MODELING TOPOLOGICAL CHANGES IN DEFORMABLE REGISTRATION

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ABSTRACT

Topological changes are common in brain MR images for aging or disease studies. For deformable registration algorithms, which are formulated as a variational problem and solved by the minimization of certain energy functional, topological changes can cause false deformation in the resulting vector field, and affect algorithm convergence. In this work, we focus on the effect of topological changes on diffeomorphic and inverse-consistent deformable registration algorithms, specifically, diffeomorphic demons and symmetric LDDMM. We first use a simple example to demonstrate the adverse effect of topological changes on these algorithms. Then, we propose a novel framework that can be imposed onto any existing diffeomorphic and inverse-consistent deformable registration algorithm. Our framework renders these registration algorithms robust to topological changes, where the output will consist of two components. The first is a deformation field that presents only the brain structural change which is the expected vector field if the topological change did not exist. The second component is a label map that provides a segmentation of the topological changes appeared in input images.

Index Terms— Deformable registration, topological change, segmentation

1 Introduction

Many deformable registration algorithms on brain MR images have been proposed to reveal the structural difference among brains of distinct subjects or shape changes of a brain over time [1, 2]. However, subjects may have not only structural changes, but also altered tissue characteristic, which leads to local image intensity changes. For brain MR images, intensity changes are commonly found in aging- or disease-related studies. For example, conditions such as brain tumor, multiple sclerosis (MS), or white matter hyperintensity, i.e., Leukoaraiosis, all result in local intensity changes in brain MR images. For clinical applications, being able to register the images of diseased brains with intensity changes is of great importance. However, most currently available deformable registration algorithms aim at revealing structural changes without specifically considering the impact of local intensity changes. Medical images taken for the same field of view of healthy individuals generally contain the same anatomical shapes and have level-sets of the same topology, up to measurement noise. However, in the presence of a lesion or a tumor, the corresponding area with intensity change will insert new iso-contours into the level-sets of the images, referred to as topological change. One approach to register images with topological changes is to allow the spatial grid as well as the image intensity to deform [3]. However, by doing so, the registration need to be solved by minimizing an energy functional defined over the two distinct deformations, which makes the search of optimal transformations complex and numerically unstable. Another approach is to embed an N-dimensional (N-d) image into an (N+1)-d Reimannian space, which converts images with topological changes into continuous surfaces. Registration can then be performed by simultaneously deforming N-d spatial grid and intensity [4]. However, it is difficult to find a proper mapping to balance the deformation of the spatial grid and that of the intensity.

Topological changes in brain MR images can be caused by different pathology mechanics. For example, the growth of cancer tumors pushes their surrounding tissue aside. MS and Leukoaraiosis lesions cause density changes of white matter, which is independent of brain structural change. As a result, before examining the pathological nature of a topological change, one should not make assumptions on the underlying deformation. Taking this into consideration, some existing methods target only images with tumors [5], where the registrations rely on a pre-computed tumor model. However, the required prior information makes the registration process less automatic. More importantly, they cannot register images with all types of topological changes and are thus less general.

In this work, instead of pre-determining the pathological nature of a topological change, we propose a two-round registration framework that can be imposed onto any existing diffeomorphic and inverse-consistent deformable registration algorithms. This framework performs two rounds of conventional registration. The first round is a coarse registration with a loose stopping criteria. After the coarse registration, the evolution of the deformation field is examined to isolate image regions with intensity differences that have not been minimized during the coarse registration process, i.e., topological changes. Then the isolated topological changes are replaced by interpolating the intensity of their neighborhoods. After this image-repairing step, a second round of registration is performed with a normal stopping criteria to obtain the desired structural deformation field. Using this framework, two distinct outputs are obtained. The first output is a registration field that captures only the structural changes of a brain, which is the expected output had the topological changes not
Fig. 1: Registration of simple images with topological change. (a) and (b) input images; (c) glyph view of deformation field from diffeomorphic demons; (d) zoom-in view of (c) around the topological change; (e) deformation field from symmetric LDDMM; (f) zoom-in view of (e) around the topological change.

occurred. The second output is a binary label map that identifies the segmented the topological changes.

2 Effect of topological changes

Registration is modeled as a variational problem in many state-of-the-art deformable registration algorithms, e.g., demons [1, 6] and LDDMM [2, 7], where the deformation field is computed using different optimization schemes. Diffeomorphic transformations are numerically more stable and physically more realistic solutions, which ensures both the transformations and its inverse are continuous and differentiable. Thus, diffeomorphic transformations can serve as an image metric representing image similarities. Meanwhile, inverse consistency, i.e., the resulting deformation field will remain the same if the source and target images are swapped, is an important constraint that makes sure the registration result is not biased toward the source or target images. Inverse consistency can be achieved by using symmetric image similarity measures in the energy function, i.e., 

\[ \text{Sim}(I_1, I_0, \phi) = \frac{1}{2}(\text{Sim}(I_1, I_0 \circ \phi^{-1}) + \text{Sim}(I_0, I_1 \circ \phi)), \]

where \( \phi \) is a diffeomorphic transformation. As a result, the diffeomorphic and inverse consistent versions of deformable registration algorithms are currently of the greatest interest to researchers. However, as will be shown in the following example, when registering images with topological changes, both diffeomorphism and inverse consistency will cause or amplify certain problems.

Fig.1 gives a simple example. Suppose a pair of 2-d images, \( I_0 \) (Fig.1(a)) and \( I_1 \) (Fig.1(b)), are to be co-registered. Clearly, \( I_0 \) carries a topological change with much lower intensity. The glyph views of registration results using diffeomorphic demons\(^1\) are shown by Fig.1(c) and (d), and those using symmetric LDDMM\(^2\) are given in Fig.1(e) and (f). These results demonstrate that with the symmetric intensity similarity measure, the intensity difference caused by the topological change drives a local region to deform in both algorithms. Note that the local deformations around the topological change are simply driven by the local intensity discrepancy and are not related to the pathological nature of the topological change, and as such we call them false deformation. Furthermore, the smoothing effect, which is caused by confining the transformation to be diffeomorphic, spreads this false deformation over an enlarged neighborhood. To summarize, topological change causes at least two problems:

1) It induces false deformation, which is mixed with the deformation field of structural change. This causes problems to subsequent quantitative studies on the resulting deformation fields, e.g., in deformation-based morphometry, the regions with false deformation will be associated with local growth/shrinkage.

2) The existence of topological changes continuously drives the deformation, where the gradient of the energy function and image residual may not drop to a sufficiently small value during the registration process. This potentially causes confusion on when to terminate the registration process.

3 Proposed registration framework

As discussed earlier, it is not practical to model the growth of a topological change without the prior knowledge of its pathological nature. Instead, a more general approach is to separate the regions with topological changes, and perform registration free from the impact of these regions. In doing so, the result of registration algorithm reveals only structural changes, while a segmentation label map, as a by-product, can be used to identify the regions with topological changes for further clinical study. In the following, we propose a two-round registration framework that can be imposed onto any currently available diffeomorphic and inverse-consistent deformable registration algorithms. For illustration purpose, we take symmetric LDDMM as an example algorithm to generate experiment results. However, since our proposed framework does not interfere with the execution of the existing registration algorithms, the results of adopting other registration methods in the proposed framework, e.g., diffeomorphic demons, are expected to show similar improvement. In addition, because the registration algorithm we used is inverse consistent, in the following discussion we assume the source image \( I_0 \) is the one contains topological change. The same operation can be performed for target image \( I_1 \), if it is the one that contains topological change, by exchanging the forward and backward deformations.

We use the simple 2-d images \( I_0 \) and \( I_1 \) in Fig.1 (a) and (b) as inputs to explain the proposed framework. The first round of registration takes the original input images with the topological changes, where we expect the the image residual and gradient of the energy function will not decrease to sufficiently small values. Thus, we force the registration to terminate at iteration \( n \) when the energy gradient drops to a local minimum, i.e., not decreasing during certain number of iterations. This is the reason that we refer to this round of registration as coarse registration. We study the pattern how image intensity dissimilarity drops over iterations during the

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\(^1\)The implementation is from http://www.insight-journal.org/browse/publication/644, by Vercauteren et. al.

\(^2\)This is our implementation of the algorithm by Beg et. al.[2], with the symmetric image similarity measure.
coarse registration to detect topological changes. Specifically, in each iteration \( k \), we compute an absolute image residual \( \text{Diff}_k = |I_0 \circ \phi_k^{-1}I_1| \). Since all the \( \text{Diff}_k \)'s are computed in the image space of \( I_0 \), and the the topological change to be identified is within \( I_0 \), we need to back propagate the absolute image residuals into the image space of \( I_0 \), which is done by \( \text{Diff}_k \circ \phi_k \). These back propagated absolute image residues are summed up to obtain a total difference \( \text{Diff} = \sum_k \text{Diff}_k \), as shown in Fig. 2(a). From Fig. 2(a) we can see that the intensity discrepancies between \( I_0 \) and \( I_1 \) caused by structural differences are gradually shrinking as the registration process proceeds. Hence, these regions appear only in some of the \( \text{Diff}_k \)'s and consequently have a low intensity in \( \text{Diff}_f \). On the other hand, image regions with different topology can not be co-registered through a diffeomorphic transformation. Thus, those intensity disagreements caused by topological changes can not be minimized as the registration proceed and are accumulate in \( \text{Diff}_f \). In addition, the interpolation error and the local mismatch caused by smoothness constraints also cause intensity differences accumulated in \( \text{Diff}_f \). These intensity differences happen along the contrast boundaries in \( I_1 \). To isolate topological changes, we also deform \( I_1 \) into the image space of \( I_0 \) as \( I_1 \circ \phi_n \), which is shown in Fig. 2(b). The edge map of the deformed target image is computed as \( \text{GM} = 1 - |\nabla(I_1 \circ \phi_n)| \ast K \) (Fig. 2(c)), where \( |\nabla(I_1 \circ \phi_n)| \) is the norm of the first order image gradients and \( K \) is a Gaussian smoothing kernel used to control the spread of detected edges. Both the total difference \( \text{Diff}_f \) and the edge map \( \text{GM} \) are then normalized within [0, 1]. By performing a pixel-wise multiplication as \( \text{Diff}_f \odot \text{GM} \), we obtain a probabilistic atlas \( P \) (Fig. 2(d)) for the topological changes in \( I_0 \). P is thresholded at a trained value that corresponds to a good operating point on the ROC curve for topological change separation. In both the 2-d and 3-d registration experiments presented in this paper, a threshold of 0.5 is used. The result of this thresholding operation is a binary mask with the detected topological changes on the foreground. Note that the regions identified by this binary mask tend to be smaller than the actual topological change, due to the partial volume effect commonly seen in medical images. A simple morphological operation, e.g., a 8-neighborhood dilation of the foreground in the binary mask can be used to obtain a refined segmentation of topological change, which is shown as a blue musk in Fig. 2(e). The intensity of the region corresponding to a topological change is then interpolated by the median intensity value of the neighbors surrounding the region. This operation provides us a repaired image \( I_0' \) (Fig. 2(f)). \( I_0' \) and \( I_1 \) are then taken as inputs to the deformable registration algorithm with the usual stopping criteria, which outputs the final deformation fields \( \phi \) and \( \phi^{-1} \). The glyph plot of the resulting \( \phi \) is shown in Fig. 2(g) and (h). By comparing these results to those in Fig. 1(c)-(e), we clearly see that the false deformation caused by the topological change has been eliminated.

Our proposed framework is summarized as follows:

**Algorithm 1:**

**Initialize** total difference \( \text{Diff}_f = 0 \)

**Coarse registration** iteration \( k \):
- compute gradient of energy function: \( \nabla E \);
- update deformation field and its inverse: \( \phi_k \) and \( \phi_k^{-1} \);
- compute absolute image difference: \( \text{Diff}_k = |I_0 \circ \phi_k^{-1} - I_1| \);
- back propagate \( \text{Diff}_k \) and update total difference: \( \text{Diff}_{f,+} = \text{Diff}_k \circ \phi_k \);
- update energy function: \( E \);

Coarse registration is forced to terminate with a loose stopping criteria after \( n \) iterations with the resulting deformation fields \( \phi_n \) and \( \phi_n^{-1} \):

**Coarse registration post-processing** : repair \( I_0 \)
- compute gradient magnitude of deformed target image: \( \text{GM} = 1 - |\nabla(I_1 \circ \phi_n)| \ast K \);
- normalize GM and \( \text{Diff}_f \) to [0, 1];
- compute probability map of topological changes: \( P = \text{Diff}_f \odot \text{GM} \);
- threshold \( P \), followed by a slight dilation, to obtain a binary label map of topological changes;
- segmented topological changes are interpolated using the intensity values of their neighborhood, leading to a repaired version of the input image \( I_0' \).

**Fine registration** replace \( I_0 \) by its repaired version \( I_0' \) to re-perform registration with normal stopping criteria, and output deformation field \( \phi \) and \( \phi^{-1} \).

**4 Results**

Our proposed framework is used to register two 3-d image volumes, where one of them carries simulated MS lesions. The image volume is obtained from the McConnell Brain Imaging Center Simulated Brain Database[8]. The axial, coronal and sagittal views of the healthy image volume is shown in Fig. 3(a), and we use it as the target image \( I_1 \). To generate source image \( I_0 \), simulated MS lesion is introduced into \( I_1 \) [8]. To simulate brain structural change we further created a non-linear diffeomorphic deformation field and applied to the image with MS lesion, which is shown in Fig. 3(b).

We perform a coarse registration to obtain the total difference \( \text{Diff}_f \), which is multiplied with the edge map of deformed \( I_1 \) to obtain the probabilistic atlas of lesion \( P \), as shown in Fig. 3(c). \( P \) is then threshold and dilated to obtain a binary label map of possible lesions in \( I_0' \). This label map
5 Conclusion and future work

In this work, we propose a novel framework to register images with topological changes. It has the flexibility to be imposed onto any currently existing deformable registration algorithm, that is inverse consistent and diffeomorphic. Our framework outputs a final registration field with reduced false deformations. Also, a binary label map of topological changes can be obtained as a by-product. Note that our method is able to pick up MS lesions which are typically of low contrast, less focal, and could be close to the ventricle. When mixing with structural differences between the brains in the input images, we do not expect these lesions to be identified by globally align the input volumes and simply look for the intensity differences. We acknowledge that the thresholding and interpolation steps used in the current registration framework may not be robust enough in more complicated registration problems, e.g., under the impact of imaging noise and bias or when topological changes occur on the boundaries between different tissue types. We are currently working on an updated framework where the topological changes will be compensated through an optimization process, instead of a hard thresholding.

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6 References