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Registration

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Abstract

The goal of image registration is to find a 1–1 point-wise correspondence between two images, a subject image and a target image. Knowing the pointwise correspondence between two brain images allows comparison of structural and functional imaging data such as regions of interest, functional data (e.g., fMRI, EEG, MEG, DTI), and geometric shapes. The image registration process also allows creation of probabilistic anatomical atlases (Mazziotta et al., Neuroimage 2(2): 89–101, 1995; Thompson, J Comput Assist Tomogr 21(4):567–581, 1997; Thompson et al., Detecting disease-specific patterns of brain structure using cortical pattern matching and a population-based probabilistic brain atlas. In: IPMI2001. Lecture notes in computer science, pp 488–501, 2001), automatic segmentation by label transfer, modality fusion, morphological analysis (Hua, Neuroimage 43(3):458–469, 2008), and many other applications. Image registration techniques strive to find a one-to-one correspondence between subject and target images to perform this task. This correspondence is defined by a smooth deformation field. This deformation field captures the geometric variations in the two images. In this chapter, we will review various techniques for image registration that are specifically designed for human brain.

Keywords

Image registration; Brain; MRI

1 Introduction

Registration of brain images is an essential step in multi-subject and multi-modality brain image analysis. Studies of anatomical changes in the brain over time or differences in brain anatomy between populations require that the data first be transformed to a common coordinate system in which anatomical structures in the brain scans are aligned. Similarly, longitudinal studies within subject or group analyses of functional data also require that the brain images are anatomically aligned. The morphological differences in the brains can be analyzed using techniques such as MRI-volumetry [1] that uses segmentations of regions of interests (ROIs), either manually or automatically, voxel based morphometry (VBM) [2] that studies voxel-wise intensity statistics, deformation based morphometry (DBM) [3], which analyzes spatial position differences, and tensor based morphometry (TBM) [4] that analyzes the deformation tensors at every voxel computed from Jacobian of the deformation field. These techniques rely on the 1–1 pointwise correspondence established by image registration as well as the resulting deformation fields that aligns the images.

The goal of image registration is to find a one-to-one correspondence between biological homologous points between two brain imaging scans. This correspondence is represented by a mathematical transformation called deformation or warping field. The idea of image registration originates from the continuum mechanics and perhaps was first applied for biological structures in the works of D'Arcy Thompson in his book *On Growth and Form* [5]. Figure 1 shows his application of deformation grids for warping coordinate grids to deform skulls of primates and humans.

The human brain can be analyzed either as a surface represented by the cerebral cortex or the volume that contains cortical as well as sub-cortical structures. Since the cerebral cortex of the brain is highly folded, it is often convenient to model it as a 2D surface and use surface registration techniques. On the other hand, volumetric registration techniques are often applied where we are interested in cortical as well as sub-cortical structures.

In this chapter, we will focus on anatomical registration of brain images based on T1 MRI. We will first describe the surface based registration techniques that focus on alignment of the cerebral cortex. Next we will describe volumetric registration techniques that try to align brain volumes and in the end we will describe surface-constrained volumetric registration techniques (combined registration techniques) that try to align cortical surface as well as the sub-cortical structures. Finally, we will review existing intensity based linear and nonlinear image registration approaches commonly used.

2 Surface Registration

Human cerebral cortex is often modeled as a highly convoluted sheet of gray matter. A triangular mesh representation of cortical surfaces is generated using software such as BrainSuite (http://brainsuite.org), FreeSurfer (https://surfer.nmr.mgh.harvard.edu/), BrainVisa (http://brainvisa.info/), etc. Since it is often not possible to align this highly convoluted cortex in the 3D space, a necessary first step for cortical registration is cortical surface parameterization that maps the cortical surface to a sphere as in FreeSurfer or BrainVisa or squares as in BrainSuite (Fig. 2). Inter- and intra-subject comparison involving anatomical changes over time or differences between populations requires the spatial alignment of the cortical surfaces, such that they have a common coordinate system that is anatomically meaningful. Sulcal curves are fissures in the cortical surface and are commonly used as surrogates for the cytoarchitectural boundaries in the brain. Therefore, there is also great interest in direct analysis of the geometry of these curves for studies of disease propagation, symmetry, development, and group differences (e.g. [6, 7]). Labels of cortical regions of interest (ROIs) or sulcal curves that are required for these studies can be produced using manual [8] or automatic delineation [9, 10]. The manual delineation is often performed using interactive software tools [8] which, however, can be a tedious and subjective task that also requires substantial knowledge of neuroanatomy and is therefore confounded by intra- and inter-rater variability. This variability is reduced to some extent using rigorous definitions of a sulcal tracing protocol and extensive training as described in [8, 11].

An alternative approach to this problem is to use automatic surface registration to align surface curvature or sulcal depth [12].The mean curvature is used as it represents the sulci fundi with negative values and gyral crowns with positive values; therefore, its alignment leads to accurate registration of the cortex. The curvature maps generated are then transferred to the unit square using the point correspondence established by the p-harmonic maps. The alignment of the curvature maps is then performed by minimizing the cost function which is a weighted sum of a curvature matching penalty and a 3D coordinate matching penalty, regularized by an elastic energy. This step, as shown in Fig. 3, establishes a 1–1 correspondence between the subject and target cortical surfaces such that the sulcal and gyral patterns on the two brains are aligned. This correspondence can then be used to transfer data or labels from one brain image to the other.

3 Volume Registration

The most popular approach for brain image registration is the volumetric registration based on intensity information in anatomical T1 image. A piecewise affine transformation termed Talairach normalization [13, 14] was the first commonly used volumetric alignment technique. This method is constrained to be piecewise affine and uses a restricted set of anatomical landmarks. Therefore it results in a relatively poor alignment across subjects. Automated intensity-based registration methods overcome this constraint and also allow non-rigid deformations [15, 16].

Intensity-based volumetric image registration can be formulated in terms of an optimization problem:

$$\hat{h} = \arg\min_{h}\left(C_{\mathrm{sim}}(T, S, h) + \lambda C_{\mathrm{reg}}(h)\right)$$

where the transformation h minimizes the weighted sum of a similarity function C_{sim}, which defines a metric between corresponding features in the pair of images being matched, and a regularization function C_{reg}, which resolves the ambiguities among the set of transformations that minimize the similarity function by selecting a smooth transformation. The regularization parameter λ determines the degree of the smoothing imposed by the regularizer. Most of the image registration techniques can be placed in this framework. With this formulation, we now consider each of the three major components that define the most registration methods: feature selection and similarity metrics, transformation parameterization, choice of regularizing function. Table 1 lists many of the similarity measures, parameterizations, and regularization operators that have been used to produce many of the commonly used image registration algorithms.

Small deformation models such as polynomial warps and linear elastic deformations do not guarantee preservation of topology for larger deformations [17, 18]. The viscous fluid approach [18] and more recent approaches using large-deformation diffeomorphic metric mapping [19–21] were developed to address the problem of ensuring diffeomorphic maps and can register the objects whose alignment requires large deformations while conserving their topology.

One important consideration, apart from topology preservation, is inverse consistency of image registration [17]. A deformable image registration is called inverse consistent, if the correspondence between two images, obtained by reciprocal registration, is invariant to the order of the choice of source and target. More precisely, let S and T be the source and target images, and h and g be the forward and backward transformations obtained by a given registration method. Therefore $S \xrightarrow{h} T$ and $T \xrightarrow{g} S$; then an inverse consistent registration satisfies $h \circ g = I_d$ and $g \circ h = I_d$, where I_d is the identity map. The property of inverse consistency is applied explicitly by minimizing the difference between $h \circ g$ as well as $g \circ h$ to I_d [17] or by modifying the cost function such that the resulting forward map, generated by minimization of that cost function is inverse consistent [22]. Additional constraints such as transitivity can be imposed to get more desirable results.

In addition, the choice of a regularizer is an important consideration and can significantly affect the quality of the registration. A regularizer is used to constrain the transformation and ensure that the deformation is smooth and invertible. One common way to select a regularizer is to assign a continuum mechanical law to the deforming image medium. For instance, in elastic registration [23], the image is regarded as embedded in an elastic medium. A force is applied based on the chosen similarity function that pulls the template into agreement with the study, while linear elastic forces attempt to restore it to its original shape. Elastic registration is not guaranteed to produce 1–1 mapping and often is unsuitable for large deformations. In fluid registration, for instance, the image is treated as a viscous fluid that follows the Navier–Stokes equation, with a velocity field that is the derivative of the deformation field. The fluid flow allows large deformations while ensuring 1–1 mapping. These approaches often are computationally very expensive and can take hours for registering brain scans. Therefore, a demons algorithm [24, 25] was proposed that models image registration as a diffusion process. The demons algorithm and its variants (e.g., [26]) have become increasingly more popular than the fluid registration due to their speed.

4 Combined Approaches

Since cytoarchitecture and function of the cortex is closely related to the folding pattern of the cortex, it is important when comparing brain anatomy and function in two or more subjects that their cortical surfaces are aligned. For this reason, there has been an increasing interest in development of volumetric brain registration algorithms that also align the cortical surface accurately. Similarly, in inter-subject longitudinal studies or group analyses of functional data such as fMRI and DTI it is important that the cortical surfaces of the subjects are aligned when brain registration is performed. Several methods have been developed that perform the surface constrained volumetric registration [27–31]. Here we describe our approach to brain image registration based on harmonic maps that combines the surface and volumetric registration approaches producing a volumetric alignment in which there is also an accurate one-to-one correspondence between points on the two cortical surfaces [29, 32]. This approach is implemented in SVReg software available with BrainSuite (http://brainsuite.org).

We perform volumetric alignment of brains by first extending the surface registration to the entire volume [29] (Fig. 4). This begins with two surfaces that have been aligned using the surface registration process. For each brain, the unit-square representations of the brain surfaces are mapped onto the unit sphere. The interior brain volume is then mapped to the unit ball. This is achieved by extrapolating from the surface to the interior of the sphere while minimizing the harmonic energy of the map from brain to sphere. The harmonic mapping gives one-to-one correspondence between the two brains based on their respective maps to the unit sphere. This provides an initial registration based solely on the initial alignment of cortical geometry. Such initialization ensures that cortical features are aligned. However, since the interior mapping is based solely on geometry of the cortex, subcortical features tend to be misaligned. A refinement of this mapping is computed by minimizing the elastic bending energy driven by an intensity matching forces. The output of this process is a one-to-one point correspondence between the two brain volumes. The cortical constraint ensures that one cortical surface maps precisely onto the other (Fig. 5).

5 Conclusion

Image registration is a very active and fast moving field of research that produced a number of software tools available on regular basis in the public domain. Most registration approaches are included in some popular software for brain imaging investigation as: Automated Image Registration (AIR), ANTs, FreeSurfer, BrainSuite, FSL, LDDMM, ITK, CARET, and SPM. A comprehensive comparison of 14 of these software is performed in [33]. In this chapter, we reviewed basic techniques of brain image registration, which is an essential step for brain image analysis, trying to encompass the widest cohort of methods available.

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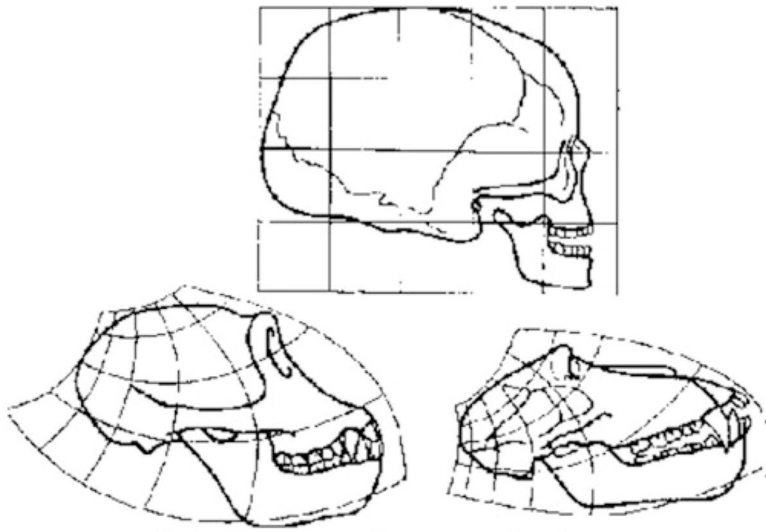

Fig. 1.
Image registration as change of coordinates

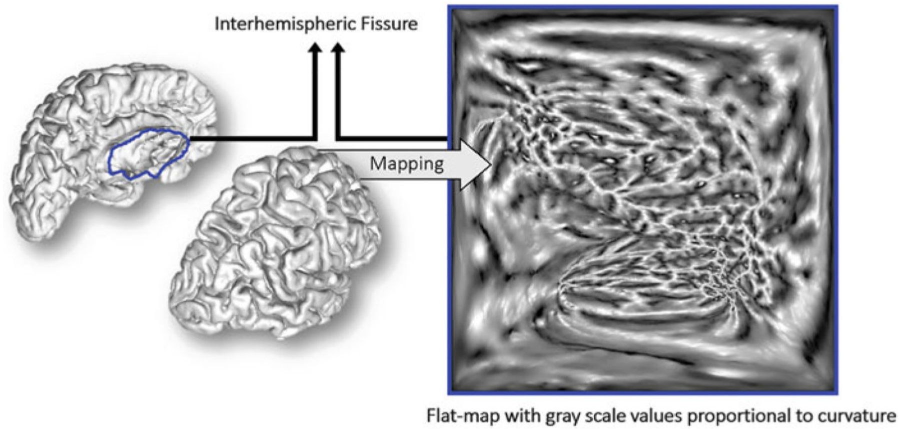

Fig. 2.
Surface parameterization of the cortex is done by constraining the interhemispheric fissure to the unit square and rest of the cortex is mapped inside the unit square by using *p* harmonic maps

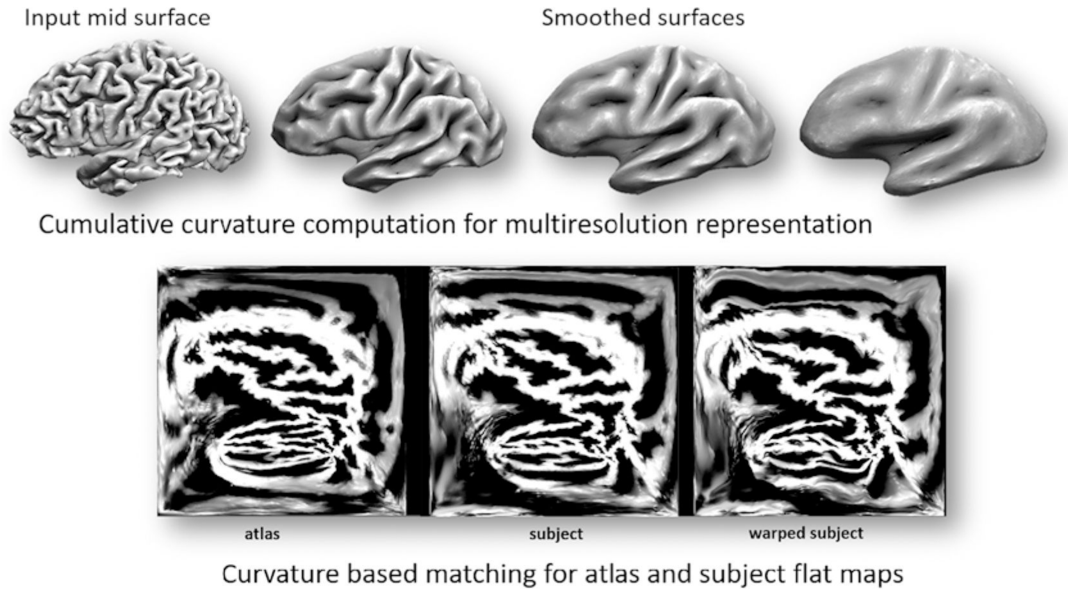

Fig. 3.

Curvature alignment is performed by first generating a multiresolution representation of the mean curvature (top row) and then performing the alignment of the curvature in the flat 2D space

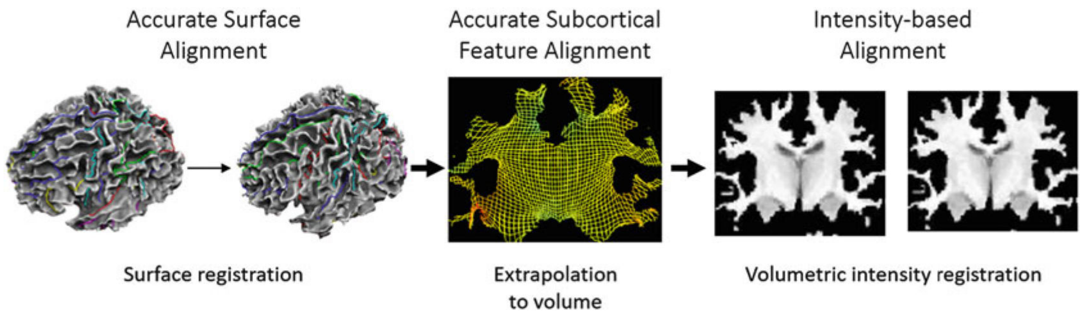

Fig. 4.
Surface-constrained volumetric registration

Fig. 5.
SVReg registration showing good alignment at the cortical as well as sub-cortical structures

Table 1

Registration methods

Corresponding feature (dimensionality)	Transformation parameterization (dimensionality)	Regularization/constraints (deformation type)
Landmark (0-D)	Rigid (low)	None
Contour (1-D)	Affine (low)	Thin-plate spline (small)
Surface (2-D)	Talairach (low)	Differential operators (small)
Sub-volume (3-D)	Polynomial (low-medium)	Prior distributions (small)
Intensity difference (N-D)	B-spline(medium-high)	Elasticity (small or large)
Cross correlation (N-D)	Thin-plate spline (medium)	Viscous fluid (large)
Intensity demons (N-D)	Discrete cosine (medium-high)	Inverse consistency (small or large)
Intensity vectors (N-D)	Fourier series (medium-high)	
Intensity variance (N-D)	Wavelet (medium-high)	
Mutual information (N-D)	Discrete lattice (high)	