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FAST NONRIGID IMAGE REGISTRATION USING STATISTICAL DEFORMATION MODELS LEARNED FROM RICHLY-ANNOTATED DATA

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Abstract

Nonrigid image registrations require a large number of degrees of freedom (DoFs) to capture intersubject anatomical variations. With such high DoFs and lack of anatomical correspondences, algorithms may not converge to the globally optimal solution. In this work, we propose a fast, two-step nonrigid registration procedure with low DoFs to accurately register brain images. Our method makes use of a statistical deformation model based upon a principal component analysis of deformations learned from a manually-segmented dataset to perform an initial registration. We then follow with a low DoF nonrigid transformation to complete the registration. Our results show the same registration accuracy in terms of volume of interest overlap as high DoF transformations, but with a 96% reduction in DoF and 98% decrease in computation time.

Index Terms

nonrigid registration; statistical deformation models; dimensionality reduction

1. INTRODUCTION

Multi-subject medical image analyses utilize nonrigid image registration for the task of spatial normalization. For example, in order to make meaningful conclusions across a population in functional imaging studies, it is necessary to bring corresponding regions of functional activation into alignment via anatomical registration. A variety of nonrigid registration algorithms have been proposed for intersubject registration [1]. Nonrigid registrations have large degrees of freedom (DoFs) and are able to accommodate large deformations. However, the success of such nonrigid registrations to find a globally optimal deformation is made difficult by the large dimensionality of the search space and the presence of many local minima. Anatomical variations between subjects exacerbate this problem further, making registration an ill-posed problem. These problems can potentially lead to misregistration and subsequently false analyses.

A variety of nonrigid registration methods and atlases exist for spatial normalization of functional areas [2]. Rueckert *et al.* [3] proposed constructing statistical deformation models (SDMs) to statistically characterize free form deformation (FFD) nonrigid registrations [4]

from a training set of previously observed deformations using principal component analysis (PCA). PCA is attractive because it has the potential to drastically reduce the registration dimensionality. Wouters *et al.* [5] and Kim *et al.* [6] implemented fast nonrigid registration methods that optimized the linear PCA coefficients, but the accuracy of their training deformations lacked veracity. In contrast, we constrain our SDM training deformations to be accurate with respect to labeled images.

As the main contribution of this paper, we propose a two-step registration process to perform fast nonrigid image registration using a FFD model. The first step performs a high-resolution FFD registration using a low-dimensional PCA SDM. To train our SDM, we leverage a dataset of manual, gold-standard segmented images to create a set of high-resolution nonrigid registrations. We then follow our initial PCA registration with a second registration; however, rather than finishing with a high-dimensional nonrigid registration similar to Kim *et al.* [6], we utilize a low-resolution FFD. In this manner, the initial PCA registration captures the principal components of deformation while the second registration accounts for the remaining anatomical variability. We demonstrate our approach using brain data in the functional image analysis context. By exploiting richly-annotated images to form a low-dimensional SDM, our proposed method is able to achieve high-accuracy volume of interest (VOI) overlap equivalent to a high-resolution FFD, but does so with a 96% reduction in transformation DoFs and a corresponding 98% speedup in computation time.

2. METHODS

We begin with a description of our method for creating accurate registrations with respect to the functional areas of the brain in Section 2.1. We then present our proposed low-dimensional nonrigid registration scheme in Section 2.2.

2.1. Constructing the SDM training set

Because we want to accurately register functional areas of the brain for a group of subjects, we select a database containing gold-standard, manual segmentations of functional VOIs. The UCLA Laboratory of Neuroimaging (LONI) Probabilistic Brain Atlas (LPBA40) [7] contains bias field-corrected (BFC) skull-stripped images I_i and functional VOI label images L_i for $i = 1, \dots, 40$ subjects. Each label image L_i has 56 manually labeled VOIs of functionally eloquent areas of the brain. Additionally, we create a set of point surfaces S_i for each label VOI in L_i . With these images as input, our nonrigid registration pipeline consists of four steps shown in Figure 1: initial affine registration, integrated intensity-point nonrigid registration, reference image bias-correction, and then another application of integrated registration.

We perform affine registration to the MNI Colin 27 brain using robust point matching [8], denoting this transformation $T_{i \rightarrow \text{MNI}}$ ($i \rightarrow j$ indicates linear registration from space i to j). Applying this transformation, we resampled all LPBA40 images to MNI space with $181 \times 217 \times 181$ volumes of 1mm^3 isotropic resolution. We then selected one subject at random (subject 1) to be used as an initial reference image for nonrigid registration. Using both the images $I_{i \rightarrow \text{MNI}}$ and label surfaces $S_{i \rightarrow \text{MNI}}$, we nonrigidly register the remaining 39 subjects to $I_{1 \rightarrow \text{MNI}}$ and $S_{1 \rightarrow \text{MNI}}$ with an integrated intensity and point-feature algorithm [9]

to constrain correspondence of the functional VOIs. This algorithm uses a FFD transformation model with 5mm control point spacing and minimizes the sum of squared differences similarity measure to produce the transformations $T_{i \rightsquigarrow 1 \rightarrow \text{MNI}}$ ($i \rightsquigarrow j$ indicates nonrigid registration from space i to j).

The registrations at this point are biased toward our choice of reference (subject 1). To

correct for this bias, we compute the mean transformation $\bar{T} = \frac{1}{N-1} \sum_{i=2}^N T_{i \rightsquigarrow 1 \rightarrow \text{MNI}}$ and apply the inverse transformation $\bar{T}^{-1}$ to subject 1. We denote this bias-corrected reference (BCR) image and surface I_{BCR} and S_{BCR} , respectively. The final stage of our pipeline then reregisters the 39 subjects to the BCR using the same integrated registration as before. The final, nonrigid transformations $T_{i \rightsquigarrow \text{BCR}}$ compose our SDM's training set.

In addition to the transformations, we create an atlas composed of an anatomical and a label image. The mean intensity anatomical brain image $I_{\text{Atlas}} = \frac{1}{N-1} \sum_{i=2}^N T_{i \rightsquigarrow \text{BCR}} \circ I_i$, where $\circ$ is the transformation operator, is a representation of all anatomies from the training set. We compute the corresponding label image L_{Atlas} using a majority-vote of the nearest-neighbor interpolated labels $T_{i \rightsquigarrow \text{BCR}} \circ L_i$.

2.2. Low-dimensional nonrigid registration using SDMs

We propose a two-step, low-dimensional, registration process to nonrigidly register a sample image I to our atlas reference I_{Atlas} . First, we apply a sparsely parameterized FFD transformation model T_{SDM} as an initial registration, and then follow with a second, traditional, FFD registration T_{FFD} . Assuming that I has already been registered to I_{Atlas} with an affine transformation, our nonrigid registration is the combination of two transformations

$$T(\mathbf{x}) = T_{\text{FFD}}(\mathbf{x}) \circ T_{\text{SDM}}(\mathbf{x}).$$

We use the registrations described in the previous section to create a SDM of the nonrigid FFD transformation. For each transformation $T_{i \rightsquigarrow \text{BCR}}$, let $\mathbf{d}_i \in \mathbb{R}^{3M}$ be the vector of M concatenated FFD control point displacements in 3D. We linearly approximate the distribution of the deformation $\mathbf{d}$ using PCA

$$\mathbf{d} = \bar{\mathbf{d}} + \Phi \mathbf{w} \quad (1)$$

where $\bar{\mathbf{d}} = \frac{1}{N} \sum_{i=1}^N \mathbf{d}_i$ is the mean deformation of the N training registrations, Φ is the matrix of orthogonal principal components, and $\mathbf{w}$ is the vector of model co-efficients. We compute the principal components using the eigensystem decomposition of the covariance matrix

$\mathbf{C} = \frac{1}{N-1} \sum_{i=1}^N (\mathbf{d}_i - \bar{\mathbf{d}})(\mathbf{d}_i - \bar{\mathbf{d}})^T$. In general, the number of control points for high-resolution FFD deformations is much greater than the number of training deformations, $M \gg N$, which makes the eigendecomposition of $\mathbf{C}$ intractable. Instead, we compute the

eigendecomposition of the $N \times N$ system $\frac{1}{N-1} \sum_{i=1}^N (\mathbf{d}_i - \bar{\mathbf{d}})(\mathbf{d}_i - \bar{\mathbf{d}})^T$ [10]. Using this

formulation, $\Phi = (\phi_1 | \phi_2 | \dots | \phi_N) \in \mathbb{R}^{3M \times N}$ is a matrix of N eigenvectors $\phi_i \in \mathbb{R}^{3M}$ with corresponding eigenvalues λ_i , and $\mathbf{w} \in \mathbb{R}^N$.

The model coefficients $\mathbf{w}$ compactly parameterize a high-dimensional FFD transformation $\mathbf{d}$ in Equation 1. We write this FFD transformation $T_{\text{SDM}}(\mathbf{x}; \mathbf{d})$ for all points $\mathbf{x}$ in the reference image domain Ω defined by atlas template I_{Atlas} . Our proposed algorithm nonrigidly registers an image I to I_{Atlas} by solving for the coefficients $\mathbf{w}$ in the following equation

$$\hat{T}_{\text{SDM}} = \arg \max_{\mathbf{w}} J(I_{\text{Atlas}}(\mathbf{x}), T_{\text{SDM}}(\mathbf{x}; \bar{\mathbf{d}} + \Phi \mathbf{w}) \circ I(\mathbf{x})) \quad (2)$$

where J is a similarity metric evaluated at all points $\mathbf{x} \in \Omega$. We use conjugate gradient optimization with multiple image resolutions to maximize the normalized mutual information (NMI) of the sample image I and I_{Atlas} . Following the initial SDM registration, we deform I using $\hat{T}_{\text{SDM}}$ such that $I' = \hat{T}_{\text{SDM}} \circ I$. We then register I' to the atlas I_{Atlas} using a low-resolution FFD, T_{FFD} , with 15mm control point spacing by maximizing NMI.

3. RESULTS

We evaluated registration accuracy using the Dice overlap measure for each of the 56 VOIs in the label images L_i , and summarized these values by calculating the mean Dice overlap as a global measure of registration quality. In practice, we noted that small improvements in the Dice overlap measure actually corresponded to large improvements in registration as VOI boundaries aligned better. Since we predicated our SDMs upon the existence of accurately registered training deformations, we first present the results of our initial registrations in Section 3.1 and follow with the results of our low-dimensional registration approach in Section 3.2. We implemented our algorithms on the GPU using the CUDA parallel programming platform as part of BioImage Suite [11].

3.1. Assessing the SDM training set

We evaluated our integrated registration approach by assessing how well our atlas explained the registration training set in comparison to atlases created using affine registration and intensity-only nonrigid FFD registration. For integrated registration, we equally weighted the intensity and point-feature contributions by setting the point-feature weighting proportion to 0.5. The intensity-only registration used the framework from Section 2.1, but with the point-feature weighting proportion set to 0. We qualitatively visualized anatomical alignment using mean intensity images of 39 subjects, leaving subject 1 out. Figure 2 shows mean intensity images for each of the 3 registration methods. Our proposed method appears much sharper than both the affine and intensity-only FFD indicating better anatomical correspondence. To quantitatively assess registration, we computed the mean overlap for all 39 subjects with respect to each method's majority-vote label image (shown in Figure 2), and summarized the results in Table 1. The integrated registrations performed significantly better than the intensity-only method in terms of mean overlap (paired t-test, $p = 1.5 \times 10^{-8}$).

3.2. Evaluating low-dimensional nonrigid registration

To demonstrate our approach, we performed *leave-one-out* experiments. For each subject j , we calculated $\mathbf{d}$ and Φ in Equation 1 using $T_{i \rightarrow \text{BCR}} \forall i = 2, \dots, 40, i \neq j$. We then registered image I_j to I_{Atlas} by first solving for Equation 2, and then again using the FFD transformation. We repeated these tests using different numbers of non-zero modes of variation in $\mathbf{w}$. We compared our method to affine registration and multi-resolution FFD registration with control point spacings of 15 and 5mm, denoted as FFD₁₅ and FFD₅, respectively. All registrations used I_{Atlas} as a reference and L_{Atlas} (both shown in Figure 2) for overlap computation. Rather than recomputing L_{Atlas} for each leave-one-out test, we used all 39 label images assuming that a single subject would have little effect on the majority-vote results.

Figure 3 shows that over the first 10 modes of variation, our method performed comparable or better than high-resolution FFD₅. We noted that the PCA registration saturated in terms of performance after 3 modes; however, we observed the highest mean overlap using 3 modes after the final FFD registration. Using more modes, we observed a small decrease in performance of our method that is most likely explained by the PCA model overfitting to the nuances of the training set.

Table 2 summarizes how our approach using 3 modes of variation performed. For the given image sizes, FFD₁₅ and FFD₅ required 2,535 and 60,236 control points, respectively, which translated to 7,605 and 180,708 DoFs in 3D. Our approach reduced the DoFs to 7, 605+ m where m is the number of modes of variation. For 3 modes, this meant both a 95.8% reduction in DoFs and a subsequent 97.5% reduction in computational time for the same level of registration quality as FFD₅ with respect to mean overlap. Figure 4 shows an example registration result of a single subject using our approach.

4. CONCLUSION

Our proposed registration method achieves similar registration accuracy as a high DoF FFD transformation, but does so with a 96% reduction in DoFs and on average a 98% reduction in computational time. While the PCA SDM registration individually does not perform as well as the low-resolution FFD registration, by adding SDM registration as an initial transformation and then performing another, single level of low-resolution intensity registration we see a jump in performance that rivals high-resolution FFD intensity registration. We hypothesize that the low DoF SDM transformation gets the registration out of many initial local minima by providing gross deformations accounted for by the first few modes of variation, with optimal number of modes 3. In the future, we aim to explore dictionary learning as an alternative dimensionality reduction method.

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Fig. 1.

Our proposed registration framework takes a dataset with gold-standard segmentations as input and creates a set of high-resolution nonrigid transformations that are accurate with respect to the segmented VOIs. We use these registrations as the training set for our SDM.

Fig. 2.

Mean intensity images of 39 subjects after (a) affine, (b) intensity-only FFD, and (c) our integrated intensity-point nonrigid registration. We overlaid the corresponding atlas labels (d–f) on images (a–c), respectively. We used (c) as the anatomical reference image I_{Atlas} for our SDM registration approach and (f) as the atlas labels L_{Atlas} .

Fig. 3.

Leave-one-out mean Dice overlap results of the initial PCA SDM and final proposed registration methods compared to affine, and intensity FFD registration with 15 and 5mm control points spacing. Our proposed method performs similar to the high resolution FFD with 5mm control point spacing but does so with 96% fewer DoFs. All values are mean $\pm$ std for 39 subjects.

Fig. 4.

Visualizing our proposed registration method. (a) LPBA40 subject 7 before nonrigid registration, (b) after the initial PCA SDM registration using 3 modes of variation, and (c) after the final FFD registration. In (b) and (c), we overlaid an isotropic grid to better visualize the nonrigid deformation. Figure 2(c) shows the reference image to which we registered this image.

Table 1

Mean Dice overlap of the 39 subjects in the training set after affine, intensity-only FFD, and our integrated nonrigid registrations. Reported values are mean $\pm$ std with respect to each method's corresponding atlas (shown in Figure 2).

Method	Mean Overlap
Affine	73.56 $\pm$ 2.32
Intensity FFD	79.68 $\pm$ 1.34
Integrated intensity/point FFD	81.76 $\pm$ 1.11

Table 2

Registration results comparing our proposed method (using 3 modes of variation) with intensity-only FFD registrations using 15 and 5mm control point spacing. Reported values are mean $\pm$ std for 39 subjects. Computational times were measured using an NVIDIA GeForce GTX 580 GPU.

Method	DoFs	Mean Overlap	Compute Time (m)
Affine	12	72.18 $\pm$ 2.30	-
Intensity FFD ₁₅	7,605	77.41 $\pm$ 1.53	1.08 $\pm$ 0.42
Intensity FFD ₅	180,708	78.09 $\pm$ 1.26	73.85 $\pm$ 1.39
PCA SDM	3	74.40 $\pm$ 1.39	0.75 $\pm$ 0.02
Proposed method	7,608	78.37 $\pm$ 1.06	1.85 $\pm$ 0.41