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LoAd: A locally adaptive cortical segmentation algorithm

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ABSTRACT

Thickness measurements of the cerebral cortex can aid diagnosis and provide valuable information about the temporal evolution of diseases such as Alzheimer's, Huntington's, and schizophrenia. Methods that measure the thickness of the cerebral cortex from in-vivo magnetic resonance (MR) images rely on an accurate segmentation of the MR data. However, segmenting the cortex in a robust and accurate way still poses a challenge due to the presence of noise, intensity non-uniformity, partial volume effects, the limited resolution of MRI and the highly convoluted shape of the cortical folds. Beginning with a well-established probabilistic segmentation model with anatomical tissue priors, we propose three post-processing refinements: a novel modification of the prior information to reduce segmentation bias; introduction of explicit partial volume classes; and a locally varying MRF-based model for enhancement of sulci and gyri. Experiments performed on a new digital phantom, on BrainWeb data and on data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) show statistically significant improvements in Dice scores and PV estimation ($p<10^{-3}$) and also increased thickness estimation accuracy when compared to three well established techniques.

Introduction

The thickness of the cortex has been found to have an important correlation to various diseases such as Alzheimer's (Lerch et al., 2005; Du et al., 2007; Lehmann et al., in press), Huntington's (Rosas et al., 2008), schizophrenia (Nesvåg et al., 2008), and also to normal ageing (Shefer, 1973; Salat et al., 2004; Thambisetty et al., 2010). Automatic extraction of measurements from the cortex, such as thickness, has the potential to provide a biomarker for diagnosis and disease progression (Desikan et al., 2009). However, algorithms for the reliable extraction of the cortical layer are still in need of improvement. From a technical point of view, this problem is intrinsically complex due to the convoluted shape of the cortex and the fact that its normal thickness (2.5 ± 1.5 mm, (von Economo, 1929) is close to the typically acquired MRI voxel dimensions ($\approx$1 mm isotropic). This task is further hampered by the presence of noise, partial volume (PV) effects and intensity non-uniformity (INU) across the image.

Segmentation of the brain into its different tissue types has been proposed using methods based on morphological operations (Mangin et al., 1995), edge detection (Tang et al., 2000), fuzzy c-means (Pham, 2002; Wang and Fei, 2009) and probabilistic models. Probabilistic mixture models fitted with the expectation maximisation (EM) algorithm form the basis of several image segmentation methods (Wells et al., 1996; Van Leemput et al., 1999b; Zhang et al., 2001; Ashburner and Friston, 2005). These EM-based image segmentation algorithms were shown to be among the most accurate and robust (Klauschen et al., 2009). Wells et al. (1996) segments the brain into three main tissue types (white matter, grey matter and cerebrospinal fluid), modelling each class as normal distribution after log transformation to make the bias field additive, and assumes a Gaussian distributed bias field model to correct for intensity non-uniformity. Van Leemput et al. (1999b) added a spatial consistency model based on a Markov Random Field (MRF), explicit modelling of the INU with polynomial basis functions, and some prior information about the brain anatomy to initialise and locally constrain the segmentation. Ashburner and Friston (2005) combined image registration with tissue classification, and bias field correction in an elegant unified framework. Despite these advances, the problems of intensity non-uniformity (INU), partial volume effect (PV), noise, image artefacts, limited resolution and the great degree of natural variability, mean that the local intensity difference is not enough to provide an accurate segmentation of fine structures. These problems can lead to an

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[1] Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (http://www.loni.ucla.edu/ADNI). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. ADNI investigators include (complete listing available at http://www.loni.ucla.edu/ADNI/Collaboration/ADNI_Citation.shtml).

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incorrect delineation of problematic areas like PV-corrupted grey matter folds, resulting in incorrect segmentations. The use of prior knowledge may also cause problems in areas that have a high degree of natural variability, as the prior information is representative of a sample of a normal population and might not describe a particular subject. The use of probabilistic priors becomes more problematic when an atlas derived from a normal population is used to segment patients with different anatomical or pathological characteristics.

The methods described above are global brain segmentation methods, and are not specifically designed for the cortical layer. In this paper we are interested specifically in cortical segmentation as an input to a voxel-based cortical thickness algorithm. Cortical thickness estimation methods can be broadly categorised into two types: surface-based (Fischl and Dale, 2000; Kim et al., 2005) and voxel-based methods (Jones et al., 2000; Hutton et al., 2008; Lohmann et al., 2003; Acosta et al., 2009). Surface-based approaches fit a triangulated mesh to the internal and external surface of the cerebral cortex. These surface-based methods work in the continuous domain and can achieve sub-voxel accuracy and robustness to image noise due to mesh smoothness constraints. However, these methods are computationally very demanding (normally above 10 h), and often require laborious manual interaction at several stages. Surface-based methods can also produce biased results due to the implicit surface model and topology constraints (MacDonald et al., 2000; Srivastava et al., 2003; Kim et al., 2005; Thompson et al., 2005; Scott et al., 2009).

In contrast, voxel-based techniques that work directly in the 3D voxel grid are much more computationally efficient but are more prone to noise, PV and INU effects and topological errors. To locally improve the detection of PV corrupted sulci, Han et al. (2004) and Acosta et al. (2008) used the information derived from a distance based cost function as a post processing step to try to solve this problem. Hutton et al. (2008) used a layering method based on mathematical morphology to detect deep sulci. However, these approaches are post processing steps; they do not take the new information into account to improve the segmentation. They are also only concerned with improvements in the delineation of deep sulci though the same problems can occur in thinned gyri due to white-matter tissue loss, PV effects and structural readjustments.

In this paper we improve a probabilistic segmentation framework with three novel modifications in order to reduce the influence of the priors in an anatomically coherent way and improve the PV estimation and the delineation of deep sulci and gyri (Fig. 1). Both the solution of the EM algorithm and the information derived from a geodesic distance function are used to locally modify the priors and the weighting of the MRF, enabling the detection of small variations in intensity while maintaining robustness to noise. An MRF energy matrix derived from the anatomical properties of the brain is used to add topological and shape knowledge to the MRF. Although full topological correctness is not ensured, the proposed MRF energy matrix improves the topological characteristics of the segmentation and reduces the PV layer thickness, making it more in line with the theoretical anatomical limit. The implicit modelling of PV and the reduction of the PV layer thickness obviates the need for an empirical threshold to distinguish between pure and mixed voxels and eases the problem of achieving subvoxel accuracy when calculating the cortical thickness.

Method

Intensity model and MRF regularisation

Starting from the image model developed by Van Leemput et al. (1999b), let $i \in \{1,2,\cdots,n\}$ index the n voxels of an image domain. For coregistered multimodal datasets, intensities form feature vectors $y_i \in \mathcal{R}^m$; for simplicity, we assume unimodal data with $m=1$. Let z_i denote the tissue type to which voxel i belongs. For K tissue types, $z_i = e_k$ for some k, $1 \le k \le K$ where e_k is a unit vector with the kth component equal to one and all the other components equal to zero.

As in Van Leemput et al. (1999a) we represent an INU bias field as a linear combination $\sum_{j=1}^{J} c_j \phi_j$ of J smoothly varying basis functions $\phi_j(x)$, where x denotes the spatial position and $C=\{c_1, c_2, \ldots, c_j\}$ denote the bias field parameters. For mathematical convenience and similarly to Garza-Jinich et al. (1999), Wells et al. (1996), Van Leemput et al. (1999b) and Zhang et al. (2001), we assume that the intensity of the voxels that belong to class k are normally distributed after log transformation with mean μ_k and standard deviation σ_k grouped in $\theta_k = \{\mu_k, \sigma_k\}$. Let $\Phi_y = \{\theta_1, \theta_2, \ldots, \theta_K, C\}$ represent the overall model parameters. This log transformation of the data makes the multiplicative bias field additive, ameliorating problems with numerical stability and enabling the existence of a linear least square solution for the coefficient optimisation (Van Leemput et al., 1999b).

Defining Φ_y as the model parameters, the overall probability density for y_i is

$$f\left(y_i \mid \Phi_y\right) = \sum_k f\left(y_i \mid z_i = e_k, \Phi_y\right) f(z_i = e_k) \tag{1}$$

with

$$f\left(y_i \mid z_i = e_k, \Phi_y\right) = G_{\sigma_k}\left(y_i - \mu_k - \sum_j c_j \phi_j(x_i)\right) \tag{2}$$

where $G_{\sigma_k}()$ denotes a zero-mean normal distribution with standard deviation σ_k. Eq. (1) can be seen as a mixture of normal distributions.

Thus, by assuming statistical independence between voxels, the overall probability density for the full image can be given by

$$f\left(y \mid \Phi_y\right) = \prod_i f\left(y_i \mid \Phi_y\right) \tag{3}$$

The Maximum Likelihood (ML) parameters for Φ_y can be found by maximisation of $f(y|\Phi_y)$, giving the following update equations for the model parameters:

$$\mu_k^{(m+1)} = \frac{\sum_{i=1}^{n} p_{ik}^{(m+1)} \left(y_i - \sum_{j=1}^{J} c_j^{(m)} \phi_j(x_i)\right)}{\sum_{i=1}^{n} p_{ik}^{(m+1)}} \tag{4}$$

Fig. 1. Segmentation of a BrainWeb T1-weighted dataset with 3% noise and 20% INU: left) BrainWeb ground truth segmentation; centre) MAP with MRF but without the proposed improvements; right) proposed method.