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# Cortical surface registration using spherical thin-plate spline with sulcal lines and mean curvature as features

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## ABSTRACT

Analysis of cortical patterns requires accurate cortical surface registration. Many researchers map the cortical surface onto a unit sphere and perform registration of two images defined on the unit sphere. Here we have developed a novel registration framework for the cortical surface based on spherical thin-plate splines. Small-scale composition of spherical thin-plate splines was used as the geometric interpolant to avoid folding in the geometric transform. Using an automatic algorithm based on anisotropic skeletons, we extracted seven sulcal lines, which we then incorporated as landmark information. Mean curvature was chosen as an additional feature for matching between spherical maps. We employed a two-term cost function to encourage matching of both sulcal lines and the mean curvature between the spherical maps. Application of our registration framework to fifty pairwise registrations of T1-weighted MRI scans resulted in improved registration accuracy, which was computed from sulcal lines. Our registration approach was tested as an additional procedure to improve an existing surface registration algorithm. Our registration framework maintained an accurate registration over the sulcal lines while significantly increasing the cross-correlation of mean curvature between the spherical maps being registered.

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## 1. Introduction

The cortex of the brain is regarded as a highly folded sheet (i.e., surface) of gray matter, which implies that the cortical surface is a two-dimensional (2D) manifold in a three-dimensional (3D) space. Analysis of cortical patterns plays a key role in neuroimaging studies (Gholipour et al., 2007). Cortical patterns refer to features that characterize the brain cortex; they include sulcal lines, gyral lines, sulcal depth, curvature, surface area, gray matter density, and cortical thickness. For example, Thompson et al. (2004) used cortical thickness, gray matter density, and gyral lines for comparison of a diseased group (i.e., Alzheimer's disease and schizophrenia patients) with a normal group. Fillard et al. (2007) used tensor fields to model the variability of the cortex via sulcal lines. In all of these applications, it is essential to bring two or more cortical patterns into spatial alignment, so that they may be compared in the same spatial framework for appropriate analysis of cortical patterns. The

process of spatial alignment, commonly known as registration, is therefore an important element in neuroimaging analysis.

Volumetric registration of the brain based on intensity features is commonly performed (Hill et al., 2001); its aim is correct registration of the whole brain volume on average. However, the cortical surface is only a small fraction of the 3D volume of the brain, so an accurate volume registration does not necessarily mean an accurate cortical surface registration. Volume registration methods often lack sensitivity for correct registration of complex cortical patterns (Hellier et al., 2003). Surface-based registration in which the features are derived solely from the surface of interest will have better sensitivity for registering cortical surfaces. Many surfacebased registration methods have adopted sulcal and gyral lines for explicit modeling of cortical geometry (Gholipour et al., 2007). In general, surface-based registration methods are better suited for correct registration of cortical patterns (Hellier et al., 2003).

Mapping of the complex cortical surface onto an equivalent domain to perform an analysis is common. A simple 2D domain, including a square or the surface of a sphere, is preferred, as the analysis becomes more tractable. Some researchers map the cortical surface to a canonical square (Thompson et al., 2004). This process requires an expert who can identify the anatomical structure known as the inter-hemispheric fissure, which is constrained

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to be the boundary of the unit square. Many researchers map the cortical surface to a canonical spherical space (Fischl et al., 1999; Robbins, 2003; Zou et al., 2007). Spherical representation of the cortical surface allows a common scale-invariant framework to compare cortical surfaces, as large and small brains are mapped onto the same unit sphere. Another advantage is that deeply hidden structures are brought to the surface, and can be easily visualized. In addition, optimization occurs over a 2D parameter space reduced from the 3D space of the volumetric registration. Sulcal and gyral lines are the surface landmarks that are most commonly utilized for registration of different brains (Van Essen, 2004). These landmarks are typically used to define anatomical structures in the cortex. Many existing surface registrations enforce matching sulcal landmarks (Robbins, 2003; Van Essen, 2004), which guarantees accurate registration for areas where sulcal lines exist. However, correct registration of sulcal lines does not imply correct registration of the entire cortex. One reason is that the area of sulcal lines is a small portion; thus, registration of sulcal lines would lead to correct registration of only parts of the cortex, not the whole cortex. The other reason is that the sulcal lines themselves have inherent variability (Paus et al., 1996). A sulcal line of a patient might differ significantly depending on the expert or the computer algorithm chosen to produce the sulcal lines. Zou et al. (2007) proposed a registration algorithm that is sensitive to correct registration of both the sulcal lines and the entire cortex. To implement matching of the entire global cortex, they adopted a method utilizing spherical thin-plate splines (TPS) to implement sulcal line matching, and minimized the mean curvature difference between the cortical surfaces.

We propose a similar registration framework based on spherical TPS and mean curvature matching. Zou et al. (2007) used the spherical TPS in its original form while our method uses a novel modified version of spherical TPS to approximate the widely accepted large deformable diffeomorphic metric mapping (LDDMM). Zou et al. (2007) validated their algorithm using the Dice overlap index over a few anatomical regions; however, systematic quantification was missing. The Dice overlap index measure is based on the region of interest (ROI) and is less sensitive to registration errors occurring within the ROI than is a measure such as landmark distance. To validate our method, we performed systematic computation of sulcal landmark distances over the seven sulcal landmarks.

Spherical TPS is a natural extension of the well known geometric interpolant TPS into the spherical space (Wahba, 1981). TPS has been widely adopted in volumetric registration, where the 3D spatial coordinates are interpolated. Among all geometric interpolants, TPS is known for maximal smoothness (Bookstein, 1989); thus, it is well suited for modeling smooth geometric deformations. TPS-based methods are well suited for modeling landmarks. Landmarks are modeled as collections of corresponding points in TPS based methods. Some researchers have used spherical TPS to model deformation between two cortical surfaces (Zou et al., 2007). Some went further and modeled the landmarks as parameterized corresponding curves (Durrleman et al., 2007) in a LDDMM setting. The most accurate modeling of cortical landmarks (e.g., sulcal lines) is that of Durrleman et al. (2007); however, it is computationally expensive.

The main contributions of this study are: (1) we have developed a novel spherical TPS based surface registration method; (2) we have validated the method with seven different sulcal lines from thirty brain scans; and (3) we have tested our algorithm as an additional post-processing procedure to improve an existing surface registration algorithm, the Montreal Neurological Institute (MNI)'s surface registration algorithm. Our registration framework utilizes the following components: (1) surface-based registration; (2) spherical representation of the brain; (3) sulcal lines as surface landmarks; and (4) spherical TPS as a geometric function.

#### 2. Materials and methods

## 2.1. Subjects

The sample for this study consisted of 30 normal patients who underwent high-resolution T1-weighted volume magnetic resonance imaging (MRI) at the Samsung Medical Center, Seoul, South Korea. The Mini-Mental State Examination (MMSE) was also performed. The study group had no history of neurological or psychiatric illnesses or abnormalities. The mean age of the control group was  $71.7 \pm 4.9$  (mean  $\pm$  STD), and the ratio of sexes was 12/18 (male/female). Cognitive functioning of the control subjects was confirmed to be within normal limits, as assessed by MMSE and neuropsychological testing. We obtained informed consent from all patients. The study was approved by the Institutional Review Board of the Samsung Medical Center.

### 2.2. MRI scan acquisition

Three dimensional T1-weighted SPGR scans were acquired using a 1.5 T MRI scanner (GE Signa, Milwaukee, WI, USA) with the following imaging parameters: coronal slice thickness, 1.5 mm; echo time, 7 ms; repetition time, 30 ms; number of excitations, 1; flip angle,  $45^{\circ}$ ; field of view,  $22 \pm 22$  cm; and matrix size,  $256 \times 256$  pixels. A total of 30 scans were collected.

## 2.3. Cortical surface extraction and pre-processing

Input images were processed using the MNI software (Ad-Dabbagh et al., 2006; Robbins et al., 2004), which includes a surface registration algorithm that performs cortical surface extraction and a non-rigid registration of cortical surfaces. Details of cortical extraction are described below. Using an affine transformation, native MR images were first normalized into a standardized stereotaxic space and then corrected for intensity non-uniformity. The registered and corrected volumes were then classified into white and gray matter, cerebrospinal fluid, and background using a neural-net classifier. Next, the Constrained Laplacian-based Automated Segmentation with Proximities (CLASP) algorithm (Kim et al., 2005) was used for automatic extraction of the hemispheric surfaces of the cortex. With the extracted surface, we applied a 2D non-rigid registration algorithm based on the geodesic distance from the gyral crown vertex with an appropriate smoothing term (Robbins et al., 2004). Simply put, the registration encourages matching of gyral patterns with appropriate smoothing. Our registration algorithm (to be described later) is an additional procedure to improve upon the existing MNI's surface registration algorithm.

## 2.4. Automatically extracted sulcal lines

Sulcal lines are major landmarks on the cortical surface. A sulcal line is commonly defined as a valley in the cortical surface with high curvature within the sulcus. We adopted an algorithm for automatic extraction and labeling of major sulcal lines (Lyu et al., 2010; Seong et al., 2010). The algorithm adopted anisotropic skeletons of sulcal regions to follow the highly variable shape of the cortical surface and was shown to be robust to local shape variability in different human brains (Seong et al., 2010). We performed automatic extraction of seven sulcal lines. They included the superior temporal, central, post central, superior frontal, inferior frontal, parieto-occipital, and calcarine sulcal lines; for the remainder of this study, the term "seven sulcal lines for the left hemisphere of one patient, where the sulcal lines are assigned numbers; superior temporal (number 1), central (number 2), post central (number 3),

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