Regression Analysis of Correlations for Correlated Data

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Abstract

Correlated data are ubiquitous in today’s data-driven society. A fundamental task in analyzing these data is to understand, characterize and utilize the correlations in them in order to conduct valid inference. Yet explicit regression analysis of correlations has been so far limited to longitudinal data, a special form of correlated data, while implicit analysis via mixed-effects models lacks generality as a full inferential tool. This paper proposes a novel regression approach for modelling the correlation structure, leveraging a new generalized z-transformation. This transformation maps correlation matrices that are constrained to be positive definite to vectors with unrestricted support, and is order-invariant. Building on these two properties, we develop a regression model to relate the transformed parameters to any covariates. We show that coupled with a mean and a variance regression model, the use of maximum likelihood leads to asymptotically normal parameter estimates, and crucially enables statistical inference for all the parameters. The performance of our framework is demonstrated in extensive simulation. More importantly, we illustrate the use of our model with the analysis of the classroom data, a highly unbalanced multilevel clustered data with within-class and within-school correlations, and the analysis of the malaria immune response data in Benin, a longitudinal data with time-dependent covariates in addition to time. Our analyses reveal new insights not previously known.

Keywords: Correlogram; Correlated data analysis; Correlation matrix; Generalized z-transformation; Regression modeling; Testing random effects.

1 Introduction

1.1 Background

Correlated data arise in numerous fields in a variety of forms. In epidemiology, social sciences, biology, public health, psychology, and economics, for example, a large number of datasets are longitudinal where multiple observations are collected on individuals over time, or clustered where the observations are grouped, sometimes under multiple levels of grouping. A fundamental feature of these data is that the observations are not independent due to within-group or within-subject correlations. Understanding, accounting for, modelling, and utilizing these correlations are fundamental for valid inference in any statistical model. Moreover, there are numerous occasions where correlations can be of central scientific interest to draw inferential conclusions. Naturally, a statistician’s take on this important problem is to develop regression

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models in using covariates to account for the correlations. However, there are several major interrelated challenges that have prevented the current approaches for modelling correlation matrices from achieving desirable capacity:

1. These matrices are inherently positive definite and have ones on their diagonals, making the elements in these matrices lie in a highly constrained space;

2. The dimensions of these matrices are dependent on the numbers of the observations in the subjects or clusters and hence can vary substantially for unbalanced data;

3. Although there is a notion of ordering of observations within-subject for some correlated data such as longitudinal data, in general many correlated data such as clustered data are not ordered.

1.2 Literature review

In the specialized area for modelling temporally dependent data, there is a line of research on explicitly and parsimoniously modelling the covariances with unconstrained parametrization via Cholesky-type decompositions. Note that modelling covariances is different from modelling correlations since the former does not impose unity constraints on the diagonals of matrices. A usual recipe is to transform the restricted supports of the covariance matrices to un-restricted ones; then regression modelling approaches are exploited by utilizing the transformed parameters. Among others, Pourahmadi (1999) proposed to factor the inverse covariance matrix via the modified Cholesky decomposition with entries having autoregressive interpretation, and Zhang and Leng (2012) suggested factoring the covariance matrix itself such that the entries in this decomposition are moving average parameters. see also Pourahmadi (2000), Pan and Mackenzie (2003), Ye and Pan (2006), and Leng, et al. (2010). For explicit regression analysis of correlations in longitudinal data, Zhang, et al. (2015) explored the use of hyperspherical coordinates to parametrize a correlation matrix via angles that are easy to model via regression. Since these Cholesky-type decompositions are tied to the known ordering of the observations, they are highly effective for modelling longitudinal data, but unfortunately unsuitable for other general correlated data where no ordering information is available.

For implicitly modelling correlations and covariances, one of the most celebrated approach is mixed-effects models (Laird and Ware, 1982). We call them implicit because their modelling of covariance is by incorporating random effects, typically in an additive manner to the fixed effects. As a result, the marginal variance of the response scales quadratically with the random effects; and the between-observations correlations are also implicitly determined. This intrinsic tie between the marginal variances and the correlations may restrict the capacity of mixed-effects models; in a great many applications, it is more
reasonable to allow investigating these two components separately. While mixed-effects models naturally fit categorical random effects such as grouping variables, they offer very limited options for incorporating heterogeneous variance due to continuous random effects, and the variance extrapolation beyond the range of the variables can be problematic. In addition, the need to have positive definite covariance estimates puts constraints on the identifiability and complexity of the random effects that can be handled and hence it is not tractable to study models with more flexible random effects specifications.

While the versatility of the mixed-effects model has been increasingly recognized in many applied fields, there are challenging difficulties when it comes to its statistical inference. There are unresolved issues involving some of the most basic aspects, including, for example, identifying the number of parameters in a mixed-effects model, determining the degrees of freedom for various statistics, and subsequently quantifying their asymptotic distributions. It could be practically difficult to address problems such as model selection (Muller, et al., 2013), and even specification of the structure of the random effects (Barr, et. al., 2013; Bates, et al., 2015, cf.). When it comes to testing fixed effects, the familiar F-tests and t-tests widely used for linear models are known inconvenient due to the need to estimate the random effects and the ambiguity of their degrees of freedom (Bolker and others, 2021; Faraway, 2015, cf.), although some progress has been made in using likelihood ratio tests (LRTs) for simple and unbalanced datasets with one variance component (Crainiceanu and Ruppert, 2004). As a result, no associated p-values are presented when fitting mixed-effects models using R package lme4 (Bates, 2006; Baayen, et al., 2008). More difficulties and ambiguity arise when testing random effects for which LRTs are often suggested although without rigorous justification (Baayen, et al., 2008, cf.). Critically, for testing the existence of random effects, the limiting distributions of the corresponding LRTs have to be analyzed case-by-case (Self and Liang, 1987; Chen and Liang, 2010), and even so, it is often found that their approximation accuracy could be quite poor in finite samples (Crainiceanu and Ruppert, 2004), due to the fact that the parameter value being tested is on the boundary of its space. The shortage of justified and conveniently accessible inferential approaches for the mixed-effects models has resulted in confusing, and sometimes contradictory recommendations about what tests to use, how and when, not only by applied workers but also by professional statisticians (Bolker and others, 2021; Luke, 2017). We refer to Bates, et al. (2014), Song (2007), Faraway (2016), and Jiang (2017), among many others, for further discussions.

1.3 Our contributions

This paper makes the first attempt in proposing a novel, simple, flexible, unified inferential tool for modelling correlations for general correlated data, regardless they are ordered or not. As a regression model, our approach relates the entries in correlation matrices to any covariates via a new un-restricted parametrization
of parameters and thus simultaneously addresses the three challenges outlined in Section 1.1. In particular, our model explores a new device built upon a recent discovery on the parametrization of the correlation matrix that can be viewed as a generalization of the Fisher’s z-transformation of a univariate correlation coefficient (Archakov and Hansen, 2021). Analogous to extending the support of the correlation coefficient from the unit interval to the whole real line, the new parametrization extends the support of a correlation matrix from a restricted space to an un-restricted one. A remarkable advantage of the new parametrization is its order-invariance: re-ordering the variables in the correlation matrix results in the same re-ordering of the components in the new parametrization. Thus, our approach allows the transformed correlation matrices to be order-invariant and different-dimensional, and yet guarantees their positive definiteness. The two merits – un-restricted support and order-invariance – make the new parametrization an ideal device for modelling the correlation structures of clustered data; see our comparative examples in Section 2.2 and real data examples in Section 3. The modelling of correlation via an explicit regression model makes the measurements of quantities such as degrees of freedom straightforward, as opposed to that in the mixed effects model. Most importantly, the correlation model proposed in this paper enables us to employ the golden-standard maximum likelihood and thus inference becomes extremely easy and accessible. For example, our framework allows the testing of the existence of random effects in a straightforward manner as we illustrate in Section 4. Finally, we remark that although only linear models are studied in this paper, our proposed framework allows viable extensions to semi-parametric and non-parametric modelling of correlation matrices.

The following notations are used in this paper. For a symmetric matrix \( A \in \mathbb{R}^{m \times m} \), the operator \( \text{vecl}(A) \in \mathbb{R}^{m \times (m-1)/2} \) stacks the lower off-diagonal elements of \( A \) into a vector. The operator \( \text{diag}(\cdot) \) is used in two ways. When applied to a vector \( v = (v_1, \ldots, v_m)' \in \mathbb{R}^m \), \( \text{diag}(v) \) becomes a diagonal matrix with diagonal terms being \( v_1, \ldots, v_m \). When applied to \( A \), \( \text{diag}(A) \) extracts the diagonals of \( A \) to return a length-\( m \) vector. We use \( e^A \) and \( \log A \) to denote matrix exponential and logarithm of \( A \), defined respectively as \( e^A = Q \text{diag}(e^{\lambda_1}, \ldots, e^{\lambda_m})Q' \) and \( \log A = Q \text{diag}(\log \lambda_1, \ldots, \log \lambda_m)Q' \), where \( A = Q \text{diag}(\lambda_1, \ldots, \lambda_m)Q' \) is the eigen-decomposition of \( A \) with \( Q \) an orthonormal matrix. When logarithm is applied to a vector \( v \), we define \( \log v = (\log v_1, \ldots, \log v_m)' \).

The rest of the paper is organized as follows. Section 2 introduces the generalized z-transformation, outlines the correlation model and compares it to the mixed-effects model, presents maximum likelihood for parameter estimation, and provides the theoretical results. We present two data analyses in Section 3 to illustrate the advantages of our framework over mixed-effects models when observations are not ordered, and over Cholesky-type decompositions when analyzing ordered data. Extensive simulation is provided in Section 4 to demonstrate the finite-sample performance of our methods in comparison to its competitors. A
brief conclusion is made in Section 5. All the proofs are relegated to the Appendix.

2 Methodology

2.1 Generalized z-transformation

For a correlation $\rho \in (-1, 1)$, the Fisher’s z-transformation is defined as $z = \frac{1}{2} \log \frac{1+\rho}{1-\rho} \in \mathbb{R}$. In addition to transforming a restricted parameter to an un-restrictive one, z-transformation has the remarkable property of stabilizing variance. Archakov and Hansen (2021) recently discovered a matrix operation in the same spirit, transforming the restricted support of a correlation matrix to an un-restricted one. The transformation defines a mapping $f$ from a correlation matrix $R \in \mathbb{R}^{m \times m}$ to an $m(m-1)/2$-dimensional vector denoted as $\gamma$ via

$$\gamma = f(R) = \text{vecl}(\log R). \quad (1)$$

Note that the resulting $\gamma$ contains the same number of free parameters in a correlation matrix. We will refer to this transformation as generalized z-transformation hereafter. The mapping $f(R)$ has the following remarkable properties.

(a) **One-to-one mapping between $R$ and $\gamma = f(R)$**. Archakov and Hansen (2021) shows that for any real symmetric matrix $G \in \mathbb{R}^{m \times m}$, there exists a unique vector $x^* \in \mathbb{R}^m$, such that $e^{G[x^*]}$ is a correlation matrix, where $G[x^*]$ denotes the matrix $G$ with $x^*$ replacing its diagonal. To find $x^*$, they further show that the sequence

$$x_{(k+1)} = x_{(k)} - \log \text{diag}(e^{G[x_{(k)}]})$$

satisfies $x_{(k)} \to x^*$ as $k \to \infty$ with arbitrary initial vector $x_{(0)} \in \mathbb{R}^m$. Thus, to recover $R = f^{-1}(\gamma)$ with a given $\gamma$, one just needs to make a symmetric matrix $G$ with its lower off-diagonal elements equal to the corresponding elements in $\gamma$ and apply the above iteration to find $x^*$. The resulting correlation matrix is $R = e^{G[x^*]}$.

(b) **Order-invariance**. Suppose that $R_x = \text{corr}(x)$ and $R_y = \text{corr}(y)$, where the elements of random vector $x$ is a permutation of the elements of $y$. Then the elements of $\gamma_x = f(R_x)$ is a permutation of the elements of $\gamma_y = f(R_y)$.

Property (a) implies that for any $m(m-1)/2$-dimensional vector $\gamma$, we can identify a unique $m \times m$
dimensional correlation matrix that satisfies (1). Importantly the entries in $\gamma$ are un-restricted. Property (b) indicates that the parametrization by $\gamma$ is order-invariant.

2.2 Parsimonious modelling of the correlation matrix

Based on the transformation in (1), we propose regression analysis for modelling the correlation matrix. We assume that we observe $n$ groups of dependent data, with size $m_i$ for the $i$th group. Denote $R_i = (\rho_{ijk})$ ($i = 1, \ldots, n$) as the correlation matrices of the $n$ groups, and $\gamma_i = (\gamma_{ijk})$ ($i = 1, \ldots, n; 1 \leq k < j \leq m_i$) as their generalized z-transformations. Let $y_{ij}$ be the $j$th observation of group $i$ associated with covariate $x_{ij}$; then $\rho_{ijk} = \text{corr}(y_{ij}, y_{ik})$ by taking $x_{ij}$ as fixed. Our proposal for the correlation model is simply

$$\gamma_{ijk} = w'_{ijk} \alpha,$$

where $\alpha$ is an unknown parameter which will be referred to as the matrix log-correlation parameters, and $w_{ijk} \in \mathbb{R}^d$ are observations $j$ and $k$ dependent covariates used to model the correlation. A simple choice of $w_{ijk}$ is the difference of the covariates at observations $j$ and $k$ for subject $i$. One consideration of this choice is that the resulting correlation matrix will be stationary if the covariate is time. For more general continuous covariates other than time, such a choice is advantageous in avoiding concerns when extrapolations are needed. Of course, the construction of $w_{ijk}$ can be very flexible and tailor-made to suit practical scenarios; a few examples are provided below and more can be found in data analysis. This results in a highly parsimonious device – one parameter $\alpha$ accounting for $n$ correlation matrices of arbitrary sizes for modelling general dependent data.

We now provide five concrete examples to illustrate a wide variety of models that our device can handle. In some of these examples, with some abuse of notations, we use the indices $i, j$ and $k$ differently from those in (2) in to highlight the structures of intended correlated data under discussion.

Example 1: The device in (2) can conveniently model the correlation structure in temporally dependent data. For example, for modelling longitudinal data, the covariates $w_{ijk}$ can be simply taken from the $j$th and $k$th measurements of the $i$th subject ($i \in \{1, \ldots, n\}; j, k \in \{1, \ldots, m_i\}$) including their observed time $t_{ij}$ and $t_{ik}$ and other time-dependent variables. In this case, (2) can be applied in a similar spirit as in Pourahmadi (1999) and Zhang, et al. (2015).

Example 2: For clustered data with nested random effects, a typical mixed-effects model can be denoted as

$$y_{ijk} = g(x_{ijk}) + u_i + v_{ij} + \epsilon_{ijk},$$
where three indices \( i, j \) and \( k \) are needed for the notation to maintain the usual interpretations of the indices in the context of mixed-effects models. Here \( g(x_{ijk}) \) is the fixed effects properly specified as a function of covariates \( x_{ijk} \). The additive random errors are independent and satisfy \( u_i \sim N(0, \sigma^2_u) \), \( v_{ij} \sim N(0, \sigma^2_v) \), and \( \epsilon_{ijk} \sim N(0, \sigma^2) \). Then \( \text{cov}(y_{ij}, y_{ik}) = \sigma^2_u + \sigma^2_v \) for two observations sharing two common random effects, and \( \text{cov}(y_{ij}, y_{jk}) = \sigma^2_u \) for two observations sharing one common random effect. All the other cases are un-correlated.

The induced correlation structure from this mixed-effects model can be modelled via the device in (2) by taking \( w_{ijk} = (w_{ijk,0}, w_{ijk,1})' \) where \( w_{ijk,0} = 1 \) is the intercept, and \( w_{ijk,2} = 1 \) if the \( j \)th and the \( k \)th observations are in the same group sharing two common random effects, and \( w_{ijk,2} = 0 \) otherwise. By construction, \( \gamma_{ijk} = \alpha_0 + \alpha_1 \) or \( \gamma_{ijk} = \alpha_0 \). It is straightforward to verify that there is a one-to-one correspondence between \( \alpha = (\alpha_0, \alpha_1)' \) and \( (\sigma^2_u, \sigma^2_v)' \) and hence our parametrization can capture this mixed-effects model.

**Example 3**: As a generalization of Example 2, one may consider \( v_{ij} \sim N(0, \sigma^2_v), l = 1, \ldots, L \) in \( y_{i01\ldots L} = g(x_{i01\ldots L}) + u_{i0} + v_{ij} + \epsilon_{ijk} \) to allow heterogeneous random effects in \( v \). Then \( \text{cov}(y_{ij}, y_{ij'}) = \sigma^2_u + \sigma^2_v \) for two observations sharing two common random effects, and other covariances remain the same as in Example 2.

The induced correlation structure from this mixed-effects model can be modelled via the device in (2) by taking \( w_{ijk} = (w_{ijk,0}, w_{ijk,1}, \ldots, w_{ijk,L})' \) where \( w_{ijk,0} = 1 \) is the intercept, and \( w_{ijk,l} \) is the dummy variable defined as \( w_{ijk,l} = 1 \) if the \( j \)th and the \( k \)th observations are in the same group sharing the same \( v_{ij} \) and \( w_{ijk,l} = 0 \) otherwise.

**Example 4**: For multiple-level clustered data with \( L + 1 \) levels, a linear mixed-effects model is

\[
y_{i01\ldots L} = g(x_{i01\ldots L}) + u_{i0} + u_{i01} + \ldots + \epsilon_{i01\ldots L}
\]

where additive random effects are independent, satisfying \( u_{i0\ldots il} \sim N(0, \sigma^2_u) \) for \( l = 0, \ldots, L - 1 \). Then \( \text{cov}(y_{i0\ldots il+1\ldots L}, y_{i0\ldots ii'_{l+1}\ldots L}) = \sum_{i=0}^{l} \sigma^2_u \) for two observations sharing common \( l + 1 \) levels of random effects.

Analogously, by appropriate coding in (2), one can set \( \gamma_{ijk} = \sum_{i=0}^{l} \alpha_l \) for two observations sharing common \( l + 1 \) levels of random effects.

**Example 5**: In crossed random-effects models, the units at the same level of a hierarchy are simultaneously classified by more than one factor. For example, a two-level additive variance components model can be
denoted as
\[ y_{i(jk)} = g(x_{i(jk)}) + u_j + v_k + \epsilon_{i(jk)}, \]
where additive random effects are independent and satisfy \( u_j \sim N(0, \sigma_u^2) \), \( v_k \sim N(0, \sigma_v^2) \) and \( \epsilon_{i(jk)} \sim N(0, \sigma^2) \).

Then \( \text{cov}(y_{i(jk)}, y'_{i(jk)}) = \sigma^2_u + \sigma^2_v \), \( \text{cov}(y_{i(jk)}, y'_{i(j'k)}) = \sigma^2_u \) and \( \text{cov}(y_{i(jk)}, y'_{i(j'k)}) = \sigma^2_v \).

The induced correlation structure from this mixed-effects model can be modelled via the device in (2) by taking \( w_{ijk} = (w_{ijk,0}, w_{ijk,1}, w_{ijk,2})' \) where \( w_{ijk,0} = 1 \) is the intercept. The two dummy variables are defined as \( w_{ijk,1} = 1 \) if the two individuals share the same \( u \) effect and \( w_{ijk,1} = 0 \) otherwise, and \( w_{ijk,2} = 1 \) if the two individuals share the same \( v \) effect and \( w_{ijk,2} = 0 \) otherwise.

The above five examples demonstrate a wide range of correlation structures that the new device is able to handle when correlations are mainly determined by grouping indicator variables. In its full generality, the form of the correlation model in (2) can be ANOVA or ANCOVA type, similar to analogous mean models, to deal with categorical and continuous variables that may influence the correlations in a unified fashion; see our real data examples in Section 3.

2.3 Correlogram for continuous covariates

While categorical variables related to grouping factors are obvious choices to be included in our correlation model, deciding what continuous variables to include in the model can be more challenging, especially when data are highly unbalanced across groups and not ordered. Below we establish a key property – whose proof is given in the Appendix – of the generalized z-transformation that facilitates a convenient approach to decide the relevance of a continuous variable to our correlation model.

Denote \( \rho_i = \text{vecl}(R_i) \) as the vector containing the lower off-diagonal elements of \( R_i \). Recall that \( \gamma_i = \text{vecl}(\log R_i) \) denotes the vector containing the lower off-diagonal elements of the matrix logarithm of \( R_i \). We now characterize one key property of the Jacobian \( \partial \rho_i / \partial \gamma_i \); the explicit form of this \( m_i (m_i - 1)/2 \times m_i (m_i - 1)/2 \) Jacobian matrix is given in the Appendix.

**Proposition 1.** The diagonal elements of \( \partial \rho_i / \partial \gamma_i \) are all nonnegative, i.e., \( \partial \rho_{iik} / \partial \gamma_{iik} \geq 0 \) \( (i = 1, \ldots, n; 1 \leq k < j \leq m_i) \), implies that \( \rho_{ijk} \) and \( \gamma_{ijk} \) have the same monotonicity.

Proposition 1 provides the foundation for an exploratory analysis of the influence of continuous variables on the correlation, because it states that \( \rho_{ijk} \) and \( \gamma_{ijk} \) move in the same direction. The property of this proposition can be employed for the examination of the correlogram which defines the dependence of the matrix log-correlations \( \gamma \) on the covariate \( w \). The correlogram can be seen as an analogue to the variogram in analyzing longitudinal data for examining the pattern in variances. We now discuss how to visualize
correlogram using its empirical estimate.

For balanced ordered data, empirical correlation matrices of the residuals can be computed after fitting a suitable mean model. From there the corresponding correlogram can be constructed by applying the transformation (1) directly on the empirical correlation matrices, and then plotting the matrix log-correlations against those covariates used for ordering. Constructing a correlogram for un-balanced and un-ordered correlated data is more challenging since it is difficult, sometimes even impossible, to empirically calculate matrix log-correlations. We provide the following procedure to examine instead the relationship between correlations and covariates.

Step 1. Fit a suitable mean and variance model and obtain the (standardized) residuals;

Step 2. For a continuous covariate, use local stratification or smoothing to obtain the estimate of the correlation as a function of each continuous covariate. While there are many choices that one can use, for this paper, we will explore the use of local-averaging after stratifying the corresponding variable;

Step 3. Examine the empirical correlations and the groups both obtained in Step 2.

If we see systematic monotonic trend in the last step, according to Proposition 1, it will manifest itself in the relationship between $\gamma_{ijk}$ and the corresponding covariates. An example is found in Figure 2, where plots depicting decreasing patterns in the strength of correlations with two continuous variables will imply similar trends in the related correlograms, leading directly to the inspection of the usefulness of these variables in modelling correlations.

2.4 Model specification and estimation

Having developed a regression model for the correlations, we complement it by including the following regression models of the mean and the log-variances

$$g(\mu_{ij}) = x_{ij}' \beta, \quad \log(\sigma^2_{ij}) = z_{ij}' \lambda,$$

where $\mu_{ij}$ and $\sigma^2_{ij}$ ($i = 1, \ldots, n; j = 1, \ldots, m_i$) are respectively the conditional mean and variance for the $j$th measurement of the $i$th subject, $x_{ij}$ and $z_{ij}$ are $p \times 1$ and $q \times 1$ vectors of generic covariates for modelling the mean and the log-variances respectively, $g(\cdot)$ is a known link function, which is assumed to be monotone and differentiable; an example is the identity function as in linear models for Gaussian data. The specification of the three models for the mean, variance and correlation structures in (2) and (3) stipulates the number of parameters unequivocally as $p + q + d$, which can then be easily utilized to decide the degrees of freedoms
for various statistics of interest. In contrast, in the mixed-effects type of models, it is not clear what one should regard as the degrees of freedom for random effects terms (Bates, 2006; Baayen, et al., 2008; Faraway, 2015).

Let \( \mu_i = (\mu_{i1}, \ldots, \mu_{im_i})' \), \( D_i = \text{diag}(\sigma_{i1}, \ldots, \sigma_{im_i}) \) and \( \omega_i = (\beta', \alpha', \lambda')' \). Write \( \nu_i = y_i - \mu_i \) as the random error associated with the \( i \)th subject. Then \( \Sigma_i = \text{cov}(\nu_i) = D_i R_i D_i \). If \( y_i \) is Gaussian, the log-likelihood is given by

\[
l(\omega) = -\frac{1}{2} \sum_{i=1}^{n} \left( \log |D_i R_i D_i| + \nu_i' D_i^{-1} R_i^{-1} D_i^{-1} \nu_i \right).
\]

Then the following score equations based on the log-likelihood (4) can be obtained by direct calculations:

\[
S_1(\beta; \alpha, \lambda) = \sum_{i=1}^{n} X'_i \Delta_i \Sigma_i^{-1} (y_i - \mu_i) = 0,
\]

\[
S_2(\alpha; \beta, \lambda) = \sum_{i=1}^{n} W'_i (\partial \rho_i / \partial y_i)' \text{vecl} \left( R_i^{-1} \hat{R}_i R_i^{-1} - R_i^{-1} \right) = 0,
\]

\[
S_3(\lambda; \beta, \alpha) = \frac{1}{2} \sum_{i=1}^{n} Z'_i (h_i - 1_{m_i}) = 0,
\]

where \( X_i, W_i \) and \( Z_i \) are respectively the \( m_i \times p, m_i(m_i - 1)/2 \times d \) and \( m_i \times q \) matrices that contain the relevant observed covariates, and \( 1_{m_i} \) is the \( m_i \times 1 \) vector with elements 1.

We define the negative expected Hessian matrix \( I(\omega) = -\mathbb{E} \left( \frac{\partial^2 \ell}{\partial \omega \partial \omega'} \right) \). Following (5), it is shown in Appendix that the block expression of \( I(\omega) \) satisfy

\[
I_{11}(\omega) = \sum_{i=1}^{n} X'_i \Delta_i \Sigma_i^{-1} \Delta_i X_i, I_{22}(\omega) = \sum_{i=1}^{n} W'_i (\partial \rho_i / \partial y_i)' J_i \partial \rho_i W_i,
\]

\[
I_{33}(\omega) = \frac{1}{4} \sum_{i=1}^{n} Z'_i (R_i^{-1} \circ R_i + 1_{m_i}) Z_i, I_{12}(\omega) = I'_{21}(\omega) = 0,
\]

\[
I_{13}(\omega) = I'_{31}(\omega) = 0, I_{23}(\omega) = I'_{32}(\omega) = \frac{1}{2} \sum_{i=1}^{n} W'_i (\partial \rho_i / \partial y_i)' H_i Z_i,
\]

where \( \circ \) denotes the Hadamard product. Denote by \( \eta_i = \text{vecl}(R_i^{-1} \hat{R}_i R_i^{-1} - R_i^{-1}) = (\eta_{ijk}), 1 \leq k < j \leq m_i \) and \( \phi_i = h_i - 1_{m_i} = (\phi_{il}), 1 \leq l \leq m_i \) for \( i = 1, \ldots, n \). Then, the \( m_i(m_i-1)/2 \times m_i(m_i-1)/2 \) matrix \( J_i \) in \( I_{22}(\omega) \) and \( m_i(m_i-1)/2 \times m_i \) matrix \( H_i \) in \( I_{23}(\omega) \) can be respectively expressed as \( J_i = \mathbb{E}(\eta_i \eta'_i) \) and \( H_i = \mathbb{E}(\eta_i \phi'_i) \), since the negative expected Hessian matrix is equate to the Fisher information matrix \( I(\omega) = \mathbb{E}(\partial \ell / \partial \omega \partial \omega') \).
The calculation of each element of $J_i$ and $H_i$ is given in Proposition 2.

We then estimate $\omega$ by maximizing the log-likelihood in (4) via an iterative Newton-Raphson algorithm. An application of the quasi-Fisher scoring algorithm on Equation (5) directly yields the numerical solutions for these parameters. Since the negative expected Hessian matrix $I(\omega)$ is block diagonal consisting of one block corresponding to $\beta$ and the other to $\alpha$ and $\lambda$, it is natural to iterate between updating $\beta$ and $(\alpha', \lambda')'$. The computation needed to find the solution is summarized in Algorithm 1.

**Algorithm 1 Quasi-Fisher Scoring Algorithm**

**Input:** Starting value: $\beta^{(0)}$, $\alpha^{(0)}$ and $\lambda^{(0)}$, set $k = 0,$

**Output:** An estimate of $\omega$.

1: repeat
2: Compute $\Sigma_i$ by using $\alpha^{(k)}$ and $\lambda^{(k)}$. Update $\beta^{(k+1)}$ as

$$
\beta^{(k+1)} = \beta^{(k)} + I^{-1}_1(\omega)S_1(\beta, \alpha, \lambda)|_{\beta = \beta^{(k)}}.
$$
3: Given $\beta = \beta^{(k+1)}$, update $\alpha^{(k+1)}$ and $\lambda^{(k+1)}$ by using

$$(\alpha^{(k+1)}\lambda^{(k+1)}) = (\alpha^{(k)}\lambda^{(k)}) + \left[ \begin{pmatrix} I_{22}(\omega) & I_{23}(\omega) \\ I_{32}(\omega) & I_{33}(\omega) \end{pmatrix}^{-1} \begin{pmatrix} S_2(\alpha; \beta, \lambda) \\ S_3(\lambda; \beta, \alpha) \end{pmatrix} \right]|_{\alpha = \alpha^{(k)}, \lambda = \lambda^{(k)}}.
$$
4: Set $k = k + 1.$
5: until a desired convergence criterion is met.

Since the likelihood function is not a global convex function of the parameters on their support, it can only be guaranteed that the algorithm converges to a local optimum. To choose a reasonable initial value, we assume $\Sigma_i$ to be identity matrices initially and use the least-squares estimator as the initial value of $\beta$ in first equation of (4). Then we initiate $\alpha$ and $\lambda$ using the least-squares estimation based on the residuals. Our numerical experience shows that this iterative algorithm converges very quickly, usually in a few iterations.

## 2.5 Properties

We summarize the computation of $J_i$ and $H_i$ in the negative expected Hessian matrix in the following proposition:

**Proposition 2.** Let $a_{ijk}$ be the $(j, k)$th element of $R_i^{-1}$. Then the $(\frac{(2n-k)(k-1)}{2} + j - k, \frac{(2n-s)(s-1)}{2} + l - s)$th element of $J_i$ is given by $\mathbb{E}(\theta_{ijk} \theta_{ils}) = a_{ijl}a_{iks} + a_{iks}a_{ijl}(1 \leq k < j \leq m_i; 1 \leq s < l \leq m_i)$, and the $(\frac{(2n-k)(k-1)}{2} + j - k, l)$th element of $H_i$ is given by $\mathbb{E}(\phi_{ijl} \phi_{jkl}) = a_{ijl} \delta_{jl} + a_{ijkl}(1 \leq k < j \leq m_i; 1 \leq l \leq m_i)$, where $\delta_{jk}$ is unity when $j = k$ and zero otherwise.

For theoretical analysis, we make the following regularity assumptions.
(A1) The dimensions $p, q$ and $d$ of covariates $x_{ij}$, $z_{ij}$ and $w_{ijk}$ are fixed, and $\max_{1 \leq i \leq n} m_i$ is bounded.

(A2) The parameter space $\Omega$ of $(\beta', \alpha', \lambda')'$ is a compact set in $\mathbb{R}^{p+d+q}$, and the true value $\omega_0 = (\beta'_0, \alpha'_0, \lambda'_0)'$ is in the interior of $\Omega$.

(A3) As $n \to \infty$, $n^{-1} I(\omega_0)$ converges to a positive definite matrix $I(\omega_0)$.

Assumption (A1) is routinely made in the analysis of correlated data. Assumption (A2) is a conventional assumption for theoretical analysis of the maximum likelihood approach. Notably, given our model formulation, it is natural to assume that the true values of the parameters are not on the boundary of the parameter space. Assumption (A3) is a natural requirement for the regression analysis in unbalanced longitudinal data modelling. We establish the following asymptotic results for the maximum likelihood estimator, which support the statistical inference associated with the model parameters.

**Theorem 1.** Under regularity assumptions (A1)–(A3), as $n \to \infty$, we have that

(a) the maximum likelihood estimator $\hat{\omega}$ is strongly consistent for the true value $\omega_0$, and

(b) $\hat{\omega} = (\hat{\beta}', \hat{\alpha}', \hat{\lambda}')'$ is asymptotically normally distributed such that $\sqrt{n}(\hat{\omega} - \omega_0) \xrightarrow{d} N(0, I(\omega_0)^{-1})$, where $I(\omega_0)$ is the Fisher information matrix defined in assumption (A3) and $\xrightarrow{d}$ means convergence in distribution.

Note that $\beta$ is asymptotically independent of $\alpha$ and $\lambda$, because $\beta$ concerns the mean and $\alpha$ and $\lambda$ are parameters of the covariances. This independence are well known for Gaussian distributions. A consistent estimator of $I(\omega_0)$ is $I(\hat{\omega})$ which can be used for inference. Based on Theorem 1 and Chernoff (1954), we immediately obtain the following Corollary 1, which is of essential importance in statistical inference applications, including testing the existence of random effects.

**Corollary 1.** Suppose that $\omega \in \Omega$, and that both $\Omega_0$ and $\Omega - \Omega_0$ are non empty subsets of $\Omega$. Denote the dimensions of $\Omega$ and $\Omega_0$ as $k$ and $r$, with $k > r$, respectively. Then for testing

$$H_0 : \omega \in \Omega_0 \ vs \ H_1 : \omega \in \Omega_1 = \Omega - \Omega_0,$$

if we define the log likelihood ratio test statistic as

$$2 \log LR = 2 \left( \sup_{\omega \in \Omega} l(\omega) - \sup_{\omega \in \Omega_0} l(\omega) \right),$$

then we have $2 \log LR \xrightarrow{d} \chi^2_{k-r}$ as $n \to \infty$. 

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Thanks to the simple formulation of our model and the fact that our parameters are unconstrained, we can see that there is no ambiguity regarding the number of parameters in the model and thus deriving the distribution of various LRTs is straightforward. These are in stark contrast to similar LRTs in the mixed-effects model; so we advocate the use of our approach as an appealing competitor for analyzing correlated data in practice.

3 Real Data Analysis

3.1 The classroom data

We apply our method to the classroom dataset evaluating math achievement scores conducted by researchers at the University of Michigan (West, et al., 2014). In this study, first- and third-grade students were randomly selected from classrooms in a national U.S. sample of elementary schools. Thus there are within-class and within-school clusters where the former is nested within the latter. After omitting items with missing values, the dataset has 1081 students from 285 classrooms in 105 schools. The number of students in each school varies from 2 to 31, making this dataset highly unbalanced. We consider Mathgain as the response variable, which measures the change in a student’s math achievement scores from the spring of kindergarten to the spring of first grade. There are eight covariates including individual-level, classroom-level, and school-level variables with a mixture of categorical and continuous ones as detailed in Table 1.

Table 1: Covariates in the classroom data

| Covariate  | Description (range) |
|------------|----------------------|
| Student-level |                       |
| Sex        | Indicator variable (0 = boy, 1 = girl) |
| Minority   | Indicator variable (0 = nonminority student, 1 = minority student) |
| Mathkind   | Student’s math score in the spring of their kindergarten year [290, 629] |
| Ses        | Student socioeconomic status [-1.61, 3.21] |
| Classroom-level |                   |
| Yearstea   | First-grade teacher’s years of teaching experience [0, 40] |
| Mathprep   | First-grade teacher’s mathematics preparation: number of mathematics content and methods courses [1, 6] |
| Mathknow   | First-grade teacher’s mathematics content knowledge, higher values indicate higher content knowledge [-2.50, 2.61] |
| School-level |                   |
| Housepov   | Percentage of households in the neighborhood of the school below the poverty level [0.012, 0.564] |

West, et al. (2014) recommended the following linear mixed-effects model chosen by the Bayesian information criterion (BIC)

\[
\text{Mathgain}_{ijk} = \beta_0 + \beta_1 \text{Sex} + \beta_2 \text{Minority} + \beta_3 \text{Mathkind} + \beta_4 \text{Ses} \\
+ \beta_5 \text{Yearstea} + \beta_6 \text{Mathprep} + \beta_7 \text{Mathknow} + s_i + c_{ij} + \epsilon_{ijk}, \quad (6)
\]
where $i, j, \text{ and } k$ index schools, classes, and individuals respectively, $s_i \sim N(0, \sigma_s^2)$ and $c_{ij} \sim N(0, \sigma_c^2)$ are nested random effects, respectively capturing the within-school effect and within-class effect nested in schools, and $\varepsilon_{ijk} \sim N(0, \sigma^2)$ incorporates all the remaining variations. The random effects are considered independent as in West, et al. (2014). Fitting this linear mixed-effects model via function `lmer()` in R package `lme4` gives a log-likelihood $-5160.1$ which has the optimal BIC value $98.78$. The need to model the two random effects in $s_i$ and $c_{ij}$ is partially reflected in Figure 1, where one can see clearly between-class variations in the response. This mixed-effects model will serve as a benchmark in our analysis.

![Boxplots of Mathgain for students in selected classrooms in the first three schools.](image)

**Figure 1:** Boxplots of Mathgain for students in selected classrooms in the first three schools.

While the above mixed-effects model offers an effective mechanism to model classroom and school effects – the two grouping factors – as random effects, an important question arises as to whether other variables may have played a role in influencing the correlations between observations. Among others, investigating the impact of students’ math score in the spring of their kindergarten year (Mathkind) and socioeconomic status (Ses) – two continuous variables – can be of interest. Intuitively, students in the same class with similar math scores in their kindergarten or similar socioeconomic status tend to perform similarly when it comes to math achievements, simply because students with similar backgrounds tend to undertake similar educational paths and interact more. To test this out, we obtain the residuals $\tilde{\epsilon}_{ijk}$ of each student by subtracting the fixed effects in model (6). We standardize $\tilde{\epsilon}_{ijk}$ by dividing it by the fitted standard deviation of model (6), obtaining standardized residuals as $\tilde{\epsilon}_{ijk}$. Then we calculate the empirical correlations confined to pre-defined subgroup $S$ as

$$
\hat{\rho}_{ij}^S = \frac{1}{N_{ij}^S} \sum_{k<k'} \tilde{\epsilon}_{ijk} \tilde{\epsilon}_{ijk'} I(|V_{ijk} - V_{ijk'}| \in S),
$$

where $V$ stands for Mathkind or Ses that we are concerned about, $S$ is created by stratifying their difference, and $N_{ij}^S$ is the total number of different pairs in the subgroup. We examine the data by creating three subgroups – small difference: $S = (0, 40]$ for Mathkind or $S = (0, 0.3]$ for Ses; mid difference: $S = (40, 120]$
for Mathkind or $S = (0.3, 0.6]$ for Ses, and large difference: $S = (120, 240]$ for Mathkind or $S = (0.6, 0.9]$ for Ses. The empirical distributions of $\hat{\rho}_{ij}^S$ are shown by boxplots in Figure 2, where clear decreasing trends are seen, indicating that the mathgains are indeed more correlated among students whose Mathkind or socioeconomic statuses differ relatively less. This finding in the correlation structure is remarkable. Accounting for correlation of this kind is important in drawing valid inferences, by appropriately quantifying the strength of the data evidence.

![Boxplots of Correlations](Figure 2)

**Figure 2:** Correlogram: boxplot of the pairwise correlations with different Mathkind and Ses gap.

Besides the graphical illustration, we also perform formal hypothesis tests for the effects of various variables. To compare with the linear mixed-effects model in (6), we first consider the same mean model of (6), and model log-variances by $\log \sigma^2 = \lambda_0$ and matrix log-correlations by

$$\gamma_{ijk} = \alpha_0 + \alpha_1 w_{ijk,1}, \quad (7)$$

where $i$ is the index of the schools, $j, k$ are the $j$th and $k$th individuals therein. In this correlation model, we use $\alpha_0$ to capture the school effect; we define $w_{ijk,1} = 1$ if student $j$ and student $k$ come from the same classroom and $w_{ijk,1} = 0$ otherwise. Thus, $w_{ijk,1}$ captures the classroom effect. The $p$-values of the school and class effects using our model and those of these two variables when they are used as random effects in the linear mixed-effects model are presented in Table 2. Note that from Example 2 in Section 2.2, these tests are equivalent in this case for the two methods. All the $p$-values are all very small, indicating that school and classroom are useful variables for capturing correlations.

Next, we demonstrate using a few LRTs to test the effects of the four student-level covariates in addition to class and school. Towards this, we add $\alpha_2 w_{ijk,2}$ to model one of the four student-level covariates, and test if $H_0 : \alpha_2 = 0$. For example, if we test the Sex effect, then $w_{ijk,2}$ is defined as the absolute difference of the Sex between student $j$ and student $k$; dummy variables for the other three tests are created in a similar way. For the linear mixed-effects model, we add each of the student-level covariates as a random effect nested in schools to model (6), and test if the corresponding random effect exists. We remark that
the testings of the random effects of the two categorical variables Sex and Minority are equivalent for the two methods, while those for the two continuous variables Mathkind and Ses are not. The $p$-value of the four tests are present in Table 2. We can see that there is a marked difference in the $p$-values for Minority, Mathkind and Ses. The simulation in Section 4 suggests that these inference results based on our approach are trustworthy, corroborating the theory in Section 2.5, while those based on the mixed-effects model may not.

**Table 2:** $p$-values of LRTs by using the linear mixed-effects model (LMM) and our proposed approach (Proposed).

|            | School  | School:Class | Sex   | Minority | Mathkind | Ses   |
|------------|---------|--------------|-------|----------|----------|-------|
| LMM        | $1.08 \times 10^{-11}$ | 0.0011       | 0.2818 | 0.0485   | 0.9999   | 0.9750 |
| Proposed   | $2.37 \times 10^{-12}$ | 0.0023       | 0.2387 | 0.1166   | 0.0027   | 0.1567 |

Since the LRTs of Sex and Minority via our approach are not significant at 0.05 level, and recognizing from correlogram that the omission of Mathkind term or socioeconomic status in the random effects as an inadequacy of the mixed-effects model in (6), we attempt our proposed approach in developing a more effective model for the correlation structure by specifying

$$
\gamma_{ijk} = \alpha_0 + \alpha_1 w_{ijk,1} + \alpha_2 w_{ijk,2} + \alpha_3 w_{ijk,3},
$$

where the definition of $w_{ijk,1}$ is the same as that in (7), $w_{ijk,2}$ is defined as the absolute difference of the Mathkind between student $j$ and student $k$, and $w_{ijk,3}$ is defined as the absolute difference of the Ses between student $j$ and student $k$. For the other two models in (3), we consider the same structure as in (6) for the mean model, and model the marginal log-variances using the same seven covariates.

Given the many terms in our mean, log-variances and correlation models, we selectively examine the following three models of particular interest: the benchmarking mixed-effects model in (6), our full model with all the covariates, which gives a log-likelihood $-4154.59$ and BIC value 80.02, and our model when chosen by minimizing BIC, which gives a log-likelihood $-4157.54$ and BIC value 79.81. The mean analysis and covariance analysis of these three models are presented in Table 3. In addition, the estimated random effects parameters of the linear mixed-effects model are $\sigma_s^2 = 75.19$, $\sigma_c^2 = 86.68$ and $\sigma^2 = 713.83$, respectively. Note that unlike our proposed approach, the standard errors of the estimate random effects parameters in the linear mixed-effects model are not straightforward to obtain and not made available in `lme4`.

Compared with the mixed-effects model in (6), we observe that both our models are better in terms of the log-likelihood and the BIC value. The improvement in our models compared with the mixed-effects model indicates that the proposed approach is effective in including Mathkind or Ses as covariates for the
Table 3: Analysis of the classroom data: The estimated values of parameters and their standard errors. LMM: Linear mixed-effects model; Our full: our full model; Our BIC: Our model chosen by BIC.

| Mean | Intercept | Sex | Minority | Mathkind | Ses | Yearstea | Mathprep | Mathknow |
|------|-----------|-----|----------|----------|-----|----------|----------|----------|
| LMM  | 282.02_{11.70} | -1.34_{1.72} | -7.87_{2.43} | -0.48_{0.02} | 5.42_{1.28} | 0.04_{0.12} | 1.09_{1.15} | 1.91_{1.15} |
| Our full | 276.42_{12.76} | -1.43_{1.68} | -7.18_{2.48} | -0.46_{0.02} | 5.15_{1.28} | 0.05_{0.11} | 0.88_{0.09} | 2.14_{1.11} |
| Our BIC | 275.28_{12.71} | -1.08_{1.68} | -6.97_{2.42} | -0.46_{0.02} | 5.34_{1.29} | 0.07_{0.11} | 0.91_{1.14} | 1.99_{1.14} |

| Log-variance | Intercept | Sex | Minority | Mathkind | Ses | Yearstea | Mathprep | Mathknow |
|--------------|-----------|-----|----------|----------|-----|----------|----------|----------|
| Our full     | 8.329_{0.547} | -0.087_{0.084} | -0.191_{0.099} | -0.003_{0.001} | 0.118_{0.059} | -0.003_{0.004} | -0.032_{0.043} | -0.045_{0.043} |
| Our BIC      | 7.742_{0.490} | -0.002_{0.001} | 0.128_{0.058} | -0.000072_{0.0002} | -0.000016_{0.0002} | -0.000074_{0.0003} |

| Matrix log-correlation | School | Classroom | Mathkind | Ses |
|-----------------------|--------|-----------|----------|-----|
| Our full              | 0.096_{0.019} | 0.078_{0.025} | -0.000072_{0.0002} | -0.000016_{0.0002} |
| Our BIC               | 0.093_{0.019} | 0.081_{0.025} | -0.000074_{0.0003} |

correlations. Remarkably, the effects of Mathkind and Ses in our full model and the effect of Mathkind in our model chosen by BIC are all negative, matching our empirical observation from Figure 2. However, in the mixed-effects model, if we add Mathkind as a random effect nested in school, the variance estimator of Mathkind becomes zero, indicating that covariance caused by continuous variables of this kind is not compatible with the mixed-effects model. There are also interesting results from the log-variance model part. The coefficient of Mathkind is negative in both our models, suggesting that higher math scores in kindergarten leads to lower variance in Mathgain. On the other hand, the coefficient of Ses is positive in these two models, implying that higher socioeconomic status is associated with higher variance in Mathgain.

3.2 Malaria immune response data in Benin

As another application of our proposed model, we apply it to a malaria immune response data set studied by Adjakossa, et al. (2016), where the response is the level of the protein IgG1_A1 in the children assessed at 3, 6, 9, 12, 15, and 18 months. This response was obtained by using two recombinant P. falciparum antigens to perform antibody quantification by Enzyme-Linked ImmunoSorbent Assay standard methods developed for evaluating malaria vaccines by the African Malaria Network Trust (AMANET [www.amanet148trust.org]). Due to missingness, the number of measurements for each individual varies from 2 to 5. In total, this data set contains 316 individuals with 1292 measurements. Together, there are seven covariates as described in Table 4. An interesting aspect of this dataset is that the measurements of each child were ordered according to time, but the exact time when a measurement was taken was not recorded. Another interesting aspect of this dataset is that two time-dependent variables pred_trim and nutri_trim are available.

Since the exact time of measurements is not recorded, we use $t_i = (1, \ldots, m_i)'$ as measured times for
Table 4: Covariates in the malaria immune response data

| Covariate     | Description (range)                                                                 |
|---------------|------------------------------------------------------------------------------------|
| CO.IgG1_A1    | measured concentration of IgG1_A1 in the umbilical cord blood [-4.59, 8.21]          |
| M3.IgG1_A1    | predicted concentration of IgG1_A1 in the child’s peripheral blood at 3 months [-5.83, 4.13] |
| ap            | placental apposition (0=apposition, 1=non apposition)                                |
| hb            | hemoglobin level [5.7, 17.1]                                                        |
| inf_trim      | number of malaria infections in the previous 3 months [1, 5]                        |
| pred_trim     | quarterly average number of mosquitoes child is exposed to [0.028, 24.25]            |
| nutri_trim    | quarterly average nutrition scores [0, 1]                                           |

subject $i$. This assignment of time may mis-align some observations with time but given the data provided, it is probably the best that one can do. Since now the data are aligned, we select all the individuals with 4 and 5 measurements and use them to calculate the empirical $4 \times 4$ and $5 \times 5$ correlation matrices respectively. These estimated correlation matrices allow us to assess the correlogram. By examining matrix log-correlations $\gamma$ versus the time lag and pre_trim difference respectively in Figure 3, it seems that $\gamma$ has a decreasing trend with pre_trim difference while its relationship with the time lag is not clear. This makes sense since malaria is caused by a parasite which is passed to humans through mosquito bites, so that the covariate pred_trim is highly correlated to the concentration of IgG1_A1. On the other hand, time itself is not that useful, especially considering that mosquito bites are highly seasonal and thus time difference does not offer much insight.

![Figure 3: Malaria immune response data. (a): the empirical matrix log-correlations against time lag; (b) the empirical matrix log-correlations against pred_trim difference.](image-url)

To compare methods, we also apply the approaches in Pourahmadi (1999) and Zhang, et al. (2015) that require ordering of the observations, which is available in this dataset. Additionally, it is interesting to compare the performance between approaches when the ordering is not maintained. Towards these, we conduct the following analysis, by first taking advantage of the time-dependent covariate pred_trim.
as covariates. The robustness of different methods is then examined by randomly permuting the order of pred_trim and then taking the permuted observations as if they are ordered as such. In particular, we consider the following three specifications, taking the same mean model that has all the covariates in a linear regression:

- “time model”: This specification favors approaches requiring ordering. We use a polynomial of $t_{ij}$ for the log-variance model and a polynomial of the time lag for the correlation model for our approach and that in Zhang, et al. (2015), and use a polynomial of $t_{ij}$ for the log-innovation model and a polynomial of the time lag for the autoregressive model for the modified Cholesky decomposition in Pourahmadi (1999). The optimal models all turn out to have $q = 1$ and $d = 1$ when using BIC as the criterion to choose an optimal model;

- “pred_trim model”: This specification uses indirectly the original ordering of the data. Use pred_trim for the log-variance model and the difference between the $j$th and $k$th pred_trim of individual $i$ for the correlation model for our approach and that in Zhang, et al. (2015), and use pred_trim for the log-innovation model and the pred_trim difference for the autoregressive model for the modified Cholesky decomposition in Pourahmadi (1999);

- “permuted pred_trim model”: This specification randomly permutes the ordering, mincing a case with un-ordered clustered dependence. It is similar to the above pred_trim model but with the measurements of each child randomly permuted. All the approaches under comparison will use the permuted order as the true order to construct their models. This random permutation is conducted 50 times and the results are averaged.

The results are presented in Table 5. We can see clearly that the proposed method outperforms the other two approaches, with or without knowing the ordering of the measurements. While the methods of Pourahmadi (1999) and Zhang, et al. (2015) are satisfactory when the ordering is known, they clearly fail to fit the data if the correct ordering is not maintained. The best model for fitting this data is from our approach with the variable pred_trim as the covariate. The use of pred_trim instead of the time in our model agrees with our exploratory analysis in Figure 3. In Figure 4, we further compare the fitted curves of $\gamma$ and log-$\sigma^2$ versus time and pred_trim respectively, when using time or pred_trim in our model. It can be seen that the log-variance increases with the increase of the average number of mosquitoes a child was exposed to, which is consistent with our understanding of malaria immune response.
### Table 5: Malaria immune response data: Comparison of different models

| Model     | Our approach | Pourahmadi (1999) | Zhang, et al. (2015) |
|-----------|--------------|-------------------|----------------------|
|           | log-likelihood | BIC | log-likelihood | BIC | log-likelihood | BIC |
| time      | −1241.65 | 8.059 | −1244.09 | 8.093 | −1244.96 | 8.098 |
| pred_trim | −1233.04 | 8.004 | −1240.16 | 8.050 | −1237.37 | 8.032 |
| permuted  | −1233.04 | 8.004 | −1707.99 | 11.01 | −6361.83 | 40.47 |

**Figure 4:** Malaria immune response data: the dotted lines indicate the asymptotic 95% confidence intervals: (a) the fitted matrix log-correlations against time lag; (b) the fitted log-variances against time; (c) the fitted matrix log-correlations against pred_trim difference; (d) the fitted log-variances against pred_trim.

### 4 Simulation

In this section, we investigate the finite sample performance of the proposed method via three studies. In Study 1, the data are generated from our model to validate our theory. In Study 2 and Study 3, we generate data inspired by the classroom data and compare our approach to the linear mixed-effects model to demonstrate the usefulness of our approach.

**Study 1.** The data sets are generated from the following model

\[
\begin{align*}
\gamma_{ijk} &= \alpha_0 + w_{ijk1} \alpha_1 + w_{ijk2} \alpha_2 \\
\log(\sigma_{ij}^2) &= \lambda_0 + z_{ij1} \lambda_1 + z_{ij2} \lambda_2
\end{align*}
\]

\[
y_{ij} = \beta_0 + x_{ij1} \beta_1 + x_{ij2} \beta_2 + e_{ij} \\
(i = 1, \ldots, n; j = 1, \ldots, m_i)
\]
where \( m_i - 1 \sim \text{binomial}(6, 0.8) \) gives rise to different numbers of repeated measurements \( m_i \) for each subject, the covariate \( x_{ij} = (x_{ij1}, x_{ij2})' \) is generated from a multivariate normal distribution with mean \( \mathbf{0} \), marginal variance 1 and correlation 0.5, and we set \( z_{ij} = x_{ij} \). For \( w \), we set \( w_{ijk} = (1, u_{ij} - u_{ik}, (u_{ij} - u_{ik})^2)' \) with \( u_{ij} \) generated from the uniform \((0, 1)\) distribution. The values of the parameters are found in Table 6. We generate 1,000 data sets and consider sample sizes \( n = 50, 100, \) or 200.

We use the mean absolute biases (MAB) of the estimated parameters to illustrate the estimation accuracy. We also compare the sample average of 1,000 standard errors (SE) based on the estimated Fisher information matrix, and the sample standard deviation (SD) of 1,000 estimated parameters. Table 6 summarizes the simulation results. It is obvious that all the biases are small and decrease rapidly with the increase of the sample size \( n \). We can also see that SE and SD are quite close, especially for large \( n \), indicating that our standard error formula works well.

**Table 6:** Simulation results for Study 1. All the results have been multiplied by 100.

| Parameter | True value | \( n=50 \) | \( n=100 \) | \( n=200 \) |
|-----------|------------|------------|------------|------------|
| \( \beta_0 \) | 1.0 | 6.70 8.58 8.40 | 4.81 6.05 6.10 | 3.33 4.32 4.25 |
| \( \beta_1 \) | -0.5 | 3.31 4.14 4.18 | 2.31 2.87 2.87 | 1.63 2.02 2.05 |
| \( \beta_2 \) | 0.5 | 2.88 3.59 3.65 | 2.04 2.59 2.59 | 1.49 1.85 1.86 |
| \( \alpha_0 \) | 0.3 | 3.70 4.47 4.66 | 2.58 3.15 3.23 | 1.76 2.24 2.22 |
| \( \alpha_1 \) | -0.2 | 6.59 7.68 8.32 | 4.13 5.10 5.19 | 3.05 3.73 3.85 |
| \( \alpha_2 \) | 0.3 | 13.36 15.66 16.67 | 8.69 10.38 10.81 | 6.40 7.79 7.93 |
| \( \lambda_0 \) | -0.5 | 10.29 12.51 12.69 | 7.41 8.77 8.99 | 4.89 6.24 6.19 |
| \( \lambda_1 \) | 0.5 | 7.04 8.14 8.83 | 4.66 5.58 5.86 | 3.27 3.94 4.10 |
| \( \lambda_2 \) | -0.3 | 6.48 7.58 8.08 | 4.46 5.38 5.52 | 3.18 3.93 4.03 |

**Study 2.** In this study, we compare the estimation accuracy of the proposed approach with the linear mixed-effects model under three different scenarios inspired by the classroom data in Section 3.1. We set sample sizes as \( n = 50, 100 \) or 200 and generate clustered data from the following model

\[
y_{ijk} = \beta_0 + x_{ijk,1}\beta_1 + x_{ijk,2}\beta_2 + \varepsilon_{ijk},
\]

where \( i = 1, \ldots, n; j = 1, \ldots, m_i; k = 1, \ldots, k_{ij} \). For all the cases considered here, we set \( \beta_0 = (1, -0.5, 0.5)' \) and generate the covariate \( x_{ijk} = (x_{ijk,1}, x_{ijk,2})' \) from a bivariate normal distribution with mean \( \mathbf{0} \), marginal variance 1 and correlation 0.5.

In case I, we generate the error from a linear mixed-effects model by taking \( \varepsilon_{ijk} = u_i + v_{ij} + \epsilon_{ijk} \), where \( u_i, v_{ij} \) and \( \epsilon_{ijk} \) are independent and all follow the standard normal distribution. To be consistently
comparable, we consider balanced data sets where \( m_i = 2 \) and \( k_{ij} = 5 \) for all \( i \) and \( j \). In this case, the linear mixed-effects model and our approach, using the specification in Example 2 in Section 2.2, estimate the same covariance structure.

In case II, we generate data similar to the unbalanced classroom data where \( m_i \) is uniform on \( \{2, 3, 4\} \) and \( k_{ij} - 1 \sim \text{binomial}(4, 0.8) \). We generate \( \varepsilon_{ijk} \) from our model in (2) with \( \gamma_{ikk'} = \alpha_0 + \alpha_1 w_{ikk'} + \alpha_2 |t_{ik} - t_{ik'}| \) with \( t_{ik} \) following the uniform distribution on \([0, 1] \). Here \( w_{ikk'} = 1 \) if \( k \)th and \( k' \)th observations are in the same group and \( w_{ikk'} = 0 \) otherwise. For simplicity, we set \( \log(\sigma^2_{\varepsilon_{ij}}) = \lambda_0 \), and set \( \alpha_0 = (0.2, 0.3, -0.2)' \) and \( \lambda_0 = 1 \). In this case, the covariance model for the linear mixed-effects model is misspecified.

In case III, we take the same setting on \( m_i \) and \( k_{ij} \) as in case II and let \( \varepsilon_{ijk} = u_i + v_{ij} + \varepsilon_{ijk} \), where \( u_i \) and \( v_{ij} \) both follow the standard normal distribution as in case I, but with \( \varepsilon_{ijk} \) having an autoregressive AR(1) correlation structure in the sense that \( \text{corr}(\varepsilon_s, \varepsilon_{s'}) = 0.85\rho^{\mid s - s'\mid} \) for \( \rho = 0.6 \) corresponding to moderately correlated errors. In this case, both approaches use misspecified models for the covariance.

We use the following error measurements to compare the performance of the two competing methods

\[
\| \hat{\mu}_d \| = \frac{1}{n} \sum_{a=1}^{n} \| x'_a (\hat{\beta} - \beta_0) \| \quad \text{and} \quad \| \hat{\Sigma}_d \| = \frac{1}{n} \sum_{a=1}^{n} \| \hat{\Sigma}_a - \Sigma_{0a} \| ,
\]

which are the \( \ell_2 \)-norm of the difference between the estimated mean and the true mean, and the Frobenius norm of the difference between the true covariance matrix and its estimate. Table 7 presents the average norms with their standard errors over 1000 replicates. In case I where data are generated from the linear mixed-effects model, our approach performs almost the same as the mixed-effects model approach. In case II when the data is generated from our model, it is not surprising that our method performs much better. In case III when both methods are misspecified, our method still performs better, especially for estimating the covariance matrices. The simulation results together with our real data examples clearly demonstrate that the proposed approach is more adaptive and flexible for capturing the correlations of correlated data, even when the model is misspecified.

\textit{Study 3.} This study is for demonstrating the use of our approach for inference when testing the presence of random effects.

The data are generated in a way similar to case I in Study 2 with sample size \( n = 50 \) where \( u_i \sim N(0, \sigma_u^2) \), \( v_{ij} \sim N(0, \sigma_v^2) \) and \( \varepsilon_{ijk} \sim N(0, 1) \) are independent. That is, the data are generated from the linear mixed-effects model. For each simulation setup, we repeat the experiments 200 times. We are interested in testing various hypotheses regarding the magnitude of \( \sigma_u^2 \) and \( \sigma_v^2 \). A recommended test for the linear mixed-effects model is the LRT as implemented in \texttt{lme4} whose performance we now examine. As we have
Table 7: Comparison between the method proposed and the linear mixed-effects model.

| Case      | Size | Proposed model |          | Mixed-effects model |          |
|-----------|------|----------------|----------|---------------------|----------|
|           |      |                | $\|\hat{\mu}_d\|$ | $\|\hat{\Sigma}_d\|$ | $\|\hat{\mu}_d\|$ | $\|\hat{\Sigma}_d\|$ |
| Case I    | $n = 50$ | 0.153,0.096 | 0.288,0.172 | 0.153,0.096 | 0.287,0.167 |
|           | $n = 100$ | 0.115,0.075 | 0.201,0.107 | 0.115,0.075 | 0.199,0.102 |
|           | $n = 200$ | 0.084,0.058 | 0.132,0.075 | 0.084,0.058 | 0.130,0.075 |
| Case II   | $n = 50$ | 0.159,0.105 | 0.227,0.149 | 0.160,0.108 | 0.993,0.180 |
|           | $n = 100$ | 0.101,0.066 | 0.131,0.082 | 0.112,0.088 | 0.674,0.085 |
|           | $n = 200$ | 0.078,0.043 | 0.101,0.053 | 0.084,0.056 | 0.560,0.067 |
| Case III  | $n = 50$ | 0.138,0.111 | 0.371,0.143 | 0.141,0.110 | 1.228,0.370 |
|           | $n = 100$ | 0.098,0.049 | 0.309,0.081 | 0.103,0.056 | 1.151,0.303 |
|           | $n = 200$ | 0.080,0.041 | 0.282,0.078 | 0.083,0.052 | 1.090,0.206 |

shown in Example 2 in Section 2.2, a test regarding $\sigma_u^2$ or $\sigma_v^2$ corresponds to a test regarding $\alpha_0$ and $\alpha_1$ which are defined therein. A trivial application of Corollary 1 suggests that the LRT via our approach is asymptotically $\chi^2$ distributed with its degrees of freedom determined by the number of constraints under the null hypothesis. For the mixed-effects model approach however, statistical inference is not easy due to the absence of analytical results for the null distributions of parameter estimates (Bates, et al., 2014).

When testing the existence of random effects for example, the true parameter value is at the boundary of the support of the variance parameter, making the asymptotic distribution of the LRT not generally tractable.

With the above discussion in mind, we examine various scenarios to test the magnitude and the existence of the random effects. First, we test $H_0 : \sigma_u^2 = \sigma_v^2 = 1$, where $\sigma_u^2$ and $\sigma_v^2$ are in the interior of their respective parameter space. When data are generated under this null, we know that the LRT will follow $\chi^2_2$ asymptotically, regardless whether the mixed-effects model or our model is used. This is confirmed in Figure 5 (a) and (e) when the quantile-quantile (Q-Q) plots of the LRT statistics versus the $\chi^2_2$ distribution is examined. In the next three settings, we examine the existence of the random effects by testing the following hypotheses:

- $H_0 : \sigma_v^2 = 0$ for the linear mixed-effects model, or equivalent $H_0 : \alpha_1 = 0$ for the proposed approach;
- $H_0 : \sigma_u^2 = 0$ for the linear mixed-effects model, or equivalent $H_0 : \alpha_0 = 0$ for the proposed approach;
- $H_0 : \sigma_u^2 = \sigma_v^2 = 0$ for the linear mixed-effects model, or equivalent $H_0 : \alpha_0 = \alpha_1 = 0$ for the proposed approach.

The Q-Q plots of the LRT statistics versus the corresponding $\chi^2$ distributions under the three hypotheses
above are plotted in the second to the last columns in Figure 5. It is clear that while the variance components are at the boundary of their parameter spaces, a substantial discrepancy exists between the empirical distribution of the test statistics and the reference distribution for the linear mixed-effects model. In contrast, our approach remains valid. Indeed, Baayen, et al. (2008) commented, in a different context, that though the LRT is often chosen as the test statistic to use for these tests in linear mixed-effects models, the asymptotic reference distribution of a $\chi^2$ does not apply, giving rise to mis-calibrated $p$-values for variance parameters if these $p$-values are computed using the $\chi^2$ reference distribution.

We close with a remark that the limiting distribution of the LRT for the mixed-effects model in this case is known non-standard; see Self and Liang (1987) and Chen and Liang (2010). The analytical procedure is case-by-case for testing various random effects, and its finite sample approximation is known inaccurate (Crainiceanu and Ruppert, 2004), rendering substantial barriers for testing the random effects in the mixed-effects model in practice. Our approach, in contrast, provides a simple and justified solution.

5 Conclusion

We have proposed a novel regression analysis of correlations for general correlated data including clustered and longitudinal studies. Our model can deal with highly unbalanced clusters and groups and provide a
parsimonious characterization of various correlation structures. Our approach builds on the generalized
z-transformation that permits un-restrictive parameters, to relate quantities in this transformation to
covariates via a regression model. Together with a mean model and a model for the logarithm of the
marginal variances, the proposed method represents a flexible and attractive framework with easy and
accessible inferential tools rooted in maximum likelihood. Through simulations and data analysis, we have
demonstrated that our modelling framework can be more robust to model misspecification and offer a
valuable alternative to the mixed-effects modelling approach. Moreover, our approach is straightforward
for statistical inference, especially when testing the existence of random effects, an open problem that the
mixed-effects model has difficulty with. In the analysis of the classroom data, this flexibility is demonstrated
by including continuous variables in the regression analysis of the correlations. The analysis of the malaria
immune data further reminds us that in longitudinal data modelling, the correlation between the observations
of the same subject some times can be better represented by important time-dependent covariates other
than time.

We identify several directions for future work. First, since the parameters in our parametrization are
unconstrained, it is natural to model the matrix log-correlations non-parametrically or semi-parametrically.
Second, we only consider the scenario when the response variable is Gaussian. When departure from
normality happens, it will be interesting to consider a wider family of distributions such as multivariate
t-distributions for modelling correlated data. Finally, we have only considered continuous response variables
in this paper. It will be interesting to extend the developed framework to deal with categorical responses.
These and other generalizations of the method in this paper will be reported elsewhere.

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Appendix A  Technical details

Some useful formulas. We start from a formula in Archakov and Hansen (2021):

\[
\frac{\partial \rho_i}{\partial \gamma_i} = E_l \left( I - A_i E'_d (E_d A_i E'_d)^{-1} E_d \right) A_i (E_l + E_u)',
\]

where \( A_i = \partial \text{vec} R_i / \partial \text{vec} G_i \), vec is the matrix column vectorization operator, \( G_i = \log R_i \) and the matrices \( E_l, E_u \) and \( E_d \) are elimination matrices, such that \( \text{vec} R_i = E_l \text{vec} R_i, \text{vec} R'_i = E_u \text{vec} R_i \) and
Therefore, the eigenvalues of
\[ Q_i \Lambda_i Q_i' \]
where \( \Lambda_i \) is the diagonal matrix containing the eigenvalues \( \lambda_{i1}, \ldots, \lambda_{im_i} \) of \( G_i \), and \( Q_i \) is an orthonormal matrix (i.e. \( Q_i' = Q_i^{-1} \)) containing the corresponding eigenvectors.

According to Linton and McCrorie (1995), \( \partial \text{vec} R_i = A_i \partial \text{vec} G_i \), where

\[
A_i = (Q_i \otimes Q_i) \Xi_i (Q_i \otimes Q_i)',
\]

is a \( m_i^2 \times m_i^2 \) matrix and \( \Xi_i \) is an \( m_i^2 \times m_i^2 \) diagonal matrix whose elements are given by

\[
\xi_{ijk} = \Xi_i((j-1)m_i+k,(j-1)m_i+k) = \begin{cases} e^{\lambda_{ij}}, & \text{if } \lambda_{ij} = \lambda_{ik} \\ e^{\lambda_{ij}} - e^{\lambda_{ik}} / \lambda_{ij} - \lambda_{ik}, & \text{if } \lambda_{ij} \neq \lambda_{ik} \end{cases}
\]

for \( i = 1, \ldots, n \) and \( j, k = 1, \ldots, m_i \). Clearly, we have \( \xi_{ijk} = \xi_{ikj} \) for all \( i \) and \((j, k)\). Moreover, \( A_i \) is a symmetric positive definite matrix, because all the diagonal elements of \( \Xi_i \) are strictly positive. For convenience, in the following proofs, we use \( (M)_{ij} \) for the \((i, j)\)th element of the matrix \( M \).

*Proof of Proposition 1.* Since \( A_i \) is a symmetric positive definite matrix, we can decompose \( A_i \) as \( A_i = Q_i Q_i' \), where \( Q_i \) is a positive matrix. Then, we have

\[
I - A_i E_d' (E_d A_i E_d')^{-1} E_d = I - Q_i Q_i' E_d' (E_d Q_i Q_i' E_d')^{-1} E_d Q_i Q_i^{-1},
\]

where \( Q_i' E_d' (E_d Q_i Q_i' E_d')^{-1} E_d Q_i \) is a symmetric idempotent matrix whose eigenvalues are either 0 or 1. Therefore, the eigenvalues of \( Q_i Q_i' E_d' (E_d Q_i Q_i' E_d')^{-1} E_d Q_i Q_i^{-1} \) are 0 or 1, which implies that the eigenvalues of \( I - A_i E_d' (E_d A_i E_d')^{-1} E_d \) are 0 or 1, too. Denote by \( B_i = A_i - A_i E_d' (E_d A_i E_d')^{-1} E_d A_i \). Thus, \( B_i \) is a semi-positive definite symmetric matrix.

Since \( \partial \rho_i / \partial \gamma_i = E_i B_i (E_i + E_u)' \), the diagonal element \( \partial \rho_{ijk} / \partial \gamma_{ijk} (1 \leq k < j \leq m_i) \) is given by

\[
\frac{\partial \rho_{ijk}}{\partial \gamma_{ijk}} = B_i; j+m_i(k-1), j+m_i(k-1) + B_i; j+m_i(k-1), k+m_i(j-1).
\]

Note that \( B_i \) is also the Jacobian of \( \partial \text{vec} R_i / \partial \text{vec} G_i \), but the diagonal elements of \( R_i \) are constrained to one. Because of the symmetry of \( \partial \text{vec} R_i / \partial \text{vec} G_i \), it is easy to verify that

\[
B_i; j+m_i(k-1), j+m_i(k-1) = B_i; k+m_i(j-1), k+m_i(j-1).
\]
The semi-positive definiteness of $B_i$ implies that the principal sub-matrix of $B_i$ satisfies

$$B_{i:j+m_i(k-1),j+m_i(k-1)} B_{i:k+m_i(j-1),k+m_i(j-1)} \geq B_{i:j+m_i(k-1),k+m_i(j-1)}^2,$$

so that

$$B_{i:j+m_i(k-1),j+m_i(k-1)} \geq B_{i:j+m_i(k-1),k+m_i(j-1)},$$

which implies that $\partial \rho_{ijk}/\partial \gamma_{ijk} = B_{i:j+m_i(k-1),j+m_i(k-1)} + B_{i:j+m_i(k-1),k+m_i(j-1)} \geq 0$. □

We have the following intermediate result that is useful in our derivations.

**Lemma 1.** Suppose that $\epsilon \in \mathbb{R}^d$ and $\epsilon \sim \mathcal{N}(0, I_d)$. Then for any $d \times d$ matrix $B$, $\mathbb{E}(\epsilon \epsilon' B \epsilon') = B + B' + \text{tr}(B) I_d$, where $I_d$ is an identity matrix and $\text{tr}(\cdot)$ is the trace of matrix.

**Proof.** Without loss of generality, we assume $\epsilon = (\epsilon_1, \ldots, \epsilon_d)'$, so that $\epsilon_i, i = 1, \ldots, d$ are i.i.d standard normal variables, and we have $\mathbb{E}(\epsilon_i^2) = 1$ and $\mathbb{E}(\epsilon_i^4) = 3$. Denote by $B = (b_{ij})_{i,j=1}^d$. Then it is easy to compute

$$\epsilon' B \epsilon = \sum_{m=1}^d \sum_{n=1}^d b_{mn} \epsilon_m \epsilon_n.$$

Thus, the $(i, j)$th element of $\mathbb{E}(\epsilon \epsilon' B \epsilon')$ is given by

$$\mathbb{E}[\epsilon_i \sum_{m=1}^d \sum_{n=1}^d b_{mn} \epsilon_m \epsilon_n] = \begin{cases} 2b_{ii} + \sum_{k=1}^d b_{kk}, & \text{if } i = j, \\ b_{ij} + b_{ji}, & \text{if } i \neq j. \end{cases} \quad (9)$$

Then, it is easy to rewrite (9) in matrix form $\mathbb{E}(\epsilon \epsilon' B \epsilon') = B + B' + \text{tr}(B) I_d$. □

We then compute the score equations below.

**Score equations.** The calculation of $S_1(\beta; \alpha, \lambda)$ is straightforward and is omitted.

To calculate $S_2(\alpha; \beta, \lambda)$ we rewrite the log-likelihood (4) as

$$l(\omega) = -\frac{1}{2} \sum_{i=1}^n \left( \log |D_i^2| + \log |R_i| + \text{tr} \left( R_i^{-1} \tilde{R}_i \right) \right). \quad (10)$$

Since $\rho_i = \text{vecl}(R_i) = (\rho_{ijk}), (1 \leq k < j \leq m_i)$ and $\frac{\partial \log |R_i|}{\rho_{ijk}} = 2(R_i^{-1})_{jk}$, by chain rule we have

$$\frac{\partial \log |R_i|}{\partial \gamma_i} = \sum_{k<j} \left( \frac{\partial \log |R_i|}{\rho_{ijk}} \right) \frac{\partial \rho_{ijk}}{\partial \gamma_i} = 2 \sum_{k<j}(R_i^{-1})_{jk} \frac{\partial \rho_{ijk}}{\partial \gamma_i} = 2 \left( \frac{\partial \rho_i}{\partial \gamma_i} \right)' \text{vecl}(R_i^{-1}),$$
and

\[
\frac{\partial \text{tr} \left( R_i^{-1} \hat{R}_i \right)}{\partial \gamma_i} = \sum_{j,k=1}^{m_i} \frac{\partial \text{tr} \left( R_i^{-1} \hat{R}_i \right)}{\partial R_i^{-1}} \frac{\partial (R_i^{-1})_{jk}}{\partial \gamma_i} = \sum_{j,k=1}^{m_i} (\hat{R}_i)_{jk} \frac{\partial (R_i^{-1})_{jk}}{\partial \gamma_i} = \left( \frac{\partial \rho_i}{\partial \gamma_i} \right)^t \sum_{j,k=1}^{m_i} (\hat{R}_i)_{jk} \frac{\partial (R_i^{-1})_{jk}}{\partial \rho_i}.
\]

(11)

Because \( \frac{\partial (R_i^{-1})_{jk}}{\partial R_i} = \frac{\partial R_i^{-1}}{\partial (R_i^{-1})_{jk}} = -R_i^{-1} E_{jk} R_i^{-1} \), where \( E_{jk} \) is the selection matrix with 1 in its \((j, k)\)th element and zero otherwise, by the definition of \( \rho_i = \text{vecl}(\hat{R}_i) \) we have

\[
\frac{\partial (R_i^{-1})_{jk}}{\partial \rho_i} = -2 \text{vecl}(R_i^{-1} E_{jk} R_i^{-1}).
\]

(12)

Here, the 2 in the right-hand side of (12) is due to a change in an element of \( \rho_i \) affecting two symmetric entries in the matrix \( R_i \). Substituting equation (12) in equation (11), we obtain

\[
\frac{\partial \text{tr} \left( R_i^{-1} \hat{R}_i \right)}{\partial \gamma_i} = -2 \left( \frac{\partial \rho_i}{\partial \gamma_i} \right)^t \sum_{j,k=1}^{m_i} (\hat{R}_i)_{jk} \text{vecl}(R_i^{-1} E_{jk} R_i^{-1}) = -2 \left( \frac{\partial \rho_i}{\partial \gamma_i} \right)^t \text{vecl}(R_i^{-1} \hat{R}_i R_i^{-1}).
\]

Therefore,

\[
\frac{\partial l(\omega)}{\partial \alpha} = -\frac{1}{2} \sum_{i=1}^{n} W_i' \left( \frac{\partial \log |R_i|}{\partial \gamma_i} + \frac{\partial \text{tr} \left( R_i^{-1} \hat{R}_i \right)}{\partial \gamma_i} \right) = \sum_{i=1}^{n} W_i' \left( \frac{\partial \rho_i}{\partial \gamma_i} \right)^t \text{vecl}(R_i^{-1} \hat{R}_i R_i^{-1} - R_i^{-1}),
\]

and this establishes \( S_2(\alpha; \beta, \lambda) \).

To calculate \( S_2(\lambda; \beta, \alpha) \), it is easy to see that \( \frac{\partial \log |D_i^2|}{\partial \lambda} = Z_i' \mathbf{1}_{m_i} \), where \( \mathbf{1}_{m_i} \) is \( m_i \times 1 \) vector with elements 1. Since the parameter \( \lambda \) is only on the diagonal elements of \( D_i \) for \( i = 1, \ldots, n \), by chain rule, we have

\[
\frac{\partial \text{tr} \left( R_i^{-1} D_i^{-1} \nu_i' D_i^{-1} \nu_i \right)}{\partial \lambda} = \sum_{j=1}^{m_i} \left( \frac{\partial \text{tr} \left( R_i^{-1} D_i^{-1} \nu_i' D_i^{-1} \nu_i \right)}{\partial D_i^{-1}} \right)_{jj} \frac{\partial \sigma_i^{-1}}{\partial \lambda} = -\sum_{j=1}^{m_i} (R_i^{-1} D_i^{-1} \nu_i' D_i^{-1})_{jj} \frac{2 \sigma_{ij}}{\sigma_{ij} \partial \lambda}.
\]

\[
= -\sum_{j=1}^{m_i} (R_i^{-1} D_i^{-1} \nu_i' D_i^{-1})_{jj} \frac{\partial \log (\sigma_{ij}^2)}{\partial \lambda} = -Z_i' \text{diag} \left( R_i^{-1} D_i^{-1} \nu_i' D_i^{-1} \right).
\]
Thus
\[
\frac{\partial l(\omega)}{\partial \lambda} = \frac{1}{2} \sum_{i=1}^{n} Z_i' (\text{diag}(R_i^{-1}D_i^{-1}\nu_i\nu_i'D_i^{-1}) - 1_{m_i}),
\]
and we have completed the derivation. \( \square \)

The proof of Proposition 2 and the calculation of the Fisher information matrix. The calculation of \( I_{11}(\omega) \) is trivial. Since \( \Sigma_i, i = 1, \ldots, n \) only depend on \( \alpha \) and \( \lambda \), it is easy to see that \( I_{12}(\omega) = 0 \) and \( I_{13}(\omega) = 0 \).

Recall that \( \eta_i = \text{vecl}(R_i^{-1}\hat{R}_iR_i^{-1} - R_i^{-1}) = (\eta_{ijk}), 1 \leq k < j \leq m_i \). For \( I_{22}(\omega) \), the key is to compute the \( \frac{m(m-1)}{2} \times \frac{m(m-1)}{2} \) matrix \( J_i = \mathbb{E}(\eta_i') \). Since \( \mathbb{E}((R_i^{-1}\hat{R}_iR_i^{-1})_{jk}) = (\mathbb{E}(R_i^{-1}\hat{R}_iR_i^{-1}))_{jk} = (R_i^{-1})_{jk} \), the \( \frac{(2n-k)(k-1)}{2} + j - k, \frac{(2n-s)(s-1)}{2} + l - s \)th element of \( J_i \) for \( 1 \leq k < j \leq m_i, 1 \leq s < l \leq m_i \) is given by
\[
\mathbb{E}(\eta_{ijk}\eta_{ils}) = \mathbb{E} \left[ (R_i^{-1}\hat{R}_iR_i^{-1})_{jk}(R_i^{-1}\hat{R}_iR_i^{-1})_{ls} \right] - a_{ijk}a_{ils},
\]
where \( a_{ijk} \) is the \( (j,k) \)th element of \( R_i^{-1} \). Denote by \( \epsilon_i = R_i^{-1/2}D_i^{-1/2}\nu_i \) so that \( \epsilon_i \sim \mathcal{N}(0, I_{m_i}) \) and \( R_i^{-1}\hat{R}_iR_i^{-1} = R_i^{-1/2}\epsilon_i\epsilon_i'R_i^{-1/2} \). Let \( T_{ij} \) be the \( j \)th column of \( R_i^{-1/2} \). We have \( T_{ij}'T_{ik} = a_{ijk} \), and \( (R_i^{-1}\hat{R}_iR_i^{-1})_{jk} = T_{ij}'\epsilon_i\epsilon_i'T_{ik} \).

Thus
\[
\mathbb{E} \left[ (R_i^{-1}\hat{R}_iR_i^{-1})_{jk}(R_i^{-1}\hat{R}_iR_i^{-1})_{ls} \right] = T_{ij}'\mathbb{E}((\epsilon_i\epsilon_i'T_{ik}T_{il}'\epsilon_i\epsilon_i')T_{is}) - a_{ijk}a_{ils} = a_{ijkl}a_{iks} + a_{ijsla_{ikl}},
\]
and this proves the first part of Proposition 2.

Similarly, recall that \( \phi_i = h_i - 1_{m_i} = (\phi_{il}), 1 \leq l \leq m_i \), where \( h_i = \text{diag}(R_i^{-1}D_i^{-1}\nu_i\nu_i'D_i^{-1}) \). Then for \( I_{23}(\omega) \), the key is to compute the \( \frac{m(m-1)}{2} \times m_i \) matrix \( H_i = \mathbb{E}(\eta_i\phi_i') \). Since \( \mathbb{E}(h_i) = 1_{m_i} \), the \( \frac{(2n-k)(k-1)}{2} + j - k, 1 \leq l \leq m_i \)th element of \( H_i \) for \( 1 \leq k < j \leq m_i, 1 \leq l \leq m_i \) is given by
\[
\mathbb{E}(\eta_{ijk}\phi_{il}) = \mathbb{E} \left[ (R_i^{-1}\hat{R}_iR_i^{-1})_{jk}(R_i^{-1}\hat{R}_i)_{il} \right] - a_{ijk}.
\]
Note \( R_i^{-1}D_i^{-1}\nu_i\nu_i'D_i^{-1} = R_i^{-1/2}\epsilon_i\epsilon_i'R_i^{-1/2} \), and denote by \( P_{ij} \) the \( j \)th column of \( R_i^{-1/2} \). We have \( P_{ij}'P_{ik} = \rho_{ijk} \), \( T_{ij}'P_{ik} = \delta_{jk} \), and \( (R_i^{-1}\hat{R}_i)_{il} = T_{il}'\epsilon_i\epsilon_i'P_{il} \). Thus
\[
\mathbb{E} \left[ (R_i^{-1}\hat{R}_iR_i^{-1})_{jk}(R_i^{-1}\hat{R}_i)_{il} \right] = T_{ij}'\mathbb{E}((\epsilon_i\epsilon_i'T_{ik}T_{il}'\epsilon_i\epsilon_i')P_{il}).
\]
By using Lemma 1 we have

$$
\mathbb{E}(\eta_{ijk}\phi_{jl}) = T_{ij}'T_{ik}T_{il}'P_{il} + T_{ij}'T_{il}T_{ik}'P_{il} + T_{ij}'\text{tr}(T_{ik}T_{il}')P_{il} - a_{ijk} = a_{ijl}\delta_{jl} + a_{ilk}\delta_{kl}.
$$

This completes the proof of Proposition 2.

For $I_{33}(\omega)$, the key is to compute the $m_i \times m_i$ matrix $\mathbb{E}(\phi_i\phi_i')$. According to the proof above, the $(j,k)$th element of $\mathbb{E}(\phi_i\phi_i')$ for $j,k = 1, \ldots, m_i$ can be calculated as

$$
\mathbb{E}(\phi_{ij}\phi_{ik}) = \mathbb{E}\left[ (R_{i}^{-1}\hat{R}_{i})_{jj}(R_{i}^{-1}\hat{R}_{i})_{kk} \right] - 1,
$$

and

$$
\mathbb{E}\left[ (R_{i}^{-1}\hat{R}_{i})_{jj}(R_{i}^{-1}\hat{R}_{i})_{kk} \right] = T_{ij}'\mathbb{E}(\epsilon_i\epsilon_i'P_{ij}T_{ik}'\epsilon_i\epsilon_i')P_{ik}.
$$

Similarly, using Lemma 1 we have

$$
\mathbb{E}(\phi_{ij}\phi_{ik}) = T_{ij}'P_{ij}T_{ik}'P_{ik} + T_{ij}'T_{ik}P_{ij}'P_{ik} + T_{ij}'\text{tr}(P_{ij}T_{ik}')P_{ik} - 1 = a_{ijk}\rho_{ijk} + \delta_{jk}.
$$

Thus, we have $\mathbb{E}(\phi_i\phi_i') = R_{i}^{-1} \circ R_{i} + I_{m_i}$, where $\circ$ denotes the Hadamard product.

Proof of Theorem 1. The proof follows standard steps under the regularity conditions; we omit the details here.