Mixed Effects Model for Functional Surfaces with Applications to Cortical Surface Task fMRI

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Abstract
Motivated by cortical surface task fMRI, we propose a framework for jointly modeling the geometry and functionality in high-dimensional functional surfaces. The proposed model characterizes effects of subject-specific covariates and exogenous stimuli on functional surfaces while accounting for the mutual-influence of their geometry and the functionality. This is accomplished through a computationally efficient estimation method developed for the proposed mixed effects model, incorporating regularized estimation of the precision matrix of random effects. We apply the proposed approach to cortical surface task fMRI data of the Human Connectome Project and discover geometric shapes of cortical surface and activated regions in the fMRI associated with demographics and task stimuli. In particular, new modes of correspondence between the shapes and activation relevant to emotion processing are revealed.

Keywords: Cortical surface task fMRI, functional surfaces, Riemann manifold, mixed effects model, Cholesky decomposition, principal component analysis, Human Connectome Project

1 Introduction

1.1 Cortical Surface Task fMRI

When studying the function of the human brain in cognitive, emotional and behavioral tasks, functional magnetic resonance imaging (fMRI) has served as an important tool Huettel et al. (2009). The processing method (Glasser et al. (2013)) that maps fMRI signals to a two-dimensional (2D) manifold representing the cerebral cortical surface is gaining increasing

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popularity as cortical surface fMRI provides a more intuitive representation of functional distance compared to 3D volumetric fMRI: adjacent vertices on the cortical surface usually have similar activation behavior, while nearby voxels in the volume fMRI often serve distinct neural functions (Glasser et al. (2013); Mejia et al. (2020)).

Surface fMRI also preserves the geometric shape of subjects’ cortical surfaces, which has two crucial implications for the analysis. First, the geometric variability in different subjects’ cortical surfaces is preserved, enabling an analysis of variation of the geometry in addition to the analysis of variation of the functionality to be undertaken. Second, the geometry and the functionality of the cortical surface have been shown to influence each other, requiring any analysis to incorporate such effects. Surface fMRI carries information of both the geometry and functionality of the cortical surface and enables examination of their relations. A well known example is that London taxi drivers were found to have greater gray matter volume in mid-posterior hippocampi and less volume in anterior hippocampi compared to bus drivers (Maguire et al. (2006)). In a recent study Stahn et al. (2019) found that after a 14-month journey in Antarctica, nine expeditioners lost significant volume in the hippocampus which is critical for learning, memory and emotion processing.

1.2 Past Work on Analyzing Cortical Surface fMRI

Past work on analyzing cortical surface fMRI has focused on the analysis of functionality alone. Poline et al. (2016); Friston et al. (1995); Worsley and Friston (1995); Worsley et al. (1996); Andrade et al. (2001); Genovese et al. (2002); Hagler Jr. et al. (2006); Smith and Nichols (2009); Lindquist and Mejia (2015); Barch et al. (2013) model the activation of functional signals at each individual vertex on the cortical surface with general linear models (GLM) and adjust for multiple comparison with thresholding and clustering methods.

Studies have shown pitfalls of voxel/vertex-wise analysis including reduced power (Ishwaran and Rao (2011)) and sensitivity to voxel/vertex size and smoothing (Woo et al. (2014)).
Vertex-wise methods also fail to account for the underlying spatial dependence between vertices and information contained in the totality of the data. To address these issues, Formisano et al. (2004) proposed a new approach of spatial independent component analysis. Bayesian methods with spatial priors on activation regions have also been proposed (Friston et al. (2002b,a); Penny et al. (2005); Sidén et al. (2017)). Mejia et al. (2020) proposed a spatial GLM model for task-based cortical surface fMRI with a stochastic partial differential equation prior for latent activation regions. In these studies, different geometric shapes of subjects were registered to a common template and functional signals were aligned according to the registration. Analyzing the aligned functional signals alone eliminates information on geometric variability among the subjects and excludes information on associations between the geometry and functionality of cortical surfaces from subsequent analyses. Lila and Aston (2020) proposed a framework for studying the geometric and functional variability in cortical surfaces simultaneously. The authors generalized the model proposed by Charlier et al. (2017), which represented functional surfaces as a metamorphosis, by introducing random variables to capture both the geometric and functional variability in the subjects. Lila and Aston (2022) extended the approach to analyze brain shape and functional connectivity represented by covariance matrices of resting state fMRI time series.

1.3 The Proposed Scheme of Analysis

Questions remain in studying the geometry and functionality of cortical surfaces, particularly in task based studies. First, it is of interest to model the variability in both geometry and functionality as functions of covariates, including demographics and health measurements, and exogenous stimuli in tasks during fMRI scans. There are three challenges in this task: 1. Functionality captured by fMRI signals defined on distinct domains of cortical surfaces of different subjects needs to be mapped to a common domain. 2. The dimensionality of both the geometric shapes and functionality are large and requires dimension reduction methods.
3. In task fMRI, the subjects’ functions are expected to vary at different stages of tasks and have an extra temporal dimension. Therefore, modeling of the functions need to account for the time series aspect of the data and the temporal correlations among the observations.

Second, models are needed to capture correlations between the geometry and the functionality of the cortical surfaces for revealing meaningful relations between the shape and functions of the brain. Omitting or mis-specifying such correlations may also induce bias in studying the effects of the subject-specific and stimuli covariates on the geometry and the functionality. Due to potential correlations between the geometry and the functionality, the effects of the covariates on the geometry and the functionality cannot be sufficiently analyzed in separate models, and a unified model to incorporate the effects as well as the correlations is required.

To address these unsolved issues, we propose a unified mixed effects model framework for functional surfaces including cortical surface task fMRI. The proposed model characterizes effects of subject-specific covariates and exogenous stimuli with fixed effects and mutual-influences of the geometry and the functionality with random effects. In the mixed effects model, the multi-variate outcomes are projections on geometric and functional PCs, obtained using the stochastic metamorphism model (Lila and Aston (2020)) and a functional principal component analysis (fPCA). To model the mutual influence of the geometry and functionality, we introduce random effects with a structured covariance matrix. The covariance structure and the positive-definiteness constraint are guaranteed via the proposed parameterization of the Cholesky decomposition of the precision matrix (inverse of the covariance matrix). The focus and approach of this work are different from Lila and Aston (2022) as the outcomes of interest here are the geometry and functionality of cortical surface characterized by the time series of high-dimensional task fMRI signals instead of functional connectivity measured by covariance matrices of resting state fMRI, in which the temporal dimension is compressed.

We propose an iterative estimation method for the mixed effects model. In particular, the estimation of the precision matrix is scalable by utilizing results in Bickel and Levina 4.
(2008) that the estimation of the Cholesky decomposition of the precision matrix can be converted to parallel regularized regressions (studies with similar focus on sparse estimation of the covariance and precision matrix can be found in Banerjee et al. (2008); Meinshausen and Bühlmann (2006); Levina et al. (2008); Pourahmadi and Daniels (2002); Rothman et al. (2008, 2009, 2010); Rocha et al. (2008); Wu and Pourahmadi (2003); Friedman et al. (2008); Pourahmadi (2011); Wang et al. (2010); Bondell et al. (2010)). Comparing to the Restricted Maximum Likelihood Estimation (REML, c.f. Thompson Jr (1962); Jiang (1996)) methods, the propose approach is computationally efficient especially for the high dimensionality of this particular application, and is more flexible in parameterizing the precision/covariance matrices while ensuring the positive definiteness.

1.4 Task fMRI of the Human Connectome Project (HCP)

We conduct a comprehensive analysis on the cortical surface task fMRI data of 100 unrelated young healthy adults from the Human Connectome Project (HCP) (WU-Minn Consortium (2018)), focusing on measures taken from the emotion processing task (Hariri et al. (2002)). During the task, participants were asked to match pictures on the bottom and top of the screen, which showed either faces with emotions of anger or fear or geometric shapes (control). Tasks were presented to the participants in blocks, each consisted of six 3-second trials of the same type (face or shape). For each individual participant, a time series of 176 tfMRI scans were taken during the trials and the intermittent resting periods in-between. In addition to the tfMRI scans, the geometric shapes ($xyz$ coordinates) of the cortical surfaces of participants were measured in the structural MRI.

With the proposed approach we reveals effects of demographics including age and gender on both the geometric shapes of the cortical surfaces and the activated functional regions identified by the fMRI, as well as effects of task stimuli on the functional activated regions. Age and gender are found to have more significant associations with functionality than with
geometry of the cortical surface. Associations between the emotion processing task stimuli and activated regions show that functional areas associated with the emotion processing include the inferior and middle temporal, somatosensory and motor cortex, auditory association cortex, orbital and polar frontal cortex, primary visual cortex, parahippocampal, and fusiform. Results also demonstrate the advantage of the proposed approach in statistical power when revealing meaningful associations between the covariates and the functionality of the cortical surface due to its ability of dealing with large dimensionality of the fMRI time series in their full temporal dimension. Furthermore, the proposed approach enables discovery of several modes of correspondence between geometric shapes and functionality of cortical surfaces in processing emotions. Regions of activation in parts of the inferior temporal, occipitotemporal sulcus, fusiform gyri and temporal lobe are found to have potential correspondences with the geometric shapes of these regions.

To our knowledge, this study is among the first attempts to model the geometry and functionality of cortical surface task fMRI jointly. Given the emerging opportunities and challenges brought by the relatively new cortical surface fMRI data format, our study provides a novel tool for the new data format and demonstrates how to address important substantive problems such as those in Stahn et al. (2019) and contributes to the advances in methodology developments for studying brain images, especially cs-fMRI.

The paper is organized as follows. Section 2 introduces the statistical representation of cortical surface task fMRI and formulates the proposed mixed effects model. Section 3 delineates the estimation pipeline. Section 4 studies the HCP data with the proposed methods and compares findings with existing clinical studies. Some concluding remarks are then provided. In the appendix, we set out some simulations studies which provide further justification for the methodology proposed.
2 A Mixed Effects Model for Cortical Surfaces tfMRI

2.1 The Functional Manifold Model

We adopt the functional manifold framework proposed by Charlier et al. (2017) in which the geometry is characterized by a metamorphosis from a template manifold and the functionality is characterized by functions on the manifold. Suppose there are $N$ subjects, each has a time series of $T$ task fMRI scans and a structural MRI. The data of the $i$th subject are denoted by $\{(M_i, Y_i(t)) : t = 1, \ldots, T\}$, where $M_i$ is a time-invariant two-dimensional manifold embedded in $\mathbb{R}^3$ denoting the geometric shape of cortical surface and $Y_i(t) \in L^2(M_i)$ is a time series of square integrable functions on $M_i$ denoting the time series of functional fMRI blood-oxygen-level-dependent (BOLD) signals.

As in Lila and Aston (2020), the variability in the geometry and functionality is represented by subject-specific random vector fields. First, let $M_i = \varphi(v_i, \cdot) \circ M_0$, where $M_0$ is a template manifold, usually the mean shape of the subjects' cortical surfaces, and $\varphi(v_i, \cdot) : \mathbb{R}^3 \rightarrow \mathbb{R}^3$ be a deformation operator indexed by a subject specific $v_i$, where $\{v_i : i = 1, \ldots, N\}$ are independent and identically distributed (i.i.d.) samples of a random field $V$ defined in a Hilbert space. $\varphi$ can be further represented by a diffeomorphism determined by its initial momenta $m_0$ defined on a finite set of control points on $M_0$. Intuitively, the initial momenta are vectors in $\mathbb{R}^3$ at selected vertices of the template manifold, indicating the directions and magnitudes to “drag” the template $M_0$ towards the subject-specific shape $M_i$. For more details, see Miller et al. (2006); Younes (2010); Charlier et al. (2017).

The functionality $Y_i(t)$ defined on the domain of $M_i$ can be mapped to the domain of $M_0$ with the inverse deformation $\varphi^{-1}(v_i, \cdot)$. Suppose $Y_i(t) = X_i(t) \circ \varphi^{-1}(v_i, \cdot)$ then $\{X_i(t) : t = 1, \ldots, T\}$ denote the fMRI scans mapped to the template shape. As in Lila and Aston (2020), we model the variability in the functionality with $X_i(t) = \mu(t) + \delta Z_i(t)$, where $\mu$ is the mean function, $\delta$ is a scalar, and the $\{Z_i(t) : i = 1, \ldots, N\}$ are i.i.d. realizations of...
a discrete time stochastic process \( \{ Z(t) : t = 1, \ldots, T \} \) where each \( Z(t) \in L^2(M_0) \).

We further assume a finite principal components (PC) decomposition for both the geometry and functionality:

\[
v_i = \sum_{j=1}^{K^G} a^G_{ij} \psi^G_j, \quad Z_i(t) = \sum_{j=1}^{K^F} a^F_{ij}(t) \psi^F_j,
\]

where \( K^G \) and \( K^F \) are numbers of geometric and functional PCs adequate for explaining most of the variability, \( a^G_{ij} \) is the projection coefficient of \( V_i \) on the \( j \)th geometric basis \( \psi^G_j \) and \( a^F_{ij}(t) \) is the projection coefficient of \( Z_i \) on the \( j \)th functional basis \( \psi^F_j \) at time \( t \) (Riesz and Sz Nagy (1955)).

### 2.2 Model Notation

We propose a mixed effects model to study effects of subject-specific covariates on the geometry and functionality of cortical surface tfMRI as well as the correlation between the geometry and functionality. We model \( \mathbf{a} = (\mathbf{a}^G, \mathbf{a}^F) \), where \( \mathbf{a}^G \in \mathbb{R}^{N \times K^G} \) and each \( a^G_{ij} \) denotes the \( i \)th subject’s projection coefficient on the \( j \)th geometric PC. \( \mathbf{a}^F \in \mathbb{R}^{N \times (T \cdot K^F)} \) and each row \( \mathbf{a}_i^F = (\mathbf{a}_{i1}^F, \ldots, \mathbf{a}_{iK^F}^F) \), where \( \mathbf{a}_{ik}^F = (a_{ik}^F(1), \ldots, a_{ik}^F(T)) \) denotes the \( i \)th subject’s projection coefficients on the \( k \)th functional principal component at time \( t = 1, \ldots, T \).

We model effects of two types of covariates. The first is time-invariant covariates such as age and gender which have same values during the period of the experiments. Denote the number of time-invariant covariates by \( p_u \) and let \( \mathbf{U} = (\mathbf{U}_1, \ldots, \mathbf{U}_{p_u}) \in \mathbb{R}^{N \times p_u} \) denote the matrix of all time-invariant covariates. The second type is time varying covariates such as the task signals/phases in studying the brain’s response to exogenous stimuli using task fMRI. Denote the number of time varying covariates by \( p_w \). Let \( \mathbf{W} = (\mathbf{W}_1, \ldots, \mathbf{W}_{p_w}) \in \mathbb{R}^{(N \cdot T) \times p_w} \), where \( \mathbf{W}_k = (W_{1,k}(1), \ldots, W_{N,k}(1), \ldots, W_{1,k}(T), \ldots, W_{N,k}(T))^T \) denotes the column vector of time series of the \( k \)th time-varying covariate for all \( N \) subjects.

Assume the functionality represented by \( \{ \mathbf{a}_i^F \} \) is affected by both \( \mathbf{U} \) and \( \mathbf{W} \), but \( \{ \mathbf{a}_i^G \} \) is not affected by time-varying covariates \( \mathbf{W} \). This is because the geometric shape of a subject is considered to be the same during the short period of task fMRI scanning. This could be
relaxed in the case of longitudinal imaging studies. Let $\alpha^G$ denote effects of time-invariant covariates $U$ on the geometric projections $a^G$, $\alpha^F$ denote the effect of $U$ on functional projection coefficients $a^F$, and $\beta$ denote the effect of the time-varying covariates $W$ on the functional projections.

To model the correlations between the geometry and functionality, we introduce random effects $\gamma = (\gamma^G, \gamma^F)$, where $\gamma^G \in \mathbb{R}^{N \times K^G}$ and $\gamma^F \in \mathbb{R}^{N \times (T \cdot K^F)}$. Assume the rows $\gamma_i \sim \text{i.i.d.} \mathcal{N}(0, \Sigma_\gamma)$ and $\Sigma_\gamma$ follows the structure:

$$
\Sigma_\gamma = \begin{bmatrix}
\Sigma_{GG} & \Sigma_{GF_1} & \cdots & \cdots & \Sigma_{GF_{K^F}} \\
\Sigma_{GF_1}^T & \Sigma_{F_1 F_1} & 0 & \cdots & 0 \\
\vdots & 0 & \ddots & \ddots & \vdots \\
\vdots & \vdots & \ddots & \ddots & 0 \\
\Sigma_{GF_{K^F}}^T & 0 & \cdots & 0 & \Sigma_{F_{K^F} F_{K^F}}
\end{bmatrix}.
$$

In (1), $\Sigma_{GG} = \text{diag}\{\sigma^2_{G1}, \ldots, \sigma^2_{G_{K^G}}\}$ is the covariance matrix of $(\gamma^G_{i1}, \ldots, \gamma^G_{iK^G})$ for any $i$. For each $i$ and $k = 1, \ldots, K^F$, $\Sigma_{F_k F_k}$ is the temporal covariance matrix among $\{\gamma^F_{i,(k-1)T+t} : t = 1, \ldots, T\}$. For each $j \in \{1, \ldots, K^G\}$ and $t \in \{1, \ldots, T\}$, $\Sigma_{GF_k}(j, t)$ is the covariance between $\gamma^G_{ij}$ and $\gamma^F_{i,(k-1)T+t}$. The off-diagonal elements in $\Sigma_{GG}$ and the non-diagonal blocks except for $\{\Sigma_{GF_k}, \Sigma_{GF_k}^T : k = 1, \ldots, K^F\}$ are assumed to be zero, reflecting the zero correlations among the projection coefficients on the geometric PCs and among the projections on the functional PCs.

Let $\epsilon^G \in \mathbb{R}^{N \times K^G}$ and $\epsilon^F \in \mathbb{R}^{N \times (TK^F)}$ denote the independent errors in measuring the geometry and functionality that cannot be explained by the fixed effects nor the random effects. They are assumed to be independent of $\gamma$. Assume the rows $\epsilon^G_i \sim \mathcal{N}(0, \sigma^2_{\epsilon} I_{K^G})$, and $\epsilon^F_i$ follows i.i.d. $\mathcal{N}(0, \sigma^2_{\epsilon} I_{T \cdot K^F})$.

Let $\text{vec}(\cdot)$ indicate the operator than reshapes a matrix to a vector by column, then the
joint distribution of $a^G$ and $a^F$ is characterized by the mixed effects model

$$a^G_{N\times K^G} = U_{N\times p_u} \alpha^G_{p_u\times K^G} + \gamma^G_{N\times K^G} + \epsilon^G_{N\times K^G},$$

(2)

$$\text{vec} [a^F_{N\times (T\cdot K^F)}] = \text{vec} [(U_T, W)_{(NT)\times(p_u+p_w)} \cdot (\alpha^F_{K^F\times p_u}, \beta^F_{K^F\times p_u})^T] + \text{vec} [\gamma^F_{N\times (T\cdot K^F)} + \epsilon^F_{N\times (T\cdot K^F)}].$$

Note $U_T = (U^T, \ldots, U^T)^T$ is the expansion of $U$ by repeating it $T$ times.

### 2.3 Parameterization of $\Sigma$

The covariance matrix of the outcome is $\Sigma = \Sigma_\gamma + \sigma^2 I_{K^G+T\cdot K^F}$. Not all parametrizations of $\Sigma$ lead to positive definite matrices required for a *bona fide* covariance matrix, even if each of the blocks $\Sigma_{GG}$, $\Sigma_{F_k F_k}$ and $\Sigma_{GF_k}$ in $\Sigma_\gamma$ is a well defined covariance matrix.

To address this issue we parameterize the precision matrix $\Sigma^{-1}$. Assume the following Cholesky decomposition

$$\Sigma^{-1} = L^T D^{-1} L,$$

(3)

where $D$ is a diagonal matrix with all positive elements and $L$ is a lower triangular matrix with all diagonal elements equal to 1. Then the covariance matrix has the Cholesky decomposition $\Sigma = L^{-1} D (L^{-1})^T$, where $L^{-1}$ is also lower triangular, which guarantees the positive definiteness of $\Sigma$.

For a random vector $(\gamma_1, \ldots, \gamma_p)$ from any distribution with mean 0 and covariance matrix $\Sigma$, elements of $D$ and $L$ in (3) can be written as regression coefficients (Pourahmadi (1999), Levina et al. (2008), Rothman et al. (2010)). For $j > 1$, write $\gamma_j = \sum_{k=1}^{j-1} \zeta_{jk} \gamma_k + \xi_j$, where $\{\zeta_{jk}\}$ are the coefficients of the best linear predictor of $\gamma_j$ by $\{\gamma_k : k = 1, \ldots, j - 1\}$ and $\xi_j$ is the residual. Let $\xi_1 = \gamma_1$, $\sigma_j^2 = \text{Var}(\xi_j)$ and $\zeta = \{\zeta_{jk}\}$, then $L = I - \zeta$, and $D = \text{Diag} \{\sigma_1^2, \ldots, \sigma_p^2\}$. Therefore, $\Sigma^{-1}$ can be parameterized with regression coefficients $\zeta$ and residual variances $\{\sigma_j^2\}$.

For the fixed effects to be identifiable, the design matrices $U$ and $(U_T, W)$ need to
be of full rank. The covariance matrix $\Sigma$ is identifiable if and only if $\Sigma_{GG}$, $\Sigma_{F_kF_k}$ and $\Sigma_{GF_k}$ are identifiable for all $k = 1, \ldots, K^F$, and there exists a $k \in \{1, \ldots, K^F\}$, such that for some $t \in \{1, \ldots, T\}$, the diagonal element $\{\Sigma_{F_kF_k}\}_{(t,t)}$ is a function of elements in $\Sigma_{F_kF_k} + \sigma_k^2 I_{T \cdot K^F}$. For example, if $\{\Sigma_{F_kF_k} : k = 1, \ldots, K^F\}$ are temporal covariance matrices of time series from AR($p$) models with coefficients $(\phi_1^k, \ldots, \phi_p^k)$ and $p < T - 1$, then $\Sigma$ is identifiable.

3 Parameter Estimation

In this section we delineate the estimation procedure for two groups of parameters: 1. those in characterizing variability in the geometry and functionality of cortical surface tffMRI in Section 2.1, in which the most important are the geometric and functional PC projections, and 2. parameters in the mixed effects model (2).

3.1 Estimation of the PC projections

In practice, the data of each subject is available in a discretized format. For each $i$, the geometric shape of cortical surface given by the structural MRI is a triangulated mesh $M_i^T$ of vertices on the surface as an approximation of the manifold $M_i$, and the function $Y_i(t)$ at each time/scan $t$ is represented by a piecewise affine mapping $Y_i^T(t) : M_i^T \rightarrow \mathbb{R}$.

First, subject-specific geometric shapes $\{M_i^T\}$ are deformed to a common mean shape $M_0^T$ (using the MATLAB package fshapesTK (Charlier et al. (2017))). The output is the estimated initial momenta $\{\hat{m}_i^0\}$ of the deformations. Then the geometric PCs and projection scores are estimated from the subject-specific deformations and it suffices to calculate the PC decomposition of $\{\hat{m}_0^i\}$, since the deformations are fully characterized by the initial momenta (Miller et al. (2015)). The output of the geometric PC analysis is the top $K^G$ PCs of the initial momenta and associated projection scores. $K^G$ is determined by examining the variance explained by the PCs, in the usual scree plot type approach. A pre-residualization
In the next step we estimate the functional PCs and projection scores. The observed functions \( \{Y^T_i(t)\} \) are first mapped to the domain of \( M^T_0 \) with the estimated deformation. Specifically, let \( X^T_i(t) = Y^T_i(t) \circ \varphi(\hat{v}_i, \cdot) \), where \( \{\hat{v}_i\} \) are determined by \( \{\hat{m}_0\} \) obtained in the previous step. Then we apply the SM-fPCA algorithm developed by Lila et al. (2016) to \( \{X^T_i(t)\} \) to estimate the functional PCs and the associated projection coefficients.

Similar to the principal component analysis for the subjects' geometric shapes, covariates that have potential effects on the functionality are pre-residualized before estimating the PCs. Additional details in estimating the geometric and functional PCs are available in the Supp. Material.

### 3.2 Estimation of the Mixed Effects Model

Parameters of interest in the mixed effects model (2), are fixed effects \( \alpha^G, \alpha^F, \beta \) and the precision matrix \( \Sigma^{-1} \). To simplify the likelihood, let \( p = K^G + TK^F \). Then \( a = (a^G, a^F) \in \mathbb{R}^{N \times p} \), and \( \text{vec}(a) \sim N(XB, (\Sigma_\gamma + \sigma^2 _{\epsilon} \otimes I_p) \otimes I_N) \), where \( \otimes \) denotes the Kronecker product,

\[
X = \begin{bmatrix}
I_{KG} \otimes U & 0 \\
0 & I_{KF} \otimes (U_T, W)
\end{bmatrix} \in \mathbb{R}^{(Np) \times (K^G p_u + K^F (p_u + p_w))}
\]

and \( B = (\text{vec}(\alpha^G)\top, \text{vec}((\alpha^F, \beta)\top)\top)\top \) is the re-shaped fixed effects vector.

Parameters in the mixed effects model (2) are estimated based on the likelihood function. To estimate \( \Sigma \), let \( \tilde{\gamma} := (\gamma^G + \epsilon^G, \gamma^F + \epsilon^F) \) denote the random effects combined with the errors, then \( \tilde{\gamma}_i \overset{iid}{\sim} N(0, \Sigma) \). We will use the parameterization \( \Sigma^{-1} = L\top D^{-1} L \), \( L = I - \zeta \) with \( \zeta \) being regression coefficients in \( \tilde{\gamma}_j = \sum_{k=1}^{j-1} \zeta_{jk} \hat{\gamma}_k + \xi_j \), and \( D = \text{Cov}(\xi) = \text{Diag}\{\sigma^2_1, \ldots, \sigma^2_p\} \).

If \( \{\tilde{\gamma}_j\} \) are observed, elements in \( L \) and \( D \) can be estimated by regressing observed \( \hat{\tilde{\gamma}}_j \) on
all of $\hat{\gamma}_k : k < j$.

We also impose Lasso regularization on the regression coefficients $\{\zeta_{jk}\}$ for two reasons. First, with large $K^G$, $K^F$ and $T$, the number of parameters to estimate in the regressions can easily exceed the number of subjects $N$, making ordinary least squares estimation intractable. Second, sparsity of the non-zero regression coefficients is closely related to the structure of the covariance matrix (1). Proposition 3.1 (proof in supp. material) states that under mild conditions, the matrix $L$ preserves the zero blocks in $\Sigma$. This ensures no inherent functional equivalence coming through correlations with the same geometric components. Figure 1 in the supp. material exhibits an example of structures of $\Sigma$, $\Sigma^{-1}$ and corresponding $L$ to demonstrate the results of Proposition 3.1.

**Proposition 3.1.** For $k_1, k_2 \in \{1, \ldots, K^F\}$, define the following partial equivalence relation:

$k_1 \sim k_2$ if and only if there exists $g \in 1, \ldots, K_G$ such that $\{\Sigma_{GF_{k_1}}\}_g, \neq 0$ and $\{\Sigma_{GF_{k_2}}\}_g, \neq 0$, where $\{\cdot\}_g, \cdot$ denotes the $g$th row of a matrix. Suppose $\Sigma^{-1}$ has Cholesky decomposition $L^T D^{-1} L$ and $L = I - \zeta$. Then for $k_1, k_2 \in \{1, \ldots, K^F\}$ and $k_1 < k_2$, $\zeta_{ji} = 0$ for all $i \in \{K^G + (k_1 - 1)T + 1, \ldots, K^G + k_1 T\}$ and $j \in \{K^G + (k_2 - 1)T + 1, \ldots, K^G + k_2 T\}$ whenever $k_1 \sim k_2$.

The regression coefficients $\{\zeta_{jk}\}$ are estimated by minimizing the $L^1$ regularized least squared distance:

$$\arg \min_{\{\zeta_{j1}, \ldots, \zeta_{j,j-1}\}} \|\hat{\gamma}_j - \sum_{k=1}^{j-1} \zeta_{jk}\hat{\gamma}_k\|^2 + \lambda_j \|\zeta_j\|_1$$

(5)

where $\lambda_j$ is the penalty parameter. Values of $\{\lambda_j\}$ can be determined using cross validation. An alternative method of choosing $\{\lambda_j\}$ is to define a vector $\tau = (\tau_1, \ldots, \tau_p)$, where $\tau_j$ is the number of non-zero coefficients allowed in the $j$th regression, and to select $\lambda_j$ so that $\#\{k : \zeta_{jk} \neq 0\} = \tau_j$. The latter is especially suitable for our application, as the number of nonzero elements in the $j$th regressions can be approximated by the desired number of
non-zero elements in the $j$th row of the structured covariance matrix (1), and the latter can be computed given values of $K^G$, $K^F$, $T$, and $j$.

Elements in the diagonal matrix $D$ are estimated by

$$
\hat{\sigma}_j^2 = \frac{1}{N - \#\{k : \zeta_{jk} \neq 0\}} \| \hat{\gamma}_j - \sum_{k=1}^{j-1} \hat{\zeta}_{jk} \hat{\gamma}_k \|^2.
$$

(6)

Given the estimates $\hat{D} = \text{Diag}\{\hat{\sigma}_1^2, \ldots, \hat{\sigma}_p^2\}$ and $\hat{L} = I - \hat{\zeta}$, we estimate the precision matrix with $\Sigma^{-1} = \hat{L}^\top \hat{D}^{-1} \hat{L}$ and the covariance matrix with $\Sigma = \hat{L}^{-1} \hat{D}[\hat{L}^{-1}]^\top$. Estimations of coefficients in each regression are independent and can be computed in a parallel manner, making the estimation scalable in high dimensional scenarios.

### 3.3 An Iterative Estimation Algorithm for Mixed Effects Model

We propose an iterative algorithm to estimate the fixed effect coefficients $\mathbf{B}$ and the covariance matrix $\Sigma$ in the presence of unobserved random effects and errors. In the initial step, assume there are no random effects. The fixed effect coefficients are estimated by regressing $\text{vec}(\mathbf{a})$ on the design matrix $\mathbf{X}$. Then the random effects are estimated with residuals of the regression, and the precision matrix is estimated with (5) and (6). Given the estimate of $\Sigma^{-1}$, the estimate of fixed effect coefficients are updated with the generalized least squares estimator (Lindstrom and Bates (1990))

$$
\hat{\mathbf{B}} = [\mathbf{X} \Sigma^{-1} \otimes \mathbf{I}_N]^{-1} \cdot \mathbf{X} \Sigma^{-1} \otimes \mathbf{I}_N \text{vec}(\mathbf{a}).
$$

The above steps are repeated until convergence criteria for both the fixed and random effect parameters are satisfied. For the fixed effects, the $L^2$ norm of the difference between estimates in the $n$ and $(n+1)$ steps $\Delta(\mathbf{B}^{(n+1)}, \mathbf{B}^{(n)}) = \| \text{vec}(\mathbf{B}^{(n+1)}) - \text{vec}(\mathbf{B}^{(n)}) \|^2$ is compared to a given criterion $C_B$. For covariance of the random effects, the Kullback-Leibler divergence $\Delta_{KL}(\Sigma^{(n+1)}, \Sigma^{(n)}) = \text{tr}[\Sigma^{(n)}^{-1} \Sigma^{(n+1)}] - \ln |\Sigma^{(n)}| - \Sigma^{(n+1)} - p$ is compared to a given criterion $C_\Sigma$.

If further identifiable parametrization is assumed for $\Sigma_\gamma = \Sigma_\gamma(\rho)$, where $\rho$ is a set
of unknown parameters, then $\rho$ and $\sigma^2_\epsilon$ can be estimated by minimizing the objective

$$\Delta_{KL}(\Sigma_\gamma(\rho) + \sigma^2_\epsilon I_p, \hat{\Sigma}) = \text{tr}((\hat{\Sigma}^{-1}(\Sigma_\gamma(\rho) + \sigma^2_\epsilon + I_p)) - \ln(|(\hat{\Sigma}^{-1}(\Sigma_\gamma(\rho) + \sigma^2_\epsilon + I_p)| - p$$

over admissible values of $\rho$ and $\sigma^2_\epsilon$. An example of further parametrization is to assume an AR($p$) structure for the temporal correlations among the functional PC projections.

To test on the fixed effects $B$, we use the Wald-type testing statistic based on the following estimator of variance of $\hat{B}$ (see, for example, Demidenko (2013)): $[X'(\hat{\Sigma}^{-1} \otimes I_N)X]^{-1}$. The test statistic for $\hat{B}_i$ is $\hat{B}_i / \text{diag}([X'(\hat{\Sigma}^{-1} \otimes I_N)X]^{-1})_i$, which follows the standard normal distribution under the null hypothesis $B_i = 0$.

## 4 Application to the HCP Cortical Surface Task fMRI

In this section we conduct a comprehensive analysis on the HCP task fMRI data. The cortical surface tMRI data were processed with HCP pipeline (as found in “fMRISurface” (Glasser et al. (2013), WU-Minn Consortium (2018)) and converted to .csv for statistical analysis using software Connectome Workbench and AFNI package (Cox (1996))). For each subject, the processed data consist of a structural MRI scan with the $xyz$ coordinates of 32,492 vertices on each hemisphere (left and right), indicating the geometric shape of the cortical surface, and a time series of $T = 176$ fMRI scans of BOLD signal values of each of the vertices, indicating the functionality in emotion processing tasks. Here we focus on analyzing data of the left hemisphere. In addition, time-invariant age and gender variables and time series of task stimuli were extracted from the event (EV) files of the data. We analyze the effect of time invariant variables and the task stimuli on both the geometry and the time series of functional fMRI scans at their full temporal dimension $T = 176$. We also analyze the data in a collapse version of $T = 3$ as a reference (results in Supp Material). The comparison between the full and collapse dimension data analysis demonstrates that there are significant advantages to be able to use the full temporal dimension of data made
possible by the proposed approach.

4.1 Data Analysis

The Conte69 cortical surface (Van Essen et al. (2012)) is used as the template shape in estimating the initial momenta of deformations of subject-specific shapes with the fshapesTK package (Charlier et al. (2017)). The principal components (PCs) of the initial momenta are extracted as the geometric PCs (visualizations in the Supp. material).

Then we map subjects’ functions defined on the subject-specific shapes to the common template and extract the functional PCs defined on the template. To reduce computation time we averaged each subject’s fMRI signals by experiment phases before obtaining the PCs.

Due to the high dimensionality of both the geometry and functionality of the tfMRI data, a large number of PCs are required to explain the majority of the geometric (top 30 explains 50%) and functional variability (top 20 explains 70%) in the subjects. The variability in the geometric shapes is especially large as all vertices on the hemispheres rather than regions of interest are under examination. Here we use a preliminary step to select geometric and functional PCs to include in the mixed effects model. In particular, we are interested in PCs that are most relevant to the emotion processing task. To this end we conduct pair-wise Pearson’s tests on the correlations between the subjects’ projection coefficients on the top 20 geometric PCs and the projections of the fMRI signals during the “face” phase on the top 10 functional PCs. Table 1 in the Supp. Material shows the combinations of the functional and geometric PCs with largest correlations, and we include the top 10 functional PCs and the top 10 geometric PCs according in the table for subsequent analyses.

The time-invariant covariates included in the mixed effects model are the age and gender. There are four categories of age (22-25, 26-30, 31-35, and 36+) and two of gender (female and male). Including the intercept and using the age group of 22-25 and female as baseline
values, the effective number of the time-invariant covariates is $p_u = 5$.

The time-varying covariates are the indicators of task phases for each subject during the experiment. There are three phases: the “resting” phase when subjects are in the intermissions between task trials, “face” when subjects are asked to match faces with fearful or angry expressions, and “shape” when subjects are asked to match pictures of shapes without emotional indications. The indicators of the three phases are linear dependent and we use the resting phase as the baseline. The effective number of the time-varying covariates is thus $p_w = 2$.

The mixed effects model for the $i$th subject is

$$a^G_i = \text{Age}_i \cdot \alpha^G_{\text{Age}} + \text{Gender}_i \cdot \alpha^G_{\text{Gender}} + \gamma_i^G + \epsilon_i^G,$$

$$a^F_i(t) = \text{Age}_i \cdot \alpha^F_{\text{Age}} + \text{Gender}_i \cdot \alpha^F_{\text{Gender}} + \text{Task}_i(t) \cdot \beta + \gamma_i^F(t) + \epsilon_i^F,$$

where $a^G_i$ denotes the projection coefficients on the geometric PCs and $a^F_i(t)$ denotes the projection coefficients on the functional PCs at time $t$. Age$_i$ and Gender$_i$ denote the vector of dummy variables of age and gender categories. The corresponding effect sizes are $\alpha^G_{\text{Age}}$ and $\alpha^G_{\text{Gender}}$ on the geometric PC projections and $\alpha^F_{\text{Age}}$ and $\alpha^F_{\text{Gender}}$ on the functional PC projections. Task$_i(t)$ denotes the time series of task phase indicators with effect size $\beta$ on the functional projection coefficients.

### 4.2 Results and Interpretations

We conduct data analysis in two settings. The first is a complete-time setting in which the full time series of $T = 176$ fMRI signals for each subject are preserved. The second is a collapse/compressed setting in which time series of fMRI signals are aggregated by the $T = 3$ experiment phases and the averages of fMRI signals are used for subsequent analysis.
### 4.2.1 Estimation of the Fixed Effects

Tables 1, 2 and 3 show the estimated fixed effects coefficients in the \( T = 176 \) model setting.

Results of setting \( T = 3 \) are available in the Supp. Material.

| PC1   | PC3   | PC4   | PC5   | PC6   | PC10  | PC12  | PC13  | PC15  | PC17  |
|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Gender: M | 3.03** | -1.36 | -0.56 | 1.64* | -0.11 | -0.05 | 0.03  | -0.42 | 0.80  | 0.52  |
| Age: 26-30 | 0.90  | 0.38  | 0.16  | -0.49 | -0.35 | 0.25  | 0.05  | -0.22 | -0.28 | -0.42 |
| Age: 31-35 | 0.67  | -0.48 | -0.34 | 0.19  | -0.21 | 0.02  | -0.07 | -0.84 | 0.04  | -0.12 |
| Age: 36+  | 0.84  | 0.57  | -2.07 | -0.02 | -2.81 | 0.51  | -0.03 | 2.48  | -1.05 | -1.32 |

Table 1: Model Setting \( T = 176 \): Fixed effects \( \alpha^G \) of time-invariant covariates on estimated geometric PC projections. Significance levels: 0.1 (.), 0.05 (*), 0.01 (**), 0.001 (†).

| PC1   | PC2   | PC3   | PC4   | PC5   | PC6   | PC7   | PC8   | PC9   | PC10  |
|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Gender: M | 1.53† | -1.66† | 2.15† | 0.01  | 0.19† | -0.36† | 0.16† | 0.06* | -0.43† | -0.31† |
| Age: 26-30 | 0.74† | -0.90† | 1.08† | -0.41† | 0.32† | -0.11* | -0.43† | 0.55† | 0.12* | 0.33† |
| Age: 31-35 | 0.57** | -0.84† | 1.45† | 0.15  | 0.66† | -0.08 | -0.28† | 0.69† | -0.53† | 0.25† |
| Age: 36+  | 0.58  | 4.60† | -1.73† | -4.19† | -3.94† | 1.70† | -0.37* | -1.03† | -1.76† | 0.23  |

Table 2: Model Setting \( T = 176 \): Fixed effects \( \alpha^F \) of time-invariant covariates on estimated functional PC projections \((\times 10^4)\). Significance levels: 0.1 (.), 0.05 (*), 0.01 (**), 0.001 (†).

| PC1   | PC2   | PC3   | PC4   | PC5   | PC6   | PC7   | PC8   | PC9   | PC10  |
|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Face  | 0.51  | 1.71  | -1.01 | 2.61† | -0.78 | 1.02* | -0.97* | 1.55** | 1.46† | 0.60* |
| Shape | 3.59* | 1.00  | -0.31 | 1.35* | 0.55  | 0.66  | 0.31  | 0.66  | 2.02† | 0.51  |

Table 3: Model Setting \( T = 176 \): Fixed effects \( \beta \) of task phases on estimated functional PC projections \((\times 10^2)\). Significance levels: 0.1 (.), 0.05 (*), 0.01 (**), 0.001 (†).

Comparing the results of the \( T = 3 \) and \( T = 176 \) settings, the estimated fixed effects of the time-invariant covariates on the geometry are similar in the two settings, which is expected given that the shapes are invariant to task phases and should not vary with different treatments of time of the tfMRI time series. Not many PCs are found to be significantly associated with age and gender, except for PC1 and PC5, which are associated with gender.

These results are reasonable, as geometric PC1 and PC5 (Figure 2 in Supp. Material) mainly explains the overall size, either inflated or deflated, of the cortical surface comparing to the template, and males are known to have larger brains by volume than females.
For both settings, age and gender have more significant associations with functional PCs than with geometric PCs, indicating more important roles of the demographic factors as well as high heterogeneity in emotion processing among the population. More significant fixed effects of the time-invariant covariates on the functional PC projections are revealed in the $T = 176$ setting, as the effective sample size is much larger and more information is preserved. Similar phenomenon can be observed in estimates of the effects $\beta$ of time-varying covariates, demonstrating improved statistical power of the complete-time model setting and the capability of the proposed estimation methods in dealing with the large dimensionality of the complete time data.

Figure 1: Functional PCs associated with the emotion processing task visualized on the template surface. Top: lateral view. Bottom: medial surface. Red color indicates higher values (largest 0.02) and blue color indicates lower values (smallest value -0.02) of the pre-residualized BOLD fMRI signals.

Figure 1 visualizes the functional PCs 4, 6, 7, 8, 9, 10 which are significantly associated with emotion processing task as indicated by the fixed effects of the “face” task phase indicator on the corresponding projection coefficients. Functional areas associated with the emotion processing task as shown by the deeper colored regions on the PCs are: the inferior and middle temporal, somatosensory and motor cortex, auditory association cortex, orbital and polar frontal cortex, primary visual cortex, parahippocampal, and fusiform. Our results supplement those of the analysis on the volumetric subcortical fMRI data by Barch et al. (2013), which discovered that there was activation of the amygdala extending into the hippocampus, as well as activation in medial and lateral orbital frontal cortices and visual
regions including fusiform and ventral temporal cortex.

4.2.2 Estimation of the Random Effects

An important aspect of the results is the covariance matrix of the random effects, which characterizes the relation between the geometry and functionality of the cortical surfaces.

Figure 3 in the Supp. Material shows significant associations in the $T = 3$ setting between the projections on the geometric and functional PCs via the $L$ matrix in the Cholesky decomposition $\Sigma^{-1} = L^\top D^{-1} L$. A non-zero $(i,j)$th element in $L$ suggests potential association between the $i$th geometric and $j$th functional PCs. Figures 2 visualizes geometric PCs $6, 10, 12, 15, 17$ found to be associated with the functional PCs (in Figure 1) that are relevant to the emotion processing task. We plot the resulting manifolds by applying deformations $\varphi(c \cdot \psi_j^G, \cdot)$ to the template manifold, where $\psi_j^G$ denotes the vector field associated with initial momenta of the $j$th geometric PC. The initial momenta are multiplied by scalers $c = -15, -1, 1, 7$, selected to illustrate how shapes of the cortical surface vary with different values of projection scores.

![Figure 2: Geometric PCs 6,10,12,15,17 associated with functional PCs relevant to emotion processing (lateral view). Top row: deformations of template manifold with geometric PCs’ initial momenta $\varphi(c \psi_j^G, \cdot)$ for $j = 6, 10, 12, 15, 17$ and $c = 1$ (white) and $c = 7$ (blue). Bottom row: deformations of template manifold with $\varphi(c \psi_j^G, \cdot)$ for $c = -1$ (white) and $c = -15$ (blue).](image)

In particular, Figure 3 provides a side-by-side comparison of functional PC6 and geometric PC6, in which potential influence of the geometry and the functionality of the cortical surface can be observed. Regions of activation marked by deep red and blue colors on the functional PC (bottom), especially near the inferior temporal and fusiform gyri, have a
visible correspondence with the geometric shape (top) of the regions: the blue/white colors on the top right panel, which indicate inflated/deflated gyri, are matched with the deep blue/red colors on the bottom right of activated areas. The occipitotemporal sulcus in white (top right panel) also has an apparent correspondence with the deep red color in the functional PC colormap (bottom right panel). A similar correspondence can be seen in the temporal lobe area. These results are interesting as they hint potential associations between the development in shapes of regions and the functionality of those regions.

Figure 3: A comparison of geometric PC6 (top) and functional PC6 (bottom)

5 Concluding Remarks

In this paper we propose a framework for jointly modeling the geometric and functional variability in functional surfaces including cortical surface task fMRI. We characterize effects of subject-specific covariates and exogenous stimuli on both the geometry and functionality while accounting for their mutual-influences with a unified mixed effects model. We also develop a computationally efficient estimation method for the proposed mixed effects model by iteratively estimating the fixed effects and elements in the Cholesky decomposition of the precision matrix of random effects. In particular, elements in the rows of the Cholesky decomposition are estimated via regularized regressions to circumvent the computational burdens in dealing with high dimensional covariance matrices. The proposed method is
scalable and automatically guarantees the positive-definiteness of the estimated precision/covariance matrix.

We apply the proposed method to the HCP cortical surface task fMRI data in both the complete time setting with $T = 176$ and the condensed setting with $T = 3$. We analyze the fixed effects of age and gender and task stimuli on both geometry and functionality of subjects’ cortical surface fMRI data as well as the covariance between the geometry and functionality. The proposed approach reveals patterns of geometric shapes and activated regions associated with the covariates, as well as unique modes of correspondence between the shapes of the cortical surface and functionality related to emotion processing.

In the appendix, we further examine the performance and computational efficiency of the proposed method with a comprehensive simulation study using synthetic data and demonstrate its advantage when compared to other methods including REML. The proposed method performs especially well when the covariance matrix is of high dimensions.

While we focus on the analysis of vertex-wise cortical surface data, the model and method proposed here can be readily applied to study of morphology and functionality of regions of interest (ROI) on the cortical surface. In fact, in studying ROIs, since the geometry and functional signal in individual vertex is summarized in the corresponding ROI, with proper registration of each subject’s geometry, the ROI level data need not go through the fPCA procedure to reduce the dimensionality. Therefore the mixed model and the estimation method proposed here can be directly applied to the ROI level functional surface data.

The proposed model and method can be applied beyond cerebral cortical surfaces and to studying functional surfaces in general. For example, Gee et al. (2018) studies the association between cortical mass surface density (CMSD), which is closely correlated with risk of hip fracture, and the shape of proximal femoral neck bone via statistical parametric mapping (SPM). The model and method in our paper can be adopted for the femoral neck bone data to study the bone shape and CMSD jointly while accounting for covariates relevant to both
the shape and the CMSD.

There are several possible future directions for us to pursue. First, as in all studies on functional data, the alignment of subject-specific functions to a common domain induces identifiability issues, which will be carried to statistical analyses of the aligned functions. This issue is alleviated in our study, as the proposed joint model is able to capture the variability in both geometry and functionality of the functional surfaces. To improve the alignment of the functions, prior knowledge on functional regions such as functional atlas or ROIs as well as landmarks can be incorporated to the registration step.

Second, in modeling the variability in functionality, an alternative approach is to use the multilevel PCA (Di et al. (2009)) to further separate the inter- and intra-subject (temporal) variability of the aligned tfMRI signals. Then one can link the multilevel PC projects to the covariates to study their effects on the functionality at different phases of the tasks.

Third, in the proposed model and estimation method we do not impose extra constraints on the elements of the covariance matrix other than the regularization on elements in the Cholesky decomposition of the precision matrix. As a result the estimation of the covariance matrix is flexible and adapts well to a wide range of covariance structures. If prior knowledge implies further constraints on the covariance matrix, elements in the Cholesky decomposition can be re-parameterized to satisfy, at least approximately, the desired structure of the covariance matrix.

Finally, if multiple modalities of the functional surfaces are available for the subjects, such as different types of fMRI including resting state and task fMRI, and Diffusion Tensor Imaging (DTI), the proposed model can be extended to characterize the covariance among different modalities.

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A Appendix: Simulation Studies

A.1 Generation of the Functional Manifolds

We further demonstrate the proposed approach with synthetic functional manifolds that resemble cortical surface task fMRI, but with a lower dimensionality to reduce the computational workload and enable testing in different scenarios.

First we create $K^G$ geometric PCs and $K^F$ functional PCs using a template manifold $\mathcal{M}_0$ resembling the human brain stem created by Lila et al. (2016) (see figure in Supp. Material). To generate shapes associated with geometric PCs, we create $K^G$ orthogonal deformation momenta to map $\mathcal{M}_0$ to manifolds associated with the PCs. The functional PCs are mappings from $\mathcal{M}_0$ to $\mathbb{R}$ and are generated to have correspondence with the geometric PCs. For the $k$th functional PC, large values (red) are generated on vertices where the shape of the $k$th geometric PC is inflated, and smaller values (blue) are generated on vertices where the $k$th geometric PC are deflated. The generated PCs are visualized on the top row of Figure 4, in which the shapes represent the geometric PCs while the colormap on top of the shapes represents the functional PCs.

![Figure 4: The geometric and functional PCs visualized by overlaying colormaps of functional PCs on shapes of geometric PCs with the same indices. Top row: the PCs in the generative model. Bottom row: estimated PCs from one simulation run of 200 subjects.](image)

The simulation study is conducted under a small temporal-dimension setting with $T = 5$ and a large temporal-dimension setting with $T = 50$. For each setting we run 20 independent simulations. In each simulation run, $N = 200$ subjects’ functional surfaces are generated from the $K^G = 5$ geometric and $K^F = 5$ functional PCs in Figure 4. Each subject’s projection coefficients $a = (a^G, a^F)$ on the geometric and functional PCs are generated as the outcomes of the mixed effects model (2). For the mixed effects model $p_u = 2$ time-invariant covariates are sampled independently from $U_1 \sim N(3, 3)$ and $U_2 \sim t_3 + 3$. In addition, $p_w = 2$ time-varying signals $W$ are generated for all subjects to resemble the stimuli in the task fMRI (see the Supp. Material for plots of the signals). For the fixed effects coefficients, we select vec$(\alpha^G) = (1, 0, 0, 1, 0.5, 0.5, 0.2, 0.6, 1.5, 0.5)$ for effect sizes of $U$ on the geometric PC projections, vec$(\alpha^F) = (1, 1, 0.5, 1.5, 0.5, 0.5, 1, 0, 0, 1)$ for effect sizes of $U$ on the functional PC projections, and vec$(\beta) = (0, 0, 1, 0.5, 0.5, 1.5, 0.5, -0.3, -0.7)$ for effect sizes of $W$ on the functional projections.

The random effects $\gamma$ in the mixed effects model are sampled independently from $N(0, \Sigma_\gamma)$, where $\Sigma_\gamma$ is constructed using the Cholesky decomposition (3). The constructed
\( \Sigma_\gamma \) has blocks \( \Sigma_{GG} = \text{Diag}(25,16,9,4,1) \) and each of \( \{ \Sigma_{Fk,Fk} : k = 1,\ldots,5 \} \) following approximately the covariance matrix of an AR(1) model with variances \((30,20,10,5,1)\), respectively. The blocks \( \Sigma_{GF_k} \) are constructed to contain significantly non-zero values to represent the covariance between the geometry and functionality. Finally, errors \( \epsilon \sim \mathcal{N}(0,\sigma_\epsilon^2) \) with \( \sigma_\epsilon = 0.5 \) are generated independently of the random effects. In constructing the covariance matrices, we do not impose further parametrization on \( \Sigma_\gamma \), and thus the covariance matrix is identifiable up to \( \Sigma = \Sigma_\gamma + \sigma_\epsilon^2 I \).

The deformation operator \( \phi_i \) for mapping the \( i \)-th subject’s shape from the template \( M_0 \) is calculated as the linear combination of the geometric PCs with the projection coefficients \( a_{Gi} \) as the weights. Similarly, the function of the \( i \)-th subject at each time \( t \), defined on the domain of \( M_0 \), are obtained by calculating the linear combinations of the functional PCs weighted by \( a_{Fi}(t) \). Finally, the observed function of the \( i \)-th subject, defined on the subject-specific domain \( M_i \), is given by the composite of \( \phi_i \) and the function on \( M_0 \).

The propose estimation approach is applied to the generated synthetic functional manifolds. To examine the effectiveness of the proposed estimation for the mixed effects model, we also estimate the mixed effects model with actual values of \( (a^G, a^F) \) as the outcome to separate errors in the mixed effects model estimation from those induced in estimating the deformations and extracting the PCs.

We compare results using the proposed method with two alternative methods for mixed effects model estimation, whenever the alternatives are computationally feasible. The first is to use an iterative algorithm similar to the proposed but without any regularization on the elements in the Cholesky decomposition of \( \Sigma^{-1} \). The second is to use restricted maximal likelihood estimation (REML). Here we implement a modified REML algorithm based on the R package \texttt{lme4} (Bates et al. (2015)). In the modified REML estimation, we assume the structure of \( \Sigma \) including the zero blocks is known \textit{a priori} to avoid the computational burden in optimizing over the complete set of \( p(p+1)/2 \) parameters. Not all parameter settings guarantee the positive definiteness of the covariance matrix, without which the REML cannot proceed. To address this issue we implement truncations in which non-positive eigenvalues of the covariance matrix given the proposed parameter setting are replaced with \( 10^{-5} \) so that the resulting matrix is positive definite. We also estimate the fixed effects without accounting for the random effects and include the results in the comparison.

### A.2 Estimation Results

#### A.2.1 \( K^G = 5, K^F = 5, T = 5, N = 200 \)

Figure 5 summarizes the estimation of the fixed effects via box plots. The left panel shows the square roots of the mean squared errors (MSE) from all simulation runs in which the estimates are obtained with the actual PC projection coefficients. Results are averaged by fixed effect types: \( \alpha^G, \alpha^F \) and \( \beta \), and methods: proposed, REML, estimation without accounting for random effects, and estimation without imposing regularization on the covariance matrix. The right panel shows the results obtained from the estimated PC projection coefficients.
With the actual values of PC projections $\mathbf{a}$, different methods have similar performance in estimating $\alpha^G$, except for the procedure without imposing regularization on the covariance matrix, which leads to larger errors. In estimating $\alpha^F$ and $\beta$, the procedure without accounting for random effects under-performs comparing to the other methods. The proposed method and REML have the best performance, which is not surprising, as the other two methods either over-simplifies the covariance matrix as the identity matrix or fails to recognize the sparsity in the covariance structure. The right panel of Figure 5 demonstrates to what extent the fixed effects estimation is affected by the biased introduced in the geometric registration of the manifolds and the estimation of the PCs. The median errors nearly doubled compared to the estimates with the actual $\mathbf{a}$, and the comparison of performances of different methods is similar to that with the actual $\mathbf{a}$.

Figure 6 compares estimation of the covariance matrix with the actual PC projection coefficients with the square roots of the MSE in each element. The proposed method is able to recover the structure of the covariance matrix with high precision, including the temporal covariance of the time series $\alpha^F$ and the covariance between the geometric and functional PC projections (color bands on the top left corner of the matrix). The procedure without regularizing the covariance matrix is able to recover most of the covariance structure, but has many false recoveries of non-zero elements in the matrix. REML performs much worse than the aforementioned two methods, suffering from large errors in estimating the non-zero elements in the covariance matrix. The MSE of REML in Figure 6 contains apparent
color blocks, indicating REML fails to recover most of the covariance structure, despite the fact that the positions of zero elements in the matrix are already given “for free” in the simulations. It is also worth noting that REML’s performance relies heavily on the initial value. Additional figures are available in the Supp. Material for estimation results of the covariance matrix obtained with the estimated PC projection coefficients. Although less accurate due to errors induces in the estimation of deformation and PCs, the proposed method still has satisfactory performance comparing to the other methods, which suffer from false recoveries of non-zero elements in the covariance matrix.

Regarding computational efficiency, the proposed method took about 8 seconds to finish the estimation, the method without regularization took 6.8 seconds, and the REML took 13.5 minutes. Here the REML method is given an advantage of knowing the zero blocks in the covariance matrix, a much reduced number of parameters needs to be optimized over. In more practical scenarios, the estimation with REML is expected to take a longer time.

### A.2.2 \( K^G = 5, K^F = 5, T = 50, N = 200 \)

We also examine a large-T scenario that reflects the realistic dimension of cortical surface fMRI data. Same parameters are used in generating the functional manifolds.

We also apply the “no regularization on the covariance matrix” method to compare with the proposed method. With \( T = 50 \), elements in the covariance matrix can no longer be estimated with the regression method due to over-fitting when the number of elements exceeds the number of subjects. Here we modify the estimation algorithm: in each iteration the covariance matrix is estimated with a truncated empirical covariance matrix whose non-positive eigenvalues are replaced with a small positive constant. In this large \( T \) setting, the REML becomes computationally infeasible and thus no results are available for the comparison.

The left panel of Figure 7 summarizes estimates of fixed effect coefficients via boxplots grouped by fixed effect types and methods. It is apparent that the fixed effects estimation is heavily affected when the covariance matrix is estimated poorly with the “without regularization” method, which is expected as the empirical covariance matrix performs poorly in the high dimensional scenario. Estimation with the proposed method is comparable to the method without accounting for random effects. The right panel of Figure 7 displays the estimation results with estimated PC projections. Due to the additional errors induced during the geometric registration and the PC estimation, the errors increases by about 50% for all three methods.

![Figure 7: Estimation of fixed effects, grouped by methods and fixed effects type. Left: with actual PC projection coefficients. Right: with estimated PC projection coefficients.](image)
Due to the dimensionality of the covariance matrix, instead of showing the estimated covariance matrix averaged over the simulations, we show in Figure 8 the density curves of square roots of MSE for each element in the covariance matrix. The density curve of proposed method peaks at near zero and has the majority of mass concentrated in $[0, 1.5]$. The curve of the “no regularization” method shifts towards large values of the error, indicating a worse performance. Additional figures are available in the Supp. Material. Both methods needed about 6 minutes to finish the estimation procedure. Attempts of the REML took longer than 9 hours without finishing the estimation and were aborted.
Supplementary Material of *Mixed Effects Model for Cortical Surface Task fMRI*

1 Proof of Proposition 3.1

![Figure 1: Example of Σ (left) and the corresponding Σ⁻¹ (middle) and L (right) in which K^G = 5, K^F = 5, T = 3.](image)

**Proof.** Suppose a random vector $\gamma$ follows a multivariate distribution with mean $0$ and covariance matrix $\Sigma_\gamma$ and the inverse of the covariance has Cholesky decomposition $\Sigma_\gamma^{-1} = L^\top L$. Then $L = I - \zeta$ in which $\zeta_{ji}$ is the coefficient of $\gamma_i$ in the best linear predictor of $\gamma_j$ by $\{\gamma_k : k = 1, \ldots, j - 1\}$. Let $\gamma_{j-} = (\gamma_1, \ldots, \gamma_{j-1})$, then $\zeta_j = (\gamma_{j-}, \gamma_{j-})^{-1} \cdot (\gamma_{j-}, \gamma_j)$, where $\zeta_j$ is the $j$th row of $\zeta$ and $\langle X_1, X_2 \rangle = E(X_1^\top X_2)$. To simplify the notation, suppose for now $j > K^G + (k_2 - 1)T + 1$ and let $m = j - (K^G + (k_2 - 1)T + 1)$. Then

\[
\langle \gamma_{j-}, \gamma_{j-} \rangle = \begin{bmatrix}
\Sigma_{GG} & \Sigma_{GF_1} & \cdots & \cdots & \{\Sigma_{GF_{k_2}}\}_{1:m} \\
\Sigma_{GF_1}^\top & \Sigma_{F_1F_1} & 0 & \cdots & 0 \\
\vdots & 0 & \ddots & \ddots & \vdots \\
\vdots & \vdots & \ddots & \ddots & 0 \\
\{\Sigma_{GF_{k_2}}\}_{1:m}^\top & 0 & \cdots & 0 & \{\Sigma_{F_{k_2}F_{k_2}}\}_{1:m,1:m}
\end{bmatrix}, \tag{1}
\]
where \{·\}_{1:m,·}, \{·\}_{·,1:m} and \{·\}_{1:m,1:m} denote the first \(m\) rows, first \(m\) columns and the first \(m\) rows and columns of a matrix, respectively. The inverse \((\gamma_{j-}, \gamma_{j-})^{-1}\) can be written in terms of blocks in (1): let \(A = \Sigma_{GG}, C = [\Sigma_{GF_1}, \cdots, [\Sigma_{GF_{k_2}}]_{1:m}]^T\), and \(D = \text{Diag}([\Sigma_{F_1 F_1}, \cdots, [\Sigma_{F_{k_2} F_{k_2}}]_{1:m,1:m}]\), then

\[
(\gamma_{j-}, \gamma_{j-})^{-1} = \begin{bmatrix}
A^{-1} + A^{-1}C(D - CA^{-1}C)^{-1}CA^{-1} & -(D - CA^{-1}C)^{-1}CA^{-1} \\
-(D - CA^{-1}C)^{-1}CA^{-1} & (D - CA^{-1}C)^{-1}
\end{bmatrix}. \tag{2}
\]

In the next step we show that \((D - CA^{-1}C)^{-1}\) is symmetric, and \(j \in \{(k-1)T+1, \cdots, (k-1)T\}\) such that \(k \approx k_2\) and \(k \neq k_2\). A permutation matrix \(P\) can be applied to the matrix \(D - CA^{-1}C\) to make \(P(D - CA^{-1}C)P^T\) block-diagonal: select \(P\) such that left-multiplying \(P\) with a matrix moves each block of rows indexed by \{(k-1)T+1, \cdots, kT\} (except for \(k = k_2\) where the row indices are \{(k-1)T+1, \cdots, (k-1)T+m\}) in the matrix to make blocks with semi-equivalent \(k\) adjacent. Consequently \((P(D - CA^{-1}C)P^T)^{-1}\) is also block-diagonal. Reverting the permutations gives \((D - CA^{-1}C)^{-1} = P^T \cdot (P(D - CA^{-1}C)P^T)^{-1} \cdot P\) and leads to the desired results.

Since \(k_1 \approx k_2\), for all \(g \in 1, \cdots, K\) such that \([\Sigma_{GF_{k_2}}]_{g,·} \neq 0\), \(- (D - CA^{-1}C)^{-1}CA^{-1}\) is block-diagonal. Given \((\gamma_{j-}, \gamma_{j-}) = \{[\Sigma_{GF_{k_2}}]_{m+1,0}, \cdots, 0, [\Sigma_{F_{k_2} F_{k_2}}]_{m+1,·}\}^T\), we have \(\zeta_{ij} = \{\gamma_{j-}, \gamma_{j-}\}^{-1}_{i,·}, \{\gamma_{j-}, \gamma_{j-}\} = \{-(D - CA^{-1}C)^{-1}CA^{-1}\}^{-1}_{i,·}, \{\Sigma_{GF_{k_2}}\}_{m+1} + \{[D - CA^{-1}C]^{-1}\}^{-1}_{i,·}, \{\Sigma_{F_{k_2} F_{k_2}}\}_{m+1,·} = 0.\)

\[\square\]

2 Technical Details of Registration of Manifolds and Estimation of Principal Components

2.1 Estimation of the Geometric Principal Components

The first step of the estimation procedure is to extract the values of the subject-specific vector fields \(\{v_i : i = 1, \ldots, N\}\) that index the deformation operator \(\varphi(v_i,·) : \mathcal{M}_0 \to \mathcal{M}_i\). This step is often referred to as the registration of the shapes. Given the vector field \(v\), the deformation operator \(\varphi\) is assumed to satisfy \(\varphi(v_0, x) = \phi_v(1, x)\), where \(\phi_v(1, x)\) is the solution to \(\partial \phi_v(s, x) / \partial s = v_s \circ \phi_v(s, x)\) with initial condition \(\phi_v(0, x) = x\).

It is further assumed \(v_s(·) = \sum_{k=1}^{n_g} K_{g}(\phi_v(s, c_k),·) m_{k,s}\), where \(K_{g}(x, y) = \exp(-\|x - y\|^2/(2\sigma_y^2))\) is the deformation momentum in the \(k\)th control point at time \(s\). In practice, the \(d\) points on the discretized template \(\mathcal{M}_0^d \subset \mathbb{R}^3\) are usually selected as the control points, so that \(n_d = d\) and \(v_i\) can be fully characterized by the subject-specific momenta \(\{m_{k,s} : s \in [0,1], k = 1, \ldots, d\}\). For each \(i\), assume \(v_i\) minimizes the objective \(D^2(\varphi(v_i,·) \circ \mathcal{M}_0, \mathcal{M}_i) + \lambda \int_0^1 \|v_s\|_D^2 ds\) where \(D\) is a mismatching functional and \(\lambda\)
is a penalty parameter for the energy of the deformation, and a natural estimator of \( v_i \) is

\[
\hat{v}_i = \arg \min_v D^2(\phi(v, \cdot) \circ M^T_0, M^T_i) + \lambda \int_0^1 \left\| \nu_i \right\| ds.
\]

If the vertices of \( M^T_i \) and \( M^T_0 \) have a known one-one correspondence, then a natural choice of \( D \) is the Euclidean distance in \( \mathbb{R}^3 \). If the correspondence between vertices of \( M^T_i \) and \( M^T_0 \) is unknown, methods have been developed by Vaillant and Glaunès (2005) and Vaillant et al. (2007) for the definition of \( D \) in matching \( M^T_i \) and \( M^T_0 \).

The objective in 3 can be solved backwards and the solution is fully determined by a vector field \( \{ \hat{m}^i_{k,0} \} \) termed the initial momenta (for details, see Miller et al. (2015)). Consequently, the deformation of the \( i \)th subject can be characterized by estimate of the vector field \( \hat{v}_i \), which in turn is characterized by the estimated initial momenta \( \{ \hat{m}^i_{k,0} : k = 1, \ldots, d \} \) on the \( d \) nodes of the triangular mesh. The MATLAB package \( \text{fshapesTK} \) can be used to solve for the initial momenta for each subject. For details of the solution to the optimization problem, see Charlier et al. (2017).

The principal component decomposition \( V_i = \sum_{j=1}^{K^G} a^G_{ij} G_j \) is estimated by the decomposition of \( \hat{v}_i \). Since \( \{ \hat{v}_i \} \) is fully characterized by the initial momenta \( \{ \hat{m}^i_{k,0} \} \), it suffices to calculate the decomposition of the momenta. For each \( i \), format the estimated momenta as a matrix \( \hat{M}_i \in \mathbb{R}^{d \times 3} \), in which the \( k \)th row is \( \hat{m}^i_{k,0} \). Then let \( \hat{M} \in \mathbb{R}^{N \times 3d} \) be the data matrix where the \( i \)th row is \( \text{vec}(\hat{M}_i) \) (the vectorization of \( \hat{M}_i \) by column), and the geometric PCs are estimated by the empirical PCs from decomposing \( \hat{M} \). Finally, the projection coefficients are estimated by calculating the projections of the initial momenta of the subject’s deformation on the empirical PCs.

It is worth noting that an extra step can be applied prior to the principal component analysis to increase the accuracy of the estimation. Given covariates that are believed to have effects on the subjects’ geometry, it is advantageous to regress the estimated initial momenta on the covariates and conduct the principal component analysis on the residuals of the regression. This extra step of pre-residualization reduces the covariance induced by sharing the same covariates among different columns of the initial momenta at different vertices and increases the accuracy in recovering the original PCs.

### 2.2 Estimation of the Functional Principal Components with SM-fPCA

The next step is to estimate the functional texture PCs \( \hat{\psi}^F_j \) and the corresponding projection coefficients \( \hat{a}^F_j \). In the model for the functionality: \( Y_i(t) = X_i(t) \circ \varphi^{-1}(v_i, \cdot) \), where \( X_i(t) = \mu(t) + \delta Z_i(t) \) and \( Z_i(t) = \sum_{j=1}^{K^F} a^F_j(t) \psi^F_j \), to estimate the functional PCs, the observed texture functions \( \{ Y_i^T(t) \} \) need to be mapped back to the domain of the template manifold \( M^T_0 \) by the estimated deformation functional. Specifically, let \( X_i^T(t) = Y_i^T(t) \circ \varphi(\hat{v}_i, \cdot) \), where \( \{ \hat{v}_i \} \) are estimated in the previous registration step.
Extra steps of registration can be applied to $X^F_t(t)$ under the rationale that the textures of different subjects should have an underlying mean effect if aligned properly. Especially in the situation of no landmarks are present in the geometric registration, additional registration of the texture after the geometric registration might be preferred. See Lila and Aston (2017) for details on the functional registration.

Given the estimated texture $X^F_t(t)$ mapped back to the template $M^T_0$, we apply the SM-fPCA method proposed in Lila et al. (2016) to calculate the estimates of the functional PCs and the corresponding projection coefficients.

The first PC $\psi^F_1$ is estimated by minimizing the objective

$$\hat{\psi}^F_1 = \arg \min_{\psi} \sum_{i=1}^n \sum_{t=1}^T \sum_{j=1}^d (X^F_{i,t}(p_j) - \bar{X}^T(p_j) - a_{i,t}\psi(p_j))^2 + \lambda \| \Delta \psi \|_{L^2(M^T_0)},$$  

(4)

where $\{p_j\}$ are vertices on $M^T_0$, $\bar{X}^T(p_j)$ is the average of $X^F_{i,t}(p_j)$ over all $i = 1, \ldots, N$ and $t = 1, \ldots, T$, and $a_{i,t}$ is the projection of the residual $X^F_{i,t}(p_j) - \bar{X}^T(p_j)$ on $\psi$. To continue the estimation, $X^F_{i,t}(p_j) - \bar{X}^T(p_j)$ in (4) is replaced by $X^F_{i,t}(p_j) - \bar{X}^T(p_j) - \sum_{k=1}^{K-1} \hat{a}_{i,t,k}\hat{\psi}^F_k(p_j)$ so that $\{\hat{\psi}^F_K : K = 2, \ldots, K^F\}$ can be obtained iteratively by minimizing the objective. The calculation is done with the MATLAB package SM-fPCA developed by Lila et al. (2016).

Similar to the principal component analysis for the subjects’ geometric shapes, an extra step of regressing the textures on covariates that are considered to have effects on the functionality is conducted before estimating the PCs to eliminate the covariance induced by the shared covariates.
Algorithm 1 Estimation of the Mixed Effects Model

1: procedure Mixed\((X, \text{vec}(a), K^G, K^F, T, C_B, C_{\Sigma}, n_{\text{iter}})\)
2: Let \(\hat{\gamma}(0) = 0, B(0) = 0, \Sigma(0) = I_{p \times p}\), and \(\Delta_1 = \Delta_2 = C > \max(C_B, C_{\Sigma})\)
3: Let \(n = 1\)
4: while \((\Delta_1 \geq C_B \text{ or } \Delta_2 \geq C_{\Sigma})\) and \(n < n_{\text{iter}}\) do
5: \(B^{(n)} = [X^T([\Sigma^{(n-1)}]^{-1} \odot I_N)]^{-1} \cdot X^T([\Sigma^{(n-1)}]^{-1} \odot I_N) \text{vec}(a)\) \(\triangleright\) Update \(B\)
6: \(\Delta_1 = \Delta(B^{(n)}, B^{(n-1)})\)
7: \(\hat{\gamma}^{(n)} = \text{vec}(a) - XB^{(n)}\) \(\triangleright\) Update \(\hat{\gamma}\)
8: for \(j = 1\) to \(p\) do
9: if \(j \leq K_G\) then
10: \(\zeta_j = \arg\min_{(\zeta_{j1}, \ldots, \zeta_{j,j-1})} \|\hat{\gamma}_j - \sum_{k=1}^{j-1} \zeta_{jk} \hat{\gamma}_k(n)\|^2\)
11: else
12: \(\zeta_j = \arg\min_{(\zeta_{j1}, \ldots, \zeta_{j,j-1})} \left(\|\hat{\gamma}_j - \sum_{k=1}^{j-1} \zeta_{jk} \hat{\gamma}_k(n)\|^2 + \lambda_j \|\zeta_j\|_1\right)\)
13: \(\tau_j = \#\{\zeta_{jk} : \zeta_{jk} \neq 0\}\)
14: \(\hat{\sigma}_j^2 = \frac{1}{N-\tau_j}\|\hat{\gamma}_j(n) - \sum_{k=1}^{j-1} \zeta_{jk} \hat{\gamma}_k(n)\|^2\)
15: \(\hat{\Lambda} = I - \zeta, \hat{D} = \text{Diag}\{\hat{\sigma}_j^2\}, \hat{D}^{-1} = \text{Diag}\{\hat{\sigma}_j^{-2}\}\)
16: \([\Sigma^{(n)}]^{-1} = \hat{\Lambda}^T \hat{D}^{-1} \hat{\Lambda}, \Sigma^{(n)} = \hat{\Lambda}^{-1} \hat{D}[\hat{\Lambda}^{-1}]^T\)
17: \(\Delta_2 = \Delta_{KL}(\Sigma^{(n)}, \Sigma^{(n-1)})\)
18: \(n \leftarrow n + 1\)
19: return \(B = B^{(n)}, \hat{\Sigma} = \Sigma^{(n)}\)
4 Additional Figures and Results in Data Analysis

Figure 2 visualizes the first 5 geometric PCs by showing the resulting surfaces of mapping the template according to the deformations given by the initial momenta of the PCs (standardized).

![Geometric PCs](image)

Figure 2: First 5 geometric PCs (in blue) comparing to the template manifold (in white). Blue areas on each surface show where the corresponding PC manifold expands comparing to the template, while white areas show where the PC manifold shrinks from the template manifold.

Table 1 shows the combinations of the functional and geometric PCs with largest correlations sorted by p-values.

| Functional | Geometric | Correlation | p-value |
|------------|-----------|-------------|---------|
| 7          | 6         | 0.37        | 1.8E-04 |
| 5          | 6         | 0.36        | 1.9E-04 |
| 3          | 1         | 0.36        | 2.1E-04 |
| 8          | 3         | -0.36       | 2.8E-04 |
| 6          | 17        | 0.34        | 5.2E-04 |
| 3          | 12        | 0.30        | 2.2E-03 |
| 5          | 10        | 0.29        | 3.8E-03 |
| 9          | 5         | -0.26       | 8.5E-03 |
| 6          | 6         | 0.25        | 1.0E-02 |
| 2          | 4         | -0.25       | 1.2E-02 |
| 3          | 4         | -0.23       | 2.0E-02 |
| 2          | 5         | -0.22       | 2.6E-02 |
| 2          | 19        | -0.22       | 3.0E-02 |
| 6          | 19        | 0.20        | 4.2E-02 |

Table 1: Significant correlations between projection coefficients on top geometric and functional components.

Figure 3 shows significant associations in the $T = 3$ setting between the projections on the geometric and functional PCs via the $L$ matrix in the Cholesky decomposition $\Sigma^{-1} = L^T D^{-1} L$. A non-zero $(i, j)$th element in $L$ suggests potential association between the $i$th geometric and $j$th functional PCs.
Figure 3: Model Setting $T = 3$: associations between the geometric and functional components via the estimated $L$ matrix. Deeper colors indicate larger absolute values if the $L$ matrix. White indicates corresponding values in $L$ is zero.

Figure 4 shows the medial surface view of Geometric PCs 6, 10, 12, 15, 17.

Figure 4: Geometric PCs 6, 10, 12, 15, 17 associated with functional PCs (medial surface view). Top row: deformations of template manifold $\varphi(c\psi_{G,j}^i, \cdot)$ for $j = 6, 10, 12, 15, 17$ and $c = 1$ (white) and $c = 7$ (blue). Bottom row: deformations of template manifold $\varphi(c\psi_{G,j}^i, \cdot)$ for $c = -1$ (white) and $c = -15$ (blue).

5 Additional Figures and Results in Simulation Studies

Figure 5 shows the front and back views of the template manifold used in the simulation studies. Figure 6 shows the generated geometric overlaid with the generated functional PCs with the same indices.
Figure 5: Template manifold for generating geometric PCs. Left: front view. Right: back view.

Figure 6: The geometric and functional PCs visualized by overlapping colormaps of functional PCs on shapes of geometric PCs with the same indices. Top row: the PCs in the generative model. Bottom row: estimated PCs from one simulation run of 200 subjects.

Figure 7 shows the two time-varying signals $W_1$ and $W_2$ used in generating the synthetic fMRI signals.

Figure 7: Stimuli signal 1 (left) and 2 (right) in the simulation studies ($T = 5$)
5.1 Simulation Setting $T = 5$

Figure 8 shows the averaged estimates of the covariance matrix with different methods given actual values of the PC projection coefficients.

![Averaged estimates of covariance matrix](image)

Figure 8: Average of estimated covariance matrix using different methods compared to actual covariance matrix (estimates obtained with actual PCs). Top left: actual covariance matrix. Top right: proposed method. Bottom left: without regularization of elements in covariance. Bottom right: REML.

Figures 9 and 10 show estimation results of the covariance matrix obtained with the estimated PC projection coefficients. Figure 9 compares the estimated covariance matrix averaged over the 20 simulation runs to the actual. Figure 10 compares the square roots of the MSE in each element of the covariance matrix with different methods.

Due to the errors induced in those procedures the covariance matrix estimation is less accurate with all three methods. However, the proposed method is still able to recover most of the actual covariance matrix, except for a section in the covariance between the geometric and functional PC projections, possibly due to the incomplete separation of functional PC 1 and PC 2. Again the method without regularizing the covariance matrix has more false recoveries of non-zero elements and hence the extra noise in the MSE plot. REML continues to suffer from poor estimation performance, falsely recognizing zero elements in the covariance matrix as non-zero and failing to recover the majority of the covariance structure.
Figure 9: Average of Estimated covariance matrix using different methods compared to actual (with estimated PCs).

Figure 10: Square root of MSE of estimated covariance matrices using different methods (with estimated PCs).

Figure 11 compares the square roots of the MSE with different methods where the estimates are obtained with the actual projection coefficients. Figure 12 displays the results with estimated PC projections.
Figure 11: Square root of MSE of estimated covariance matrices using different methods (with estimated PCs).

Figure 12: Square root of MSE of estimated covariance matrices using different methods (with estimated PCs).

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