AN APPROACH FOR INTERSUBJECT ANALYSIS OF 3D BRAIN IMAGES BASED ON CONFORMAL GEOMETRY

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ABSTRACT

Recent advances in imaging technologies, such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and Diffusion Tensor Imaging (DTI) have accelerated brain research in many aspects. In order to better understand the synergy of the many processes involved in normal brain function, integrated modeling and analysis of MRI, PET, and DTI across subjects is highly desirable. The current state-of-art computational tools fall short in offering an analytic approach for intersubject brain registration and analysis. In this paper we present an approach which is based on landmark constrained conformal parameterization of a brain surface from high-resolution structural MRI data to a canonical spherical domain. This model allows natural integration of information from co-registered PET as well as DTI data and lays a foundation for the quantitative analysis of the relationship among diverse datasets across subjects. Consequently, the approach can be extended to provide a software environment able to facilitate detection of abnormal functional brain patterns in patients with neurological disorder.

Index Terms— Conformal Mapping, Brain Image Analysis, Information Integration, Registration.

1. INTRODUCTION

Advanced imaging technologies have accelerated brain research in many aspects [10, 12, 13]. In order to enable comparison of localized functional information across individuals, various brain mapping techniques have been developed in recent years [3, 5]. Most of them achieves standardization by non-linear spatial warping of individual's brains to an anatomical template and then performs all data analyses in template space. Furthermore, as human cortical brain surfaces are highly convoluted, conventional geometric shape analysis methods based on Euclidean geometry, e.g., FreeSurfer [2] or BrainVoyager [7, 8], are suboptimal in handling the complexity of the cortical mantel. As an example, given two points on the cortical surface that are close to each other in R^3, their geodesic distance might be very long. The inconsistency between the Euclidean distance in the embedding space and the Riemannian metric distance on the surface makes conventional mapping algorithms suboptimal. Methods based on Euclidian distances are problematic when brains are analyzed which largely differ in size and shape, frequently encountered in analyses that include both pediatric and adult brains [11].

Recently, conformal mapping techniques have gained a wider application in brain mapping [1]. For example, Hurdal and Stephenson proposed a discrete mapping approach that uses spherical packing in order to produce a "flattened" image of the cortical surface onto a sphere or onto an Euclidean or hyperbolic plane [6]. They obtained maps that are quasi-conformal approximations to classical conformal maps. Furthermore, Gu et al. proposed to optimize the conformal parameterization by composing an optimal Möbius transformation so that it minimizes the landmark mismatch energy [4] and Wang et al. introduced the application of compound energy (harmonic and landmark matching energy) to optimize the brain conformal mapping [14, 15].

In this paper we present the development of Conformal Brain Model (e.g., CBM, a unit sphere with brain cortical surface parameterization) based on high-resolution volumetric MR images, serving as a homotopic canonical space for subsequent data representation and integration. The landmark constrained conformal mapping procedure is used to determine the homotopic location of cortical surface in each subject's native space. This characteristic sets this method apart from other techniques which perform spatial warping of image volumes to a predefined template, such as Statistical Parametric Mapping (SPM) [3]. Our method integrates complementing imaging data within the homotopic brain model, CBM, allowing statistical analysis across subjects. The normative brain pattern with respect to PET tracer concentrations and DTI fiber tracts can be derived from control subjects of various ages. Subsequently, the decision whether a particular cortical element derived from a patient falls into the normal range is based on this normative pattern. This data structure provides universal access and quantification to each individual's brain functional information (from PET) and neural network information (from DTI).

2. BRAIN MAPPING USING CONFORMAL GEOMETRY

In differential geometry, surfaces are modeled as manifolds. A manifold M is a topological space with a set of local coordinate charts $\{(U_i, \Phi_i)\}$, where U_i are open sets on M, the union of U_i covers M, Φ_i: $U_i \rightarrow R^2$ is a homeomorphism that maps U_i to the planar parameter domain. One point p on M can be covered by multiple local coordinate charts (U_i, Φ_i) and (U_j, Φ_j), the coordinate transition function Φ_{ij}: $\Phi_j \circ \Phi_i^{-1}$ converts one local parameters $\Phi_i(p)$ to another one $\Phi_j(p)$.

A *Riemannian metric* on surface M is a differential quadratic form. On a local coordinate chart, the metric can be represented as

$$ds^2(u,v) = E(u,v)du^2 + 2F(u,v)dudv + G(u,v)dv^2$$

where (u, v) are the local coordinates. A *Riemann* surface is a two-dimensional manifold, such that all transition functions are analytic functions, and on each chart the Riemannian metric has a special form

$$ds^2(u,v) = e^{2\lambda(u,v)}(du^2 + dv^2)\,. \qquad (1)$$

This kind of local coordinates are called *isothermal coordinates*. Suppose Φ: $M \to N$ is a diffeomorphism between two Riemann surfaces. Suppose (U, Ψ) is a chart on M, (x, y) is the local isothermal coordinates; (V, Ω) is a chart on N, (u, v) is the corresponding local isothermal coordinates, $\Phi(U) \subset V$. Then Φ restricted on U induces a map between parameter domains, Φ: (x, y) $\to$ ($u(x, y)$, $v(x, y)$). If

$$\frac{\partial u}{\partial x} = \frac{\partial v}{\partial y}, \frac{\partial u}{\partial y} = -\frac{\partial v}{\partial x} \qquad (2)$$

holds for any restrictions of Φ, then Φ is called a *conformal map* between M and N. Conformal means angle preserving. Suppose γ_1, γ_2 are two arbitrary curves on M intersect at the point p with angle α, Φ is a conformal map from M to N, then $\Phi(\gamma_1)$ and $\Phi(\gamma_2)$ are two curves on N, intersect each other at the point $\Phi(p)$ with angle α. Angle preserving property is very valuable for real applications. Because the local shape features are preserved after mapping, it is convenient and reliable to conduct registration and alignment in the parametric domains.

Due to the fact that the cortical surface of a brain is a genus zero surface and topologically equivalent to a sphere, conformal mapping provides a convenient way to parameterize brain surfaces without angular distortion, which is computed by minimizing the harmonic energy of the map [4], i.e., for genus zero surfaces M_1, M_2, f: $M_1 \to M_2$ is conformal if and only if f is harmonic. Based on this fact, we can easily compute the conformal mapping between genus zero surfaces by minimizing the harmonic energy. In practice, we use the triangular mesh to approximate genus zero surfaces. Discrete harmonic energy and Laplacian operator are defined as in [4].

Suppose $f \in C^{\mathrm{PL}}$, where $C^{\mathrm{PL}}(K)$ represent a linear space consisting of all piecewise linear functions defined on the simplicial complex K, the implicit energy is defined as:

$$E = \sum_{\{u,v\}\in K} k_{u,v} \left\| f(u) - f(v) \right\|^2 \qquad (3)$$

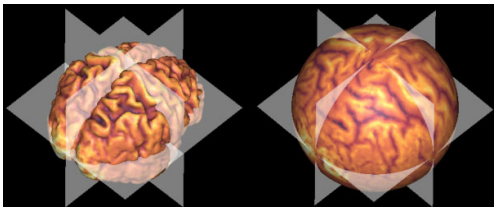
where u, v denote vertices, $\{u, v\}$ denotes the edge linking between u and v. $k_{u,v}$, are constant. The *discrete Laplacian* is the linear operator $\Delta : C^0K \to C^0K$ on the space of piecewise linear functions on K, Δ is defined by the formula

$$\Delta f = \sum_{\{u,v\}\in K} k_{u,v}(f(v) - f(u))\,. \qquad (4)$$

The function f minimizes the harmonic energy, if and only if $\Delta f(v)$'s tangential component is zero for every interior vertex v of K. Note that the corresponding triangular mesh of a genus zero surface does not have boundary edges.

For a vector valued function $\vec{f} : M_1 \to R^3$, $\vec{f} = \{f_0, f_1, f_2\}$, $f_i \in C^{\mathrm{PL}}$ (i=0, 1, 2), the energy of $\vec{f}$ is computed by $E(\vec{f}) = \sum_{i=0}^{2} E(f_i)$. In a similar way, the piecewise Laplacian of $\vec{f}$ is computed by $\Delta\vec{f} = (\Delta f_0, \Delta f_1, \Delta f_2)$. More specifically, since M_2 is S^2, then the conformal mapping $\vec{f} : M_1 \to S^2$ can be constructed by using the steepest descent method, which is not unique but forms a so-called Möbius group [4].

With the zero mass-center constraint, all conformal maps are restricted to a 3D Euclidean rotation group. In order to determine a unique mapping, we first manually align the original surface to a pre-defined orientation strictly. For example, in cortical surface mapping (Figure 1), we define the Cartesian coordinate system by locate the coordinate origin at the mass center of the surface. The yz plan is defined by the brain's hemisphere plane and xy plane passes the originating points of the central sulci which are close to the hemispheric cleft. This configuration ensures a unique solution of the computation.



(a) (b)

Figure 1: (a) shows the brain cortical surface with its mass center positioned at the coordinate origin, the yz plane aligned to the hemisphere plane and the originating points of the central sulcus near hemisphere clefts defines the xy plane. (b) shows the conformal mapping of the brain cortical surface to a unit sphere.

3. LANDMARK CONSTRAINED CONFORMAL MAPPING

Conformally mapping brain surfaces to a unit sphere does not guarantee a consistent alignment of the anatomical features across subjects. In order to relate and compare anatomical features or functional activations across subjects, it is necessary to establish a mapping that specifies a unique correspondence between each location in one brain and the corresponding location in another, namely, to bring the two brains into registration. Since gyral and sulcal landmarks are typically accurate indicators of the many functional areas, it seems likely that using these features to drive the registration of the cortical surfaces will result in a more accurate alignment of corresponding functional areas. In this section, we present a novel method to register brain surfaces in the parameter domain, which not only explicitly match those labeled landmarks, but also make use of surface's intrinsic geometry via conformal mapping to optimize the alignment for other anatomical features.

After mapping the cortical surface of each individual subject onto a sphere, we morph them to register with an average, canonical template, guided by a combination of feature-alignment (sulcus/gyrus) and isometry-preserving forces (conformal geometry). In detail, major landmarks are aligned on the spherical domain by recomputing the conformal mapping with hard coded landmark constraints. As shown in Figure 2, some features, such as occipital pole, frontal pole, the hemispheric cleft and the left and right central sulci, are used, while we explicitly enforce that the hemispheric cleft must be mapped onto the hemispherical circle of the canonical domain (unit sphere) and that the frontal pole and occipital pole must be mapped to the south and north poles of the

unit sphere, respectively. In order to determine a standard location for the landmark of left and right central sulci in the parametric domain, we choose the brain of one adult to be conformally mapped to the unit sphere without constraining the location of both central sulci. The generated result is regarded as the *Standard Conformal Brain Model*. We use it as the exemplary template indicating the locations of major landmarks, as well as other cortical structures in the spherical domain. Once this template is established, other subjects' cortical surfaces can be conformally mapped to this template model with landmarks constrained at specific locations, such as aligning its central sulci with the corresponding ones of the standard CBM. Figure 2(a) shows the original cortical surface used as the template. The hemispheric cleft and both the central sulci are highlighted in blue, while the frontal and occipital poles are marked using a yellow point and a purple point, respectively. The standard CBM is shown in Figure 2(b), where the hemispheric cleft is mapped as the meridian and the frontal and occipital poles are mapped to the north and south poles of this model. Note that the central sulci are conformally mapped without constraints in this case. A subjects' cortical surface and its corresponding CBM are shown in Figure 2(c) and Figure 2(d), respectively.

To achieve the aforementioned mapping, let's suppose that C_1 and C_2 are two cortical surfaces we want to compare and that $f_1: C_1 \to S^2$ is the canonical cortical surface mapping. We manually label the major anatomical features as landmarks on the two cortical surfaces as discrete point sets based on the initial surface rendering of the brain, as shown in Figure 2 (a) and (c). We denote them as $\{ p_i \in C_1 \}$ and $\{ q_i \in C_2 \}$, with p_i matching to q_i. We proceed to compute a map $f_2 : C_2 \to S^2$ from C_2 to S^2. First, we still use the result of a normal conformal mapping as the initial condition. With an initial computation of conformal map, we assume that the corresponding features of the cortical surfaces for both the canonical template and the individual subject are very close to each other at the spherical domain. Then, the landmark-constrained optimization is computed, which still minimizes the harmonic energy, but every labeled point is constrained to be aligned with its counterpart on C_1 at the spherical domain.

Our *landmark constrained conformal cortical surface mapping* approach is as follows:

Algorithm: Input (aligned mesh M, step length δt, energy difference threshold δE), output ($\vec{f}_2 : C_2 \to S^2$) where $\vec{f}_2$ minimizes the harmonic energy based on the pre-assigned constraints.

(a). Compute conformal mapping $\vec{f}_{2\,cnf} : C_2 \to S^2$ using the steepest descent method [4]. The difference here is that we use vertex projection instead of Gauss map, which is computed by

$$P(v) = \frac{v - c}{\|v - c\|}, v \in M$$

where $P(v)$ is the projection map from M to S^2 at v, and c is the mass center of M.

(b). Assign each vertex q_i that is labeled as point on the landmarks to its constrained location indicated by p_i. Then compute constrained harmonic energy E_0.

(c). For each vertex $v \in M$, compute absolute derivative $D\vec{f}$ by

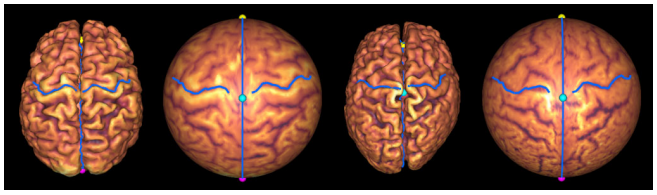
$$D\vec{f}(v) = \Delta\vec{f}(v) - (\Delta\vec{f}(v))^{\perp}.$$

Then, with the steepest descent algorithm, the offset for each vertex is computed by $\delta\vec{f}(v) = -D\vec{f}(v) \times \delta t$.

(d). Update $\vec{f}(v)$ (vertices) by $\delta\vec{f}(v)$ and then "pull" each vertex q_i back to its original position.

(e). Compute current energy E, if $\|E - E_0\| < \delta E$, return $\vec{f}(v)$ which is the constrained conformal mapping from its original domain. Otherwise, replace E_0 by E and repeat steps (b) to (e).

The result is shown by Figure 2 (b) and (d). Note that, the anatomical features in Figure 2 (a) and (c) appear to be very different from each other. With our proposed algorithm, the landmarks of Figure 2 (d) are now exactly aligned to that of Figure 2 (b). Note that, after inspection to the result of such parametric registration, we observe that local adjustments for the lankmark matching do not generate any significant conformality degradation over the domain.



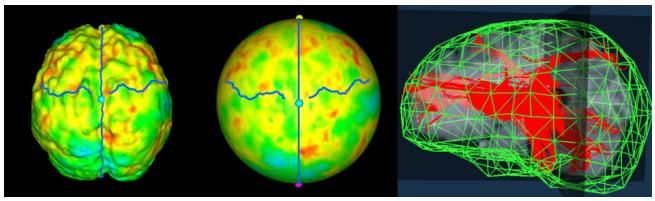
(a) (b) (c) (d)

Figure 2: (a) shows the template brain cortical surface with hemisphere cleft, central sulci, etc. as the landmarks. (b) shows the result of mapping the cortical surface of (a) onto the unit sphere by the normal conformal mapping. (c) shows the cortical surface of a subject, with the same anatomical landmark specified. (d) shows the result of the cortical surface registration for the subject at the spherical domain.

4. MULTIMODEL IMAGING INFORMATION INTEGRATION

To model multimodality imaging data (MRI, PET, and DTI) obtained from an individual subject using the CBM model, we first co-register all image modalities to the original MRI and then extract the brain. Once the homologous CBM is established, all results derived in native space from co-registered MR, PET, and DTI data is integrated in the CBM and the spatial/functional relationship between such diverse datasets can be determined using rigorous statistical analysis. Note that we do not transform or parameterize PET or DTI volume data directly. All information from PET, DTI, and EEG is computed strictly based on individuals' brain data in their native spaces in order to avoid any distortion. Specifically, the PET data is sampled based on the "inverse gradient" method. In order to match the resolution of the MR surface to the surface of PET for sampling, the high-resolution MR surface is smoothed and the direction of the normal vector (gradient) is calculated in each surface voxel. The co-registered PET image volume is sampled in the direction of the inverse gradient (into the cortical mantel up to a pre-defined depth) yielding PET sampling values. Functionally abnormal cortical regions can then be objectively determined using statistical group analysis methods. Furthermore, the depth of these cortical regions can be extended so that the volumes include fiber tracts which

terminate at the cortical/white matter junction. Fiber tracts will be calculated in native space based on co-registered DTI data. Connection strength between standardized cortical volume elements can be calculated and measured quantitatively. Figure 3 shows an example of information integration in the CBM model. For DTI data we currently employ the probability fiber tracking algorithm [5, 9]. The PET information and the fiber tracts can be transferred, parameterized and stored in its CBM model. Based on the CBM and its integrated information, our computational framework can provide many novel, accurate, and objective tools to aid in analysis of multimodal imaging data in this uniform data structure.



(a) (b) (c)

Figure 3: Integration of PET and DTI information in a brain's CBM model. (a) Inverse gradient fusion of MR and PET data. (b) The CBM model with mapped PET information. (c) Rendering of fiber tracts in the same subject. The connectivity strength can be mapped to the CBM as well.

5. CONCLUSION AND DISCUSSION

This paper has presented an analytic approach for intersubject brain analysis based on landmark constrained conformal mapping of the brain. This novel conformal mapping allows reproducible transformation of each subject's brain to a canonical spherical domain and is the basis for subsequent statistical analysis of cortical surface across subjects. The CBM model does not only serve as the unit of statistical analysis of PET images across individuals' brains, but is also the basis for a quantitative assessment of fiber tract connectivity strength between anatomical territories of the brain. The evaluation of the intersubject registration accuracy will be conducted in the near future. In addition, advanced data mining and analysis tools will be developed based on the CBM data structure.

6. ACKNOWLEDGEMENT

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