Nonrigid Image Registration of Brain MR Images Using Normalized Mutual Information

Smita Pradhan and Dipti Patra

Abstract Registration is an advanced technique which maps two images spatially and can produce an informative image. Intensity-based similarity measures are increasingly used for medical image registration that helps clinicians for faster and more effective diagnosis. Recently, mutual information (MI)-based image registration techniques have become popular for multimodal brain images. In this chapter, normalized mutual information (NMI) method has been employed for brain MR image registration. Here, the intensity patterns are encoded through similarity measure technique. NMI is an entropy-based measure that is invariant to the overlapped regions of the two images. To take care of the deformations, transformation of the floating image is performed using B-spline method. NMI-based image registration is performed for similarity measure between the reference and floating image. Optimal evaluation of joint probability distribution of the two images is performed using parzen window interpolation method. The hierarchical approach to nonrigid registration based on NMI is presented in which the images are locally registered and nonrigidly interpolated. The proposed method for nonrigid registration is validated with both clinical and artificial brain MR images. The obtained results show that the images could be successfully registered with 95 % of correctness.

Keywords Medical image registration · Mutual information · Normalized mutual information · B-spline method

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1 Introduction

Image registration is the process of transforming different sets of data into one coordinate system. Registration methods can be classified by a number of characteristics, which include the type of transformation and the registration measure. Although it has applications in many fields, medical image registration is important among them. Medical image registration has a wide range of potential applications, but the emphasis is on radiological imaging. Modern three-dimensional treatment radiation planning is based on sequences of tomographic images. Computed tomography (CT) has the potential to quantitatively characterize the physical properties of heterogeneous tissue in terms of electron densities. Magnetic resonance (MR), is very often superior to CT, especially for the task of diferentiating between healthy tissue and tumor tissue. Positron emission tomography (PET), single photo emission tomography (SPECT), and MRS (magnetic resonance spectroscopy) imaging have the potential to include information on tumor metabolism. They have specific properties and deliver complementary information. The images supply important information for delineation of tumor and target volume, and for therapy monitoring.

A widespread survey of image registration methods have been published by Brown and Zitova et.al. They have classified the image registration techniques as intensity-based methods and feature-based methods [1, 2]. In intensity-based methods, similarity measure has an important role, which quantifies the relationship of transformation between the images. The most commonly used similarity measures are based on intensity differences, intensity cross correlation, and information theory. Among them, mutual information (MI) has gained wide interest in the medical image registration field [3]. When the assumptions of corresponding intensities are not one-to-one related, maximization of mutual information (MMI) is widely applicable [4]. Pluim et al. proposed to combine MI with an image gradient-based term that favors similar orientation of edges in both images [5].

As MI is computed on voxel-by-voxel basis, it does not take the spatial information inherent to the original image. To overcome this drawback, variations of MI have been proposed. Pluim et al., suggested interpolation artifacts in similarity measures [6]. Likar et al. developed a hierarchical image subdivisions strategy, that decomposes the nonrigid matching problem into an elastic interpolation of numerous local rigid registration [7]. For overlapping sub regions of the image, a nonrigid registration scheme was proposed by extending the intensity joint histogram with a third channel representing a spatial label by Chen et al. [8]. Rueckert et al. employed for transformation modeling the multiresolution scheme [9]. Studholme et al. employed normalized mutual information (NMI) for nonrigid registration of serial brain magnetic resonance imaging (MRI) due to the local intensity changes, which are mainly caused by imaging distortions and biological changes of the brain tissue [10]. The optimization algorithm for nonrigid medical image registration based on cubic b-spline and maximization of MI is derived in [11].

MI faces difficulties for registration of small-sized images. To overcome this limitation, Andronache et al. used the MI for global registration and cross correlation to register the small image patches [12]. Besides the Shanon's entropy, other divergence measures have been used such as Tsallis entropy by Khader et al. [13].

In image registration, finding homologous landmarks is a challenging task due to lack of redundancy in anatomical information, in different modalities. Intensity-based techniques circumvent these problems as they do not require any geometrical landmarks. Their basic principle is to search, the transformation that maximizes a criterion measuring the intensity similarity of corresponding voxels. In this chapter, the registration scheme has been proposed using similarity measure-based method by incorporating NMI. The NMI approach is a robust similarity measure technique used for multimodal medical image registration. Moreover, the NMI-based registration is less sensitive to the changes in the overlap of two images. Here, we propose a non-rigid image registration approach by optimizing the NMI as similarity measure and B-spline method for modeling the transformation of the deformation field between the reference and floating image pairs.

2 Problem Statement

Here the NMI-based similarity measure is used as a matching criterion to solve the image alignment problem.

Let A and B be two misaligned images to be registered where A is the reference image and B is the floating image. The floating image B is a deformed image with a deformation field. The deformation field is described by a transformation function T(r, μ) where μ is the set of transformation parameter to be determined. The image registration problem may be formulated as an optimization problem

$$\overset{\wedge}{\mu} = \arg\max_{\mu} NMI(A(r), B(T(r; \mu))) \qquad (1)$$

For alignment of the transformed target image B($T(r; \mu)$) with the reference image A, we need the set of transformation parameters $^-$ that maximizes the image cost function $NMI(A(r), B(T(r; \mu)))$.

3 Problem Formulation

3.1 Registration by Normalized Mutual Information

The notion of image registration based on MI has been proposed by Maintz et al. [3]. The MI of two images is a combination of the entropy values of the images. The entropy of an image can be computed by estimation of the probability distribution of the image intensities [5].
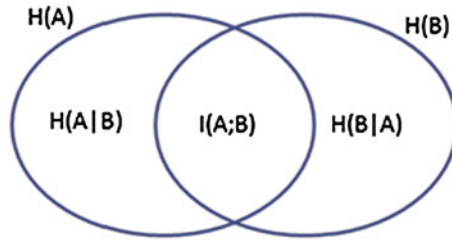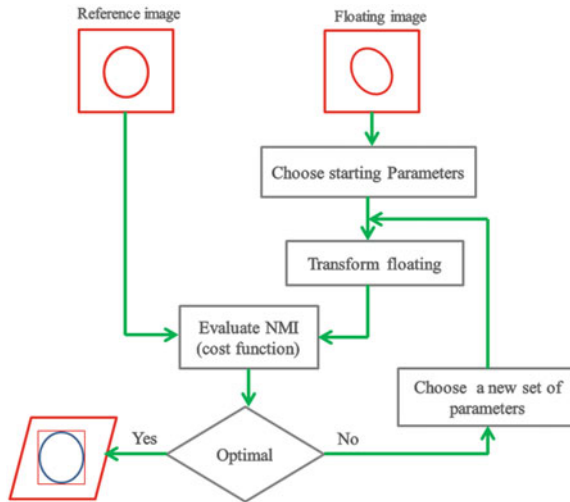
Fig. 1 Mutual Information of two images

Fig. 2 Block diagram of NMI

If A and B are two random variables, then the amount of information that one variable contains about another is evaluated by MI (Fig. 1) which is given as

$$I_{(A:B)} = \sum_{a,b} p_{A,B}(a,b) \log \left(\frac{p_{A,B}(a,b)}{p_A(a) p_B(b)} \right) \qquad (2)$$

where $P_A(a)$ and $P_B(b)$ are the marginal probability mass function and $P_{AB}(a,b)$ is the joint probability mass function. MI is related to the entropies by

$$I(A, B) = H(A) + H(B) - H(A, B) \qquad (3)$$

where H(A) and H(B) are the entropies of A and B and H(A, B) is the joint entropy defined as (Fig. 2)

$$H(A) = -\sum_a p_A(a).\log p_A(a)$$

$$H(B) = -\sum_b p_B(b).\log p_B(b)$$

$$H(A, B) = -\sum_{a,b} p_{a,b}(a, b).\log p_{a,b}(a, b) \tag{4}$$

The MI of two images determines the uncertainty of one of the images when the other is known. MI is assumed to be maximum when the images are registered. According to Studholme et al., the registration quality might decrease despite an increasing MI value whenever overlap between voxel occurs. At that time, MI is maximum but the quality of the registration is not optimal [10]. To counter the effect of increasing MI with decreasing registration quality NMI is considered. The transformation yielding the highest NMI value is assumed to be the optimal registration of two images. An estimate of the intensity distribution of the images is necessary to compute the NMI value. NMI is a well-established registration quality measure which can be defined in terms of image entropies,

$$NMI(A, B) = \frac{H(A) + H(B) - H(A, B)}{H(A, B)} \tag{5}$$

3.2 Optimization Using Parzen Window

To calculate the NMI between the reference image A and the floating image B using a transformation $T(r; \mu)$, the joint histogram $H(a, b; \mu)$ has been taken. The popular Parzen window interpolation method is formulated to obtain the joint histogram. Parzen window places a kernel at a particular bin r and updates all the bins falling under the kernel with the corresponding kernel value. The parzen window joint histogram is given by;

$$H(a, b; \mu) = \sum_{r \in A} w_a(I_A(r_a) - a)w_b(I_B(T(r_a; \mu)) - b) \tag{6}$$

where $I_A(r)$: intensity of A, $I_B(r)$: intensity of B, $T(r; \mu)$, maps every reference position r_a to the corresponding floating position $r_b = T(r_a; \mu)$ with a given set of parameters μ. w_a and w_b are the Parzen window kernels used to distribute an intensity over the neighboring bins.

3.3 Transformation Model

The transformation model defines how one image can be deformed to match another; it characterizes the type and number of possible deformations. Several transformation models have been proposed for nonrigid image registration. In this chapter, we adopt the second order B-splines model for transformation of deformed image. By contrast, B-splines are only defined in the vicinity of each control point; perturbing the position of one control point only affects the transformation in the neighborhood of the point. Because of this property, B-splines are often referred to as having "local support". B-spline based nonrigid registration techniques are popular due to their general applicability, transparency, and computational efficiency. The B-spline model is situated between a global rigid registration model and a local nonrigid model at voxel scale. Its locality or nonrigidity can be adapted to a specific registration problem by varying the mesh spacing and thus the number of degrees of freedom.

Let Φ denote a $rx \times ry$ mesh of control points $\Phi_{i,j}$ with a uniform spacing Δ. Then, the 2D transformation at any point $r = [x, y]^T$ in the target image is interpolated using a linear combination of a B-spline convolution kernel as follows:

$$T(r; \mu) = \sum_{ij} \eta_{ij} \beta^2 \left(\frac{r - \phi_{ij}}{\Delta} \right) \tag{7}$$

where $\beta^{(2)}(r) = \beta^{(2)}(x)\beta^{(2)}(y)$ is a separable B-spline convolution kernel, and η_{ij} are the deformation coefficients associated to the control points $\Phi_{i,j}$.

3.4 Simulation and Results

The optimization of nonrigid transformation using B-spline interpolation method leads to align the images. The time required for optimization steps to reach registration can be used as a measure of computational speed. The interpretation of NMI function is based on dispersion of the joint histogram, meaning the less dispersed the joint histogram, the better the two images are assumed to be registered. Under this interpretation, minimization of the dispersion of the joint histogram is related to maximization of NMI value.

The registrations were performed for a set of deformed brain MR images in our simulation. In the first set, a T1 weighted brain MR image and a deformed image that are considered as reference and floating images and, are shown in Fig. 3a, b respectively. The deformation field is shown in Fig. 3c. The registered image is shown in Fig. 3d. The joint histograms of the two images before registration and after registration are shown in Fig. 3e and f respectively. It can be seen that the histogram is not dispersed, rather focused after registration using NMI-based similarity measure. The dispersion shows the misalignment between the images with a
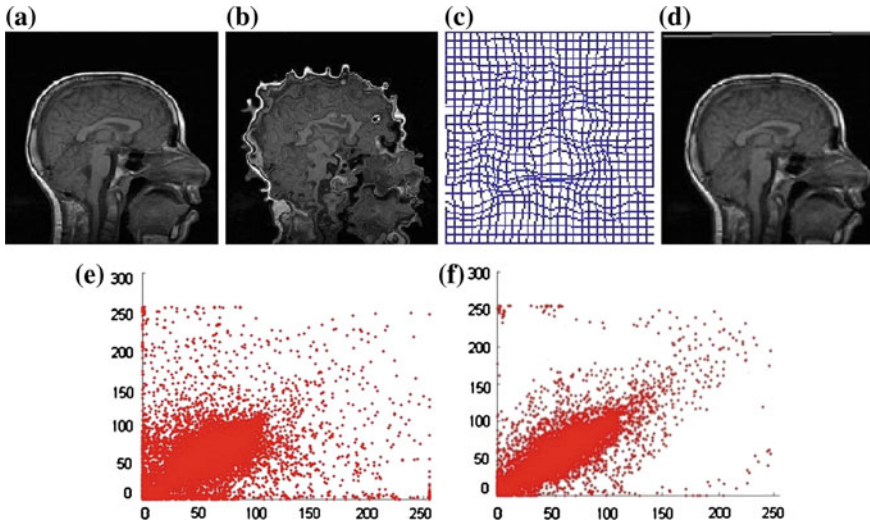
Fig. 3 a Floating image **b** Reference image **c** Deformation field **d** Registered image **e** Joint histogram before registration **f** Joint histogram after registration

percentage of 4.009. The optimization timing or computational timing is recorded as 41.14 s.

Another set of MR images are taken, where Fig. 4a is the floating image which is deformed and rotated with an angle of 30 %. The reference image is shown in Fig. 4b. The floating image is first rotated for best alignment with the reference one shown in Fig. 4c. The deformation field is presented in Fig. 4d. The joint histogram of Fig. 4a, b is shown in Fig. 4f, where it can be observed that the histogram is dispersed due to misalignment between the two images. But in case of Fig. 4g it can been seen that the histogram is very much focused after the registration process. The computation time for optimal registration is recorded as 18.51 s.

The optimized NMI value, the percentage of misregistration error (MRE), and the computational time for optimization metrics for both experiments are presented in Table 1. The normalized value signifies the alignment between the two images after registration process. The higher the value of NMI means more alignment of the images. MRE is misregistration error calculated by considering the registered image with respect to the reference images. Less value of MRE means best alignment of the images. Computational time is the time required for optimal registration. From

Table 1 Calculated NMI value with % age of Mis-reg Error and comp. time

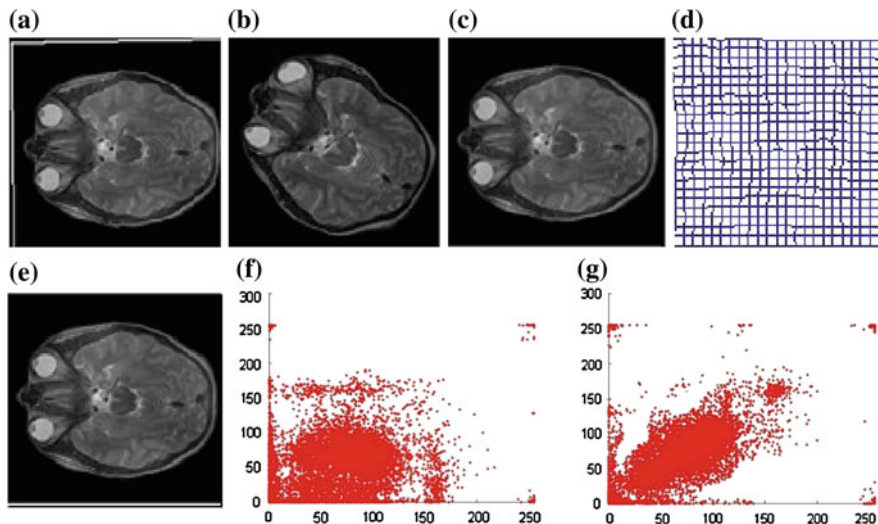| Image	NMI value	MRE (%)	Comp. timing (s)
Figure 3	0.2880	4.0090	18.51
Figure 4	0.3960	7.5041	41.14

Fig. 4 **a** Floating image **b** Reference image **c** 30° rotated floating image **d** Deformation field **e** Registered image **f** Joint histogram before registration **g** Joint histogram after registration

the table, it can be concluded that the optimization process for aligning the images takes more time with a low percentage of misalignment and vice versa.

4 Conclusion

In this paper, intensity-based technique is applied for alignment problem as we can work directly with the volumetric data. We propose the registration scheme by optimizing the NMI as similarity measure. This measure produces accurate registration results on both artificial and clinical brain images that we have tested. B-spline method is used for modeling the nonrigid deformation field of the target image with respect to the reference image. Parzen window interpolation method is employed for joint histogram plot. Current attempts are made to register the image with multimodal images. This work can be extended towards multimodal brain image registration.

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