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Segmentation of longitudinal brain MR images using bias correction embedded fuzzy c-means with non-locally spatio-temporal regularization ☆

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ABSTRACT

We propose an automated method for segmentation of brain tissues in longitudinal MR images. In the proposed method, images acquired at each time point are first separately segmented into white matter, gray matter, and cerebrospinal fluid by bias correction embedded fuzzy c-means. Intensities differences are then defined as similarities of each voxel to the cluster centroids. After being normalized in inter-class, the similarities are incorporated into a non-local means de-noising formula to regularize the segmentation in both spatial and temporal dimensions. Non-locally regularization results are used to compute final membership functions for the segmentation. To improve time performance, we accelerate the modified de-noising algorithm using CUDA and obtain a 200× performance improvement. Quantitative comparison with the state-of-the-art methods on BrainWeb dataset demonstrate advantages of the proposed method in terms of segmentation accuracy and the ability to consistently segment brain tissues in an arbitrary number of longitudinal brain MR image series.

1. Introduction

Brain atrophy, observed in a variety of neurodegenerative disorders, such as multiple sclerosis (MS), Alzheimer's disease (AD), Huntington's disease, and Parkinson's disease, generally manifests itself as volume changes in brain tissues [1,2]. Due to its non-invasive nature and excellent soft tissue contrast, magnetic resonance imaging (MRI) has been widely used by various image processing technologies, such as segmentation, to reveal changes of human brain in basic and clinical neuroscience studies [3,4]. Thus, segmentation of magnetic resonance (MR) images of human brain into anatomically meaningful tissues such as white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF) is crucial for measurement of subtle but complex changes of human brain quantitatively [5,6].

Since it is labor-intensive, time-consuming, and sensitive to inter- and intra-observer variability, manual segmentation suffers from lacks of reproducibility and ability of maintaining consistency for entire dataset of a study [7,6]. Therefore, many efforts have been devoted to developing automated methods in the literature for analysis of brain atrophy in MR images [8–17]. But most of the methods are proposed merely in view of cross-sectional (3D) images of human brain [8–13]. It is obvious that 3D segmentations are not able to provide adequate longitudinal stability because images at each single time point are segmented separately [18–20]. In contrast, segmentation of a series of 3D image sequences of the same subject simultaneously has been shown to be able to increase the accuracy of brain atrophy measurement [21,3]. That is to say that segmentation of longitudinal brain MR images (images at multiple time points) consistently is crucial to the measurement of subtle volume changes of brain tissues [22,23]. In [24], Smith et al. presented a fully automated method to analyze changes of human brain longitudinally. They first automatically distinguish brain tissues from non-brain tissues and then registered the brain MR images while estimated skull images were used to constrain scaling and skew. They finally estimated brain surface motion by tracking surface points of the brain in subvoxel accuracy [25,26]. This method has already been incorporated into a soft package named SIENA (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/SIENA) for analysis of brain change in both single-time-point (cross-sectionally) and two-time-point (longitudinally). In [12],

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Zhang et al. proposed a method to segment brain MR images by using a hidden Markov Random Field (MRF) model and the Expectation–Maximization (EM) algorithm. Their method has been generalized and integrated into FMRIB Software Library (FSL) as a tool named FMRIB's Automated Segmentation Tool (FAST, http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FAST) with the ability of correcting the spatial intensity inhomogeneities and simultaneously segmenting the brain image into WM, GM, and CSF. As a brain imaging software package developed by the Martinos Center, Freesurfer (FSF, http://freesurfer.net/) includes volumetric segmentation and longitudinal processing functions for brain image analysis [27]. The segmentation method in Freesurfer is based on voxel intensities and Talairach anatomical atlases where images are automatically processed for longitudinal analysis within the longitudinal stream to extract reliable volume estimations [28]. Xue et al. proposed a temporally consistent and spatially adaptive longitudinal MR brain image segmentation method named CLASSIC in [29].Their method incorporates image-adaptive clustering, spatio-temporal smoothness constraints, and image warping to jointly segment a series of brain MR images of the same subject aiming at obtaining accurate measurements of rates of change of regional and global brain volumes from serial MR images and estimating the morphological changes of the brain, such as atrophy [29]. Although a few longitudinal segmentation methods have been proposed in the literature, segmentation of MR brain images longitudinally is still an open problem and is challenging due to the large size of brain MR images especially at multiple time points, the limitation of available a priori knowledge, and the presence of noise and intensity inhomogeneities (well known as bias field) [30]. Fig. 1 shows an example of intensity overlaps between different brain tissues caused by noise and intensity inhomogeneity.

As one of the well known clustering methods, fuzzy c-means (FCM) has been widely studied in the literature for its application to image segmentation [31]. But traditional FCM and hard c-means are both sensitive to noise and lacks the ability to deal with intensity inhomogeneity [32]. To overcome this drawback, Ahmed et al. proposed a bias corrected fuzzy c-means (BCFCM) method by taking consideration of the correlation among neighboring pixels [33]. Chen and Zhang modified BCFCM to improve its time performance and robustness to noise and outliers [34]. However, final clustering results of methods proposed by Ahmed et al. and Chen and Zhang are both heavily affected by a parameter used to adjust influence of the neighboring pixels. Therefore, Yang and Tsai proposed a generalized type of BCFCM in [35] where the parameter is estimated automatically under a learning scheme. However, all the above mentioned improvements of BCFCM are without pay any attention to correct the bias field from the image. In this paper, we propose a fully automated method for segmentation of brain tissues longitudinally. Besides being able to deal with the intensity inhomogeneities inherently, the proposed method is effective in segmenting brain tissues in arbitrary number of MR image series. In the method, a bias correction embedded FCM (BCEFCM) is first proposed to segment 3D MR image sequences of each time point separately and estimate the bias field simultaneously. A non-locally spatio-temporal regularization is then introduced to ensure segmentation consistency of the proposed method. The regularization is defined on similarities of intensities between voxels and cluster centroids. Specifically, after being normalized in inter-class, the similarities are incorporated into a non-local means de-noising formula by summing them together and introducing a time component integral to regularize longitudinal images non-locally in both spatial and temporal dimensions. It is obvious that the proposed method is also able to overcome negative influences of noise as well because of the existing of non-local means de-noising. Membership functions are finally updated with non-local means de-noising results, and are further used to decide which class the voxels should be classified into.

The rest of this paper is organized as follows. The framework and formulation of the proposed method are described in Section 2. Experimental results, quantitative evaluation, and discussions are given in Section 3. This paper is finally concluded in Section 5.

2. Method

In this paper, we suppose that the MR images of different time points have already been rigidly registered in the same coordinate system and non-brain tissues have already been removed from the images. For the images used in this paper, maximization of mutual information and a fast robust automated brain extraction tool, BET, are used to register each image case and strip non-brain tissues from the images, respectively [36,37]. Before performing segmentation, longitudinal MR image series denoted by $\mathbf{I} = (I_1, I_2, \ldots, I_T)$, which include T image sequences, are first rigidly registered to the first image sequence in the same image domain Ω with six degree of freedom. Given a brain MR image I_t acquired at time point $t \in [1, T]$, we view it as a function $I_t : \Omega \rightarrow R$ defined on the continuous image domain $\Omega \subset R^2$. It has been well known that the observed image can be described by a product of the true image intensity J_t and the unknown bias field b_t, namely,

$$I_t(\mathbf{x}) = b_t(\mathbf{x})J_t(\mathbf{x}) + n_t(\mathbf{x}), \tag{1}$$

where $\mathbf{x} \in \Omega$ and n_t is zero-mean additive noise. The true image J_t characterizes an intrinsic physical property of brain tissues, which ideally takes a specific intensity $c_{t,i}$ for the i-th type of tissues and is therefore assumed to be piecewise constant. That is to say, the true image J_t approximately takes N distinct constant values $c_{t,1}$, $c_{t,2}$, …, and $c_{t,N}$ in disjoint regions $\Omega_{t,1}$, $\Omega_{t,2}$, …, and $\Omega_{t,N}$,

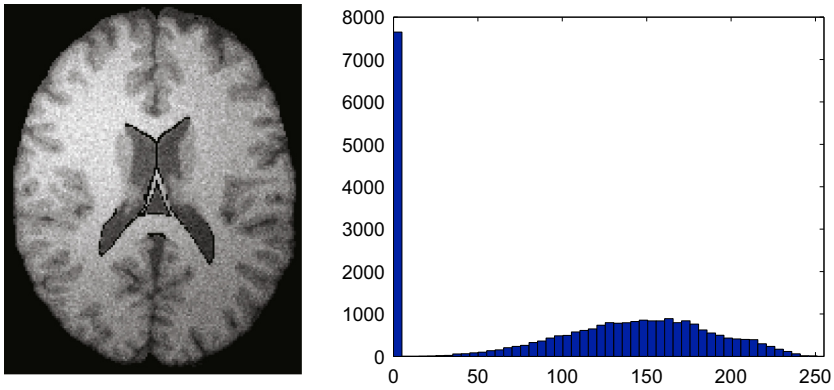

Fig. 1. Appearance and intensity histograms of a brain image corrupted by both noise and intensity inhomogeneity.