NON-RIGID REGISTRATION OF MEDICAL IMAGES: PURPOSE AND METHODS, A SHORT SURVEY

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ABSTRACT

Non-rigid registration is an important topic in the medical imaging community and a variety of methods have been proposed to solve this problem. This manuscript serves as an introduction to a special session dedicated to non-rigid registration. Its intent is to provide the reader with a sense for the type of problems to be solved and the range of solutions that have been proposed. Each of the speakers in the session has years of experience in the field and has been instrumental in developing an approach that fits into one of the categories discussed herein.

1. NON-RIGID REGISTRATION, WHY?

Image registration consists in finding a transformation that realigns two or several images (in 2D) or image volumes (in 3D). It is a common and fundamental problem in the area of medical imaging. The most common example is the registration of several imaging modalities, i.e., images acquired from the same subject with several image acquisition devices such as SPECT (Single Photon Emission Tomography), MR (Magnetic Resonance), or US (Ultrasound) images. This type of registration is clinically important because each imaging modality provides specific information that needs to be fused by the clinicians. Practitioners can look at images side by side and try to integrate the information mentally. This mental mapping process is, however, difficult to achieve because structures visible in one imaging modality may not be visible in the others and because images may have been acquired at a different orientation.

Image registration techniques can be categorized into two very broad categories: rigid-body and non-rigid methods. Rigid body methods involve the computation of transformations with six degrees of freedom (in 3D): three rotation angles and three translation vectors. Methods designed to compute automatically rigid body transformation for intra- and inter-modality problems have been developed over the years. These algorithms are now mature and often available clinically in software packages offered by imaging device manufacturers. A good survey of currently available methods and algorithms can be found in [1].

Rigid-body problems are, however, only a small fraction of the spectrum of registration problems to be solved. More often than not, medical image registration problems require the computation of a transformation with much more degrees of freedom. These will be called here non-rigid transformations. Algorithms designed to compute automatically these non-rigid transformation have also been proposed over the years but they are much less mature than their rigid counterpart, rarely available in the clinical setting, and often tested on very specific applications.

Non-rigid registration problems can themselves be classified into the following broad tasks:

1) Intra-modality, intra-subject registration: The images to be registered have been acquired from the same patient and on the same scanner. This situation occurs when serial images are acquired as is done for functional MR (fMRI), PET studies, or pre- and post contrast injection. For these studies, image volumes are acquired over time, possibly hours, and the patient may even be moved in and out of the scanner. Motion between image volumes needs to be corrected before the data is analyzed, which requires realigning each image volume to a common reference. This type of registration is also required to assess response to therapy. Series of MR images can, for instance, be acquired over several months to track tumor response to radiation. If the image volumes contain non-rigid structures or organs such as the chest, abdomen, or breast non-rigid registration methods are called for.

2) Intra-modality, inter-subject registration: The images to be registered have been acquired on the same device but from different subjects. This type of registration is important for two major tasks: (1) statistical atlas creation and (2) atlas-based segmentation.

Statistical atlases are used for population comparison. A good example is the generation of activation maps created with functional MRI (fMRI). fMRI permits the visualization of brain activity when performing various cognitive or motor tasks. Individual activation maps (i.e.,

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brain regions that are activated when a task is performed) can be created. But meaningful comparison between subjects and across populations requires the spatial normalization of these maps. This is achieved by registering all the brains to a reference brain (the atlas).

Atlas-based segmentation is the exact opposite of atlas creation. Segmentation consists in computing automatically the boundary of structures of interest in an image. Segmenting structures and substructures in medical images is a difficult problem because their boundaries can be poorly defined, images are noisy, or their spatial resolution is limited. A possible solution is to create one image volume in which structures of interest have been labeled, possibly by hand. Atlas-based segmentation then consists in registering the atlas to another brain volume to be segmented. Once the transformation has been computed, labels assigned to regions can simply be applied to corresponding regions in the other volume.

3) Inter-modality, intra-subject registration: The images to be registered have been acquired from the same subject but on various devices. This problem has been introduced previously and it is the most common in the clinical arena. It requires integrating and fusing information from several imaging modalities (most often MR, PET, and CT). Again, if the images contain non-rigid structures and organs, rigid-body registration methods are inadequate. Non-rigid inter-modality, intra-subject registration is also required for applications such as the correction of geometric distortions in MR images.

4) Inter-modality, inter-subject registration: The images to be registered have been acquired on different devices and from different subjects. This situation happens, for instance, when several MR image volumes acquired on different scanners at different institutions need to be registered. Even though both volumes are MR volumes, differences between scanners and in acquisition parameters can be such that the contrast characteristics between image volumes substantially different. So much so that methods developed for intra-modality applications fail.

2. NON-RIGID REGISTRATION, HOW?

A wide variety of non-rigid registration methods have been and are still being proposed. Conceptually, the non-rigid registration problem (as is the rigid case) can be cast into an optimization problem. It consists in computing the transformation that minimizes the differences between two image volumes to be registered. This can be formalized as follows:

$$\arg\max_{(T)} F(TB(\mathbf{x}), A(\mathbf{x}), T)$$

In which $F, T, A,$ and TB are a similarity measure, a transformation, the first image, and the second image to which transformation T has been applied, respectively. Non-rigid registration methods proposed in the literature differ both by the type of transformations they allow to warp one image onto the other and by the similarity measure they use to compute the optimal transformation. It is difficult to derive a taxonomy for these methods because two methods can use the same similarity measure and a different class of transformation. Conversely, two methods can use the same class of transformations but different similarity measures. Here we will attempt to classify these techniques according to the type of transformation they use and we will mention in each category if more than one similarity measure has been used.

2.1. Affine and polynomial transformations

In 3D the rigid body transformation has 6 degrees of freedom. This class of transformation can be extended to a full affine transformation with 12 degrees of freedom to take into account unknowns such as voxel dimensions or gantry tilt or to transformations relying on higher order polynomials (see for instance the AIR ---Automated Image Registration--- [2] package). Another approach proposed by Collins [3] has been to compute an overall non-rigid registration by combining a set of local rigid or affine transformations. The measures of similarity used for this type of transformation are typically based on the intensity value of the images and range from correlation to mutual information. Mutual information is a measure of similarity that has been widely used for medical image registration problems. Introduced by Shannon as early as 1948 [4] it has been independently proposed for medical image registration by researchers at MIT [5] and the KUL [6]. It has been widely used for rigid-body inter-modality registration problems and was shown to be both robust and accurate in a large inter-site retrospective validation study [7]. It is also commonly used for non-rigid registration problems.

2.2 Transformations based on smooth basis functions

Instead of modeling the deformation field with polynomials, other basis functions have been proposed. These include trigonometric basis functions, radial basis functions such as thin-plate splines, multiquadratics or Gaussian. Compactly supported basis functions such as B-splines or other radially symmetric compactly supported basis functions have also been used. Often, the formulation of the problem includes a smoothness term introduced to maintain the correctness of the transformation. For instance, Meyer [8] uses interpolating thin-plate splines in the following way. Approximately homologous points are identified in the images to be registered. Based on the location of these landmarks, a non-rigid transformation is computed for the entire image using thin-plate splines as interpolant. The transformation is then applied to the image to be deformed and a measure of similarity between this image and the reference image is computed. An optimizer is subsequently used to displace the position of the reference points in one of the images to maximize the value of the similarity measure (mutual information). Thin-plate splines can also be used to approximate rather than interpolate the deformation field to include uncertainty about the location of the landmarks as proposed in [9]. A related approach was proposed by Rueckert et al. [10]. Rather than relying on thin-plate splines, these authors model the deformation field using B-splines placed on a regular grid. The deformation field that registers one image onto the other is then computed by adjusting the position of the control points. In this work mutual information is also used as the measure of similarity. Kybic et al. [11] have used a very similar approach but instead of relying on mutual information as a measure of similarity, they have used the square of the intensity differences. This allows them to compute an analytical expression for the gradient but limits their algorithm to intra-modality problems. One of the problems associated with spline-based techniques is their computational complexity. An optimum needs to be found in a high dimensional parameter space (> 300,000 for typical 3D medical image registration problems). Approaches have been proposed to reduce the complexity of the problem. For instance Rohde et al. [12] propose to use compactly supported radial basis functions that do not need to be placed on a regular grid. This allows these authors to modify the deformation field only where the registration is deemed inaccurate. A criterion based on the gradient of the similarity measure (mutual information) is used to identify regions in the images that are incorrectly registered. Another approach used to reduce the computational complexity has been put forth by Schnabel et al. [13]. In this work, B-splines placed on a regular grid are used but only a fraction of these are included in the optimization procedure. They propose several criteria to decide whether or not the control point of a particular spline is included in the set of control points to be optimized.

2.3 Physical models

Elastic registration techniques (see for instance [14]) rely on a physical model of the objects to be deformed and assume these to be elastic entities. Deformation of the images is then, in general, governed by the Navier equations for elastically isotropic and homogeneous substances:

$$\mu\nabla^2\mathbf{u}(\mathbf{x}) + (\lambda+\mu)\nabla(\nabla\mathbf{u}(\mathbf{x})) + \mathbf{F}(\mathbf{x}) = 0$$

In which $\mathbf{F}(\mathbf{x})$ are the external forces distributed over the substance that drive the deformation and $\mathbf{u}(\mathbf{x})$ the computed displacements that result from these forces. When the relation between forces and displacement is governed by these equations, the resulting transformation is smooth and preserves the topology of the objects. A number of approaches have been proposed to define the forces $\mathbf{F}(\mathbf{x})$, ranging from intensity-based similarity measures such as correlation to corresponding points on contours or line segments. Some authors have also proposed to relax the homogeneity assumption [15] to permit the spatial adaptation of the elastic properties of the material. Because of their smoothness, elastic transformations limit the range of deformations these capture. An alternative approach based on viscous-fluid transformations has been proposed by Christensen et al. [16]. This increases the complexity of the computations substantially but a fast convolution-based implementation has been proposed by Bro-Nielsen and al. [17].

2.5 Optical flow-based methods

The optical flow constraint equation was derived to estimate the motion between two successive frames in an image sequence [18]. It is based on the assumption that the intensity value of a given point in the image does not change over small time increments. This constraint can be expressed as $\vec{v}.\vec{\nabla}I = -I_t$ in which $\vec{v}$, $\vec{\nabla}I$, and I_t are the unknown motion vector between the images, the intensity gradient of the image, and the temporal derivative of the image, respectively. This equation is underconstrained (a problem known as the aperture problem) and a number of regularization scheme have been proposed to address this issue. A simple way to enforce smoothness is to decouple the computation of the motion field and its regularization as proposed by Thirion [19]. This is done by first computing the motion field without constraints, and then smoothing it using, for instance, a Gaussian filter. In general, the algorithm is applied in a hierarchical way and a mechanism is used to maintain compatibility between the forward and the reverse motion fields. This is done by computing the motion field T12 (the transformation warping image 1 onto image 2) and the motion field T21 (the transformation warping image 2 onto image 1) and distributing the residual R=T12 °T21 (with ° indicating composition) onto these two fields. This construct, coupled with the smoothing of the field prevents its tearing as well as crossing over of neighborhood pixels. Another optical-flow based method has also been proposed by Hellier et al. [20]. Here the authors rely on robust estimators that allow them to estimate deformation fields that are not globally smooth. The deformation field they compute is the one that minimize a cost function that contains two terms: a similarity measure and a smoothness term. To reduce the computational cost associated with this technique, a multiresolution/multigrid strategy is employed and an adaptive partitioning method is proposed The domain is first decomposed into cubes. Cubes are then subdivided into subcubes based on information from a segmentation mask and the quality of the deformation obtained so far in the cube. Within each cube, the deformation field is modeled using an affine transformation.

A common problem of methods that do not rely on any anatomical information such as optical-flow based techniques is the difficulty to realign sulci and gyri across subjects. The topology and shape of deep brain structures are similar from one subject to the other but there is a wide variation at the cortical level. To address this problem Hellier et al. [21] augment their cost function to include a term that allows them to use sparse constraints derived from homologous sulci in two image volumes. Sulci are extracted from these images using so-called active ribbons. Robust estimators are relied upon to permit registrations in which sulci do not match exactly to take into account possible segmentation errors and topological differences between subjects. A related approach has been proposed recently by Hartmann [22] to include sulcal constraints in the framework proposed by Thirion.

2.7 Registration based on homologous surfaces

Difficulty in matching precisely cortical structures have lead some groups to take the opposite tack and to drive the deformation using homologous structures identified in the volumes. Thompson et al. [23], for instance, identify semi-automatically a number of surfaces in the volumes to be registered. These include portions of the ventricular system, the outer edge of the cerebral cortex, and a number of deep sulcal surfaces. Surfaces are parameterized and displacement vectors for each point on the surfaces are computed. Displacement vectors for each voxel in the 3D volume are finally obtained form the computed surface displacement vectors by interpolation.

3. DISCUSSION AND CONCLUSION

Non-rigid registration is an evolving field with a wide spectrum of applications. It is also a field that has not reached the same level of maturity as its rigid counterpart and issues such as robustness, speed, or validation need to be resolved before it gains wide acceptance in the clinical arena. Papers presented in this session will discuss these as well as other current challenges.

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