P. R. Krishnaiah, ed., *Handbook of Statistics, Vol. 1*
©North-Holland Publishing Company (1980) 41–87

2

Multivariate Analysis of Variance of Repeated Measurements

Neil H. Timm

1. Introduction

The analysis of variance of multiple observations on subjects or units over several treatment conditions or periods of time is commonly referred to in the statistical and behavioral science literature as the repeated measures situation or repeated measures analysis. Standard textbook discussions of repeated measurement designs employing mixed-model univariate analysis of variance procedures are included in Cox (1958), Federer (1955), Finny (1960), John (1971), Kempthorne (1952), Kirk (1968), Lindquist (1953), Myers (1966), Quenouille (1953) and Winer (1971), to name a few. Recently, Federer and Balaam (1972) published an extensive bibliography of repeated measurement designs and their analysis through 1967 and Hedayat and Afsarinejad (1975) discussed the construction of many of the designs. Coverage of the analysis of variance of repeated measures designs by the above authors has been limited to standard situations employing univariate techniques. The analysis of repeated measurements are discussed from a multivariate analysis of variance point of view in this chapter.

2. The general linear model

The generalization of the analysis of variance procedure to analyze repeated measurement designs utilizing the multivariate analysis of variance approach employs the multivariate general linear model and the testing of linear hypotheses using p-dimensional vector observations. From a multivariate point of view, n independent p-dimensional repeated measurements are regarded as p-variate normal variates $\mathbf{Y}_i$, $i=1,2,\ldots,n$, with a common unknown variance-covariance matrix Σ and expectations

$$E(\mathbf{Y}_i)=x_{i1}\boldsymbol{\beta}_1+x_{i2}\boldsymbol{\beta}_2+\cdots+x_{iq}\boldsymbol{\beta}_q,\quad i=1,2,\ldots,n, \tag{2.1}$$

where the x_{ij}'s are known constants and the $\boldsymbol{\beta}_j$'s are unknown p-component parameter vectors. Letting the $p\times q$ matrix $B'=(\boldsymbol{\beta}_1\boldsymbol{\beta}_2\cdots\boldsymbol{\beta}_p)$, the $p\times n$ matrix $Y'=(\mathbf{Y}_1\mathbf{Y}_2\cdots\mathbf{Y}_n)$ and the $n\times q$ matrix $X=[x_{ij}]$, expression (2.1) is written as

$$E(Y)=XB. \tag{2.2}$$

Since each row vector $\mathbf{Y}_i$ of Y is sampled from a p-variate normal population with variance-covariance matrix Σ, we may write the variance of the matrix Y as

$$V(Y)=I_n\otimes\Sigma \tag{2.3}$$

where the symbol $\otimes$ represents the direct or Kronecker product of two matrices. The combination of the formulas (2.2) and (2.3) are referred to as the multivariate Gauss–Markoff setup.

To estimate the unknown parameter vectors in the matrix B, the normal equations

$$X'XB=X'Y \tag{2.4}$$

are solved. Letting $\hat{B}$ be a solution to the normal equations, the least squares estimator of an estimable parametric vector function

$$\psi=\mathbf{c}'B=c_1\boldsymbol{\beta}_1+c_2\boldsymbol{\beta}_2+\cdots+c_q\boldsymbol{\beta}_q, \tag{2.5}$$

for known c_i, is

$$\hat{\psi}=\mathbf{c}'\hat{B}=c_1\hat{\boldsymbol{\beta}}_1+c_2\hat{\boldsymbol{\beta}}_2+\cdots+c_q\hat{\boldsymbol{\beta}}_q. \tag{2.6}$$

To estimate the unknown elements σ_{ij} of the matrix Σ, the sum of squares and cross products (SSP) matrix due to error is computed. This matrix is obtained by evaluating

$$S_e=Y'Y-Y'X\hat{B} \tag{2.7}$$

where $\hat{B}$ is any solution to the normal equations. Letting the rank of the design matrix be $r\leqslant q$, the degrees of freedom due to error is $n-r=\nu_e$, and $(1/\nu_e)S_e$ results in an unbiased estimator of Σ.

To test the hypothesis H_0 that $\psi=\mathbf{c}'B$ has a specified value ψ_0, we proceed by using Hotelling's generalized T^2 statistic (see Hotelling, 1931 and Bowker, 1960) and Theorem 2.1 (Rao, 1973, p. 541).

THEOREM 2.1. *Let S have a central Wishart distribution with k degrees of freedom, represented by $S\sim W_p(k,\Sigma)$, and let $\mathbf{d}$ be normally distributed with* *mean* $\boldsymbol{\delta}$ *and variance-covariance matrix* $c^{-1}\Sigma$ *with constant* c *greater than zero, represented by* $\mathbf{d} \sim N_p(\boldsymbol{\delta}, c^{-1}\Sigma)$, *such that* S *and* $\mathbf{d}$ *are independent. Hotelling's generalized* T^2 *statistic is defined by*

$$T^2 = ck\mathbf{d}' S^{-1}\mathbf{d},$$

and

$$\left(\frac{k-p+1}{p}\right)\frac{T^2}{k} \sim F(p, k-p+1, c\tau^2),$$

which is a noncentral F *distribution with noncentrality parameter* $c\tau^2 = c\boldsymbol{\delta}'\Sigma^{-1}\boldsymbol{\delta}$.

Since S_e *has a central Wishart distribution,* $S_e \sim W_p(\nu_e, \Sigma)$, *and* $\hat{\boldsymbol{\psi}} \sim N_p(\boldsymbol{\psi}, \mathbf{c}'(X'X)^{-}\mathbf{c}\Sigma)$, *independent of* S_e, *where* $(X'X)^{-}$ *is a generalized inverse of* $X'X$, *and* $\mathbf{c}'(X'X)^{-}\mathbf{c} > 0$ *if* $\boldsymbol{\psi}$ *is estimable,*

$$\left(\frac{\nu_e - p + 1}{p}\right)\frac{(\hat{\boldsymbol{\psi}} - \boldsymbol{\psi}_0)' S_e^{-1}(\hat{\boldsymbol{\psi}} - \boldsymbol{\psi}_0)}{\mathbf{c}'(X'X)^{-}\mathbf{c}} = F \tag{2.8}$$

has a noncentral F *distribution and the null hypothesis* H_0: $\boldsymbol{\psi} = \boldsymbol{\psi}_0$ *is rejected at the significance level* α *if* $F > F^{\alpha}(p, \nu_e - p + 1)$. *Alternatively, since*

$$1 + \frac{T^2}{\nu_e} = \frac{|S_e|}{|S_e + S_h|},$$

where $S_h = (\mathbf{c}'(X'X)^{-}\mathbf{c})^{-1}(\hat{\boldsymbol{\psi}} - \boldsymbol{\psi}_0)(\hat{\boldsymbol{\psi}} - \boldsymbol{\psi}_0)' \sim W_p(1, \Sigma)$ *under the null hypothesis, the ratio*

$$B = \frac{|S_e|}{|S_e + S_h|} \sim B\left(\frac{\nu_e - p + 1}{2}, \frac{p}{2}\right) \tag{2.9}$$

has a central beta distribution when H_0 *is true so that rejecting for large values of* F *is equivalent to rejecting* H_0 *for small values of* B.

To test the hypothesis H_0 that ν_h independent estimable functions have a specified value Γ, the null hypothesis H_0 is written as

$$H_0\colon CBA = \Gamma \tag{2.10}$$

where the $\nu_h \times q$ matrix C is of rank $\nu_h \leqslant r$ and A is any $p \times u$ matrix of rank $u \leqslant p \leqslant n - r$. Following the test of H_0 that $\boldsymbol{\psi} = \boldsymbol{\psi}_0$, we compute the matrix S_h known as the SSP matrix ("sum of squares + products") due to the hypothesis using the formula

$$S_h = (C\hat{B}A - \Gamma)'(C(X'X)^{-}C')^{-1}(C\hat{B}A - \Gamma). \tag{2.11}$$

Furthermore,

$$S_e = A'Y'\left[I - X(X'X)^{-}X'\right]YA, \tag{2.12}$$

and S_h are independently distributed; $S_e \sim W_u(n-r, A'\Sigma A)$ and $S_h \sim W_u(\nu_h, A'\Sigma A, \cdot)$. Departure from the null hypothesis may be detected by comparing the matrices S_e and S_h.

Having computed the matrices S_e and S_h for the null hypothesis (2.10), several procedures have been recommended for testing that the hypothesis H_0 is true. All of the procedures proposed are dependent on the roots of one of the following determinantal equations.

$$\begin{aligned} &(\mathrm{a}) \qquad |S_h - \lambda S_e| = 0, \\ &(\mathrm{b}) \qquad |S_e - \nu(S_e + S_h)| = 0, \\ &(\mathrm{c}) \qquad |S_h - \Theta(S_h + S_e)| = 0 \end{aligned} \tag{2.13}$$

with roots ordered from largest to smallest for $i = 1, 2, \ldots, s = \min(\nu_h, u)$. Wilks (1932) proposed testing H_0 using

$$\Lambda = \frac{|S_e|}{|S_e + S_h|} = \prod_{i=1}^{s} v_i = \prod_{i=1}^{s} (1+\lambda_i)^{-1} = \prod_{i=1}^{s} (1-\Theta_i) \tag{2.14}$$

and to reject H_0 if $\Lambda < U^{\alpha}(u, \nu_h, \nu_e)$. Lawley (1938) and Hotelling (1951) suggested the statistic

$$\begin{aligned} T_0^2 &= \nu_e \operatorname{Tr}\left(S_h S_e^{-1}\right) = \nu_e \sum_{i=1}^{s} \lambda_i \\ &= \nu_e \sum_{i=1}^{s} \left(\frac{1-v_i}{v_i}\right) = \nu_e \sum_{i=1}^{s} \left(\frac{\Theta_i}{1-\Theta_i}\right) \end{aligned} \tag{2.15}$$

and to reject H_0 if T_0^2 is greater than some constant k^* to attain a predetermined level of significance. The symbol Tr denotes the trace of a matrix. Roy (1957) recommended the largest root statistic

$$\Theta_1 = \frac{\lambda_1}{1+\lambda_1} = 1 - v_1 \tag{2.16}$$

and to reject the hypothesis if $\Theta_1 > \Theta^{\alpha}\ (s, m, n)$ where $m = (|\nu_h - u| - 1)/2$, $n = (\nu_e - u - 1)/2$ and $s = \min(\nu_h, u)$. Pillai (1960) approximated the distribution of the following trace criterion proposed by Bartlett (1939) and

Nanda (1950):

$$V = \mathrm{Tr}\left[S_h(S_h+S_e)^{-1}\right] = \sum_{i=1}^{s}\Theta_i = \sum_{i=1}^{s}\frac{\lambda_i}{1+\lambda_i} = \sum_{i=1}^{s}(1-v_i) \quad (2.17)$$

and to reject the hypothesis if $V > V^{\alpha}$ (s,m,n). Tables for each of the criteria are collected in Timm (1975). For a review of the literature on the distribution of Λ, T_0^2, Θ, and V, the reader is referred to Krishnaiah (1978). In general no one multivariate criterion is uniformly best; we have selected to use Wilks' Λ-criterion to illustrate the analysis of repeated measurement designs from a multivariate analysis of variance point of view. When $s=1$, all criteria are equivalent.

Several alternative criteria have been proposed by authors to test the null hypothesis represented in (2.10). Of particular importance is the step-down procedure proposed by J. Roy (1958) and the finite intersection tests developed by Krishnaiah (1965). In addition, tests based on the ratio of roots are discussed in the paper by Krishnaiah and Waikar (1971).

Following the test of a multivariate hypothesis of the form H_0: $CBA=\Gamma$, simultaneous confidence intervals for the parametric estimable functions $\psi = \mathbf{c}'B\mathbf{a}$, for vectors $\mathbf{c}$ in the row space of C and arbitrary vectors $\mathbf{a}$, may be obtained for each of the multivariate test criteria. Evaluating the expression

$$\hat{\psi} - c_0\left(\mathbf{a}'\left(\frac{S_e}{\nu_e}\right)\mathbf{a}\mathbf{c}'(X'X)^{-}\mathbf{c}\right)^{\frac{1}{2}} \leqslant \psi \leqslant \hat{\psi} + c_0\left(\mathbf{a}'\left(\frac{S_e}{\nu_e}\right)\mathbf{a}\mathbf{c}'(X'X)^{-}\mathbf{c}\right)^{\frac{1}{2}} \quad (2.18)$$

$100(1-\alpha)\%$ simultaneous confidence intervals for all $\psi = \mathbf{c}'B\mathbf{a}$ may be constructed where c_0 is selected to maintain a $(1-\alpha)$ confidence set. The critical constant c_0 for each multivariate criterion has the following values (Gabriel, 1968):

Wilks:

$$c_0^2 = \nu_e\left(\frac{1-U^{\alpha}}{U^{\alpha}}\right), \quad (2.19a)$$

Lawley–Hotelling:

$$c_0^2 = \nu_e U_0^{\alpha} = T_{0,\alpha}^2, \quad (2.19b)$$

Roy:

$$c_0^2 = \nu_e\left(\frac{\Theta^{\alpha}}{1-\Theta^{\alpha}}\right), \quad (2.19c)$$

Bartlett-Nanda-Pillai:

$$c_0^2 = \nu_e\left(\frac{V^\alpha}{1-V^\alpha}\right). \tag{2.19d}$$

The critical values U^α, Θ^α, U_0^α, and V^α correspond to those procured in testing the multivariate hypothesis H_0: $CBA=\Gamma$ at the significance level α.

3. One-sample repeated measurement design

Suppose a random sample of n subjects are measured (in the same metric scale with the same origin and unit) at p treatment levels so that the general organization of the data may be represented as in Table 3.1.

The data in Table 3.1 may be analyzed as a special application of the multivariate general linear model. The p repeated measures for the ith subject is regarded as a p-variate vector observation

$$\mathbf{Y}_i = \boldsymbol{\mu} + \boldsymbol{\varepsilon}_i, \qquad i=1,2,\ldots,n, \tag{3.1}$$

where $\boldsymbol{\mu}$ is a $p\times 1$ vector of treatment means and $\boldsymbol{\varepsilon}_i$ is a $p\times 1$ vector of random errors. Furthermore, we assume that $\boldsymbol{\varepsilon}_i \sim IN_p(\mathbf{0},\Sigma)$ so that $E(\mathbf{Y}_i)=\boldsymbol{\mu}$.

The usual hypothesis of interest for the design is that the treatment means $\mu_1,\mu_2,\ldots,\mu_p$, the elements of the vector $\boldsymbol{\mu}$, are equal:

$$H_0\colon \mu_1=\mu_2=\cdots=\mu_p. \tag{3.2}$$

Representing H_0 as $CBA=\Gamma$, the matrices C, B, A and Γ take the following form:

$$\underset{(1\times 1)}{C} = [1], \qquad \underset{(1\times p)}{B} = [\mu_1,\mu_2,\ldots,\mu_p],$$

$$\underset{p\times(p-1)}{A} = \begin{pmatrix} I_{p-1} \\ \hdashline -\mathbf{1}' \end{pmatrix}, \qquad \underset{1\times(p-1)}{\Gamma} = [0],$$

where $\mathbf{1}$ denotes a vector of unities.

With the $n\times p$ matrix $Y=[y_{ij}]$ and the $n\times 1$ design matrix $X=\mathbf{1}$, expressions for S_e and S_h are readily obtained using (2.11) and (2.12) with $\hat{B}=(X'X)^{-1}X'Y$. If H_0 is true,

$$\Lambda = \frac{|S_e|}{|S_e+S_h|} \sim U(p-1,1,n-1)$$

Table 3.1
Data for a one-group repeated measurement design

Subjects	Treatments					
	T_1	T_2	.	.	.	T_p
S_1	y_{11}	y_{12}	.	.	.	y_{1p}
S_2	y_{21}	y_{22}	.	.	.	y_{2p}
.	.	.	.	.	.	.
.	.	.	.	.	.	.
.	.	.	.	.	.	.
S_n	y_{n1}	y_{n2}	.	.	.	y_{np}

and H_0 is rejected if $\Lambda < U^{\alpha}\ (p-1,1,n-1)$ or since $s=\min(\nu_h,u)=\min(1,p-1)=1$, the hypothesis is rejected if

$$\left(\frac{n-p+1}{p-1}\right)\left(\frac{1-\Lambda}{\Lambda}\right) > F^{\alpha}(p-1,n-p+1),$$

or equivalently if

$$\left(\frac{n-p+1}{p-1}\right)\frac{T^2}{(n-1)} > F^{\alpha}(p-1,n-p+1),$$

since when $s=1$, $T^2/\nu_e=(1-\Lambda)/\Lambda$.

EXAMPLE 3.1. Using the data in Table 3.2, the mean reaction time of subjects to five probe words are investigated (Timm, 1975, p. 233).

Table 3.2
Sample data: one-group analysis

Subjects	Probe-word positions				
	1	2	3	4	5
1	51	36	50	35	42
2	27	20	26	17	27
3	37	22	41	37	30
4	42	36	32	34	27
5	27	18	33	14	29
6	43	32	43	35	40
7	41	22	36	25	38
8	38	21	31	20	16
9	36	23	27	25	28
10	26	31	31	32	36
11	29	20	25	26	25

Calculations show that

$$\Lambda = \frac{|S_e|}{|S_e + S_h|} = 0.2482$$

or $T^2 = 30.29$ and

$$\left(\frac{n-p+1}{p-1}\right)\frac{T^2}{(n-1)} = \left(\frac{7}{4}\right)\frac{30.29}{10} = 5.30.$$

The hypothesis is rejected at the $\alpha = 0.05$ level if $\Lambda < U^{0.05}(4,1,10) =$ 0.057378 or

$$\frac{n-p+1}{p-1}\,\frac{T^2}{(n-1)} > F^{0.05}(4,7) = 4.12$$

so that H_0 is rejected.

Employing the formula (2.18), confidence intervals for $\psi = \mu_1 - \mu_5$ and $\psi = \mu_1 - \mu_2$ are easily evaluated:

$$-7.09 \leqslant \mu_1 - \mu_5 \leqslant 17.82 \quad \text{(N.S.)},$$
$$0.86 \leqslant \mu_1 - \mu_2 \leqslant 20.24 \quad \text{(Sig.)}.$$

In the analysis of the one-group repeated measurements design from a multivariate analysis of variance point of view, no restrictions were placed on the structure of the variance-covariance matrix Σ (except that $n > p$ to ensure a positive definite estimate). If, however, mixed model univariate assumptions are established for a set of data, a univariate analysis is readily obtained from a set of multivariate calculations provided the post matrix A is orthogonalized so that $A'A = I$.

To illustrate following Bock (1963), suppose the mean vector $\boldsymbol{\mu}$ in the multivariate model has the form

$$\boldsymbol{\mu} = \mu\mathbf{1} + \boldsymbol{\beta} \tag{3.3}$$

where $\boldsymbol{\beta}' = (\beta_1, \beta_2, \ldots, \beta_p)$. Furthermore, suppose $\boldsymbol{\varepsilon}_i$ is represented by

$$\boldsymbol{\varepsilon}_i = s_i\mathbf{1} + [\varepsilon_{ij}] \tag{3.4}$$

and that $\boldsymbol{\varepsilon}_i \sim IN_p(\mathbf{0}, \Sigma)$ so that the population variance-covariance matrix of the repeated measures has the uniform covariance structure

$$\Sigma = \sigma_s^2 \mathbf{1}\mathbf{1}' + \sigma^2 I. \tag{3.5}$$

Such a decomposition yields the univariate mixed model

$$y_{ij} = \mu + s_i + \beta_j + \varepsilon_{ij} \tag{3.6}$$

where the subjects are a random sample from a population in which $s_i \sim IN(0, \sigma_s^2)$ jointly independent of the errors ε_{ij} and $\varepsilon_{ij} \sim IN(0, \sigma^2)$. The parameters in (3.6) have the interpretation: μ is an unknown constant, s_i is a random component associated with subject i, β_j is a fixed treatment effect, and ε_{ij} is a random error component. A test of the null hypothesis

$$H_0\colon \beta_1 = \beta_2 = \cdots = \beta_p$$

is provided by the ratio

$$F = \frac{\mathrm{SSH}/(p-1)}{\mathrm{SSE}/(n-1)(p-1)} \sim F(\nu_h^*, \nu_e^*).$$

The degrees of freedom for the F ratio are obtained from the multivariate test by the formula $\nu_h^* = R(A)\nu_h = (p-1)1 = (p-1)$ and $\nu_e^* = R(A)\nu_e = (p-1)(n-1)$ where $R(A)$ denotes the rank of A. Furthermore, selecting A so that $A'A = I$, $\mathrm{SSH} = \mathrm{Tr}(S_h)$ and $\mathrm{SSE} = \mathrm{Tr}(S_e)$. Thus, the univariate mixed model analysis is merely a special case of the more general multivariate analysis.

If the variance-covariance matrix Σ has the structure given in (3.5), then the mean square ratio for testing the equality of the fixed treatment effects have an exact F-distribution. As shown by Bock (1963), a necessary and sufficient condition for an exact F-test is that the transformation of the error matrix by an orthogonal contrast matrix results is the scalar matrix $\sigma^2 I$. Box (1950) and Lee, Krishnaiah and Chang (1976) developed procedures to test for uniform covariance structure. Bock (1975) and Huynh and Feldt (1970) review the general structure case. Whenever, the condition for the exact F-distribution is satisfied, the univariate model should be used to analyze repeated measurement data.

When the variance-covariance matrix Σ is arbitrary, Greenhouse and Geisser (1959) and Huynh and Feldt (1976) proposed a conservative F-test procedure for testing for the equality of treatment effects using the univariate mixed model analysis. However, as discussed by Geisser (1979), such a procedure is to be avoided when an exact multivariate procedure exists.

4. The I-sample repeated measurement design

Letting

$$\mathbf{Y}'_{ij} = (y_{ij1}, y_{ij2}, \ldots, y_{ijp}) \sim IN_p(\boldsymbol{\mu}_i, \Sigma)$$

the p-variate observation of the jth subject within the ith group is represented as

$$\mathbf{Y}_{ij} = \boldsymbol{\mu}_i + \boldsymbol{\varepsilon}_{ij}, \quad i = 1, 2, \ldots, I; j = 1, 2, \ldots, N_i \tag{4.1}$$

and $N = \sum_{i=1}^{I} N_i$ where $\boldsymbol{\mu}_i = (\mu_{i1}, \mu_{i2}, \ldots, \mu_{ip})$ is a $1 \times p$ vector of means and $\boldsymbol{\varepsilon}_{ij}$ is a vector of random errors. From (4.1) the data matrix Y is an $N \times p$ matrix, the parameter matrix B is

$$\underset{(I \times p)}{B} = \begin{bmatrix} \mu_{11} & \mu_{12} & \cdots & \mu_{1p} \\ \mu_{21} & \mu_{22} & \cdots & \mu_{2p} \\ \cdot & \cdot & \cdots & \cdot \\ \cdot & \cdot & \cdots & \cdot \\ \cdot & \cdot & \cdots & \cdot \\ \mu_{I1} & \mu_{I2} & \cdots & \mu_{Ip} \end{bmatrix} \tag{4.2}$$

and the design matrix X is of the form

$$\underset{(N \times 1)}{X} = I_N \otimes \mathbf{1}_{N_i} \quad \text{with} \quad i = 1, 2, \ldots, I.$$

The primary hypotheses of interest for the I-sample data are:
H_{01}: Are the profiles for the I groups parallel?
H_{02}: Are there differences among treatments?
H_{03}: Are there significant differences among groups?
To test the hypothesis of group differences, the hypothesis in terms of the elements of B is

$$H_{03}: \boldsymbol{\mu}_1 = \boldsymbol{\mu}_2 = \cdots = \boldsymbol{\mu}_I \tag{4.3}$$

which is identical to the test for differences in means employing the one-way multivariate analysis of variance (MANOVA) model. Representing the hypothesis as $CBA = \Gamma$, the matrices C, A and Γ for B defined in (4.2) are selected:

$$\underset{(I-1) \times I}{C} = \left(I_{I-1} \vdots -\mathbf{1}\right), \quad A = I_p \quad \text{and} \quad \Gamma = 0. \tag{4.4}$$

With $\nu_h = R(C) = I - 1$, $\nu_e = N - R(X) = N - I$ and $u = R(A) = p$, the hypothesis H_{03} is rejected at the level α if

$$\Lambda = \frac{|S_e|}{|S_e + S_h|} < U^{\alpha}(p, I-1, N-I). \tag{4.5}$$

The parameters for the other multivariate criteria are $s = \min(\nu_h, u) = \min(I-1, p)$, $m = (|\nu_h - u| - 1)/2 = (|I-p-1|-1)/2$ and $n = (\nu_e - u - 1)/2 = (N-I-p-1)/2$.

To test for differences in treatments, the hypothesis is stated as

$$H_{02}: \begin{bmatrix} \mu_{11} \\ \mu_{21} \\ \cdot \\ \cdot \\ \cdot \\ \mu_{I1} \end{bmatrix} = \begin{bmatrix} \mu_{12} \\ \mu_{22} \\ \cdot \\ \cdot \\ \cdot \\ \mu_{I2} \end{bmatrix} = \cdots = \begin{bmatrix} \mu_{1p} \\ \mu_{2p} \\ \cdot \\ \cdot \\ \cdot \\ \mu_{Ip} \end{bmatrix},$$

and the matrices C, A and Γ take the form

$$\underset{p\times(p-1)}{A} = \begin{pmatrix} I_{p-1} \\ \hline -\mathbf{1}' \end{pmatrix}, \quad C = I_I \quad \text{and} \quad \Gamma = 0,$$

where the $R(C) = \nu_h = I$ and the $R(A) = u = p-1$. Forming the Λ-ratio, the hypothesis is rejected at the level α if

$$\Lambda = \frac{|S_e|}{|S_e + S_h|} < U^{\alpha}(p-1, I, N-I). \tag{4.6}$$

In addition, $s = \min(I, p-1)$, $m = (|I-p+1|-1)/2$ and $n = (N-I-p)/2$.

To test for parallelism of profiles or interaction between groups and treatments, the hypothesis may be stated as

$$H_{01}: \begin{bmatrix} \mu_{11} & - & \mu_{12} \\ \mu_{12} & - & \mu_{13} \\ \vdots & & \vdots \\ \mu_{1(p-1)} & - & \mu_{1p} \end{bmatrix} = \cdots = \begin{bmatrix} \mu_{I1} & - & \mu_{I2} \\ \mu_{I2} & - & \mu_{I3} \\ \vdots & & \vdots \\ \mu_{I(p-1)} & - & \mu_{Ip} \end{bmatrix}, \tag{4.7}$$

and the matrices C, A and Γ become

$$\underset{(I-1)\times I}{C} = (I_{I-1} \,\vdots\, -\mathbf{1}), \quad \underset{p\times(p-1)}{A} = D_{p-1}\begin{pmatrix} 1 \\ -1 \end{pmatrix} \quad \text{and} \quad \underset{(I-1)\times(p-1)}{\Gamma} = 0,$$

where D_{p-1} is a $(p-1)$-diagonal matrix with diagonal elements $\binom{1}{-1}$, the

$R(C)=\nu_h=I-1$, $R(A)=u=p-1$ and $\nu_e=N-I$. For the parallelism hypothesis, $s=\min(I-1,p-1)$, $m=(|I-p|-1)/2$ and $n=(N-I-p)/2$.

For valid multivariate tests of differences in group and treatment mean vectors, we did not assume that the statistic for testing the parallelism hypothesis was nonsignificant so that the multivariate tests may be confounded with interaction. If there is no interaction between groups and treatments, alternative tests for group mean differences and differences in treatment means may be of interest that are special cases of the multivariate tests. In terms of the parameters in the matrix B, the tests for group and treatment mean difference become

$$H_{03}^{(g)}:\ \frac{\sum_{j=1}^{p}\mu_{1j}}{p}=\cdots=\frac{\sum_{j=1}^{p}\mu_{Ij}}{p} \tag{4.8}$$

$$H_{02}^{(t)}:\ \frac{\sum_{i=1}^{I}\mu_{i1}}{I}=\cdots=\frac{\sum_{i=1}^{I}\mu_{ip}}{I}. \tag{4.9}$$

Since the number of subjects within each group are unequal, the test for treatment differences $H_{02}^{(t)}$ is an unweighted test that is independent of the sample sizes N_i. An alternative test to $H_{02}^{(t)}$ is the weighted test

$$H_{02}^{(t_w)}:\ \frac{\sum_{i=1}^{I}N_i\mu_{i1}}{N}=\cdots=\frac{\sum_{i=1}^{I}N_i\mu_{ip}}{N}. \tag{4.10}$$

Depending on whether the loss of subjects was due to the treatments or independent of the treatment, the weighted or unweighted tests would be selected, respectively.

To test the hypothesis $H_{03}^{(g)}$, the matrices C and A are selected to represent it in the form $CBA=0$:

$$\underset{(I-1)\times p}{C}=\left(I_{I-1}\vdots-\mathbf{1}\right),\qquad \underset{(p\times 1)}{A}=\left[1/p\right].$$

To test $H_{02}^{(t)}$, the matrix $\Gamma=0$ and C and A take the form:

$$\underset{(1\times I)}{C}=\left(\frac{1}{I}\mathbf{1}'\right)\quad\text{and}\quad \underset{p\times(p-1)}{A}=D_{p-1}\begin{pmatrix}1\\-1\end{pmatrix}.$$

Alternatively, to test $H_{02}^{(t_w)}$, A is as defined for $H_{02}^{(t)}$, but the matrix $1\times I$ matrix $C=(N_1/N,\ldots,N_I/N)$.

Selecting A such that $A'A=I$ for the test of $H_{03}^{(g)}$, $\nu_h=I-1$ and $\nu_e=N-I$,

$$\Lambda=\frac{|S_e|}{|S_e+S_h|}\sim U(1,I-1,N-I).$$

However, if $\nu_h = 1$ or $s = \min(\nu_h, u) = 1$,

$$\frac{\nu_e - u + 1}{|u - \nu_h| + 1} \frac{1 - \Lambda}{\Lambda} \sim F(u - \nu_h + 1, \nu_e - u + 1),$$

so

$$F_g = \frac{\nu_e}{I} \frac{1 - \Lambda}{\Lambda} \sim F(\nu_h, \nu_e).$$

Furthermore, since A is selected so that $A'A = I$,

$$S_h = \mathrm{SSH} = p \sum_i N_i (y_{j\cdot\cdot} - y_{\cdot\cdot\cdot})^2,$$

$$S_e = \mathrm{SSE} = p \sum_i \sum_j (y_{ij\cdot} - y_{i\cdot\cdot})^2,$$

which is identical to the hypothesis and error sum of squares obtained employing a univariate mixed model split-plot design (Geisser, 1979).

For the tests of $H_{02}^{(t)}$ or $H_{02}^{(t_w)}$, the criterion $\Lambda \sim U(p-1, 1, N-I)$. However, since $\nu_h = 1$, $\Lambda = (1 + T^2/\nu_e)^{-1}$ and T^2 for the tests of $H_{02}^{(t)}$ and $H_{02}^{(t_w)}$ become, respectively,

$$T_t^2 = I^2 \left(\sum_{i=1}^{I} \frac{1}{N_i} \right)^{-1} \mathbf{Y}'_{\cdot\cdot} A (A'SA)^{-1} A' \mathbf{Y}_{\cdot\cdot},$$

where

$$\mathbf{Y}_{\cdot\cdot} = \sum_{i=1}^{I} Y_{i\cdot}/I \quad \text{and} \quad S = \frac{Y'\left[I - X(X'X)^{-1}X'\right]Y}{N - I},$$

and

$$T_{t_w}^2 = N \overline{\mathbf{Y}}'_{\cdot\cdot} A (A'SA)^{-1} A' \overline{\mathbf{Y}}'_{\cdot\cdot}$$

where

$$\overline{\mathbf{Y}}_{\cdot\cdot} = \sum_{i=1}^{I} N_i \mathbf{Y}_{i\cdot}/N.$$

Relating T_t^2 or $T_{t_w}^2$ to an F statistic, the formula

$$F = \left(\frac{(N - I - p + 2)}{(p - 1)} \right) \frac{T^2}{(N - I)} \sim F(p - 1, N - I - p + 2)$$

is employed.

As in the one sample repeated measurement design, the mixed model analysis of the data in Table 4.1 may be recovered from certain of the multivariate tests provided the post matrix A is selected such that $A'A = I$. As discussed by Kirk (1968, Chapter 8), the univariate mixed model may

Table 4.1
Kirk's data: two-group analysis

		B_1	B_2	B_3	B_4
	S_1	3	4	7	7
A_1	S_2	6	5	8	8
	S_3	3	4	7	9
	S_4	3	3	6	8
	S_1'	1	2	5	10
A_2	S_2'	2	3	6	10
	S_3'	2	4	5	9
	S_4'	2	3	6	11

be written as

$$y_{ijk}=\mu+\alpha_i+\beta_k+\gamma_{ik}+s_{(i)j}+\varepsilon_{(i)jk}$$
$$i=1,2,\ldots,I;\, j=1,2,\ldots,N_i;\; k=1,2,\ldots,p \tag{4.11}$$

where $s_{(i)j}\sim IN(0,\sigma_s^2)$, $\varepsilon_{(i)jk}\sim IN(0,\sigma^2)$ and $s_{(i)j}$ and $\varepsilon_{(i)jk}$ are jointly independent so that Σ takes the form within each group,

$$\Sigma=\sigma_s^2\mathbf{1}\mathbf{1}'+\sigma^2 I. \tag{4.12}$$

The parameters in the model are defined: μ = overall constant, α_i = ith group effect, $s_{(i)j}$ = effect of the jth subject measured as the ith group, β_k = kth treatment effect γ_{ik} = group by treatment interaction, and $\varepsilon_{(i)jk}$ = subject by treatment interaction plus a random error component.

We have already seen that in the presence of no interaction the test of H_g: $\alpha_1=\alpha_2=\cdots=\alpha_I$ is identical to the test $H_{03}^{(g)}$. If Σ takes the form specified in (4.12), the test of

$$H_\gamma:\ \gamma_{ik}-\gamma_{i'k}-\gamma_{ik'}+\gamma_{i'k'}=0$$

may be recovered from the H_{01} test of parallelism when $A'A=I$. In this situation, $\nu_h^*=\nu_h R(A)=(I-1)(p-1)$, $\nu_e^*=\nu_e R(A)=(N-I)(p-1)$, and $\mathrm{SSH}=\mathrm{Tr}(S_h)$ and $\mathrm{SSE}=\mathrm{Tr}(S_e)$. In the absence of interaction, the test of differences in treatments has two representations because of the unequal number of subjects in each group.

$$H_\beta:\ \text{all } \beta_j \text{ are equal},$$

$$H_{\beta_w}:\ \beta_j+\sum_{i=1}^{I} N_i\alpha_i/N \text{ are equal for all } j,$$

where H_β is the unweighted test and H_{β_w} is the weighted test. The univariate tests are obtained from the tests $H_{02}^{(t)}$ and $H_{02}^{(t_w)}$, respectively, provided A is chosen so that $A'A=I$ in the multivariate case. For either univariate test, the degrees of freedom are $\nu_h^* = \nu_h R(A) = 1(p-1) = p-1$ and $\nu_e^* = \nu_e R(A) = (N-I)(p-1)$. Furthermore, the SSH$=\mathrm{Tr}(S_h)$ and SSE $=\mathrm{Tr}(S_e)$. However, remember that the matrix C for each multivariate test was defined differently. The mixed model hypotheses are not related to the multivariate tests H_{02} and H_{03}.

EXAMPLE 4.1. Using the data in Table 4.1 taken from Kirk (1968, p. 274), a multivariate and univariate analysis are illustrated.

To demonstrate how we would test H_{01}, H_{02}, and H_{03}, Kirk's data are reanalyzed. For Kirk's data,

$$\underset{(2\times 4)}{B} = \begin{pmatrix} \mu_{11} & \mu_{12} & \mu_{13} & \mu_{14} \\ \mu_{21} & \mu_{22} & \mu_{23} & \mu_{24} \end{pmatrix}, \qquad \underset{(10\times 2)}{X} = \begin{pmatrix} \mathbf{1}_{(5\times 1)} & \mathbf{0} \\ \mathbf{0} & \mathbf{1}_{(5\times 1)} \end{pmatrix}$$

and

$$\underset{(2\times 4)}{\hat{B}} = \begin{pmatrix} 3.75 & 4.00 & 7.00 & 8.00 \\ 1.75 & 3.00 & 5.50 & 10.00 \end{pmatrix}.$$

To test H_{03}, the matrices $C=(1,-1)$ and $A=I_2$ are selected. To test H_{02}, the matrices

$$C = I_2 \quad \text{and} \quad A = \begin{bmatrix} 1 & 0 & 0 \\ -1 & 1 & 0 \\ 0 & -1 & 1 \\ 0 & 0 & -1 \end{bmatrix} = D_3\begin{pmatrix} 1 \\ -1 \end{pmatrix}$$

are used. Finally, H_{01} may be tested by using

$$C = (1-1) \quad \text{and} \quad A = \begin{bmatrix} 1 & 0 & 0 \\ -1 & 1 & 0 \\ 0 & -1 & 1 \\ 0 & 0 & -1 \end{bmatrix} = D_3\begin{pmatrix} 1 \\ -1 \end{pmatrix}.$$

In all cases, $\Gamma=0$. The MANOVA table for the analysis is shown in Table 4.2.

Alternatively, testing $H_{03}^{(g)}$, $H_{02}^{(t)}$, and H_{01} by selecting A such that $A'A=I$, the following matrices are employed.

$$H_{03}^{(g)}\colon\ C=(1,-1), \qquad A' = \left(\tfrac{1}{2}, \tfrac{1}{2}, \tfrac{1}{2}, \tfrac{1}{2}\right)$$

$$H_{02}^{(t)}\colon\ = \left(\tfrac{1}{2}, \tfrac{1}{2}\right), \qquad A = \begin{bmatrix} 0.707107 & 0.408248 & 0.288675 \\ -0.707107 & 0.408248 & 0.288675 \\ 0.000000 & -0.816497 & 0.288675 \\ 0.000000 & 0.000000 & -0.866025 \end{bmatrix}.$$

Table 4.2
Multivariate analysis I

Hypothesis	MSP = SSP/ν	DF	Λ	p-value
H_{03}	$\begin{pmatrix} 8.00 & & & (\text{Sym}) \\ 4.00 & 2.00 & & \\ 6.00 & 3.00 & 4.50 & \\ -8.00 & -4.00 & -6.00 & 8.00 \end{pmatrix}$	1	0.137	0.1169
H_{02}	$\begin{pmatrix} 3.25 & & (\text{Sym}) \\ 7.75 & 30.50 & \\ 11.75 & 28.50 & 42.50 \end{pmatrix}$	2	0.004	0.0002
H_{01}	$\begin{pmatrix} 2.00 & & (\text{Sym}) \\ -1.00 & 0.50 & \\ 7.00 & -3.50 & 24.50 \end{pmatrix}$	1	0.144	0.0371
Error				
H_{03}	$\begin{pmatrix} 1.250 & & & (\text{Sym}) \\ 0.677 & 0.677 & & \\ 0.583 & 0.333 & 0.500 & \\ 0.000 & 0.167 & 0.167 & 0.677 \end{pmatrix}$	6		
H_{02}	$\begin{pmatrix} 0.583 & & (\text{Sym}) \\ -0.250 & 0.500 & \\ 0.083 & 0.167 & 0.833 \end{pmatrix}$	6		
H_{01}	$\begin{pmatrix} 0.583 & & (\text{Sym}) \\ -0.250 & 0.500 & \\ 0.083 & 0.167 & 0.833 \end{pmatrix}$	6		

Table 4.3
Multivariate Analysis II

Hypothesis	SSP	DF	Λ	p-value
$H_{03}^{(g)}$	3.125	1	0.250	0.2070
$H_{02}^{(t)}$	$\begin{pmatrix} 2.250 & & (\text{Sym}) \\ 10.825 & 52.083 & \\ 17.759 & 85.442 & 140.167 \end{pmatrix}$	1	0.027	0.0014
H_{01}	$\begin{pmatrix} 1.000 & & (\text{Sym}) \\ 0.000 & 0.000 & \\ 4.287 & 0.000 & 18.375 \end{pmatrix}$	1	0.144	0.0371
Error				
$H_{03}^{(g)}$	9.378	6		
$H_{02}^{(t)}$	$\begin{pmatrix} 1.752 & & (\text{Sym}) \\ 0.144 & 1.584 & \\ 0.408 & 2.004 & 5.790 \end{pmatrix}$	6		
H_{01}	$\begin{pmatrix} 1.752 & & (\text{Sym}) \\ 0.144 & 1.584 & \\ 0.408 & 2.004 & 5.790 \end{pmatrix}$	6		

To test H_{01}, the matrix C defined to test $H_{03}^{(g)}$ and the matrix A defined to test $H_{02}^{(t)}$ are used. The MANOVA table for this analysis is displayed in Table 4.3.

From the entries in Table 4.3, univariate F-ratios for testing for groups, treatments and treatment by group interactions are immediately obtained:

$$F_g = \frac{3.125/1}{9.378/6} = \frac{3.125}{1.563} = 2.00 \sim F(1,6),$$

$$F_t = \frac{194.50/3}{9.126/18} = \frac{64.83}{0.51} = 127.88 \sim F(3,18),$$

$$F_{gt} = \frac{19.375/3}{9.126/18} = \frac{6.46}{0.51} = 12.74 \sim F(3,18).$$

The hypothesis (ν_h^*) and error (ν_e^*) degrees of freedom for each univariate F-ratio are obtained by multiplying the degrees of freedom for each multivariate test by the rank of the normalized post matrix A corresponding to the test. For the F_t ratio, $\nu_h^* = \nu_h R(A) = 1 \cdot 3 = 3$ and $\nu_e = \nu_e R(A) = 6 \cdot 3 = 18$. The others follow similarly.

5. Factorial design structures

In many applications of repeated measurement designs, subjects receive treatments in low-order factorial combinations where the sequence of administration is randomized independently for each subject. That is, suppose groups of subjects are randomly assigned to I methods and the set of subjects receive BC treatment combinations. For the $I=2$ group case, the data may be organized as in Table 5.1.

To analyze the data in Table 5.1, we represent the observation vector of repeated measures as

$$\mathbf{Y}_{ij} = \boldsymbol{\mu}_i + \boldsymbol{\varepsilon}_{ij}, \quad i = 1,2,\ldots,I, j = 1,2,\ldots,J_i, \tag{5.1}$$

so that the parameter matrix of means take the form

$$B = \begin{pmatrix} \mu_{11} & \mu_{12} & \mu_{13} & \mu_{14} & \mu_{15} & \mu_{16} & \mu_{17} & \mu_{18} & \mu_{19} \\ \mu_{21} & \mu_{22} & \mu_{23} & \mu_{24} & \mu_{25} & \mu_{26} & \mu_{27} & \mu_{28} & \mu_{29} \end{pmatrix}, \tag{5.2}$$

Table 5.1
A 3^2 factorial design structure

Group	Subjects within groups	B_1			B_2			B_3		
		C_1	C_2	C_3	C_1	C_2	C_3	C_1	C_2	C_3
A_1	1	y_{1111}	y_{1112}	y_{1113}	y_{1121}	y_{1122}	y_{1123}	y_{1131}	y_{1132}	y_{1133}
	2	y_{1211}	y_{1212}	y_{1213}	y_{1221}	y_{1222}	y_{1223}	y_{1231}	y_{1232}	y_{1233}
	.	.	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.	.	.
	J_1	y_{1J_111}	y_{1J_112}	y_{1J_113}	y_{1J_121}	y_{1J_122}	y_{1J_223}	y_{1J_131}	y_{1J_132}	y_{1J_133}
A_2	1	y_{2111}	y_{2112}	y_{2113}	y_{2121}	y_{2122}	y_{2123}	y_{2131}	y_{2132}	y_{2133}
	2	y_{2211}	y_{2212}	y_{2213}	y_{2221}	y_{2222}	y_{2223}	y_{2231}	y_{2232}	y_{2233}
	.	.	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.	.	.
	J_2	y_{2J_211}	y_{2J_212}	y_{2J_213}	y_{2J_221}	y_{2J_222}	y_{2J_223}	y_{2J_231}	y_{2J_232}	y_{2J_233}

and

$$X=\begin{pmatrix} \mathbf{1}_{J_1} & \mathbf{0} \\ \mathbf{0} & \mathbf{1}_{J_2} \end{pmatrix}$$

for the two group case. Furthermore, we assume that $\varepsilon_{ij} \sim IN_p(\mathbf{0}, \Sigma)$.

Corresponding to the multivariate formulation is the classical univariate mixed model.

$$\begin{aligned} y_{ijkm} &= \mu + \alpha_i + \beta_k + \gamma_m + (\alpha\beta)_{ik} + (\alpha\gamma)_{im} + (\beta\gamma)_{km} \\ &\quad + (\alpha\beta\gamma)_{ikm} + s_{(i)j} + (\beta s)_{(i)jk} + (\gamma s)_{(i)jm} + \varepsilon_{(i)jkm}, \qquad (5.3) \\ & i = 1,2,\ldots,I; \quad j = 1,2,\ldots,J_i; \\ & k = 1,2,\ldots,K; \quad m = 1,2,\ldots,M, \end{aligned}$$

where $s_{(i)j} \sim IN(0, \rho\sigma^2)$, $(\beta s)_{(i)jk} \sim IN(0, \rho\sigma^2)$, $(\gamma s)_{(i)jm} \sim IN(0, \rho\sigma^2)$, $\varepsilon_{(i)jkm} \sim IN(0, (1-\rho)\sigma^2)$, and $\varepsilon_{(i)jkm}$, $(\gamma s)_{(i)jm}$, $(\beta s)_{(i)j}$ are jointly independent. As in the preceding two sections, we will illustrate how from the multivariate analysis the standard univariate results may be recovered.

The first hypothesis of interest employing the multivariate model is to see whether there is an interaction between A and the levels of B, C and BC which as in Section 4.1 we call the test of parallelism. Following the formulation for testing interaction (parallelism) for the design in Section 4.1, the matrices needed to test for parallelism, with the hypothesis stated in the form $CBA = 0$, are

$$C = (1, -1), \qquad A = \left[\underbrace{\begin{matrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ -1 & 1 \\ -1 & 1 \\ -1 & 1 \\ 0 & -1 \\ 0 & -1 \\ 0 & -1 \end{matrix}}_{B} \quad \underbrace{\begin{matrix} 1 & 0 \\ -1 & 1 \\ 0 & -1 \\ 1 & 0 \\ -1 & 1 \\ 0 & -1 \\ 1 & 0 \\ -1 & 1 \\ 0 & -1 \end{matrix}}_{C} \quad \underbrace{\begin{matrix} 1 & 0 & 0 & 0 \\ -1 & 1 & 0 & 0 \\ 0 & -1 & 0 & 0 \\ -1 & 0 & 1 & 0 \\ 1 & -1 & -1 & 1 \\ 0 & 1 & 0 & -1 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 1 & -1 \\ 0 & 0 & 0 & 0 \end{matrix}}_{BC}\right]. \tag{5.4}$$

The first two columns of the post matrix A are formed to evaluate AB, the next two are used to investigate AC, and the last four, constructed from the first two by taking Hadamard vector products, are used to test ABC. Normalizing the post matrix A so that $A'A = I$ and separating out the submatrices associated with AB, AC and ABC, we sum certain of the diagonal elements of the SSP matrix and the error matrix in the test of parallelism to construct univariate F-ratios.

To test BC, given that the parallelism hypothesis is tenable, the matrices

$$C = (1, -1), \qquad A = \begin{bmatrix} A_1 & 0 \\ 0 & A_1 \\ -A_1 & -A_1 \end{bmatrix} \quad \text{and} \quad A_1 = \begin{bmatrix} 1 & 0 \\ 0 & 1 \\ -1 & 1 \end{bmatrix} \tag{5.5}$$

are used. The post matrix A is constructed by arranging the elements of B in table form (Table 5.2) and forming linearly independent contracts such that

$$\eta_{ij} - \eta_{i'j} - \eta_{ij'} + \eta_{i'j'} = 0.$$

Normalizing A, the univariate F-ratio for testing BC is immediately obtained. If the parallelism hypothesis is not tenable, we may test BC with

Table 5.2
Rearranged means

	C_1	C_2	C_3		C_1	C_2	C_3
B_1	$\mu_{11} = \eta_{11}$	$\mu_{12} = \eta_{12}$	$\mu_{13} = \eta_{13}$	B_1	$\mu_{21} = \eta_{11}$	$\mu_{22} = \eta_{12}$	$\mu_{23} = \eta_{13}$
B_2	$\mu_{14} = \eta_{21}$	$\mu_{15} = \eta_{23}$	$\mu_{16} = \eta_{23}$	B_2	$\mu_{24} = \eta_{21}$	$\mu_{25} = \eta_{12}$	$\mu_{26} = \eta_{23}$
B_3	$\mu_{17} = \eta_{31}$	$\mu_{18} = \eta_{32}$	$\mu_{19} = \eta_{33}$	B_3	$\mu_{27} = \eta_{31}$	$\mu_{28} = \eta_{32}$	$\mu_{29} = \eta_{33}$

$(BC)^*$ by using $C=I_2$ and the post matrix A defined in (5.5). The univariate test of BC is not obtained from testing $(BC)^*$.

To test the main effect hypothesis A, B, and C under parallelism and no BC interaction, we use the following matrices for C and the post matrices A when the hypotheses are expressed in the form $CBA=0$:

$$(A):\quad C=(1,-1),\qquad A=\mathbf{1}_9,$$

$$(B):\quad C=(1,1),\qquad A=\begin{bmatrix} \mathbf{1}_3 & \mathbf{0}_3 \\ \mathbf{0}_3 & \mathbf{1}_3 \\ -\mathbf{1}_3 & -\mathbf{1}_3 \end{bmatrix},$$

$$(C):\quad C=(1,1),\qquad A=\begin{bmatrix} \mathbf{a} & \mathbf{b} \\ \mathbf{a} & \mathbf{b} \\ \mathbf{a} & \mathbf{b} \end{bmatrix}, \tag{5.6}$$

where $\mathbf{a}'=(1,0,1)$ and $\mathbf{b}'=(0,1,-1)$. Normalizing the post matrix A in (5.6), univariate tests are immediately obtained from the multivariate tests. Tests of A, B and C which do not require parallelism are denoted by A^*, B^*, and C^*. In each case, the post matrix A is identical to the corresponding matrices in (5.6), however, the matrices C take the form:

$$(A^*)\colon C=(1,-1),\qquad (B^*)\colon C=I_2,\quad \text{and}\quad (C^*)\colon C=I_2.$$

To write each of the multivariate hypotheses in terms of the elements of B given in (5.2), we merely substitute the hypothesis test matrix C and the post matrix A into the general expression $CBA=0$ for each hypothesis. To test each of the preceding hypotheses, the expressions $S_h = (C\hat{B}A)'[C(X'X)^{-1}C']^{-1}(C\hat{B}A)$, $S_e = A'Y[I-X(X'X)^{-1}X']YA$ are evaluated where $\hat{B}$ is a matrix of means.

Example 5.1. Using the data in Table 5.3 the hypotheses discussed and the relationship to the univariate mixed model are illustrated.

To obtain univariate tests from appropriate multivariate tests, we stated that one may take the $\mathrm{Tr}(S_h)$ and the $\mathrm{Tr}(S_e)$ and divide the result by ν_h^* and ν_e^*, respectively. That is, $\mathrm{MSH}=\mathrm{Tr}(S_h)/\nu_h\cdot R(A)$, and $\mathrm{MSE}=\mathrm{Tr}(S_e)/\nu_e\cdot R(A)$. Since $\mathrm{MSP}=\mathrm{SSP}/\nu$, we see that the hypothesis mean square and the error mean square can alternatively be obtained by averaging the diagonal elements of MSP matrices. This approach is illustrated for the example.

To illustrate the construction of the multivariate tests discussed, the MSP matrices are displayed in Table 5.4; the post matrix A for each hypothesis without an asterisk (*) has been normalized so that $A'A=I$.

Averaging the diagonal elements of the hypothesis test matrices of AB, AC and ABC within Paral, BC, C, B and A in Table 5.4 and the diagonal

Table 5.3
Factorial structure data

		B_1			B_2			B_3		
		C_1	C_2	C_3	C_1	C_2	C_3	C_1	C_2	C_3
	s_1	20	21	21	32	42	37	32	32	32
	s_2	67	48	29	43	56	48	39	40	41
	s_3	37	31	25	27	28	30	31	33	34
	s_4	42	40	38	37	36	28	19	27	35
A_1	s_5	57	45	32	27	21	25	30	29	29
	s_6	39	39	38	46	54	43	31	29	28
	s_7	43	32	20	33	46	44	42	37	31
	s_8	35	34	34	39	43	39	35	39	42
	s_9	41	32	23	37	51	39	27	28	30
	s_{10}	39	32	24	30	35	31	26	29	32
	s'_1	47	36	25	31	36	29	21	24	27
	s'_2	53	43	32	40	48	47	46	50	54
	s'_3	38	35	33	38	42	45	48	48	49
	s'_4	60	51	41	54	67	60	53	52	50
A_2	s'_5	37	36	35	40	45	40	34	40	46
	s'_6	59	48	37	45	52	44	36	44	52
	s'_7	67	50	33	47	61	46	31	41	50
	s'_8	43	35	27	32	36	35	33	33	32
	s'_9	64	59	53	58	62	51	40	42	43
	s'_{10}	41	38	34	41	47	42	37	41	46

elements of the correspondent error matrices, univariate split-split plot F-ratios are immediately constructed. To illustrate

$$F_{ABC}(4,72)=\frac{(5.513+2.604+11.704+47.535)/4}{(20.357+31.497+8.778+27.700)/4}=\frac{16.84}{22.08}=0.76,$$

$$F_{BC}(4,72)=\frac{(1872.113+0.104+270.937+297.735)/4}{(44.424+0.099+34.188+9.622)/4}=\frac{610.22}{22.08}=27.64,$$

$$F_{AC}(2,36)=\frac{(4.033+2.178)/2}{(7.815+20.801)/2}=\frac{3.11}{14.31}=0.22,$$

$$F_{C}(2,36)=\frac{(261.075+166.736)/2}{(23.475+5.141)/2}=\frac{213.91}{14.31}=14.95,$$

$$F_{AB}(2,36)=\frac{(0.033+18.678)/2}{(96.313+97.551)/2}=\frac{9.36}{96.93}=0.10,$$

$$F_{B}(2,36)=\frac{(154.133+480.711)/2}{(119.417+74.448)/2}=\frac{317.42}{96.93}=3.29,$$

$$F_{A}(1,18)=\frac{3042.22}{356.05}=8.54.$$

Hyp.	DF	MSP	Λ	p-value
Paral	1	$\begin{bmatrix} 0.033 & & & & & & & \text{(Sym)} \\ 0.789 & 18.678 & & & & & & \\ 0.367 & 8.679 & 4.033 & & & & & \\ 0.269 & 6.378 & 2.964 & 2.178 & & & & \\ -0.429 & -10.147 & -4.715 & -3.465 & 5.513 & & & \\ -0.295 & -6.974 & -3.241 & -2.381 & 3.789 & 2.604 & & \\ -0.625 & -14.785 & -6.871 & -5.049 & 8.032 & 5.521 & 11.704 & \\ -1.529 & -29.797 & -13.846 & -10.174 & 16.188 & 11.126 & 23.587 & 47.535 \end{bmatrix}$	0.809	0.9392
BC	1	$\begin{bmatrix} 1872.113 & & & \text{(Sym)} \\ 13.965 & 0.104 & & \\ -712.198 & -5.313 & 270.937 & \\ 746.587 & 5.569 & -284.020 & 297.735 \end{bmatrix}$	0.225	<0.0001
C	1	$\begin{pmatrix} 261.075 & \text{(Sym)} \\ 208.640 & 166.736 \end{pmatrix}$	0.325	<0.0001
B	1	$\begin{pmatrix} 154.133 & \text{(Sym)} \\ 272.201 & 480.711 \end{pmatrix}$	0.676	0.0356
A	1	3042.22	0.678	0.0091
$(BC)^*$	2	$\begin{bmatrix} 3870.251 & & & \text{(Sym)} \\ 1956.651 & 989.300 & & \\ 723.750 & 364.200 & 166.500 & \\ 1508.051 & 762.200 & 285.900 & 588.100 \end{bmatrix}$	0.209	0.0012
C^*	2	$\begin{pmatrix} 783.23 & \text{(Sym)} \\ 933.67 & 1113.03 \end{pmatrix}$	0.316	0.0005
B^*	2	$\begin{pmatrix} 506.50 & \text{(Sym)} \\ 980.40 & 1944.40 \end{pmatrix}$	0.670	0.1357
A^*	1	(deleted, lack of space)	0.533	0.5114
Error				
Paral	18	$\begin{bmatrix} 96.313 & & & & & & & \text{(Sym)} \\ 25.606 & 97.551 & & & & & & \\ 20.619 & 1.749 & 7.815 & & & & & \\ 9.998 & 24.640 & 6.836 & 20.801 & & & & \\ -9.445 & 10.182 & 0.982 & 16.135 & 20.357 & & & \\ 14.754 & -7.007 & 10.144 & 18.444 & 18.335 & 31.497 & & \\ 22.132 & 5.946 & 2.214 & 0.538 & -0.256 & 2.997 & 8.778 & \\ 20.531 & 25.214 & -0.870 & 6.548 & 9.002 & 5.106 & 12.761 & 27.700 \end{bmatrix}$		

In Example 5.1, we illustrated the analysis of a repeated measurement experiment with a 3^2 factorial design within the vector (subject) observation and a simple one-way design for the subjects (vectors). Numerous alternatives to this arrangement are possible and easily analyzed employing multivariate procedures.

6. Crossover/changeover design

Implicit in the vector valued analysis of repeated measurement data has been the assumption that the experimenter randomized the order of treatments for each subject independently to eliminate sequence effects and that there was sufficient delay between treatments to minimize residual or carryover treatment effects.

Suppose that in a repeated measurement experiment that sufficient time existed between the administration of two treatments, but it was felt that a sequence effect may be present. To assess it, a one sample multivariate design may be modified as shown in Table 6.1 to analyze sequence, treatment (represented by a and b) and period effects. The setup for the data in Table 6.1 is identical to the design discussed in Section 4. The parameter matrix is

$$B=\begin{pmatrix} \mu_{11} & \mu_{12} \\ \mu_{21} & \mu_{22} \end{pmatrix}. \tag{6.1}$$

The test for treatments becomes

$$H_T\colon \mu_{11}+\mu_{22}=\mu_{12}+\mu_{21} \tag{6.2}$$

Table 6.1
Two-period crossover design

Sequence	Subjects within sequence	Periods P_1	P_2
AB	S_1	a	b
	S_2	a	b
	S_3	a	b
	S_4	a	b
	S_5	a	b
BA	S_1	b	a
	S_2	b	a
	S_3	b	a
	S_4	b	a
	S_5	b	a

the primary hypothesis of interest. A test for sequence may be represented as

$$H_S: (\mu_{11}+\mu_{12})/2=(\mu_{21}+\mu_{22})/2. \tag{6.3}$$

Finally, to test for periods, we may use

$$H_P: (\mu_{11}+\mu_{21})/2=(\mu_{12}+\mu_{22})/2. \tag{6.4}$$

In a design with p periods, there are $p!$ possible sequences. When the number of periods is larger than 3, generating 6 possible sequences, one may sample from among the sequences.

The ten subjects in Table 6.1 may be grouped into five pairs, each pair forming a 2×2 Latin Square for periods and treatments as illustrated in Table 6.2. This design would be appropriate if the period effect varies from subject to subject. In the simple crossover design, the period effect is assumed to be the same for all subjects. Thus, for a series of Latin Squares, we may assess period $\times$ square variation.

Table 6.2
Series of Latin Squares

		Periods	
Squares	Subjects within squares	P_1	P_2
Square 1	S_1	a	b
	S_2	b	a
Square 2	S_1	a	b
	S_2	b	a
Square 3	S_1	a	b
	S_2	b	a
Square 4	S_1	a	b
	S_2	b	a
Square 5	S_1	a	b
	S_2	b	a

As suggested by Cochran and Cox (1957), the data in Table 6.2 may be viewed as an incomplete four way layout or r replicate Latin Squares. Thus, we have a square by subject by period by treatment design. Letting r represent the number of squares and d the size of the square, the rd^2 degrees of freedom for the incomplete design may be partitioned as follows.

Incomplete design	df
Squares	$r-1$
Subjects	$d-1$
Subjects × squares	$(d-1)(r-1)$
Periods	$(d-1)$
Periods × squares	$(d-1)(r-1)$
Treatments	$d-1$
Residual	$r(d-1)^2-(d-1)$
"Total"	rd^2-1

For the simple crossover design (Table 6.1) and the Series of Latin Squares (Table 6.2), the following results.

Simple crossover design	
Sequences	$r-1$
Subjects within sequences	$r(d-1)$
Periods	$d-1$
Treatments	$d-1$
Residual	$(d-1)(rd-2)$
"Total"	rd^2-1

Series of squares	
Squares	$r-1$
Subjects within squares	$r(d-1)$
Periods	$d-1$
Periods × squares	$(d-1)(r-1)$
Treatments	$d-1$
Residual	$r(d-1)^2-(d-1)$
"Total"	rd^2-1

To analyze the data in Table 6.2, from a multivariate point of view, the data ignoring empty cells are organized as a one-group multivariate design:

	P_1		P_2	
	A_1	B_1	A_1	B_2
S_1	a	b	a	b
S_2	a	b	a	b
S_3	a	b	a	b
S_4	a	b	a	b
S_5	a	b	a	b

with parameter matrix $B=(\mu_1\, \mu_2\, \mu_3\, \mu_4)$.

To test for period effects,

$$H_p\colon (\mu_1+\mu_2)/2=(\mu_3+\mu_4)/2$$

the matrices C and A are:

$$C=1 \quad \text{and} \quad A'=(1/2, 1/2, -1/2, -1/2). \tag{6.5}$$

To test for treatment effects,

$$H_T: (\mu_1+\mu_3)/2=(\mu_2+\mu_4)/2,$$

the matrices C and A are:

$$C=1 \quad \text{and} \quad A'=(1/2,-1/2,1/2,-1/2). \tag{6.6}$$

To assess the effect of squares or blocks, the data are organized as in Table 6.2. Now, however, the parameter matrix takes the form

$$B'=\begin{pmatrix} \mu_{11} & \mu_{21} & \mu_{31} & \mu_{41} & \mu_{51} \\ \mu_{12} & \mu_{22} & \mu_{32} & \mu_{42} & \mu_{52} \end{pmatrix}.$$

To test for squares, the matrices C and A are:

$$C=\left(I_4 \vdots -\mathbf{1}\right), \qquad A=(\mathbf{1}_2). \tag{6.7}$$

EXAMPLE 6.1. Cochran and Cox (1957, p. 130) give data for comparing the speeds of two calculators A and B. The order of the machines was balanced and assigned to subjects who performed operations first on one machine and then on the other. The dependent variable was the time (seconds minus 2 minutes) taken to calculate a sum of squares. The data for the experiment are shown in Table 6.3.

To analyze the data from a multivariate point of view, the data are reorganized as in Table 6.4 for the within subject analysis.

Table 6.3
Cochran and Cox data

Squares	Subjects within blocks	First (P_1) calculation	Second (P_2) calculation
Square 1	S_1	A 30	B 14
	S_2	B 21	A 21
Square 2	S_1	A 22	B 5
	S_2	B 13	A 22
Square 3	S_1	A 29	B 17
	S_2	B 13	A 18
Square 4	S_1	A 12	B 14
	S_2	B 7	A 16
Square 5	S_1	A 23	B 8
	S_2	B 24	A 23

Table 6.4
Within subject analysis

	P_1		P_2	
Subjects	A_1	B_1	A_2	B_2
S_1	30	21	21	14
S_2	22	13	22	5
S_3	29	13	18	17
S_4	12	7	16	14
S_5	23	24	23	8

Forming the matrices

$$C=1 \quad \text{and} \quad A'=\begin{bmatrix} \frac{1}{2} & \frac{1}{2} & -\frac{1}{2} & -\frac{1}{2} \\ \frac{1}{2} & -\frac{1}{2} & \frac{1}{2} & -\frac{1}{2} \end{bmatrix} \tag{6.8}$$

so that $A'A=I$, the MS_h and MS_e matrices are:

$$\begin{aligned} \mathrm{MS}_h &= \begin{pmatrix} 64.80 & (\mathrm{Sym}) \\ 144.00 & 320.00 \end{pmatrix} \\ \mathrm{MR}_e &= \begin{pmatrix} 30.425 & (\mathrm{Sym}) \\ 9.625 & 11.625 \end{pmatrix} \end{aligned} \tag{6.9}$$

with $\nu_h=1$ and $\nu_e=4$. Since $A'A=I$ and the $R(A)$ for each test is 1, the appropriate F-ratios from the analysis are obtained from the diagonals of the matrices in (6.9) and ANOVA Table 6.5 results.

To analyze the effects of squares, the data are organized as in Table 6.6. Using $C=(I_4\vdots-1)$ and $A'=(0.707107, 0.707107)$, the F-ratio for the test for differences in squares is

$$F=\frac{218.3/4}{139.5/5}=\frac{54.5750}{27.9000}=1.9561 \sim F(4,5).$$

Table 6.5
Latin Square series within subject analysis

Source	df	MS	F	p-values
Period	1	64.80	2.1298	0.2183
Treatment	1	320.00	27.5269	0.0064
Error period	4	30.425		
Error treatment	4	11.625		

Table 6.6
Block analysis

Squares	Subjects Within Blocks	P_1	P_2
Square 1	S_1	30	14
	S_2	21	21
Square 2	S_1	22	5
	S_2	13	22
Square 3	S_1	29	17
	S_2	13	18
Square 4	S_1	12	14
	S_2	7	16
Square 5	S_1	23	8
	S_2	24	23

Table 6.7
ANOVA for Cochran and Cox data

Source	SS	df	MS	F	p-value
Between					
Squares	218.30	4	54.575	1.9561	0.2397
Subjects within squares	139.50	5			
Within					
Periods	64.80	1	64.800	2.1298	0.2183
Treatments	320.00	1	320.000	27.5269	0.0064
Error periods	121.70	4	30.425		
Error treatment	46.50	4	11.625		
"Total"	910.80	19			

Using the multivariate split design approach because of the incomplete vector observations, we combine the results into one table, Table 6.7. As usual, subjects are random and squares, periods, and treatments are fixed.

While it is possible to recover the analysis of univariate designs with incomplete within subject vector data from a multivariate point of view, the variations in the reorganization of the data for the multivariate analysis are complex because the multivariate approach requires complete vectors.

7. Multivariate repeated measurements

In the preceding designs, each subject was observed at several experimental treatment conditions and one variate was measured. In many experimental situations, data on several variates are observed repeatedly

Treatment subject	t_1	t_2	$\cdots$	t_q
A_i s_i	$y_{ij1}=\begin{bmatrix} y^{(1)}_{ij1} \\ y^{(1)}_{ij2} \\ \vdots \\ y^{(1)}_{ijp} \end{bmatrix}$	$y_{ij2}=\begin{bmatrix} y^{(2)}_{ij1} \\ y^{(2)}_{ij2} \\ \vdots \\ y^{(2)}_{ijp} \end{bmatrix}$	$\cdots$	$y_{ijq}=\begin{bmatrix} y^{(q)}_{ij1} \\ y^{(q)}_{ij2} \\ \vdots \\ y^{(q)}_{ijp} \end{bmatrix}$

Fig. 7.1. p-variate observations over q conditions.

over several experimental conditions. Designs with multivariate observations on p variates over q conditions are called multivariate or multi-response repeated measurement designs since the multivariate observations are not commensurable at each treatment condition, but are commensurable over conditions a variable at a time (Fig. 7.1).

Since each of the p-variates are observed over q conditions, it is convenient to rearrange the data in Fig. 7.1 by variates for a multivariate repeated measures analysis so that each variate is observed over q periods (Fig. 7.2). The data matrix Y for the analysis is of order $N \times pq$, where the first q columns correspond to variable one, the next q to variable 2, the next q to variable 3 and so on up to the pth variable. Alternatively, using the data as arranged in Fig. 7.2, a multivariate mixed model analysis of variance procedure may be used to analyze multi-response repeated measures data. This would be done by simply extending the univariate sum of squares to sum of squares and products matrices and calculating multivariate criteria to test hypotheses. However, for such an analysis we must not only assume a restrictive structure on the variance-covariance matrix associated with each variable over q conditions but that the structure on each variance-covariance matrix between variables across conditions is constant. This is even more restrictive than the univariate assumptions and for this reason is not usually recommended. Instead, a multivariate approach should be used.

Treatment subject	1	2	$\cdots$	1p
A_i s_i	$y_{ij1}=\begin{bmatrix} y^{(1)}_{ij1} \\ y^{(2)}_{ij1} \\ \vdots \\ y^{(q)}_{ij1} \end{bmatrix}$	$y_{ij2}=\begin{bmatrix} y^{(1)}_{ij2} \\ y^{(2)}_{ij2} \\ \vdots \\ y^{(q)}_{ij2} \end{bmatrix}$	$\cdots$	$y_{ijp}=\begin{bmatrix} y^{(1)}_{ijp} \\ y^{(2)}_{ij2} \\ \vdots \\ y^{(q)}_{ijp} \end{bmatrix}$

Fig. 7.2. Data layout for multivariate repeated measures design.

Table 7.1
Means for multivariate repeated measurements data

	Variables								
	1			2			3		
Conditions	C_1	C_2	C_3	C_1	C_2	C_3	C_1	C_2	C_3
Treatments A_1	μ_{11}	μ_{12}	μ_{13}	μ_{14}	μ_{15}	μ_{16}	μ_{17}	μ_{18}	μ_{19}
Treatments A_2	μ_{21}	μ_{22}	μ_{23}	μ_{24}	μ_{25}	μ_{26}	μ_{27}	μ_{28}	μ_{29}

To analyze profile data for multivariate measurements arranged as in Fig. 7.2, the general linear model is again used. Letting $p=q=3$, for the arrangement of population parameters shown in Table 7.1, we consider some hypotheses which might be of interest for multi-response data.

The first hypothesis of interest for profile data is whether the profiles for each variable are parallel. That is, is there an interaction between conditions and treatment? The hypothesis may be stated as

$$\begin{aligned} H_{(AC)^*}\colon & (\mu_{11}-\mu_{12},\mu_{12}-\mu_{13},\ldots,\mu_{18}-\mu_{19}) \\ & =(\mu_{21}-\mu_{22},\mu_{22}-\mu_{23},\ldots,\mu_{28}-\mu_{29}). \end{aligned} \tag{7.1}$$

The matrices C and A to test $H_{(AC)^*}$ are

$$C_{(AC)^*}=(1-1) \quad \text{and} \quad \underset{9\times 6}{A}=D\begin{bmatrix} 1 & 0 \\ -1 & 1 \\ 0 & -1 \end{bmatrix}. \tag{7.2}$$

To test for differences in treatments, H_{A^*}, where H_{A^*} is

$$H_{A^*}\colon \boldsymbol{\mu}_1=\boldsymbol{\mu}_2, \tag{7.3}$$

the matrices

$$C_{A^*}=(1-1) \quad \text{and} \quad A=I_9 \tag{7.4}$$

are constructed. For differences in conditions,

$$H_{C^*}\colon \begin{bmatrix} \mu_{11} \\ \mu_{21} \\ \mu_{14} \\ \mu_{24} \\ \mu_{17} \\ \mu_{27} \end{bmatrix} = \begin{bmatrix} \mu_{12} \\ \mu_{22} \\ \mu_{15} \\ \mu_{25} \\ \mu_{18} \\ \mu_{28} \end{bmatrix} = \begin{bmatrix} \mu_{13} \\ \mu_{23} \\ \mu_{16} \\ \mu_{26} \\ \mu_{19} \\ \mu_{29} \end{bmatrix}, \tag{7.5}$$

the test matrices are

$$C_{C^*} = I_2 \quad \text{and} \quad \underset{9\times 6}{A} = D\begin{bmatrix} 1 & 0 \\ -1 & 1 \\ 0 & -1 \end{bmatrix}. \tag{7.6}$$

Given parallelism, tests for differences between the two treatments and among conditions are written as

$$A: \begin{bmatrix} \sum_{j=1}^{3} \mu_{1j}/3 \\ \sum_{j=4}^{6} \mu_{1j}/3 \\ \sum_{j=7}^{9} \mu_{1j}/3 \end{bmatrix} = \begin{bmatrix} \sum_{j=1}^{3} \mu_{2j}/3 \\ \sum_{j=4}^{6} \mu_{2j}/3 \\ \sum_{j=7}^{9} \mu_{2j}/3 \end{bmatrix}, \tag{7.7}$$

and

$$C: \begin{bmatrix} \sum_{i=1}^{2} \mu_{i1}/2 \\ \sum_{i=1}^{2} \mu_{i4}/2 \\ \sum_{i=1}^{2} \mu_{i7}/2 \end{bmatrix} = \begin{bmatrix} \sum_{i=1}^{2} \mu_{i2}/2 \\ \sum_{i=1}^{2} \mu_{i5}/2 \\ \sum_{i=1}^{2} \mu_{i8}/2 \end{bmatrix} = \begin{bmatrix} \sum_{i=1}^{2} \mu_{i3}/2 \\ \sum_{i=1}^{2} \mu_{i6}/2 \\ \sum_{i=1}^{2} \mu_{i9}/2 \end{bmatrix}, \tag{7.8}$$

respectively. Hypothesis test matrices to test hypotheses A and C become

$$\begin{aligned} C_A &= (1, -1), & \underset{9\times 3}{A} &= D\begin{bmatrix} \frac{1}{3} \\ \frac{1}{3} \\ \frac{1}{3} \end{bmatrix}, \\ C_C &= \left(\tfrac{1}{2}, \tfrac{1}{2}\right), & \underset{9\times 6}{A} &= D\begin{bmatrix} 1 & 0 \\ 0 & 1 \\ -1 & 1 \end{bmatrix}. \end{aligned} \tag{7.9}$$

Provided the post matrix A, for hypotheses stated as $CBA = 0$, is normalized so that $A'A = I$, multivariate mixed model multivariate criteria are immediately obtained from the multivariate approach for the hypotheses A, C, and $(AC)^*$. This is not the case for the hypotheses A^* and C^*.

Example 7.1. To illustrate the tests of several multivariate hypotheses and to show how one may recover mixed model results from a multivariate

Table 7.2

Individual measurements utilized to assess the changes in the vertical position of the mandible at three time points of activator treatment

	Subject	SOr-Me (mm)			ANS-Me (mm)			Pal-MP angle (degrees)		
Group	Number	1	2	3	1	2	3	1	2	3
	1	117.0	117.5	118.5	59.0	59.0	60.0	10.5	16.5	16.5
	2	109.0	110.5	111.0	60.0	61.5	61.5	30.5	30.5	30.5
	3	117.0	120.0	120.5	60.0	61.5	62.0	23.5	23.5	23.5
	4	122.0	126.0	127.0	67.5	70.5	71.5	33.0	32.0	32.5
T_1	5	116.0	118.5	119.5	61.5	62.5	63.5	24.5	24.5	24.5
	6	123.0	126.0	127.0	65.5	61.5	67.5	22.0	22.0	22.0
	7	130.5	132.0	134.5	68.5	69.5	71.0	33.0	32.5	32.0
	8	126.5	128.5	130.5	69.0	71.0	73.0	20.0	20.0	20.0
	9	113.0	116.5	118.0	58.0	59.0	60.5	25.0	25.0	24.5
	Means	119.33	121.72	122.94	63.22	64.00	65.61	24.67	25.17	25.11
	1	128.0	129.0	131.5	67.0	67.5	69.0	24.0	24.0	24.0
	2	116.5	120.0	121.5	63.5	65.0	66.0	28.5	29.5	29.5
	3	121.5	125.5	127.0	64.5	67.5	69.0	26.5	27.0	27.0
	4	109.5	112.0	114.0	54.0	55.5	57.0	18.0	18.5	19.0
T_2	5	133.0	136.0	137.5	72.0	73.5	75.5	34.5	34.5	34.5
	6	120.0	124.5	126.0	62.5	65.0	66.0	26.0	26.0	26.0
	7	129.5	133.5	134.5	65.0	68.0	69.0	18.5	18.5	18.5
	8	122.0	124.0	125.5	64.5	65.5	66.0	18.5	18.5	18.5
	9	125.0	127.0	128.0	65.5	66.5	67.0	21.5	21.5	21.6
	Means	122.78	125.72	127.28	64.28	66.00	67.17	24.00	24.22	24.29

analysis, the data provided by Dr. Tom Zullo in the School of Dental Medicine at the University of Pittsburgh and displayed in Table 7.2 are used.

Tests of differences between groups (7.3), differences among conditions (7.5) and the interactions between groups and conditions (7.1) are the primary hypotheses of interest. Alternatively, given that the interaction hypothesis is tenable, tests for differences between groups and differences

Table 7.3

Multivariate profile analysis of Zullo's data

Hypotheses	Wilks' Λ	DF	p-value
$(AC)^*$	0.583	(6, 1, 16)	0.3292
A^*	0.422	(9, 1, 16)	0.3965
C^*	0.026	(6, 2, 16)	<0.0001
A	0.884	(3, 1, 16)	0.6176
C	0.034	(6, 1, 16)	<0.0001

among conditions, as defined in (7.7) and (7.8), may be tested. Using Wilks' Λ-criterion to test the hypotheses, the results are displayed in Table 7.3.

As mentioned previously, mixed model multivariate tests are obtained from the appropriately normalized multivariate hypotheses in Table 7.3. To see this, consider the hypothesis and error mean square and product matrices for testing C; the matrices were obtained by normalizing the 9×6 post matrix A given in (7.9) so that $A'A=I$ for the hypothesis given in (7.8) when written in the form $CBA=0$.

$$\mathrm{MSP}_C=\begin{bmatrix} 148.028 & & & & & (\mathrm{Sym}) \\ -26.927 & 4.898 & & & & \\ 96.391 & -17.521 & 62.674 & & & \\ 2.927 & -0.532 & 1.904 & 0.058 & & \\ 13.383 & -2.434 & 8.708 & 0.265 & 1.210 & \\ -7.493 & 1.363 & -4.875 & -0.148 & -0.677 & 0.379 \end{bmatrix}$$

$$\mathrm{MSP}_E=\begin{bmatrix} 0.606 & & & & & (\mathrm{Sym}) \\ -0.277 & 0.337 & & & & \\ 0.457 & -0.199 & 0.556 & & & \\ -0.042 & 0.089 & -0.202 & 1.148 & & \\ -0.425 & 0.161 & -0.279 & 0.055 & 1.163 & \\ 0.233 & -0.116 & 0.183 & -0.049 & -0.634 & 0.383 \end{bmatrix}$$

Averaging the "circled" diagonal elements of the above matrices, the MSP_C and MSP_E matrices for the multivariate mixed model test of C are obtained:

$$\mathrm{MSP}_C=\begin{bmatrix} 76.463 & & (\mathrm{Sym}) \\ 47.894 & 31.366 & \\ 7.373 & 4.280 & 0.795 \end{bmatrix}$$

$$\mathrm{MSP}_E=\begin{bmatrix} 0.472 & & (\mathrm{Sym}) \\ 0.273 & 0.852 & \\ -0.271 & -0.164 & 0.773 \end{bmatrix}.$$

The degrees of freedom associated with the multivariate mixed model matrices are ν_h^* and ν_e^*, obtained from the formula $\nu_h^*=\nu_h\cdot R(A)/p=1\cdot 6/3=2$ and $\nu_e^*=\nu_e\cdot R(A)/p=16\cdot 6/3=32$, where p denotes the number of variables, $R(A)$ is the rank of the post matrix A, and ν_h and ν_e are the hypothesis and error degrees of freedom associated with Wilks' Λ-criterion for testing C as shown in Table 7.3. Wilks' Λ-criterion for testing C using the multivariate mixed model is $\Lambda = 0.0605$ which is compared to $U^{0.05}_{(3,2,32)} = 0.663$. The p-value for the test is less than 0.0001.

Analyzing the data a variable at a time using three univariate mixed model split-plot designs, the univariate F-ratios for testing C are immediately obtained from the multivariate mixed model analysis. The univariate F-ratios are:

Variables	F-value	p-value
SOr	76.463/0.472 = 162.1	< 0.0001
ANS	31.366/0.852 = 36.82	< 0.0001
Pal	0.795/0.773 = 1.03	0.3694

8. Growth curve analysis

While the standard MANOVA model (SMM) is applicable in many experimental situations, the model has several limitations if an experimenter wants to analyze and fit growth curves to the average growth of a population over time. To analyze data obtained from a growth curve experiment, Potthoff and Roy (1964) developed the growth curve model (GCM) which is a simple extension of the standard MANOVA model.

The model considered by Potthoff and Roy is given by

$$\begin{aligned} E(Y_0) &= XBP, \\ V(Y_0) &= I_n \otimes \Sigma_0 \end{aligned} \tag{8.1}$$

where Y_0 $(n \times q)$ is a data matrix, X $(n \times m)$ is a known design matrix, B $(m \times p)$ is a matrix of unknown nonrandom parameters, P $(p \times q)$ is a known matrix of full rank $p \leqslant q$, Σ_0 $(q \times q)$ is positive definite and the rows of Y_0 are independently normally distributed.

Comparing the GCM with the SMM, we see that only the post matrix P has been added to the model. This implies that each response variate can be expressed as a linear regression model of the form

$$E(\mathbf{y}_i) = P'\boldsymbol{\beta}_i,$$

where $\mathbf{y}_i$ $(q \times 1)$ is the observation vector for the ith subject and $\boldsymbol{\beta}_i$ is a vector of unknown parameters.

To analyze (8.1), Potthoff and Roy suggested the transformation

$$Y = Y_0 G^{-1} P' (P G^{-1} P')^{-1} \tag{8.2}$$

where G $(q \times q)$ is any symmetric positive definite weight matrix either nonstochastic or independent of Y_0 such that $PG^{-1}P'$ is of full rank. Employing the transformation in 8.2, the matrix Y $(n \times p)$ will be distributed mutually independently normal with unknown *p.d.* variance-covariance matrix

$$\underset{(p\times p)}{\Sigma} = \left[PG^{-1}P'\right]^{-1} PG^{-1}\Sigma_0 G^{-1}P'(PG^{-1}P')^{-1},$$

and mean $E(Y) = XB$. Hence, by using (8.2) we have reduced the GCM to the SMM with minor limitations on the selection of G.

Motivation for the selection of the transformation in (8.2) by Potthoff and Roy is contained in Appendix B of their (1964) paper; they show that the BLUE of an estimable linear parametric function $\psi = \mathbf{c}'B\mathbf{a}$ (where the estimability conditions are that $\mathbf{c}$ belongs to the space spanned by $X'X$ and $\mathbf{a}$ belongs to the space spanned by the columns of P) is given by

$$\psi = \mathbf{c}'\hat{B}\mathbf{a},$$
$$\hat{B} = (X'X)^{-}X'Y_0\Sigma_0^{-1}P'\left(P\Sigma_0^{-1}P'\right)^{-1}. \tag{8.3}$$

Since (8.1) reduces to (8.2) under (8.2) we see that

$$\hat{B} = (X'X)^{-}S'Y_0G^{-1}P'(PG^{-1}P')^{-1},$$

with G replacing Σ_0 in (8.3), $\hat{B}$ is very close to the BLUE.

To test hypotheses of the form

$$H_0\colon CBA = \Gamma \tag{8.4}$$

under (8.1), we merely have to substitute Y defined in (8.2) into the expression for S_h and S_e in (2.11) and (2.12). The degrees of freedom for the hypotheses is $\nu_h = R(C)$ and the degrees of freedom for error is $\nu_e = n - R(X) = n - r$.

Setting $\Gamma = 0$ in (8.4) and letting Y be defined as in (8.2), the hypotheses and error sum of square and products matrices take the following form.

$$S_h = A'Y'X(X'X)^{-}C'\left[C(X'X)^{-}C'\right]^{-1}C(X'X)^{-}X'YA,$$
$$S_e = A'Y'\left[I - X(X'X)^{-}X'\right]YA, \tag{8.5}$$

where $\nu_h = R(C)$ and $\nu_e = n - r$.

Under the SMM, no criteria is uniformly most powerful (Schatzoff, 1966; Olson, 1974). This is also the case for the GCM; however, in the GCM we have the additional problem of selecting the weight matrix G

when $p<q$. If $p=q$, the transformation in (8.2) reduces to

$$Y=Y_0P^{-1},$$

or if P is an orthogonal matrix so that $P^{-1}=P'$,

$$Y=Y_0P'$$

and there is no need to choose G. This was the approach taken by Bock (1963a) and the one used in the development of the MULTIVARIANCE package (Bock, 1963b, 1975; Finn, 1972 [MULTIVARIANCE VI incorporates the Potthoff–Roy analysis using S_e to estimate Σ]). If $p<q$ the choice of G is important since it affects the variance of $\hat{\psi}$ which increases as G^{-1} departs from Σ_0^{-1}, the power of the tests and the widths of confidence bands.

A simple choice of G is to set $G=I$. Then

$$Y=Y_0P'(PP')^{-1}.$$

Such a choice of G will certainly simplify one's calculations; however, it is not the best choice in terms of power since information is lost by reducing Y_0 to Y unless G is set equal to Σ_0. The estimator of $\hat{\psi}=\mathbf{c}'\hat{\mathbf{B}}\mathbf{a}$, when it is estimable and G is set equal to I, is the BLUE of ψ assuming $\Sigma_0=\sigma^2I$.

To try to avoid the arbitrary choice of the matrix G in Potthoff and Roy's model and its effect on estimates and tests, Rao (1965, 1966, 1967, 1972) and Khatri (1966) independently developed an alternative reduction of model (8.1) to a conditional model.

$$E(Y|Z)=XB+Z\Gamma \tag{8.6}$$

where Y $(n\times p)$ is a data matrix, X $(n\times m)$ is a known design matrix, B $(m\times p)$ is a matrix of unknown nonrandom parameters, Z $(n\times h)$ is a matrix of covariates and Γ $(h\times p)$ is a matrix of unknown regression coefficients.

To reduce (8.1) to (8.6) a $q\times q$ nonsingular matrix $H=(H_1H_2)$ is constructed so that the columns of H_1 form a basis for the vector space spanned by the rows of P, $PH_1=\mathrm{I}$ and $PH_2=0$. When the rank of P is p, H_1 and H_2 can be selected as

$$H_1=G^{-1}P'(PG^{-1}P')^{-1}, \qquad H_2=I-H_1P,$$

where G is an arbitrary positive definite matrix. Such a matrix H is not unique; however, estimates and tests are invariant for all choices of H

satisfying the specified conditions (see Khatri, 1966). Hence, G in the expression for H_1 does not affect estimates or tests under (8.6). By setting

$$
\begin{aligned}
Y &= Y_0H_1 = Y_0G^{-1}P'(PG^{-1}P')^{-1},\\
Z &= Y_0H_2,
\end{aligned}
\tag{8.7}
$$

$E(Y)=XB$ and $E(Z)=0$; thus, the expected value of Y given Z is seen to be of the form specified in (8.5) (Khatri, 1966; Grizzle and Allen, 1969). Using (8.6), the information contained in the covariates $Z = Y_0H_2$, which is ignored in the Potthoff–Roy reduction, is utilized.

Both Rao and Khatri argued that the BLUE under the conditional model of $\psi = \mathbf{c}'B\mathbf{a}$ is more efficient than that obtained by Potthoff and Roy since their estimator includes information in Z ignored by Potthoff and Roy. This is not the case. As shown by Lee (1974) and Timm (1975) employing the standard multivariate analysis of covariance (MANCOVA) model,

$$\hat{B} = (X'X)^{-}X'Y_0S^{-1}P'(PS^{-1}P')^{-1} \tag{8.8}$$

where $S = Y_0'[I - X(X'X)^{-}X']Y_0$. Khatri (1966) using the maximum likelihood procedure obtained the same result for $\hat{B}$. Thus, if $p<q$, Rao's procedure using $q-p$ covariates, Khatri using maximum likelihood methods and Potthoff and Roy's method weighting by $G^{-1}=S^{-1}$ are identical. Setting $G=I$ in the Potthoff and Roy method is equivalent to not including any covariates in the Rao–Khatri reduction. When $p=q$, H_2 does not exist.

Testing the hypothesis

$$H_0\colon\ CBA = \Gamma$$

where $\Gamma = 0$, is not the same under the Potthoff and Roy and Rao–Khatri reductions. Employing the standard MANCOVA model,

$$
\begin{aligned}
S_h &= A'Y'X(X'X)^{-}C'(CRC')^{-1}C(X'X)^{-}X'YA,\\
S_e &= A'(PS^{-1}P')^{-1}A,
\end{aligned}
\tag{8.9}
$$

where

$$R = (X'X)^{-} + (X'X)^{-}X'Y_0\left[S^{-1} - S^{-1}P'(PS^{-1}P')^{-1}\right]Y_0X(X'X)^{-},$$

$$Y = Y_0S^{-1}P'(PS^{-1}P')^{-1},$$

$$\nu_h = R(C), \qquad \nu_e = n-r-h \quad \text{and} \quad h = q-p.$$

Although Potthoff and Roy's approach does not allow G to be stochastic unless it is independent of Y_0, it is interesting to compare (8.6) and (8.9) if $G=S$. Then

$$\begin{aligned}
S_e &= A'Y\left[I - X(X'X)^{-}X'\right]YA \\
&= A'(PS^{-1}P')^{-1}PS^{-1}Y_0\left[I - X(X'X)^{-}X'\right]Y_0S^{-1}P'(PS^{-1}P')^{-1}A \\
&= A'(PS^{-1}P')^{-1}P'(PS^{-1}P')^{-1}A \\
&= A'(PS^{-1}P')^{-1}A,
\end{aligned}$$

which, except for the degrees of freedom for error, is identical to S_e obtained under the Rao–Khatri reduction. The sum of squares and products matrix S_h, however, is not the same.

The development of the GCM by Potthoff and Roy and the subsequent Rao–Khatri reduction has caused a great deal of confusion among experimenters trying to use the model in growth curve studies. A paper which helped to clarify and unify the methodologies was by Grizzle and Allen (1969). They also developed a procedure for selecting only a subset of the $q-p$ covariates.

Potthoff and Roy's analysis of the GCM was developed by introducing the transformation

$$Y = Y_0G^{-1}P'(PG^{-1}P')^{-1}$$

to reduce the GCM to the SMM. To avoid having a test procedure that was dependent on an arbitrary positive definite matrix G, Rao (1965) and Khatri (1966) proposed an alternative reduction to the standard MANCOVA model which did not depend on G. Their procedure, as discussed by Grizzle and Allen (1969), depends on selecting the "best" set of $q-p$ covariates. In addition, one may question the use of covariates that are part of the transformed variables of the dependent variables being analyzed. To avoid these problems, Tubbs, Lewis and Duran (1975) developed a test procedure to test

$$H_0\colon CBA = \Gamma,$$

employing maximum likelihood methods directly under the GCM.

Under the GCM, the maximum likelihood estimator of B is

$$\hat{B} = (X'X)^{-}X'Y_0S^{-1}P'(PS^{-1}P')^{-1} \tag{8.10}$$

and under H_0: $CBA = \Gamma$

$$\hat{B}_{H_0} = \hat{B} - (X'X)^{-} C'\left[C(X'X)^{-} C'\right]^{-1}(C\hat{B}A - \Gamma)$$
$$\times \left[A'(PS^{-1}P)^{-1}A\right]^{-1} A'(PS^{-1}P')^{-1}. \tag{8.11}$$

Using the likelihood ratio criterion due to Wilks,

$$S_h = (C\hat{B}A - \Gamma)'\left[C(X'X)^{-} C'\right]^{-1}(C\hat{B}A - \Gamma),$$
$$S_e = A'(PS^{-1}P')^{-1}A, \tag{8.12}$$

where $\nu_h = R(C)$ and $\nu_e = n - r$.

Comparing this result with that proposed by Rao and Khatri, we see that each S_h is different, but have the same degrees of freedom and that S_e is identical for both procedures, but have different degrees of freedom. However, as pointed out by Kleinbaum (1973), both procedures are asymptotically equivalent since they have the same asymptotic Wishart distributions. No information is available about the two procedures for small samples or about the relative power of each procedure.

In the analysis of growth curve data, observations at some time points may be missing either by chance or design so that each dependent variate is not measured on each subject. In addition, the design matrix X may not be the same for each dependent variate. While these problems have been discussed in the literature by Trawinski and Bargmann (1964), Srivastava and Roy (1965) and Srivastava (1966, 1967, 1968), extending the theory of the SMM, Kleinbaum (1973) developed a generalized growth curve model (GGCM) for estimating and testing hypotheses when observations are missing either by chance or design with different design matrices corresponding to different response variates.

As discussed by Srivastava (1967) and more generally by Kleinbaum (1970), to obtain BLUE of every parametric function $\psi = \mathbf{c}'B\mathbf{a}$ in complex multivariate linear models (linear models with design matrices that are not the same for each dependent variate) that are independent of the unknown elements of the variance-covariance matrix, requires additional restrictive conditions on the model (see, e.g., Kleinbaum, 1970, p. 58). This led Kleinbaum (1973) to consider Best Asymptotically Normal (BAN) estimators for the GGCM which use consistent estimators of Σ_0 and generally yield nonlinear estimators with variances that are in large samples the minimum that could be achieved by linear estimators if Σ_0 were known.

To test hypothesis of the form H_0: $CBA=0$ assuming a GCM with $p<q$, three frequentist analyses have been suggested to applied researchers over the past decade.

Potthoff and Roy: Using the transformation $Y=Y_0G^{-1}P'(PG^{-1}P')^{-1}$ and forming the estimator $\hat{B}=(X'X)^{-}X'Y$, the hypothesis and error matrices are formed:

$$\begin{aligned} S_h &= A'Y'X'(X'X)^{-}C'\left[C(X'X)^{-}C'\right]^{-1}C(X'X)^{-}X'YA, \\ S_e &= A'Y'\left[I-X(X'X)^{-}X'\right]YA, \end{aligned} \tag{8.13}$$

where $\nu_h=R(C)$, $\nu_e=n-r$ and G is any symmetric positive definite weight matrix either non-stochastic or independent of Y_0 such that $PG^{-1}P'$ is of full rank.

Tubbs, Lewis and Duran: Using maximum likelihood procedures, which is equivalent to setting $G=S$ in the Potthoff and Roy model, they obtain

$$\begin{aligned} \hat{B} &= (X'X)^{-}X'Y_0S^{-1}P'(PS^{-1}P')^{-1}=(X'X)^{-}X'Y, \\ S_h &= A'YX(X'X)^{-}C'\left[C(X'X)^{-}C'\right]^{-1}C(X'X)^{-}X'YA, \\ S_e &= A'Y'\left[I-X(X'X)^{-}X'\right]YA=A'(PS^{-1}P')^{-1}A, \end{aligned} \tag{8.14}$$

where $\nu_h=R(C)$, $\nu_e=n-r$, $S=Y_0'[I-X(X'X)^{-}X']Y_0$ and $Y=Y_0S^{-1}P'(PS^{-1}P')^{-1}$.

Rao–Khatri: Using a conditional model with

$$\begin{aligned} \hat{B} &= (X'X)^{-}X'Y_0S^{-1}P'(PS^{-1}P')^{-1}=(X'X)^{-}X'Y, \\ Y &= Y_0S^{-1}P'(PS^{-1}P')^{-1}, \\ S &= Y_0'\left[I-X(X'X)^{-}X'\right]Y_0, \end{aligned}$$

the matrices

$$\begin{aligned} S_h &= A'Y'X(X'X)^{-}C'(CRC')^{-1}C(X'X)^{-}X'YA, \\ S_e &= A'(PS^{-1}P')^{-1}A, \\ R &= (X'X)^{-}+(X'X)^{-}X'Y_0\left[S^{-1}-S^{-1}P'(PS^{-1}P')^{-1}PS^{-1}\right]Y_0X(X'X)^{-}, \end{aligned} \tag{8.15}$$

are formed where $\nu_h=R(C)$ and $\nu_e=n-r-q+p$. While the procedure of Rao and Khatri has been "accepted" as the usual procedure employed in growth curve studies over the years and is asymptotically equivalent to the procedure proposed by Tubbs, Lewis and Duran, we do not know which of the procedures are best in small samples. Perhaps the determination cannot be answered on the basis of power, but on whether in assessing growth the notion of conditional versus unconditional inference is being raised (Bock, 1975).

While the work of Kleinbaum has begun to address the data problems we have in analyzing data in the behavioral sciences, his procedure may lead to spurious test statistics since it depends on the method used to estimate $\hat{\Sigma}_0$ in the construction of the BAN estimator.

In this section, we have reviewed the classical frequentist analysis of the growth curve model for modeling the average growth curve for a population. Geisser (1979) reviews the basic sampling distribution theory for determining confidence bounds for growth curves and more importantly considers Bayesian procedures which may be used to analyze individual growth curves.

Example 8.1. To illustrate the application of the GCM for a set of data, the data given in Table 7.2 are utilized.

From the mean plots of the data in Table 7.2 for each group and variable (Figure 8.1) it appears that the growth curves for the three

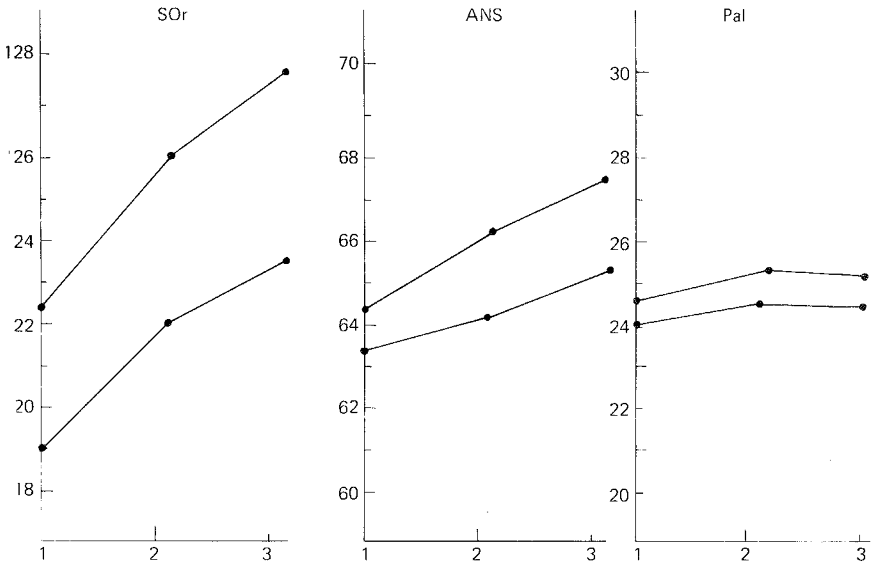

Fig. 8.1. Mean plots for data in Table 7.2.

variables are at least linear. Some other questions of interest for the data include:

(1) Are the growth curves for the two groups parallel for one or more variables?

(2) If we have parallel growth curves, for some variables, are they coincident?

(3) What are the confidence band(s) for the expected growth curve(s)?

Depending on whether we take $p=q=3$ when analyzing the data in Table 7.2, the procedure used to answer questions (1), (2), and (3) will differ. For illustrative purposes, we will demonstrate both techniques using a program developed at the Educational Testing Service called ACOVSM (Jöreskog, van Thillo, and Gruvaeus, 1971).

Assuming that $p=q=3$, the matrix B for the data in Table 7.2 is

$$B=\begin{pmatrix} \beta_{10} & \beta_{11} & \beta_{12} & \theta_{10} & \theta_{11} & \theta_{12} & \xi_{10} & \xi_{11} & \xi_{12} \\ \beta_{20} & \beta_{21} & \beta_{22} & \theta_{20} & \theta_{21} & \theta_{22} & \xi_{20} & \xi_{21} & \xi_{22} \end{pmatrix},$$

with P defined as

$$P=\begin{bmatrix} A_1 & 0 & 0 \\ 0 & A_1 & 0 \\ 0 & 0 & A_1 \end{bmatrix} \quad \text{and} \quad A_1=\begin{bmatrix} 1 & 1 & 1 \\ 1 & 2 & 3 \\ 1 & 4 & 9 \end{bmatrix},$$

B is estimated by

$$\hat{B}=$$

$$\begin{pmatrix} 115.778 & 4.139 & -0.583 & 63.278 & -0.472 & 0.417 & 23.611 & 1.333 & -0.278 \\ 118.444 & 5.028 & -0.694 & 62.000 & 2.555 & -0.278 & 23.622 & 0.456 & -0.078 \end{pmatrix}.$$

To test for parallelism,

$$H_p\colon (\beta_{11} \quad \beta_{12} \quad \theta_{11} \quad \theta_{12} \quad \xi_{11} \quad \xi_{12}) = (\beta_{21} \quad \beta_{22} \quad \theta_{21} \quad \theta_{22} \quad \xi_{21} \quad \xi_{22})$$

simultaneously for all variables, the matrices

$$C=(1-1), \qquad A=\begin{bmatrix} A_1 & 0 & 0 \\ 0 & A_1 & 0 \\ 0 & 0 & A_1 \end{bmatrix}, \quad \text{where} \quad A_1=\begin{bmatrix} 0 & 0 \\ 1 & 0 \\ 0 & 1 \end{bmatrix},$$

are used. Wilks' Λ-criterion for the test is $\Lambda=0.583$ and comparing Λ with $U^{0.05}_{(6.1,16)}=0.426$, the parallelism test is not rejected. The p-value for the test is $\alpha_p=0.3292$.

Given parallelism, we next test for coincidence again assuming $p=q$. For this test, $C=(1-1)$ and $A=I_9$. Computing Wilks' Λ-criterion, $\Lambda=0.422$. Since tables for the U distribution are not available for $U^{\alpha}=U^{0.05}_{(9,1,16)}$, we may compute either Rao's multivariate F-statistic, $F=1.216$ with 9 and 8 degrees of freedom, or Bartlett's Chi-square statistic, $\chi^2=9.915$ with 9 degrees of freedom; both are approximations of the general U-distribution (Rao, 1973, p. 556). The p-values for the two criteria are $\alpha_p=0.3965$ and $\alpha_p=0.3575$, respectively, indicating that we would not reject the coincidence hypothesis.

Treating the data in Table 7.2 as data obtained from a single group, the common regression function for all variables is

$$\hat{B}=(117.111 \quad 4.583 \quad -0.639 \quad 62.639 \quad 1.041 \quad 0.069 \quad 23.617 \quad 0.894 \quad -0.178).$$

Instead of analyzing Zullo's data with $p=q$, suppose that we decided a priori or through a statistical test that the regression model for each variable was linear. Then, $p<q$ and

$$B=\begin{pmatrix} \beta_{10} & \beta_{11} & \theta_{10} & \theta_{11} & \xi_{10} & \xi_{11} \\ \beta_{20} & \beta_{21} & \theta_{20} & \theta_{21} & \xi_{20} & \xi_{21} \end{pmatrix}.$$

Using the Rao–Khatri model with $G=S$, we test the coincidence hypothesis using the matrices $C=(1-1)$ and $A=I_6$. For this test, $\Lambda=0.440$ and comparing Λ with $U^{0.05}_{(6,1,13)}=0.271$, we conclude that the growth curves for each group are coincident for all variables. The p-value for the test is $\alpha_p=0.2300$. However, with $p<q$ and $G=S$, the models fit to each variable take the following form

$$y_{\mathrm{SOr}}=121.210+1.820t$$
$$y_{\mathrm{ANS}}=63.285+1.196t$$
$$y_{\mathrm{Pal}}=25.045-0.023t$$

which, as expected, do not agree with the models arrived at by taking $G=I$ since $p<q$.

Comparing the three regression models which may have been obtained using Zullo's data, the observed and predicted values for the models are displayed in Table 8.2.

Using Wilks' Λ-criterion, we may construct $(1-\alpha)\%$ simultaneous confidence bands for each variable and each model (Geisser, 1979).

Table 8.2
Regression models

Observed means	Quadratic ($p=q$)	*Predicted means* Linear ($p<q, G=I$)	Linear ($p<q, G=S$)
121.056	121.355	121.268	121.210
123.722	123.721	123.296	123.030
125.111	125.109	125.324	124.850
63.750	63.750	62.408	63.825
65.000	64.999	63.727	65.021
66.389	66.386	65.048	66.217
24.333	24.333	24.210	25.045
24.694	24.693	24.393	25.022
24.700	24.697	24.576	24.999

9. Summary

In this chapter we have illustrated through several examples the analysis of repeated measurement data employing multivariate methods using several standard designs. We hope that through the examples selected that the MANOVA model will replace the standard univariate techniques that occur in practice (Federer, 1975, 1977) when univariate mixed model assumptions are not satisfied.

References

Bartlett, M. S. (1939). A note on tests of significance in multivariate analysis. *Proc. Cambridge Phil. Soc.* **35**, 180–185.

Bartlett, M. S. (1950). Tests of significance in factor analysis. *Brit. J. Psychol.* (Statist. Section) **3**, 77–85.

Bock, R. D. (1963a). Programming univariate and multivariate analysis of variance. *Technometrics* **5**, 95–117.

Bock, R. D. (1963b). Multivariate analysis of variance of repeated measurements. In: C. W. Harris, ed., *Problems of Measuring Change*, University of Wisconsin Press, Madison, 85–103.

Bock, R. D. (1975). *Multivariate Statistical Methods in Behavioral Research*, McGraw-Hill, New York.

Bowker, A. H. (1960). A representation of Hotelling's T^2 and Anderson's classification statistic. In: I. Olkin et al., eds., *Contributions to Probability and Statistics*, Stanford University Press, Stanford, 142–149.

Box, G. E. P. (1950). Problems in the analysis of growth and wear curves. *Biometrics* **6**, 362–389.

Cochran, W. G. and Cox, G. M. (1957). *Experimental Designs* (2nd ed.), Wiley, New York.

Cox, D. R. (1958). *Planning of Experiments*, Wiley, New York.

Federer, W. T. (1955). *Experimental Design-theory and Application*, Macmillan, New York.

Federer, W. T. and Balaam, L. N. (1972). *Bibliography on Experiment and Treatment Design Pre-1968*, Oliver and Boyd, Edinburgh.

Federer, W. T. (1975). The misunderstood split plot. In: R. P. Gupta, ed., *Applied Statistics*, North-Holland, Amsterdam, Oxford, 9–39.

Federer, W. T. (1977). Applications and concepts of repeated measures designs when residual effects are present. Technical Report BU-603-M, Cornell University.

Finn, J. (1972). *MULTIVARIANCE: Univariate and Multivariate Analysis of Variance, Covariance and Regression, Version 5*, Release 3 (1976). National Educational Resources, Chicago.

Finny, D. J. (1960). *An Introduction to the Theory of Experimental Design*. The University of Chicago Press, Chicago.

Gabriel, K. R. (1968). Simultaneous test procedures in multivariate analysis of variance. *Biometrika* **55**, 489–504.

Geisser, S. (1979). Growth curve analysis. *Handbook of Statistics Vol. I.*, North-Holland, New York.

Greenhouse, S. W. and Geisser, S. (1959). On methods in the analysis of profile data. *Psychometrika* **24**(a), 95–112.

Grizzle, J. and Allen, D. M. (1969). Analysis of growth and dose response curves. *Biometrics* **25**, 357–381.

Hedayat, A. and Afsarinejad, K. (1975). Repeated measurements design I. In: J. N. Srivastava ed., *A Survey of Statistical Designs*: *I*. North-Holland, Amsterdam, Oxford, 229–242.

Hotelling, H. (1931). The generalization of student's ratio. *Ann. Math. Statist.* **2**, 360–378.

Hotelling, H. (1951). A generalized T-test and measure of multivariate dispersion. In: *Proceedings of the Second Berkeley Symposium on Mathematics and Statistics*, University of California Press, Berkeley, 23–41.

Huynh, H. and Feldt, L. S. (1970). Conditions under which mean square ratios in repeated measurement designs have exact F-distributions. *J. Amer. Statist. Assoc.* **65**, 1582–1589.

Huynh, H. and Feldt, L. S. (1976). Estimation of the Box correction for degrees of freedom from sample data in randomized block and split-plot designs. *J. Educational Statist.* **1** (1), 69–82.

John, P. W. M. (1971). *Statistical Design and Analysis of Experiments*. Macmillan, New York.

Jöreskog, K., van Thillo, M. and Gruvaeus, G. T. (1971). A general computer program for analysis of covariance structures including generalized MANOVA. Research Bulletin RB-71-1. Princeton, New Jersey: Educational Testing Service.

Kempthorne, O. (1952). *The Design and Analysis of Experiments*. Wiley, New York.

Khatri, C. G. (1966). A note on a MANOVA model applied to problems in growth curve. *Ann. Inst. Statist. Math.* **18**, 75–86.

Kirk, R. E. (1968). *Experimental Design—Procedures for the Behavioral Sciences*. Brooks and Cole, Monterey, CA.

Kleinbaum, D. G. (1970). Estimation and hypothesis testing for generalized multivariate linear models. Mimeo Series No. 696, Institute of Statistics, University of North Carolina, Chapel Hill, NC.

Kleinbaum, D. G. (1973). A generalization of the growth curve model which allows missing data. *Journal of Multivariate Analysis*, **3**, 117–124.

Krishnaiah, P. R. (1965). Multiple comparison procedures in multi-response experiments. *Sankhya A* **27**, 31–36.

Krishnaiah, P. R. (1969). Simultaneous test procedures under general MANOVA models. In: P. R. Krishnaiah, ed., *Multivariate Analysis II*, Academic Press, New York, 121–142.

Krishnaiah, P. R. (1978). Some recent developments on real multivariate distributions. In: P. R. Krishnaiah, ed., *Developments in Statistics Vol. 1*, Academic Press, New York, 135–169.

Krishnaiah, P. R. and Waikar, V. B. (1971). Simultaneous tests for equality of latent roots against certain alternatives I. *Ann. Inst. Statist. Math.* **23**, 451–468.

Lawley, D. N. (1938). A generalization of Fisher's z-test. *Biometrika* **30**, 180–187.

Lee, J. C., Krishnaiah, P. R. and Chang, T. C. (1976). On the distribution of the likelihood ratio test statistic for compound symmetry. *South African Statistical J.* **10**, 49–62.

Lee, Y. H. K. (1974). A note on Rao's reduction of Potthoff and Roy's generalized linear model. *Biometrika* **61**, 349–351.

Lindquist, E. F. (1953). *Design and Analysis of Experiments in Psychology and Education*. Houghton–Mifflin, Boston.

Myers, J. L. (1966). *Fundamentals of Experimental Design*. Allyn and Bacon, Boston.

Nanda, D. N. (1950). Distribution of the sum of roots of a determinantal equation under a certain condition. *Ann. Math. Statist.* **21**, 432–439.

Olson, C. L. (1974). Comparative robustness of six tests in multivariate analysis of variance. *J. Amer. Statist. Assoc.* **69**, 894–908.

Pillai, K. C. S. (1960). *Statistical Tables for Tests of Multivariate Hypotheses*. Statistical Center, University of the Philippines, Manila.

Potthoff, R. F. and Roy, S. N. (1964). A generalized multivariate analysis of variance model useful especially for growth curve problems. *Biometrika* **51**, 313–326.

Quenouille, M. H. (1953). *The Design and Analysis of Experiments*. Griffin, London.

Rao, C. R. (1965). The theory of least squares when the parameters are stochastic and its application to the analysis of growth curves. *Biometrika* **52**, 447–458.

Rao, C. R. (1966). Covariance adjustment and related problems in multivariate analysis. In: P. R. Krishnaiah, ed., *Multivariate Analysis*. Academic Press, New York, 87–103.

Rao, C. R. (1967). Least square theory using an estimated dispersion matrix and its application to measurement of signals. *Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics*, University of California Press, Berkeley, CA, 355–372.

Rao, C. R. (1972). Recent trends of research work in multivariate analysis. *Biometrics* **28**, 3–22.

Rao, C. R. (1973). *Linear Statistical Inference and its Applications* (2nd ed.). Wiley, New York.

Roy, J. (1958). Step-down procedure in multivariate analysis. *Ann. Math. Statist.* **29**, 1177–1187.

Roy, S. N. (1957). *Some Aspects of Multivariate Analysis*. Wiley, New York.

Schatzoff, M. (1966). Sensitivity comparisons among tests of the general linear hypothesis. *J. Amer. Statist. Assoc.* **61**, 415–435.

Srivastava, J. N. and Roy, S. N. (1965). Hierarchal and p-block multiresponse designs and their analysis. In: C. R. Rao, ed., *Mahalanobis Dedicatory Volume*. Pergamon Press, New York.

Srivastava, J. N. (1966). Some generalizations of multivariate analysis of variance. In: P. R. Krishnaiah ed., *Multivariate Analysis*. Academic Press, New York, 129–145.

Srivastava, J. N. (1967). On the extension of Gauss–Markov theorem to complex multivariate linear models. *Ann. Inst. Statist. Math.* **19**, 417–437.

Srivastava, J. N. (1968). On a general class of designs for multiresponse experiments. *Ann. Math. Statist.* **39**, 1825–1843.

Timm, N. H. (1975). *Multivariate Analysis with Applications in Education and Psychology*. Brooks/Cole, Monterey, CA.

Trawinski, I. M. and Bargmann, R. E. (1964). Maximum likelihood estimation with incomplete multivariate data. *Ann. Math. Statist.* **35**, 647–658.

Tubbs, J. D., Lewis, T. O. and Duran, B. S. (1975). A note on the analysis of the MANOVA model and its application to growth curves. *Comm. Statist.* **4**, 643–653.

Wilks, S. S. (1932). Certain generalizations in the analysis of variance. *Biometrika* **24**, 471–494.

Winer, B. J. (1971). *Statistical Principles in Experimental Design* (2nd ed.). McGraw-Hill, New York.