the results, our proposed method performs significantly better than the other methods, and motivates the use of 4^{th}-order tensors for registering DW-MRI datasets. Figure 1 (right) shows a quantitative comparison of the above results by measuring the distance between the corresponding misaligned tensors by using the measure defined in section 2.2. The results conclusively validate the accuracy of our method and demonstrate its superior performance compared to the other existing methods.

Furthermore, another dataset (shown in Fig. 2 left) was simulated using [13], by stretching the fibers of Fig.1a along the x-axis by a factor s. In this simulation the fiber orientations were taken to form an angle $\phi' = atan(tan(\phi)/s)$ with x-axis, where ϕ is the original angle between the fiber orientation and x-axis, which was used in the simulation of dataset in Fig. 1a.

In order to demonstrate the need of the tensor re-transformation operation defined in section 2.4, we registered the dataset in Fig. 1a with that in Fig. 2(left)

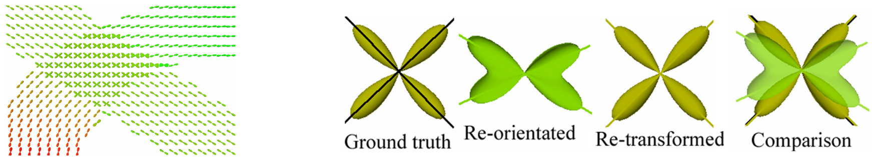

Fig. 2. Left: Simulated dataset generated by stretching the fibers of Fig 1a. Rest of the plates: Comparison of results after registering dataset in Fig.2(left) to that of Fig.1a using tensor re-orientation only and our proposed tensor re-transformation.

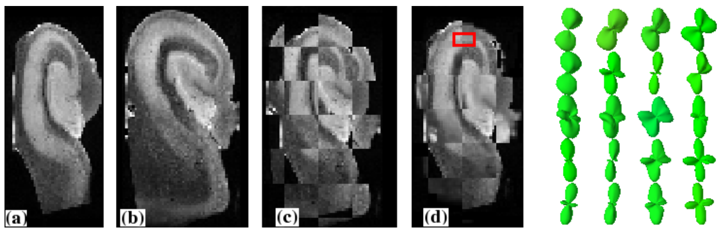

Fig. 3. a and b) S_0 images from two HARDI volumes of human hippocampi. c,d) datasets before and after registration. Tensors from the ROI in (d) showing crossings.

by using: a) re-orientation only in Eq. (5), and b) our proposed re-transformation operation. Fig. 2 depict: a single tensor from the crossing region of the dataset in Fig. 2(left) after registering the datasets using the two methods. By observing the results, we conclude that by re-orienting only the tensors, the fiber orientations were inaccurately estimated, and this motivates the use of our proposed re-transformation.

In the data acquisition first an image without diffusion-weighting was collected, and then 21 diffusion-weighted images were collected with a 415 mT/m diffusion gradient (T_d =17 ms, δ = 2.4ms, b = 1250 s/mm^2). Figure 3 shows two S_0 images from the two 3D volumes (a,b), and two "checkers" images showing the datasets before (c) and after registration (d). A "checkers" image is a way to display two images at the same time, presenting one image in the half boxes, and the other in the rest of the boxes. Based on knowledge of hippocampal anatomy, fiber crossings are observed in several hippocampal regions such as CA3 stratum pyramidale and stratum lucidum. Therefore, one should employ our 4th-order tensor method instead of DTI registration. By observing Fig.3d all the hippocampal regions were successfully alligned by our method, transforming appropriately the fiber crossings Fig. 3(right).

4 Conclusions

Registration of DW-MRI datasets has been commonly performed by using either scalar or DTI information [17]. However scalar or 2^{nd}-order tensorial approximation fails to represent complex local tissue structures, such as fiber crossings, resulting in inaccurate transformations in regions where such complex structures are present. In this paper we presented a method for registering diffusion weighted MRI represented by 4^{th}-order tensor fields. This method employs a novel scale and rotation invariant distance measure between 4^{th}-order tensors. We also proposed a 4^{th}-order tensor re-transformation operation and showed that it plays essential role in the registration procedure. We applied our method to both synthetically generated datasets from simulated MR signal, and real high angular resolution diffusion weighted MR datasets. We compared and validated our method, showing superior performance over other existing methods.

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