# **On Image Registration In Magnetic Resonance Imaging**

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### Abstract

Image registration is used in many fields for mapping one image to another. In magnetic resonance imaging (MRI) applications, one of the main uses is for correction of motioninduced artifacts so that subsequent image analysis would be more reliable. This paper gives an introduction to some image registration problems in MRI and functional MRI applications, describes certain commonly used image registration procedures, and discusses their major features. Two potential research topics for improving current image registration procedures are also discussed.

## 1. Introduction

Image registration aims to geometrically match up images or image volumes for structure localization and difference detection. It has been widely used in medical diagnostics, treatment planning and evaluation, disease and intervention monitoring, image-guided surgery and therapy, and so forth. A common application of this technique is to integrate useful information from different sources (e.g., CT, PET, SPECT, X-ray, ultrasound, and magnetic resonance images [1],[2]), or to register images obtained at different times [3]. In this paper, we introduce some commonly used image registration procedures and their applications in magnetic resonance imaging (MRI).

In MRI applications, one major purpose of image registration is to study image variations, ranging from intersubject anatomical comparisons of brain images [4],[5], intra-subject monitoring of pathological development [6], to matching an observed image with a reference template [4],[5]. In cases of intra-subject or temporal variation registration, observed images could be a time series acquired in a short period of time at one occasion, or a time series acquired at several occasions. In the first case, differences between the reference and consecutive images are mostly object-related, since noise patterns and other environment-related artifacts would be similar. However, this may not be true in the second case. For instance, noise patterns at different occasions could be different due to different acquisition settings. Such noise pattern variations have not been well-addressed in image registration applications. Thus, image registration methods could be fortified if such issues are handled properly.

In Section 2, a brief introduction about MRI, functional MRI (fMRI), and aquisition artifacts is given. An overview of some commonly used registration methods is presented in Section 3. Section 4 discusses two potential research topics for improving current image registration procedures

# 2. MRI, fMRI, and Aquisition Artifacts

MRI is a technique used mainly for assessing pathological or other physiological conditions in living tissues, by visualizing the inside of living organisms [7]. In simple terms, its methodological basis lies in: (i) different tissues have different compositions and physical properties, such as water molecule densities, from which the tissue type at a given position can be determined, and (ii) these differences, in water molecule density say, can be depicted as various image contrasts using the MRI technique.

When a part (e.g., head) of a body is placed in a uniform magnetic field of a given direction, say, the z direction, the hydrogen nuclei of water in that part would align themselves in parallel or anti-parallel with the field, creating a net magnetization, and rotate with the Larmor frequency of angular velocity  $w_0$ . The basis of MRI lies in manipulating the local magnetic field such that the local resonant frequency would differ at different locations, which is achieved by applying additional, small, linear magnetic field gradients. In a MR scanner system, three orthogonally positioned gradient coils would produce such magnetic fields that vary linearly along their respective axes (e.g., x, y, and z axes), and these small fields are added to the main magnetic field. Turning on the coils in any particular combination would produce a field gradient along any desired direction. After applying radiofrequency (RF) pulses transmitted by a separate RF coil, emitted radiation is absorbed by nuclei. Consequently, the net magnetization is tipped away from the main z axis; the nuclei continue their rotation, and as the excited nuclei relax back to the initial lower-energy alignment along the main field, RF signals are re-emitted and received by a RF receiver coil. Along the z direction, suppose a particular perpendicular slice of the body part at  $z = z_0$  is to be imaged. Then, a RF pulse with frequency corresponding to that slice position would excite the nuclei in that plane. Considering only the proton density and spin relaxation, the received signal can be expressed by

$$S_{z_0}(k_x, k_y) = \int \int_{\Omega_{z_0}} m(x, y, z_0) \exp[i2\pi(k_x x + k_y y)] dxdy,$$
(1)

where  $\Omega_{z_0}$  denotes the 2-dimensional (2-D) region of the slice,  $m(x, y, z_0)$  is the density of hydrogen protons at (x, y), and  $k_x$  and  $k_y$  are the frequency change rates along the x and y directions of the local magnetic fields. Note that some constant multipliers have been ignored on the right-hand-side of (1) for simplicity. It can be seen that  $S_{z_0}(k_x, k_y)$  is a Fourier transformation of  $m(x, y, z_0)$ . Therefore, if we have signals  $S_{z_0}(k_x, k_y)$  in frequency domain, for all  $k_x, k_y = 1, 2, \ldots, n$ , then  $m(x, y, z_0)$  can be determined in spatial domain at  $n \times n$  regularly spaced pixels by the discrete inverse Fourier transformation (see [8], Chapter 7), as demonstrated in Figure 1.



# Figure 1. (a) Signals in frequency domain. (b) Corresponding image obtained by the discrete inverse Fourier transformation of (a).

fMRI is a technique for measuring the hemodynamic response related to neural activity in the brain or spinal cord of humans or other animals. When neurons are activated, blood supply to active regions would increase and the supply of oxygenated hemoglobin to the regions would be greater than the local oxygen consumption, which would lead to local signal increases in active regions. By acquiring a time series of brain images during some activation tasks, such regional signal changes in the time series can be correlated with the activation tasks and the brain's functional structure can hence be studied [9],[10].

Equation (1) is only a theoretical model for describing MRI image acquisition. In practice, there will be many different artifacts in the received signal due to various reasons, including hardware imperfections, signal dropouts caused by field inhomogeneity and susceptibility effects, movement of the imaged object, and so forth. Some of these artifacts are shown in Figure 2. In fMRI, brain activation accounts for an additional source of intensity changes, apart from pointwise noise and other artifacts. These activationrelated changes can be obscured by artifacts, and vice versa. It is reported that motion-related intensity shifts of onetenth of a voxel can amount to a 2% signal change, which is above the level of detected activation-related signal changes by most clinical magnetic resonance (MR) systems [11]. Therefore, if artifacts are not treated properly, then fMRI analysis could be misleading. On the other hand, activationrelated intensity changes can bias detection of artifacts, vielding erroneous correction of such artifacts [12]. These issues pose a challenge on MRI image registration.



Figure 2. (a)-(d): Relatively clean images. (e)-(h): Their contaminated versions.

# 3. Image Registration

Assume that R(x, y) and M(x, y) are a reference image and an image to register with, respectively. Then, the major goal of image registration is to find a geometrical transformation T such that M(T(x, y)) is as close to R(x, y) as possible. Mathematically, the image registration problem can be formulated as the following maximization problem:

$$T_{opt} = \arg \max_{T \in \Omega_T} S(R, M(T)), \tag{2}$$

where  $T_{opt}$  denotes the optimal transformation, S is a selected similarity metric, and  $\Omega_T$  is the space of all possible transformations. In (2), if a dissimilarity metric is used, then "max" should be replaced by "min".

In MR applications, a conventional registration process consists of some of the following five steps: 1) image preprocessing, 2) feature selection, 3) transformation specification, 4) selection of a similarity or dissimilarity metric, and 5) optimization. As mentioned earlier, observed MR images often contain various artifacts. Image pre-processing is mainly for deleting the artifacts so that image registration would be more reliable. See [8] for a detailed introduction about image pre-processing techniques.

One way to solve the maximization problem (2) is that Ncorresponding points are first selected in the two images and then an optimal transformation is searched to best match the two point sets in the two images. More specifically, let  $(x_i, y_i), i = 1, 2, ..., N$  and  $(X_i, Y_i), i = 1, 2, ..., N$ be two point sets in R(x, y) and M(x, y), respectively. Then, the task of mapping M to R becomes the problem of finding a transformation T(x, y) such that  $T(x_i, y_i)$  are close to  $(X_i, Y_i)$ . This transformation T can be regarded as a coordinate transformation, which transforms the coordinates of the N points in the image R to the coordinates of the corresponding N points in the image M. Thus, it is often referred to as a coordinate transformation in the literature [13]. If it is required that  $T(x_i, y_i) = (X_i, Y_i)$ , for  $i = 1, 2, \ldots, N$ , then T is also called an interpolation transformation [14].

Feature selection is mainly for the *direct* matching algorithms mentioned above. It entails extracting characteristics to establish correspondence between two images to register. Landmarks or control points, which are often the preferred features, can be selected manually, or automatically by a computer [15]. Lines or curves are often detected through gradient-based methods. Regions, centroids or templates are usually determined by ways of thresholding and segmentation [16].

In certain applications, feature selection can be a very complicated and challenging process. In such cases, rather than selecting features to match, we can search a transformation such that R and M match each other the best in terms of a similarity metric defined by image intensities. This type of *indirect* registration procedures requires no prior knowledge of correspondence between two sets of selected features. Because of this flexibility, they have become popular within MR applications. However, computation involved in such intensity-based procedures would be relatively complex, compared to the feature-based matching procedures.

Transformations can be divided into parametric or nonparametric ones. In the context of motion detection in MR, they often operate with three different motion types: rigidbody, non-rigid body and affine models [17]. Rigid-body transformations assume a global motion in which distance between any two points on an object is unchanged during motion. This model deals with translation and rotation only, and hence has 3 parameters or degrees of freedom (2 for translations and 1 for in-plane rotation) in 2D, and 6 parameters in 3D (3 for translations and 3 for rotations). Non-rigid models are similarly defined, but on a local basis, see e.g., [17]. Affine transformations are sometimes considered as extended rigid-body transformations, but are more versatile in accounting for a larger extent of global deformation, by incorporating scaling and shearing in addition to translation and rotation, and by preserving line parallelism. A typical affine transformation has 12 degrees of freedom in 3D cases [4].

Parametric transformations, such as the rigid-body and affine motion models, generally include global motion assumptions. The widely used linear transformation in 2D is:

$$\begin{cases} X = \alpha(x\cos\Delta\phi + y\sin\Delta\phi) + \Delta x \\ Y = \alpha(-x\sin\Delta\phi + y\cos\Delta\phi) + \Delta y \end{cases}$$
(3)

where  $(\Delta x, \Delta y, \Delta \phi)$  are three motion parameters and  $\alpha$ is a parameter accounting for any scaling. Model (3) can be easily extended to 3D cases, and in the case of  $\alpha$  = 1, it describes rigid-body motions. Such assumptions of global translation and rotation have been applied in both the feature-based direct matching algorithms, such as in the Principal Axes approach[18], and the intensity-based registration methods. Model (3) has been commonly used in applications [19]. A reason for this lies in the ease of implementation and computation. Another advantage of this transformation is its feature preservation property (e.g., a line maps to a line), and hence it does not introduce additional distortions to the related images. On the other hand, global motion assumptions are sometimes too restrictive to describe real complex deformations well, although it has been shown in the literature that model (3) can work well in many applications.

Non-parametric transformations do not assume specific parametric forms. Therefore, they are more flexible than their parametric counterparts. They are mainly used in general registration applications for directly matching known corresponding features. Instead of imposing and applying a pre-specified parametric transformation onto data, a non-parametric transformation is adaptive to data. To this end, both interpolation and approximation methods have been proposed for MR registration. Numerous interpolation techniques exist in the general field of image registration, spanning from thin-plate splines to multiquadric methods [20]. In the MR literature, spline-based procedures have been proposed for accommodating physical object deformation[4],[13]. Approximation methods are widely used for handling non-rigid motions. Many general registration techniques based on approximation have been applied to MR, including approaches such as the piecewise linear or cubic approximations [21], [15], weighted mean or weighted linear methods [21], and so forth. Instead of fitting a model globally using all data points, approximation methods are often performed over sub-regions defined by the data points. Compared to some interpolation-based procedures, they are usually easier to implement and more robust to noise and outliers. A drawback is that good accuracy is only obtained within the span of sub-regions.

No matter the choice of a registration method, its implementation is almost always closely linked to optimizing certain similarity (or, dissimilarity) measure for best match between two images. Finding a most suitable similarity measure has been and still is the subject of much research[22]. Numerous similarity metrics have been suggested in MR registration. Some commonly used ones can be categorized broadly into 3 groups, briefly discussed below.

The first group of similarity metrics requires that the reference image R(x, y) and the transformed image M(T(x, y)), obtained by transforming image M(x, y) using a proper transformation T, are as close to (or, correlated with) each other as possible. Among such metrics, the following least-squares metric is the classical and most widely employed one:

$$\min_{T \in S_T} \sum_{i=1}^{N} \left[ R(x_i, y_i) - M(T(x_i, y_i)) \right]^2,$$
(4)

where  $\{(x_i, y_i), i = 1, 2, ..., N\}$  are N points in R selected for matching the two images. This metric is implemented in many of the standard software packages used in MR today, such as packages AIR and SPM. Another metric is defined by the sample standard deviation of the ratios

$$r(x_i, y_i) = \frac{M(T(x_i, y_i))}{R(x_i, y_i)}, \text{ for } i = 1, 2, \dots, N.$$

By this metric, a good transformation T should make this sample standard deviation small, or minimize the variability of the ratios defined above. More recent implementations also include a group of measures based on statistical correlations between R(x, y) and M(T(x, y)). A good transformation T should make such correlations large.

The second group of similarity metrics are entropybased. For a random variable  $\xi$  with a discrete distribution  $\{p_j, j = 1, 2, ..., k\}$ , the entropy of this distribution, defined by  $H(\xi) = -\sum_{j=1}^{k} p_j \log p_j$ , provides a measure of uncertainty about  $\xi$ . So, intuitively, if T is a good transformation, then association between R(x, y) and M(T(x, y))should be strong; consequently,

$$H(R) + H(M(T)) - H(R, M(T))$$

should be large, where H(R, M(T)) denotes the entropy of the joint intensity distribution of (R, M(T)), because it can be checked that H(R) + H(M(T)) is the entropy of the joint intensity distribution of (R, M(T)) when R and M(T) are assumed independent. In the literature, there are a number of different entropy-based similarity metrics. One such metric is H(R - M(T)), which is the entropy of R - M(T). A good transformation T should make H(R - M(T)) small. See [1] and [23] for more related discussions.

The above two groups of similarity metrics are all quite sensitive to noise and other artifacts. This would influence the performance of registration and would even lead to misregistration in some cases. To overcome such limitations, various robust metrics have been proposed in the literature. A general robust measure can be described by

$$\sum_{i=1}^{N} \rho \left[ R(x_i, y_i), M(T(x_i, y_i)) \right],$$

where  $\rho$  is a loss function. In the literature, there are many *robust*  $\rho$  functions proposed. One seen in the registration literature is the Geman-McClure  $\rho$ , defined by

$$\rho(x,y) = \frac{(x-y)^2}{c^2 + (x-y)^2}$$

where the scale parameter c controls its ability to diminish the possible effect of outliers. This function is commonly used in MR applications, since it has certain robustness to outliers, is relatively simple to compute and implement, and is found to be more efficient than some other robust metrics [2], [24]. Another popular robust metric is defined by (4) after replacing the summation by "median", and the corresponding registration procedure is often referred to as the least median squares procedure [2], [25].

Robust metrics are useful in applications when outliers are a real issue. In fMRI applications, temporal image intensity variations due to measured brain activity can be generally considered as "outliers"; thus, robust metrics are particularly important in such applications.

# 4. Discussions

We have discussed some commonly used image registration methods in MR applications. When matching features are selected beforehand, existing methods either take a parametric approach by specifying a parametric form for the matching transformation, or search for a transformation by interpolation or approximation without specifying any parametric form. When matching features are not available, most existing methods take the parametric approach using all available image intensities, although some methods specify the transformation more flexibly based on certain physical models[29]. In some applications, it might be challenging to specify matching features, and parametric transformations may not describe differences among images well. In such cases, it would be good if we can propose some nonparametric registration methods, without specifying any parametric form on the transformation and without selecting matching features beforehand.

As discussed in Section 3, existing registration methods often pre-process images to minimize the effect of noise and other artifacts before matching images. In the literature, several image restoration procedures can be found for preprocessing purposes [26],[27]. See [28] for an overview. It should be noted that artifacts handled by these preprocessing procedures are usually within a same observed image, while artifacts and variations handled by most existing registration methods are between two or more images to register. Quite often, when noise and other artifacts are removed by a pre-processing procedure, some true image structures (e.g., small edges, roofs/valleys) would also be altered to a certain degree, making the subsequent image matching less efficient. Therefore, it might be interesting to combine image pre-processing and image matching in a single procedure, or to suggest some image registration methods which can accommodate artifacts within individual images.

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