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Nonparametric Estimation of Cortical Thickness via Heat Kernel Smoothing

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Introduction

The cerebral cortex has the topology of a 2D highly convoluted sheet. The cortical thickness has been used to characterize the brain shape [2]. The thickness measurements are always contaminated with noise. The noise may come from a scanner or due to the partial volume effect. In order to increase the signal-to-noise ratio and smoothness of measurements on data defined on the cortex, diffusion smoothing has been usually used before [1, 2]. We present a completely new smoothing technique that is simpler than diffusion smoothing for the estimation of the cortical thickness.

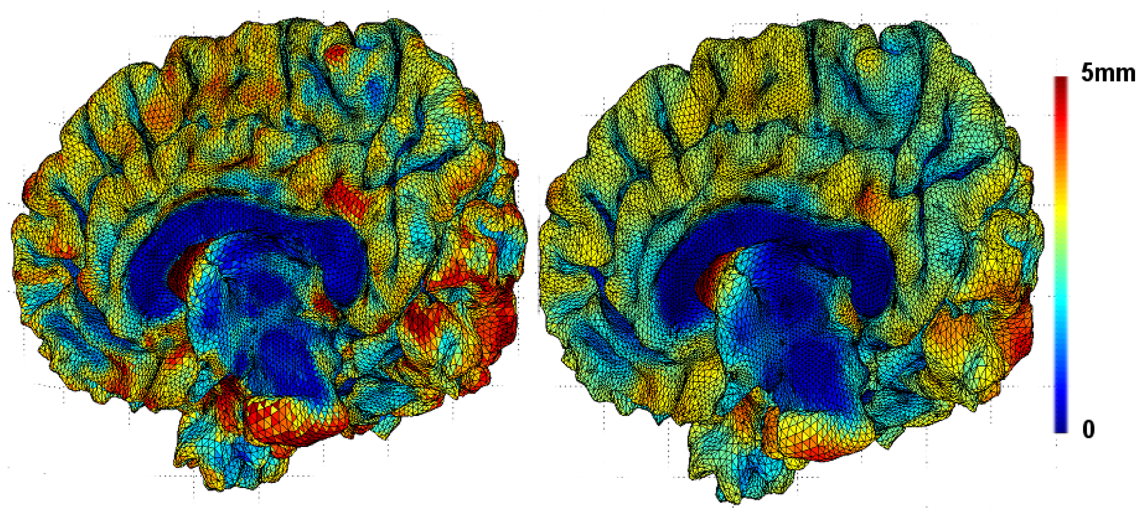

Figure 1: Left: original cortical thickness of the right hemisphere of an autistic subject. Right: heat kernel smoothing with $\sigma = 0.5$ and $k = 100$ iterations.

Methods

The cortical surfaces are segmented from T1 weighted magnetic resonance images using a deformable surface algorithm (FreeSurfer) [5]. The cortical thickness is computed as the minimum distance between the outer and inner cortical surfaces. The thickness measurement Y is assumed to follow the additive model of true signal θ plus noise ϵ on the cortex $\partial\Omega$:

$$Y(p) = \theta(p) + \epsilon(p), p \in \partial\Omega. \quad (1)$$

We assume ϵ to be a zero mean Gaussian random field. To overcome the complexity of solving diffusion equations to estimate θ on the cortex [2], we have developed a much simpler method based on the heat kernel smoothing which generalizes Gaussian kernel smoothing in Euclidean space. We define *heat kernel smoothing estimator* of θ to be the convolution

$$\widehat{\theta}(p) = K_\sigma * Y(p) = \int_{\partial\Omega} K_\sigma(p,q) Y(q)\, d\mu(q) \quad (2)$$

where $\mu(q)$ is a surface measure and heat kernel K_σ is defined in terms of the eigenvalues of the Laplace-Beltrami operator. Based on the *parametrix expansion* [6],

$$K_\sigma(p,q) \approx \frac{1}{(2\pi\sigma)^{1/2}}\Big[\exp -\frac{d^2(p,q)}{2\sigma^2}\Big] u_0(p,q)$$

where $d(p,q)$ is the geodesic distance between x and y. The first term $u_0(p,q) \to 1$ as $p \to q$. When the manifolds is flat, $u_0(p,q) = 1$ and $d(p,q) = \|p - q\|$, the Euclidean distance between p and q so the heat kernel K_σ becomes Gaussian kernel

$$G_\sigma(p,q) = \frac{1}{(2\pi\sigma)^{1/2}} \exp\Big[-\frac{\|p-q\|^2}{2\sigma^2}\Big].$$

Since kernel K_σ is not a probability distribution on manifolds, we normalize kernel in a small geodesic ball $B_p = \{q \in \partial\Omega : d(p,q) \le r\} \subset \partial\Omega$:

$$\widetilde{K}_\sigma(p,q) = \frac{\exp\big[-\frac{d^2(p,q)}{2\sigma^2}\big]\mathbf{1}_{B_p}(q)}{\int_{B_p}\exp\big[-\frac{d^2(p,q)}{2\sigma^2}\big]\, d\mu(q)} \quad (3)$$

where indicator function $\mathbf{1}_{B_p}$ is defined as $\mathbf{1}_{B_p}(q) = 1$ if $q \in B_p$ and $\mathbf{1}_{B_p}(q) = 0$ otherwise.

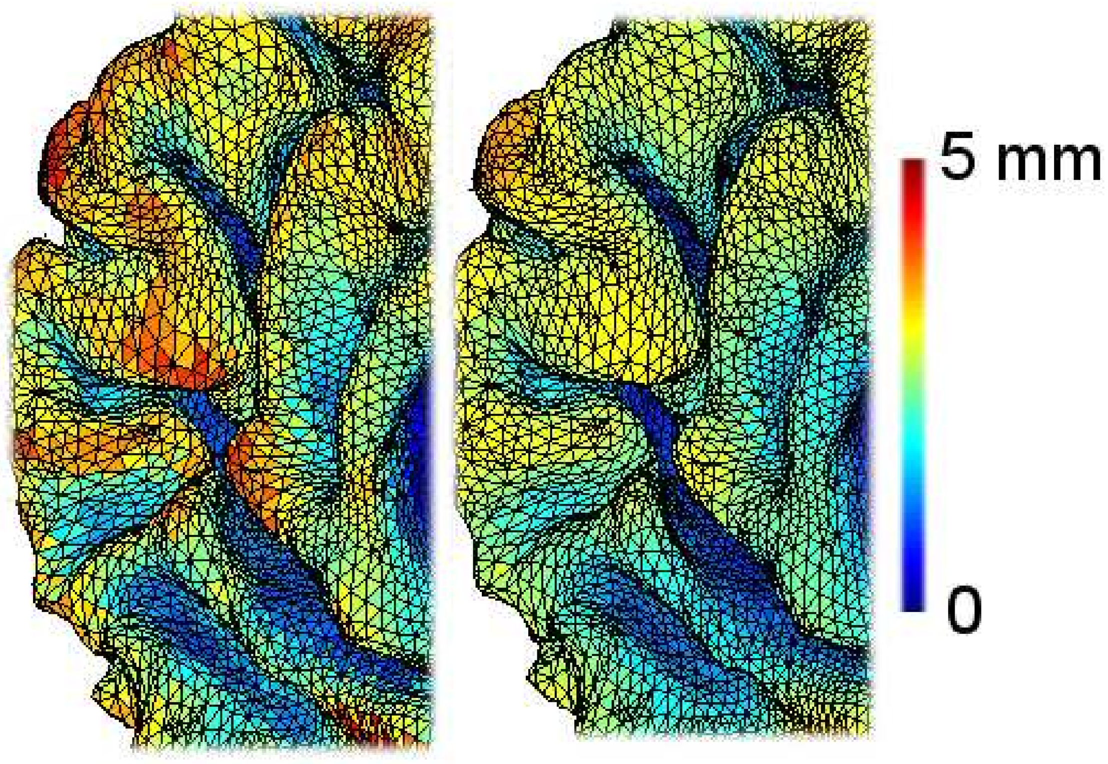

Figure 2: Cortical thickness computed at the posterior right hemisphere of the autistic brain and its iterated heat kernel smoothing with $\sigma = 0.5$ and $k = 100$ iterations.

We present a couple of selected properties of a heat kernel smoother. Other properties can be found in [3].

Theorem 1 *$K_\sigma * Y$ is the unique solution of the following initial value problem after time $t = \sigma^2/2$:*

$$\frac{\partial f}{\partial t} = \Delta f, \;\; f(p,0) = Y(p) \quad (4)$$

where Δ is the Laplace-Beltrami operator.

Theorem 2 *Heat kernel smoother minimizes the sum of weighted squared residuals*

$$\int_{\partial\Omega} K_\sigma(p,q)\big[Y(q) - \theta\big]^2\, d\mu(q).$$

Theorem 3 *If the covariance function of Y in (1) is decreasing isotropic function of the form $R_Y(p,q) = \rho(d(p,q))$, then*

$$\mathbf{Var}[K_\sigma * Y(p)] \le \mathbf{Var}Y(p) \textit{ for each } p \in \partial\Omega.$$

Hence heat kernel smoothing will reduce the variability of cortical thickness measurements.

Theorem 4 *Heat kernel smoothing with large bandwidth can be decomposed into multiple kernel smoothing with smaller bandwidth via*

$$\underbrace{K_\sigma * \cdots * K_\sigma}_{k \text{ times}} * f = K_{\sqrt{k}\sigma} * f.$$

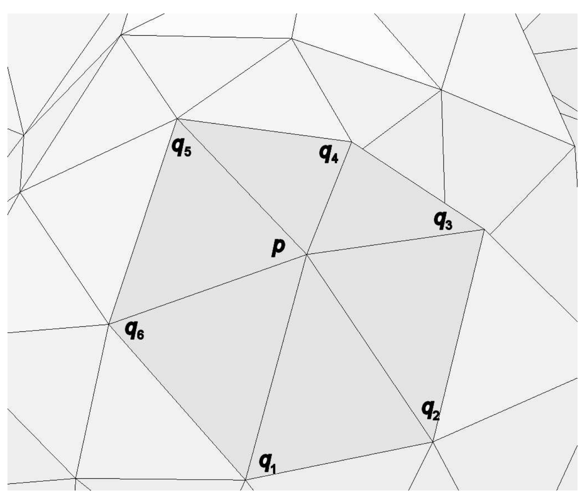

Figure 3: Typical triangular mesh with $m = 6$ neighboring vertices around $p = q_0$.

For triangular mesh that represents the cortical thickness, it is natural to take a discrete measure μ in defining convolution. Let $q_1, \cdots, q_m$ be neighboring vertices of $p = q_0$ (Figure 3). Then the discrete version of heat kernel is given by

$$\widetilde{W}_\sigma(p,q_i) = \frac{\exp\big[-\frac{\|p-q_i\|^2}{2\sigma^2}\big]}{\sum_{j=0}^m \exp\big[-\frac{\|p-q_j\|^2}{2\sigma^2}\big]}$$

and discrete convolution

$$\widetilde{W}_\sigma * Y(p) = \sum_{i=0}^m \widetilde{W}_\sigma(p,q_i) Y(q_i).$$

This is the generalization of *Nadaraya-Watson estimator* [4] defined in Euclidean space to manifolds.

Results

Heat kernel smoothing with large bandwidth $\sigma = 5$ mm is performed iteratively with smaller bandwidth $\sigma = 0.5$ mm. Figure 1 and 2 shows before and after heat kernel smoothing. Heat kernel smoothing decrease the variability (Theorem 3) while increasing the Gaussianess (Figure 4) which would be useful for random field based multiple comparison.

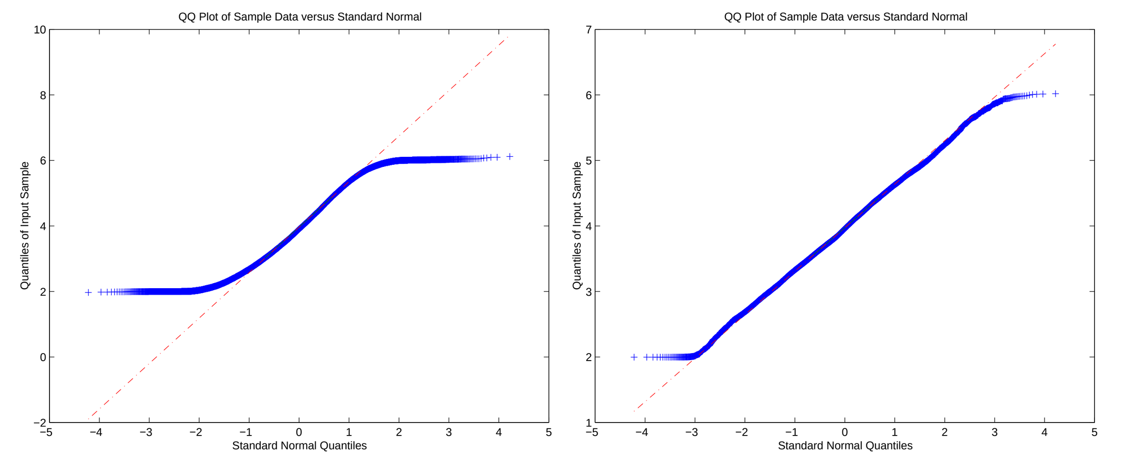

Figure 4: QQ-plot of the original cortical thickness measure. Right: QQ-plot after heat kernel smoothing with $\sigma = 5$ mm.

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