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ATLAS CONSTRUCTION FROM HIGH ANGULAR RESOLUTION DIFFUSION IMAGING DATA REPRESENTED BY GAUSSIAN MIXTURE FIELDS

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Abstract

Groupwise image registration is an essential part of atlas construction which is a very import and challenging task in medical image analysis. In this paper, we present a novel atlas construction technique using a groupwise registration of high angular resolution diffusion (MR) imaging datasets each of which is represented by a Gaussian Mixture field. To solve the registration problem, an L_2 distance is used to measure the similarity between two Gaussian Mixtures, which leads to an energy function whose gradient can be computed in closed form. A projection method is developed to construct a “sharp” (not blurred) atlas from the result of this groupwise registration. Synthetic and real data experiments are presented to demonstrate the efficacy of the proposed method.

Index Terms

HARDI; Gaussian Mixture Fields; Groupwise registration; Atlas Construction

1. INTRODUCTION

Groupwise image registration and image atlas construction is a very important and challenging task in medical image analysis. It has many applications in image segmentation and statistical analysis of a group of subject images. Several researcher groups have tackled variations of this problem and reported their results in literature [1, 2, 3, 4]. Most of these are on groupwise registration and atlas construction from scalar images or segmented shapes.

Diffusion-Weighted MR Imaging (DW-MRI) is a powerful noninvasive technique that can capture the information of water diffusion in tissues and thus infer its structure *in vivo*. Serval methods have been reported in litrature to model and estimate the diffusivity functions from the MRI signals. One popular method is the so called Diffusion Tensor Imaging(DTI) [5] which approximates the diffusivity function at a voxel by a positive definite matrix. A DTI based atlas will obviously provide more information than conventional scalar image based atlas [6] since DTI contains both scalar and directional information. Atlas construction requires the DTI data to be groupwise registered and in this

regard, until recently, most of the DTI registration techniques reported in literature were pairwise registration methods [7, 8, 9, 10]. Some of the existing DTI based atlases are built by coregistration techniques as in [11] but a DTI based groupwise registration and atlas construction methods was reported in [12].

It is however well known that the DTI model cannot resolve complex tissue structure such as fiber crossings. To handle this problem, several higher order models [13, 14, 15, 16] based on High Angular Resolution Diffusion Imaging (HARDI) dataset were reported in literature. Several recent works were reported for the HARDI pairwise registrations [10, 17, 18, 19], and shown to outperform DTI based registration especially in aligning fiber crossing regions [10]. But very few works have been reported in the groupwise registration for HARDI dataset, except a 4-th order tensor field based groupwise registration reported in [17] which extended the unbiased atlas construction technique in [1] to handle 4-th order tensor fields by using novel distances.

In this paper, we present a novel atlas construction method for HARDI datasets represented by a Gaussian Mixture Field (GMF) generated by the algorithm described in [15]. GMF is a field of zero mean 3D Gaussian mixture models one each at each lattice point of the field. We use the L_2 distance between GMFs to measure the dissimilarity between two Gaussian mixture fields as was defined in [18]. And we significantly extended the framework in [1] to construct the atlas from a set of GMFs. A novel mean GMF computation method is also presented along with the groupwise registration process. The key contributions of our paper are: 1. A GMF based groupwise registration is proposed which is the first of its kind; 2. An objective function involving the L_2 distance between Gaussian mixtures is used that leads to a closed form expression for the distance and the gradient computation. 3. A minimal distance projection is defined and used to obtain a “sharp” (non-blurry) atlas which is useful in atlas based segmentation. Experiments along with comparisons are presented to demonstrate the performance of our algorithm.

The rest of the paper is organized as follows: The method for atlas construction on GMF is presented in section 2, along with the atlas construction framework in 2.1, followed by the distance metric in 2.2, and the implementation and mean GMF computation in 2.3. In section 3, we present synthetic and real data experiments along with comparisons to other existing methods. And the conclusion is in 4.

2. METHODS

2.1. Image Atlas Construction Framework

An atlas of a set of images/shapes etc. is commonly defined as an average over the set, which is taken to be a representative of the set. The problem with simply taking an average as the atlas is that the average tends to be rather blurred and is not effective for use in tasks such as, atlas-based segmentation or atlas-based registration etc. Mathematically speaking, this can be caused due to the fact that the average may not necessarily belong to the same abstract space (e.g., space of brain images) defined by the original data set. For instance, the technique described in [1] searches for the average in the image space without a constraint on the space of images, which can lead to a blurred atlas image. To solve this problem, in [3], the atlas is constrained to be deformed diffeomorphically from a super template which needs to be pre-selected; And in [2, 20, 21] the structure of the subject image space is learned from the dataset, using which the atlas is computed. These methods need registrations between all the image pairs in the dataset ($O(N^2)$ registrations), which makes the approach computationally expensive for large datasets.

In this paper, we define the space of images of interest to us (spinal cord images) to be spanned by a set of GMFs $\{I_n\}_{n=1}^N$ and denoted by $S = \bigcup_n \mathcal{O}(I_n)$, where $\mathcal{O}(I_n) = \{J: J = I_n \circ \mathbf{T}, \mathbf{T} \in \text{Diff}\}$ is the orbit spanned by the image I_n and all the diffeomorphic deformations $\mathbf{T}_n: \Omega \rightarrow \Omega$, where Ω denotes the domain of the image. Thus, finding the atlas I can be viewed as solving the following problem

$$m^*, \mathbf{T}_1^*, \dots = \underset{m, \mathbf{T}_1, \dots}{\operatorname{argmin}} \sum_n E(I_n \circ \mathbf{T}_n, I_m \circ \mathbf{T}_m) + \varphi(\mathbf{T}_n)$$

And the final atlas could be defined as $\hat{I} = \Phi_{m^*}^{-1}[I_{m^*} \circ \mathbf{T}_{m^*}]$, where Φ_{m^*} is the Jacobian of the deformation $\mathbf{T}_{m^*}$, and $\Phi_{m^*}^{-1}[\cdot]$ denotes the re-orientation operation discussed in section 2.2. Solving this problem directly would make the computational complexity similar to $\mathcal{O}(N^2)$ pairwise registrations. What we would like to do, is to achieve an approximate solution using a two step procedure.

In the first step, we try to find a intermediate atlas in the space of all images, which can be viewed as solving the optimization problem (similar as [1] but generalized to GMFs)

$$I, \mathbf{T}_1, \dots = \underset{I, \mathbf{T}_1, \dots}{\operatorname{argmin}} \sum_n E(I_n \circ \mathbf{T}_n, I) + \varphi(\mathbf{T}_n) \quad (1)$$

where, in this paper, the data term energy function $E(\cdot)$ is defined as a sum of squared voxelwise distance (details in 2.2)

$$E(I_n \circ \mathbf{T}_n, I) = \int_{\Omega_I} \text{dist}_{\Phi_n}^2(I_n \circ \mathbf{T}_n(\mathbf{x}), I(\mathbf{x})) d\mathbf{x} \quad (2)$$

φ is the penalty term used to enforce the smoothness constraint on the deformation. The deformation can be modeled as a diffeomorphism, and parametrized by a velocity field

$\frac{\partial \mathbf{T}_n}{\partial t} = \mathbf{v}_n(\mathbf{T}_n(\mathbf{x}, t), t)$. Thus the deformation can be computed as

$\mathbf{T}_n(\mathbf{x}) = \mathbf{x} + \mathbf{d}_n(\mathbf{x}) = \mathbf{x} + \int_0^1 \mathbf{v}_n(\mathbf{x}(t), t) dt$, where $\mathbf{d}_n$ represents the displacement field. The smoothness constraint we use here is given by,

$$\varphi(\mathbf{T}_n) = \lambda * \log(\det(\Phi_n)) * (1 - \det(\Phi_n)) + \int_{\Omega_I} \int_0^1 \|L\mathbf{v}_n(\mathbf{x}, t)\|^2 dt. \quad (3)$$

Where, L is a linear operator, and the first term in Equation 3 imposes additional smoothness as in [22].

In the second step, we project the intermediate atlas to the space S by solving another distance minimization

$$\hat{I} = \Phi_{m^*}^{-1}[I_{m^*} \circ \mathbf{T}_{m^*}]$$

$$m^*, \mathbf{T}^* = \underset{m, \mathbf{T}}{\operatorname{argmin}} E(I_n \circ \mathbf{T}, I) \quad (4)$$

and the projection result $\hat{I}$ is our final atlas.

2.2. L_2 Distance and Re-orientation for GMs

We use the L_2 distance as a dissimilarity measure between two Gaussian mixture densities (GMs), which can be computed in a closed form [18]. Let $f(\mathbf{r}) = \sum_{i=1}^M \eta_i G(\mathbf{r}; 0, \Sigma_i)$ and $g(\mathbf{r}) = \sum_{j=1}^N \rho_j G(\mathbf{r}; 0, \Gamma_j)$ be two Gaussian mixture density functions, where $\mathbf{r} \in \mathbb{R}^3$ is the displacement vector and η_i, ρ_j denote the mixture weights of the corresponding Gaussian components $G(\mathbf{r}; 0, \Sigma_i)$ and $G(\mathbf{r}; 0, \Gamma_j)$ with covariance matrices Σ_i and Γ_j respectively. The L_2 distance between f and g can be written as a quadratic function of the mixture weights $dist^2(f, g) = \boldsymbol{\eta}^t \mathbf{A} \boldsymbol{\eta} + \boldsymbol{\rho}^t \mathbf{B} \boldsymbol{\rho} - 2 \boldsymbol{\eta}^t \mathbf{C} \boldsymbol{\rho}$, where $\boldsymbol{\eta} = (\eta_1, \dots, \eta_M)^t$ and $\boldsymbol{\rho} = (\rho_1, \dots, \rho_N)^t$, and $\mathbf{A}_{M \times M}$, $\mathbf{B}_{N \times N}$ and $\mathbf{C}_{M \times N}$ are the matrices generated by the Gaussian components, see [18] for details.

A re-orientation operation is needed for image transformation, when the image value at each pixel/voxel is related to the image coordinates and is not rotationally invariant [23]. In this case, the image value should change according to the image coordinates. Otherwise, an artifact might be introduced due to this transformation. As in [18], the Preservation of Principal Direction (PPD) re-orientation is extended to GMs, and it is the only re-orientation strategy that can capture the change of angle between fiber crossings during a non-rigid transformation. In this paper, we adopt this re-orientation strategy, and the energy function with reorientation would be $dist_{\Phi}^2(f, g) = \boldsymbol{\eta}^t \mathbf{A}_{\Phi^{-1}} \boldsymbol{\eta} + \boldsymbol{\rho}^t \mathbf{B} \boldsymbol{\rho} - 2 \boldsymbol{\eta}^t \mathbf{C}_{\Phi^{-1}} \boldsymbol{\rho}$, where computation of $\mathbf{A}_{\Phi^{-1}}$ and $\mathbf{C}_{\Phi^{-1}}$ can be found in [18].

2.3. Mean GMF Computation

We employ an (iterative) greedy algorithm to solve the problem in Equation 1. Given the initialization of atlas I and $\{\mathbf{T}_n\}$, in each iteration step, we first fix the deformations and update the atlas by optimizing w.r.t. I . $I^{new} = \underset{I}{\operatorname{argmin}} \sum_n \int_{\Omega} dist_{\Phi_n}^2(I_n \circ \mathbf{T}_n(\mathbf{x}), I(\mathbf{x})) d\mathbf{x}$. Since we use an L_2 distance, the global minimum can be found as $I^{new} = \frac{\sum_n \Phi_n^{-1} [I_n \circ \mathbf{T}_n]}{N}$. However, from this formula, $I^{new}(\mathbf{x})$ would have many more components than $I_n(\mathbf{x})$ would have had, which would make the algorithm computational expensive. To solve this problem, we fixed the group of mixture components of I^{new} . Since each mixture component is zero mean, and cylindrically symmetric with fixed eigenvalues. All we need to do is to decide on the eigen vectors. In this paper, we discretize the hemi-sphere using 46 different directions, and used them as the eigen vectors (the same approach has been used in the reconstruction method [15]). Then, the only thing left is to compute the mixing weights, which is equivalent to solving the linear system at each voxel $\mathbf{A} \boldsymbol{\rho} = \sum_n \mathbf{C}_{\Phi_n^{-1}} \eta_n$. This would be easy to solve since $\mathbf{A}$ is low dimensional and full rank.

After updating the atlas, the force field can be first computed as the first order variation of data term of the objective function plus the first term on the right (enforcing additional smoothness) in Equation 3; And then the velocity field is updated as the Gaussian kernel based smoothed version of the force field [17], and the deformation field $\mathbf{T}(\mathbf{x})$ is updated using the following update equation $\mathbf{T}^{new}(\mathbf{x}) = \mathbf{T}^{old}(\mathbf{x} + \boldsymbol{\varepsilon} \mathbf{v})$.

The derivative of the objective function is computed by applying the derivative chain rule as in [18]. And the derivative of the regularization term in Equation 3 can be computed directly using the derivative for the determinant.

We employ a coarse-to-fine strategy in our registration algorithm for an efficient implementation. With initialization of the deformation set to identity, the algorithm yields

satisfactory results in 200 steps. After we get the atlas I , we can project it to S to get $\hat{I}$ by using Equation 4.

3. EXPERIMENTS

3.1. Synthetic Data Experiments

To validate the registration framework used in our atlas construction method, we first apply our method to the pairwise registration problem. For the two images case, Equation 1 would reduce to $\mathbf{T}_1, \mathbf{T}_2 = \operatorname{argmin}_{\mathbf{T}_1; \mathbf{T}_2} E(I_1 \circ \mathbf{T}_1, I_2 \circ \mathbf{T}_2) + \phi(\mathbf{T}_1) + \phi(\mathbf{T}_2)$. By using the displacement field inverse method [24], we can get $T = T_1 \circ T_2^{-1} : \Omega_{I_2} \rightarrow \Omega_{I_1}$. Thus we have a pairwise registration algorithm. We applied this algorithm to the synthetic dataset and then compared it to a GA based registration algorithm (using an SSD cost) and a DTI based registration algorithm in [8] with the same dataset.

To generate the synthetic dataset, a 3D synthetic image ($64 \times 64 \times 4$) with two crossing fiber bundles was generated and then, 20 randomly deformed images were synthesized from this by using a bspline-based non-rigid deformation. The method described in [25] was used to generate the simulated MR signals from the fiber bundles. Rician noise was added to simulate data at 4 different noise levels with $SNR = 50, 20, 10$ and 5 . The method in [15] was used to generate the GMF from the MR signals with 46 Gaussian components at each voxel.

After the data generation, we registered each of the randomly deformed images (source image) to the original image (target image) separately. To evaluate the registration, the resulting deformation obtained from the registration was applied to the noise free source image, and then the dissimilarity between the deformed source and target images were computed as the error in registration. The dissimilarity measure we used here was Hellinger distance between the displacement probability profiles (represented in spherical harmonic

coefficients) at corresponding lattice points $r = \int_{S^2} (\sqrt{f(x)} - \sqrt{g(x)})^2 dx$. Also, we computed the registration error in two different regions: (1) the whole image, (2) the region that contains only the crossing fibers.

The data sets and the results are displayed in figure 1. Figure (a) and (b) show that our method yields a slightly lower mean and standard deviation of the registration errors for the whole image, and much lower error in the fiber crossing region for all four noise levels. This demonstrates the accuracy of our HARDI registration method.

3.2. Real Data Experiments

For the real data experiments, we apply our method to the HARDI scans of a rat spinal cord at C3–5 for 7 different rats. In each scan 21 diffusion gradients were used (with Δ and the δ was set to be $13.4ms$ and $1.8ms$) with $b = 1000s/mm^2$. Also, one S_0 image is taken with b close to zero. The image resolution in the x – y plane was 128×128 , with the number of slices varying from 25 to 34. The voxel size is $35\mu m \times 35\mu m \times 300\mu m$. [15] was used to generate the GMF from the MR signals with 46 Gaussian components at each voxel.

We first apply a similarity registration to quotient out the translation, rotation and scaling factors, and apply our group-wise registration algorithm to the dataset to get an atlas I . In the following, we projected I to the space spanned by the given data samples using Equation 4 to get the “sharp” (non-blurry) atlas $\hat{I}$. The results of our atlas construction method are depicted in figure 2 (via S_0 images even though the algorithm was applied to the the GMF representation of the HARDI data), where the (a) is the voxelwise mean of S_0 images before registration, and (b) after registration. We can see that (a) is fuzzy because the structure is

not well aligned, and (b) is not. This indicates the effectiveness of our groupwise registration method. (c) is the I_{m^*} in Equation 4, and (d) is the final atlas $\hat{I}$. We can see that (b) is much more blurry than (d), and the shape of the boundary between white and grey matter is nearly the same for (b) and (d). This indicates that $\hat{I}$ could be a good representative for the whole dataset, and thus justifies the effectiveness of our method.

4. CONCLUSIONS

We have presented a novel atlas construction method from HARD-MRI data represented as GMFs. The key feature of our atlas is that it is much sharper (less blurry) than the one obtained by using state-of-the-art atlas construction methods as depicted in the results. Having a sharper (in terms of features) atlas is essential for many applications such as atlas-based segmentation, registration etc.

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Fig. 1.

Experimental results on synthetic dataset. Figure (a) and (b) are the mean and standard deviation of error for the 20 registrations from all the three methods at different noise levels in the two different ROIs.

Fig. 2.

Experimental results on real datasets depicted using S_0 images. Figure (a)–(d) are all S_0 images, with (a) the voxelwise mean before groupwise registration, and (b) after registration. (c) is the S_0 image for I_{m^*} and (d) is the S_0 image for the final atlas $\hat{I}$. Figure (e) is the diffusion profile of $\hat{I}$, and is colored by the max direction of the diffusion profile, with xyz directions mapped to RGB respectively.