CONSISTENT GROUPWISE NON-RIGID REGISTRATION FOR ATLAS CONSTRUCTION

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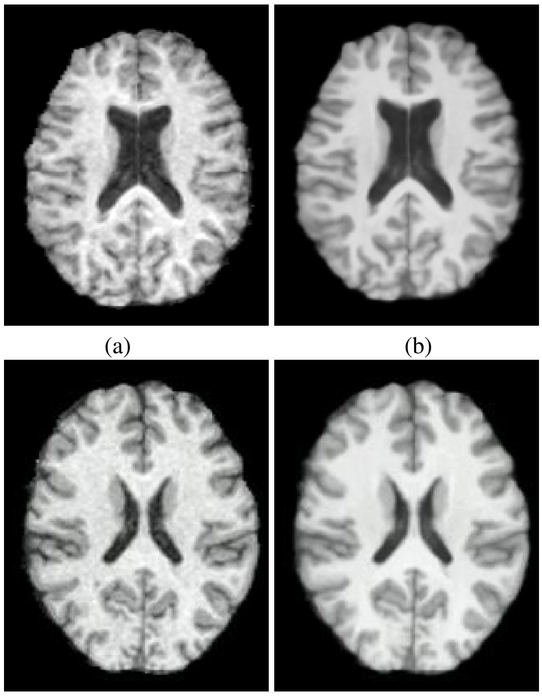
ABSTRACT

This paper describes a groupwise, non-rigid registration algorithm to simultaneously register all subjects in a population to a common reference (or *natural*) coordinate system, which is defined to be the average of the population. This *natural* coordinate system is calculated implicitly by constraining the sum of all deformations from itself to each subject to be zero. To do this, the gradient projection method for constrained optimization is applied to maximize the similarity between the images, subject to the constraint being satisfied. The algorithm has been tested on a group of 19 brain MR images acquired from a population of subjects with schizophrenia.

1. INTRODUCTION

Image registration is an important tool in medical image analysis. The use of high-dimensional non-rigid registration algorithms enables computational morphometry for volumetric studies such as [1], or the creation of population-specific atlases. This requires spatial normalization of the population, where each image is transformed to the coordinate system of a chosen reference anatomy. Typically, a pairwise registration algorithm is used to find the mapping from points in the reference space to points in the coordinate system of each image separately. This requires the a-priori selection of a reference subject from the population being studied. However, this reference may not be truly representative of the population, particularly if there is wide variation within the groups, for example, in studies of neurodegenerative disorders or in neonatal brain development. Additionally, if the deformations required to transform one image into another are too large, the performance of the registration algorithm may be degraded. This can happen if the chosen reference subject represents one extremum of the population under investigation.

Another problem associated with the use of pairwise image registration is that the atlas created, and any resulting calculations (eg: volume measurements), are dependent on the choice of reference subject. For example, Figure 1 shows MR images of two subjects taken from a study of 19 schizophrenics. These were used as two separate references to register all images in the population to, and atlases produced by averaging over the group.



(a) (b) (c) (d)

Fig. 1. Choice of reference image strongly affects atlas. (a) and (b): reference images; (c) and (d): atlases constructed from references (a) and (b) respectively.

This motivates the simultaneous registration of all subjects to a (yet unknown) reference that represents the average shape of the population. The distance between the images and the unknown reference is therefore minimized. Additionally, by registering all the images simultaneously, the resulting deformation fields will contain information about the variability across the group, and any inferences drawn will be with respect to the population as a whole. The aim of this work is to avoid altogether the need to choose a reference subject. Instead, all subjects are simultaneously registered to an imaginary coordinate system that is at the average of the population being studied. This coordinate system is not defined explicitly, but is calculated implicitly by constraining the sum of all the deformations to be zero while maximizing the similarity of all images.

In a previous work, Rueckert et al. [2] construct an atlas using pairwise registration from each subject in a group to a chosen reference anatomy. The mean deformation of the group is then applied to this atlas, to obtain a model in its natural coordinate system. If the registration were perfect, this would eliminate any bias to the choice of reference. However, in practice, residual errors in the registration have an influence on the average deformation field.

Work by Guimond et al. [3] involves using an iterative method of registration to obtain an atlas representing the average of the population. Here, subjects are first registered to a chosen reference and an atlas (model) is created. The subjects are then re-registered to this atlas, and this is repeated until the shape and intensity of the atlas converge. This, however, means that errors could be introduced when registering to an atlas in which structures are not clearly defined.

Marsland et al. [4] select the reference to be the subject from the population that minimizes the sum of distances between itself and the other images. However, this registration is still essentially pairwise from each image to the reference, and although the reference is selected automatically by the registration, it must still exist within the population.

Studholme [5] simultaneously aligns the group of images to a common space using high-dimensional non-rigid registration. A cost function is optimized with the aim of maximizing the similarity between images, while penalizing displacement from the average shape. However, this requires explicitly choosing a weighting parameter to specify the influence of the penalty term and thus how well the constraint is satisfied.

In our work, we use a high-dimensional non-rigid registration algorithm to conduct a simultaneous registration across the whole group of images. In contrast to Studholme however, we apply a fixed constraint on the optimization to *force* the sum of transformations from the reference space to the images to be zero; the similarity between the images is maximized, subject to this constraint always being satisfied.

2. METHODS

2.1. Registration

For *n* images, given a set of points in a common reference space, $\mathbf{X}_r$, and a set of points in each image space $\mathbf{X}_i, i = 1...n$, the goal of the registration is to find a set of transformations τ, each of which maps any point $\mathbf{x}_r$ in the reference space to a corresponding point $\mathbf{x}_i$ in image *i*: $\tau = \{\mathbf{T}_i : \mathbf{x}_r \mapsto \mathbf{x}_i, i = 1...n\}$.

To do this, we use a registration algorithm based on global and local components. The global component is represented by an affine transformation consisting of translations, rotations, scaling and shearing, and describes overall differences between the subjects. The local component describes any local deformation required to match the anatomies of the subjects. For this we adapt a non-rigid registration algorithm which has previously been applied successfully to a number of different registration tasks [6, 7]. A free-form deformation (FFD) model based on B-splines is used, which is a powerful tool for modelling 3D deformable objects. FFDs deform an object by manipulating an underlying mesh of control points ϕ; the resulting deformation controls the shape of the object. Increasing the resolution of the control point lattice, increases the amount of local deformation that can be achieved. In our application, we use a collection of FFDs $\mathbf{d}_i$, over the domain Ω, to deform each subject i to the common reference coordinate system, written here as the 3D tensor product of 1D cubic B-splines:

$$\mathbf{d}_i(\mathbf{x}) = \sum_{l=0}^{3}\sum_{m=0}^{3}\sum_{n=0}^{3} B_l(u)B_m(v)B_n(w)\phi^i_{a+l,b+m,c+n} \quad (1)$$

2.2. Similarity

To compare the similarity between images, normalized mutual information (NMI) is used [8]. Comparing *n* images would require an *n*-dimensional histogram, which for large numbers of images would become computationally infeasible. Instead, we have selected one arbitrary image to act as an intensity, but not as an anatomical, reference. All pairs of intensities, comprising the voxel intensity in the reference and the corresponding intensity in each image, are added to the same joint histogram. This is used to evaluate the NMI using:

$$S(\mathbf{X}_{ir}, \mathbf{X}) = \frac{H(\mathbf{X}_{ir}) + H(\mathbf{X})}{H(\mathbf{X}_{ir}, \mathbf{X})} \quad (2)$$

where $H(\mathbf{X}_{ir})$ represents the marginal entropy of the intensity reference, $H(\mathbf{X})$ represents the marginal entropy of the combined set of images and $H(\mathbf{X}_{ir}, \mathbf{X})$ denotes their joint entropy.

2.3. Constrained Optimization

To find the optimal non-rigid transformation that aligns all subjects to an average reference shape, a control point lattice is overlayed onto each subject. The control points are displaced, deforming the underlying image, until the similarity between the images is maximized, subject to the constraint that the sum of all deformations is equal to zero, ie:

Maximize: S($\mathbf{d}$)
Subject to:

$$\sum_{i=1}^{n} \mathbf{d}_i(\mathbf{x}) = 0 \quad \forall \mathbf{x} \epsilon \Omega \quad (3)$$

where the objective function S($\mathbf{d}$) denotes a measure of the similarity. Since the deformation fields are linearly dependent on the control points displacements, this is equivalent to constraining the sum of the displacements of each control point to be zero.

This is solved using Rosen's Gradient Projection Method [9], which is comparable to the method of steepest descent for unconstrained optimization. At each iteration, the directions of movement of the control points δ are found by calculating the gradient $\mathbf{g}$ of the similarity function with respect to the control point displacements. This is then multiplied by a projection matrix $\mathbf{P}$ which projects the objective function onto the constraint surface, after which the method reduces to steepest descent along the constraint.

$$\delta = -\mathbf{P}\mathbf{g} \quad (4)$$

where $\mathbf{P}$ is a block diagonal matrix and is a function of the constraints only.

3. RESULTS

To test the groupwise registration algorithm we applied the algorithm to a set of brain MR images of subjects with schizophrenia.

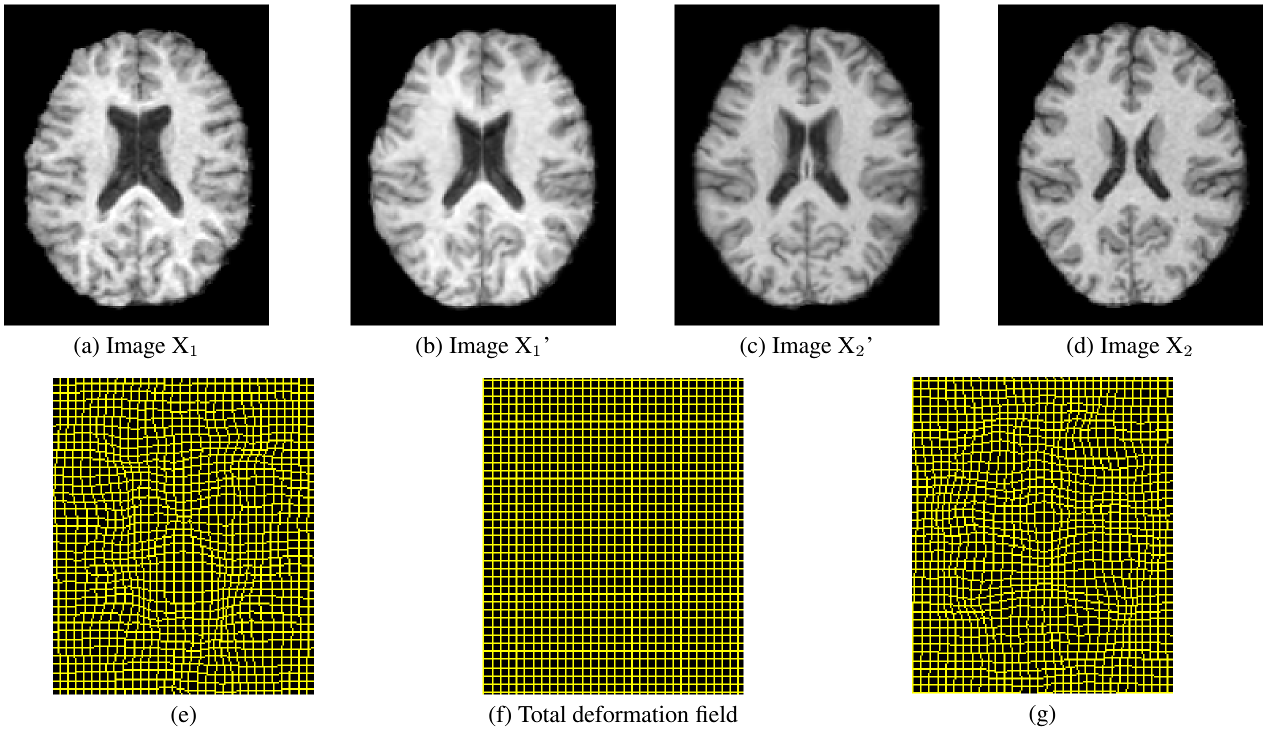


Fig. 2. (a), (d): images of the two subjects; (b), (c): resulting transformed images after registration; (e), (g): deformation fields produced in transforming (a) and (d); (f) sum of both deformation fields showing resultant coordinate system is at center of the two images.

Subjects were recruited following first diagnosis of schizophrenia and were studied with permission of the Hammersmith Hospitals Research Ethics Committee. Three dimensional (3D) T1 weighted (T1W) radiofrequency (RF) spoiled MRI (TR 21ms, TE 6ms, 152 x 256 x 114 imaging matrix, 2 NEX, 25cm FOV and 1.6mm slice thickness) were obtained on a 1.0T HPQ Plus scanner (Philips Medical Systems, Cleveland, Ohio).

3.1. Consistent registration of two images

In our first experiment we have applied the proposed registration algorithm for the consistent registration of two images: Figure 2 shows the results of applying the algorithm to two 3D brain MR images from our population, (a) and (d), with markedly different anatomies. The images are registered simultaneously to a frame of reference that is at the average of the two anatomies. The images formed by applying the resulting transformations are shown in (b) and (c): in both cases the size and shape of the ventricle is the average of the two original images. Figures 2(e) and (g) show the two deformation fields produced in order to get the above mappings. Adding the two deformation fields gives a total displacement of zero at each control point, indicating that the reference space is indeed exactly half-way between the two anatomies.

3.2. Consistent registration of n images

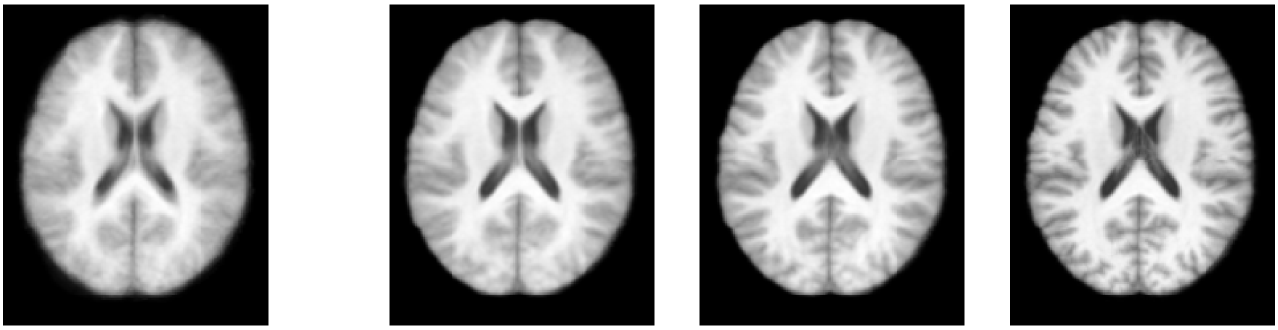
In our second experiment we have applied the proposed registration algorithm to all 19 brain MR images. The 3D images were first affinely registered to an average space. An axial slice through each image was taken and the resulting 19 2D images (matrix size 256x256) were registered using the non-rigid registration algorithm described. Atlases were constructed by averaging the transformed images after affine registration, and after non-rigid registration using increasing control point resolutions, as shown in Figure 3. The increasing clarity of the atlases shows that correspondence within the group improves with increasing mesh resolution. There are clearly limitations on the structural fidelity that can be achieved by inter-subject registration of 2D brain slices, but major features have evidently been brought into alignment by the method.

3.3. Computational Complexity

Table 1 shows the effect of registering varying numbers of images on memory requirements and time taken for registration at each control point spacing. In all these cases, 2D images of size 256x256 were used, and the program was run on a 2GHz Pentium machine with 1.5GBytes memory. When registering 3D images of size 256x256x114, the memory requirements are 1GByte for 5 images and 1.8GBytes for 10 images.

4. DISCUSSION

We have described in this paper a groupwise registration algorithm that simultaneously registers all images to a common reference space. Using a constrained optimization procedure to optimize the transformations forces this reference space to be at the average of the population. The algorithm has been tested on 19 two-dimensional MR images of the brain, which initially show



(a) Affine (b) 20mm (c) 10mm (d) 2.5mm

Fig. 3. Atlases produced after affine (a) registration, and after non-rigid registration at varying control point spacings (b)-(d).

Number of images	Time (mins) 20mm	10mm	5mm	2.5mm	Memory (MB)
2	1	2	3	5	16
5	3	9	15	24	21
10	9	22	41	66	31
15	17	35	67	112	40
19	25	49	91	155	48

Table 1. Memory and time requirements for non-rigid registration using varying numbers of 2D images (size 256x256) at different control point spacings

significantly varying ventricle sizes, with results that show good registration to an average shape. The algorithm does not require specifying any geometric reference, but an intensity reference has been chosen to evaluate the similarity during the registration. Although this is not ideal, using a multidimensional histogram to evaluate the NMI of n-images would result in increasing sparsity of the histogram and exponentially growing memory requirements as the number of images is increased. We believe however, that the choice of reference does not affect the results in a discernable way.

While the algorithm extends easily to 3D images, presently, memory requirements limit its application to only a small number of images ($<$10) on regular computers. Given the computational expense of even pairwise non-rigid registration algorithms, it seems infeasible to be able to register large numbers of 3D images on only one machine: we are therefore currently working on an implementation to be run on multiple machines.

5. ACKNOWLEDGEMENTS

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