

## Introduction

Many anatomical MRI studies on the human brain have been focused on cortical thickness of laminar structure of the cerebral cortex, a highly folded sheet of gray matter. Cortical thickness varies between 1.3mm and 4.5 mm in the various parts of the brain, with an overall average of about 2.7mm[1]. The cortical thickness is interesting in a wide variety of studies on neurodegenerative and psychiatric disorders, such as aging, Alzheimer's disease and other dementias, Huntington's disease, sclerosis and schizophrenia. Recent measurements of cortical thickness are based on segmentation information from MRI volumes. Thickness has been measured as the distance between exterior and interior surfaces (the boundary between the gray matter and cerebrospinal fluid (CSF) and the boundary between the white and gray matter)[2,3,4]. However, accurate extraction of the outer surface remains a major problem, especially when two gyri in reality separated by CSF appear fused in MRI images due to the resolution of MRI images and highly folded structure of the cortex. In this research, we provide a new direct parametric statistical model to estimate the cortical thickness, which nowhere needs the reconstruction of the exterior surface.

## Cortical Geometry

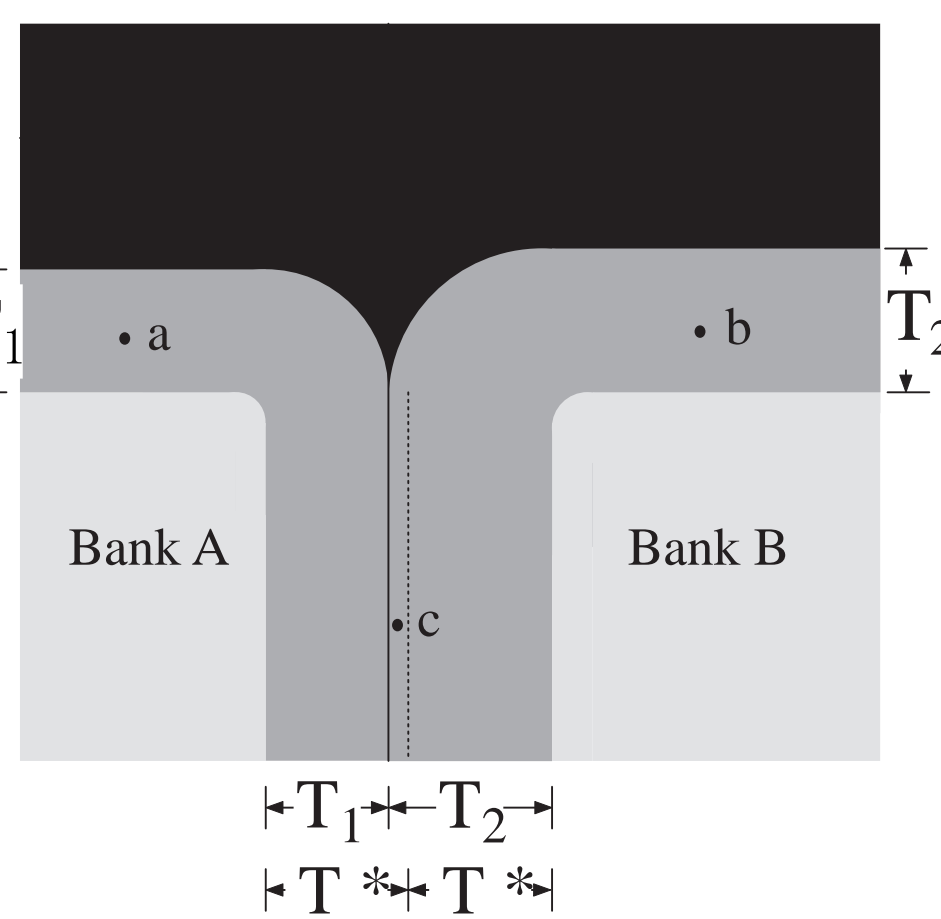


Figure 1 shows two naturally occurring 2D manifolds of the cortex, one at the boundary of gray and white matter, the other at the exterior surface of gray matter. Some of the exterior surface of gray matter is contiguous with CSF; some is contiguous with the gray matter on the other side of the sulcus. In general, the Gray/White boundary manifold is geometrically better behaved than the second Gray/CSF manifold as it does not intersect itself. We call regions of the cortex where the exterior boundaries of two different gyri touch "hidden," and places where they do not touch "exposed."

Figure 1: Illustration of Cortical Geometry.

## MRI Intensity-Distance Map

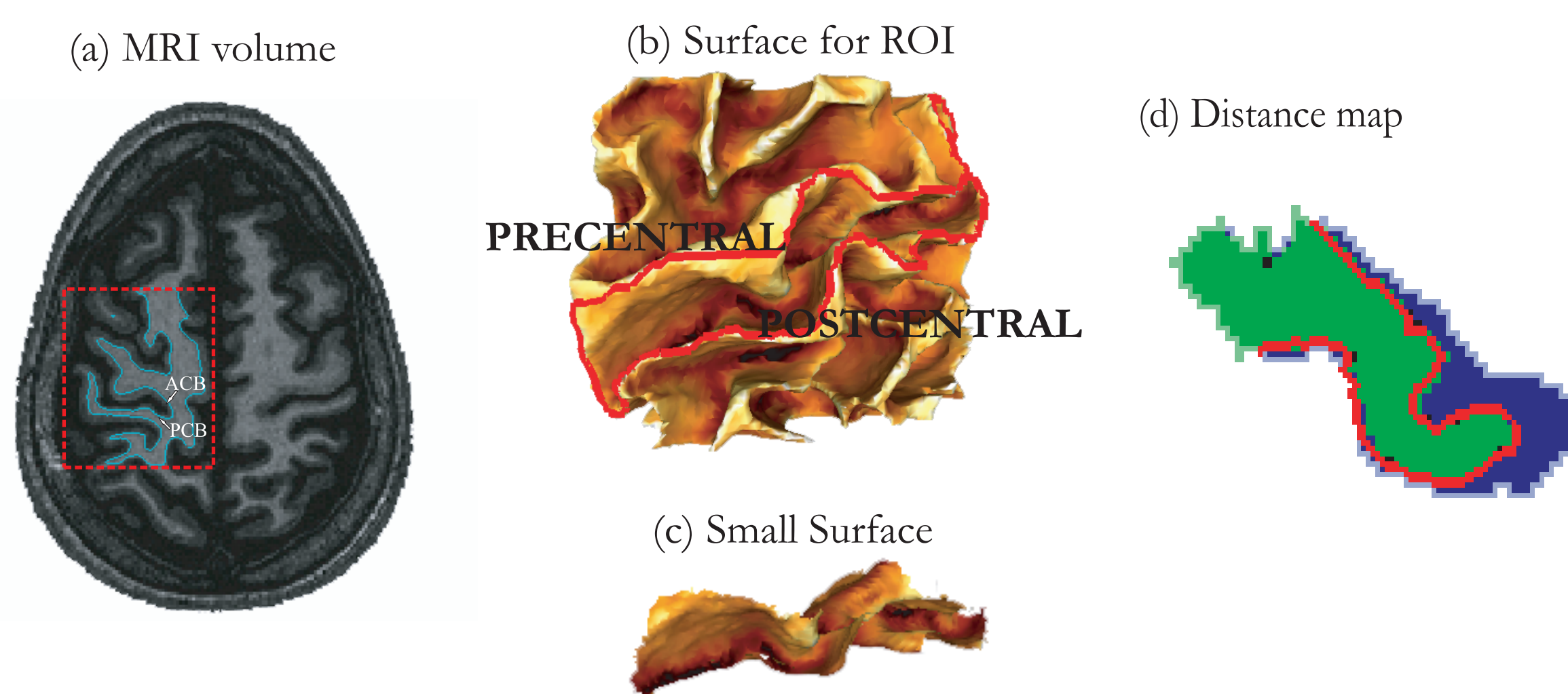


Figure 2: Cortical Distance Map. Panel (a) shows the MRI volume. The region of interest (ROI) in red is where panel (b) shows the isocontoured surface with ACB and PCB denoting the anterior and posterior banks of the central sulcus, respectively. The region marked by red line depicts the two banks of the central sulcus on the surface extracted by dynamic programming. Panel (c) shows the small surface associated with the central sulcus. Panel (d) shows the distance map containing the voxels in the ROI that are the closest to the surface shown in panel (c). Green and blue correspond to positive and negative distances, respectively.

We introduce local normal coordinate system, for which an orthogonal frame consists of two axes spanning the tangent plane to the Gray/White surface and the third normal axis measures the relative normal distance from the Gray/White surface to the center of individual voxels [5]. The MRI image intensities  $I(x_k), k=1,2,\dots,n$ , are augmented by the normal distance calculation for each voxel,  $(I,D)(x_k), k=1,2,\dots,n$ , where  $(I,D):X \rightarrow R \times R$  consists of the image intensity value and the distance to the cortical manifold. We term the joint data structure as the MRI-distance map.

## A Marked Poisson Process Model of the Intensity-Distance Histogram

A basic insight recognizes that the cortical thickness is directly evidenced by the change in tissue type as a function of the normal distance. For example, the white matter has a negative normal distance and the gray matter as well as CSF has a positive normal distance. However, CSF has a greater distance than the gray matter does.

Reference:

- [1] von Economo, C., 1929, Oxford Univ. Press, London.
- [2] Fischl B. and Dale A. M., 2000, PNAS, 97:11050-11055.
- [3] Zeng X. et. al., 1999, IEEE TMI, 18:100-111.
- [4] MacDonald D., 2000, NeuroImage, 12:340-356.
- [5] Miller M. I. et. al., 2003, PNAS, 100:15172-15177.

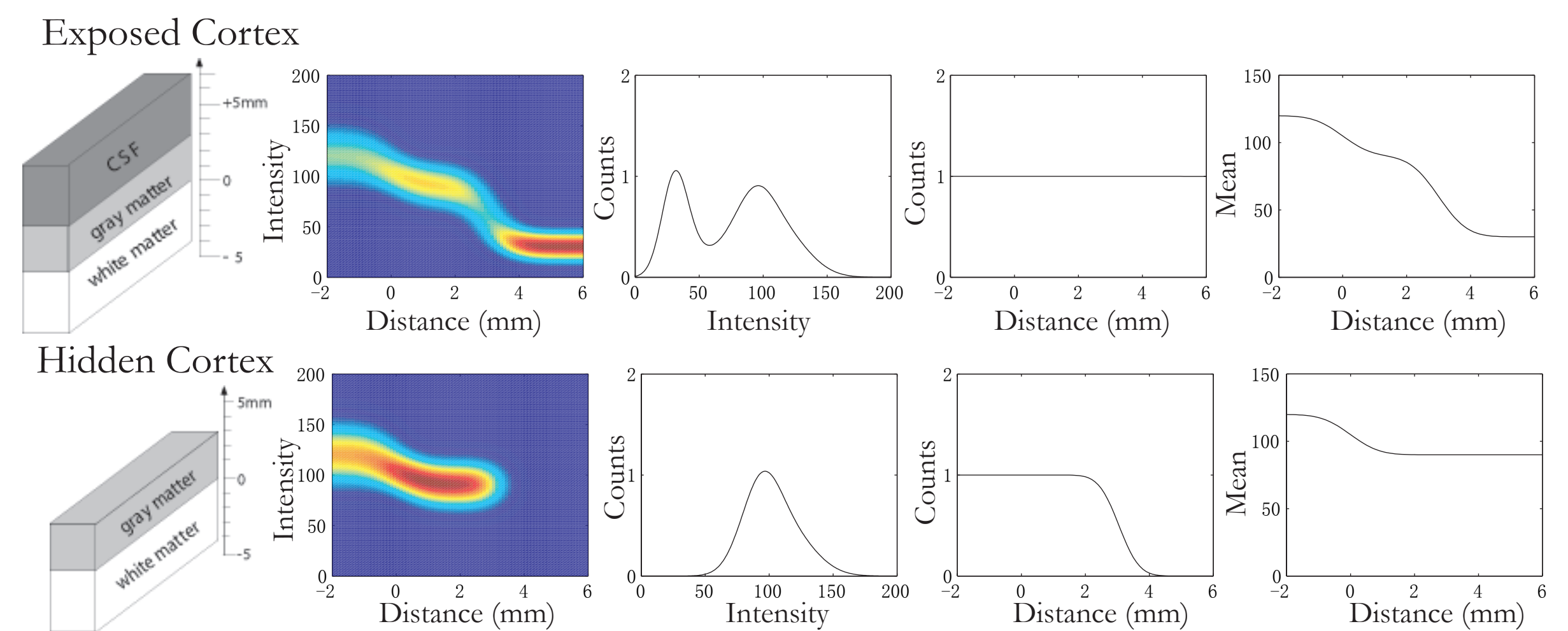


Figure 3: Column 1 illustrates geometric structures of exposed (top) and hidden (bottom) cortex. Columns 2-5 show the intensity-distance histogram, intensity histogram, distance histogram, and mean curve respectively. Rows represent simulations with effects of partial volume and surface location uncertainty.

We generate the Intensity-Distance Histogram (IDH) from the MRI-distance map, which is a two-dimensional data structure counting the number of voxels of some image intensity at a particular distance interval. The amount of voxels at various distances is modeled as a Poisson arrival process; the distribution of intensity is modeled as a Gaussian random field conditioned by the normal distances. Based on these two assumptions, the log-likelihood function of the IDH is parameterized by the cortical structural parameters, such as cortical thickness, tissue properties, as well as effects of partial volume and surface location uncertainty.

## Results and Discussion

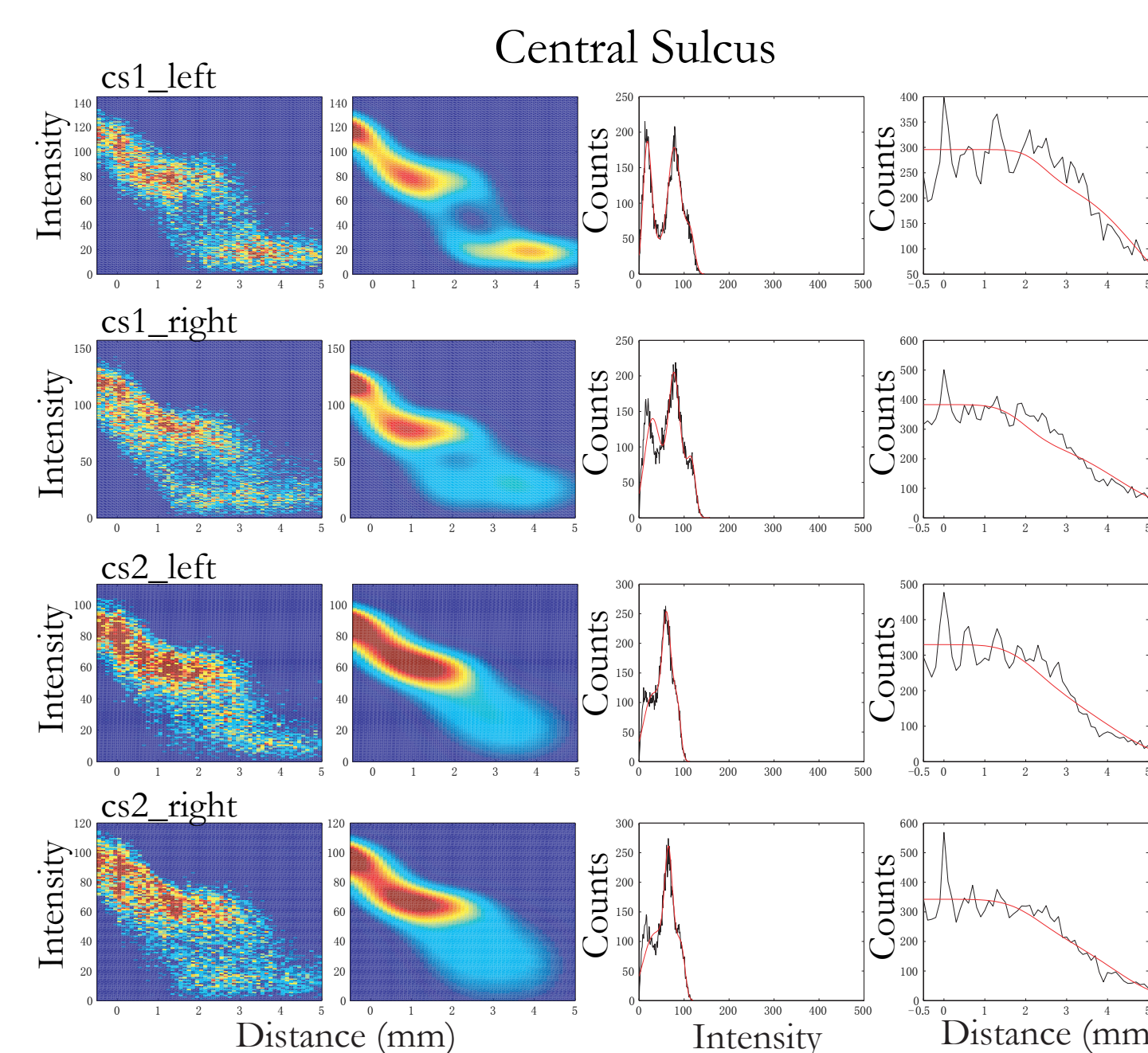


Figure 4: Optimal fits to the anterior and posterior banks of the central sulcus. Columns 1-4 show measured IDH, fitted IDH, intensity histogram and distance histogram, respectively. Black lines depict the measured data; red lines depict the fitted curves. Measured and fitted IDHs are plotted using identical color scale.

To validate and test the model, we estimated cortical thicknesses for anterior and posterior banks in the left and right central sulcus of 6 healthy subjects (anterior and posterior banks of the central sulcus as identified in Figure 2). These two banks are remarkable for having the largest difference in cortical thickness when the cortex moves from a sulcus to a gyrus[1]. We hypothesized that our model would successfully replicate von Economo's observations.

Figure 4 gives representative fits for the central sulcus via four different measures, including measured IDH, fitted IDH, conventional image intensity histogram and count-rate versus distance histogram. In the measured IDHs, the two thicknesses for anterior and posterior banks of the central sulcus clearly are shown by intensity changes in the normal distance. It is also shown in the fitted IDHs. Overall, the model can capture the structure of the IDH. As our Cramer-Rao bound results (Figure 5) show the estimates of cortical thickness are highly concentrated around the true cortical thickness values in order of 0.01 mm, which implies the model we described is able to give precise estimation of cortical thickness for small pieces of cortex.

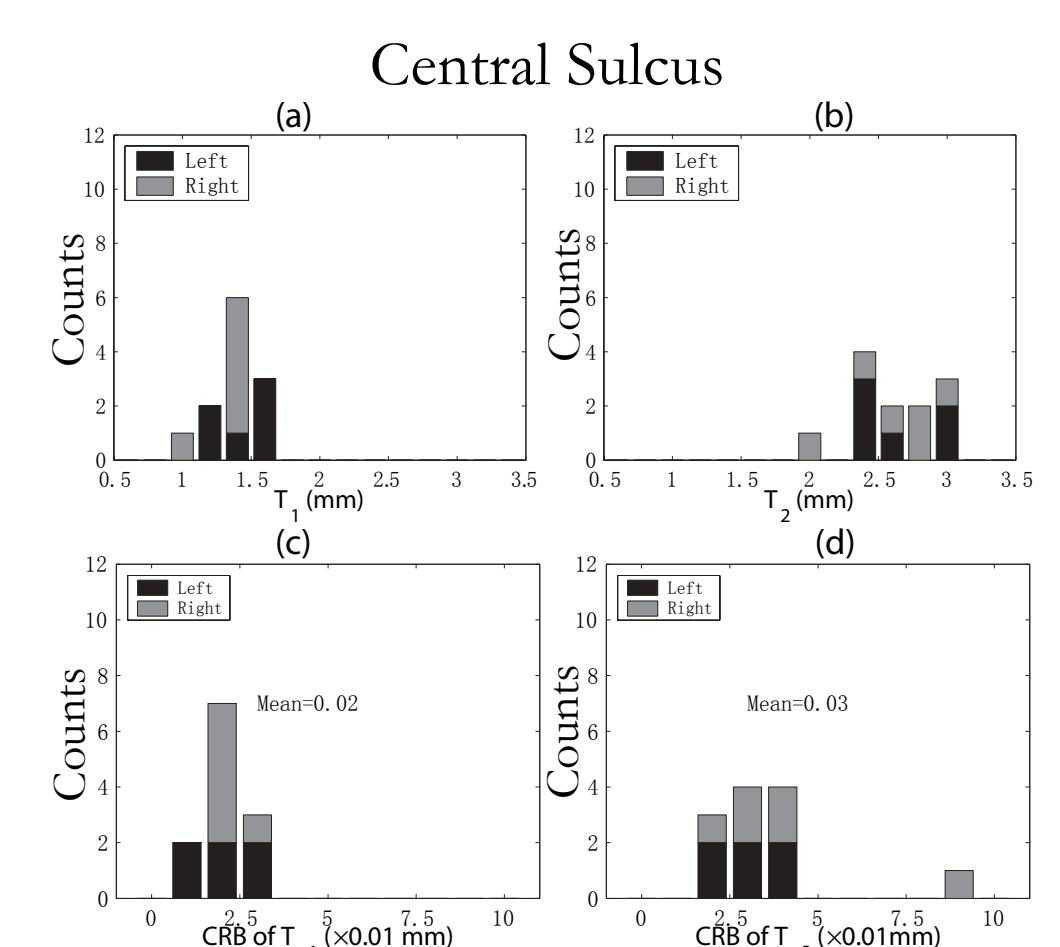


Figure 5: Distributions of thicknesses and square root of their Cramer-Rao Bounds for the central sulcus data.

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