MEASURING CORTICAL THICKNESS FROM VOLUMETRIC MRI DATA

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ABSTRACT

Cortical thickness is one of the most fundamental measurements for population and longitudinal studies in brain imaging. Therefore, measuring cortical thickness from MRI data is an important topic in computational brain imaging. In this work we present a new approach for measuring cortical thickness that is based on fitting balls into the gray matter mantle of the brain by maximizing the amount of probability-weighted gray matter that is contained in each ball. Previous methods often solely measure the distance between the extracted inner and outer boundary surfaces of the gray matter, and ignore the underlying probabilities that are assigned to each voxel in the MRI volume, a natural consequence of noise and partial volume effects present in MRI. Moreover, our proposed framework works directly on the volumetric data, without relying on an accurate segmentation, which is only used as an initial condition for the optimization step. We present the underlying concepts of the proposed framework and examples.

Index Terms— Magnetic resonance imaging, thickness measurement, computational anatomy.

1. INTRODUCTION

Neuroscience has shown a long term interest in measuring cortical thickness, beginning with the manual measurements of [1, 3]. In recent years automatic approaches have been proposed that estimate cortical thickness from Magnetic Resonance Imaging (MRI), e.g., [4, 8, 9, 10, 19]. Measurements of the cortical thickness support neuroscientists in their investigations of normal and abnormal change in the cerebral cortex and are therefore of great current interest (see [17] and the references therein). Studies have suggested that various diseases such as AIDS or Alzheimer may affect the cortical thickness [18]. Thus, by measuring the change of the cortical thickness one hopes to earlier detect certain diseases and provide better cures for the patients.

Cortical thickness varies over different regions of the brain in the range of $2 - 5mm$. Ideally, one would like to measure cortical thickness in-vivo as the length of the axonal connections along the columnar organization of the cortex [9, 10]. However, due to the current limited resolution of MRI (usually $1\ mm^3$, improving at high magnetic fields), the axonal connections are not distinguishable and thus such a measurement is not currently possible. Therefore, alternative measurements for cortical thickness based on MRI data have been proposed. These approaches can be categorized into *surface* and *volume* based methods. Most of the existing methods work with the boundary surfaces of white matter and gray matter (WM/GM surface, inner surface) and gray matter and cerebro-spinal fluids (GM/CSF surface, outer surface). Once these surfaces are extracted from the MRI data, surface based methods either compute the minimum Euclidean distance between points on the inner surface to points on the outer surface [4, 8, 9, 11], or solve the Laplace equation, [6, 7], and measure cortical thickness along the characteristics of the heat flow from inner to outer surface (see Fig. 1 for an illustration). A Bayesian construction of cortical thickness based on the extracted surfaces was proposed by [12]. The volume based method of [10] is purely voxel-based and avoids the extraction of the said boundary surfaces as meshes. The voxels are (hard) classified into belonging to WM, GM, CSF and then cortical thickness is estimated using a 3D Euclidean distance transform w.r.t. the voxels of the WM boundary.

With the approach proposed in the present paper we aim at improving currently available methods in the following main directions. So far, once the segmentation of the MRI volume data into WM, GM and CSF voxels is performed, it is ignored that each voxel actually has a certain probability of belonging to either WM, GM or CSF. This is a natural consequence of partial volume effects and noise in the MRI, and ignoring these probabilities translates into throwing away important available information. To bring these probabilities back into cortical thickness estimation, we employ a set of balls that we center in the gray matter mantle by optimizing their position and radius via minimizing an appropriate energy function. The cortical thickness is then estimated from

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the optimized set of balls. We thereby avoid accurate hard segmentation, which is often problematic and not achievable, and use the whole MRI data and not just the results of hard labelling processes. Our underlying approach is presented in Section 2 and initial results are discussed in Section 3. Before this, we briefly review some previous work in the subject.

1.1. Previous Work

There are various ways of measuring cortical thickness in the literature and the research community has not yet agreed on a precise definition of a thickness measure that can be computed from MRI brain data. Here we discuss previous work that uses the extracted inner and outer surfaces for distance computations. These methods suffer from inaccuracy in the segmentation process and discard in the way important available information at the moment they make hard labelling decisions. The connections of these works with ours will be clear after their presentation.

So-called *coupled surface methods* [4, 11] define the cortical thickness as the Euclidean distance between corresponding points on the inner and outer surface. This thickness measure has the disadvantage that if the surfaces are shifted then the correspondence does not yield a meaningful distance measure (Fig. 1(a)).

The *closest point methods* such as [12] compute for each point on one surface the closest point on the other surface. The main problem here is that this thickness definition is not symmetric, which means that we do not get the same measure if we interchange inner and outer surface (Fig. 1(b)). Furthermore, this definition significantly underestimates the cortical thickness in areas of high curvature (Fig. 1(b)).

Laplace methods [6, 7, 19] solve Laplace's equation for the potential between the inner and outer surface, thereby providing a more elaborated point correspondence between both surfaces. Then the length of the flow lines — which are orthogonal to both surfaces — defines the cortical thickness (Fig. 1(c)). This mathematical model has been argued to give an anatomically plausible thickness measure, it assigns to each voxel in the gray matter mantle a unique curve (flow line) that measures the thickness. Still, the method solely works with the extracted surfaces and does not take into account the probabilities with which each voxel belongs to either GM, WM, or CSF.

2. METHODS

Computing cortical thickness from MRI brain images is fundamentally based on the classification of brain matter into the major tissue classes: gray-matter (GM), white-matter (WM) and cerebro-spinal fluid (CSF). In previous work this classification is used to extract the WM/GM and GM/CSF boundary surfaces. Then the cortical thickness (i.e., the thickness of the gray matter mantle) is computed using these two boundary surfaces of the gray matter. In our work we follow these traditional steps just to get a first estimate for the cortical thickness and to generate initial positions and radii for the balls we use in our optimization procedure. These initial ball positions and radii are then subject to optimization using the original MR image information. We are thereby not so strongly affected by inaccuracies in the segmentation and we use the whole available MRI information and not just the (often wrongly) labelled one. In addition, in contrast with the above mentioned approaches, the proposed technique is not based on explicit point correspondences between the gray matter boundaries.

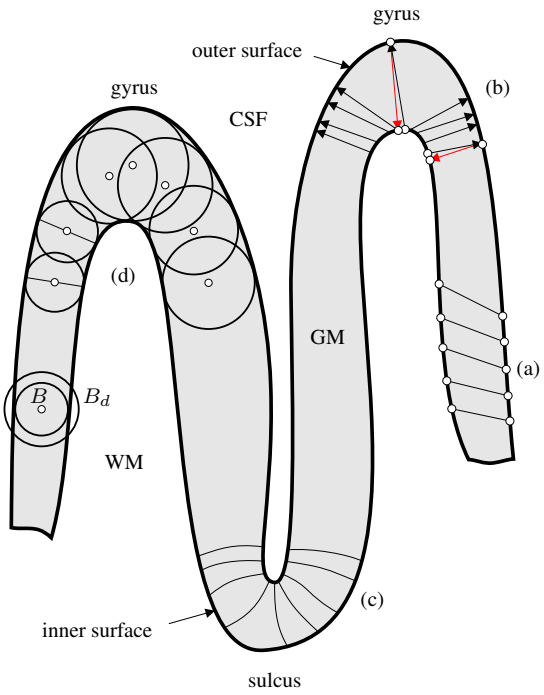

Fig. 1. *Illustrating various ways of measuring cortical thickness based on the inner and outer surface: (a) coupled-surface methods, (b) closest point methods, (c) Laplace methods, (d) our method.*

2.1. Initial Positions and Radii of Balls

The T1-weighted MRI brain volumes we used ($1\ mm^3$ isotropic voxels) were acquired at the Montreal Neurologic Institute and provided to us by Dr. Alan C. Evans. Using the Brain Extraction Tool[1] [16], skull stripping was performed and afterwards the inner and outer surfaces were extracted using FreeSurfer[2] [5]. Using topologically correct triangle meshes of the inner and outer surface we compute pairs (a_i, b_i) of corresponding closest points on both surfaces as in [4]. Then the midpoint $c_i = 1/2(a_i + b_i)$ gives the initial center position for the ball B_i and $r_i = \|a_i - b_i\|$ is the initial radius. While most prior techniques will end up here (with variations in the computation of the correspondences and distances, which we

[1] *Brain Extraction Tool (BET)*, see http://www.fmrib.ox.ac.uk/fsl/bet/
[2] *FreeSurfer*, see http://surfer.nmr.mgh.harvard.edu/

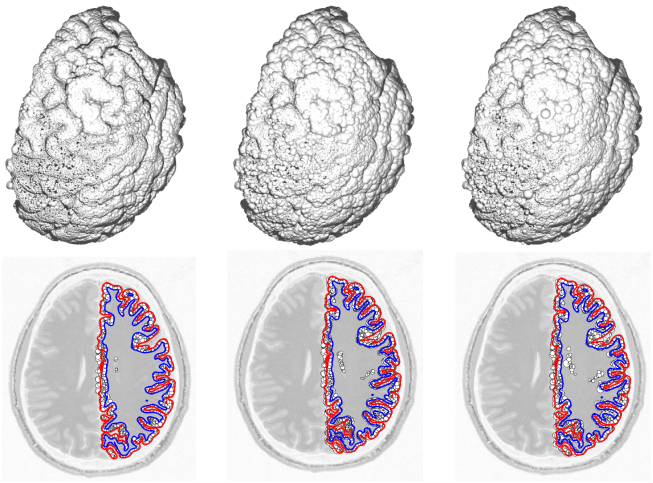

Fig. 2. *Balls used for cortical thickness estimation: (left) the initial position, (middle) radius optimization, (right) simultaneous radius and center position optimization.*

could incorporate as well), this is just the initialization for our proposed approach, further optimizing for the position and radius of these balls.

2.2. Partial Volume Estimation

Due in part to the limited spatial resolution of the scanning devices and the strongly folded structure of the brain, noise is introduced in medical images, including that which is known as the *partial volume effect* (PVE). In addition to being noisy, a single voxel in an MR image may be composed as a mixture of tissue types and hence a so-called soft segmentation method is advantageous over a strict classification into exactly one class. The partial volume effect may lead to erroneous surface segmentation, [15], and thus wrong cortical thickness estimates if the measure is solely based on the extracted inner and outer surface. Note that considering the average gray matter thickness and the MRI resolution, an error in one voxel classification could lead to thickness estimations biased by 25-50%.

Partial volume estimation, i.e. the estimation of the amount of each tissue type within each voxel, has received considerable interest in the literature (see [14] and the references therein). Since partial volume estimation is not the topic of the present paper, for illustration of our proposed framework we use a naive Bayes classifier, [2], and obtain a posterior probability P_{GM}, P_{WM}, and P_{CSF} of each voxel belonging to GM, WM, and CSF. However, we are aware that a more sophisticated approach such as the one presented in [14] would likely improve our results. In order to achieve sub-voxel accuracy and better control over the PVE problem, we sub-sample the voxel data. Using trilinear interpolation we divide each voxel into first 8 smaller congruent cubes and then by repeating the procedure into a total of 64 sub-voxels.

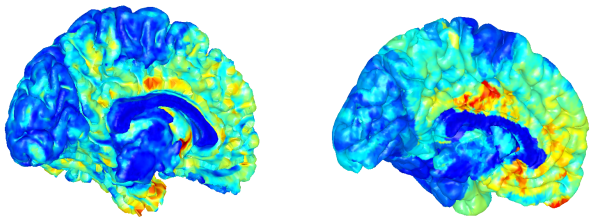

Fig. 3. *Computed thickness color coded onto the outer surface of two different hemispheres (blue thinner, red thicker).*

2.3. The Optimization Function

Given a ball B with center $c = (x, y, z)$ and radius r, we formulate the following objective function,

$$F(x, y, z, r) = \sum_{v \in B} P_{GM}(v) - \alpha P_{WM}(v) - \beta P_{CSF}(v), \quad (1)$$

where we sum the posterior probabilities over all sub-voxels v contained in the ball B. The goal is to maximize the objective function to get a ball that contains as much gray matter as possible and as little white matter and cerebro-spinal fluids, weighted by their actual probability (in contrast with classical approaches where voxels are pre-classified and then those in the gray matter count as "one" and outside of it count as "zero"). The parameters α and β control how strong the objective function penalizes the posterior probabilities of non-gray matter tissues.

Our optimization framework now proceeds in the following way. To correct for possible over- and underestimates in the initial thickness we first solely optimize the radius of each ball by minimizing the modified objective function $F(r)$ where the only variable is the radius r. Then we build a priority queue such that those balls that need further optimization are processed first. To quickly assess the current quality of a ball we use the ball B and an offset ball B_d with radius $r + d$. Then we classify the sub-voxels inside the mantle $B_d \backslash B$. A ball is in good position if B only contains gray matter voxels with a probability greater than $1/2$ and if $B_d \backslash B$ contains for all three matters (GM, WM, CSF) voxels with a probability greater than $1/2$. According to the priority queue build with the ball and offset ball ("bad" balls are dealt with first), we now optimize the center position and the radius with a trust region optimization [13] maximizing $F(x, y, z, r)$ of Equ. (1).

3. EXAMPLES AND DISCUSSION

We present results of our algorithm on two different MRI brain volumes. Fig. 2 shows the set of balls in their initial position, after radius optimization, and in their final optimized position. Fig. 2 (top row) illustrates the complete set of balls. Fig. 2 (bottom row) shows one slice of the MRI data overlaid with the intersection curves of the inner and outer surface

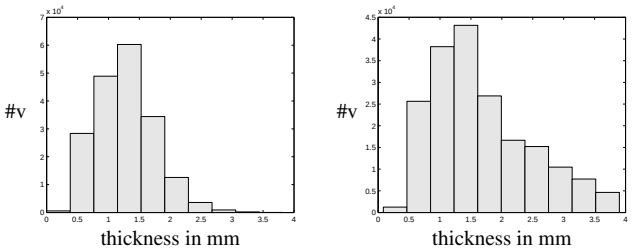

Fig. 4. *Initial and final thickness distribution for one brain.*

and the circular intersections of the set of balls. Figure 3 illustrates the computed thickness color coded on the outer surface for two different hemispheres. Figure 4 illustrates the initial and final thickness distribution. The shift towards a slightly larger thickness is expected since we start with a conservative estimation.

There are a number of issues we would like to further improve in future work. The current black box trust region optimizer we are using lets some balls blow up. On average roughly 3% of all balls suffer from these numerical instabilities and these balls are clearly seen in Fig. 2 as the ones that are obviously too large and out of place. Since currently each ball is optimized independently from the other balls the overall set of balls is not distributed optimally. We plan to address this issue by means of a relaxation that shall distribute the balls more regularly throughout the gray matter. By means of decimation we would like to optimize the number of balls necessary to give a sufficiently detailed cortical thickness measure. To validate our results we need to compare them to thickness estimates computed with other approaches.

To avoid using the extracted inner and outer surfaces we could employ the following user interaction. A human expert clicks one point as the center for the first ball inside the gray matter mantle. This seed ball is then optimized automatically and we could propagate balls further throughout the whole gray matter mantle.

Results in these directions will be reported elsewhere.

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