Published in final edited form as:

Proc IEEE Int Symp Biomed Imaging. 2018 April ; 2018: 683–686. doi:10.1109/ISBI.2018.8363666.

A COMPUTATIONAL METHOD FOR LONGITUDINAL MAPPING OF ORIENTATION-SPECIFIC EXPANSION OF CORTICAL SURFACE AREA IN INFANTS

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Abstract

The dynamic expansion of the human cortical surface during infancy is largely driven by the increase of surface area in two orthogonal directions: 1) the expansion parallel to the folding orientation (i.e., increasing the lengths of folds) and 2) the expansion perpendicular to the folding orientation (i.e., increasing the depths of folds). The knowledge on this would help us better understand the cortical growth mechanisms and provide important insights into neurodevelopmental disorders, but still remains scarce, due to the lack of dedicated computational methods. To address this issue, we propose a novel method for longitudinal mapping of orientation-specific expansion of cortical surface area in these two orthogonal directions during early infancy. We apply our method to 30 healthy infants, and for the first time reveal the orientation-specific longitudinal cortical surface expansion maps during the first postnatal year.

Index Terms

Orientation fields; cortical folding; longitudinal development; surface expansion; graph cuts

1. INTRODUCTION

At term birth, all primary and secondary cortical folds are established, but the surface area is only one-third of that of adults [1]. During the first year, the cortical surface expands 80%, with region-specific patterns [1]. Abnormal cortical surface expansion during infancy is related to many neurodevelopmental disorders. For example, infants who later develop autism present a larger surface area expansion from 6 to 12 months than the control infants [2]. As cortical folds have characteristic orientations [3, 4], the postnatal cortical surface expansion can be mainly decomposed into two orthogonal directions in the tangent plane of cortical folding: 1) The expansion parallel to the folding orientation (i.e., increasing the lengths of cortical folds), denoted as $\mathbf{p}_a$; 2) The expansion perpendicular to the folding orientation (i.e., increasing the depths of cortical folds), denoted as $\mathbf{p}_e$, as shown in Fig. 1. Although the emergence of tertiary folds after birth also leads to the increase of surface area, this value is relatively small, compared to the expansion in the tangent plane, as the cortical folding degree only increases 16%, while the surface area expands 80% in the first postnatal year [5]. Hence, studying orientation-specific surface expansion can help us 1) better

quantify cortical development and understand its mechanisms, thus better modeling the early brain development, and 2) better localize and understand the cortical abnormality in neurodevelopmental disorders, thus helping early identification of their biomarkers. However, due to the lack of dedicated computational methods, our knowledge on orientation-specific surface expansion during infancy remains scarce. These facts have spurred us to develop the first computational method to fill the gaps in both the methodology and knowledge.

2. MATERIALS AND METHODS

2.1. Image Acquisition and Processing

Longitudinal brain MRI scans at year 0 and year 1 were acquired from 30 normal infants (17 males/13 females). Infants were scanned unsedated by using a Siemens 3T scanner with a circular polarized head coil. T1-weighted images were obtained by using the parameters: TR = 1900 ms, TE = 4.38 ms, inversion time = 1100 ms, Flip Angle = 7°, and resolution = 1×1×1 mm³. T2-weighted images were acquired with the parameters: TR = 7380 ms, TE = 119 ms, Flip Angle = 150°, and resolution = 1.25×1.25×1.95 mm³.

We first reconstructed cortical surfaces from infant MR images using the UNC Infant Pipeline [6] and then mapped all cortical surfaces onto a spherical space [7]. To establish longitudinal cortical correspondences, we aligned each spherical surface at year 0 onto its corresponding surface at year 1 using spherical demons [8]. To establish cross-sectional cortical correspondences, we aligned each spherical surface at year 1 onto the UNC 4D Infant Cortical Surface Atlas [6] (<https://www.nitrc.org/projects/infantsurfatlas>). Based on these deformation fields, we resampled all the cortical surfaces as a standard-mesh tessellation with 163,842 vertices, thus establishing vertex-to-vertex correspondences across subjects and ages. For each vertex, we computed its sulcal depth (the distance to the nearest vertex on the cerebral hull surface), the maximum principal curvature (Fig. 2) and the maximum principal direction.

2.2 Mapping Orientation-specific Surface Expansion

The proposed method for longitudinal mapping of orientation-specific expansion of cortical surface contains three major steps. First, to derive the two orientation fields perpendicular ($\mathbf{p}_e$) and parallel ($\mathbf{p}_a$) to cortical folds, we propose to adaptively fuse the gradient field of sulcal depth and the maximum principal direction field, by formulating this task as a discrete labeling problem, and solving it by graph cuts. Then, based on the longitudinal deformation field of the cortical surface, we estimate the Jacobian matrix at each vertex, by solving a least-squares problem, and derive its stretch tensor. Finally, we project the stretch tensor into the two orthogonal orientations separately to obtain the orientation-specific expansion. Each step is detailed below.

To estimate $\mathbf{p}_e$, we take advantage of both the normalized gradient field of sulcal depth $\mathbf{p}_e^g$ and the maximum principal direction field $\mathbf{p}_e^c$. As shown in Fig. 3, on the highly-bended regions at gyral crests and sulcal bottoms, the maximum principal direction field $\mathbf{p}_e^c$ is more

reliable and informative for estimating $\mathbf{p}_e$, as $\mathbf{p}_e^g$ is noisy and unreliable, due to small and ambiguous gradients. On the turning corners and flat regions at sulcal walls, the gradient field $\mathbf{p}_e^g$ is more reliable and useful for estimating $\mathbf{p}_e$, due to the ambiguity in computing $\mathbf{p}_e^c$.

On the flat regions at wide sulcal bottoms and gyral crests, both $\mathbf{p}_e^g$ and $\mathbf{p}_e^c$ are unreliable and ambiguous, where the reliable and informative orientation fields from neighboring regions can be leveraged to estimate $\mathbf{p}_e$. Hence, we design an energy function to formulate this task as a discrete labeling problem, i.e., assigning an orientation label $\mathbf{l}$ indicating the orientation $\mathbf{p}_e$ for each vertex based on $\mathbf{p}_e^g$ and $\mathbf{p}_e^c$ adaptively, and then solve it effectively by using a graph cuts method [9].

Letting f be the sulcal depth map on the cortical surface M_0 , the gradient vector of sulcal depth at the vertex $\mathbf{v}_i$ on the tangent plane is $\mathbf{g}(\mathbf{v}_i) = \nabla_{M_0} f(\mathbf{v}_i)$. Unlike in the image space with regular grids, $\mathbf{g}(\mathbf{v}_i)$ on the surface manifold cannot be directly computed. We use the first order of Taylor's theorem to approximate the sulcal depth at vertex $\mathbf{v}_i$ with its first-ring neighborhood vertex $\mathbf{v}_j$ as: $f(\mathbf{v}_i) \approx f(\mathbf{v}_j) + \mathbf{g}(\mathbf{v}_j)^\top \cdot (\mathbf{v}_i - \mathbf{v}_j)$. Hence, we minimize the following error that constrains the gradient vector $\mathbf{g}(\mathbf{v}_i)$ to sit in the tangent plane:

$$\mathbf{g}(\mathbf{v}_i) = \underset{\hat{\mathbf{g}}}{\operatorname{argmin}} \left\{ \sum_{\mathbf{v}_j \in \mathcal{N}(\mathbf{v}_i)} (f(\mathbf{v}_i) - f(\mathbf{v}_j) - \hat{\mathbf{g}}(\mathbf{v}_i)^\top \cdot (\mathbf{v}_i - \mathbf{v}_j))^2 + \|\mathcal{N}(\mathbf{v}_i)\| (\hat{\mathbf{g}}(\mathbf{v}_i)^\top \cdot \mathbf{n}(\mathbf{v}_i))^2 \right\},$$

(1)

where $\mathcal{N}(\mathbf{v}_i)$ is the neighborhood of vertex $\mathbf{v}_i$ and $\mathbf{n}(\mathbf{v}_i)$ is the normal direction of $\mathbf{v}_i$. The field $\mathbf{p}_e^g(\mathbf{v}_i)$ in the tangent plane is obtained as: $\mathbf{p}_e^g(\mathbf{v}_i) = \mathbf{g}(\mathbf{v}_i) / \|\mathbf{g}(\mathbf{v}_i)\|$.

Given the normalized gradient field of sulcal depth $\mathbf{p}_e^g$ and the maximum principal direction field $\mathbf{p}_e^c$, we aim to minimize the following energy function for deriving $\mathbf{l}$:

$$E = \sum_{\mathbf{v}_i} D(\mathbf{l}(\mathbf{v}_i), \mathbf{p}_e^g(\mathbf{v}_i), \mathbf{p}_e^c(\mathbf{v}_i)) + \sum_{\mathbf{v}_i, \mathbf{v}_j \in \mathcal{N}} S(\mathbf{l}(\mathbf{v}_i), \mathbf{l}(\mathbf{v}_j)). \quad (2)$$

The first term in Eq. (2) is a data term to adaptively keep $\mathbf{l}(\mathbf{v}_i)$ close to $\mathbf{p}_e^g(\mathbf{v}_i)$ or $\mathbf{p}_e^c(\mathbf{v}_i)$. The second term is a smoothness term to eliminate the unreliable and noisy orientations by propagating the reliable orientations from neighbors to the problematic regions. For each vertex $\mathbf{v}_i$, $\mathbf{l}(\mathbf{v}_i)$ is its label from the finite label space, which is defined as 81 orientations uniformly distributed on a unit hemisphere. Note that, in our application, a direction and its opposite direction will be regarded as the same. The number of orientation labels is determined by gradually increasing the numbers, while visually assessing the resulted

orientation field. We found that 81 orientation labels are already dense enough to generate promising results.

The data term in Eq. (2) is computed as:

$$D(\mathbf{l}(\mathbf{v}_i), \mathbf{p}_e^g(\mathbf{v}_i), \mathbf{p}_e^c(\mathbf{v}_i)) = w_g(\mathbf{v}_i) \cdot D^g(\mathbf{l}(\mathbf{v}_i), \mathbf{p}_e^g(\mathbf{v}_i)) + w_c(\mathbf{v}_i) \cdot D^c(\mathbf{l}(\mathbf{v}_i), \mathbf{p}_e^c(\mathbf{v}_i)), \quad (3)$$

The first term is a gradient-determined term and the second term is a curvature-determined term, defined as:

$$D^*(\mathbf{l}(\mathbf{v}_i), \mathbf{p}_e^*(\mathbf{v}_i)) = \min \{ \|\mathbf{l}(\mathbf{v}_i) - \mathbf{p}_e^*(\mathbf{v}_i)\|, \|\mathbf{l}(\mathbf{v}_i) + \mathbf{p}_e^*(\mathbf{v}_i)\| \} \quad (4)$$

Herein, * can be *g* or *c*. In Eq. (3), w_g and w_c are two spatially-adaptive weighting parameters, defined as: $w_g(\mathbf{v}_i) = 1 - e^{-\lambda_g \|\mathbf{g}(\mathbf{v}_i)\|}$, and $w_c(\mathbf{v}_i) = e^{-\lambda_c \|\mathbf{g}(\mathbf{v}_i)\|} (1 - e^{-\lambda_c |c(\mathbf{v}_i)|})$. λ_g and λ_c are the non-negative parameters used to determine the trade-off between preserving the gradient field of sulcal depth and preserving the maximum principal direction field. According to weighting parameters, on the turning corners and flat regions at sulcal walls, where $\|\mathbf{g}(\mathbf{v}_i)\|$ is typically large and $\mathbf{p}_e^g(\mathbf{v}_i)$ is more reliable and informative, $w_g(\mathbf{v}_i)$ will be large and $w_c(\mathbf{v}_i)$ will be small, thus encouraging $\mathbf{l}(\mathbf{v}_i)$ to be close to $\mathbf{p}_e^g(\mathbf{v}_i)$. On the highly-bended regions at sulcal bottoms and gyral crests, where $\|\mathbf{g}(\mathbf{v}_i)\|$ is typically small and $|c(\mathbf{v}_i)|$ is large, $\mathbf{p}_e^c(\mathbf{v}_i)$ is more reliable and informative, and thus $w_g(\mathbf{v}_i)$ will be small and $w_c(\mathbf{v}_i)$ will be large, encouraging $\mathbf{l}(\mathbf{v}_i)$ to be close to $\mathbf{p}_e^c(\mathbf{v}_i)$.

In the smoothness term in Eq. (2) is defined as:

$$S(\mathbf{l}(\mathbf{v}_i), \mathbf{l}(\mathbf{v}_j)) = (w_s(\mathbf{v}_i) + w_s(\mathbf{v}_j)) \cdot \min \{ \|\mathbf{l}(\mathbf{v}_i) - \mathbf{l}(\mathbf{v}_j)\|, \|\mathbf{l}(\mathbf{v}_i) + \mathbf{l}(\mathbf{v}_j)\| \}, \quad (5)$$

$w_s(\mathbf{v}_i)$ is a spatially-adaptive weighting parameter. It should be large on regions where both $\|\mathbf{g}(\mathbf{v}_i)\|$ and $|c(\mathbf{v}_i)|$ are small, e.g., flat regions at wide gyral crests and sulcal bottoms. On the contrary, it should be small on regions where $\mathbf{p}_e^g(\mathbf{v}_i)$ or $\mathbf{p}_e^c(\mathbf{v}_i)$ are reliable. Thus, $w_s(\mathbf{v}_i)$ is defined as:

$$w_s(\mathbf{v}_i) = e^{-(\lambda_g \cdot \|\mathbf{g}(\mathbf{v}_i)\| + \lambda_c \cdot |c(\mathbf{v}_i)|)} \quad (6)$$

The energy function in Eq. (2) is solved by the graph cuts method [9] to obtain the labeled orientations. To obtain the final orientation field $\mathbf{p}_e(\mathbf{v}_i)$, $\mathbf{l}(\mathbf{v}_i)$ is further projected to the tangent space of the cortical surface and then normalized:

$$\mathbf{p}_e(\mathbf{v}_i) = \frac{\mathbf{l}(\mathbf{v}_i) - (\mathbf{n}(\mathbf{v}_i) \cdot \mathbf{l}(\mathbf{v}_i)) \cdot \mathbf{n}(\mathbf{v}_i)}{\|\mathbf{l}(\mathbf{v}_i) - (\mathbf{n}(\mathbf{v}_i) \cdot \mathbf{l}(\mathbf{v}_i)) \cdot \mathbf{n}(\mathbf{v}_i)\|} \quad (7)$$

Accordingly, the orientation field parallel to folds is computed as: $\mathbf{p}_a(\mathbf{v}_i) = \mathbf{p}_e(\mathbf{v}_i) \times \mathbf{n}(\mathbf{v}_i)$.

To map the orientation-specific cortical surface expansions, we also compute the Jacobian matrix of the cortical deformation. At each vertex, the Jacobian matrix is the spatial gradient of the deformation field. Let $\mathbf{F}$ be the 3D deformation vector of each vertex on the cortical surface at the first time-point. The Jacobian matrix $\mathbf{J}$ is then defined by:

$$\mathbf{J} = \begin{pmatrix} \frac{\partial \mathbf{F}_x}{\partial x} & \frac{\partial \mathbf{F}_x}{\partial y} & \frac{\partial \mathbf{F}_x}{\partial z} & \frac{\partial \mathbf{F}_y}{\partial x} & \frac{\partial \mathbf{F}_y}{\partial y} & \frac{\partial \mathbf{F}_y}{\partial z} & \frac{\partial \mathbf{F}_z}{\partial x} & \frac{\partial \mathbf{F}_z}{\partial y} & \frac{\partial \mathbf{F}_z}{\partial z} \end{pmatrix}. \quad (8)$$

As the Jacobian matrix on the surface manifold cannot be directly computed, we approximate the Jacobian matrix at the vertex $\mathbf{v}_i$ using each of its first-ring neighborhood vertex $\mathbf{v}_j$ such that:

$$\mathbf{F}(\mathbf{v}_i) \approx \mathbf{F}(\mathbf{v}_j) + \mathbf{J}(\mathbf{v}_i) \cdot (\mathbf{v}_i - \mathbf{v}_j). \quad (9)$$

By minimizing the following error, $\mathbf{J}(\mathbf{v}_i)$ is estimated as:

$$\mathbf{J}(\mathbf{v}_i) = \underset{\mathbf{J}}{\operatorname{argmin}} \left\{ \sum_{\mathbf{v}_j \in \mathcal{N}(\mathbf{v}_i)} (\mathbf{F}(\mathbf{v}_i) - \mathbf{F}(\mathbf{v}_j) - \mathbf{J}(\mathbf{v}_i) \cdot (\mathbf{v}_i - \mathbf{v}_j))^2 \right\}. \quad (10)$$

However, the Jacobian matrix encodes both stretch (zooms and shears) and rotational components. The first part describes the stretch of the cortical surface, which is desired. The second part contains only the rigid deformation, which is useless in our application. We compute the stretch component by decomposing the Jacobian matrix according to the polar decomposition theorem: $\mathbf{J} = \mathbf{R}\mathbf{S} = \mathbf{S}'\mathbf{R}$, where $\mathbf{R}$ is the rotation matrix and $\mathbf{S}$ is the stretch tensor. $\mathbf{S}$ is a symmetric positive definite matrix and can be derived as: $\mathbf{S} = (\mathbf{J}^T \mathbf{J})^{1/2}$ [10]. For each vertex, given the surface deformation matrix $\mathbf{S}$ and the two orthogonal orientation fields $\mathbf{p}_e$ and $\mathbf{p}_a$, we compute the longitudinal surface expansion in the orientation fields perpendicular to folds as s_e and parallel to folds as s_a : $s_e = \mathbf{p}_e^T \mathbf{S} \mathbf{p}_e$ and $s_a = \mathbf{p}_a^T \mathbf{S} \mathbf{p}_a$.

3. RESULTS

In all our experiments, we set the parameters as $\lambda_g = 2.0$ and $\lambda_c = 4.0$, after testing their different combinations. Fig. 4 shows the estimated orientation field $\mathbf{p}_e$ on a cortical surface at year 0 by our method, which is visually perpendicular to cortical folds. To quantitatively evaluate the quality of our estimated orientation field $\mathbf{p}_e$, we compared our method with

other methods, i.e., the maximum principal direction field $\mathbf{p}_e^c$, the diffused $\mathbf{p}_e^c$ by the method in [11], and the gradient field of sulcal depth $\mathbf{p}_e^g$. And we defined a coherence measurement for an orientation field $\mathbf{p}$ at each vertex $\mathbf{v}_i$ as:

$$\text{Coh}(\mathbf{p}(\mathbf{v}_i)) = \frac{1}{|\mathcal{N}(\mathbf{v}_i)|} \sum_{\mathbf{v}_j \in \mathcal{N}(\mathbf{v}_i)} |\mathbf{p}(\mathbf{v}_i) \cdot \mathbf{p}(\mathbf{v}_j)|. \quad (11)$$

The value of Coh ranges from 0 to 1. Larger coherence values indicate that the orientation field is smoother and more coherent. Fig. 5 shows the coherence maps of $\mathbf{p}_e^c$, diffused $\mathbf{p}_e^c$, $\mathbf{p}_e^g$ and $\mathbf{p}_e$ on a randomly-selected individual cortical surface, and their histograms. As we can see, $\mathbf{p}_e$ is similar to $\mathbf{p}_e^c$ in their coherence values at gyral crests and sulcal bottoms, while is similar to $\mathbf{p}_e^g$ in their coherence values at sulcal walls. Moreover, $\mathbf{p}_e$ has large coherence values on the flat regions at gyral crests and sulcal bottoms, where $\mathbf{p}_e^c$ and $\mathbf{p}_e^g$ have small coherence values. Meanwhile, the shift towards larger coherence values in the histogram of $\mathbf{p}_e$ indicates that the orientation field is smoother and more coherent in $\mathbf{p}_e$, compared to $\mathbf{p}_e^c$, diffused $\mathbf{p}_e^c$, and $\mathbf{p}_e^g$.

We applied our method onto 30 normal infants with longitudinal cortical surfaces at 0 and 1 year of age. Fig. 6(a) and (b) show the population-average cortical surface expansion maps in the orientation fields *perpendicular* to cortical folds and *parallel* to cortical folds, respectively. The cortical surface expands remarkably in both orientations, with region-specific and orientation-specific patterns. By using paired t-test with $p < 0.01$ after correction for multiple comparisons based on random field theory [12], the red/blue clusters represent the regions with the expansion being significantly larger/smaller than the average expansion in each orientation. Specifically, regions with high-expansion *perpendicular* to cortical folds include the superior parietal, inferior parietal, lateral occipital, posterior middle temporal, precuneus, cingulate regions, postcentral gyrus and Heschl's gyrus. In contrast, regions high-expansion *parallel* to cortical folds contain the superior parietal, inferior parietal, lateral occipital, anterior temporal, postcentral, fusiform, medial orbitofrontal, lingual, and cuneus regions.

Fig. 6(c) shows the difference of cortical surface expansion maps in the two orientations of the 30 infants during the first year. Many regions show different expansion degrees in the two orthogonal orientations. Specifically, the Heschl's gyrus, posterior middle temporal gyrus, parietal-occipital junction region, a portion of fusiform gyrus, and cingulate cortex exhibit larger expansions in the orientation *perpendicular* to cortical folds than in the orientation *parallel* to cortical folds. In contrast, the anterior temporal cortex, orbitofrontal cortex, pars triangularis, lingual gyrus, fusiform gyrus, cuneus cortex, and medial superior frontal cortex exhibit larger expansions in the orientation *parallel* to cortical folds than in the orientation *perpendicular* to cortical folds. The red/blue clusters represent the cortical

regions where the expansion *perpendicular* to cortical folds is significantly larger/smaller than the expansion *parallel* to cortical folds, after correction for multiple comparisons.

4. CONCLUSION

This paper has three main contributions. First, we developed the first computational method for mapping longitudinal orientation-specific surface expansion in infants. Second, to accurately estimate the orientation fields of cortical folds, we proposed a novel method to adaptively fuse the gradient field of sulcal depth and the maximum principal direction field, by minimizing an energy function via graph cuts. Finally, for the first time, we revealed the orientation-specific and region-specific longitudinal cortical surface expansion maps during the first postnatal year. We will apply our method on a large-scale dataset to study the orientation-specific surface expansion at dense time points, e.g., every 3 months in the first year, and study abnormal cortical surface expansion in neurodevelopmental disorders.

Acknowledgments

This work was partially supported by NIH grants (MH100217, MH108914, MH107815, MH110274, MH109773).

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Fig. 1.

An illustration of the orientation-specific cortical surface expansion. (a) The original folds. (b) Surface expansion in the orientation parallel to folds (i.e., increasing the length of folds). (c) Surface expansion in the orientation perpendicular to folds (i.e., increasing the depth of folds). (d) Expansions in both orientations.

Fig. 2.

The maps of sulcal depth and maximum principal curvature of cortical surfaces of a representative infant at 0 and 1 year of age.

Fig. 3. The gradient field of sulcal depth and the maximum principal direction field on the cortical surface of an infant at year 0.

Fig. 4.
The estimated orientation field $\mathbf{p}_e$ on a cortical surface at year 0 by the proposed method.

Fig. 5.

The coherence maps of the maximum principal direction field p_e^c , the diffused p_e^c , the gradient field of sulcal depth p_e^g , and our estimated field p_e on a cortical surface, and their histograms.

Fig. 6.

The population-average of longitudinal orientation-specific cortical surface expansion maps of 30 subjects in the first year.