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Multi-atlas segmentation with particle-based group-wise image registration

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Abstract

We propose a novel multi-atlas segmentation method that employs a group-wise image registration method for the brain segmentation on rodent magnetic resonance (MR) images. The core element of the proposed segmentation is the use of a particle-guided image registration method that extends the concept of particle correspondence into the volumetric image domain. The registration method performs a group-wise image registration that simultaneously registers a set of images toward the space defined by the average of particles. The particle-guided image registration method is robust with low signal-to-noise ratio images as well as differing sizes and shapes observed in the developing rodent brain. Also, the use of an implicit common reference frame can prevent potential bias induced by the use of a single template in the segmentation process. We show that the use of a particle guided-image registration method can be naturally extended to a novel multi-atlas segmentation method and improves the registration method to explicitly use the provided template labels as an additional constraint. In the experiment, we show that our segmentation algorithm provides more accuracy with multi-atlas label fusion and stability against pair-wise image registration. The comparison with previous group-wise registration method is provided as well.

Keywords

groupwise registration; multi-atlas segmentation; b-spline deformation; segmentation; registration; particle system

1. INTRODUCTION

The automated segmentation of MR images has been a challenging task due to image artifacts such as intensity inhomogeneities and partial volume effects and due to different anatomical structures that shares the same tissue contrast.¹ Hence, a *prior* anatomical information is crucial to simplify the segmentation process. In atlas-based segmentation, an intensity image with a segmentation label is provided to be matched to the target image we wish to segment, and the segmentation result is then obtained by warping the label image to the target image via the transformation field estimated by the deformable image registration.

Sophisticated image registration methods,² such as Large Diffeomorphic Deformation Metric Mapping (LDDMM), have greatly helped to solve the segmentation problem, but, depending on anatomical variation among the population and characteristics of the registration method used, an atlas-based segmentation method, in particular, using a single atlas cannot always produce accurate results. For example, the segmentation result may be biased to the choice of atlas, may not be robust enough to perform a group analysis, and may not be stable in the presence of irrelevant structures such as non-brain voxels.

Group-wise approaches that simultaneously consider multiples of atlases have received more and more attention in recent years due to their importance in population analyses. Group-wise approaches in atlas-based segmentation can be classified into two categories: 1) multi-atlas label fusion; and 2) group-wise image registration. Using a pair-wise image registration between an atlas and the target image, multi-atlas label fusion method makes use of more than one atlas to mediate potential bias associated with using a single atlas and applies label fusion method to create the final segmentation. This method requires additional computational costs to independently perform image registration per each atlas, but several empirical studies have recently shown that the method is more accurate than single atlas-based segmentation. Most existing label fusion methods are based on a weighted voting scheme where each atlas contributes to the final segmentation according to a non-negative weight and atlases more similar to the target image yield larger weights. Among weighted voting methods, those that derive weights from local similarity between the atlas and target have been most successful in practice allowing the weights to vary spatially.

In contrast to multi-atlas label fusion, the use of group-wise image registration helps to improve registration performance by simultaneously registering a group of images rather than a pair of images. For instance, the use of a population atlas has shown to be more robust than using only external atlases since the population atlas can capture the variation of a population more closely than the external one. The creation of an unbiased population atlas based on diffeomorphic deformable registration is originally proposed by Joshi et al.³ Meanwhile, Hamm et al.⁴ presented a tree-based registration method for group-wise registration such that the intrinsic anatomical manifold is learned by a manifold learning technique and represented as a tree rooting from the geodesic mean image. The path between two images on the tree provides a series of small deformations so that it can guide large deformation registration which is hardly successful for pair-wise registration. These methods improve the accuracy of registration by considering a group of images, but they are fundamentally based on iterative pair-wise registrations or using the similarity metric derived from pair-wise registration.

Rather than using a pair-wise registration, the proposed segmentation method applies a group-wise registration that evaluates a group-wise similarity metric and gradually transforms all subjects toward an implicitly defined common reference frame. The use of a group-wise similarity metric enables the incorporation of a group of image features⁵ into the registration and, thus, is expected to produce robust and sound registration. In particular, we apply a particle-guided image registration method⁶ previously proposed by the authors. In the following sections, we describe the particle-guided image registration method followed

by its extension to multi-atlas based segmentation. We compare our segmentation results with expert manual segmentation and show its performance with respect to volume overlaps.

2. METHOD

The proposed segmentation method employs a particle-guided image registration to create target labels and then perform label fusion to warp candidate segmentation labels into the final segmentation using a weighted voting scheme. Since the registration method used is a core novelty of the proposed method, we first describe the particle-guided registration method in detail followed by an extension of the registration method to the multi-atlas segmentation problem.

2.1 Particle-guided Image Registration

The particle-guided group-wise image registration method⁷ is motivated by a surface-based particle correspondence method where good correspondence is sought in the principle of the minimum description length (MDL).⁸ Given the same number of particles across subjects via an initialization process, the correspondence method optimizes the distribution in particles to the direction of minimizing an ensemble entropy while maximizing a surface entropy. Since these entropy values are equivalent to the average description length of the given surfaces,⁹ the correspondence method achieves the same correspondence configuration with previous MDL-based methods, allowing the ease of implementation without relying on a specific parameterization and a flexible extension to higher dimensions.

Extending the particle correspondence method to a volume domain, our group-wise registration method employs a set of corresponding particles as a novel feature in the registration process. In detail, we first sample a set of particles in correspondence in order to guide transformation fields among a group of images. These particles are distributed inside a brain mask by maximizing a sampling entropy and are directly optimized so that each particle will be placed at corresponding positions across subjects, minimizing the group-wise intensity metric. During this optimization, a B-spline free-form deformation is estimated for each subject to constitute a common reference frame. Each particle stores position and local image intensity values to represent the appearance of structures. We match those values across subjects, minimizing a group entropy, an information theoretic similarity measure, and identify correspondences between image volumes.

2.1.1 Group-wise Registration with Dynamic Particles—Extending the particle correspondence method, our group-wise registration method employs a set of corresponding particles as a novel feature in the registration process. In detail, we first sample a set of particles in correspondence in order to guide transformation fields among a group of images. These particles are distributed inside a brain mask by maximizing a sampling entropy

$$H_S(P_i) = \frac{1}{\sigma_i^2} \sum_{j \neq i}^{n_p} (x_i - x_j) G(x_i - x_j, \sigma_j),$$

where G is a Gaussian kernel, n_p is a number of particles in a subject P_i , and σ_i is the kernel size for sampling, and simultaneously optimized so that each particle will be placed at corresponding positions across subjects minimizing a group-wise intensity metric

$$H_I(\mathcal{J}_i) = -\dim(\mathcal{J}_i) + \frac{1}{2} \ln(2\pi)^{\dim(\mathcal{J}_i)} + \log \det \Sigma,$$

where Σ is the covariance matrix of $\mathcal{J}$. The total cost function is

$$H(P) = \arg \min_{P^j \in \Omega_j} \lambda_s \sum_{i=1}^N H_S(P_i) + \lambda_I \sum_{i=1}^n H_I(\mathcal{J}_i).$$

Given the spatially varying parameter σ , the distribution of particles can be adaptive depending on salient features of an image such as edges. The schematic diagram for the behavior of two entropy values is shown in figure 2.1.1.

2.1.2 B-Spline Deformation Driven by Corresponding Particles—Since the number of particles is much less than the number of voxels, we are required to estimate a dense deformation field to provide a voxel-wise correspondence for the sake of computational efficiency. The estimation is performed by B-spline interpolation of a set of displacement vectors between corresponding particles. Here, we require a common reference frame where every subject is registered together. In order to avoid a potential bias toward a specific choice of template, we use the average of corresponding particles

$$\bar{X} = \sum_{i=1}^{n_s} X_i,$$

where X_i is a set of particles of i -th subject, and an implicit common reference frame.

The optimization of particles is performed in an iterative manner. At each iteration step, the common reference frame is constructed from the average of particles. Each set of particles is then registered to the common reference frame so that image intensity values are matched according to the ensemble entropy. Then, the particles are distributed to maximally sample the region of interest.

2.2 Multi-atlas-based Segmentation

The core idea of this paper is to use a group-wise image registration method for the generation of a set of candidate segmentation labels for label fusion. We extend the group-wise registration method in the previous subsection to incorporate prior information from the segmentation labels in the given set of atlases. The segmentation labels associated with atlases used provide important boundary information as well as their variation among the population. In order to capture the boundary information and use as a feature in the registration step, we propose a membership for each particle. Assuming there are the same number n_L of labels in each atlas and the labels are spatially disjointed, the member m_i of

particle x_i can have a value among the set $\{L_1, L_2, \dots, L_{n_L}\}$. This membership m_i of particle x_i is obtained by an initialization process for label L_i and is used to constrain the particle to move freely only inside the label region.

The proposed segmentation consists of two steps: 1) the particle initialization step; and 2) the segmentation step. In the particle initialization step, we determine the distribution of particles that will belong to atlas labels. We repeat the same sampling process for each label as follows. Let L_i be a label to be sampled during the iteration. We first compute the intersection mask M_i for each L_i across all atlases, and then randomly sample n_{L_i} particles to duplicate into each subject. Since the initial particles are sampled from the intersection of the target label, every particle is guaranteed to stay inside the label and can be distributed maintaining explicit correspondence. After the repeated sampling and distribution process,

we have $n_p = \sum_{i=1}^{i=n_L} n_{L_i}$ particles for an atlas.

The goal of the segmentation step is to register all available atlases into a novel target image and produce the set of candidates to be fused later for the final segmentation. We first perform affine registration toward a common reference frame where atlases are aligned in order to normalize the orientation and scale of the target image. After this initial alignment, we can assume there are only non-linear residual components in the deformation fields we are estimating. In order to perform group-wise image registration with multiples of atlases, we first have to sample the same number of particles in the target image. Instead of sampling from the target image, we choose to transfer the average of particles in atlases onto the target image because we cannot guarantee that a single particle will be placed at a close corresponding location of the target image. This is important in order to identify a local optimum as close as possible to the global optimum. The transfer of particles is performed by deforming the average mask into the target image. The guidance deformation field is computed by solving Laplace partial differential equations. After transferring the atlas particles into the target image, we optimize the distribution of particles not only in the target image but also in the entire atlases.

In order to improve the segmentation accuracy, we perform label fusion of warped labels. We employ a weighted majority voting scheme¹⁰ where the final is evaluated by

$$L(x) = \sum_{i=1}^{n_s} w_i(x) L_i(x).$$

Here, w_i is determined by local intensity similarity such that

$$w_i(x) = \frac{1}{Z(x)} \left[\sum_{y \in N(x)} (I_T(y) - I_i(y))^2 \right]^{-\beta},$$

where $Z(x)$ is a normalization constant.

3. RESULTS

In our experiments, we have evaluated the performance of our multi-atlas based segmentation method for structural segmentation of C57BL/6J Brookhaven atlas.¹¹ The Brookhaven atlas consists of 10 adult male C57BL/6J mouse brain images derived from T2*-weighted 3D MRM images acquired on a 17.6T magnet. With 20 segmented structures, the C57BL/6J 3D digital brain atlas database offers individual brain atlases produced by single-atlas based segmentation followed by manual corrections. For comparison, we use the congealing group-wise registration method¹² with its available codes, <http://www.insight-journal.org/browse/publication/173>. To demonstrate the advantage of group-wise registration against pair-wise registration method, we also compare the segmentation results with our method to the results with a B-spline deformable registration implemented in Slicer4. For B-spline deformation, we used $16 \times 16 \times 16$ control points grid with the cubic splines.

The volume overlap ratio of ROIs is an important criterion to demonstrate the segmentation performance. We compute Dice overlap ratios between the manual and automatic structural segmentations. For the two overlapped region A and B , the Dice overlap ratio is defined as:

$$\frac{2|A \cap B|}{(|A| + |B|)},$$

where $|\cdot|$ denotes the number of voxels in the underlying label.

After registering 10 images by each of three registration methods, we calculated the overlap ratio for each structures. For the pair-wise B-spline registration, we aligned each subject against the minimum deformation mean image. The registration against a group mean image is typically performed in single atlas-based segmentation and known to yield better performance than registering two individual subjects. Figure. 2 displays the overlap ratio on each ROI by the pair-wise B-spline registration, the congealing method, and the proposed method. The overall overlap ratio is 84% for pair-wise B-spline registration, 88% by the congealing method, and 89% by the proposed method. For the two group-wise registration methods, two results are similar in overall performance; however, the proposed method performs better in most ROIs except Caudate & Putamen where the overlap ratio is nearly identical around 94%. A very high Dice coefficient around 90% shows less variation of rodent population due to controlled environment. The visual comparison between the congealing method and our method is provided in figure 3.

The overlap ratio values for External Capsule (EC), Neocortex (NC), Cerebellum (CE), Thalamus (TH), and Hippocampus (HP) by our method and other compared methods are displayed in Table 1. It can be observed that our method produces better results than the B-spline registration method, that is, our method produces overall overlap ratio of 89%, whereas the B-spline registration method produces 84%. By checking the overlap ratio of cortical and subcortical structures, our results also outperforms the B-spline registration method in most structures. This is in fact expected results not only due to group-wise registration method but also due to multi-atlas label fusion which is known to produce

superior results. The effect of multi-atlas label fusion is shown in two different versions of our method. In a single-atlas version, the overall overlap ratio is around 83%. The advantage of group-wise method is not in its accuracy but its stability as seen in the standard deviation of results, which is lower than the pair-wise method's. The reduced standard deviation makes our group-wise method suitable to a group-wise analysis.

Also, we performed the comparison between the uniform sampling and the adaptive sampling. Since the adaptive sampling places more particles near the region of salient edges, it is expected to perform more precisely than the uniform distribution. However, the difference between two distribution schemes was negligible.

4. CONCLUSION

We proposed a novel multi-atlas based segmentation method employing a group-wise image registration method. The group-wise registration method is proposed to provide robustness and stability for the purpose of group-analysis in rodent as well as to improve the accuracy of segmentation. In our rodent structural segmentation, the group-wise method has shown better performance than the previous B-spline registration method. By constraining guiding particles into manually segmented regions, we have shown that the deformation can be constrained within the variation of given structure population. Applying this constraint, our method can be used as a rodent brain skull-stripping method which performs consistently than previous methods. We have used B-spline deformation to estimate deformation fields. However, our future work includes the use of non-parametric deformation. Also, we apply our method to more experimental data sets, to demonstrate its power in various rodent studies.

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1) Preprocessing

- The number of particles used
- Binary mask generation
- Initial particle positioning
- Affine registration across subjects

2) Reference Space Optimization

- Common reference space construction
- Optimizing corresponding particle coherence and local intensity similarity

3) Subject Space Optimization

- Regularizing particles to avoid trivial solution
- Maximizing subject's geometric information contents

Figure 1.

The top figure shows preprocessed particles, first randomly sampled, then uniformly spread to cover whole ROIs. Individual particle interaction is rendered in the middle figure. Each particle has repulsion force preventing trivial solution where every particle overlap. The last figure summarizes the interaction of corresponding particles in different subject. Due to the Ensemble entropy and the Intensity value entropy, the particles move to the coherent position.

Figure 2.

The overlap ratios of 20 ROIs in Brookhaven rodent brain images. The overlap ratios by the congealing method and our method are shown in blue and red, respectively. It can be observed that our method achieves better segmentation result in all ROI regions than the congealing method. The overall ratio is 88% for the congealing method and 89% for our method.

Figure 3.

Segmentation results produced by our method and the congealing method. The top row is showing the sagittal plane and the bottom row for the axial plane. Label description: red - Neocortex; green - External Capsule; yellow - Hippocampus; blue - Thalamus.

Average Dice coefficient ($\pm$ standard deviation) of selected brain structures by the pair-wise B-spline registration method, the proposed method with a single atlas, the group-wise coealing B-spline method, and the proposed method with multiple atlases.

Table 1

	Hippocampus	External Capsule	Thalamus	Cerebellum	Neocortex	Overall
Pair-wise B-spline	90.2 (± 2.5)	70.1 (± 5.7)	94.9 (± 0.6)	90.6 (± 3.0)	90.9 (± 2.4)	84.0 (± 1.8)
Particle-guided B-spline (single-atlas version)	90.2 (± 3.4)	70.8 (± 3.4)	94.5 (± 0.5)	90.2 (± 0.7)	90.7 (± 0.9)	83.6 (± 1.4)
Coealing B-spline (multi-atlas version)	92.8 (± 1.4)	77.9 (± 4.8)	96.1 (± 0.8)	93.0 (± 0.9)	93.3 (± 1.4)	88.0 (± 2.0)
Particle-guided B-spline (multi-atlas version)	93.6 (± 1.6)	79.9 (± 3.6)	96.6 (± 0.3)	93.7 (± 2.3)	94.1 (± 1.5)	89.0 (± 1.5)