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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 $x_j^{(g)}$ be an mp-vector of measurements on the j-th individual in the g-th group arranged as

$$x_j^{(g)}=(x_{11j}^{(g)}, \ldots, x_{1mj}^{(g)}, \ldots\ldots, x_{p1j}^{(g)}, \ldots, x_{pmj}^{(g)})',$$

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

$$\mu_j^{(g)}=(B'\otimes I_m)\xi^{(g)}+\Theta' c_j^{(g)}, \tag{1.1}$$

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, $c_j^{(g)}$'s are r-vectors of observations of covariates, $\xi^{(g)}$'s are mq-vectors of unknown parameters, Θ is an unknown $r\times mp$ parameter matrix. Let

$$X=[x_1^{(1)}, \ldots, x_{N_1}^{(1)}, \ldots\ldots, x_1^{(k)}, \ldots, x_{N_k}^{(k)}]', \quad N=N_1+\cdots+N_k.$$

Then the model of X can be written as

$$X \sim N_{N\times mp}(A\Xi(B\otimes I_m)+C\Theta, \Omega\otimes I_N), \tag{1.2}$$

where

$$A=\begin{pmatrix} 1_{N_1} & & 0 \\ & \ddots & \\ 0 & & 1_{N_k} \end{pmatrix}$$

is an $N\times k$ between-individual design matrix, 1_n is an n-vector of ones, $C=[c_1^{(1)}, \ldots, c_{N_1}^{(1)}, \ldots\ldots, c_1^{(k)}, \ldots, c_{N_k}^{(k)}]'$ is a fixed $N\times r$ matrix of covariates, rank $[A, C]=k+r(\leq N-p)$, $\Xi=[\xi^{(1)}, \ldots, \xi^{(k)}]'$ is an unknown $k\times mq$ parameter matrix. Without loss of generality, we may assume that

$BB'=I_q$. In fact, if $BB'\neq I_q$, we may replace Ξ and B by $\Xi((BB')^{1/2}\otimes I_m)$ and $(BB')^{-1/2}B$, 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

$$\Omega_s=(B_s'\otimes I_m)\Delta_s(B_s\otimes I_m)+I_p\otimes\Sigma_s,\quad 0\leq s\leq q, \tag{1.3}$$

which is naturally introduced by assuming that the first ms columns of Ξ are random, where Δ_s and Σ_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]):

$$x_j^{(g)}=\mu_j^{(g)}+(B_s'\otimes I_m)\eta_j^{(g)}+\varepsilon_j^{(g)},\quad 0\leq s\leq q, \tag{1.4}$$

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

$$V(x_j^{(g)})=(B_s'\otimes I_m)\Delta_s(B_s\otimes I_m)+I_p\otimes\Sigma_s(=\Omega_s).$$

This implies that

$$X\sim N_{N\times mp}(A\Xi(B\otimes I_m)+C\Theta,\ \Omega_s\otimes I_N). \tag{1.5}$$

A test statistic for testing $H_{0s}:\Omega=\Omega_s$ vs. $H_{1s}:\text{not}H_{0s}$ in the model (1.2) has been proposed by Yokoyama [5]. In this paper we propose test statistics for the hypotheses

$$H_{01}:\Delta_s=0 \text{ vs. } H_{11}:\Delta_s\neq 0 \tag{1.6}$$

and

$$H_{02}:F\Xi_{ms}K=0 \text{ vs. } H_{12}:F\Xi_{ms}K\neq 0 \tag{1.7}$$

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, Ξ_{ms} is the matrix which is composed of the first ms columns of Ξ. The null hypothesis H_{01} means that random effects on the elements of Ξ_{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 $B=[B_s', B_{\bar{s}}']'$, and let $\bar{B}$ be a $(p-q)\times p$ matrix such that $\bar{B}\bar{B}'=I_{p-q}$ and $B\bar{B}'=0$. Then $G=[B_s', B_{\bar{s}}', \bar{B}']'=[G_1', G_2', G_3']'=[g_1^{(1)}, ..., g_1^{(s)}, g_2^{(1)}, ..., g_2^{(q-s)}, g_3^{(1)}, ..., g_3^{(p-q)}]'$ is an orthogonal matrix of order p, and $Q=G\otimes I_m=[Q_1', Q_2', Q_3']'=[Q_1^{(1)\prime}, ..., Q_1^{(s)\prime}, Q_2^{(1)\prime}, ..., Q_2^{(q-s)\prime}, Q_3^{(1)\prime}, ..., Q_3^{(p-q)\prime}]'$ 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 $Y=H_2'XQ'=[Y_1, Y_2, Y_3]=[Y_1^{(1)}, ..., Y_1^{(s)}, Y_2^{(1)}, ..., Y_2^{(q-s)}, Y_3^{(1)}, ..., Y_3^{(p-q)}]$ and $[Y_1, Y_2]=Y_{(12)}=[Y_{(12)}^{(1)}, ..., Y_{(12)}^{(q)}]$, the model (1.5) can be reduced to a canonical form

$$H'XQ'=\begin{bmatrix} Z & \\ Y_{(12)} & Y_3 \end{bmatrix}\sim N_{N\times mp}\left(\begin{bmatrix} \mu & \\ \tilde{A}\Xi & 0 \end{bmatrix}, \Psi\otimes I_N\right), \tag{2.1}$$

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

$$\Psi=Q\Omega_sQ'=\begin{pmatrix} \Psi_{11} & 0 \\ 0 & I_{p-s}\otimes\Sigma_s \end{pmatrix} \text{ and } \Psi_{11}-I_s\otimes\Sigma_s=\Delta_s\geq 0. \tag{2.2}$$

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 μ 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

$$Y\sim N_{n\times mp}([\tilde{A}\Xi, 0], \Psi\otimes I_n), \tag{3.1}$$

where $n=N-r$. It is easily seen the maximum likelihood estimator of Ξ under H_{01} (or H_{11}) is given by $\hat{\Xi}=(\tilde{A}'\tilde{A})^{-1}\tilde{A}'Y_{(12)}$. Let $L(\Xi, \Psi_{11}, \Sigma_s)$ be the likelihood function of Y. Then we have

$$\begin{aligned} g(\Psi_{11}, \Sigma_s)&=-2\log L(\hat{\Xi}, \Psi_{11}, \Sigma_s) \\ &=n\log|\Psi_{11}|+\mathrm{tr}\,\Psi_{11}^{-1}S_{11}+n(p-s)\log|\Sigma_s|+\mathrm{tr}\Sigma_s^{-1}\left(\sum_{i=1}^{q-s}S_{22}^{(ii)}+\sum_{j=1}^{p-q}Y_3^{(j)\prime}Y_3^{(j)}\right), \end{aligned}$$

and

$$\min_{H_{01}} g(\Psi_{11}, \Sigma_s)=np\log\left|\frac{1}{np}\left(\sum_{i=1}^{q}S_{(12)(12)}^{(ii)}+\sum_{j=1}^{p-q}Y_3^{(j)\prime}Y_3^{(j)}\right)\right|+nmp, \tag{3.2}$$

where

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

and $S_{aa}^{(ii)}=Y_a^{(i)\prime}[I_n-\tilde{A}(\tilde{A}'\tilde{A})^{-1}\tilde{A}']Y_a^{(i)}$. However, since the minimum of $g(\Psi_{11}, \Sigma_s)$ under H_{11} is complicated (see Yokoyama [5]), we consider the minimization of $g(\Psi_{11}, \Sigma_s)$ under the assumption that Ψ_{11} is arbitrary positive definite instead of the restriction that $\Psi_{11}\geq I_s\otimes\Sigma_s$. The minimum is given by

$$\begin{aligned}\min g(\Psi_{11}, \Sigma_s)&=n\log\left|\frac{1}{n}S_{11}\right| \\ &+n(p-s)\log\left|\frac{1}{n(p-s)}\left(\sum_{i=1}^{q-s}S_{22}^{(ii)}+\sum_{j=1}^{p-q}Y_3^{(j)\prime}Y_3^{(j)}\right)\right|+nmp. \end{aligned} \tag{3.3}$$

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

$$\tilde{\Lambda}_1=\frac{|S_{11}|\left|\frac{1}{p-s}\left(\sum_{i=1}^{q-s}S_{22}^{(ii)}+\sum_{j=1}^{p-q}Y_3^{(j)\prime}Y_3^{(j)}\right)\right|^{p-s}}{\left|\frac{1}{p}\left(\sum_{i=1}^{q}S_{(12)(12)}^{(ii)}+\sum_{j=1}^{p-q}Y_3^{(j)\prime}Y_3^{(j)}\right)\right|^{p}} \tag{3.4}$$

for testing H_{01} vs. H_{11}. Here we note that the statistic $\tilde{\Lambda}_1$ is the LR statistic for $\Psi_{11}=I_s\otimes\Sigma_s$. The statistic $\tilde{\Lambda}_1$ can be expressed in terms of the original observations, using

$$Y_3^{(j)\prime}Y_3^{(j)}=Q_3^{(j)}D_{xx\cdot c}Q_3^{(j)\prime}, \quad S_{11}=Q_1D_{xx\cdot ca}Q_1', \quad S_{aa}^{(ii)}=Q_a^{(i)}D_{xx\cdot ca}Q_a^{(i)\prime}, \tag{3.5}$$

where $D_{xx\cdot c}=D_{xx}-D_{xc}D_{cc}^{-1}D_{cx}$, $D_{xx\cdot ca}=D_{xx\cdot c}-D_{xa\cdot c}D_{aa\cdot c}^{-1}D_{ax\cdot c}$ and

$$D=[X, C, A]'[X, C, A]=\begin{pmatrix} D_{xx} & D_{xc} & D_{xa} \\ D_{cx} & D_{cc} & D_{ca} \\ D_{ax} & D_{ac} & D_{aa} \end{pmatrix}. \tag{3.6}$$

Lemma. *When the hypothesis H_{01} is true, the h-th moment of $\tilde{\Lambda}_1$ is*

$$\begin{aligned} E(\tilde{\Lambda}_1^h)&=\frac{p^{mph}}{(p-s)^{m(p-s)h}}\frac{\Gamma_{ms}\left(\frac{1}{2}(n-k)+h\right)}{\Gamma_{ms}\left(\frac{1}{2}(n-k)\right)} \\ &\times\frac{\Gamma_m\left(\frac{1}{2}\{n(p-s)-k(q-s)\}+(p-s)h\right)\Gamma_m\left(\frac{1}{2}(np-kq)\right)}{\Gamma_m\left(\frac{1}{2}\{n(p-s)-k(q-s)\}\right)\Gamma_m\left(\frac{1}{2}(np-kq)+ph\right)}, \end{aligned}$$

where $\Gamma_m(\cdot)$ *is the multivariate gamma function defined by* $\Gamma_m(n/2)=\pi^{m(m-1)/4}\prod_{j=1}^{m}\Gamma((n-j+1)/2)$.

proof. The statistic $\tilde{\Lambda}_1$ can be written as

$$\tilde{\Lambda}_1=\frac{|S_{11}|\left|\frac{1}{p-s}\left(\sum_{i=1}^{q-s}S_{22}^{(ii)}+\sum_{j=1}^{p-q}Y_3^{(j)\prime}Y_3^{(j)}\right)\right|^{p-s}}{\left|\frac{1}{p}\left(\sum_{i=1}^{s}S_{11}^{(ii)}+\sum_{i=1}^{q-s}S_{22}^{(ii)}+\sum_{j=1}^{p-q}Y_3^{(j)\prime}Y_3^{(j)}\right)\right|^{p}}.$$

Under H_{01}, it is easy to verify that S_{11}, S_{22} and $Y_3'Y_3$ are independently distributed as Wishart distributions $W_{ms}(n-k, I_s\otimes\Sigma_s)$, $W_{m(q-s)}(n-k, I_{q-s}\otimes\Sigma_s)$ and $W_{m(p-q)}(n, I_{p-q}\otimes\Sigma_s)$, respectively. From this, the h-th moment of $\tilde{\Lambda}_1$ can be obtained.

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

Theorem. *When the hypothesis* H_{01} *is true, an asymptotic expansion of the distribution function of statistic* $-n\rho_1\log\tilde{\Lambda}_1$ *is*

$$P(-n\rho_1\log\tilde{\Lambda}_1\leq x)=P(\chi^2_{f_1}\leq x)+O(M^{-2})$$

for large $M=n\rho_1$, *where* $f_1=\frac{1}{2}ms(ms+1)$ *and* ρ_1 *is defined by*

$$f_1n(1-\rho_1)=\frac{1}{12}ms\Big\{6(ms+1)k+2m^2s^2+3ms-1$$
$$+\frac{1}{(p-s)p}\{6(p-q)^2k^2-6(m+1)(p-q)k+2m^2+3m-1\}\Big\}.$$

In a special case $q=p$,

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

Next we consider the exact LR criterion $\Lambda_1^{n/2}$ for H_{01} vs. H_{11}, based on the distribution of Y. Let

$$\hat{\Psi}_{11}=\frac{1}{n}S_{11},\quad \hat{\Sigma}_s=\frac{1}{n(p-s)}\left(\sum_{i=1}^{q-s}S_{22}^{(ii)}+\sum_{j=1}^{p-q}Y_3^{(j)\prime}Y_3^{(j)}\right).$$

For the case $\hat{\Psi}_{11}-I_s\otimes\hat{\Sigma}_s\geq 0$, the LR statistic Λ_1 is equal to $\tilde{\Lambda}_1$. However, if it is not the case, Λ_1 becomes very complicated. As a simple bound for Λ_1, consider

$$\overline{\Lambda}_1=\begin{cases}\tilde{\Lambda}_1, & \text{if } \hat{\Psi}_{11}-I_s\otimes\hat{\Sigma}_s\geq 0,\\ 1, & \text{elsewhere.}\end{cases} \tag{3.7}$$

Then we have $\tilde{\Lambda}_1\leq\Lambda_1\leq\overline{\Lambda}_1$. We note that Λ_1 agrees with $\overline{\Lambda}_1$ 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 $\Xi=[\Xi_{ms}, \Xi_{\overline{ms}}]$. Then, from (3.1) we have

$$\begin{aligned} &Y_1\sim N_{n\times ms}(\tilde{A}\Xi_{ms}, \Psi_{11}\otimes I_n),\\ &Y_{(23)}\sim N_{n\times m(p-s)}([\tilde{A}\Xi_{\overline{ms}}, 0], (I_{p-s}\otimes\Sigma_s)\otimes I_n). \end{aligned} \tag{4.1}$$

Since Y_1 and $Y_{(23)}$ are independent and all information about Ξ_{ms} is contained in Y_1, we may start from the model for Y_1. Here we assume again that Ψ_{11} 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

$$\tilde{\Lambda}_2=|I_l+V_HV_e^{-1}|^{-1} \tag{4.2}$$

for testing H_{02} vs. H_{12}, where $V_e=K'S_{11}K$,

$$V_H=K'\hat{\Xi}'_{ms}F'(F(\tilde{A}'\tilde{A})^{-1}F')^{-1}F\hat{\Xi}_{ms}K,\quad \hat{\Xi}_{ms}=(\tilde{A}'\tilde{A})^{-1}\tilde{A}'Y_1.$$

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

$$S_{11}=Q_1D_{xx\cdot ca}Q_1',\quad \tilde{A}'\tilde{A}=D_{aa\cdot c},\quad \hat{\Xi}_{ms}=D_{aa\cdot c}^{-1}D_{ax\cdot c}Q_1', \tag{4.3}$$

where the submatrices of the matrix D are defined in (3.6). Under H_{02}, it is easy to verify that V_e and V_H are independently distributed as $W_l(n-k, K'\Psi_{11}K)$ and $W_l(d, K'\Psi_{11}K)$, respectively. Therefore, the h-th moment of $\tilde{\Lambda}_2$ is obtained from that $\tilde{\Lambda}_2$ is distributed as a lambda distribution $\Lambda_l(d, n-k)$ and is given by

$$E(\tilde{\Lambda}_2^h)=\frac{\Gamma_l\left(\frac{1}{2}(n-k)+h\right)\Gamma_l\left(\frac{1}{2}(n-k+d)\right)}{\Gamma_l\left(\frac{1}{2}(n-k)\right)\Gamma_l\left(\frac{1}{2}(n-k+d)+h\right)}. \tag{4.4}$$

The null distribution of statistic $-n\rho_2\log\tilde{\Lambda}_2$ has an approximate chi-squared distribution with degrees of freedom $f_2=dl$. For an asymptotic expansion of the distribution function of the statistic, see, e.g., Siotani, Hayakawa and Fujikoshi [4, p. 250].

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