Longitudinal functional principal component modelling via Stochastic Approximation Monte Carlo

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Abstract: The authors consider the analysis of hierarchical longitudinal functional data based upon a functional principal components approach. In contrast to standard frequentist approaches to selecting the number of principal components, the authors do model averaging using a Bayesian formulation. A relatively straightforward reversible jump Markov Chain Monte Carlo formulation has poor mixing properties and in simulated data often becomes trapped at the wrong number of principal components. In order to overcome this, the authors show how to apply Stochastic Approximation Monte Carlo (SAMC) to this problem, a method that has the potential to explore the entire space and does not become trapped in local extrema. The combination of reversible jump methods and SAMC in hierarchical longitudinal functional data is simplified by a polar coordinate representation of the principal components. The approach is easy to implement and does well in simulated data in determining the distribution of the number of principal components, and in terms of its frequentist estimation properties. Empirical applications are also presented.

1. INTRODUCTION

Because longitudinal data can be viewed as sparsely observed functional data (Rice, 2004), functional principal components analysis becomes an important tool for analyzing longitudinal data. Since the early contributions of Besse & Ramsay (1986), Ramsay & Dalzell (1991), and Rice & Silverman (1991), a substantial literature has developed for functional principal components

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Let $Y_{iℓ}$ be the $ℓ$th response for the $i$th subject at time $t_{iℓ}$. Then the hierarchical model we are considering takes the general form

$$Y_{iℓ} = μ(t_{iℓ}) + g_i(t_{iℓ}) + ε_{iℓ},$$

(1)

where $μ(·)$ is the fixed effects population-level function, $g_i(·)$ represents random functions associated with each individual, and $ε_{iℓ}$ is noise. The goal is to estimate the fixed-effects function $μ(·)$ and to understand the variability of the random effects functions $g_i(·)$.

It is standard in the functional data analysis literature to model the correlations among responses at different times through a mixed effects model, for example, via the Karhunen–Löeve expansion used in a number of the papers referenced above. As a modification of work by James, Hastie & Sugar (2000) and Rice & Wu (2001), to fit models such as (1), Zhou, Huang & Carroll (2008) introduced penalized spline estimation of functional principal components for longitudinal data using a mixed effects model framework. Suppose that there are $i = 1, . . . , n$ subjects, each of which contribute $ℓ = 1, . . . , m_i$ observations at times or locations $t_{iℓ}$. Let $b(t)$ be a $p \times 1$ orthogonal basis with the property that $\int b(t)b^T(t)\,dt = I_p$, and let $B_i$ be a $m_i \times p$ matrix with $ℓ$th row $b^T(t_{iℓ})$. Let $Y_i$ be the $m_i \times 1$ vector of responses for the $i$th observation. Then the model becomes

$$Y_i = B_iθμ + B_iΘ_fα_i + ε_i;$$

(2)

$$E(ε_i|B_i) = 0;$$

$$\text{cov}(ε_i|B_i) = σ^2 ε_i;$$

$$α_i = \text{Normal}[0, D_a = \text{diag}(d_1, . . . , d_M)].$$

where the principal components matrix $Θ_f$ is $p \times M$ with $p > M$, the main effects parameter $θμ$ is $p \times 1$, and the vector of principal components scores $α_i$ is $M \times 1$. In addition to the orthogonality constraint on the basis functions, for identifiability we need $Θ_f$ to be orthogonal, $Θ_f^TΘ = IM$. Thus, comparing (1) and (2), we are making the approximations that $μ(t) ≈ b^T(t)θμ$ and $g_i(t) ≈ b^T(t)Θ_fα_i$.

It is interesting to note that in common with the Karhunen–Löeve approaches, as in ours, if the number of principal components is $M = 1$, then the correlation structure of responses at different times is equicorrelated, but this is not the case when $M > 1$.

As in any kind of spline-based analysis, it is useful to think about penalizing the likelihood to ensure smoothness of fit and to avoid overfitting. In model (2), we have two functions that need to be penalized: the fixed effects functions represented as $b^T(t)θμ$ and the random effects functions represented as $b^T(t)Θ_f$. For the fixed effects function, for example, the usual device is to have a penalty parameter, here called $λ_μ$, and to penalize the likelihood by $λ_μθμ^T K θμ$, where $K$ is a so-called penalty matrix. The typical form of the penalty matrix is the integrated square of the second derivative matrix, that is, $K = \int b''(t)b''(t)^T\,dt$. Methods for constructing the orthogonal basis functions $B_i$ and for computing the penalty matrix $K$ are described by Zhou, Huang & Carroll (2008).

Enforcing smoothing of the random effects functions is somewhat more involved, because $b^T(t)Θ_f$ has $M$ columns, each of which needs to be penalized. Here is the device used by Zhou, Huang & Carroll (2008). If $θ_f$ is the $j$th column of $Θ_f$, the penalty for the random functions

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becomes \( \lambda_f \sum_{j=1}^{M} \vartheta_j^T K \vartheta_j \). Overall then, to ensure smoothness, the log likelihood is penalized by
\[ \lambda_\mu \vartheta_\mu^T K \vartheta_\mu + \lambda_f \sum_{j=1}^{M} \vartheta_j^T K \vartheta_j. \]

Of course, penalty parameters need to be estimated, and for this purpose there are a variety of possibilities. Zhou, Huang & Carroll (2008) used 10-fold crossvalidation to estimate \((\lambda_\mu, \lambda_f)\) for any given \(M\). To choose the number of principal components, they use an informal ad hoc procedure, see their Section 5.2. James, Hastie & Sugar (2000) used the informal %-variation explained and a likelihood ratio test, although they found that the performance of the latter was “ambiguous” and they recommended the use of the former.

Especially when the number of subjects is small, there will be ambiguity as to the choice of the number of principal components. We propose to acknowledge this ambiguity by taking a Bayesian approach to the problem.

An outline of this paper is as follows. In Section 2 we present the basic algorithm. Section 3 describes simulation studies, while Section 4 investigates empirical examples. Concluding remarks are presented in Section 5. Technical details are given in an appendix.

2. ALGORITHM

2.1. Parameters of the Basic Model and Their Posterior Distributions

The model is as described at (2).

In what follows, let \( \sigma_\mu^2 = \lambda_\mu^{-1} \) and \( \sigma_f^2 = \lambda_f^{-1} \). It is convenient to work with the parameterization \( \xi_1 = \log(\sigma_\epsilon) \), \( \xi_2 = \log(\sigma_\mu) \) and \( \xi_3 = \log(\text{diag}(D_\alpha)) \). We write the number of principal components as \(M\).

As described in Section 2.2, because of the restriction that \( \Theta_f^T \Theta_f = I \), we will parameterize \( \Theta_f \) in terms of auxiliary parameters \( \Omega_f \). If \( \alpha = (\alpha_1, \ldots, \alpha_n) \), the main effects vector is \( \theta_\mu \) and \( Y \) denotes the response data, then except for constants of proportionality, we write the posterior distribution of \((\Omega_f, \xi_3, \xi_2, \xi_1, \sigma_f^2, \theta_\mu, \alpha)\) given \(Y\) as \(f(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma_f^2, \theta_\mu, \alpha | Y)\), see the Appendix for details.

In formulating this problem, we face a number of challenges.

- By definition, \( \Theta_f \) is constrained to be orthogonal. We achieve this orthogonality by combining the polar coordinate approach of Zhang & Davidian (2001) with a Gram–Schmidt transformation, see Section 2.2.
- Even though \( \Theta_f \) is orthogonal by construction, it still needs to be smoothed.
- Because the models are of different dimensions, a basic reversible jump type algorithm is attractive (Green, 1995). However, we observed difficulty in accepting the death step of such an algorithm, and in order to explore the model space chose instead to implement the Stochastic Approximation Monte Carlo or SAMC algorithm of Liang, Liu & Carroll (2007).

2.2. Parameterizing \( \Theta_f \)

In this section, we show how to write \( \Theta_f \) as a function of other parameters \( \Omega_f \), in such a way that \( \Theta_f \) is orthogonal, and all elements of its first row are positive, as required by the identifiability result in Zhou, Huang & Carroll (2008).

Because \( \Theta_f \) is an orthogonal \( p \times M \) matrix with \( p > M \), we turn to a polar coordinate representation, handily provided by Zhang & Davidian (2001). Let \( \Theta_f = (\vartheta_1, \ldots, \vartheta_M) \) where \( p > M + 1 \), each \( \vartheta_j \) is \( p \times 1 \), and define the \( p \times 1 \) vector \( s_j \) as follows. Its first element is \( \sin(\gamma_{1j}) \), and its \( k \)th element for \( k = 2, \ldots, p - 1 \) is \( \sin(\gamma_{kj}) \prod_{\ell=1}^{k-1} \cos(\gamma_{\ell j}) \). Finally, its \( p \)th element is \( \prod_{\ell=1}^{p-1} \cos(\gamma_{\ell j}) \). These are thus polar coordinates in \( p - 1 \) parameters. Take \(-\pi/2 \leq \gamma_{kj} \leq \pi/2\) for all \((k, j)\) except \( k = j = 1 \), and let \( 0 \leq \gamma_{11} \leq \pi/2\) to force identifiability, see Zhou, Huang...
& Carroll (2008) for details. The matrix $s_j$ is of unit length: $s_j^T s_j = \| s_j \|^2 = 1$. Define $y_j^T = (y_{1j}, \ldots, y_{(p-1)j})$ and $\Omega_f = (y_1, \ldots, y_M)$, then we can generate $y_{kj}$ for $k = 1, \ldots, p-1$ and $j = 1, \ldots, M$ as uniform on their support.

To form an orthogonal $p \times M$ matrix, we use a Gram–Schmidt transformation. Define $\text{proj}_e(s) = (s^T e)e$. Then $\vartheta_1 = \vartheta_1$, for $k = 2, \ldots, M$, define $\vartheta_k = (I - \sum_{j=1}^{k-1} \vartheta_j^T s_j) s_k$, and $\vartheta_k = \vartheta_k/\|\vartheta_k\|$. Finally, take $\Theta_f = (\vartheta_1, \ldots, \vartheta_M)$.

Write $e^T = (1, 0, \ldots, 0)$. Note that the first element of $\vartheta_{k*}$, $e^T \vartheta_{k*}$ is $e^T (I - \sum_{j=1}^{k-1} \vartheta_j^T s_j) s_k$. To force the first element of $\vartheta_k$ to be positive, we set $\vartheta_k = \text{sign}(e^T \vartheta_{k*}) \vartheta_{k*}/\|\vartheta_{k*}\|$.

2.3. Basic Reversible Jump Algorithm

Let $M$ denote the number of principal components, and assume that it has a uniform prior distribution. We marginalized the posterior by integrating out $\theta_\mu$ and $\alpha$, resulting in the function $g(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma_f^2 | \mathbf{Y})$ given in Equation (6) in the Appendix. Let $(\Omega_f^{(v)}, \xi_3^{(v)}, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{(v)})$ denote the sample obtained at iteration $v$. Below we outline the algorithm assuming that there are only three possible principal components; however, this can easily be extended to include any number of principal components.

2.3.1. Initial step

In this step, we decide which component of the model to update at iteration $v + 1$. We let “MH” here denote a Metropolis-Hastings step, see Section 2.3.2. Birth and death steps are described in Sections 2.3.3 and 2.3.4, respectively.

- Draw $U = \text{Uniform}(0, 1)$.
- If $M = 1$ and $U < 0.5$ do “birth” step and set $\omega_{12} = 0.5$; if $M = 1$ and $U \geq 0.5$ do “MH” step.
- If $M = 2$ and $U < 1/3$ do “birth” step and set $\omega_{23} = 1/3$; If $M = 2$ and $1/3 \leq U \leq 2/3$ do “death” step and set $\omega_{21} = 1/3$; if $M = 2$ and $U \geq 2/3$ do “MH” step.
- If $M = 3$ and $U < 0.5$ do “death” step and set $\omega_{32} = 0.5$; if $M = 3$ and $U \geq 0.5$ do “MH” step.

2.3.2. Metropolis-Hastings step

In this step, we keep the dimensions of $\Omega_f^{(v)}$ and $\xi_3^{(v)}$ unchanged while the parameters are updated. Draw $U = \text{Uniform}(0, 1)$. If $U \leq 1/5$ make Move-1; if $1/5 < U \leq 2/5$, make Move-2; if $2/5 < U \leq 3/5$, make Move-3; if $3/5 < U \leq 4/5$, make Move-4, and if $4/5 < U \leq 1$ make Move-5.

In what follows, we set $\tau_1 = \tau_2 = \tau_3 = \tau_4 = 0.1$.

(a) (Move-1) Updating $\xi_1^{(v)}$ and $\xi_2^{(v)}$. Let $U_1$ and $U_2$ be independent $\text{Uniform}(−0.5, 0.5)$ random variables. Draw $\xi_1^* = \xi_1^{(v)} + 0.2U_1$ and $\xi_2^* = \xi_2^{(v)} + 0.5U_2$. Calculate the MH ratio

$$ r = \frac{f(\Omega_f^{(v)}, \xi_3^{(v)}, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)} | Y)}{f(\Omega_f^{(v)}, \xi_3^{(v)}, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)} | Y)} \cdot $$

Accept $(\xi_1^*, \xi_2^*)$ with probability $\min(1, r)$.

(b) (Move-2) Updating $\Omega_f^{(v)}$. Draw a vector $e = \text{Normal}(0, \tau_2^2 I)$ and add $e$ to a column of $\Omega_f^{(v)}$ selected at random. Denote the new $\Omega_f$ matrix by $\Omega_f^*$. Calculate the MH ratio

$$ r = \frac{f(\Omega_f^*, \xi_3^{(v)}, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)} | Y)1(\Omega_f^* \in \mathcal{A})}{f(\Omega_f^{(v)}, \xi_3^{(v)}, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)} | Y)} , $$

where $\mathcal{A}$ denotes the set $(-\pi/2, \pi/2)^{\dim(\Omega_f^*)}$. Accept $\Omega_f^*$ with probability $\min(1, r)$.  

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(c) (Move-3) Updating $\xi_{3}^{(v)}$. Let $U_3 = \text{Uniform}(-0.5, 0.5)$. Draw the $j$th component of $\xi_{3}^{*}, \xi_{3,j} = \xi_{3,j}^{(v)} + 0.1U_3$. Calculate the MH ratio

$$r = \frac{f(\Omega_f^{(v)}, \xi_3, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)}|Y)}{f(\Omega_f^{(v)}, \xi_3^{*}, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)}|Y)}.$$

Accept $\xi_{3}^{*}$ with probability $\min(1, r)$.

(d) (Move-4) Updating $\sigma_f^{2(v)}$. This can be done by a Gibbs step, see the Appendix.

(e) (Move-5) Put the elements of $\xi_{3}^{(v)}$ in descending order and exchange columns of $\Omega_f^{(v)}$ and $\Theta_f^{(v)}$ accordingly. Because identifiability requires that the elements of $D_\nu = \text{diag}[\exp(\xi_3)]$ be in descending order, this step avoids the label switching problem. Accept $\Omega_f^{*}$ and $\xi_{3}^{*}$ with probability $\min(1, r)$.

### 2.3.3. Birth step

In this step, we try to append a new column to $\Omega_f^{(v)}$ and append an element to $\xi_{3}^{(v)}$.

(a) (Angle sampling) Draw a random vector $\gamma$ from $\text{Uniform}(-\frac{\pi}{2}, \frac{\pi}{2})$, and draw $\xi^* = \text{Normal}(0, \tau_{4}^2)$. set $\Omega_f^* = (\Omega_f^{(v)}, \gamma)$ and $\xi_{3}^* = \text{diag}[\xi_{3}^{(v)}, \xi^*]$.

(b) (Proposal acceptance) Calculate the MH ratio

$$r = \frac{f(\Omega_f^{(v)}, \xi_{3}^*, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)}|Y + 1)}{f(\Omega_f^{(v)}, \xi_{3}, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)}|Y)} \frac{\tau_4}{\tau_4} \frac{\omega_{k+1,k}}{\omega_{k,k+1}}. \tag{3}$$

(c) Accept $\Omega_f^*$ and $\xi_{3}^*$ with probability $\min(1, r)$.

### 2.3.4. Death step

In this step, we try to delete a random column of $\Omega_f^{(v)}$ and the corresponding diagonal element of $\xi_{3}^{(v)}$.

$$r = \frac{f(\Omega_f^{(v)}, \xi_{3}^*, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)}|Y - 1)}{f(\Omega_f^{(v)}, \xi_{3}, \xi_2^{(v)}, \xi_1^{(v)}, \sigma_f^{2(v)}|Y)} \frac{\tau_4}{\tau_4} \frac{\omega_{k-1,k}}{\omega_{k,k-1}}. \tag{4}$$

where $\xi^{(v)}$ denotes the selected diagonal element of $\xi_{3}^{(v)}$.

The two groups of parameters, $(\Omega_f, \xi_{3})$ and $(\xi_1, \xi_2, \sigma_f^2)$, are updated in an unbalanced way in the above algorithm. This is allowed by the Gibbs sampler.

### 2.4. SAMC

Because of low acceptance rates in the death step of the algorithm in Section 2.3, we opt to implement the Stochastic Approximation Monte Carlo or SAMC algorithm (Liang, Liu & Carroll, 2007, Section 5; Liang, 2009), which is a method designed to provide samples from the entire space that are then weighted to form posterior distributions. The SAMC algorithm, especially appropriate for our problem, is given in Equation (13) of Liang, Liu & Carroll (2007). We describe the algorithm for three principal components, detailed reasoning for this is provided later.

Let $v$ be the index in the MCMC calculations. Let $\zeta = (1/3, 1/3, 1/3)$ and let $v_0$ be a tuning parameter that can be adjusted. Define $\kappa_v = v_0 / \max(v_0, v)$. Also define $\theta^{(v)} = (\theta_{v,1}, \theta_{v,2}, \theta_{v,3})^T$, 

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where $\theta_{v,j}$ is the current estimate of the $i$th normalizing constant of the target density, which in this case equals $\log(1/\xi_j)$. Let $T$ be the sampling space of allowable values of $\theta^{(v)}$. Liang, Liu & Carroll (2007) make this a very large space, but because of the exponentiation involved in the adjusted Metropolis ratio, we have restricted this to the cube $[-10, 10]^3$.

First start with $v = 1$ and $\theta^{(v)} = (\log(3), \log(3), \log(3))^T$. Let $M^{(v)}$ be the current number of principal components, and let $M^*$ be a proposal for the number of principal components. If $M^{(v)} = M^*$, the Metropolis steps in Section 2.3.2 do not change. If $M^{(v)} \neq M^*$, and if $r$ is the birth or death ratio in (3) or (4), respectively, the only thing that changes is that $r$ is multiplied by $\exp(\theta_{v,M^{(v)}} - \theta_{v,M^*})$. Let the new model be $M^{(v+1)}$. Set $\theta^* = \theta^{(v)} + \kappa_{v+1}(e_{M^{(v+1)}} - \zeta)$, where the three component vector, $e_{M^{(v+1)}}$, is all zeros except with a 1.0 in location $M^{(v+1)}$. Then if $\theta^* \in T$, we set $\theta^{(v+1)} = \theta^*$. Otherwise, we set $\theta^{(v+1)} = \theta^* + \epsilon^*$, where $\epsilon^*$ is chosen so that $\theta^* + \epsilon^* \in T$.

Having run SAMC, we are now in a position to do posterior inference. Thus for example, assuming equal prior probabilities for the three possible models, the posterior probability that the number of principal components, $M = j$, is given as

$$
\text{pr}(M = j | Y) = \frac{\sum_v^{T} \exp(\theta_{v,M^{(v)}}) I(M^{(v)} = j)}{\sum_v^{T} \exp(\theta_{v,M^{(v)}})},
$$

where $T$ is the number of iterations used to do posterior inference. Posterior quantities can be calculated similarly. For example, given that we have $j$ principal components, let $\sigma^{(v)}_{\theta}$ be the value of $\sigma_\theta$ at iteration $v$. Then

$$
E(\sigma_\theta | M = j, Y) = \frac{\sum_v^{T} \sigma^{(v)}_\theta \exp(\theta_{v,M^{(v)}}) I(M^{(v)} = j)}{\sum_v^{T} \exp(\theta_{v,M^{(v)}}) I(M^{(v)} = j)};
$$

$$
E(\sigma_{\mu} | Y) = \frac{\sum_v^{T} \sigma^{(v)}_{\mu} \exp(\theta_{v,M^{(v)}})}{\sum_v^{T} \exp(\theta_{v,M^{(v)}})}.
$$

From (5), it can be seen that our approach employs model averaging to do posterior inference.

We provide details only for the case of up to 3 principal components because, in biological data, 3 principal components usually suffice, and most algorithms become unstable for higher number of principal components, see the comments of Rice & Silverman (1991) and Hall, Müller & Wang (2006) in a different context. If more than three principal components are used in our simulations and data analyses, the 4th and higher diagonal elements of the variance matrix $\Sigma_\alpha$, which are in decreasing order, become crowded around zero, making the corresponding elements of $\Theta_f$ essentially unidentified.

3. SIMULATION DETAILS AND RESULTS

3.1. Simulation from the Model

We simulated 200 data sets from model (2) with $n = 20$ subjects, $m_1 = m_2 = 11$ equally spaced observations per subject, and with $\Theta_f = p \times M$, where $p = 5$ and $M = 1$ and $M = 2$. When $M = 1$, $D_\alpha = 1.00$, while with $M = 2$, we generated two scenarios, $D_\alpha = \text{diag}(1.00, 0.30)$ and $D_\alpha = \text{diag}(1.50, 0.75)$. We set $\sigma^2_\epsilon = 0.25$ and $\theta_\mu = (-4.09, 7.07, -7.82, 6.59, -2.10)^T$. The values of $\Omega_f$ were generated completely at random for each of the 200 data sets.

We ran SAMC with 200,000 Gibbs steps, and repeated the process 5 times with different starting values. In each case, we started by assuming 1 principal component, with $\Omega_f$ generated completely at random, and with starting values for $\xi_1 = \log(\sigma_\epsilon) = \log(\text{Uniform}(0.4, 0.6))$, $\xi_2 = \text{Uniform}(0.5, 1.5)$, $\xi_2 = \log(\sigma_\mu) = \text{Uniform}[4, 6]$ and $\sigma^2_\theta = 2c$, where $c$ yields 4.5 degrees of freedom.
freedom for the smoother matrix trace\([(B^T B + K/c)^{-1}B^T B]\). We also repeated the analysis with no smoothing: as might be expected, there was slightly more variability in this latter case.

In all cases, \(\sigma^2_\epsilon\) and \(\theta_\mu\) were estimated with little bias. In addition, the within-subject function variances \(\text{diag}\{\text{cov}(B_i|\Theta_j, \alpha_i)\}\) were estimated with only minor bias. An example of this is given in Figure 1, for the case that \(D_\alpha = \text{diag}(1.50, 0.75)\). The top left panel shows the true function and the 5th and 95th pointwise percentiles of the simulations: there is almost no bias so that the mean of the simulations is not displayed. The bottom right panel shows that the within-subject function variances are also essentially unbiased. The top right panel gives the posterior probabilities of the models: in this case, two principal components were selected for all 200 data sets. The bottom left panel gives 16 examples of the within-subject function variances.

We also compared our analysis with the method of Zhou, Huang & Carroll (2008). Their informal method choose two principal components in 90.5% of the cases, and one principal component in 7% of the cases. In Table 1, we compare the mean absolute error and the mean squared error for estimating the within-subject function variances for the method of Zhou, Huang & Carroll (2008) versus our method. SAMC had somewhat smaller mean squared errors for estimating the mean function, and much smaller mean squared errors for estimating the variance function.

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**Figure 1:** Results of the simulation study in the case of two principal components with \(D_\alpha = \text{diag}(1.50, 0.75)\), as described in Section 3.1. Top left: all 200 posterior means for \(B_i|\Theta_j, \alpha_i\). The true value is within the 200 lines. Top right: the estimated model probabilities over the 200 runs. Bottom left: For sixteen of the datasets, this gives the true (solid line) and estimated (dashed line) within-subject functional variance \(\text{diag}\{\text{cov}(B_i|\Theta_j, \alpha_i)\}\). Bottom right: the true and mean of the estimated within-subject functional variances.

[Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
Table 1: Results of the simulation study for either 1 principal component, “1PC,” or 2 principal components, “2PC.”

<table>
<thead>
<tr>
<th>Simulation</th>
<th>Method</th>
<th>Function Variance</th>
<th>Model probabilities</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>MAE    MSE</td>
<td>MAE    MSE</td>
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<tr>
<td>Model, 1PC</td>
<td>Zhou</td>
<td>0.154  0.052</td>
<td>0.281  0.301</td>
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<tr>
<td></td>
<td>SAMC</td>
<td>0.141  0.044</td>
<td>0.222  0.189</td>
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<tr>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Model, 2PC</td>
<td>Zhou</td>
<td>0.192  0.073</td>
<td>0.383  0.480</td>
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<tr>
<td>$D_\alpha$ = (1.00, 0.30)</td>
<td>SAMC</td>
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<td>0.421  0.432</td>
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<tr>
<td>Model, 2PC</td>
<td>Zhou</td>
<td>0.248  0.121</td>
<td>0.655  1.300</td>
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<tr>
<td>$D_\alpha$ = (1.50, 0.75)</td>
<td>SAMC</td>
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<tr>
<td>Function, 1PC</td>
<td>Zhou</td>
<td>0.117  0.026</td>
<td>0.323  0.236</td>
</tr>
<tr>
<td></td>
<td>SAMC</td>
<td>0.129  0.029</td>
<td>0.274  0.177</td>
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<tr>
<td>Function, 2PC</td>
<td>Zhou</td>
<td>0.210  0.089</td>
<td>0.897  2.188</td>
</tr>
<tr>
<td></td>
<td>SAMC</td>
<td>0.216  0.092</td>
<td>0.728  1.336</td>
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</tbody>
</table>

The simulations labelled “Model” are described in Section 3.1, while those labelled “Function” are described in Section 3.2. The mean absolute errors (MAE) and the mean squared error (MSE) for estimating the “Function” $E(Y|X) = B^T \theta_0$, and those for estimating the “Variance” $\text{diag}(\text{cov}(B_i, \theta | \alpha_i))$ are listed. For the method of Zhou, Huang & Carroll (2008), the “Model Probabilities” are the percentage of the times their method picks various numbers of principal components. For the SAMC methods, we list the average posterior model probabilities: the numbers in parentheses are the fraction of the time that the average model probability exceeded 50%.

3.2. Simulation Away from the Model

In this case, we simulated with $\sigma^2_\epsilon = 0.25$, and in two settings with $D_\alpha = 1.00$ and $D_\alpha = \text{diag}(1.50, 0.75)$. We used the Bspline basis functions as in Zhou, Huang & Carroll (2008) with seven basis functions. In the case of one principal component, the model is

$$Y_{i\ell} = \sin(2\pi t_\ell) + \sqrt{2} \cos(2\pi t_\ell) \alpha_i + \epsilon_{i\ell},$$

while with two principal components, and $\alpha_i = (\alpha_{i1}, \alpha_{i2})^T$,

$$Y_{i\ell} = \sin(2\pi t_\ell) + \sqrt{2} \cos(2\pi t_\ell) \alpha_{i1} + \left\{11.65(x - 0.5)^2 - \frac{\cos(2\pi t_\ell)}{\pi^2}\right\} \alpha_{i2} + \epsilon_{i\ell}.$$

We used seven basis functions with three interior knots. All functions are adequately but not exactly approximated with this number of knots. The same priors were used as above, except that...
we centred them at the estimates from Zhou, Huang & Carroll (2008). We also experimented with fixed priors as in Section 3.2, with little change in results.

The results are again reported in Table 1, with graphical representation in the two principal components case given in Figure 2. In the former, we see that SAMC very similar to the method of Zhou, Huang & Carroll (2008) for estimating the mean function \( \sin(2\pi t_j) \), and much better in terms of estimating the variance function. Figure 2 shows that there is more ambiguity in the posterior model probabilities across the simulated data sets, although in 97% of the cases two principal components have posterior probability > 0.50. We actually think that this ambiguity is a strength of our approach. If the model is not correct, then there should be ambiguity in the choice of the number of principal components, with some random data sets coming close to being fit by two principal components, and others needing 3.

4. EMPIRICAL EXAMPLES

4.1. Outline

The simulations presented in Section 3 suggest that the method of Zhou, Huang & Carroll (2008) and our SAMC method will have roughly equal performance in terms of estimating the mean.
function, but will tend to have different performance when estimating the variance function. The SAMC method of course comes endowed with Bayesian posterior credible intervals. In this section, we will describe two data sets, each with two responses, and then display the analysis of all four. All analyses used seven basis functions: the estimates of $\sigma^2_\epsilon$, $\sigma^2_\mu = 1/\lambda_\mu$, $\sigma^2_f = 1/\lambda_f$ and the first component of $D_\alpha$ from Zhou, Huang & Carroll (2008) were used as starting values. The starting value of $\Theta_f$ was random. SAMC was run with 200,000 iterations twice, and the results pooled.

4.2. RNA and CD4 Data

Our first example concerns data from an AIDS clinical trial. Both virologic and immunologic surrogate markers such as plasma HIV RNA copies (viral load) and CD4+ cell counts currently play important roles in evaluating antiviral therapies in AIDS clinical research. Both CD4+ cell counts and plasma HIV RNA copies have each been used as sole surrogate markers in AIDS clinical trials. Here we study the time course of plasma HIV RNA copies and CD4+ cell counts obtained from an AIDS clinical study conducted by the AIDS Clinical Trials Group (ACTG 315). In this study, forty-six evaluable HIV-1 infected patients were treated with potent antiviral therapy consisting of ritonavir, 3TC and AZT, see Lederman et al. (1998) and Wu & Ding (1999) for more details on this study. After initiation of potent antiviral treatment at day 0, patients were followed for up to 10 visits and at each visit both viral load and CD4+ cell counts were monitored simultaneously. The actual visit times are irregularly spaced and different for different patients. The visit time varies from day 0 (first visit) to day 196. We took logarithms for both CD4 data and RNA data and then standardized them to have mean zero and variance one. We also standardized follow up times to the unit interval. In this case, what we have been calling “time,” $t_{i\ell}$, is indeed time.

4.3. Phenotype Data

We apply our method to phenotypic longitudinal data of colonic crypts in the rat model. Colonic crypts are tube-like structures in the colon formed by cells which undergo development from stem cells to fully differentiated mature colonic cells. This development begins at the bottom of the colonic crypt where the mother stem cells divide and produce new colon cells which will mature as they travel up the crypt to the colon surface. Colonic DNA damage can change the behaviour of any cell by fundamentally altering its normal function and potentially inducing uncontrolled growth. This can contribute to carcinogenesis, see Hong et al. (2005).

In this model, the times $t_{i\ell}$ correspond to the cell locations, normalized to the unit interval. The responses are the DNA adduct levels, a measure of DNA damage, in the proximal and in the distal region of the colon. In this analysis, there were 30 subjects. The DNA adduct levels in the proximal and distal regions were log-transformed, and then standardized to have mean zero and variance one.

In this case, what we call “time” is not time, but actually location of the cell. Since stem cells, or colloquially “baby” cells are at the bottom of the crypts, with $t$ near zero, and since mature cells at the top of the crypts, $t$ near one, the functions may be thought to be functions of the age of the cells.

4.4. Results

The method of Zhou, Huang & Carroll (2008) picked one principal component in all cases. The SAMC method had posterior probabilities of one principal component equal to 1.0 for the CD4 and RNA data. However, for the distal adducts, the posterior probability of two principal components was 0.92, while for proximal data one principal component has a posterior probability of 0.60. In all cases, the posterior probability of three principal components equalled 0.00.

As expected by the simulations, the estimated posterior mean function $\beta^T(t)\theta_{\mu}$ was almost identical to that found by Zhou, Huang & Carroll (2008) (not displayed). In Figure 3, we display the posterior mean and medians of $\beta^T(t)\theta_{\mu}$, along with 90% pointwise credible intervals. In the

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adduct level, the distribution of \( t_{\ell} \) was almost uniform, and hence the lengths of the credible intervals might be expected to be nearly constant, a conjecture seen in the plots. On the other hand, in the CD4 and RNA data, the distribution of \( t_{\ell} \) is highly skewed right, with most of the observations being between 0.0 and 0.4. In this case, one would expect the credible intervals to be much wider for larger values of \( t_{\ell} \) than for smaller values, an expectation born out in the plot.

Figure 4 displays results for estimating the marginal variances \( b^T(t)\Theta_f D_f \Theta_f^T b(t) \) (magenta dot-dashed lines), the estimate from Zhou, Huang & Carroll (2008) (black solid lines) and posterior pointwise 90% credible intervals. Variance functions are of course much harder to estimate than mean functions, and as seen in the simulations here we do not expect SAMC and the method of Zhou, Huang & Carroll (2008) to be nearly identical, and they are not, although the differences are fairly small given the uncertainties.

5. DISCUSSION

We have shown how to use SAMC for Bayesian principal component selection and model estimation for longitudinal functional data. Our simulations suggest that our method is comparable to the method of Zhou, Huang & Carroll (2008) in terms of frequentist mean squared errors when estimating the mean function, and generally considerably more accurate when estimating the random variation about the mean function. While there are statistical gains in our approach, it is still MCMC based, and hence in terms of computing time generally much slower than the EM-based algorithm. Both methods scale up similarly when the number of subjects increases.
Figure 4: Results of the data analysis of Section 4. Displayed are the posterior mean variance function (dash-dotted magenta line), the estimated variance function from the method of Zhou, Huang & Carroll (2008) and labelled “pdfa” (black solid line) and 90% pointwise posterior credible intervals (blue and red dashed lines) for SAMC. The labels for each graph refer to the data set. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

An interesting case to consider would be where the random functions $g_i(\cdot)$ in (1) or their spline equivalents $b^T(\cdot) \Theta_j \alpha_i$ in (2) are spatially correlated. Problems with such spatial correlation structure have been investigated by Baladandayuthapani et al. (2008) in a Bayesian manner and by Li et al. (2007) in a frequentist manner. In unpublished work, we have developed a direct generalization of model (2) for this context, which again involves estimating the number of principal components. We believe that SAMC can be used successfully in this context.

Another interesting question is how to deal with correlation when, for example, there are pairs of responses such as might occur for familial data where different family members are followed in time (Sneddon & Sutradhar, 2004). Zhou, Huang & Carroll (2008) discuss a generalization of model (2), this may be one way of attacking the problem from the principal components framework: they use an EM-algorithm. It would not be a great leap to generalize the SAMC algorithm to handle this case.

APPENDIX
A.1 Marginal Posterior Density Computation
We provide some detail of integrations which lead to the marginal posterior density

$$f(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma_f^2 | Y).$$
Recall that $\xi_1 = \log(\sigma_e)$, $\xi_2 = \log(\sigma_\mu)$ and $\xi_3 = \log(\text{diag}(D_\alpha))$. Our prior distributions are in terms of $(\xi_1, \xi_2, \xi_3)$, but since they are not being integrated our displayed equations will use $(\sigma_e, \sigma_\mu, D_\alpha)$.

Our prior distributions were $\xi_1 = \text{Normal}(\mu_1, \sigma_1^2)$, $\xi_2 = \text{Normal}(\mu_2, \sigma_2^2)$, and $\xi_3 = \text{Normal}(\mu_3, \sigma_3^2)$. It is more tricky to penalize $\Theta_f$ as done by Zhou, Huang & Carroll (2008), because $\Theta_f$ must be orthogonal. We wrote the prior for $[\sigma^2_f | \Omega_f]$ to be $\text{IG}(A + pM/2, B + \sum_{l=1}^{M} \vartheta_j^T K \vartheta_j)$, with $A = B = 3$, where $\vartheta_j$ is the $j$th column of $\Theta_f$. This has the convenient behaviour that samples from this distribution are of the same form as samples for a smoothing parameter in an ordinary penalized spline regression without constraints, see Carroll et al. (2004). The prior distribution for $\Omega_f$ is independent uniforms on $[-\pi/2, \pi/2]$, and is written as $p(\Omega_f) = \pi^{-M(p-1)} I(-\pi/2 < \Omega_f < \pi/2)$.

Let the prior density for $(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f) = p(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f)$. Then except for a normalizing constant, the posterior density is

$$f(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f, \theta_\mu, \alpha | Y) = \prod_{i=1}^{n} \left\{ p(Y_i | \Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f, \theta_\mu, \alpha) p(\alpha | \xi_3) \right\} \times p(\theta_\mu) p(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f).$$

For convenience in displaying the equations, where it causes no confusion we will write this posterior in terms of $(\sigma_e, \sigma_\mu, D_\alpha)$, which is given as

$$(\sigma_e^2)^{-N/2} \exp\left\{ -2(\sigma_e^2)^{-1} \sum_{i=1}^{n} (Y_i - B_i \theta_\mu - B_i \Theta_f \alpha_i)^T (Y_i - B_i \theta_\mu - B_i \Theta_f \alpha_i) \right\} 
\times |2\pi D_\alpha|^{-n/2} \exp\left\{ -\frac{1}{2} \sum_{i=1}^{n} \alpha_i^T D_\alpha^{-1} \alpha_i \right\} \times |\sigma_\mu^2 K^{-1}|^{-1/2} \exp\left\{ -\frac{1}{2} \theta_\mu^T \left( \frac{K}{\sigma_\mu^2} \right) \theta_\mu \right\} \times p(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f),$$

where $N = \sum_{i=1}^{n} n_i$. Integrating with respect to $\alpha = (\alpha_1, \ldots, \alpha_n)$

$$f(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f, \theta_\mu | Y) = (\sigma_e^2)^{-N/2} \times |2\pi D_\alpha|^{-n/2} \times |\sigma_\mu^2 K^{-1}|^{-1/2} \times \left( \prod_{i=1}^{n} |C_{2i}|^{1/2} \right) \times \exp\left\{ -2(\sigma_e^2)^{-1} \sum_{i=1}^{n} R_i^T R_i - \frac{1}{2} \theta_\mu^T \left( \frac{K}{\sigma_\mu^2} \right) \theta_\mu \right\} \times \left( \prod_{i=1}^{n} |C_{1i}^T C_{2i} C_{1i} |^{1/2} \right) \times p(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f),$$

where $C_{2i} = (\Theta_f^T B_i^T \Theta_f / \sigma_e^2 + D_\alpha^{-1})^{-1}$, $C_{1i} = (R_i^T B_i \Theta_f / \sigma_e^2)$, and $R_i = Y_i - B_i \theta_\mu$. Now we integrate with respect to $\theta_\mu$ and obtain

$$f(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f | Y) = (\sigma_e^2)^{-N/2} |2\pi D_\alpha|^{-n/2} |\sigma_\mu^2 K^{-1}|^{-1/2} \left( \prod_{i=1}^{n} |C_{2i}|^{1/2} \right) \times |C_4|^{1/2} \exp\left\{ -\frac{1}{2} \sum_{i=1}^{n} Y_i^T (\sigma_e^{-2} I_{n_i} - \Psi_i) Y_i + \frac{1}{2} C_{1i}^T C_4 C_{1i} \right\} \times p(\Omega_f, \xi_3, \xi_2, \xi_1, \sigma^2_f),$$

(6)
where
\[ C_4 = (\sigma_\mu^2 K + \sigma_\epsilon^2 \sum_{i=1}^n B_i^T B_i - \sum_{i=1}^n B_i^T \Psi_i B_i)^{-1}, \quad C_3^T = (\sigma_\epsilon^2 \sum_{i=1}^n Y_i^T B_i - \sum_{i=1}^n Y_i^T \Psi_i B_i) \text{ and } \Psi_i = \sigma_\epsilon^{-1} B_i \Theta / C_{2i} \Theta B_i^T. \]

A.2 Conditional Posterior Density of \( \theta_\mu \) and \( \alpha_i \)
Easy calculations show that samples from \( \theta_\mu \) and \( \alpha_i \) given the data and the parameters can be obtained as

\[
[\theta_\mu | \Omega_f, \xi_3, \xi_2, \xi_1, \sigma_f^2, Y] = \text{Normal}(C_4 C_3, C_4);
\]
\[
[\alpha_i | \Omega_f, \xi_3, \xi_2, \xi_1, \sigma_f^2, \theta_\mu, Y] = \text{Normal}(C_{2i} C_{1i}, C_{2i}).
\]

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BIBLIOGRAPHY


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