An algorithm for registration of evolving closed surfaces

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Abstract

Magnetic resonance imaging provides three-dimensional image volumes that show the detailed structure of the brain. Such data, acquired over time from a single subject, can illuminate patterns of growth, including spatial and temporal variations. To characterize volumetric or surface growth from such longitudinal studies, it is necessary to register the image volumes themselves, or surfaces constructed from these volumes. Registration establishes a point-to-point correspondence between volumes or surfaces. In studies that compare different subjects, "inter-subject registration" establishes approximate correspondence based on similar features. In longitudinal studies, the correspondence is physical, and "intra-subject registration" can, in theory, match material points in evolving structures. Algorithms developed for "inter-subject" registration introduce artificial distortions when applied to longitudinal studies of an individual; even simple dilations are poorly registered by existing algorithms. Such distortions would prevent accurate estimates of growth during cortical development, for example. The particular problem of interest (cortical folding) occurs on a thin surface that is topologically equivalent to a closed sphere. We have developed a registration algorithm based on continuum mechanics, that is intended to minimize artifactual distortion while matching features on two surfaces obtained from the same subject at different times. After an initial correspondence brings points into approximate registration, the finite element method is applied to a spherical parameterization of the surface, to minimize a combination of a strain–energy density function and a "matching energy" function. In this paper, the algorithm is applied to a hierarchical set of test cases to establish its validity. In future studies it will be applied to characterize growth of the cortical surface in gyrencephalic mammals and humans.

Introduction

Background:

Measures of spatial and temporal variations in growth are needed to characterize morphogenetic processes such as folding of the cerebral cortex (Van Essen, 1997). Advances in anatomical imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), and optical coherence tomography (OCT) allow high resolution images of the brain to be acquired. Repetition of scans at multiple time points provides a sequence of snapshots during development. To quantify local cortical growth over time, correspondence must be established between points on the cortex at different times.

Registration is the process of determining a one-to-one correspondence between two or more *N* dimensional objects (e.g. curves, images, surfaces). In medical image analysis, inter-subject registration provides a correspondence between different subjects or groups of subjects. Intra-subject registration provides a correspondence between a single individual imaged at different times or using different imaging modalities.

Registration methods can be split into two major categories: surface-based and volume-based approaches. A large body of research describes many different volume-based registration approaches (e.g. Beg et al., 2005, Christensen et al., 1996, Davatzikos, 1996, Johnson and Christensen, 2002, Joshi and Miller, 2000, Shen and Davatzikos, 2002). A number of reviews provide a thorough analysis of volume-based registration methods (e.g. Gholipour et al., 2007, Holden, 2008). Surface-based approaches have also been well studied in the literature (e.g. Drury et al., 1999, Fischl et al., 1999, Glaunès et al., 2004, Thompson and Toga, 1996, Valliant and Glaunès, 2005). Some surface-based registration approaches are also reviewed in (Gholipour et al., 2007). For convenience, we will provide a brief review of some of those methods here. Van Essen et al. (2001) use spherical surface parameterizations to minimize surface distortions on the sphere while matching landmark curves (Van Essen et al., 2001). Fischl et al. (1999) also inflate the cortical surface to a sphere, but minimize distortions on the sphere while matching convexity, which is a surface geometry measure that is not as affected by noise as curvature (Fischl et al., 1999). Lui et al. (2004) employ a hybrid volume- and surface-based approach that first involves a volume technique to roughly align the images, and then a surface method to complete the warp (Lui et al., 2004). Shi et al. (2007) create an implicit surface representation within a narrow band from explicit surfaces. They then use 3D techniques to solve a governing partial differential equation (PDE), which minimizes a global energy term that is based on the sum of a harmonic and data energy term (Shi et al., 2007). Litke et al. (2005) parameterize open surfaces to planes, and use the finite element method to solve a PDE that minimizes a global energy term based on deformation smoothness, bending of normal vectors, and feature correspondence (Litke et al., 2005). If applied to the cortical surface, which is topologically equivalent to a sphere, this approach would require cuts to be made in the surface.

Since we are interested in quantifying growth of the cortex during development, a surface-based approach is warranted. For human studies, segmentation and surface generation algorithms are well established (e.g. Dale et al., 1999, Hill et al., 2009 Van Essen et al., 2001, Zhang et al., 2001) , although they may require some manual editing. Animal studies require segmentation to be performed manually, which is time-consuming. However, the resulting surfaces allow for shape features like curvature, sulcal depth, folding indices, and surface strain to be computed straightforwardly. Surfaces also have a well defined topology, which must be maintained to achieve an accurate registration (Van Essen et al., 1998).

Motivation:

Our goal is to calculate growth during brain development in ferrets (first 7 weeks of life) and humans (gestational age 25 weeks through term equivalent). In order to calculate growth between cortical surface representations at different time points, surfaces must be registered to one another. Existing registration algorithms designed for inter-subject registration (e.g., CARET, Van Essen et al., 2001) were evaluated first. In order to validate algorithms for intra-subject registration, two test cases were created to simulate uniform growth; in order to quantify inhomogeneous expansion of a surface, an algorithm should be able to correctly characterize uniform expansion.

For the first test case, the reference surface coordinates (**X**) were set equal to the deformed surface coordinates (**x**). For the second test case, the reference surface coordinates were multiplied by 1.25 to create the deformed (uniformly expanded) surface. For both cases, 7 exact landmark curves were used for the registration process.

$$Case\ 1:\ \boldsymbol{x} = \boldsymbol{X}$$
$$Case\ 2:\ \boldsymbol{x} = 1.25\boldsymbol{X} \qquad 1.1$$

The Lagrangian surface strain tensor is a local measure of deformation rigorously defined in terms of the spatial derivatives of the displacement field (Filas et al., 2008). If an infinitesimal circle is drawn on the reference surface, it becomes an ellipse after deformation of the surface. The principal stretches $\lambda_i = \frac{d_i}{d}$. characterize the lengths of the principal axes of this ellipse (d_1,d_2), relative to the original diameter of the circle (d) (Fig. 1). The principal strains are given by the equation (Taber 2004)

$$E_1 = \frac{1}{2}\left(\lambda_1^2 - 1\right)$$
$$E_2 = \frac{1}{2}\left(\lambda_2^2 - 1\right) \qquad 1.2$$

Surface strain was estimated between for the mapping from the reference surface to the registered surface using a method developed previously (Filas et al., 2008). Both first and second principal strains should be constant over the surface. First principal strain E_1 should equal 0 for the first case and 0.2813 for the second case. However, when an existing registration algorithm for inter-subject registration (CARET, Van Essen et al., 2001) was used, the resulting strain fields (shown in Fig. 1) suggest large spatial variations of growth throughout the cortex.

Similar results, i.e. significant artifactual non-uniform strains arising in an example of uniform growth, were obtained using algorithms of Fischl et al. (1999), Shi et al. (2007), and Vaillant and Glaunes (2005). These results suggest that a new method to minimize artifactual distortion introduced by the registration process would be very valuable for studies of development. A proposed criterion is that the magnitude of strain artifacts obtained when registering a surface to a transformed version of itself with zero or uniform growth, should be an order of magnitude smaller than true strains of interest.

In this paper, we present a surface registration method to be applied to intra-subject studies of brain development. The goal of the algorithm is to calculate displacement vectors **v** for the surface coordinates that minimize a strain-energy density function associated with surface deformation, while maximizing alignment of surface features. This can be accomplished by a mechanics-based formulation, in which displacements are governed by the equation of an elastic membrane sliding over the surface. A feature-based matching force and a viscous drag force modify the displacement field. Displacements are solved for using the finite element method. Specifically, COMSOL Multiphysics v.3.4 (COMSOL Inc, Burlington, MA) is used in combination with Matlab v.7.5 (Mathworks, Natick, MA).

Methods

Overview:

The algorithm identifies displacements **v** on a sphere that will minimize the "strain energy" of surface stretch, while simultaneously matching surface features. The underlying assumption is that the best estimate of local growth is the one that, after matching surface features, is the least distorted. The strain-energy density function is minimized by solving a partial differential equation (PDE) that describes relaxation of an elastic membrane, sliding over the surface, subject to viscous drag.

$$\rho\alpha_{dM}\frac{\partial \boldsymbol{v}}{\partial t} = \nabla \cdot \boldsymbol{P} + \boldsymbol{f} \qquad 2.1$$

Here ρ is density, α_{dM} is a viscous coefficient, $\boldsymbol{P}$ is the 1st Piola-Kirchhoff stress tensor, and $\boldsymbol{f}$ is a forcing term derived from the mismatch between surface features. Note that the viscous term on the left hand side of Eqs 2.1 differs from the inertial term common in classical mechanics. In principle, this equation can be solved by standard finite element methods on a surface embedded in 3D.

In practice, this type of equation is much easier to solve on a plane or standard spherical surface (rather than a convoluted cortical surface), largely because it is most straightforward to constrain displacements to the surface of a plane or sphere. The cortical surface is topologically equivalent to a sphere, so that a smooth map from the cortex to the sphere can be obtained by "inflation" of the cortical surface. However the objective is not to minimize distortions of the spherical surface, but to minimize the distortion of the physical surface. Accordingly, displacements in the spherical representation must be described in terms of their effect on the strain energy of the physical surface. This is achieved mathematically by using the mapping from cortical surface to sphere (see Theory below).

Another useful step in solving the problem is to convert Eqs 2.1 to its weak form (Szabó and Babuška, 1991),

$$\rho\alpha_{dM}\dot{v}_i w_i + P_{ij}w_{i,j} - f_i w_i = 0 \qquad 2.2$$

where w_i is a test function. This approach is advantageous because it does not require us to estimate the spatial derivatives of $\boldsymbol{P}$. Since $\boldsymbol{P}$ depends in turn on spatial derivatives of **v**, errors due to numerical differentiation are reduced. The specific form of $\boldsymbol{P}$ is presented below. The derivation of Eqs 2.2 is presented in the Appendix.

Theory:

In this paper, we will restrict analysis to closed surfaces embedded in 3D Euclidian point space. Let *FV* be the reference surface, with coordinates $\boldsymbol{X}$, and *fv* be the deformed surface at time t, with coordinates $\boldsymbol{x}$, where $\boldsymbol{X}, \boldsymbol{x} \in \mathcal{R}^3$ and $t \in \mathcal{R}$. Both *FV* and *fv* can be represented as spherical surfaces *SPH* and *sph* with coordinates $\boldsymbol{A}$ and $\boldsymbol{a}$, where $\boldsymbol{A}, \boldsymbol{a} \in \mathcal{R}^3$. Coordinate mappings are linear, one-to-one and at least twice differentiable, and are defined from surfaces *FV* to *fv*, *sph to fv*, and *SPH* to *sph*.

$$\begin{aligned} \boldsymbol{x} &= \boldsymbol{\chi}(\boldsymbol{X}, t) \\ \boldsymbol{x} &= \boldsymbol{\varphi}(\boldsymbol{a}) \\ \boldsymbol{a} &= \boldsymbol{\psi}(\boldsymbol{A}, t) \end{aligned} \qquad 2.3$$

For simplicity, spatial and time dependence will no longer be stated explicitly. Note that φ is not a function of time. As coordinates are displaced on *sph*, and subsequently on *fv*, the mappings *FV* to *fv* and *SPH* to *sph* change; the mapping *sph to fv* remains constant. From these linear mappings we can calculate the Jacobian matrices between the surfaces and the spherical surfaces.

$$\begin{aligned} \boldsymbol{H} &= \frac{\partial \boldsymbol{x}}{\partial \boldsymbol{a}} \\ \boldsymbol{G} &= \frac{\partial \boldsymbol{a}}{\partial \boldsymbol{A}} \end{aligned} \qquad 2.4$$

The deformation gradient tensor $\boldsymbol{F}$ relates line elements on *FV* to those on *fv* (Taber 2004).

$$\boldsymbol{F} = \frac{\partial \boldsymbol{x}}{\partial \boldsymbol{X}} \qquad 2.5$$

To solve Eqs 2.2 we need to define constitutive relationships between deformation and stress, and to specify the matching term, $\boldsymbol{f}$. The constitutive relationships are obtained from continuum mechanical models. For hyperelastic materials, the first Piola-Kirchhoff stress tensor $\boldsymbol{P}$ is obtained by differentiating the strain-energy density function W with respect to the deformation gradient tensor, $\boldsymbol{F^T}$. A number of strain-energy density functions exist for different material models. We have chosen to use a modified Neo-Hookean material model (COMSOL manual).

$$W = \frac{1}{2}(\mu(I_1^* - 3) + \kappa(J - 1)^2) \qquad 2.6$$

This form of the equation takes into account compressibility via the "bulk modulus" κ; μ is the shear modulus. Both μ and κ are constants. I_1^* is a modified form of the first invariant that is independent of volume change (COMSOL manual)

$$I_1^* = I_1 I_3^{-\frac{1}{3}} \qquad 2.7$$

I_1 and I_3 are the first and third invariants (Taber 2004).

$$\begin{aligned} I_1 &= tr(\boldsymbol{F^T F}) \\ I_3 = J^2 &= det(\boldsymbol{F^T F}) \end{aligned} \qquad 2.8$$

J is the dilatation ratio, which represents the local volume change during deformation (Taber 2004).

Once W is defined, $\boldsymbol{P}$ can be calculated by taking the derivative of W with respect to the deformation gradient (Taber 2004).

$$\boldsymbol{P} = \frac{\partial W}{\partial \boldsymbol{G^T}} \qquad 2.9$$

Note that the derivative is taken with respect to $\boldsymbol{G^T}$ instead of $\boldsymbol{F^T}$. This is because Eqs 2.2 is solved for the displacements $\boldsymbol{v}$ on *sph*. Eqs 2.6-2.9 allow for the initial stress field to be calculated; however, we need to quantify how stress changes as a function of $\boldsymbol{v}$ over time. Let us define the Jacobian between *fv* and *sph* in the same manner as Eqs 2.4 and call it $\boldsymbol{Q}$ ($\boldsymbol{Q}$ is not used in the solution, only to complete the derivation.) $\boldsymbol{F_0}$, $\boldsymbol{Q}$, $\boldsymbol{H}$, and $\boldsymbol{G_0}$ are related to one another.

$$\boldsymbol{G_0} = \boldsymbol{H^{-1} F_0 Q^{-1}} \qquad 2.10$$

Displacement of coordinates on *sph* will cause $\boldsymbol{G}$ to change over time (Taber 2004).

$$\boldsymbol{G_1} = \boldsymbol{I} + (\boldsymbol{\nabla v})^{\mathrm{T}} \qquad 2.11$$

The total Jacobian $\boldsymbol{G}$ is given by the product of $\boldsymbol{G_1}$ and $\boldsymbol{G_0}$, which can then be related back to the initial deformation gradient.

$$\boldsymbol{G} = \boldsymbol{G_1}\boldsymbol{G_0} = \boldsymbol{G_1}(\boldsymbol{H}^{-1}\boldsymbol{F_0}\boldsymbol{Q}^{-1}) \qquad 2.12$$

Solving Eqs 2.10 for $\boldsymbol{F}$, and inserting Eqs 2.11 and 2.12 gives

$$\boldsymbol{F} = \boldsymbol{H}\boldsymbol{G}\boldsymbol{Q} = \boldsymbol{H}\left(\boldsymbol{G_1}(\boldsymbol{H}^{-1}\boldsymbol{F_0}\boldsymbol{Q}^{-1})\right)\boldsymbol{Q} \qquad 2.13$$

Eqs 2.13 can be further simplified and rewritten to show the total deformation gradient as a function of $\boldsymbol{v}$.

$$\boldsymbol{F} = (\boldsymbol{H}(\boldsymbol{I} + (\nabla\boldsymbol{v})^{\mathrm{T}})\boldsymbol{H}^{-1})\boldsymbol{F_0} \qquad 2.14$$

To compute the matching force term $\boldsymbol{f}$, we employ the method described in Shi et al. (2007). An energy term is defined as the squared difference between values of some shape characteristic on the two surfaces. The first variation of this term is given by (Shi et al. 2007)

$$\boldsymbol{f} = (f_1 - f_2)\nabla f_2 \qquad 2.15$$

The variables f_1 and f_2 are scalar functions of space on the reference and deformed surfaces (the principle can be applied to vector-valued functions). In this study we use functions that decay with the absolute geodesic distance (D and d) from manually drawn landmark curves.

$$f_1 = A_1 e^{-\frac{D^2}{2{\sigma_1}^2}}$$
$$f_2 = A_2 e^{-\frac{d^2}{2{\sigma_2}^2}} \qquad 2.16$$

For cortical surface registration we draw landmarks along the base of sulci. It may be possible to use intrinsic features of the surface, like curvature magnitude or sulcal depth as matching terms to register similar surfaces. However large changes in curvature and sulcal depth occur during the first few weeks of development so that large mismatches may occur. f_1 and f_2 will typically not match exactly when the simulation has converged. Instead, solving the equation 2.2 finds a balance between matching f_1 and f_2 while minimizing the strain-energy density function on the surface. The total energy is given by

$$E_{total} = \frac{1}{2}\left(\mu(I_1^* - 3) + \kappa(J-1)^2\right) + \frac{1}{2}(f_1 - f_2)^2 \qquad 2.17$$

Non-dimensional form:

From Eqs 2.1, using the standard Neo-Hookean model, the divergence of stress can be written in terms of displacement. By applying a change of variables, Eqs 2.1 can be rewritten in a non-dimensional form (Appendix).

$$\frac{\partial U_i}{\partial \tau} = \frac{\partial^2 U_j}{\partial \xi_i \partial \xi_j} + F_i \qquad 2.18$$

The variable substitutions are given by

$$\begin{aligned} t &= t_c \tau \quad & t_c &= \frac{\rho \alpha_{dM} A_c}{\mu} \\ \boldsymbol{x} &= x_c \boldsymbol{\xi} \quad & x_c &= \sqrt{A_c} \\ \boldsymbol{u} &= u_c \boldsymbol{U} \quad & u_c &= \sqrt{A_c} \\ \boldsymbol{f} &= f_c \boldsymbol{F} \quad & f_c &= \frac{\mu}{\sqrt{A_c}} \end{aligned} \qquad 2.19$$

A_c is a characteristic area, which is defined as the surface area of the deformed sphere *sph* divided by the number of elements in the finite element mesh. The non-dimensional form of Eqs 2.1 and 2.2 allow us to most easily compare parameters and results for different cases.

Algorithm:

The commercial software packages COMSOL (finite element analysis) and Matlab are used with one another to solve all parts of this process. The surface of a sphere is generated in COMSOL with the same radius as *sph*. The variables $\boldsymbol{H}$, $\boldsymbol{F_0}$, f_1 and f_2 are calculated in Matlab from surface mesh data using custom-written functions. f_2 is a function of the current position on the surface *fv* (and correspondingly *sph*). Therefore the value f_2 must be updated as coordinates displace during registration. This is accomplished via an external function call. $\boldsymbol{H}$, $\boldsymbol{F_0}$ and f_1 are functions of the original coordinate position and therefore do not need to be updated during registration. The variables are initialized at interpolation points on the spherical surface using finite element interpolating functions (COMSOL).

The finite element mesh was generated automatically in COMSOL; approximately 600-1200 triangular mesh elements were used, with Lagrange 2nd order interpolating functions. Displacements were obtained using the time-dependent solver with the generalized minimum residual (GMRES) linear solver (Saad and Schultz, 1986) with Incomplete LU preconditioning.

The projection of spatial derivatives onto the tangent plane was calculated using functions within COMSOL. The tangential components of the spatial gradient are given by

$$(\nabla \mathbf{v})_{T} = (\boldsymbol{I} - \boldsymbol{n}\boldsymbol{n}^{T}) \cdot \nabla \mathbf{v} \qquad 2.20$$

Displacements were constrained to remain on the surface. The solution was then exported to Matlab where the surface coordinates $\boldsymbol{a}$ and $\boldsymbol{x}$ are updated. Estimation of surface strain is performed using custom software in the Matlab environment.

Results

Results from a number of examples are shown to illustrate the method. First we describe a 2D example of simultaneous matching and relaxation in the plane. We then illustrate the correction of artificial distortions introduced onto simple surfaces in 3D. Finally, the method is applied to register a cortical surface obtained by MRI of a juvenile ferret brain.

Registration of a plane surface:

The reference surface is a square in the xy-plane with boundaries at $x = \pm 3$ and $y = \pm 3$. An initial displacement field was applied to create distortions between the reference surface and corresponding deformed surface. The boundaries remain fixed.

$$x = X + \frac{0.75}{\pi^2} sin\left(\frac{2\pi}{3} X\right)$$
$$y = Y + \frac{0.75}{\pi^2} sin\left(\frac{2\pi}{3} Y\right) \qquad 3.1$$

Shape features were defined for each of the surfaces. The feature on the reference surface was offset from the corresponding feature on the deformed surface.

$$f_1 = 10e^{\frac{-25(x-0.25)^2}{2}}$$
$$f_2 = 10e^{\frac{-25x^2}{2}} \qquad 3.2$$

High values of f_1 were initially shifted by 0.25 units in the positive x-direction with respect to f_2 when mapped onto the deformed surface. For the surface features to align, the coordinates at x=0.25 should move to x=0 after registration. Specifically, if one were to draw a line (l_1) from x=-3 to x=0.25 and then another (l_2) from x=0.25 to x=3 at τ=0, after perfect registration the final lengths would each be 3 units. The Lagrangian strains E_1 and E_2 for line l_1 and l_2 should be -0.074 and 0.095 respectively.

Eqs 2.2 was solved via the finite element method (COMSOL) as described above (without mapping the problem to the sphere). Parameters are given in Table 1. The displacement field that minimized the strain-energy density function and matching cost function was used to update the coordinates on the deformed surface.

Spatial plots of the strain-energy density function before and after the registration process (Fig. 4e,f) show that the initial areas of high values of the strain–energy density function are reduced. On each side of the surface feature, the strain-energy density function approaches a constant, spatially uniform value. The difference between the surface feature terms is reduced by approximately an order of magnitude. Surface features are not matched exactly because the goal is to balance the minimization of distortion with feature matching. Principal strain values are estimated for the registration between the reference surface and deformed surface before and after the correction. High strains exist initially between the reference and deformed surface. After registration correction, strains become more uniform on either side of the surface features. The strain values obtained by our method (Fig. 5) are very close to the exact values.

Registration of a spherical surface:

The second example involves deformations on a sphere. Initial displacements were applied to the surface in spherical coordinates.

$$\begin{gathered} \phi = \Phi \\ \theta = \Theta + \frac{0.1}{\pi} sin(4\Theta) cos^2(\Phi) \\ r = R \end{gathered} \qquad 3.3$$

Surface features were defined as functions of Cartesian coordinates, and were offset spatially from one another.

$$\begin{gathered} f_1 = 10e^{\frac{-25(x-0.15)^2}{2}} \\ f_2 = 10e^{\frac{-25x^2}{2}} \end{gathered} \qquad 3.4$$

The initial deformation gradient was calculated in Matlab and imported into COMSOL along with the surface features. The Jacobian $\boldsymbol{H}$ is identity. Displacements were calculated by solution of Eqs 2.2 on the sphere using the finite element method (COMSOL).

Initial distortions, shown in Fig. 6(e) and Fig. 7(a,c), decay during registration. Because the high values of the surface features align with one another, the positive-x side of the sphere expands while the negative-x side of the sphere contracts. In the xz-plane, if a curve (l_1) is drawn from (-1,0) to (0.15,0.989) and another curve (l_2) is drawn from (1,0) to (0.15,0.989), both along the circle that lies in the plane at τ=0, after perfect registration each curve's final length should be 1.571 units. The Lagrangian strain E_1 and E_2 for curve l_1 and l_2 are -0.084 and 0.111 respectively.

In Fig.6(f), the spatial distribution of the strain-energy density function shows three regions that contain approximately uniform values. The dark band is where the high values of the surface features have aligned with one another. The regions on either side of the dark band are approximately constant, but at different values of the strain-energy density function. The principal strain estimates (Fig. 7) associated with registration complete the description. Principal strains are approximately zero in the region where the high values of the surface features overlap. The side of the sphere with positive x-coordinates has high positive strains, corresponding to expansion. The side of the sphere with negative x-coordinates has high negative strain, corresponding to compression. The difference between surface features is reduced by approximately one order of magnitude.

For the registrations of the plane and sphere, the mean of the total energy function (Eqs 2.17, Fig. 8), was determined by summing the total energy function over the surface at each time point during the solution and dividing by the number of nodes. For the both the plane and sphere case, this global measure decreases over time, approaching a constant value.

Registration of a "pumpkin" shape:

The third test case involves a sphere that expands and folds into a shape like a pumpkin. No surface features were matched for this case. Displacements in the radial direction were applied to the reference coordinates to create the deformed surface. The initial deformation gradient was calculated and imported into COMSOL. The Jacobian, $\boldsymbol{H}$, is the identity operator.

$$\phi = \Phi$$
$$\theta = \Theta \qquad 3.5$$
$$r = 1.1R + 0.1sin(4\Theta)cos(\Phi)$$

The spatial distribution of the strain-energy density function shows marked reduction its variability (Fig. 9); however, differences still exist between the outward folds and inward folds. The initial strain field (Fig. 10a,c) shows large principal strains in areas of high negative curvature. After registration, principal strain values are more uniform over the surface, but still show some spatial variation, as the surface necessarily deforms non-uniformly to accommodate the change in shape.

Registration of a cortical surface from a juvenile (P14) ferret brain:

An anatomical MRI of the brain of a 14 day-old (P14) ferret was manually segmented, and the segmented volume was used to create a representation of the cortical surface. A spherical surface corresponding to the cortical surface was also generated. To create known artificial distortions, a displacement field was applied to the spherical surface. The displaced coordinates on the sphere were projected back onto the cortical surface, creating an artificially misregistered surface.

$$\phi = \Phi$$
$$\theta = \Theta + \frac{0.05}{\pi}sin(4\Theta)cos(\Phi) \qquad 3.6$$
$$r = R$$

Surface features f_1 and f_2 were generated using landmarks drawn on the cortical surfaces (Fig. 11a,b). Only an image of the feature on the reference surface is shown. Because the two surfaces are identical, the shape features appear the same. The initial principal strain fields show regions of both high positive and negative strain estimates. Since this test case involves registering a surface to itself, the principal strains should be equal to 0. After registration, the mean and standard deviation of principal strain estimates decreased significantly (Table 2). This is consistent with Fig. 12 where the higher localized regions of strain in Fig. 12(a,c) are replaced by lower and more diffuse values in Fig. 12(b,d).

For the more complex cases (pumpkin and ferret brain) the time history of the mean of the strain-energy density function is shown in Fig. 13. In both cases the mean of the strain-energy density function starts at a maximum, decreasing toward a constant value. In the pumpkin, the spatial variation in strain does not vanish, as the surface underwent true distortion as the shape changed.

Discussion

In this paper we introduce a method to register closed surfaces in 3D based on minimization of distortion while matching surface features. Our approach is similar to the methods presented in Shi et al. (2007) and Litke et al. (2005). Shi et al. (2007) take advantage of implicit descriptions of surfaces, which allows standard numerical schemes to be implemented in 3D. Beginning from an initial map, they iteratively solve a PDE on the reference surface. The optimal registration is defined as the minimization of an energy term, which is the sum of a harmonic (smoothness) and data (geometric features) term. Landmarks are also used to aide in the registration. However, when this method was applied to analyze uniform growth of a ferret cortical surface, it was found to introduce artificial distortions between the surfaces. The implicit surface method, because it relies on discrete voxel size, may not be optimal for longitudinal registration for highly convoluted surfaces like the mammalian brain.

Litke et al. (2005) map open surfaces to the plane, which simplifies the computations considerably. A PDE that accounts for nonlinear large deformations is solved using the finite element method and a multiresolution approach. The optimal registration is defined as the minimum of an energy function, which is the sum of regularization (smoothness), matching (geometric features) and bending energies. The specific approach of Litke et al. (2005) can only be applied to open surfaces, which would involve making cuts in or only looking at part of the cortical surface. The authors do not expect a one-to-one correspondence to exist between the surfaces, while our approach requires it. We deliberately do not include a penalty on bending energy, since the distortions we wish to quantify during cortical folding include large bending deformations.

This surface registration method is aimed ultimately at longitudinal studies of cortical development. While a number of registration algorithms are available to study inter-subject differences, these algorithms introduce distortions that prevent the accurate calculation of growth. The proposed algorithm reduces these distortions by using the finite element method to solve for displacements that minimize the sum of strain and feature energy between the cortical surfaces. A hierarchical set of test cases of increasing complexity was created to validate our method. Values of parameters were chosen so that the time constant t_c and force constant f_c were similar for each of the test cases.

Simple test cases illustrate the approach and demonstrate its efficacy. Initial distortions of a plane decay, and shifted surface features are brought into registration by this approach. In the absence of surface feature matching, the strain field in our test case would be uniformly zero after registration. Matching the surface features caused expansion on one side and compression on the other. In the spherical test case, as in the planar example, initial distortions of the spherical surface decay, while shifted surface features are brought into registration. The numerical results of the registration algorithm (e.g., Figs. 7b,d) agree well with the theoretical values that would arise from exact correspondence.

The "pumpkin" test case incorporates both growth and folding of a simple shape into a more complex shape, analogous to early stages in brain development. At ages of less than one week in ferrets, and around 25 weeks GA in humans, the cerebral cortex is very smooth. Within a few days in ferrets and a few weeks in humans, brain growth and folding increase dramatically. In the pumpkin test case, after registration the strain field (e.g, Fig. 10) still varies spatially. Minimization of the strain-energy density function does not necessarily eliminate spatial variations in strain, if the surface must stretch non-uniformly to accommodate a change of shape. Note that surface features were not matched in this example; if surface features were incorporated, additional variations in final strain field would be expected.

The final test case in this paper is based on a surface created from an MR image volume of a 14 day-old ferret brain. The coordinates of the reference surface were manipulated to create a deformed surface with known distortions. The surface features were generated using the landmark lines drawn in CARET (Van Essen et al., 2001). Identical landmark lines are used to create both the reference and deformed surface features. The initial principal strain fields show regions of high positive and negative strain. Since this test case involves registration of a surface to itself, zero strain should exist between the reference and deformed surface. After registration, both the mean and standard deviation of the principal strain estimates decreased significantly (Table 2). The higher localized regions of strain before registration (Fig. 12a,c) are replaced by much lower and more diffuse values (Fig. 12b,d). This test case demonstrates that the algorithm reduces artifactual strain values in a realistic surface.

The numerical solution of the equation of motion identifies a minimum of the objective function. The current approach does not seek a global minimum, so that initial conditions are important. This method requires an initial correspondence between two surfaces to be established in a "pre-processing" step. This correspondence should lie within the neighborhood of the desired solution. The CARET algorithm (Van Essen et al., 2001) is used in our study, and many other methods exist to establish approximate correspondence. The procedure is implemented in the COMSOL/Matlab environment. The number of vertices will influence the amount of time required to run through the entire registration process. The density of the finite element mesh also affects computational requirements (memory and processing time).

Conclusion

A surface registration algorithm that minimizes physical distortions during registration of brain surfaces from an individual is an important tool. It will allow researchers to to quantify true variations in growth during development of the brain. In this paper, we present an approach that can be implemented with commercial software, and use a hierarchical set of test cases to validate. We plan to use this algorithm to study regional patterns of growth during brain development in the ferret and in human subjects.

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Appendix

Derivation of the weak form:

We follow the approach described by Szabó and Babuška (1991). Eqs 2.1 in index notation is written

$$\rho\alpha_{dM}\dot{v}_i = P_{ij,j} + f_i \qquad 5.1$$

Note that $\dot{v}$ is the derivative with respect to time. Multiplying by an arbitrary test function w_i and integrating over Ω gives

$$\int_\Omega \dot{v}_i w_i dA = \int_\Omega P_{ij,j} w_i dA + \int_\Omega f_i w_i dA \qquad 5.2$$

where w_i is a test function . The product rule is then applied to the stress divergence term.

$$P_{ij,j} w_i = \left(P_{ij} w_i\right)_{,j} - P_{ij} w_{i,j} \qquad 5.3$$

Application of the Divergence Theorem gives

$$\int_\Omega \left(P_{ij} w_i\right)_{,j} dA = \int_{\partial\Omega} P_{ij} n_j w_i ds \qquad 5.4$$

where *n* is the unit normal vector on the boundary. Eqs 5.2 can then be rewritten as

$$\int_\Omega \dot{v}_i w_i dA = \int_{\partial\Omega} P_{ij} n_j w_i ds - \int_\Omega P_{ij} w_{i,j} dA + \int_\Omega f_i w_i dA \qquad 5.5$$

Satisfying the boundary conditions separately, in the interior we are left with.

$$\int_\Omega \left(\dot{v}_i w_i + P_{ij} w_{i,j} - f_i w_i\right) dA = 0 \qquad 5.6$$

Because this must hold true for an arbitrary domain, the quantity within the integral must be equal to zero.

$$\dot{v}_i w_i + P_{ij} w_{i,j} - f_i w_i = 0 \qquad 5.7$$

Derivation of non-dimensional form:

Using the standard Neo-Hooken constitutive model, the divergence of the first Piola-Kirchoff stress can be written in terms of displacements.

$$\rho\alpha_{dM} \frac{\partial u_i}{\partial t} = \mu \frac{\partial^2 u_j}{\partial X_i \partial X_j} + f_i \qquad 5.8$$

The following relationships are used to define non-dimensional time, τ, space, ξ , displacement, U, and force, F.

$$
\begin{aligned}
t = t_c\tau \quad & t_c = \frac{\rho\alpha_{dM}A_c}{\mu} \\
\boldsymbol{X} = x_c\boldsymbol{\xi} \quad & x_c = \sqrt{A_c} \\
\boldsymbol{u} = u_c\boldsymbol{U} \quad & u_c = \sqrt{A_c} \\
\boldsymbol{f} = f_c\boldsymbol{F} \quad & f_c = \frac{\mu}{\sqrt{A_c}}
\end{aligned} \qquad 5.9
$$

A_c is the characteristic area, which is defined as the surface area divided by the number of elements in the finite element mesh. Applying the definitions in Eqs 5.9, and using the product rule during differentiation, Eqs 5.8 can be rewritten as

$$
\frac{\partial U_i}{\partial \tau} = \frac{\partial^2 U_j}{\partial \xi_i \partial \xi_j} + F_i \qquad 5.10
$$

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Table 1: Parameters for each of the test cases. N is the number of elements in the finite element mesh, Ac is the characteristic area, μ is the shear modulus, ρ is the density, α_{dM} is the damping coefficient, t_c is the time constant and f_c is the forcing constant.

Test Case	N	A_c (m^2)	μ (Pa)	$\rho\alpha_{dM}$ (kg/m^3s)	t_c (s)	f_c (N/m^3)
Plane	952	0.038	1	10	0.38	5
Sphere	1232	0.01	1	100	1	10
Pumpkin	1232	0.01	1	100	1	N/A
Ferret (P14)	592	0.53	1	10	5.3	1.4

Table 2: Registration of a cortical surface from a juvenile (P14) ferret brain: Means and standard deviations of principal strains at τ =0 and τ =6.

Time τ	max(E_1)	min(E_2)	mean$\|E_1\|$	mean$\|E_2\|$	std$\|E_1\|$	std$\|E_2\|$
0	0.0885	-0.0795	0.0196	0.0201	0.0195	0.0201
4	0.0177	-0.0256	0.0011	0.0043	0.0011	0.0023