Non-rigid Registration by Diffusion Model with the Demons Algorithm

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Abstract: Non-rigid registration becomes more and more important in biomedical imaging applications. A novel non-rigid registration method based on diffusion model with demons algorithm is proposed in this paper. The moving image is considered as a deformable grid, and it is diffusing through the contours of the objects in itself, by the action of effectors, called demons, situated in these interfaces. In order to speed up the convergence of the iteration and enhance the robustness of the algorithm, the moving image is smoothed to increase the number of the ‘demons’. The deformation field has been normalized at each iteration to ensure the stability. Our algorithm is compared with the original ‘demons’ and other developed algorithms on synthetic images and real medical images, the result shows that our algorithm has obvious speed improvement and high tolerance of large deformation and noise. Copyright © 2014 IFSA Publishing, S. L.

Keywords: Registration, Diffusion model, Demons.

1. Introduction

Image registration is a crucial step in all image analysis tasks in which the final information is gained from the combination of various data sources like in image fusion, change detection, and multi-channel image restoration [1]. In medical imaging, registration becomes more and more central to many biomedical imaging applications such as segmentation, to build statistical atlas, for planning and to follow-up treatment. Numerous algorithms for registering image data have been reported in these areas, and much work has been done in the pursuit of developing accurate and efficient nonlinear image alignment algorithms [2]. The fluid method proposed by Nielsen [3] is regarded as one of the most advanced registration method available for nonlinear medical registration task since it satisfies the general requirements of both complex and large deformations. An intensity-based fully automatic non-rigid image registration algorithm, originally known as the ‘demons’ algorithm, has been implemented for finding small deformations in temporal sequences of images [4, 5]. The main idea is to consider the objects boundaries in one image as semi-permeable membranes and to let the other image, considered as a deformable grid model, diffuse through these interfaces, by the action of effectors known as ‘demons’ situated within the membranes. Nielsen demonstrated that the Gaussian filtering used in the ‘demons’ algorithm approximates the linear elastic filter used in the viscous fluid model for deformable image registration. In addition, the body force is almost identical to his fluid model.

Many scholars have put forward to improve the ‘demons’ algorithm [6-8]. Wang et al. proposed an accelerated ‘demons’ algorithm by introducing an ‘active force’ along with an adaptive force strength adjustment during the iterative process [9].
Liu et al. presented a more meaningful, stable and noise-tolerant registration by the assisting of the segmentation to handle the simple inputs [10]; it means that the region captured by the contour contains a single object of the fixed image.

In this paper, a novel diffuse method based on the demons algorithm for image registration is inspired by both the fluid registration and the ‘demons’ algorithm. It has obvious speed improvement over the original algorithm and a high tolerance of large deformation and a strong robustness to the noise. First, we define the ‘demons’ at the pixels in the moving image whose gradient are not zero, and the moving image which considered as a deformable grid model diffuse through the action of the ‘demons’ in itself, this would speed up the convergence rate of the iteration, because the ‘demons’ would closer to the moving image than the original demons algorithm, especially when the deformation is large. Second, elastic-like algorithm such as ‘demons’ has the total displacement fields smoothed and viscous fluid-like approach has the correction fields smoothed. Here, we has the moving image smoothed while computing the gradient of it, this has the similar effect of smoothing the correction fields in viscous fluid-like approach to some extent. Moreover, smoothing the moving image has another two benefits: enhancing the robustness to noises of the algorithm and increasing the number of demons point which would accelerate the convergence of the iteration. Third, In order to ensure the stability of the registration, the magnitude of the motion vector is normalized to between 0 and 1. By our method, the accuracy and efficiency of the algorithm have been obviously improved. In addition, it led to high tolerance of large organ deformations and robustness to noise.

The remaining sections of this paper are structured as follows. First, we present the mathematical model of our approach and described the numerical procedure we employ to solve the registration problem. Next, the feasibility of our approach is illustrated, where we compare our registration with the original ‘demons’ and some other related algorithms on synthetic images and real medical images. Last, we conclude this paper.

2. Methods and Materials

2.1. Non-parametric Diffuse Model

Commonly, the basic input data to a registration process are two images: one is defined as fixed (or target) image $F$ and the other as the moving (or source) image $M$. A typical solution to the non-rigid registration problem is to look for a transformation $T$ such that

$$T' = \arg \min_T D(F, M \circ T),$$

where the function $D$ used to compute the dissimilarity and $\circ$ denotes the composition, $T$ is usually defined by its associated displacement field $U$ on the discrete image, unless we constrain the transformation to belong to some parametric space [11]. The displacement field is searched by minimizing an energy function $D$.

Thirion’s demons algorithm [4] applies the concept of diffusing model to perform image-to-image matching. It consider the objects boundaries (pixels whose gradient are not zero) in the fixed image as semi-permeable membranes and to let the moving image, considered as a deformable grid model, diffuse through these interfaces, by the action of effectors known as ‘demons’ situated within the membranes (Fig. 1a). On the contrary, in our diffusion model, we define the pixels whose gradient are not zero in the moving image as the effectors of demons, and the moving image considered as a deformable grid is diffusing by the action of these effectors (Fig. 1b).

The optical flow equation was used to estimate demons forces. For a given point $p$, let $f, m$ be the intensity of fixed image $F$ and moving image $M$ respectively, and $\nabla f$ be the gradient of the
fixed image at point $p$. The estimated displacement of the point $p$ as follow:

$$\vec{u} = \frac{(m-f)\nabla f}{|\nabla f|^2}, \quad (2)$$

This equation is unstable for small values of $\nabla f$, leading to infinite values for $\vec{u}$. Ideally, the expression should be close to zero for small $\nabla f$. Thirion achieved this by multiplying the expression of equation (2) with a multiplier of $\left( |\nabla f|/|\nabla f| + (m-f) \right)$. In order to avoid the confusing effect of a new parameter in the experiments, thirion chose to use $m-f$ instead of $k$. Then, the equation can be written as:

$$\vec{u} = \frac{(m-f)\nabla f}{|\nabla f|^2 + (m-f)^2}, \quad (3)$$

Obviously, the value of multiplier $\left( |\nabla f|/|\nabla f| + (m-f) \right)$ is different from points which have different intensity difference or gradients. And, the displacement computed by formula (3) may much smaller than the result of the formula (2), moreover it do not maintain the proportion between each pixel computed by formula (2). In this paper, we define $k$ to be a positive small constant $c$. Then, the value of multiplier $\left( |\nabla m|/|\nabla m| + c \right)$ is approximate to 1 when the gradient of the point in the fixed image is not zero and 0 when the gradient is zero. And we can rewrite the equation (3) as follow.

$$\vec{u} = \frac{(f-m)\nabla m}{|\nabla m|^2 + c}, \quad (4)$$

### 2.2. Gaussian Smooth

A common approach for estimating the parameters of the transformation in mono-modal registration problems is to minimize the mean of squared differences (MSD) criterion. One of the main drawbacks of the MSD criterion is its high sensitivity to outliers [12]. In order to overcome this shortage, we convolve the moving image with a Gaussian kernel prior to gradient computation to enhance the robustness to noise.

Partial derivative equations of elastic models smooth the displacements of the elastic body, and a viscous fluid-like approach has only the correction fields $u_s$ smoothed, since partial derivative equations of viscous fluid models smooth velocities of the fluid body. The original demons algorithm is an elastic-like algorithm and it has only the total displacement fields $U_s$ smoothed. Here, we smooth neither the displacement $U_s$ nor the correction fields $u_s$ during each of the iterations. We just smooth the moving image before the registration only once by the recursive Gaussian in ITK [13].

By smoothing the moving image, almost every point in them has its intensity gradient. This greatly increase the number of demons point which will accelerate the convergence of the iteration. Fig. 2(a) and (b) are the synthetic fixed image and moving image; Fig. 2(c) is the gradient magnitudes of the moving image, it has only a small number of demons points at the edge of the object in moving image; Fig. 2(d) is the gradient magnitudes of the smoothed moving image, obviously, almost every point around the object in moving image has its intensity gradient.

![fixed image](a)  ![moving image](b)  ![gradient magnitudes of the moving image](c)  ![gradient magnitudes of the smoothed moving image](d)

**Fig. 2.** (a) fixed image; (b) moving image; (c) the gradient magnitude of the moving image; (d) the gradient magnitude of the smoothed moving image.

By smoothing the moving image, we can rewrite the equation (4) as follow:

$$\vec{u} = \frac{(m-f)\nabla (G_s \odot m)}{|\nabla (G_s \odot m)|^2 + c}, \quad (5)$$

where $G_s$ is the Gaussian filter with standard deviation $\sigma$, and $\odot$ denote convolution.
2.3. Normalization

The value of the displacements computed by the formula (5) may be very large when the value of the difference of the intensities between the fixed image and moving image is large, in order to stabilize the numerical integration process, we normalized the correction field to a range of 0~1. For simplicity in notation, in the following, we will present the equations for the 2D case. First, for each pixel in the fixed image, compute the sum of the absolute value of $u_x$ and $u_y$, and denoted by $N$, that is

$$N = |u_x| + |u_y|.$$

$N_{max}$ denotes the maximum value of all the $N$ value. Then, we update all the value of $u$ by $u = u \cdot \left(\frac{1}{N_{max}}\right)$.

3. Result

In this section, we present three sets of experiments to demonstrate the improvements made by our proposed method respectively. In the first set, we compare the convergence rate of our improved algorithm with the original demons method and an accelerated ‘demons’ algorithm proposed by Wang [9] et al. In the second set, in order to validate the improvement of the registration precision and high tolerance of large deformations of our proposed method, we do some comparing experiments with the original demons method and Wang’s method on both synthetic images and real medical images. At last, we show that our algorithm has a perfect performance with noise in the images.

To evaluate the performance of our algorithm with respect to the original demons algorithm and Wang’s method, we use the same set of parameters for all the experiments. As required by the regularization purpose, a standard deviation ($\sigma = 1$) of the Gaussian smoothing kernel is applied to the deformation field at each iteration of the original demons algorithm and Wang’s method. Since the emphasis is on the comparison of the various schemes, no multi-resolution scheme has been used.

All of the experiments in this paper are accomplished on the computer of a single Pentium 3.0G CPU and 1.0G memory.

3.1. Validation of Acceleration

We first tested the convergence rate of the iteration of our algorithm, comparing with the original demons algorithm and Wang’s ‘active force’ method. Fig. 3 shows the incremental deformation at different iterations using the original demons algorithm (top row), Wang’s method (middle row) and our algorithm (bottom row) to match the moving image to the fixed image. In this case, the fixed image and the moving image are the same as in Fig. 2(a) and Fig. 2(b) respectively. The moving image is deformed by shift the fixed image to the right 20 pixels.

![Fig. 3](image)

**Fig. 3.** Top row: Deformation of the Moving image to match the fixed image by means of the original demons algorithm. From left to right are the deformed images in iterations 1, 100, 200, 300, 500, 1000 and 2000. Middle row: Deformation of the Moving image to match the fixed image by means of Wang’s algorithm. From left to right are the deformed images in iterations 1, 10, 30, 100, 200, 300 and 400. Bottom row: Deformation of the Moving image to match the fixed image by means of our algorithm. From left to right are the deformed images in iterations 1, 5, 10, 15, 20, 25 and 30.

It appears from the top row that the intensity flow is faster along the high-gradient region near the edge of the body contour in fixed image than in the low-gradient region near the centre of the field in fixed image. This indicates that the original demons algorithm took an unnecessary path to achieve the final result. The middle row of Fig. 3 shows selected intermediate steps from using Wang’s method which combined the active force with the original algorithm’s passive force, the intensity flow is much faster than original ‘demons’ algorithm because the demons’ force existed both in the fixed
3.2. High Tolerance of Large Deformations

Quantitative validation of a non-rigid registration algorithm for medical image is very difficult because of the general lack of known solutions in clinical situations. In addition, deformable image registration is inherently degenerative since multiple solutions may exist for a given match of image intensity. The appearance of the image after deformable image registration can serve as a qualitative preliminary assessment [9]. We evaluated our modified demons algorithm for deformable image registration in MSD and mutual information (MI).

Fig. 4(a) and 4(b) are the fixed and the moving image, the moving image is deformed from the fixed image with a known non-rigid deformation field and 20° clockwise rotation. Fig. 4(c) and (d) are the results of the registration between the fixed and moving images by the original demons algorithm and Wang’s ‘active force’ method respectively, and Fig. 4(e) is the result of our algorithm. Table 1 lists the similarity measure (MSD) before and after registrations and computing times of the registrations. MI1 and NMI1 are the mutual information and normalized mutual information of fixed image and moving image. MI2 and NMI2 are the mutual information and normalized mutual information of fixed image and the result image. Number of iteration represents the iteration times during the registrations. The units of the computing time are seconds. Obviously, the original demons algorithm can only deal with the small deformation of the moving image, and it can’t get the desired result with the large deformation. Our algorithm gets better results with less iterations and computing time.

<table>
<thead>
<tr>
<th>Methods</th>
<th>MI1/NMI1</th>
<th>MI2/NMI2</th>
<th>MSD</th>
<th>Number of Iteration</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original ‘demons’</td>
<td>1.30/0.32</td>
<td>1.99/0.49</td>
<td>766.3</td>
<td>1250</td>
<td>84.0</td>
</tr>
<tr>
<td>Wang’s method</td>
<td>1.30/0.32</td>
<td>2.02/0.50</td>
<td>345.8</td>
<td>418</td>
<td>28.4</td>
</tr>
<tr>
<td>Our algorithm</td>
<td>1.30/0.32</td>
<td>3.41/0.84</td>
<td>83.8</td>
<td>223</td>
<td>16.9</td>
</tr>
</tbody>
</table>

3.3. Anti-noise Performance

Liu et al have developed a segmentation-assisted registration [10], under that framework, a set of forces generated by the prior segmentation contours can provide an extra guidance in assisting the alignment process towards a more noise-tolerant procedure. However, this method can only handle the simple inputs; it means that the region captured by the contour contains a single object of the fixed image. Our methods do not have this restriction and can handle the more complicate inputs. In order to confirm this view, we do the experiment on both the simple synthetic images and the real medical images, the results were shown as Fig. 5 and Fig. 6 respectively.

The fixed image and moving images in Fig. 5(a) and 5(b) are the fixed and moving images in Fig. 3 added Gaussian white noise of mean 0 and variance 0.03 respectively. The previous experimental results indicate that the original demons and Wang’s method can match the moving image and fixed image with no noise perfectly. However, Fig. 5(c) and 5(d) are the results of the original demons algorithm and
Wang’s method respectively. Evidently, the original demons algorithm and Wang’s method have trouble in warping the moving image to a perfect matching, which is partially due to the numerous local energy minima resulted from the huge amount of noise existing in the images. However, the registration result generated from our algorithm shown as Fig. 5(e) is quite accurate, which indicates that our method is very helpful in pulling the moving image towards a correct matching.

We designed and carried out a similar experiment on a pair of MRI brain slices added Gaussian white noise of mean 0 and variance 0.01. Fig. 6(a) and 6(b) are the fixed and moving images respectively. Fig. 6(c) and 6(d) are the results of the original demons algorithm and Wang’s method respectively. Fig. 6(e) is the result of our algorithm. As evident, the original algorithm and Wang’s method fail to transform the moving image into a desired result, while our algorithm accurately achieves the registration goal.

### 4. Conclusion

The demons algorithm is an effective non-rigid registration technique for tracking anatomical variations within the same image modality. In this paper, we present a novel non-rigid image registration based on the ‘demons’ algorithm. Our model differs from the original ‘demons’ algorithm in: (1) our model considers the moving image as a deformable grid and it is diffusing through the contours of the objects in itself, by the action of effectors, called demons, situated in these interfaces; (2) the gradients are computed on the smoothed moving image to enhance the robust of the algorithm and increase the number of ‘demons’ in the moving image which can speed up the convergence rate of the iteration. We compare the result of our algorithm with that the original demons algorithm and Wang’s ‘active force’ method. The results demonstrated that our method could effectively accelerate the algorithm, and it provided the benefits of compensating for relatively large deformations between pairs of images and noise robust. Geometry-constrain of this model and multi-resolution processing will be the focus of our future work.

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