Analysis of multivariate growth curves with covariates

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1. Introduction

Suppose that $m$ response variables $x_1, \ldots, x_m$ have been measured at $p$ different occasions (or treatments) on each of $N$ individuals, and each individual belongs to one of $k$ groups. Let $x_{jg}$ be an $mp$-vector of measurements on the $j$-th individual in the $g$-th group arranged as

$$x_{jg} = (x_{j1}, \ldots, x_{jg}, \ldots, x_{jm})',$$

and assume that $x_{jg}$'s are independently distributed as $N_{mp}(\mu_{jg}, \Omega)$, where $\Omega$ is an unknown $mp \times mp$ positive definite matrix, $j=1, \ldots, N_p, g=1, \ldots, k$. Further, we assume that mean profiles of $x_{jg}$ are $m$-variate growth curves with $r$ covariates, i.e.,

$$\mu_{jg} = (B' \otimes I_m)\xi_{jg} + \Theta'c_{jg},$$

where $B$ is a $q \times p$ within-individual design matrix of rank $q(\leq p)$, $B' \otimes I_m$ is the Kronecker product of $B'$ and the $m \times m$ identity matrix, $c_{jg}$'s are $r$-vectors of observations of covariates, $\xi_{jg}$'s are $mq$-vectors of unknown parameters, $\Theta$ is an unknown $r \times mp$ parameter matrix. Let

$$X = [x_{1}^{(1)}, \ldots, x_{1}^{(g)}, \ldots, x_{q}^{(1)}, \ldots, x_{q}^{(k)}]', \quad N = N_1 + \cdots + N_k.$$ 

Then the model of $X$ can be written as

$$X \sim N_{N \times mp}(A \Xi (B' \otimes I_m) + C \Theta, \Omega \otimes I_m),$$

where

$$A = \begin{pmatrix} 1_{n_1} & 0 \\ \vdots & \ddots \\ 0 & 1_{n_k} \end{pmatrix}$$

is an $N \times k$ between-individual design matrix, $1_n$ is an $n$-vector of ones, $C = [c_{1}^{(1)}, \ldots, c_{n_1}^{(1)}; \ldots; c_{1}^{(k)}, \ldots, c_{n_k}^{(k)}]'$ is a fixed $N \times r$ matrix of covariates, rank $[A, C] = k + r(\leq N - p)$, $\Xi = [\xi_{1}^{(1)}, \ldots, \xi_{k}^{(1)}]'$ is an unknown $k \times mq$ parameter matrix. Without loss of generality, we may assume that
BB’ = I_q. In fact, if BB’ ≠ I_q, we may replace $E$ and $B$ by $E((BB')^{-t} \otimes I_m)$ and $(BB')^{-t}B$, respectively. The mean structure of (1.2) is a mixed MANOVA-GMANOVA model, and the GMANOVA portion is an extension of Potthoff and Roy [3] to the multiple-response case.

This paper is concerned with a family of multivariate random-effects covariance structures

$$\Omega_s = (B_s, B_s \otimes I_m) A_s (B_s \otimes I_m) + I_p \otimes \Sigma_s, \quad 0 \leq s \leq q,$$

(1.3)

which is naturally introduced by assuming that the first $ms$ columns of $E$ are random, where $A_s$ and $\Sigma_s$ are arbitrary $ms \times ms$ positive semi-definite and $m \times m$ positive definite matrices respectively, $B_s$ is the matrix which is composed of the first $s$ rows of $B$. The covariance structure (1.3) is based on the following model with differing numbers of random effects (see Lange and Laird [2]):

$$x_s^{(p)} = \mu^{(p)} + (B_s \otimes I_m) \eta^{(p)} + \epsilon^{(p)}, \quad 0 \leq s \leq q,$$

(1.4)

where $\mu^{(p)}$ is defined in (1.1), $\eta^{(p)}$ is an $ms$-vector of random effects distributed as $N_{ms}(0, A_s)$, $\epsilon^{(p)}$ is an $mp$-vector of random errors distributed as $N_{mp}(0, I_p \otimes \Sigma_s)$, $\eta^{(p)}$'s and $\epsilon^{(p)}$'s are mutually independent. Then, from (1.4) it is seen that

$$V(x_s^{(p)}) = (B_s \otimes I_m) A_s (B_s \otimes I_m) + I_p \otimes \Sigma_s (-\Omega_s).$$

This implies that

$$X \sim N_{N \times mp}(A \otimes (B \otimes I_m) + C \Theta, \Omega_s \otimes I_n).$$

(1.5)

A test statistic for testing $H_{0s} : \Omega = \Omega_s$ vs. $H_{1s} : \Omega \neq \Omega_s$ in the model (1.2) has been proposed by Yokoyama [5]. In this paper we propose test statistics for the hypotheses

$$H_{01} : A_s = 0 \quad \text{vs.} \quad H_{11} : A_s \neq 0$$

(1.6)

and

$$H_{02} : FSE_{ms} K = 0 \quad \text{vs.} \quad H_{12} : FSE_{ms} K \neq 0$$

(1.7)

in the model (1.5), where $F$ and $K$ are some known $d \times k$ and $ms \times l$ matrices of rank $F = d(\leq k)$ and rank $K = l(\leq ms)$ respectively, $SE_{ms}$ is the matrix which is composed of the first $ms$ columns of $E$. The null hypothesis $H_{0i}$ means that random effects on the elements of $SE_{ms}$ are absent.

2. Canonical reduction

In order to transform (1.5) to a model which is easier to analyze, we use a canonical
reduction. Let $B = [B_1, B_2]^T$, and let $ar{B}$ be a $(p-q) \times p$ matrix such that $\bar{B} B = I_{p-q}$ and $B \bar{B} = 0$. Then $G = [B_1, B_2, B_2]^T = [G_1, G_2, G_3]^T = [\phi^{(1)}, ..., \phi^{(q)} , \phi^{(p-q)}, \phi^{(p-q)}, ..., \phi^{(p-q)}]$ is an orthogonal matrix of order $p$, and $Q = G \otimes I_n = [Q_1, Q_2, Q_3]^T = [Q^{(1'y)}, ..., Q^{(q'y)}, Q^{(p-q'y)}, Q^{(p-q'y)}, ..., Q^{(p-q'y)}]$ is an orthogonal matrix of order $mp$. Further, let $H = [H_1, H_2]$ be an orthogonal matrix of order $N$ such that $H_1$ is an orthonormal basis matrix on the space spanned by the column vectors of $C$. Then, letting $Y = H_1 X Q' = [Y_1, Y_2, Y_3] = [Y_1^{(1)}, ..., Y_1^{(q)}, Y_2^{(1)}, ..., Y_2^{(p-q)}, Y_3^{(1)}, ..., Y_3^{(p-q)}]$ and $Y_i = Y_{11} = [Y_1^{(1)}, ..., Y_1^{(q)}, Y_2^{(1)}, ..., Y_2^{(p-q)}, Y_3^{(1)}, ..., Y_3^{(p-q)}]$ the model (1.5) can be reduced to a canonical form

$$H' X Q' = \begin{bmatrix} Z \\ Y_{111} \\ Y_{2} \end{bmatrix} \sim N_{n \times mp} \left( \begin{bmatrix} \mu \\ \bar{A} \Sigma \end{bmatrix}, \Psi \otimes I_n \right),$$

(2.1)

where $\mu = H_1 A [\varepsilon, 0] + H_1 C \Theta Q', \bar{A} = H_2 A$,

$$\Psi = Q \Theta Q' = \begin{bmatrix} \Psi_{11} \\ 0 \\ 0 \\ I_{p-q} \otimes \Sigma \end{bmatrix}$$

and $\Psi_{11} - I_{p-q} \otimes \Sigma = \Lambda_2 \geq 0$.

(2.2)

3. Test for $H_{01}$

In this section we consider the likelihood ratio (=LR) test for the hypothesis (1.6) under the model (2.1) instead of the model (1.5). Since $\mu$ in (2.1) is a free parameter matrix, for testing the hypothesis (1.6) we may consider the LR test formed by only the density of $Y$. The model for $Y$ is

$$Y \sim N_{n \times mp} ([\bar{A} \varepsilon, 0], \Psi \otimes I_n),$$

(3.1)

where $n = N - r$. It is easily seen the maximum likelihood estimator of $\varepsilon$ under $H_{01}$ (or $H_{11}$) is given by $\hat{\varepsilon} = (\bar{A}' \bar{A})^{-1} \bar{A}' Y_{111}$. Let $L(\varepsilon, \Psi_{11}, \Sigma)$ be the likelihood function of $Y$. Then we have

$$g(\Psi_{11}, \Sigma) = -2 \log L(\hat{\varepsilon}, \Psi_{11}, \Sigma)$$

$$= n \log |\Psi_{11}| + \text{tr} \Psi_{11}^2 S_{11} + n(p-s) \log |\Sigma| + \text{tr} \Sigma^{-1} \left( \sum_{i=1}^{p-q} S_{1i}^{(i'y)} + \sum_{j=1}^{p-q} Y_j^{(i'y)} Y_j^{(i'y)} \right),$$

and

$$\min_{\psi_{11}} g(\Psi_{11}, \Sigma) = n p \log \left| \frac{1}{np} \left( \sum_{i=1}^{p-q} S_{1i}^{(i'y)} + \sum_{j=1}^{p-q} Y_j^{(i'y)} Y_j^{(i'y)} \right) \right| + nmp,$$

(3.2)

where
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\[ S = Y'[I_n - \bar{A}(\bar{A}'\bar{A})^{-1}\bar{A}']Y = \begin{pmatrix} S_{11} & S_{12} & S_{13} \\ S_{21} & S_{22} & S_{23} \\ S_{31} & S_{32} & S_{33} \end{pmatrix}, \quad S_{11(12)} = \begin{pmatrix} S_{11} & S_{12} \\ S_{21} & S_{22} \end{pmatrix} \]

and \( S_{sd}^{(0)} = Y_d^{(0)}[I_n - \bar{A}(\bar{A}'\bar{A})^{-1}\bar{A}']Y_d^{(0)} \). However, since the minimum of \( g(\Psi_{11}, \Sigma_e) \) under \( H_{11} \) is complicated (see Yokoyama [5]), we consider the minimization of \( g(\Psi_{11}, \Sigma_e) \) under the assumption that \( \Psi_{11} \) is arbitrary positive definite instead of the restriction that \( \Psi_{11} \geq L_e \otimes \Sigma_e \). The minimum is given by

\[
\begin{align*}
\min g(\Psi_{11}, \Sigma_e) &= n \log \left| \frac{1}{n} S_{11} \right| \\
&+ n(p-s) \log \left| \frac{1}{n(p-s)} \left( \sum_{i=1}^{p-s} S^{(0)}_{ii} + \sum_{j=1}^{p-s} Y_d^{(0)}Y_d^{(0)} \right) \right| + nmp.
\end{align*}
\]

(3.3)

Therefore, from (3.2) we can suggest a test statistic

\[
\bar{A}_1 = \frac{|S_{11}|}{\frac{1}{p-s} \left( \frac{\sum_{i=1}^{p-s} S^{(0)}_{ii}}{\sum_{j=1}^{p-s} Y_d^{(0)}Y_d^{(0)}} \right)^{p-s}} \left[ \frac{1}{p} \left( \sum_{i=1}^{p-s} S^{(0)}_{ii} + \sum_{j=1}^{p-s} Y_d^{(0)}Y_d^{(0)} \right) \right]^p
\]

(3.4)

for testing \( H_0 \) vs. \( H_{11} \). Here we note that the statistic \( \bar{A}_1 \) is the LR statistic for \( \Psi_{11} = I_e \otimes \Sigma_e \).

The statistic \( \bar{A}_1 \) can be expressed in terms of the original observations, using

\[
Y_d^{(0)}Y_d^{(0)} = Q^{(0)}D_{xx-c}Q^{(0)}', \quad S_{11} = QD_{xx-c}Q', \quad S_{sd}^{(0)} = Q_d^{(0)}D_{xx-c}Q_d^{(0)}',
\]

(3.5)

where \( D_{xx-c} = D_{xx} - D_{xc}D_{cc}^{-1}D_{cx}, \ D_{xx-c} = D_{xx} - D_{xx-c}D_{cc}^{-1}D_{xx-c} \) and

\[
D = [X, C, A], D = \begin{pmatrix} D_{xx} & D_{xc} & D_{xa} \\ D_{cx} & D_{cc} & D_{ca} \\ D_{ax} & D_{ac} & D_{aa} \end{pmatrix}.
\]

(3.6)

Lemma. When the hypothesis \( H_0 \) is true, the \( h \)-th moment of \( \bar{A}_1 \) is

\[
E(\bar{A}_1^h) = \binom{m+n}{h} \frac{\Gamma_n\left(\frac{1}{2}(n-k)+h\right)}{\Gamma_n\left(\frac{1}{2}(n-k)\right)} \times \frac{\Gamma_n\left(\frac{1}{2}(m(p-s)-k(q-s))+(p-s)h\right)}{\Gamma_n\left(\frac{1}{2}(m(p-s)-k(q-s))\right)} \frac{\Gamma_n\left(\frac{1}{2}(np-kq)+ph\right)}{\Gamma_n\left(\frac{1}{2}(np-kq)\right)}
\]

\[
\times \frac{\Gamma_n\left(\frac{1}{2}(n(p-s)-k(q-s))+(p-s)h\right)}{\Gamma_n\left(\frac{1}{2}(n(p-s)-k(q-s))\right)} \frac{\Gamma_n\left(\frac{1}{2}(np-kq)+ph\right)}{\Gamma_n\left(\frac{1}{2}(np-kq)\right)},
\]

where \( m, n, p, q \) are the appropriate dimensions.
where $\Gamma_n(\cdot)$ is the multivariate gamma function defined by $\Gamma_n(n/2) = \pi^{n(n-1)/4} \prod_{i=1}^n \Gamma((n-j+1)/2)$.

**Proof.** The statistic $\bar{A}_1$ can be written as

$$\bar{A}_1 = \frac{1}{\left| S_{11} \right|} \frac{1}{p-s} \left( \frac{\sum_{i=1}^{p-s} Y_{\hat{y}_i}^o}{\sum_{i=1}^{p-s} Y_{\hat{y}_i}^o + \sum_{i=1}^{p-s} Y_{\hat{y}_i}^o} \right)^{p-s}.$$

Under $H_0$, it is easy to verify that $S_{11}$, $S_2$ and $Y_3 Y_5$ are independently distributed as Wishart distributions $W_{m(s)}(n-k, I_s \otimes \Sigma_s)$, $W_{m(s-q)}(n-k, I_q \otimes \Sigma_q)$ and $W_{m(p-q)}(n, I_{p-q} \otimes \Sigma_s)$, respectively. From this, the $h$-th moment of $\bar{A}_1$ can be obtained.

Using the above lemma, we can obtain an asymptotic expansion of the null distribution of statistic $-n\rho_1 \log \bar{A}_1$ by expanding its characteristic function.

**Theorem.** When the hypothesis $H_0$ is true, an asymptotic expansion of the distribution function of statistic $-n\rho_1 \log \bar{A}_1$ is

$$P(-n\rho_1 \log \bar{A}_1 \leq x) = P(\chi^2_s \leq x) + O(M^{-2})$$

for large $M = n\rho_1$, where $f_1 = \frac{1}{2} ms (ms + 1)$ and $\rho_1$ is defined by

$$f_1 n(1-\rho_1) = \frac{1}{12} ms \left\{ 6(ms+1)k + 2m^2s^2 + 3ms - 1 \right\}$$

$$+ \frac{1}{(p-s)p} \left\{ 6(p-q)^2k^2 - 6(m+1)(p-q)k + 2m^2 + 3m - 1 \right\}.$$

In a special case $q = p$,

$$\rho_1 = 1 - \frac{1}{n} \left\{ \frac{k + (2m^2s^2 + 3ms - 1)(p-s)p + 2m^2 + 3m - 1)}{6(ms+1)(p-s)p} \right\}.$$

Next we consider the exact LR criterion $\Lambda^2$ for $H_0$ vs. $H_{11}$, based on the distribution of $Y$. Let

$$\hat{\Lambda}_{11} = \frac{1}{n} S_{11}, \quad \hat{S}_2 = \frac{1}{n(p-s)} \left( \sum_{i=1}^{p-s} Y_{\hat{y}_i}^o + \sum_{i=1}^{p-s} Y_{\hat{y}_i}^o Y_{\hat{y}_i}^o \right).$$

For the case $\hat{\Lambda}_{11} - I_2 \otimes \hat{S}_2 \geq 0$, the LR statistic $\Lambda_1$ is equal to $\hat{A}_1$. However, if it is not the case, $\Lambda_1$ becomes very complicated. As a simple bound for $\Lambda_1$, consider
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Then we have \( \bar{\Lambda}_1 = \Lambda_1 \leq \Lambda_1 \). We note that \( \Lambda_1 \) agrees with \( \bar{\Lambda}_1 \) in the case \( m = s = 1 \).

4. Test for \( H_{02} \)

In this section we consider the LR test for the hypothesis (1.7), based on the distribution of \( Y \). Let \( \mathcal{E} = [\mathcal{E}_{ms}, \mathcal{E}_{mm}] \). Then, from (3.1) we have

\[
Y_1 \sim N_{n \times ms} (\bar{\Lambda} \mathcal{E}_{ms}, \mathcal{E}_{II} \otimes I_n),
\]

\[
Y_{2II} \sim N_{n \times ms} (\bar{\Lambda} \mathcal{E}_{ms}, (I_{n \times k} \otimes \mathcal{E}_k) \otimes I_n).
\]

Since \( Y_1 \) and \( Y_{2II} \) are independent and all information about \( \mathcal{E}_{ms} \) is contained in \( Y_1 \), we may start from the model for \( Y_1 \). Here we assume again that \( \mathcal{E}_I \) is arbitrary positive definite. Using a well-known technique in a general MANOVA model (see, e.g., Gleser and Olkin [1]), we can suggest a test statistic

\[
\tilde{\Lambda}_2 = |I_1 + V_n V_{\epsilon}^{-1}|^{-1}
\]

for testing \( H_{02} \) vs. \( H_{12} \), where \( V_{\epsilon} = K' S_{11} K \),

\[
V_n = K' \hat{\mathcal{E}}_{ms} F' (F\hat{A}' \hat{A})^{-1} F')^{-1} \hat{\mathcal{E}}_{ms} K, \quad \hat{\mathcal{E}}_{ms} = (\hat{A}' \hat{A})^{-1} \hat{A}' Y_1.
\]

The statistic \( \tilde{\Lambda}_2 \) can be also expressed in terms of the original observations, using

\[
S_{11} = Q_1 D_{xx-c} Q_1', \quad \hat{A}' \hat{A} = D_{aa-c}, \quad \hat{E}_{ms} = D_{aa-1} D_{xx-c} Q_1.
\]

where the submatrices of the matrix \( D \) are defined in (3.6). Under \( H_{02} \), it is easy to verify that \( V_{\epsilon} \) and \( V_n \) are independently distributed as \( W_1(n - k, K' \mathcal{E}_I K) \) and \( W_1(d, K' \mathcal{E}_I K) \), respectively. Therefore, the \( h \)-th moment of \( \tilde{\Lambda}_2 \) is obtained from that \( \tilde{\Lambda}_2 \) is distributed as a lambda distribution \( \Lambda_1(d, n - k) \) and is given by

\[
E(\tilde{\Lambda}_2^h) = \frac{\Gamma\left(\frac{1}{2}(n - k) + h\right) \Gamma\left(\frac{1}{2}(n - k + d)\right)}{\Gamma\left(\frac{1}{2}(n - k)\right) \Gamma\left(\frac{1}{2}(n - k + d) + h\right)}
\]

The null distribution of statistic \( -n \rho_2 \log \tilde{\Lambda}_2 \) has an approximate chi-squared distribution with degrees of freedom \( \rho_2 = dl \). For an asymptotic expansion of the distribution function of the statistic, see, e.g., Siotani, Hayakawa and Fujikoshi [4, p. 250].
References


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