A Fast Multi-phases Demon Image Registration for Atlas Building

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Abstract. Medical image registration is an essential branch in computer vision and image processing, and it plays a vital role in medical research, disease diagnosis, surgical navigation, and other medical treatments. However, existing methods are time-consuming; the progress of image registration is difficult to observe, and fewer works for human brain atlas building use image registration method. In this paper, we first introduce a fast multi-phase demon registration (FMDR) model for image registration and atlas building. To show the applicability of our FMDR model, we use synthetic circle data to illustrate a faster and more accurate result of our model than other benchmark methods. We also demonstrate the morphological changes of a TBI case, which shows the continuous shape changes from a diseased state to a healthy state. To illustrate the performance of our model, we use a set of T2 MRIs to estimate the template image for atlas building.

Keywords: Demon image registration · Atlas building · Shape deformation

1 Introduction

Morphological information and functional information of the different patients differ from each other even in the same modality; it is necessary to build an atlas for shape analysis. Therefore, for effective information integration–the fusion of information from various images or different time series images from the same patient is relatively remarkable. It can primarily improve the level of clinical diagnosis, treatment, disease monitoring, surgery, and therapeutic effect evaluation, for example, the fusion of anatomical images and functional images. It can provide an accurate description of anatomical location for abnormal physiological regions. Also, the fusion of images from different modalities can be applied to radiation therapy, surgical navigation, and tumor growth monitoring [1]. Therefore, image registration for atlas building is essential in the medical field.

There are many works addressed image registration problem. Elsen et al. summarized some medical image registration technologies and realize the alignment of different images [2]. Other methods include mutual information for

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multi-modalities image registration [3], Fourier transform [4]. Image registration will consume more substantial computation time, especially for 3D image registration. Plishker et al., 2007 discussed the acceleration techniques of medical image registration [5]. Nevertheless, one crucial criterion in medical image registration is anatomical structures are one-to-one corresponded with each other after image registration, while transformation has to be topology-preserving (diffeomorphic). If a geometric shape is significantly different in two or multiple images, a topology-preserving transformation is hard to generate. To solved this problem, several geodesic registration methods on manifold had been proposed, e.g., Large Deformation Diffeomorphic Metric Mapping (LDDMM) [6,7]. LDDMM provides a mathematically robust solution to the large-deformation registration problems, by finding geodesic paths of transformations on the manifold of diffeomorphisms. The advantage is that it can solve the large deformation registration problem, but the transformation is computationally very costly to compute if shape change is relatively large. Zhang et al. (2013), proposed a fast geodesic shooting algorithm for atlas building based on the metric of original LDDMM for diffeomorphic image registration, and was faster and used less memory intensive than original LDDMM method [8].

For image registration, it is useful to observe the differences between the composition of background deformations of the image and foreground deformations of geometric objects, such as TBI lesion or tumor. However, the challenge is that most of image registration methods cannot account for image appearance, and take a long time for matching images.

In this article, we propose a multi-phases demon image registration for atlas building. Our contributions are in two folds: (1) a fast and accurate demon registration model; (2) multiple stages to show the progress of shape deformations. We show experimental results of both 2D synthetic data and 3D T2 brain MRIs data. To demonstrate the applicability of our model, we recover a partial circle to a full circle shape. Our registered circle is better than other benchmark methods. Also, we show reasonable progress of changing from a diseased (hemorrhagic) state to a healthy state, while original demon registration method fails to show such progress. Finally, we demonstrate an example for atlas building to estimate template for real 3D brain images.

2 Method

In this part, we discuss the classic demon registration method and discuss our fast multi-phases demon registration (FMDR) model for atlas building.

2.1 Background

Demon Registration. For any point p, let f be the intensity in a static image (I_T, we call it as the target image in the below), and s be the intensity in a moving image (I_S, we call it as the source image in the below). Log demon registration was proposed by Thirion [9], it estimated the displacement $\mathbf{u}$ (velocity) for point p to match the corresponding point in I_S:

$$\mathbf{u} = \frac{(s-f)\nabla f}{|\nabla f|^2 + (s-f)^2}, \tag{1}$$

where $\mathbf{u} = (u_x, u_y)$ in 2D registration, and $\mathbf{u} = (u_x, u_y, u_z)$ in 3D registration; ∇f is the gradient of target image, and it is a internal edge force. $s - f$ is the external force, and $(s-f)^2$ can make velocity more stable. Later Vercauteren et al. [10] proposed standard registration model for Log demon registration, it minimizes the following energy functions:

$$E = ||I_T - I_S \circ (\phi + U)||^2 + \frac{\sigma_i^2}{\sigma_x^2}||U||^2, \tag{2}$$

where ϕ is the original transformation filed in x and y direction; U is the update transformation field in each iteration; $\circ$ is the image transformation operation; σ_i and σ_x control the uncertainty of image noise and transformation. The minimizing of E in Eq. 2 can be calculated using Taylor expansion. We can rewrite Eq. 2 for any point p as:

$$E = ||f - s + \mathbf{u}\nabla s||^2 + \frac{\sigma_i^2}{\sigma_x^2}||\mathbf{u}||^2, \tag{3}$$

Take the gradient of Eq. 3 with respect to $\mathbf{u}$, we obtain: $\nabla_{\mathbf{u}} E = 2\nabla s(f - s + \mathbf{u}\nabla s) + 2\frac{\sigma_i^2}{\sigma_x^2}\mathbf{u}$. Let $\nabla_{\mathbf{u}} E = 0$, we can get the transformation field $\mathbf{u}$ as Eq. 1, when $\sigma_i = (f - s)$ and $\sigma_x = 1$, see [10] for the details calculation of $\mathbf{u}$. But Eq. 1 only use the internal edge force of target image, Wang et al. [11] added another internal edge force for source image:

$$\mathbf{u} = \frac{(s-f)\nabla f}{|\nabla f|^2 + \alpha^2(s-f)^2} + \frac{(s-f)\nabla s}{|\nabla s|^2 + \alpha^2(s-f)^2}, \tag{4}$$

where α^2 is proposed by Cachier et al. [12] to control the force length. Equation 4 enhance the stability and the convergence speed of the velocity field.

Algorithm 1. Demon Registration

Input: Source image I_S, target image I_T, α, and number of iterations: itr
Ensure: Registered source image I'_S
1: Initialize transformation field U
2: **For** $i = 1$ to itr
3: Calculate U according to Eq. 4
4: $U = Ker \star U$
5: Update image $I'_S = I_S \circ (S + U)$
6: **end**

Ker is the Gaussian kernel for smoothing the velocity field. However, demon registration will take a long time to register source and target image if there is significant difference between them. *itr* should be large enough to guarantee a good registration results. Also, the transformation U will keep updating on I_S; there are no stages to show the changes in the image. In the following section, we will show how our multi-phases demon registration to overcome these limitations.

2.2 Multi-phases Demon Registration for Atlas Building

We define a general multi-phases model for atlas building using demon registration. Given input images $I_1, \cdots, I_N$, the atlas building task is to find a template image I to minimize the difference between I and input images. Differ from minimizing sum-of-squared distances function ($\min_I \frac{1}{N}\sum_{i=1}^{N} ||I - I_i||^2$) in [13], we aim to minimize following energy function:

$$E = \arg\min_I \frac{1}{2}\sum_{k=1}^{K}\sum_{i=1}^{N} ||I - I_{ik} \circ (\phi + U_{ik})||^2 + \frac{\alpha^2}{2}\sigma_i^2 ||U_{ik}||^2, \tag{5}$$

where U_{ik} is the update transformation field of each input image at phase k. α and σ_i control the regularity term ($||U_{ik}||^2$), which measures the smoothness of transformation. The first similarity term measures the similarity of the template image and input images).

To minimize the energy function in Eq. 5, similar to solve Eq. 2, we use Taylor expansion, and rewrite Eq. 5 as:

$$E' = \arg\min_I \frac{1}{2}\sum_{k=1}^{K}\sum_{i=1}^{N} ||I - I_{ik} + U_{ik}\nabla I_{ik})||^2 + \frac{\alpha^2}{2}\sigma_i^2 ||U_{ik}||^2, \tag{6}$$

Take the gradient of Eq. 6 with respect to U_{ik}, we obtain:

$$\nabla_{U_{ik}} E' = \nabla I_{ik}(I - I_{ik} + U_{ik}\nabla I_{ik}) + \alpha^2\sigma_i^2 U_{ik} \tag{7}$$

Let $\nabla_{U_{ik}} E' = 0$, we get the update transformation U_{ik} as:

$$U_{ik} = \frac{(I_{ik} - I)\nabla I_{ik}}{|\nabla I_{ik}|^2 + \alpha^2\sigma_i^2} \tag{8}$$

Again Eq. 8 only contains the internal force of template image I, to improve the registration convergence speed and the stability, we add another internal force of ∇I, and let σ_i be $I_i - I$, we get the new update transformation in our multi-phases model:

$$\begin{aligned} U_{ik} &= \frac{(I_{ik} - I)\nabla I_{ik}}{|\nabla I_{ik}|^2 + \alpha^2(I_{ik} - I)^2} + \frac{(I_{ik} - I)\nabla I}{|\nabla I|^2 + \alpha^2(I_{ik} - I)^2} \\ I_{ik} &= I_{i(k-1)} \circ (\phi + U_{i(k-1)}) \end{aligned} \tag{9}$$

By getting new images I_{ik}, we could calculate the close-form solution for our template I:

$$I = \frac{1}{N}\sum_{i=1}^{N}\{I_i \circ (\phi + U_{ik})\} \tag{10}$$

Also, our FMDR model is a generalized model, it also work for registrating two image with $N = 1$ in Eq. 5. Our FMDR model can not only find the corresponding positions between a source and a target image, but explain model differences in image appearances. We demonstrate advantages of our model in Sect. 3.

Algorithm 2. Multi-phase Demon Registration for Atlas Building

Input: Source images $I_1, I_2, \cdots, I_N$, noise α, number of iterations: itr', and smooth stage kk
Ensure: Template image I
1: Initialize transformation field U, and template image I
2: **For** $k = 1$ to K
3: **For** $i = 1$ to itr
4: Calculate U_{ik} according to Eq. 9
5: **if** $(k >= kk)$
$U = Ker \star U$
6: Update image $I'_S = I_S \circ (S + U)$
7: **end**
8: **end**
9: Calculate template image I according to Eq. 10

where $itr > K \times itr'$, the time complexity of Algorithm 1 is $\mathcal{O}(iter)$, and the time complexity of Algorithm 2 is $\mathcal{O}(K * iter')$. Therefore, our FMDR model is faster than original demon registration. In addition, in Algorithm 1, it applies Gaussian kernel in each iteration, which will reduce the resolution of register image. In our FMDR model, we have smooth parameter kk, which controls the smooth stage to maintain the resolution of the registered image.

3 Results

By introducing our FMDR model, which can not only find the correspondences between the source and the target image, but also observe the progress of shape deformation. We demonstrate the effectiveness of our model using one synthetic circle data, clinical TBI, and real 3D T2 MRI brain data.

3.1 Synthetic Circle Data

In this circle data, we want to restore a partial circle to a full circle, and we aim to test whether our FMDR model can recover the full shape with less computation time and maintain higher accuracy than other benchmark methods.

We compare results of our model with demon registration (DR) [10], Large Deformation Diffeomorphic Metric Mapping (LDDMM) [6] and Bayesian atlas building using diffeomorphic image registration (BADR) [13]. From Fig. 1, we can find that result of our FMDR model (Fig. 1(e)) can match perfectly in the

"C" shape, while the other methods cannot perfectly recover the shape. Especially, DR and LDDMM only recover partial of the shape. Also, we can visualize the difference between the target image and the registered results in Fig. 2. Comparing with the other three methods, our FMDR model has the lowest difference between target and final registered image since there is no yellow color in our model, and it only has some blue shallow outlines. As shown in Table 1, our FMDR use less computation time compared with original demon registration, BADR, and LDDMM.

3.2 TBI Lesion Registration

To illustrate our model can emphasize geometric shape changes, we test our model use a Traumatic brain injury (TBI) dataset [14]. We manually segment the pathology (red ellipse in Fig. 3, we aim to show the progress from a TBI lesion state 3(a) to a health state 3(b)). As shown in Fig. 4, the deformed area continuously changes until the health state, which illustrates the FMDR method

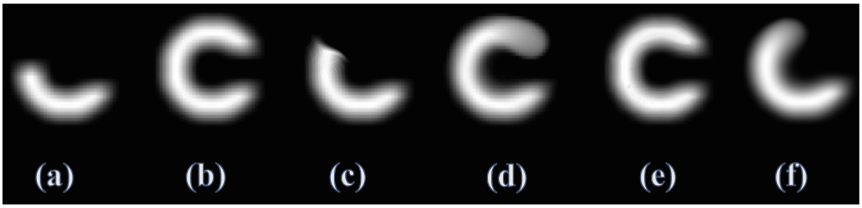


Fig. 1. Circle registration results comparisons of our FMDR model: (a) source image, (b) target image, (c) BADR, (d) LDDMM, (e) with DR, and (f) methods.

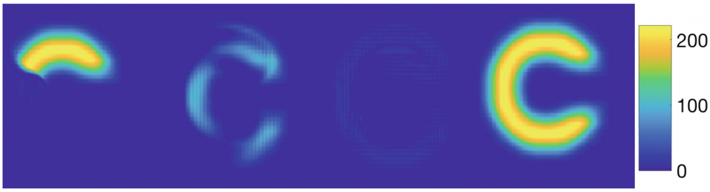


Fig. 2. Difference between the target image and registered results using different methods (from left to right: DR, BARD, FMDR, LDDMM) The color is changing from blue to yellow. Blue color means there is less difference between the source image and registered image, while yellow indicates there is a significant difference between the source and registered image.

Table 1. Computation time comparisons between FMDR, DR and LDDMM

	FMDR	DR	LDDMM
Time	**147 s**	245 s	1281 s

can represent deformation changes. However, the DR model cannot correctly show a reasonable health state.

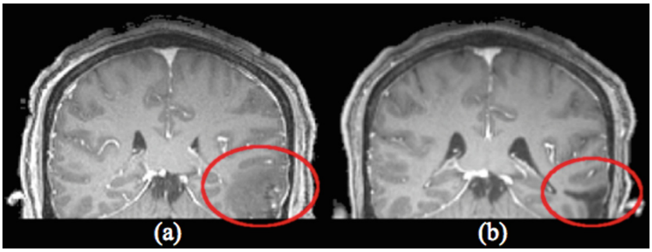


Fig. 3. Traumatic brain injury images. (a) initial scan; (b) registered scan after eight months later. The circle is TBI lesion, dramatically changes in brain lesion part, the shape is deformed. A traditional image registration cannot describe the conversion from a disease state (a: hemorrhagic) to a relative health state (b) (Image from [14], Fig. 1).

(a) The shape changes using DR

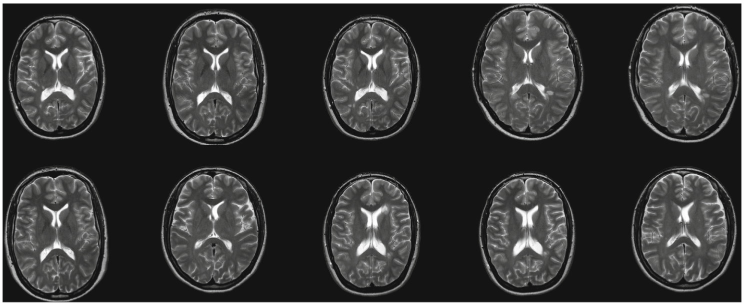
(b) The shape changes using FMDR

Fig. 4. The shape deformation comparisons of our FMDR and DR model. Our FMDR model shows correct shape changes while the DR model does not show a reasonable final health state. Notice that the presence of brain deformations, the change in the lesion's shape, and the conversion of tissue from a diseased state (hemorrhagic) to a healthy state.

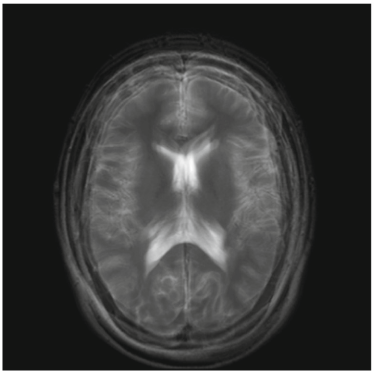
3.3 Atlas Building on 3D MRIs

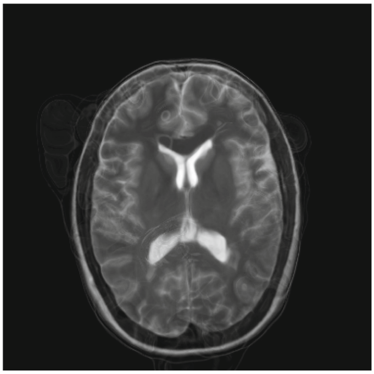
To demonstrate the effectiveness of our method on the real 3D data, we apply our FMDR model to a set of 3D T2 MRIs Fig. 5b. It is a set of Multiple Sclerosis data [15].

From Fig. 5b, the average MRIs is blur, but our estimated template image is obviously clearer than the average MRIs, and this demonstrates our FMDR model can well represent the general information for T2 images, and our method can be used to estimate the template of images which will provide a reliable reference for image fusion.



(a) Axial slices from MRIs





(b) DR template image (c) FMDR template image

Fig. 5. The estimated template image using FMDR and DR model. (a) axial view of input MRIs; (b) estimated template image using DR model; (c) estimated template image using FMDR model.

4 Discussion

One apparent strength of FMDR method is that it can accurately recover the target shape with less computational time. From the results of synthetic images (Fig. 1), we observe that FMDR has a relatively higher recovery rate than other standard image registration methods, such as Demon registration and LDDMM. Also, our FMDR model can describe the geometry shapes changes in a TBI case (Fig. 3), but our model is not limited to applying in a TBI case. It also can be used in qualifying the tumor growing process, for example, tracing the infiltrating and displacing of a brain tumor. Furthermore, this method can be useful for predicting the chronic blood perfusion changes in patients who have a stroke. However, the stage k is a hand turning parameter in our model, which can be changed with different source and target images. Although we show that our method can show the progress of TBI lesion changes, it cannot automatically segment the ROIs (e.g. in Fig. 3(a) and (b) the overlaid segmented lesion shape is manually segmented). And it will absolutely consume time, so this method may not work efficiently in a large database if we only focus on the ROIs. Therefore, our model can be improved if we can propose an addition model to segment these ROIs automatically.

5 Conclusion

In this paper, we present a novel multi-phases demon registration framework for fast and accurate atlas building. We demonstrate the performance of our model using three data sets. Our result is better than other benchmark methods using 2D synthetic data, and our model can delineate the progress of shape deformations. Also, our model can build a good template for a set of brain MRIs data. For future work, we will test our FMDR method using more 3D images. In addition, we will design new experiments for clinical application (e.g. tumor progression and prediction of chronic blood perfusion changes after stroke). Also, automatically extracting ROIs of the images will help our method in quantify the shape deformations. Furthermore, how to improve the matching accuracy and efficiency of our models need to be further explored.

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