DEPARTMENT OF STATISTICS University of Wisconsin 1300 University Ave. Madison, WI 53706

TECHNICAL REPORT NO. 1116 January 28, 2005

Model Building in Two-sphere via Gauss-Weierstrass Kernel Smoothing and Its Application to Cortical Analysis, Part II.

Moo K. Chung^{1,2}, Steve Robbins⁴, Kim M. Dalton² Shubing Wang¹, Alan C. Evans⁴, Richard J. Davidson^{2,3}

¹Department of Statistics, Biostatistics, and Medical Informatics ²Waisman Laboratory for Brain Imaging and Behavior ³Department of Psychology and Psychiatry University of Wisconsin-Madison Madison, WI 53706. USA ⁴Montreal Neurological Institute, McGill University, Canada mchung@stat.wisc.edu

Tensor-based Cortical Morphometry via Weighted Spherical Harmonic Representation

Moo K. Chung^{1,2}, Steve Robbins⁴, Kim M. Dalton² Shubing Wang¹, Alan C. Evans⁴, Richard J. Davidson^{2,3} ¹Department of Statistics, Biostatistics, and Medical Informatics ²Waisman Laboratory for Brain Imaging and Behavior ³Department of Psychology and Psychiatry University of Wisconsin-Madison Madison, WI 53706. USA ⁴Montreal Neurological Institute, McGill University, Canada mchung@stat.wisc.edu

January 28, 2006

Abstract

We present a new tensor-based morphometric framework that quantifies cortical shape variations via the concept of local area element. The local area element is obtained from the Riemannian metric tensors, which are, in turn, obtained from the smooth functional parametrization of a triangle cortical mesh. For the smooth parametrization, we have developed a novel weighted spherical harmonic (SPHARM) representation. The weighted-SPHARM differs from the classical SPHARM in a regularizing cost function. The classical SPHARM is the asymptotic limit of the weighted-SPHARM. Further, for a specific choice of weights, the weighted-SPHARM is shown to be the finite least squares approximation to the solution of an isotropic heat diffusion on a unit sphere. The main aims of this paper are to present a theoretical framework for the weighted-SPHARM, and to show how it can be used in the tensor-based morphometry. As an illustration, the methodology has been applied in the problem of detecting abnormal cortical regions in a clinical population.

1 Introduction

In many previous cortical morphometric studies, cortical thickness have been mainly used to quantify cortical shape variations in a population [12, 15, 16]. The cortical thickness measures the amount of gray matter in vertical direction on a cortical surface. We present a new tensor-based morphometry (TBM) that quantifies the amount of gray matter along the tangential direction of the cortex by com-

puting the local area element. The local area element is obtained from the Riemannian metric tensors, which are, in turn, computed from the smooth functional parametrization of a cortical mesh. For this purpose, we present a novel weighted spherical harmonic (SPHARM) representation that differs from the classical SPHARM [9, 19] in regularizing a cost function. Unlike the classical SPHARM, we weight the measurement such that the closer measurements are weighed more. The weighted-SPHARM is related to both the classical SPHARM and an isotropic heat diffusion on a unit sphere as asymptotic limits.

Let us overview some of previous studies that are related to our study. Gerig et al. (2001) used the mean squared distance (MSD) of SPHARM coefficients in quantifying ventricle surface shape in a twin study [9]. The distance based metrics widely used in deformation-based morphometry [1] do not directly quantify the amount of tissue growth and atrophy. For directly measuring the amount of tissue volume, the Jacobian determinant of the deformation field is a better metric [3]. Our local area element is the differential geometric generalization of the Jacobian determinant in Riemannian manifolds. So the area element will be able to quantify the cortical tissue growth/atrophy directly.

Shen et al. (2004) used the principal component analysis technique on the SPHARM coefficients of schizophrenic hippocampal surface in reducing the data dimension [19]. Then they performed the linear discriminant analysis and support vector machines in surface classification. In a related work, Gu et al. (2004) presented the SPHARM representation as a surface compression technique, where the main geometric feasures are encoded in the low degree spherical harmonics, while the noise will be in the high degree spherical harmonics [10]. It will be shown that our weighted-SPHARM more penalizes the high degree spherical harmonics compared to the classical SPHARM.

Bulow (2004) used spherical harmonics in developing an isotropic heat diffusion via Fourier transform on a unit sphere as form of hierarchical surface representation [2]. We will show that our weighted-SPHARM representation is related to Bulow' heat diffusion asymptotically.

Many SPHARM literatures [2, 9, 10, 19] use the both real- and imaginary-valued spherical harmonics. However, the coefficients of imaginary-valued spherical harmonic basis do not serve any purpose in SPHARM representation other than the mathematical simplicity of manipulating them. In our study, we will only use real-valued spherical harmonics with different normalizing constants. This has the effect of decreasing the number of coefficients to be estimated by half.

Once the differentiable smooth parametrization of the cortex is established by the weighted-SPHARM, we can compute the Riemmanian metric tensors and local area element. Many previous differential geometric cortical modeling is based on locally fitting a quadratic polynomial [6, 8]. The SPHARM-based global parametrization tend to be computationally expensive compared to the local quadratic polynomial based parametrization while providing more accuracy and flexibility for hierarchical representation.

2 Preliminary

In this section, we introduce mathematical notations and basic concepts in SPHARM that are needed in describing the weighted-SPHARM.

2.1 Surface parametrization

Let \mathcal{M} and S^2 be a cortical surface and a unit sphere respectively. \mathcal{M} and S^2 are realized as meshes with more than 80,000 triangle elements. It is natural to assume the cortical surface to be a smooth 2-dimensional Riemannian manifold parameterized by two parameters [7]. This parametrization is constructed in the following way. A point $p = (x, y, z) \in \mathcal{M}$ is mapped onto $u = (u_1, u_2, u_3) \in S^2$ via a deformable surface algorithm that preserves anatomical homology and the topological connectivity of meshes (Figure 1).

Let U be the inverse mapping from S^2 to \mathcal{M} . Point $u = (u_1, u_2, u_3) \in S^2$ is parameterized by the spherical coordinates:

$$(u_1, u_2, u_3) = (\sin \theta \cos \varphi, \sin \theta \sin \varphi, \cos \theta)$$



Figure 1: Cortical manifold \mathcal{M} (left) is mapped onto unit sphere S^2 (right) via a deformable surface algorithm that preserves anatomical homology [15]. For the visualization purpose, the mean curvature was computed and thresholded to better represent sulci and gyri.

with $(\theta, \varphi) \in \mathcal{N} = [0, \pi] \otimes [0, 2\pi)$. This mapping will be denoted as X, i.e. $X : \mathcal{N} \to S^2$. Then we have composite mapping $Z = U \circ X : \mathcal{N} \to \mathcal{M}$. Z is a 3D vector and it will be stochastically modeled as

$$Z(\theta,\varphi) = \nu(\theta,\varphi) + \epsilon(\theta,\varphi), \tag{1}$$

where ν is unknown true differentiable parametrization and ϵ is a random vector field on unit sphere. The computation of the Riemannian metric tensors and local area element require estimating differentiable function ν .

2.2 Spherical harmonic representation

The basis functions on the unit sphere are given as the eigenfunctions satisfying $\Delta f + \lambda f = 0$, where Δ is the spherical Laplacian:

$$\Delta = \frac{1}{\sin\theta} \frac{\partial}{\partial\theta} \left(\sin\theta \frac{\partial}{\partial\theta}\right) + \frac{1}{\sin^2\theta} \frac{\partial^2}{\partial^2\varphi}$$

There are 2l+1 eigenfunctions, denoted as $Y_{lm}(-l \le m \le l)$, corresponding to the same eigenvalue $\lambda = l(l+1)$. Y_{lm} is called the *spherical harmonic* of degree l and order m [5, 21]. For the completeness of the exposition, we write the explicit form of the 2l+1 spherical harmonics of degree l as

$$Y_{lm} = \begin{cases} c_{lm} P_l^{|m|}(\cos\theta)\sin(|m|\varphi), & -l \le m \le -1\\ \frac{c_{lm}}{\sqrt{2}} P_l^0(\cos\theta), & m = 0,\\ c_{lm} P_l^{|m|}(\cos\theta)\cos(|m|\varphi), & 1 \le m \le l, \end{cases}$$

where $c_{lm} = \sqrt{\frac{2l+1}{2\pi} \frac{(l-|m|)!}{(l+|m|)!}}$ and P_l^m is the associated Legendre polynomials of order m. Unlike many previous

SPHARM literatures [2, 9, 10, 19] that used the complexvalued spherical harmonics, we use only real-valued spherical harmonics with different normalizing constants since they are more convenient for a real-valued stochastic model (1).

For $f, h \in L^2(S^2)$, the space of square integrable functions in S^2 , the inner product is defined as

$$\langle f,h\rangle = \int_0^{2\pi} \int_0^{\pi} f(\theta,\varphi)h(\theta,\varphi) \ d\mu(\theta,\varphi),$$

where Lebesgue measure $d\mu(\theta,\varphi) = \sin\theta \ d\theta \ d\varphi$. Consider subspace

$$\mathcal{H}_k = \{ \sum_{l=0}^k \sum_{m=-l}^l \beta_i Y_{lm} : \beta_i \in \mathbb{R} \} \subset L^2(S^2),$$

which is spanned by up to k-th degree spherical harmonics. Then the least squares estimation, denoted as \hat{f} , of $f \in L^2(S^2)$ in the subspace \mathcal{H}_k is given by

$$\hat{f}(p) = \sum_{l=0}^{\kappa} \sum_{m=-l}^{\iota} \langle f, Y_{lm} \rangle Y_{lm}(p).$$

This can be stated as the following theorem. **Theorem 1.**

$$\sum_{l=0}^{k} \sum_{m=-l}^{l} \langle f, Y_{lm} \rangle Y_{lm} = \arg \min_{h \in \mathcal{H}_k} \int_{S^2} \left[f(q) - h(q) \right]^2 d\mu(q)$$

This theorem is a well known result and mainly refered as the genearlized Fourier series expansion. This is the basis of the classical SPHARM representation of closed anatomical boundaries [9, 10, 19].

3 Weighted-SPHARM

3.1 Basic theory

The classical SPHARM is only one possible representation of functional data measured on the unit sphere. We will present a more general representation technique in the framework of a local kernel regression [11]. We will call this technique as the *weighted-SPHARM* since the coefficients of SPHARM are additionally weighted by the eigenvalues of a kernel. It will be shown that the classical SPHARM is asymptotically related to the weighted-SPHARM.

First, we start with the spectral representation of positive definite kernel in S^2 . Any positive definite kernel K(p,q) in S^2 can be represented as

$$K(p,q) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} \lambda_{lm} Y_{lm}(p) Y_{lm}(q),$$
 (2)



Figure 2: The schematic comparison of the classical SPHARM and weighted-SPHARM. The classical approach estimates functional data f by minimizing the integrated squared distance between f and smooth function h. One the other hand, the weighted-SPHARM estimates f locally at each fixed p by minimizing the integrated weighted squared distance between f and h(p). The weighted-SPHARM can be viewed as a local kernel regression [11].

where eigenvalues $\lambda_{00} \geq \lambda_{1m_1} \geq \lambda_{2m_2} \geq \cdots \geq 0$ satisfy

$$\int_{S^2} K(p,q) Y_{lm}(q) \ d\mu(q) = \lambda_{lm} Y_{lm}(p).$$

This is the special case of the Mercer's theorem [5]. Without loss of generality, we assume the kernel is normalized in such a way that

$$\int_{S^2} K(p,q) \, d\mu(q) = 1. \tag{3}$$

At each fixed point p, smooth representation h of functional data f is searched in the subspace \mathcal{H}_k that minimizes the integral of the weighted squared distance between fand h. This is formulated as the following regularization problem:

$$\min_{h \in \mathcal{H}_k} \int_{S^2} K(p,q) \left[f(q) - h(p) \right]^2 d\mu(q).$$
(4)

See Figure 2 for the schematic comparison of the classical SPHARM and the weighed-SPHARM. The minimizer of (4) is given by the following theorem.

Theorem 2.

$$\sum_{l=0}^{k} \sum_{m=-l}^{l} \lambda_{lm} \langle f, Y_{lm} \rangle Y_{lm}$$
$$= \arg \min_{h \in \mathcal{H}_k} \int_{S^2} K(p,q) \left[f(q) - h(p) \right]^2 d\mu(q).$$

Proof. Let

$$h(p) = \sum_{l=0}^{k} \sum_{m=-l}^{l} \beta_{lm} Y_{lm}(p) \in \mathcal{H}_k.$$

The integral can be written as

$$I(\beta_{00}, \beta_{1-1}, \beta_{10}, \beta_{11}, \cdots, \beta_{kk}) = \int_{S^2} K(p, q) \left[f(q) - \sum_{l=0}^k \sum_{m=-l}^l \beta_{lm} Y_{lm}(p) \right]^2 d\mu(q).$$

Since the functional I is quadratic in β_{lm} , the minimum exists and it is obtained when

$$\frac{\partial I}{\partial \beta_{l'm'}} = 0 \text{ for all } l' \text{ and } m'.$$
(5)

Then solving equation (5) with equation (3), we have

$$Y_{l'm'}(p) \int_{S^2} K(p,q) f(q) \ d\mu(q)$$
 (6)

$$= \sum_{l=0}^{d} \sum_{m=-l}^{l} \beta_{lm} Y_{lm}(p) Y_{l'm'}(p).$$
(7)

Integrate the both sides of the above equation with respect to measure $\mu(p)$. Then using the othonormal conditition

$$\int_{S^2} Y_{ij}(p) Y_{lm}(p) \ d\mu(p) = \begin{cases} 1, & i = l, j = m, \\ 0, & \text{otherwise}, \end{cases}$$

we obtain

$$\begin{aligned} \beta_{l'm'} &= \int_{S^2} f(q) \, d\mu(q) \int_{S^2} Y_{l'm'}(p) K(p,q) \, d\mu(p) \\ &= \sum_{l=0}^{\infty} \sum_{m=-l}^{l} \lambda_{lm} \int_{S^2} f(q) Y_{lm}(q) \, d\mu(q) \\ &\times \int_{S^2} Y_{lm}(p) Y_{l'm'}(p) \, d\mu(p) \\ &= \lambda_{lm} \int_{S^2} f(q) Y_{l'm'}(q) \, d\mu(q). \end{aligned}$$

This proves the statement.

Now we show what happens as the dimension of \mathcal{H}_k increases. Define kernel smoothing as the integral convolution

$$K * f(p) = \int_{S^2} f(q) K(p,q) \ d\mu(q).$$
(8)

Then it can be shown that the weighted-SPHARM converges to kernel smoothing (8) as the dimension of subspace \mathcal{H}_k increases. This can be stated differently as **Theorem 3.**

$$K * f(p) = \arg \min_{h \in L^2(S^2)} \int_{S^2} K(p,q) \left[f(q) - h(p) \right]^2 \, d\mu(q).$$

Proof. The weighted-SPHARM representation can be rearranged as

$$\sum_{l=0}^{k} \sum_{m=-l}^{l} \lambda_{lm} \langle f, Y_{lm} \rangle Y_{lm}(p)$$

$$= \int_{S^2} f(q) \sum_{l=0}^{k} \sum_{m=-l}^{l} \lambda_{lm} Y_{lm}(p) Y_{lm}(q) \ d\mu(q)$$

$$\rightarrow \int_{S^2} f(q) K(p,q) \ d\mu(q) \text{ as } k \to \infty$$

The last line is from equation (2). On the other hand, from the completeness of Hilbert space $L^2(S^2)$,

$$\lim_{k \to \infty} \arg \min_{h \in \mathcal{H}_k} \int_{S^2} K(p,q) \left[f(q) - h(p) \right]^2 d\mu(q)$$

= $\arg \min_{h \in L^2(S^2)} \int_{S^2} K(p,q) \left[f(q) - h(p) \right]^2 d\mu(q).$

This proves the statement. Theorem 3 connects the weighted-SPHARM to kernel smoothing as the asymptotic limit.

We briefly explain the numerical implementation issues. We only need to numerically compute the Fourier coefficients $\langle f, Y_{lm} \rangle$ in the weighted-SPHARM. The eigenvalues λ_{lm} are given analytically from an analytical kernel. The computation for the Fourier coefficients are based on the direct numerical integration over high resolution triangle meshes with more than 80,000 triangles and the average inter-vertex distance of 0.0189 mm. The accuracy of the weighed-SPAHRM is only restricted to the mesh resolution and the Riemann sum approximation should converges to the integral as the mesh resolution increases.

Let n be the total number of nodes in the mesh. Assume triangle elements T_{k_1}, \cdots, T_{k_m} are adjacent to each other at node q_k $(1 \le k \le n)$. Then the Fourier coefficients $\langle f, Y_{lm} \rangle$ is approximated as a limit of the Riemann sum over triangle elements:

$$\int_{S^2} f(q) Y_{lm}(q) \, d\mu(q) \doteq \frac{1}{3} \sum_{k=1}^n \sum_{i=1}^{k_m} f(q_k) Y_{lm}(q_k) |T_{k_i}|.$$

=



Figure 3: Top: the original inverse mapping U is displayed in S^2 . It shows the coordinate functions projected onto S^2 . Bottom: the weighed-SPHARM representation of the coordinate functions. The color scale for coordinates is thresholded at ± 45 mm to better show the smoothing pattern of the weighted-SPHARM representation.

The weighted-SPHARM is constructed by iteratively adding each term in Theorem 2.

3.2 Gauss-Weistrass kernel and heat flow

For the choice of eigenvalues

$$\lambda_{lm} = e^{-l(l+1)\sigma},\tag{9}$$

the corresponding kernel is called the *Gauss-Weistrass kernel* and it will be denoted as

$$K_{\sigma}(p,q) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} e^{-l(l+1)\sigma} Y_{lm}(p) Y_{lm}(q).$$
(10)

The subscript σ is introduced to indicate the dependence of the additional parameter. As $\sigma \to \infty$, $\lambda_{lm} \to 1$ and the weighted-SPHARM representation converges to the classical SPHARM representation. It is interesting to note that even though the regularizing cost functions are different in Theorem 1 and Theorem 2, they are related asymptotically.

Another interesting property is observed by noting that $K_{\sigma} * f$ is the unique solution to the following isotropic heat diffusion

$$\frac{\partial g}{\partial t} = \Delta g, \ g(p, t = 0) = f(p)$$
 (11)

at time $t = \sigma^2/2$ [4, 18]. This is easily seen from the fact that K_{σ} is the Green's function of equation (11). From this property combined with Theorem 3, we conclude that

the weighted-SPHARM is the finite approximation to the isotropic heat flow in S^2 .

We have compared the numerical implementation of the weighted-SPHARM result against the analytical solution of (11). Let $f = e^{l'(l'+1)}Y_{l'm'}$ be an analytic test function. Then $K_{\sigma} * f$ can be written as

$$e^{l'(l'+1)} \sum_{l=0}^{\infty} \sum_{m=-l}^{l} e^{-l(l+1)\sigma} Y_{lm}(p) \int_{S^2} Y_{lm}(q) Y_{l'm'}(q) d\mu(q)$$
$$= e^{l'(l'+1)} \sum_{l=0}^{\infty} \sum_{m=-l}^{l} e^{-l(l+1)\sigma} Y_{lm}(p) \delta_{ll'} \delta_{mm'} = Y_{l'm'}(p),$$

where $\delta_{ll'}$ is the Kroneker's delta. The table 1 shows the comparative result for l' = 20 and selective m' with $\sigma = 0.01$ and degree k = 20. The third column shows the numerical computation of integral $\int_{S^2} Y_{l'm'}^2(p) dp =$ 1 showing the accuracy up to 3 decimal places. This shows our Riemann sum approximation provides sufficiently good accuracy, which depends on the mesh resolution. The fourth column shows the average difference between the weighed-SPHARM and the heat diffusion.

3.3 Riemannian metric tensor estimation

The weighted-SPHARM estimation $\hat{\nu}$ of the unknown true parametrization μ in equation (1) is given by

$$\widehat{\nu} = \sum_{l=0}^{k} \sum_{m=-l}^{l} \lambda_{lm} \langle Z, Y_{lm} \rangle Y_{lm}.$$

For this study, we used eigenvalue (9) corresponding to the Gauss-Weistrass kernel. The estimation of the Riemannian metric tensors requires partial derivatives of $\hat{\nu}$. Denoting partial differential operators as $\partial_1 = \partial_\theta$ and $\partial_2 = \partial_{\varphi}$, we have derivative estimations

$$\partial_i \widehat{\nu} = \sum_{l=0}^k \sum_{m=-l}^l \lambda_{lm} \langle Z, Y_{lm} \rangle \partial_i Y_{lm}(\theta, \varphi),$$

l'	m'	integral	difference
20	4	1.0001	$9.7029 \cdot 10^{-5}$
20	10	0.9999	$1.6212 \cdot 10^{-4}$
20	20	0.9999	$-1.1174 \cdot 10^{-4}$

Table 1: Numerical accuracy of the weighted-SPHARM with $\sigma = 0.01$ for degree 20, and order 4, 10 and 20. The third column checks if $\langle Y_{l'm'}, Y_{l'm'} \rangle = 1$. The last column shows the average difference between the weighted-SPHARM and the expected heat diffusion. In each case



Figure 4: Riemannian metric tensor estimation. The metric tensors g_{ij} are estimated by differentiating the weighted-SPHARM representation. Afterwards the local area element $\sqrt{\det g}$ is computed. The local area element measures the amount of are expansion and shrinking with respect to S^2 .

The partial derivatives of spherical harmonics are computed iteratively. The associated Legendre polynomials in the spherical harmonic basis are defined as

$$P_l^m(\cos\theta) = \sin^m \theta \frac{d^m}{dx^m} P_l(x) \Big|_{x=\cos\theta}$$

where $P_l(x)$ is the Legendre polynomials defined in (-1, 1) with $P_0(x) = 1$ and $P_1(x) = x$. Then for $0 \le m \le l-1$,

$$\partial_{\theta} dP_l^m(\cos \theta) = m \sin^{m-1} \theta \cos \theta \frac{d^m}{dx^m} P_l(x) \Big|_{x=\cos \theta} \\ -\sin^{m+1} \theta \frac{d^{m+1}}{dx^{m+1}} P_l(x) \Big|_{x=\cos \theta} \\ = m \cot \theta P_l^m(\cos \theta) - P_l^{m+1}(\cos \theta).$$

For m = l, since P_l is the *l*-th order polynomial, the second term vanishes. A similar recursive relationship for an alternate definition for the associated Legendre polynomial is given in [13]. Based on this iterative relation, we can compute the partial derivatives

$$\partial_{\theta} Y_{lm} = \begin{cases} c_{lm} \partial_{\theta} P_l^{|m|}(\cos \theta) \cos(|m|\varphi), & -l \le m \le -1, \\ \frac{c_{lm}}{\sqrt{2}} \partial_{\theta} P_l^0(\cos), & m = 0, \\ c_{lm} \partial_{\theta} P_l^{|m|}(\cos \theta) \sin(|m|\varphi), & 1 \le m \le l \end{cases}$$



Figure 5: Plot of σ (horizontal) vs. FWHM (vertical) showing the nonlinear functional relationship. Table 2. shows FWHM for different σ .

and

$$\partial_{\varphi}Y_{lm} = \begin{cases} |m|c_{lm}P_l^{|m|}(\cos\theta)\cos(|m|\varphi), & -l \le m \le -1, \\ 0, & m = 0, \\ -|m|c_{lm}P_l^{|m|}(\cos\theta)\sin(|m|\varphi), & 1 \le m \le l. \end{cases}$$

Then the Riemannian metric tensors are estimated as $g = (g_{ij}) = \langle \partial_i \hat{\nu}, \partial_j \hat{\nu} \rangle$ and the area element

$$G(\theta,\varphi) = \sqrt{\det g} = \sqrt{g_{11} \cdot g_{22} - g_{12}^2}$$

The area element measures the transformed area in \mathcal{M} of the unit square of the parameterized space \mathcal{N} via mapping ν .

4 Statistical inference in S^2

For the *i*-th subject $(1 \le i \le m)$, we denote the cortical manifold as \mathcal{M}_i and its area element as $G_i(\theta, \varphi)$.

The area element is influenced by the global brain size. If we enlarge the cortical coordinates by the factor of r, the area element changes by the factor of r^2 . So it is necessary to normalize G_i such that it is invariant under scaling. The affine scale invariant area element is given by

$$\widetilde{G}_i(\theta,\varphi) = \frac{4\pi G(\theta,\varphi)}{\mu(\mathcal{M}_i)},$$

where $\mu(\mathcal{M}_i)$ is the total cortical area. If we enlarge the the cortical coordinates by the factor of r, $\mu(\mathcal{M}_i)$ increases by the factor of r^2 making $\widetilde{G_i}$ invariant under affine scaling. The constant 4π is multiplied so that the normalization is

with respect to the total surface area of S^2 . Then we have the following general linear model (GLM):

$$\overline{G}_i(\theta,\varphi) = \alpha_0 + \alpha_1 \cdot \mathtt{age}_i + \alpha_2(\theta,\varphi) \cdot \mathtt{group}_i + \epsilon(\theta,\varphi),$$

where ϵ is a mean zero Gaussian random field. age_i and $group_i$ are the age and a categorical dummy variable (0 for autism and 1 for control) respectively for subject *i*. Then we test if there is any group difference in the local area element measure by testing

$$H_0: \alpha_2(\theta, \varphi) = 0 \text{ for all } \theta \text{ and } \varphi.$$

vs. $H_1: \alpha_2(\theta, \varphi) \neq 0 \text{ for some } \theta \text{ and } \varphi.$

At each point (θ, φ) , a *F*-statistic with 1 and n-3 degrees of freedom, denoted as $F(\theta, \varphi)$ is used as a test statistic. The *F*-statistic is constructed as a ratio of the residual sum of error of model fit of H_0 and H_1 . Since we need to perform the test at every (θ, φ) , this becomes a multiple comparison problem. We used the random field theory [20, 22] based thresholding to determine the statistical significance.

The probability of obtaining false positives (α -level) for the one sided alternate hypothesis in given by

$$P(\sup F(\theta, \varphi) \ge F_{\alpha}) = \sum_{i=0}^{2} \frac{\mathcal{L}_{i}(S^{2})}{\mathrm{FWHM}^{i}} \rho_{i}(y),$$

where \mathcal{L}_i is the *i*-th Lipschitz-Killing curvature or Minkowski functional [20], and ρ_i is the *i*-dimensional ECdensity [22]. FWHM denotes the full width of the half maximum of smoothing kernel K_{σ} used in the weighted sphearical harmonic representation. For the unit sphere, the Lipschitz-Killing curvatures are

$$\mathcal{L}_0(S^2) = 2, \ \mathcal{L}_1(S^2) = 0, \ \text{ and } \mathcal{L}_2(S^2) = 2\pi.$$

The EC-densities are

$$\rho_0(y) = \int_y^\infty \frac{\Gamma(\frac{m}{2})}{((m-1)\pi)^{1/2}\Gamma(\frac{m-1}{2})} \left(1 + \frac{y^2}{m-1}\right)^{-m/2} dy$$
$$\rho_2(y) = \frac{4\ln 2}{(2\pi)^{3/2}} \frac{\Gamma(\frac{m}{2})y \left(1 + \frac{y^2}{m-1}\right)^{-(m-2)/2}}{(\frac{m-1}{2})^{1/2}\Gamma(\frac{m-1}{2})}.$$

4.1 Computing FWHM

The computation for the FWHM of the Gauss-Weistrass kernel in S^2 is not trivial due to the fact there is no known close form expression for the FWHM as a function of σ . So the FWHM is computed numerically.

The Gauss-Weistrass kernel can be simplified from equation (10), via the harmonic addition theorem [21], as

$$K_{\sigma}(p,q) = \sum_{l=0}^{\infty} \frac{2l+1}{4\pi} e^{-l(l+1)\sigma} P_l^0(\cos\vartheta), \qquad (12)$$

where ϑ is the angle between p and q. Using the vector inner product \cdot , the angle can be written as $\cos \vartheta = p \cdot q$. The maximum of the Gauss-Weistrass kernel is obtained when $\vartheta = 0$ and it is given by

$$\sum_{l=0}^{k} \frac{2l+1}{4\pi} e^{-l(l+1)\sigma}$$

Now we fix $\varphi = 0$ and let p be the north pole, i.e. p = (0, 0, 1). By varying $q = (\sin \vartheta, 0, \cos \vartheta)$ for $0 \le \vartheta = \cos^{-1}(p \cdot q) \le \pi$, we have $Y_{lm} = 0$ if $m \ne 0$. Note $P_l^0(1) = 1$ for all l. Then we solve numerically for θ in

$$\frac{1}{2}\sum_{l=0}^{k}\frac{2l+1}{4\pi}e^{-l(l+1)\sigma} = \sum_{l=0}^{k}\frac{2l+1}{4\pi}e^{-l(l+1)\sigma}P_{l}^{0}(\cos\vartheta).$$

The FWHM is then 2ϑ . Table 2 in Figure 5 show the nonlinear relationship between σ and the corresponding FWHM for k = 20.

5 Application to autism study

Three Tesla T_1 -weighted MR scans were acquired for 16 autistic and 12 control right handed males. 16 autistic subjects were diagnosed with high functioning autism. The average ages are 17.1 ± 2.8 and 16.1 ± 4.5 for control and autistic group respectively. Image intensity nonuniformity was corrected using nonparametric nonuniform intensity normalization method and then the image was spatially normalized into the Montreal neurological institute (MNI) stereotaxic space using a global affine transformation. Afterwards, an automatic tissue-segmentation algorithm based on a supervised artificial neural network classifier was used to classify each voxel as cerebrospinal fluid (CSF), gray matter, or white matter [14]. Triangular meshes for outer cortical surfaces were obtained by a deformable surface algorithm [15]. The mesh starts as an ellipsoid located outside the brain and is shrunk to match the cortical boundary. By performing an affine transform on this ellipsoid, we obtain S^2 mesh, which is used in the weighted-SPHARM.

The segmented cortical meshes are normalized via a nonlinear surface-to-surface registration [17]. Cortical curvatures of two surfaces are mapped onto the sphere and they are aligned by solving a regularization problem that tries to minimize the discrepancy between two curvatures while maximizing the smoothness of the alignment in such a way that the pattern of gyral ridges are matched smoothly. This regularization mechanism produces a smooth deformation field, with very little folding. The deformation field is parameterized using a triangulated mesh and the algorithm proceeds in a coarse-to-fine manner, with four levels of mesh resolution. The surface-to-surface registration is



Figure 6: Demonstration of cortical surface normalization in S^2 showing the nonlinear alignment of central and superior temporal sulci for 149 subjects. Left: before normalization. Right: after normalization. The probability of matching increases after normalization.

completely automated and has been validated in [17]. Figure 6 demonstrates the effectiveness of this surface registration algorithm by showing the increased matching probability of superior temporal and central sulci for 149 subjects.

Afterwards, the weighted-SPHARM representation is used as an estimate for differentiable smooth parametrization of the meshes. We used parameters k = 20 and $\sigma = 0.001$. The corresponding FWHM is 0.2262 mm. The Riemannian metric tensors and the area element are computed simultaneously. Based on the general linear model framework, the statistical parametric map (F-statistic) is computed and projected on both S^2 and the average cortical surface (Figure 7). The average cortical surface is constructed by averaging the anatomically corresponding vertices in the meshes [4]. It serves as an anatomical landmark for showing where signals are detected. Then we performed the random field theory based multiple comparison correction on the F-statistic at $\alpha=0.05$ level but we did not detect any statistically significant cortical regions of local area difference although we observed maximum F-value of 9.3 (uncorrected p-value of 0.0054) at the left temporal lobe.

6 Conclusions and discussions

In this paper, we presented a theoretical framework for the weighted-SPHARM and its application in TBM. The weighted-SPHARM is used as a differentiable parametrization of the cortex. This enable us to compute the Riemannian metric tensors and local area element. The local area element is used in determining the statistical significance of the abnormal cortical tissue expan-



Figure 7: The final statistical analysis result. The F statistic is computed at every vertices of the triangle mesh in S^2 (left) and mapped onto the average cortex (right). The average cortex serves as an anatomical reference. The random field theory based multiple comparison at $\alpha = 0.05$ did not show any significant result although the maximum signal is detected at the left temporal lobe (sup F = 9.3 corresponing to uncorrected *p*-value of 0.0054).

sion/shrinking for a clinical population.

The weighted-SPHARM is a very flexible functional estimation technique for scalar and vector data defined in S^2 . It was shown that the solution to the isotropic heat diffusion in S^2 is the asymptotic limit of the weighted-SPHARM for the choice of the Gauss-Weistrass kernel. We can extend this argument further. By choosing the Green's function of a particular partial differential equation (PDE) as the kernel in the weighted-SPHARM, we can construct the finite least squares estimation of the solution of the PDE without numerically solving PDE using the finite element technique. This should serve as a spring board for investigating the wide variety of PDE based data smoothing technique in the local polynomial regression framework [11].

References

- J. Ashburner, C. Hutton, R.S.J. Frackowiak, I. Johnsrude, C. Price, and K.J. Friston. Identifying global anatomical differences: Deformation-based morphometry. *Human Brain Mapping*, 6:348-357, 1998.
- [2] T. Bulow, "Spherical diffusion for 3d surface smoothing," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. 26, pp. 1650–1654, 2004.
- [3] M.K. Chung, K.J. Worsley, T. Paus, C. Cherif, J.N. Giedd, J.L. Rapoport and A.C. Evans. A Unified Statistical Approach to Deformation-Based Morphometry, *NeuroImage* 14:595-606, 2001.
- [4] M.K. Chung, S. Robbins, Davidson R.J. Alexander A.L. Dalton, K.M., and A.C. Evans. Cortical thickness analysis in autism with heat kernel smoothing. *NeuroImage*, 25:1256-1265, 2005.

- [5] R. Courant and D. Hilbert., *Methods of Mathematical Physics, Volume 1.*, Interscience, New York, 1953.
- [6] A.M. Dale and B. Fischl. Cortical Surface-based Analysis I. Segmentation and Surface Reconstruction. *NeuroImage*, 9:179–194. 1999
- [7] C. Davatzikos and R.N. Bryan. Using a Deformable Surface Model to Obtain a Shape Representation of the Cortex. In Proceedings of the IEEE International Conference on Computer Vision, pages 2122–2127. 1995
- [8] S. Joshi, U. Grenander, and M.I. Miller, On the geometry and shape of brain sub-manifolds, *International Journal of Pattern Recognition and Artificial Intelligence: Special Issue on Processing of MR Images of the Human*. 11:1317– 1343. 1997.
- [9] G. Gerig, M. Styner, D. Jones, D. Weinberger, J. Lieberman, Shape analysis of brain ventricles using SPHARM. MM-BIA 171-178. 2001.
- [10] X. Gu, Y.L. Wang, T.F. Chan, P.M. Thompson, S.T. Yau. Genus Zero Surface Conformal Mapping and its Application to Brain Surface Mapping, *IEEE Transactions on Medical Imaging*, 23:1–10. 2004
- [11] J. Fan and I. Gijbels. Local Polynomial Modelling and Its Applications. Chapman & Hall/CRC, 1996.
- [12] B. Fischl, and M.I. Sereno, and R. Tootell, and A.M. Dale, High-resolution intersubject averaging and a coordinate system for the cortical surface *Hum. Brain Mapping*, vol. 8, pp. 272–284, 1999.
- [13] T. Khan, and A. Thomas. On derivation of the radiative transfer equation and its spherical harmonics approximation for scattering media with spatially varying refractive indices. Technical Report. 2003
- [14] K. Kollakian. Performance analysis of automatic techniques for tissue classification in magnetic resonance images of the human brain. Technical Report Master's thesis, Concordia University, Montreal, Quebec, Canada, 1996.
- [15] J.D. MacDonald, N. Kabani, D. Avis and A.C. Evans. Automated 3-D Extraction of Inner and Outer Surfaces of Cerebral Cortex from MRI. *NeuroImage*, 12:340–356, 2000.
- [16] M.I. Miller, A.B. Massie, J.T. Ratnanather, K.N. Botteron, and J.G. Csernansky. Bayesian construction of geometrically based cortical thickness metrics. *NeuroImage*, 12:676–687, 2000.
- [17] S.M. Robbins. Anatomical standardization of the human brain in euclidean 3-space and on the cortical 2-manifold. Technical Report PhD thesis, School of Computer Science, McGill University, Montreal, Quebec, Canada, 2003.
- [18] S. Rosenberg, *The Laplacian on a Riemannian Manifold*, Cambridge University Press, 1997.
- [19] L. Shen, J. Ford, F. Makedon, A. Saykin, surface-based approach for classification of 3D neuroanatomical structures. *Intelligent Data Analysis*, 8(5). 2004.
- [20] J. E. Taylor. A Gaussian Kinematic Formula. Annals of Probability. 2006. in press.

- [21] G. Wahba. Spline models for observational data. SIAM, 1990.
- [22] K.J. Worsley, S. Marrett, P. Neelin, A.C. Vandal, K.J. Friston and A.C. Evans. A Unified Statistical Approach for Determining Significant Signals in Images of Cerebral Activation. *Human Brain Mapping*, 4:58–73, 1996.