On Multiple Comparisons of Randomized Growth Curve Model

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Abstract

A completely randomized growth curve model was defined by Zerbe(1979). We propose the fully significant difference procedure for multiple comparisons of completely randomized growth curve model. The standard F test is useful tool to multiple comparisons of the completely randomized growth curve model. The proposed method is applied to experimental data.

Keywords : growth curves, multiple comparison, randomization test, S-procedure

1. Introduction

Growth curve models are commonly used for the analysis of experiments with the same experimental units which are observed repeatedly. This kinds of experiments are applied many fields, especially in the life and social sciences. The growth curve model for analysis of experiment was first proposed by Potthoff and Roy(1964) and studied by Rao(1967), Geisser(1970), Rosen(1990), Lee(1991) and Krishnaiah(1995).

Potthoff-Roy models have not been commonly used for a repeated measured design because the technique was not familiar and the available softwares for computing were not common.

However, Stanek(1990) showed that growth curves models could be fitted with the two simple ideas: the transformation of variables and the use of computer programs for multivariate and multiple regression. When the groups have different shaped profile, general growth curve models can be fitted by the methodology of Stanek(1990).

In this paper, we consider that a growth curve model with observations which are correlated across time and across groups or treatments. We assume that the r different treatments are to be compared and the data consists of measurements of a single growth variable x which

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is measured for the same set of n individuals at p different time points.

By applying earlier work by Foutz(1984), Foutz, Jensen, and Anderson(1985), we have the appropriate multiple-comparisons procedure to compute a randomization analysis of growth and response curves.

Zerbe and Murphy(1986) discussed two multiple comparisons procedures for the supplement randomization analysis of growth curves. One is used an extension of the Scheffé method to control the experimentwise Type 1 error rate for all possible contrast curves. The other is used a step wise testing procedure to control a family of Type 1 error rates.

In this paper, we propose an extension of the "S-procedure" to capitalize on the approximate F test suggested by Zerbe(1979). These results are often useful in clinical trials when the same group of patients is used for comparing different treatments.

2. Growth curve model and hypothesis testing about τ

Potthoff and Roy(1964) defined the growth curve model such as

$$X_{p\times n} = B_{p\times m}\ \xi_{m\times r}\ A_{r\times n} + \varepsilon_{p\times n} \tag{2-1}$$

where ξ is unknown, B and A are known matrices of ranks $m < p$ and $r < n$, respectively. Further, the columns of ε are independent p-variate normal with mean vector 0 and common covariance matrix Σ.

Therefor, the cumulative distribution function of X is

$$G(X \mid \xi, \Sigma) \sim N(B\xi A\ ,\ \Sigma \otimes I_N) \tag{2-2}$$

where ξ denote the vector of the regression or growth curve coefficients, $\otimes$ denotes the Kronecker product and $G(\cdot)$ the cumulative distribution function.

The design matrix B is defined such as

$$B = \begin{bmatrix} 1 & t_1 & t_1^2 & \cdots & t_1^{m-1} \\ 1 & t_2 & t_2^2 & \cdots & t_2^{m-1} \\ \vdots & \vdots & \vdots & & \vdots \\ 1 & t_p & t_p^2 & \cdots & t_p^{m-1} \end{bmatrix} \tag{2-3}$$

and matrix A is that

$$A = diag[\ E_{1n_1},\ E_{1n_2},\ \cdots,\ E_{1n_r}\ ] \tag{2-4}$$

The block diagonal matrix A with E_{1n_j} , $j = 1, 2, \cdots, r$ has the diagonal blocks and null matrices elsewhere. A is called 'group indicator' matrix since its elements 1 and 0 indicate the group from which an observation comes.

Zerbe(1979) defined growth curve model with the basic assumptions of the completely randomized design. Consider the completely randomized design in which n subjects are assigned with r treatment groups, n_i in group i, and let $x_{ij}(t)$ be the growth curve observed over the time t for the subject assigned position j in group i ($t \in [a, b]$, $i = 1, 2, \cdots, r$; $j = 1, 2, \cdots, n_i$).

Let $\psi_{ik}(t)$ be the growth curve that the kth of the n subjects would realize when he were assigned to group i. Hence $x_{ij}(t)$ is the same as $\psi_{ik}(t)$ when subject k is assigned to position j in group i. Consider the mathematical model for the population of all nr possible growth curves such as

$$\psi_{ik}(t) = \mu(t) + \tau_i(t) + \varepsilon_k(t) \tag{2-5}$$

where

$$\begin{aligned} \mu(t) &= \bar{\psi}_{..}(t) \\ \tau_i(t) &= \bar{\psi}_{i.}(t) - \bar{\psi}_{..}(t) \\ \varepsilon_i(t) &= \bar{\psi}_{k}(t) - \bar{\psi}_{..}(t) \end{aligned} \tag{2-6}$$

The model (2-5) consists of the grand mean growth curve, the effect curve due to group i, and the error curve for subject k, respectively.

The model (2-5) is based on the population of all possible time-response curves and the probability structure induced by the completely randomized design. Kempthorne(1955), Zerbe(1979) derived a statistical model for the sample of random response curves $X_{ij}(t)$ (of which the $x_{ij}(t)$ are realization) such as

$$X_{ij}(t) = \mu(t) + \tau_i(t) + E_{ij}(t) \tag{2-7}$$

In the model (2-7), $E_{ij}(t)$ are random error curves satisfying

$$E[\, E_{ij}(t) = 0\,] \text{ and}$$

$$E[\, E_{ij}(t)\, E_{i'j'}(u)\,] = (\delta_{ii'}\, \delta_{jj'} - 1/n)\sigma(t, u) \tag{2-8}$$

where $\delta_{ii'} = 1$ if $i = i'$ and 0 if $i \neq i'$, and $\sigma(t, u)$ measures the covariability between subject errors at times t and u.

To test of equality of the vectors of growth curve coefficients for the r groups, we establish the null hypothesis

$$H_0 : \tau_1(t) = \tau_2(t) = \cdots = \tau_r(t) \tag{2-9}$$

We denote ith group's sample mean such as

$$\overline{X}_{i.}(t) = \sum_{j=1}^{n_i} X_{ij}(t) / n_i \tag{2-10}$$

(2-10) is the pointwise best minimum variance linear unbiased estimator of $\mu(t) + \tau_i(t)$. And we denote total group's sample mean such as

$$\overline{X}_{..}(t) = \sum_{i=1}^{r} \sum_{j=1}^{n_i} X_{ij}(t) / n \tag{2-11}$$

(2-11) is equal to the constant, $\mu(t) + \overline{\tau}_{.}(t)$, where $\overline{\tau}_{.}(t) = \sum_{i=1}^{r} n_i \tau_i / n$.

The randomization test discussed by Kempthorne(1955) provided a test for groups effects at specified time. Kempthorne's suggestion is now generalized to test for the case of unequal group sizes. Let

$$B(t) = \sum_{i=1}^{r} n_i \{\, \overline{X}_{i.}(t) - \overline{X}_{..}(t) \}^2 \tag{2-12a}$$

$$W(t) = \sum_{i=1}^{r} \sum_{j=1}^{n_i} \{\, X_{ij}(t) - \overline{X}_{i.}(t) \}^2 \tag{2-12b}$$

and

$$T(t) = \sum_{i=1}^{r} \sum_{j=1}^{n_i} \{ X_{ij}(t) - \overline{X}_{..}(t)\}^2 \qquad (2\text{-}12c)$$

Then (2-12a), (2-12b), and (2-12c) are between, within, and total sum of squares at time t respectively. Therefore

$$F_{01}(t) = [B(t)/(r-1)] / [(r-1)\widehat{\sigma}^2(t)] \qquad (2\text{-}13)$$

where $\widehat{\sigma}^2(t) = W(t)/(n-r)$, is appropriate statistic for the null hypothesis (2-9).

The degrees of freedom of the approximate F test are approximately $r-1$ and $n-r$. Let $f_\alpha(t)$ denote the 100($1-\alpha$)% point of the exact distribution of $F_{01}(t)$. Then

$$1-\alpha = \Pr\{F_{01}(t) \langle f_\alpha(t) \mid H_0\} \qquad (2\text{-}14)$$

3. Multiple comparison procedure

The null hypothesis

$$H_0 : \; c_l\tau_l(t) - c_m\tau_m(t) = 0 \qquad (3\text{-}1)$$

$c_l + c_m = 0$, $1 \le l \langle m \le r$, can be tested by the confidence region test method.

Let

$$B_\tau(t) = \sum_{i=1}^{r} n_i\{(\overline{X}_{i.}(t) - \tau_i(t)) - (\overline{X}_{..}(t) - \overline{\tau}_.(t))\}^2 \qquad (3\text{-}2)$$

The (3-2) denotes the between-groups sum of squares at time t for the variables $X_{ij}(t) - \tau_i(t)$. Converting Scheffé's notation for the randomization blocks design to ours for a completely randomized design at time t, Scheffé(1959) proposes that the distribution of $X_{ij}(t) - \tau_i(t)$ are the same as $X_{ij}(t)$ under the null hypothesis. Hence, regardless of the true values of the treatment effect curves $\tau_i(t)$, $F_\tau(t) = B_\tau(t) / [(r-1)\widehat{\sigma}^2(t)]$ is distributed exactly like the statistic $F_{01}(t)$ under the null hypothesis. Then we have the following probability regardless of $\tau_i(t)$

$$1-\alpha = \Pr\{F_\tau(t) \ \langle f_\alpha(t)\} \tag{3-3}$$

An approximate method of multiple comparisons is in the usual way when $f_\alpha(t)$ is replaced by its more usual normal theory counterpart based on $(r-1)$ and $(n-r)$ degrees of freedom.

Scheffé(1959) also indicated that the approximation of $f_\alpha(t)$ by the 100($1-\alpha$) % point of a standard F distribution with synthesized degrees of freedom which is discussed by Zarbe(1979) is not possible for purpose of constructing simultaneous confidence limits since their calculation also depends on unspecified $\tau_i(t)$'s. The synthesized degrees of freedom can be used in simultaneous testing when the experimenter's concern is to control the experimentwise error rate α only, i.e., when global null hypothesis prevails. For other situations, say where $\tau_l(t) - \tau_m(m) = 0$ with the remaining $\tau_i(t)'s$ unspecified, the synthesized degrees of freedom could not be evaluated.

In this problem, Baker and Collier(1966) indicated that $f_\alpha(t)$ can be reasonably well approximated by the 100($1-\alpha$) % point of a standard F distribution with $r-1$ and $n-r$ degrees of freedom regardless of $\tau_i(t)'s$. For this reason Scheffé(1959) remarks that "the S-procedure is a good approximation under the randomization model to the extent that the normal-theory test of the global null hypothesis holds its nominal significance level under the randomization model."

< Theorem 3-1 > The exact $(1-\alpha)$-level simultaneous confidence intervals for all contrasts $\sum_{i=1}^{r} c_i\theta_i$ using the S-procedure work out to be

$$\sum_{i=1}^{r} c_i\theta_i \in \left[(c_i \overline{Y}_i \pm \{(r-1)F_\alpha(r-1, v)\}^{1/2} S \left(\sum_{i=1}^{r} \frac{c_i}{n_i} \right)^{1/2} \right] \tag{3-4}$$

where $\overline{Y}_i$ is the sample mean for the ith treatment $(1 \le i \le r)$ and $S^2 = MS_{error}$ with $v = \sum_{i=1}^{r} n_i - r$ d.f. For pairwise comparisons, intervals given by (3-4) simplify to the following conservative $(1-\alpha)$-level simultaneous confidence intervals:

$$\theta_i - \theta_j \in \left[\overline{Y}_i - \overline{Y}_j \pm \{ (r-1) F_\alpha (r-1, v) \}^{1/2} S \left(\frac{1}{n_i} + \frac{1}{n_j} \right)^{1/2} \right]$$
$$, \quad 1 \le i < j \le r \qquad (3\text{-}5)$$

(proof) See Halperin and Greenhouse(1958).

Now let us extend these results for a point in time to an interval of time. we can use confidence intervals for $c_l \tau_l(t) - c_m \tau_m(t)$, $1 \le l < m \le r$.

$$c_l \tau_l(t) - c_m \tau_m(t) \in [(c_l \overline{X}_{l.}(t) - c_m \overline{X}_{m.}(t)) \pm \sqrt{ (r-1) F_\alpha (t; r-1, n-r) S(t) \left(\frac{c_l^2}{n_l} + \frac{c_m^2}{n_m} \right) }] \qquad (3\text{-}6)$$

where $S(t) = W_\alpha(t) / (n-r)$

For pairwise comparison, when we take $c_l = 1$ and $c_m = -1$, the intervals given by (3-6) simplify to the following conservative $(1-\alpha)$-level simultaneous confidence intervals :

$$\tau_l(t) - \tau_m(t) \in [(\overline{X}_{l.}(t) - \overline{X}_{m.}(t)) \pm \sqrt{ (r-1) F_\alpha (t; r-1, n-r) S(t) \left(\frac{1}{n_l} + \frac{1}{n_m} \right) }] \qquad (3\text{-}7)$$

For testing null hypothesis (3-1), F-test rejects H_0 at level α when

$$F_{02} = \frac{ (\overline{X}_{l.}(t) - \overline{X}_{m.}(t))^2 }{ S(t) \left(\frac{1}{n_l} + \frac{1}{n_m} \right) } > F_\alpha (t; r-1, n-r) . \qquad (3\text{-}8)$$

The test procedure based on (3-8) is often referred to in the literature as the fully significant difference.

4. Illustration

A balanced completely randomized design experiment was reported by Frey et al. (1991) to analyze the effects of dietary ingestion of sodium zeolite A(SZA) on the growth and physiology of weanling quarter horses. Forty five animals were randomly assigned to three groups of dietary SZA; control=A, 0.66% SZA=B, 2.0% SZA=C . Plasma silicon concentration were among the many variables measured before and at 3, 6, and 9 hours after ingestion at 84 days into the diet.

To test equality of growth curve coefficients of three groups, we establish the null hypothesis $H_0 : \tau_1(t) = \tau_2(t) = \tau_3(t)$. From (2-13), we have $F_{01} = 50.292$ and p-value=7.124E-12. Therefore, there is not enough evidence that three growth curve coefficients are equal.

<Table 1> shows the result of multiple comparison for growth curve coefficients of three groups using (3-8). From <Table 1>, we know that growth curve coefficients of group (A and B) are not different but group (B and C) and (C and A) are significantly different with significant α=0.05.

<Table 1> Result of multiple comparison.

	F_{02}	p-value
GroupA and GroupB	1.23402	0.334746
GroupB and GroupC	7.93332	0.001195
GroupC and GroupA	37.3813	4.73E-10

5. Conclusion

The test of homoscedasticity and the inference of growth curve coefficient were studied Potthoff and Roy(1964). After Ptthoff and Roy(1964), others suggested the inference of growth curve. But there are a few studies for the randomized growth curve model suggested by Zerbe(1979) because this model is known less than Potthoff and Roy's.

In this paper, we propose the fully significant difference procedure for multiple comparisons of completely randomized growth curve model. The standard F test is useful tool to multiple comparisons of the completely randomized growth curve model.

In numerical example, we know that suggested method can be used to multiple comparison for growth curve coefficients of three groups. But in case there are many groups and many coefficient in growth curve model, we need more study.

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