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A generative probability model of joint label fusion for multi-atlas based brain segmentation

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ABSTRACT

Automated labeling of anatomical structures in medical images is very important in many neuroscience studies. Recently, patch-based labeling has been widely investigated to alleviate the possible mis-alignment when registering atlases to the target image. However, the weights used for label fusion from the registered atlases are generally computed independently and thus lack the capability of preventing the ambiguous atlas patches from contributing to the label fusion. More critically, these weights are often calculated based only on the simple patch similarity, thus not necessarily providing optimal solution for label fusion. To address these limitations, we propose a generative probability model to describe the procedure of label fusion in a multi-atlas scenario, for the goal of labeling each point in the target image by the best representative atlas patches that also have the largest labeling unanimity in labeling the underlying point correctly. Specifically, sparsity constraint is imposed upon label fusion weights, in order to select a small number of atlas patches that best represent the underlying target patch, thus reducing the risks of including the misleading atlas patches. The labeling unanimity among atlas patches is achieved by exploring their dependencies, where we model these dependencies as the joint probability of each pair of atlas patches in correctly predicting the labels, by analyzing the correlation of their morphological error patterns and also the labeling consensus among atlases. The patch dependencies will be further recursively updated based on the latest labeling results to correct the possible labeling errors, which falls to the Expectation Maximization (EM) framework. To demonstrate the labeling performance, we have comprehensively evaluated our patch-based labeling method on the whole brain parcellation and hippocampus segmentation. Promising labeling results have been achieved with comparison to the conventional patch-based labeling method, indicating the potential application of the proposed method in the future clinical studies.

1. Introduction

With the advent of magnetic resonance (MR) imaging technique, image analysis on MR images plays a very important role in quantitatively measuring the structure difference between either individuals or groups (Fennema-Notestine et al., 2009; Paus et al., 1999; Westerhausen et al., 2011). In many neuroscience and clinic studies, some regions-of-interest (ROIs), e.g., hippocampus, in the human brain are specifically investigated due to their close relation to brain diseases such as dementia (Devanand et al., 2007; Dickerson et al., 2001; Holland et al., 2012). Consequently, automatic accurate labeling and measurement of anatomical structures become significantly important in those studies to deal with large amount of clinical data. However, automatic labeling still remains a challenging problem because of the complicated brain structures and high inter-subject variability across individual brains.

Recently, patch-based labeling methods have emerged as an important direction for the multi-atlas based segmentation (Coupe et al., 2011; Rousseau et al., 2011; Wang et al., 2012; Wang et al., 2011; Yan et al., 2013). The basic assumption in these methods is that, *if two image patches are similar in appearances, they should have the same anatomical label* (Rousseau et al., 2011). Most patch-based labeling methods perform label fusion in a non-local manner. Specifically, to label a patch in the target image, all possible candidate patches from different atlases are considered, with their contributions weighted according to the patch similarities w.r.t. the target patch. In this way, these non-local based labeling methods can alleviate the influences from the possible registration errors.

Although patch-based labeling methods are effective in many applications, they still have several limitations:

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(1) All candidate patches from atlases contribute to the label fusion, according to their similarities to the target patch. However, even the atlas patches with high appearance similarity could still bear the wrong labels, thus undermining the label fusion result due to the lack of power in suppressing the misleading patches.
(2) If a majority of candidate patches have wrong labels, those patches will dominate the conventional label fusion procedure and lead to incorrect labeling results (Wang et al., 2012). The reason is that most label fusion methods independently treat each candidate patch during label fusion, thus allowing those highly correlated candidate patches to repeatedly produce the labeling errors.
(3) The weights calculated from patch appearance are often directly applied for label fusion. Although these weights are optimal for patch representation, i.e., making the combination of candidate patches close to the target patch, these weights are not necessarily optimal for label fusion.
(4) Most current label fusion methods complete the label fusion right after sequentially labeling each image point in the image domain, thus lacking a feedback mechanism to help correct possible labeling errors.

In this paper, we propose a novel patch-based labeling method, where a generative probabilistic model is presented to predict the labels based on the observations of registered atlas images. Specifically, the goals are (1) to seek for the best representation of the underlying target patch from a set of similar candidate atlas patches, and (2) to achieve the largest labeling consensus, among the entire candidate atlas patches, in predicting the label for each target point. For the first goal, we introduce the concept of sparse representation (Tibshirani, 1996; Vinje and Gallant, 2000; Zhang et al., 2012a, 2012b, 2012c) by imposing a non-Gaussian sparsity prior (Seeger et al., 2007; Seeger, 2008) on the label fusion weights. Thus, our method, equipped with sparsity constraint, is able to alleviate the issue of ambiguous patches by representing each target patch with only a small number of atlas patches, instead of all candidate atlas patches. For the second goal, we propose to measure the labeling unanimity through the joint probability of patch dependencies, which encodes the risk for any pair of candidate patches to produce labeling error simultaneously. In our probability model, we describe the dependency probability in two ways. First, we measure the pairwise correlation of morphological error patterns for any pair of candidate patches, in order to penalize those candidate patches with simultaneously incorrect labels. Second, we further inspect whether the latest label fusion result achieves the largest labeling consensus among the candidate patches. Since the estimation of dependency probability is related with the currently estimated labels, our label fusion method offers the feedback mechanism by iteratively improving the label fusion result with the gradually refined estimation of the dependency probability. To this end, we present an efficient EM-based solution to infer the optimal labels for the target image.

In terms of joint label fusion, our work is close to (Wang et al., 2012), which also measured the joint labeling risk between two patches. However, our generative probability model has several unique improvements. First, the joint distribution of patch dependency is measured by not only the error pattern but also the labeling consensus w.r.t. the latest estimated label. Second, the label fusion method in (Wang et al., 2012) lacks of the feedback mechanism as in our method to examine the current label fusion result and further refine the estimation of dependency. Third, our method takes advantages of sparsity constraint to obtain robust label fusion results to suppress misleading patches. As we will point out later, our method can be regarded as a generalized solution of most existing patch-based labeling methods (Artaechevarria et al., 2009; Coupe et al., 2011; Rousseau et al., 2011; Tong et al., 2012; Zhang et al., 2012a).

We demonstrated the labeling performance on NIREP-NA0 dataset (Christensen et al., 2006) with 32 manually delineated ROIs and also the ADNI (Alzheimer's Disease Neuroimaging Initiative) dataset with manually labeled hippocampi. Compared to the conventional patch-based labeling method (Coupe et al., 2011; Rousseau et al., 2011), our method achieves more accurate labeling results on both datasets. In the following, we first present our novel generative probability model for label fusion in Section 2. Then, we evaluate it in Section 3, by comparison with the conventional patch-based methods. Finally, we conclude the paper in Section 4.

2. Method

Let $\boldsymbol{S}$ be the set of N atlas images $\boldsymbol{I} = \{I_k|k = 1, \ldots, N\}$ and their corresponding label maps $\boldsymbol{L} = \{L_k|k = 1, \ldots, N\}$, which have been already registered to the target image T (that will be labeled) by linear/non-linear registration methods (Vercauteren et al., 2008, 2009; Wu et al., 2013, 2007, 2012a, 2010). For each point $v \in \Omega_{I_k}$, $\vec{L}_k(v)$ is a binary vector of $\{0, 1\}^M$ representing the particular label at the point v, where M is the total number of labels. The goal of label fusion is to propagate the labels from the registered atlases to the target image T. For each point $u \in \Omega_T$ in the target image T, its label $\vec{L}_T(u)$ will be estimated through the interaction between the target patch $\mathcal{P}_T(u)$ centered at point u and all possible candidate patches $\mathcal{P}_k(v)$ at the registered atlas image I_k. The spatial location v is usually confined to a relatively small neighborhood $n(u) \subset \Omega_T$. Given the weight $w_k(u, v)$ for the pair of $\mathcal{P}_T(u)$ and $\mathcal{P}_k(v)$, we can estimate the label vector $\theta(u)$ for the target point u as

$$\vec{\theta}(u) = \frac{\sum_{k=1}^{N} \sum_{v \in n(u)} w_k(u, v) \cdot \vec{L}_k(v)}{\sum_{k=1}^{N} \sum_{v \in n(u)} w_k(u, v)}. \tag{1}$$

It is worth noting that $(\vec{\theta}(u) = [\theta^1(u), \ldots, \theta^m(u), \ldots, \theta^M(u)]$ is a vector of continuous likelihood for each possible label at point u after label fusion. Then, the final label of the point u can be determined by binarizing the fuzzy assignment $\vec{\theta}(u)$ to a binary vector $\vec{L}_T(u) = [l^1(u), \ldots, l^m(u), \ldots, l^M(u)]$

$$l^m(u) = \begin{cases} 1, & \text{if } \theta^m(u) \text{ has the highest value} \\ 0, & \text{otherwise} \end{cases}. \tag{2}$$

In the following, we will first introduce the conventional patch-based labeling method with non-local averaging in Section 2.1. Then, we will present our generative probability model for label fusion in Section 2.2. The inference of probability model will be presented in Section 2.3, followed by the discussion in Section 2.4. Our whole method will be summarized in Section 2.5.

2.1. Conventional patch-based labeling method by non-local averaging

The principle of conventional patch-based labeling method is originated from the non-local strategy which is widely used in the computer vision area, such as image/video denoising (Buades et al., 2005) and super-resolution (Protter et al., 2009). The applications in medical images can also be found in (Awate and Whitaker, 2006; Manjón et al., 2011). The overview of patched-based method is shown in Fig. 1(a). Hereafter, for each target point $u \in \Omega_T$, we use the column vector $\vec{y}$ to vectorize the target patch $\mathcal{P}_T(u)$ centered at u (red box in Fig. 1(a)). In order to account for the registration uncertainty, a set of candidate atlas patches (pink boxes in Fig. 1(a)) are included in a search neighborhood $n(u)$ (blue boxes in Fig. 1(a)) from different atlas images. For clarity, we arrange each candidate patch $\mathcal{P}_k(v)$ into a column vector $\vec{a}_j$ and then assemble them into a dictionary matrix $\mathbf{A} = [\vec{a}_j]_{j=1,\ldots,Q}$, where