

Tensor Spectral Matching of Diffusion Weighted Images

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Abstract. Very preterm birth coincides with a period of major development in the brain, with striking changes in volume, cortex folding and significant change at the microstructural level. Diffusion MRI is sensitive to motion of water on the scale of microns, allowing us to investigate some of these changes. Mapping of diffusion tensors is a challenging process, and existing methods fail to account for the major changes that take place between 30 and 40 weeks equivalent gestational age. In this paper we introduce the spectral matching in the context of non-linear registration of diffusion images. Spatial correspondences are defined with respect to the main spectral modes of the images, which are global descriptors of the tensor information. We apply tensor spectral matching (TSM) in two different ways: by estimation of spatial correspondences uniquely based on the spectral decomposition of diffusion tensor images, and by combination of TSM with a standard diffusion tensor registration algorithm (TSM-DTI-TK). We validate the proposed approaches on 20 adult controls, and we compare it to the state-of-art registration method. We then apply these methods to longitudinal diffusion data acquired from 6 extremely preterm-born infants scanned shortly after birth and at term equivalent age. The experimental results combining TSM with standard tensor registration outperform the state-of-art when applied to both adult and preterm data. Having a reliable anatomical correspondence in preterm infants allows us to quantify microstructural changes and to work towards developing biomarkers of neurological impairment.

1 Introduction

The last 10 weeks of pregnancy represent a period of drastic changes in size, appearance and connectivity of the fetal brain, when the cortex develops from a lissencephalic state and increases dramatically in volume and surface area[1]. Premature birth implies that these brain changes will take place under the harsh conditions of the extrauterine environment and preterm birth is associated with increased rates of adverse neurological outcomes. Hence, there is wide interest in investigating the effects of prematurity on brain development during the preterm period[2].

Diffusion tensor magnetic resonance imaging (DT-MRI) is a water diffusion imaging technique that provides insight into the white matter organisation of the human brain[3]. DT-MRI may allow us to observe and quantify developmental changes during the preterm period, providing additional information about the microstructural change of white matter. Furthermore, water diffusion measures could be correlated with the cortical changes that take place during this period, since tension along axons in white matter is one of the hypotheses for cortical folding[4]. In order to study the developmental changes in the white matter during the preterm period, we need an accurate correspondence between the longitudinal diffusion weighted images. This can be done by means of diffusion tensor registration.

Several diffusion tensor image registration techniques have been proposed based on different matching criteria, like optimising tensor reorientation in an analytic manner through a derivative-based formulation[3] or through the matching of their principal eigenvectors within a diffeomorphic registration framework[5]. Spatial correspondence in standard non-linear registration algorithms is usually defined in order to optimise the similarity between *local* image features. However, when there are drastic anatomical changes such as during the preterm period, an algorithm to cope with the very large spatial deformations is needed to provide a reliable description of the underlying growth. For this purpose, we require a registration algorithm accounting for *global* anatomical descriptors, as provided, for example, by non-linear registration based on the matching of the Laplacian eigenmodes associated with an image.

Spectral matching has been proposed in the context of volume as well as surface registration[6, 7], and it has been already successfully applied to the challenging problem of registration of longitudinal cortical surfaces of preterm infants[8]. In spectral matching techniques, the spatial correspondences are defined with respect to the main spectral modes of the images, which are isometry-invariant descriptors of global geometric properties, hence accounting for large displacements and usually robust to the local variability of the image features. Spectral matching of tensor images is thus a promising approach when dealing with large anatomical variations, like those occurring in early brain development.

In this work we introduce the spectral matching in the context of non-linear registration of diffusion tensor images. We first extend the definition of the graph Laplacian of an image to DTIs, to provide a novel representation of the global geometrical properties of diffusion tensors via their spectral components. We then introduce the tensor spectral matching (TSM) registration of DTI images, to define spatial correspondences through the matching of the spectral components associated to the graph Laplacian. Finally, we combine TSM and the state-of-art algorithm for tensor registration, to provide a novel optimal registration framework (TSM-DTI-TK) accounting for both global and local tensor's properties. The experimental results show that TSM-DTI-TK outperforms standard registration approaches when applied to both adult data and the challenging problem of longitudinal registration of preterm infant data. The proposed pipeline thus represents a promising tool to investigate brain development dur-

ing this crucial period, how it is affected by preterm birth and how it might influence neurological outcome. Additionally this type of research might start to illuminate the debate on the mechanical role of tissue growth on the observed cortical folding pattern, information that is only measurable in foetal and neonatal cohorts of this type.

2 Tensor Spectral Matching

The tensor spectral matching algorithm is based on two main processing steps: 1) computation of the tensor spectral components associated with diffusion weighted images, and 2) subsequent estimation of their spatial correspondences. These steps are detailed in the following sections.

Tensor Spectral Components Let \mathbf{R} be a diffusion tensor image associating at each voxel x a tensor defined as a semi-positive definite symmetric 3-by-3 matrix: $\mathbf{R}(x) \in SPD(3)$. The estimation of the tensor spectral components requires the construction of the general Laplacian matrix \mathcal{L} associated to the diffusion weighted image \mathbf{R} . Its size is $N \times N$, where N is the number of voxels in the image.

The graph Laplacian is computed as $\mathcal{L} = D^{-1}(D - W)$, where W is the weighted adjacency matrix W , and D is the degree matrix. The adjacency matrix W is the matrix representation of the weighted graph describing the local image similarities. The nodes of the graph are the image voxels, while the weights of edges represent their correspondences with respect to the neighbouring locations. For each pair of neighbouring voxels x_i and x_j , $x_i \neq x_j$, we estimate the entry W_{ij} of the adjacency matrix depending on both their Euclidean distance, and on the similarity of the associated tensor information $\mathbf{R}(x_i)$ and $\mathbf{R}(x_j)$. This is quantified by the log-Euclidean distance of SPD matrices: $dist(\mathbf{R}(x_i), \mathbf{R}(x_j))_T = \|\log(\mathbf{R}(x_i)) - \log(\mathbf{R}(x_j))\|$, where $\|\cdot\|$ is the L_2 norm [10]. The proposed similarity measure is therefore computed as:

$$W_{ij} = \exp\left(\frac{dist(\mathbf{R}(x_i), \mathbf{R}(x_j))_T^2}{\sigma^2}\right) / (\|x_i - x_j\|^2), \quad (1)$$

where σ is a measure of the image noise, and is here computed as the average tensor distance in the graph: $\sigma = mean_{i,j}(dist(\mathbf{R}(x_i), \mathbf{R}(x_j)))$.

The degree matrix D is the diagonal matrix whose entries D_{ii} are the sum of the weights of the graph edges associated to the voxels x_i : $D_{ii} = \sum_j W_{ij}$.

The graph spectrum of the diffusion tensor image is finally given by the eigen-decomposition of the general graph Laplacian $\mathcal{L} = \mathbf{U}\Lambda\mathbf{U}^{-1}$, and it is thus identified by the eigenvalues $\Lambda = (\lambda_0, \lambda_1, \dots, \lambda_N)$, and by their associated *tensor spectral components* $\mathbf{U} = (U_0, U_1, \dots, U_N)$. In particular, the tensor spectral components U_1, \dots, U_N represent the fundamental modes of vibrations of the image, and respectively describe increasing complexity of its geometric features, from coarse to fine scales.

Estimating Spatial Correspondences Between Spectral Components

Given reference and floating diffusion tensor images \mathbf{R} and \mathbf{F} , let $\mathbf{U}^{\mathbf{R}}$, and $\mathbf{U}^{\mathbf{F}}$ be the correspondent tensor spectral components obtained with the decomposition detailed in the first part of this section. The spectral matching algorithm aims at estimating the spatial correspondences between \mathbf{R} and \mathbf{F} by optimising the correspondences between the spectral coordinates defined by the first k components of $\mathbf{U}^{\mathbf{R}}$, and $\mathbf{U}^{\mathbf{F}}$. In this work we follow the computational scheme introduced in [7]. Briefly, the first k tensor spectral components are initially corrected for their sign ambiguity and multiplicity. Then, by using the corrected components as well as the fractional anisotropy map of each image and their coordinate grid, we create the *spectral representations* $\tilde{\mathbf{R}} = (U_1^{\mathbf{R}}, U_2^{\mathbf{R}}, \dots, U_k^{\mathbf{R}}, FA^{\mathbf{R}})$ and $\tilde{\mathbf{F}} = (U_1^{\mathbf{F}}, U_2^{\mathbf{F}}, \dots, U_k^{\mathbf{F}}, FA^{\mathbf{F}})$ of respectively reference and floating images.

Tensor Spectral Matching (TSM): DTI registration through spectral matching

Inspired by the classical spectral matching of medical images [11], we propose here the tensor spectral matching (TSM) of DTIs in order to establish spatial correspondences uniquely based on the spectral properties of diffusion tensors. Thus, we estimate the spatial transformation $\phi(x)$ by optimising the similarity between the spectral representations $\tilde{\mathbf{R}}$ and $\tilde{\mathbf{F}}$. The transformation is finally estimated with a nearest-neighbours search, by including a local regularisation term based on the minimisation of the harmonic energy associated to the transformation. In what follows, the optimal parameter for the trade-off between similarities of the spectral representations and transformation regularity has been estimated by cross-validation. The experiments of Section 3 were repeated for several regularisation parameters and we selected the minimal one which guaranteed, for all the pair-wise registration performed, positive Jacobian determinant values.

Combining global spectral features with local tensor information: TSM-DTI-TK

TSM optimizes the correspondences based on global spectral information only. Therefore it does not account for local tensor properties, such as the local tensor orientation. On the contrary, standard tensor registration methods (such as DTI-TK [3]), optimise the local tensor similarity while explicitly account for tensor alignment. However they are usually not sensitive enough in order to model large displacements. We propose here a novel registration framework, TSM-DTI-TK, to account for both *global* spectral features and *local* tensor information. The proposed approach is based on defining the initial global tensor correspondences via TSM registration. The resulting deformation is then used to initialise DTI-TK in order to optimise the tensor matching with respect to the local tensor properties.

3 Validation of Tensor Spectral Matching on Adult Data

The tensor spectral matching (TSM) and TSM-DTI-TK were compared to the DTI-TK¹ tensor non-linear registration method[3], which is considered to be the state-of-art registration method for diffusion tensors [9]. The registration parameters used for DTI-TK were the default ones proposed by the developers. The comparison was based on the group-wise registration of diffusion weighted images to a common anatomical template. The registration quality was measured by quantitative and qualitative assessment of the similarity between the FA maps computed from the resampled and template tensor images. Furthermore, we look at overall differences between the alignment of the principal directions of the tensors of the resampled diffusion tensor images and of the template.

Experimental Data and Image Processing. Data was collected from 20 adolescents on a Philips Achieva 3T MRI machine. Diffusion-weighted data was acquired across four b-values at $b = \{0, 300, 700, 2000\}mm^2/s$ at TE=70ms (2.5x2.5x3.0mm). Tensor maps were created by using a non-linear least square fit to the diffusion data. The reference atlas chosen for this experiment is the freely-available one provided in the DTI-TK toolbox.

All the 20 subjects' diffusion images were initially linearly registered to the atlas by accounting for the tensor orientation[3]. The linearly aligned images were subsequently non-linearly registered to the atlas with TSM, DTI-TK and TSM-DTI-TK, and resampled in the atlas space with respect to the tensor orientation using Finite Strain [12]. Fractional anisotropy maps of the resulting diffusion tensor images were finally estimated from the resampled tensors.

Results. Figure 1 shows the average FA maps obtained when using TSM, DTI-TK and TSM-DTI-TK. We note that the images look very similar after all three methods, indicating that the alignment performed by the different algorithms leads to visually similar anisotropy properties of the resulting resampled diffusion tensors. Figure 2 shows the mean absolute difference in FA and angle between the principal directions of the template and resampled tensors for all three methods in the entire brain. It can be observed that although TSM provides a very good global registration, it underperforms DTI-TK when it comes to tensor alignment and reorientation. However, TSM-DTI-TK outperforms both methods, likely due to the optimisation of the log-Euclidean similarity measure between tensors as it is more sensitive to FA than the principal directions. To this initial anisotropy optimisation of TSM by minimising the log-Euclidean tensor similarity, DTI-TK explicitly optimises the rotation as a refinement step, providing a better result.

¹ <http://www.nitrc.org/projects/dtitk>

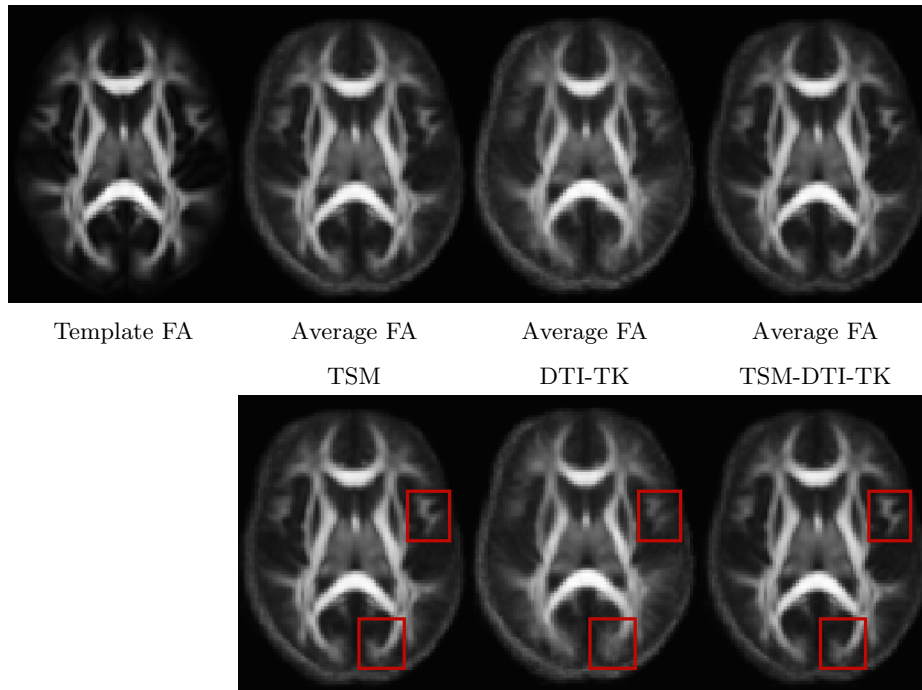


Fig. 1: Visual comparison of TSM, DTI-TK and TSM-DTI-TK when registering adult data. When using TSM, global features look sharper

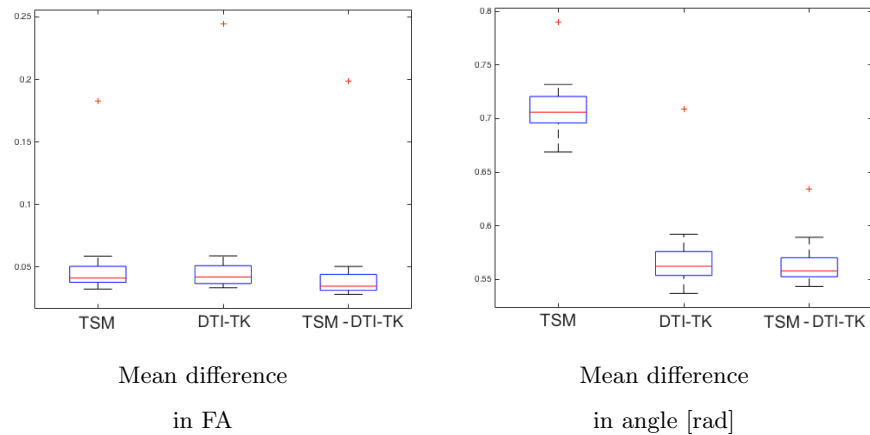


Fig. 2: Boxplots of mean absolute differences in FA and angle between the principal directions of the original template tensors and resampled tensors on the adult data.

4 Application of TSM-DTI-TK to Longitudinal Preterm-Born Infant Data

In this section we show that the TSM-DTI-TK can be successfully applied for the analysis of developmental changes in the white matter of preterm infants and that it outperforms TSM and DTI-TK for this particular problem.

Experimental Data and Image Processing. We acquired T₁-weighted and diffusion-weighted images for six preterm-born infants (Mean Gestational Age at Birth (GAB) of 26.2 ± 0.9 weeks) on a Philips Achieva 3T MRI machine. The infants were imaged at first shortly after birth, at average gestational age (GA) of 31.4 ± 1.1 weeks and then at around equivalent term at average GA of 42.8 ± 2.8 weeks. T₁-weighted data was acquired at a resolution of $0.82mm \times 0.82mm \times 0.5mm$ at TR/TE = 17/4.6ms, acquisition duration 462s. The diffusion weighted data had a resolution of $1.75mm \times 1.75mm \times 2mm$. We acquired six volumes at $b = mm^2/s$, 16 directions at $b = 750mm^2/s$ and 32 at $b = 2000mm^2/s$ with TR/TE = 9s/60ms.

We initially aligned and scaled our images using an affine transformation as described in Section 3, so that both TSM and DTI-TK have the same starting point. We then used TSM and DTI-TK to register the term scan to the preterm space for each individual infant, as well as the proposed framework TSM-DTI-TK.

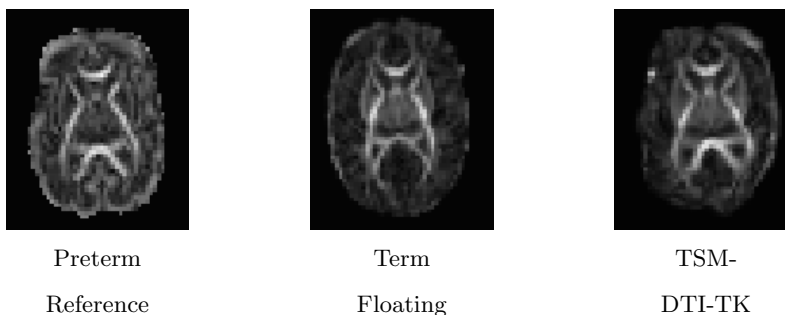


Fig. 3: Visual comparison of the resampled FA maps in the same preterm-born infant longitudinally after registration using the TSM-DTI-TK framework

Results Figure 3 (a) and (b) show an example of the diffusion images of the same infant at preterm and term equivalent and its registration, from term to preterm, by using the TSM-DTI-TK (c). As shown by Figure 4: DTI-TK does not modify much the affine transformation; TSM improves the alignment and the FA difference is decreased, although the orientation is not improved; TSM-DTI-TK improves the tensor orientation dramatically. While DTI-TK cannot cope with the large deformations that are taking place even when using different

parameters, TSM is able to capture this development. TSM-DTI-TK improves matching of shape, anisotropy and tensor orientation.

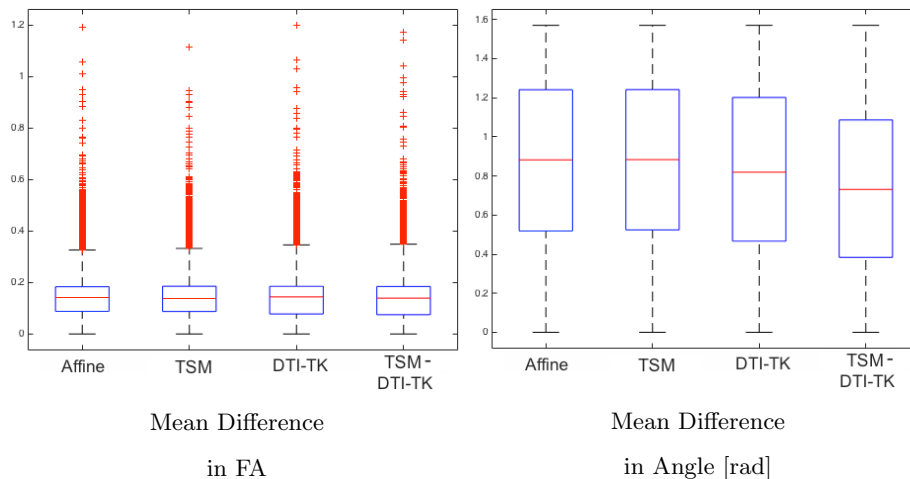


Fig. 4: Boxplots of mean absolute differences in FA in white matter and angle orientation in the white matter for the preterm infant data (all subjects)

5 Discussion

In this work we proposed a novel registration framework for diffusion weighted images (TSM-DTI-TK) based on the spectral decomposition of the diffusion tensors images and the state-of-the-art algorithm for tensor registration. When applied alone, TSM was found to be comparable globally to DTI-TK, the state-of-the-art registration method, on adult data, however it underperforms DTI-TK when it comes to tensor alignment and reorientation, which is expected since DTI-TK minimises the angle between tensors as part of its optimisation process. Tensor orientation in the spectral matching is conceptually difficult but could be added using an iterative strategy. Thus, combining TSM with DTI-TK (TSM-DTI-TK) provides a novel optimal registration framework accounting for both global and local tensor’s properties, improving the DTI-TK alone result. Moreover, TSM-DTI-TK outperformed DTI-TK alone when applied to longitudinal diffusion data from preterm-born infants. The favourable preliminary results on the preterm cohort were enabled by the proposed *global* representation of tensor features obtained through the spectral decomposition strategy introduced in this paper.

The proposed registration framework represents a very promising tool for the study of large morphological changes in the white matter of infants, a problem which, to the best of our knowledge, has not been addressed before. In the future, this registration technique will allow us to quantify the changes in diffusion

parameters over the preterm period on a voxel-wise basis. We will investigate correlations with white matter development and changes occurring in the cortex over the same timeframe, which may elucidate relationships between the cortical surface folding and the establishment of cortico-cortical connections. Medical image computing techniques of this type are fundamental to establish, *in vivo*, what leads to the developmental differences seen between preterm children and their term-born peers.

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