Surface-Based Morphometry

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Glossary

Surface conformal parameterization A method to flatten surfaces with the property that the flattened surfaces have minimal angle distortions from the original surfaces.

Surface conformal representation Surface conformal factor and mean curvature, which represent the intrinsic and extrinsic features of a surface, respectively. They uniquely determine a surface in R^3, up to a rigid motion.

Surface fluid registration An algorithm extending the image fluid registration method to surfaces, with correction for distortions introduced by surface parameterization.

Introduction

When registering structural MR images, the volume-based methods (e.g., Christensen et al., 1996) have much difficulty with the highly convoluted cortical surfaces due to the complexity and variability of the sulci and gyri. Early research (Fischl et al., 1999; Thompson et al., 2000; Van Essen et al., 2001) has demonstrated that surface-based brain mapping may offer advantages over volume-based brain mapping as a method to study the structural features of the brain, such as surface deformation, as well as the complexity and change patterns in the brain due to disease or developmental processes.

Preprocessing for Surface-Based Morphometry

In a typical surface-based morphometry pipeline, after MRI intensity is corrected with nonparametric nonuniform intensity normalization method, the images are usually spatially normalized into the stereotaxic space using a global affine transformation. Afterward, an automatic tissue-segmentation algorithm is used to classify each voxel as the cerebrospinal fluid (CSF), gray matter (GM), white matter (WM), or different subcortical structures such as the hippocampus and lateral ventricle. Usually, marching cube algorithm (Lorensen and Cline, 1987) is used to generate the cortical or subcortical surface meshes. Because the human cerebral cortex has a 3-D highly convoluted topology structure, additional algorithms, such as Laplace–Beltrami operator-based method (Shi et al., 2013b), are applied to remove the geometric and topological outliers and generate robust and accurate meshes for the following surface-based morphometry analyses.

Brain Surface Conformal Parameterization

Parameterization of brain cortical and subcortical surfaces is a fundamental problem for surface-based morphometry. Sometimes, it is also called brain surface flattening. The goal of surface parameterization is to find some mappings between brain surfaces and some common flattening surfaces, that is, some surfaces with constant Gaussian curvature. After that, these common spaces serve as canonical spaces for surface registration and morphometry analysis. Brain surface parameterization has been studied extensively. A good surface parameterization preserves the geometric features and facilitates the following surface signal processing. Some research proposed quasi-isometric mappings (Schwartz et al., 1989) or area-preserving mappings (Brechbühler et al., 1995). Another branch of research used concepts from conformal geometry to compute brain surface conformal parameterization (Angenent et al., 1999; Hurdal and Stephenson, 2004). In addition to angle-preserving property, conformal parameterization provides a rigorous framework for representing, splitting, matching, and measuring brain surface deformations.

According to differential geometry theory, a general surface can be conformally mapped to one of three canonical spaces, the unit sphere, the Euclidean plane, and the hyperbolic space. For a closed genus-zero surface, the spherical conformal mapping method (Gu et al., 2004) can conformally map it to a sphere by minimizing its harmonic energy (**Figure 1(a)**). For brain surface analysis, sometimes, we introduce landmark curves to annotate important anatomical regions. After surfaces are cut open along these given landmark curves, one may get a surface with multiple holes. Euclidean Ricci flow method (Wang et al., 2012) or holomorphic 1-form method (Wang et al., 2010) can conformally map them to the Euclidean plane (**Figure 1(b)** and **1(c)**). To model a topologically complicated lateral ventricular surface, hyperbolic conformal geometry emerges naturally as a candidate method because it can induce hyperbolic conformal parameterizations without any singularities (Shi et al., 2012; **Figure 1(d)**). Such a set of global brain surface conformal parameterization methods are technically sound and numerically stable. They may increase computational accuracy and efficiency when solving partial differential equations using grid-based or metric-based computations.

Brain Surface Registration

Brain surface registration or warping can be achieved by first mapping each of the 3-D surfaces to a canonical parameter space such as a sphere (Bakircioglu et al., 1999; Fischl et al., 1999; Styner et al., 2006) or a planar domain (Pantazis et al., 2010; Thompson and Toga, 2002). A flow, computed in the parameter space of the two surfaces, induces a correspondence field in 3-D. The flow can be computed by aligning curvature,

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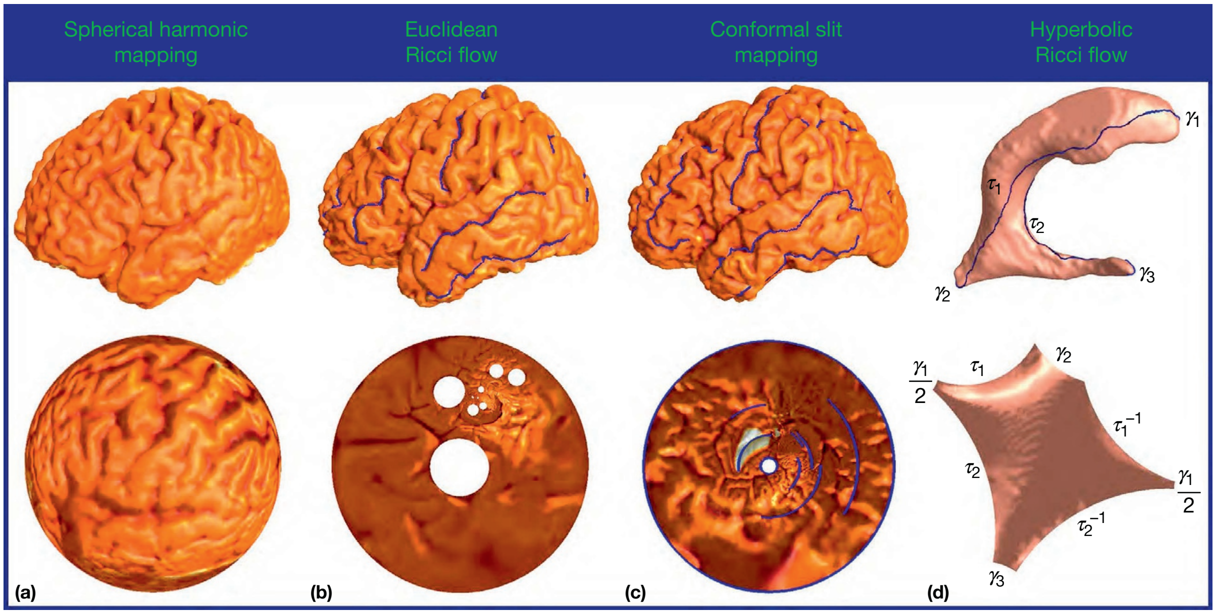

Figure 1 Illustration of different brain surface conformal parameterization methods.

sulcal depth, or other geometric maps of the surfaces, as applied in FreeSurfer (Dale et al., 1999; Fischl et al., 1999), or by aligning the surface parameterizations, as applied in spherical harmonics (Styner et al., 2006), or by aligning meaningful landmark curves, as applied in the cortical pattern matching algorithm (Thompson and Toga, 2002). Another set of brain surface warping methods (e.g., Vaillant and Glaunes, 2005) is based on the large deformation diffeomorphic metric mapping framework (Miller et al., 2002). They compute diffeomorphic registrations between individual and template surfaces by generating time-dependent diffeomorphisms in a metric space.

Next, we use a recently developed surface fluid registration algorithm (Shi et al., 2013a) as an example to highlight some key steps involved in a typical brain surface registration pipeline (as shown in Figure 2).

A brain surface is first conformally mapped onto a planar rectangle space with holomorphic 1-form method (Wang et al., 2011). Figure 2(b), 2(c), 2(f), and 2(g) shows the conformal parameterizations of the study and template surfaces, respectively; Figure 2(b) and 2(f) uses texture mapping to show the angle-preserving property. Figure 2(c) and 2(g) is the visualization of parameter space, from which we can see that the geometric features of original surfaces are well preserved. The local conformal factor (Shi et al., 2013a), computed from surface conformal parameterization, encodes a lot of geometric information about the surface. It can also be used to compute surface mean curvatures. With differential geometry theories, one can prove that the conformal factor and mean curve uniquely determine a closed surface in $\mathbb{R}^3$, up to a rigid motion. We call them *the conformal representation of a surface*. In the system, the conformal factor and mean curvature are summed up, and the dynamic range of the summation is linearly scaled to form the feature image of a surface, as show in Figure 2(d) and 2(h). Surface conformal parameterization is capable of introducing fine-grained grid on surfaces and converting a 3-D surface registration problem to a 2-D image registration problem in the parameter domain. So surfaces in the parameter domain are aligned with the fluid registration method to maintain a smooth, one-to-one mapping (Christensen et al., 1996). For a manifold fluid registration, the traditional Navier–Stokes equation is extended to a general form with a compensation term to correct for the area distortion introduced by surface parameterization. With conformal parameterization, the compensation term is simplified to the conformal factor. The inverse consistent image registration algorithm (Christensen and Johnson, 2001) is incorporated in the system to jointly estimate the forward and inverse transformations between a pair of feature images and to ensure the symmetry of the registration, as shown in Figure 2(i). Since conformal mapping and fluid registration generate diffeomorphic mappings, a diffeomorphic surface-to-surface mapping is then recovered that matches surfaces in 3-D.

Surface-Based Morphology Statistics

Since image intensities vary among scans, surface-based morphology may provide robust and biologically sound shape statistics to characterize variations of brain shapes. Generally speaking, surface-based morphology statistics can be classified into two classes: One is the class of transformation-invariant global shape descriptors that requires no surface registration; the second class of features is some local measurements defined on particular locations after the brain surface registration among the population. The first class of features is usually concise and intrinsic to surface structure, and the second class of features may lend themselves to immediate visualization. The choice between different types of features usually depends on specific applications.

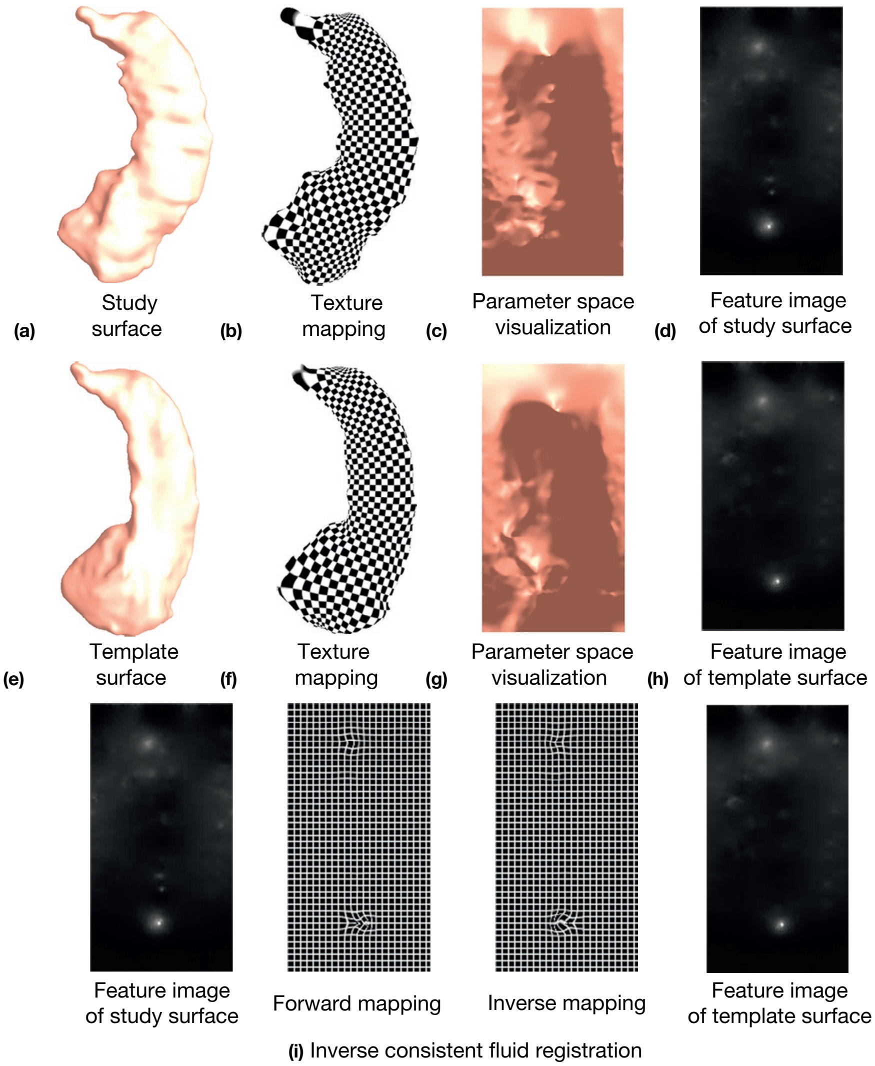

Figure 2 Hippocampal surface registration with inverse consistent surface fluid registration algorithm. Adapted from Shi, J., Thompson, P. M., Gutman, B., et al. (2013). Surface fluid registration of conformal representation: Application to detect disease effect and genetic influence on hippocampus. *NeuroImage*, *78*, 111–134, with permission.

Global Transformation-Invariant Shape Descriptors

The spherical harmonic representation uses a set of coefficients that are associated with a specific set of spherical harmonics. A spherical harmonic is an eigenfunction of the Laplace–Beltrami operator defined on the sphere. There is a countable set of spherical harmonics that form an orthonormal basis for the Hilbert space of square integrable functions. Similar to Fourier series defined on planar domain, the spherical harmonics together with their coefficients can be used to represent general functions defined on a unit sphere. These coefficients are also called frequency coefficients and they induce rotation-invariant shape descriptors. A brain surface can be represented as a vector-valued function defined on the sphere via conformal or area-preserving mapping of its surface to the sphere. The brain surface (or functions defined on brain surfaces) can then be decomposed in terms of linear combination of spherical harmonics. The vector-valued spectrum, that is, the harmonic coefficients expressed as components of a vector, can be used to analyze the shape. The main geometric features are encoded in the low-frequency part. By filtering out the high-frequency coefficients, one can smooth the surface and compress the geometry. By comparing the low-frequency coefficients, one can match surfaces and compute the similarity of surfaces (Chung et al., 2007; Gutman et al., 2009).

Surfaces can also be classified by conformal geometry. Two surfaces are conformally equivalent if they can be conformally mapped to each other. The conformal equivalence classes form a finite dimensional shape space, which is called the modular space. The universal covering space of the modular space is the Teichmüller space. The Teichmüller shape representations are intrinsic and invariant under conformal transformations and rigid motions. Wang et al. (2009) computed the Teichmüller space coordinates with hyperbolic Yamabe flow method and applied them for lateral ventricular surface classification.

Kurtek et al. (2011) proposed the q-map representation of surfaces and used it to study subcortical structure shapes. The L^2 distances between the q-maps are invariant to surface reparameterizations; thus, this method removes the parameterization variability. There is also certain interest to study isometry-invariant features in computer vision field. Such features may be useful for longitudinal brain surface-based morphometry study and they deserve some further exploration.

Point-to-Point Local Surface Measurements

Thickness measurements

A popular local measurement is the brain structure thickness. Brain GM is a 2-D highly convoluted shell of the human cerebral cortex. The interface between the GM and the CSF is the outer cortical surface, while the interface between the GM and WM is the inner cortical surface. The thickness of the GM shell is usually referred as *the cortical thickness*. A variety of methods to estimate cortical thickness have been proposed. For some subcortical structures, such as the hippocampus and lateral ventricle, their long tube shape makes it natural to define a distance between each surface point to the middle axis of its shape contour, that is, *the radial distance* (Pizer et al., 1999; Thompson et al., 2004). The thickness measures are biologically intuitive and are defined on every surface point and may be compared across subjects based on the one-to-one surface registration results. Since different clinical populations are expected to show different patterns of cortical thickness or radial distance variations, such thickness measurements have been frequently used as a quantitative index for characterizing clinical populations.

Tensor-based morphometry and multivariate tensor-based morphometry

After establishing a one-to-one correspondence map between a pair of surfaces, the Jacobian matrix J of the map is computed as its derivative map between the tangent spaces of the surfaces. Surface tensor-based morphometry (TBM) and its variant, multivariate tensor-based morphometry (mTBM), are defined to measure local surface deformation based on the local surface metric tensor changes. Practically, in the triangle mesh surface, the derivative map is approximated by the linear map from one face $[v_1, v_2, v_3]$ to another $[w_1, w_2, w_3]$. First, we isometrically embed the triangles $[v_1, v_2, v_3]$ and $[w_1, w_2, w_3]$ onto the plane; the planar coordinates of the vertices of v_i, w_j are denoted using the same symbols v_i, w_j. We can explicitly compute the Jacobian matrix for the derivative map:

$$J = [w_3 - w_1, w_2 - w_1][v_3 - v_1, v_2 - v_1]^{-1}$$

Then, we use multivariate statistics on deformation tensors and adapt the concept to surface tensors. We define the deformation tensors as $S = (J^T J)^{1/2}$. The TBM intends to study statistics of Jacobian determinant $\det(J)$ or $\log(\det(J))$.

For mTBM, we consider a new family of metrics, the 'log-Euclidean metrics' (Arsigny et al., 2006). These metrics make computations on tensors easier to perform, as the transformed values form a vector space, and statistical parameters can then be computed easily using standard formulas for Euclidean spaces. In practice, the matrix logarithm of the surface deformation tensor is a 2×2 symmetrical matrix and has two duplicate off-diagonal terms. The mTBM extracts the three distinct components of the $\log(S)$ and forms a 3×1 vector. The mTBM computes statistics from the Riemannian metric tensors that retain the full information in the deformation tensor fields and thus may be more powerful in detecting surface difference than many other statistics.

Recent researches indicate that the cortical thickness and cortical surface area are genetically independent (Panizzon et al., 2009). We proposed to combine the thickness and mTBM feature to form a new multivariate statistics (Wang et al., 2011). Since thickness and mTBM measure complementary surface morphometry information, the new multivariate morphology features may offer a more complete set of surface statistics and boost statistical power.

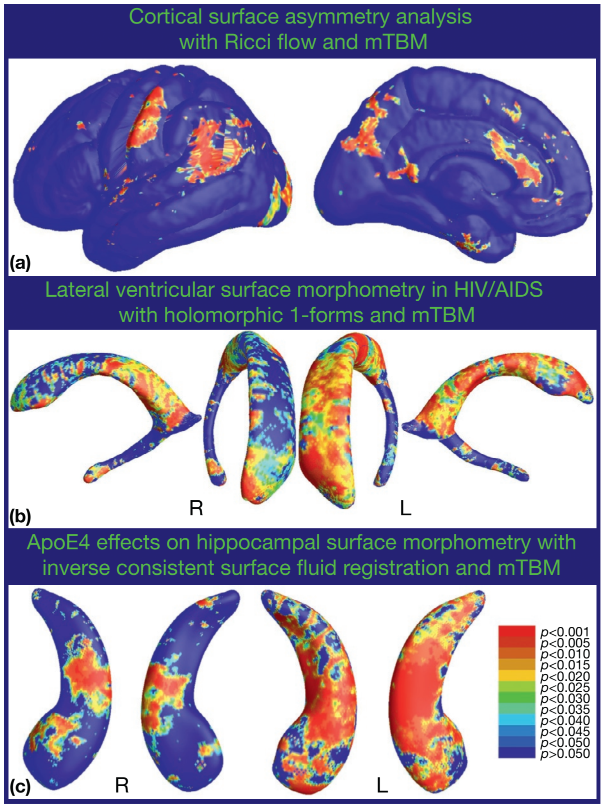

Figure 3 Applications of mTBM in group difference analyses. (a) The brain asymmetry study results in 14 healthy control subjects; (b) statistical p-map from ventricular surfaces between 11 HIV/AIDS patients and 8 matched control subjects; (c) statistical p-map from all nondemented subjects in Alzheimer's Disease Neuroimaging Initiative (ADNI) baseline subjects between ApoE e4 carriers and noncarriers ($N = 558$). Adapted from Wang, Y., Zhang, J., Gutman, B., et al. (2010). Multivariate tensor-based morphometry on surfaces: Application to mapping ventricular abnormalities in HIV/AIDS. *NeuroImage*, *49*(3), 2141–2157, with permission; Wang, Y., Shi, J., Yin, X., et al. (2012). Brain surface conformal parameterization with the Ricci flow. *IEEE Transactions on Medical Imaging*, *31*(2), 251–264, with permission; Shi, J., Thompson, P. M., Gutman, B., et al. (2013). Surface fluid registration of conformal representation: Application to detect disease effect and genetic influence on hippocampus. *NeuroImage*, *78*, 111–134, with permission.

Statistical Inference and Applications of Surface-Based Morphometry

The surface-based morphology statistics can be directly used to assess group difference between a clinical population and normal controls, study the simultaneous effects of multiple factors or covariates of interest, and evaluate disease burden, progression, and response to interventions. Specifically, Student's t-test (for univariate statistics) and Hotelling's T^2 test together with Mahalanobis distance may be used for group difference study and Pearson correlation for correlation study. A rich set of machine learning algorithms, such as support vector machine, may use the obtained morphology statistics for disease diagnosis and prognosis research.

Given maps of surface-based morphology statistics, multiple comparisons methods, such as false discovery rate methods and permutation methods, may be employed to assign overall (corrected) p-values of the map (or the features in the map), corrected for multiple comparisons. As a result, the generated surface p-maps (usually by permutation tests) can help visualize the most statistically significant areas, and the corrected p-values quantify the global statistical significance over the whole brain cortical or subcortical surfaces.

Surface-based morphometry has been widely used to in human brain mapping research (Fischl et al., 1999; Thompson et al., 2000; Van Essen et al., 2001). **Figure 3** illustrates several p-maps from our prior work that show the group differences detected by mTBM in different applications.

See also: **INTRODUCTION TO METHODS AND MODELING**: Bayesian Multiple Atlas Deformable Templates; Cortical Thickness Mapping; False Discovery Rate Control; Rigid-Body Registration; Tissue Classification.

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