Symmetric Diffeomorphic Normalisation of Fibre Orientation Distributions

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Introduction

Diffusion tensor (DT) imaging [1] permits in vivo investigation of white matter changes. However, the results are difficult to interpret due to the presence of crossing fibres in at least one third of white matter voxels [2]. Multiple fibres within a voxel can be resolved by computing diffusion or Fibre Orientation Distributions (FOD) using methods such as Q-ball imaging [3] and Constrained Spherical Deconvolution (CSD) [4]. Higher order models have improved fibre tractography studies [2], and more recently voxel based analysis [5].

Registration is an important step in group analyses of fibre tracts or their diffusion properties. Initial registration approaches employed scalar valued images such T1-weighted or DT invariants such as fractional anisotropy. More advanced methods have used the full DT, thereby including tract orientation information, which has been shown to improve the detection of white matter differences [6]. More recently, a number of higher order registration methods have been developed to utilise the additional information in regions of crossing fibres [7, 8]. This is particularly important for current [5] and future voxel-based analysis methods aimed at investigating differences in a multi-fibre context. For example, in [5], a crossing fibre model [2] is used to compare partial volume fractions (PVF) of fibre bundles between groups, based on the premise that PVF is more readily interpretable than FA in regions with crossing fibres. In this type of analysis, it is possible that results may be biased if the registration is based on DT information. Pathology-induced changes to the PVF of a given fibre bundle will alter the shape of the tensor, thereby potentially influencing registration results. However, the same PVF changes would not affect the peak fibre orientations within FODs and are therefore less likely to affect the registration.

In this work, we present a novel method for registration of FODs using a Symmetric Diffeomorphic Normalisation (SyN) approach [9]. We assess its performance by evaluating its ability to recover known applied deformation fields, and demonstrate this method by generating a group average FOD template.

Methods

We implemented a SyN registration method as described in [9] to register FODs computed using CSD [4]. Diffeomorphic registration guaranties a smooth, invertible, one-to-one mapping with a positive Jacobian determinant over the entire domain. This is particularly advantageous for FOD registration because DWI data not only needs to be mapped to template space, but also reoriented using a local affine model defined by the Jacobian matrix. We employ a method for reorienting FODs that was recently proposed [8] where FODs are approximated by the sum of a number of equally distributed, weighted, spherical harmonic (SH) delta functions. To reorient the FOD, each delta function orientation is modified using the Jacobian matrix. The final FOD is formed by summing up the SH coefficients of each re-oriented delta function using the weights initially computed to approximate the original FOD.

We investigated two different metrics for the optimisation cost-function. The first involves minimising the sum of squared difference of the FOD SH coefficients [8]. The second involves maximising an adapted form of the cross-correlation metric defined in [9]. Here the cost function to be maximised is the sum of the cross correlation of each SH coefficient image. At each voxel we compute the gradient of the cost function for each SH coefficient image as described in [9]. The gradient contribution from each SH component is then averaged to obtain the overall gradient for the voxel.

Reorientation of FODs was performed at each iteration based on the output of the previous iteration using 300 delta functions. To reduce noise, registration was performed using a SH degree ($lmax$) of 4 and the final transformations were applied to $lmax$ 8. FODs were interpolated by linear interpolation of the SH coefficients [8].

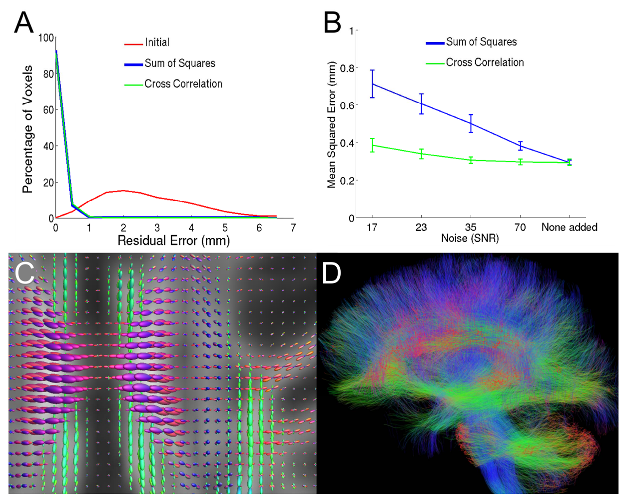

Figure 1. **A**. Cumulative frequency plot of the residual error (Euclidean distance) between the computed and ground truth deformation fields. **B**. The mean squared error between the computed and ground truth deformation fields with different levels of Rician noise. **C**. An axial view of the group average FOD template overlaid on average FA map. **D**. Group average probabilistic fibre tractography results performed on the group average template.

Experiments and Results

The proposed registration method was assessed using data from 10 healthy volunteers, collected on a 3T Siemens Trio (60 DW directions, b=3000 s/mm^2, 2.5mm isotropic voxels). FODs were computed using MRtrix [10]. A validation study was performed as follows. First, realistic deformation fields were generated by registering FA maps from 9 of the subjects to a 10th template using a Fast Free Form Deformation method [11]. These generated deformation fields were then applied to FOD images to create a series of target images. Each subject was registered to their corresponding target using the proposed SyN FOD registration method and both metrics described above. A two-level multilevel resolution approach was used, and regularisation was performed using 3mm Gaussian smoothing on the velocity field. The cross-correlation metric was computed with a radius of 3 voxels. Figure 1a shows the cumulative frequency distribution of the residual error (measured by Euclidean distance) between the computed and ground truth deformation for each metric. Both metrics successfully recover the applied deformation field with sub voxel accuracy, with no significant difference between them. To investigate the robustness of each metric to noise, the validation was repeated with various levels of added noise. This was achieved by convolving each FOD within each subject with the response function used in CSD. The resulting signal profile was sampled along 60 gradient directions. Various levels of Rician distributed noise were added, and the FODs were re-estimated using CSD for registration. Figure 1b contains a plot of the mean squared error between the computed and generated deformation fields for various noise levels. It is observed that the cross correlation metric is more robust to noise than the sum of squares metric.

To further illustrate the utility of the proposed method, we generated an unbiased group atlas using an iterative averaging approach. To obtain the initial FOD template, FA maps were affine registered to the same space and resulting transformations were applied to FOD images and averaged. Each of the 10 subjects was non-linearly registered to the initial template using the cross correlation metric. The resulting normalised images were averaged and used to update the template for the following iteration. This process was repeated until the template remained stable (10 iterations). Figure 1c shows an axial slice of the final group average template. Images are displayed with FODs ($lmax$ 8) overlaid on the average FA map.

A potential application of the group FOD template is to obtain group-wise tractography results. Such an approach has been previously explored for DTI [12], but has not to date been feasible for higher order models. Figure 1d shows whole brain probabilistic tractography performed on the group average template (Figure 1c) using MRtrix with default parameters [10].

Discussion and Conclusion

We have implemented a Symmetric Diffeomorphic registration algorithm to spatially normalise FODs. The proposed method is able to register images with computation times of less than 1 hour and is therefore able to be employed in large scale population studies. Accurate spatial alignment using higher order models will be increasingly important in the analysis of white matter regions containing multiple fibre populations.

References

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