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OPTIONS FOR ANALYZING UNBALANCED SPLIT- PLOT EXPERIMENTS: A CASE STUDY

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ABSTRACT

Unbalanced split-plot experiments present many analysis problems. This paper discusses some of the difficulties by comparing the results of the analysis recommended by Milliken and Johnson (1984) to a set of minimal sufficient statistics using a small experiment from Milliken and Johnson as a case study. The estimators used by Milliken and Johnson are not necessarily the best (smallest variance) estimators. A set of minimal sufficient statistics is used to show that the whole plot error term suggested by Milliken and Johnson does not have a distribution that is proportional to an exact chi-square distribution and is not always independent of parameter function estimators. Other options for analyzing unbalanced split-plot experiments and unbalanced repeated measures experiments in which the repeated measures satisfy the Huyhn-Feldt (1970) conditions are proposed.

Keywords: random effect, mixed model, variance component, Huyhn-Feldt

1. INTRODUCTION

The purpose of this paper is to identify options for analyzing unbalanced split-plot experiments and unbalanced repeated measures experiments where the repeated measures satisfy the Huyhn-Feldt (1970) conditions. A case study will be used to investigate the relationship between a set of minimal sufficient statistics and the estimates of effects and error terms obtained by applying the procedures for analyzing unbalanced split-plot experiments described by Milliken and Johnson (1984).

Consider an example given by Milliken and Johnson (1984). This unbalanced split-plot experiment has unequal numbers of whole plot experimental units in the two treatment groups and has some subplot measurements missing.

Example 1.

From a group of five depressed patients, three received a drug and two received a placebo. The patients were scored on a test designed to measure depression one week after treatment and two weeks after treatment. Some patients did not return for the second examination resulting in \( n = 8 \) observations. The data are reported in Table 1. The means model for an observed response in this example is

\[
Y_{ijk} = \mu + \delta_{ik} + \epsilon_{ijk}
\]

for \( i=1,2; k(1)=1,2; k(2)=3,4,5; \) and \( j=1,2. \) It is assumed that the error contributed by the \( j \)th week of the \( k \)th patient in the \( i \)th treatment group, \( \epsilon_{ijk} \), is distributed \( N(0, \sigma_e^2) \). It is also assumed that the error contributed by the \( k \)th patient in the \( i \)th treatment group, \( \delta_{ik} \), is distributed \( N(0, \sigma_d^2) \) and that all error terms are distributed independently of each other.
Table 1. Treatment Received and Depression Scores

<table>
<thead>
<tr>
<th>Patient</th>
<th>Treatment</th>
<th>Score Week 1</th>
<th>Score Week 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Placebo</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>Placebo</td>
<td>22</td>
<td>--</td>
</tr>
<tr>
<td>3</td>
<td>Drug</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>4</td>
<td>Drug</td>
<td>23</td>
<td>--</td>
</tr>
<tr>
<td>5</td>
<td>Drug</td>
<td>26</td>
<td>24</td>
</tr>
</tbody>
</table>

In matrix notation this model can be written as \( y = X\mu + \delta + \epsilon \)

\[
y = \begin{bmatrix} Y_{11} \\ Y_{12} \\ Y_{13} \\ Y_{21} \\ Y_{22} \\ Y_{23} \\ Y_{24} \\ Y_{25} \\ Y_{26} \\ Y_{27} \end{bmatrix} = \begin{bmatrix} 24 \\ 22 \\ 25 \\ 23 \\ 26 \\ 22 \\ 24 \end{bmatrix}, \quad X = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}, \quad Z = \begin{bmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix},
\]

\[
\mu = \begin{bmatrix} \mu_{11} \\ \mu_{12} \\ \mu_{13} \\ \mu_{21} \\ \mu_{22} \end{bmatrix}, \quad \delta = \begin{bmatrix} \delta_{1 \cdot} \\ \delta_{2 \cdot} \\ \delta_{3 \cdot} \end{bmatrix}, \quad \epsilon = \begin{bmatrix} \epsilon_{11} \\ \epsilon_{12} \\ \epsilon_{13} \\ \epsilon_{21} \\ \epsilon_{22} \\ \epsilon_{23} \\ \epsilon_{32} \\ \epsilon_{33} \end{bmatrix}.
\]

2. A SET OF MINIMAL SUFFICIENT STATISTICS

In this section a set of minimal sufficient statistics for Example 1 are given. The minimal sufficient statistics were obtained in Remmenga (1992) using procedures described by Hultquist and Atzinger (1972), hereafter referred to as HA. HA require that the observation vector \( y \) be transformed via a full rank transformation, denoted by \( R \), so that the transformed covariance matrix is diagonal. Denote Var[\( y \)] by \( \Sigma \), then \( R \) is chosen so that

\[
\text{Var}[Ry] = RR' = R(\sigma^2 ZZ' + \sigma_i^2 I)R'
\]

will be a diagonal matrix. Next, HA partition \( R \) into \( s \) submatrices so that \( R' = [R_1', R_2', \ldots, R_s'] \) with each \( R_i \) having dimension \( m_i \times n \), where \( \zeta_i, \ell = 1, 2, \ldots, s \) are the distinct diagonal elements of \( RR' \) and \( m_i \) is the multiplicity of \( \zeta_i \).

For each \( \ell \), HA require that an orthogonal matrix \( G_i = \frac{G^{(1)}_i}{G^{(2)}_i} \) of dimension \( m_i \times m_i \) be found such that \( G^{(1)}_i \) has dimension \( q_i \times m_i \) and \( G^{(2)}_i R_i R_i' G^{(1)}_i = 0 \), where \( q_i \) is the rank of \( R_i X \). When they exist, the statistics \( G^{(1)}_i R_i y \) are denoted by \( u_i \) and the statistics \( y' R_i G^{(2)}_i G^{(1)}_i R_i y \) are denoted by \( v_i \).

For Example 1, in which \( s = 3 \), one set of choices for \( R, G_1, G_2, \) and \( G_3 \) result in the statistics
\[ u_1 = \begin{bmatrix} u_{11} \\ u_{12} \end{bmatrix} = \begin{bmatrix} \sqrt{\frac{1}{2}} (Y_{111} + Y_{121}) \\ \frac{1}{2} (Y_{213} + Y_{223} + Y_{215} + Y_{225}) \end{bmatrix} \]

\[ u_2 = \begin{bmatrix} u_{21} \\ u_{22} \end{bmatrix} = \begin{bmatrix} \sqrt{\frac{1}{2}} (Y_{214} + Y_{112}) \\ \sqrt{\frac{1}{2}} (Y_{214} - Y_{214}) \end{bmatrix} \]

\[ u_3 = \begin{bmatrix} u_{31} \\ u_{32} \end{bmatrix} = \begin{bmatrix} \sqrt{\frac{1}{2}} (Y_{111} - Y_{121}) \\ \frac{1}{2} (Y_{213} - Y_{223} + Y_{215} - Y_{225}) \end{bmatrix} \]

\[ v_1 = \{ \frac{1}{2} (Y_{213} + Y_{223}) - \frac{1}{2} (Y_{215} + Y_{225}) \}^2 \]

\[ v_3 = \{ \frac{1}{2} (Y_{213} + Y_{223}) - \frac{1}{2} (Y_{223} + Y_{215}) \}^2 \] (\( v_2 \) does not exist.)

It can be shown that

\[ \begin{bmatrix} u_{11} \\ u_{12} \end{bmatrix} \sim N \left[ \frac{1}{2} (\mu_{11} + \mu_{12}), \left( \frac{\sigma_e^2 + 2\sigma^2 + \sigma^2}{\sigma_e^2 + 2\sigma^2} \right) \right] \]

\[ \begin{bmatrix} u_{21} \\ u_{22} \end{bmatrix} \sim N \left[ \frac{1}{2} (\mu_{21} + \mu_{11}), \left( \frac{\sigma_e^2 + \sigma^2}{\sigma_e^2 + \sigma^2} \right) \right] \]

\[ \begin{bmatrix} u_{31} \\ u_{32} \end{bmatrix} \sim N \left[ \frac{1}{2} (\mu_{11} - \mu_{12}), \left( \frac{\sigma_e^2}{\sigma_e^2} \right) \right] \]

\[ \frac{v_1}{\sigma_e^2 + 2\sigma^2} \sim \chi^2(1), \text{ and } \frac{v_3}{\sigma_e^2} \sim \chi^2(1). \]

The statistics \( u_{11}, u_{12}, u_{21}, u_{22}, u_{31}, u_{32}, v_1 \) and \( v_3 \) are also stochastically independent by the HA procedure. Because the set \( \{ \zeta_i: l = 1, 2, 3 \} \) is a linearly independent set of distinct diagonal elements of \( (\text{PER})^{-1} \), the statistics \( u_{11}, u_{12}, u_{21}, u_{22}, u_{31}, u_{32}, v_1 \) and \( v_3 \) are minimal sufficient statistics for the parameters \( \mu_{11}, \mu_{12}, \mu_{21}, \mu_{22}, \sigma_e^2 \) and \( \sigma^2 \).

3. MILLIKEN AND JOHNSON’S ANALYSIS

This section restates some results given in Analysis of Messy Data, Volume 1: Designed Experiments, in which the example from Section 1 was analyzed according to the procedures described by Milliken and Johnson (1984), hereafter referred to as MJ.

First, consider the estimators of the parameters \( \mu_{11}, \mu_{12}, \mu_{21} \) and \( \mu_{22} \). The estimator of \( \mu_{11} \) given by MJ is

\[ \hat{\mu}_{11} = (Y_{111} + Y_{112})/2 \text{ with } \text{Var}[^{1,2} \hat{\mu}_{11}] = (\sigma_e^2 + \sigma^2)/2. \]

Before estimating \( \mu_{12} \), the missing value \( Y_{122} \) is estimated in MJ. The missing value \( Y_{122} \) should be estimated in such a way that the between
patient error sums of squares and the within patient error sums of squares are not increased. Thus MJ take

\[ \hat{y}_{122} = y_{112} - y_{111} + y_{121} \]

and give the estimator of \( \mu_{12} \) as

\[ \hat{\mu}_{12} = (y_{121} + \hat{y}_{122})/2 = (2y_{12} + y_{112} - y_{111})/2 \]

with \( \text{Var}[\hat{\mu}_{12}] = (3\sigma^2 + \sigma_1^2)/2 \).

The estimator of \( \mu_{21} \) given by MJ is

\[ \hat{\mu}_{21} = (y_{213} + y_{214} + y_{215})/3 \]

with \( \text{Var}[\hat{\mu}_{21}] = (\sigma^2 + \sigma_2^2)/3 \).

To estimate \( \mu_{22} \), the missing value \( y_{224} \) is estimated. MJ take

\[ \hat{y}_{224} = y_{214} - (Y_{213} + y_{215})/2 - (y_{223} + y_{225})/2 \]

Then, one estimator of \( \mu_{22} \) is

\[ \hat{\mu}_{22} = (y_{223} + \hat{y}_{224} + y_{225})/3 \]

\[ = (y_{223} + y_{214} - (Y_{213} + y_{215})/2 - (y_{223} + y_{225})/2)/3 \]

with \( \text{Var}[\hat{\mu}_{22}] = (2\sigma^2 + \sigma_3^2)/3 \).

Estimating functions of the parameters \( \mu_{11}, \mu_{12}, \mu_{21}, \) and \( \mu_{22} \) can be achieved by taking functions of the estimated parameters. Estimates of some linear functions of the parameters, their variances and estimated standard errors for the data in Table 1 are reported in Table 2.

<table>
<thead>
<tr>
<th>Parameter Function</th>
<th>Estimate</th>
<th>Variance</th>
<th>Estimated Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \mu_{11} )</td>
<td>23</td>
<td>( 1/2(\sigma^2 + \sigma_1^2) )</td>
<td>1.041</td>
</tr>
<tr>
<td>( \mu_{12} )</td>
<td>17</td>
<td>( 3/2(\sigma^2 + 1/3\sigma_1^2) )</td>
<td>1.155</td>
</tr>
<tr>
<td>( \mu_{21} )</td>
<td>24.667</td>
<td>( 1/3(\sigma^2 + \sigma_2^2) )</td>
<td>0.850</td>
</tr>
<tr>
<td>( \mu_{22} )</td>
<td>22.167</td>
<td>( 2/3(\sigma^2 + 1/3\sigma_2^2) )</td>
<td>1.009</td>
</tr>
<tr>
<td>( \mu_{11} - \mu_{21} )</td>
<td>20</td>
<td>( 1/2(\sigma^2 + \sigma_3^2) )</td>
<td>1.041</td>
</tr>
<tr>
<td>( \mu_{12} - \mu_{21} - \mu_{22} )</td>
<td>23.417</td>
<td>( 1/4(\sigma^2 + 4/3\sigma_3^2) )</td>
<td>0.837</td>
</tr>
<tr>
<td>( \mu_{11} - \mu_{12} - \mu_{21} - \mu_{22} )</td>
<td>-3.417</td>
<td>( 3/4(\sigma^2 + 10/9\sigma_3^2) )</td>
<td>1.336</td>
</tr>
<tr>
<td>( \mu_{11} - \mu_{12} - \mu_{21} + \mu_{22} )</td>
<td>23.833</td>
<td>( 13/24(\sigma^2 + 5/13\sigma_3^2) )</td>
<td>0.672</td>
</tr>
<tr>
<td>( \mu_{12} - \mu_{21} - \mu_{22} )</td>
<td>19.583</td>
<td>( 13/24(\sigma^2 + 5/13\sigma_3^2) )</td>
<td>0.731</td>
</tr>
<tr>
<td>( \mu_{11} - \mu_{12} - \mu_{21} + \mu_{22} )</td>
<td>4.25</td>
<td>( 3/4\sigma_3^2 )</td>
<td>0.807</td>
</tr>
<tr>
<td>( \mu_{11} - \mu_{12} - \mu_{21} + \mu_{22} )</td>
<td>3.5</td>
<td>( 3\sigma_3^2 )</td>
<td>1.614</td>
</tr>
</tbody>
</table>

The variances of linear functions of estimated parameters are functions of the variance components \( \sigma^2 \) and \( \sigma_3^2 \). One way to estimate these variances is to estimate the variance components. MJ recommend estimating the variance components by fitting the model sequentially; fitting all fixed effects before fitting the random effects. Then the estimator of \( \sigma_3^2 \) given by MJ is the mean square error or

\[ \hat{\sigma}_3^2 = y'(I - WW')y/v_2 \]
where \( W = [X, 2] \) and \( v_2 = Tr(I - WW') \). MJ estimate \( \sigma_i^2 \) by taking a linear combination of the sums of squares for Patient(Treatment), denoted \( SS\text{PATIENT}(\text{TREATMENT}) \), and \( \sigma_i^2 \). Fitting fixed effects in the model before fitting the random effects results in

\[
SS\text{PATIENT}(\text{TREATMENT}) = y'(WW' - XX')y
\]

which has \( v_1 = Tr(WW' - XX') \) degrees of freedom. Using the method of moments, MJ take a linear combination of \( SS\text{PATIENT}(\text{TREATMENT}) \) and \( \sigma_i^2 \) such that \( E[k_1 \sigma_i^2 + k_2 \text{(SSPATIENT(TREATMENT))}] = \sigma_i^2 \).

For Example 1, the expected value of \( SS\text{PATIENT}(\text{TREATMENT}) \) is

\[
E[SS\text{PATIENT}(\text{TREATMENT})] = (4 \sigma_i^2)/3 + \sigma_i^2.
\]

Thus the estimator of \( \sigma_i^2 \) is given by MJ as

\[
\hat{\sigma}_i^2 = 3(SS\text{PATIENT}(\text{TREATMENT}) - \hat{\sigma}_i^2)/4.
\]

For the data in Table 1, \( SS\text{PATIENT}(\text{TREATMENT}) = 2.806, v_1 = 3, \hat{\sigma}_i^2 = 0.25, v_2 = 1 \) and thus \( \hat{\sigma}_i^2 = 1.917 \).

Estimates of the variances or standard errors of the estimates are obtained by substituting the estimates for \( \sigma_i^2 \) and \( \sigma_i^2 \) for the parameters in Table 2. For example, s.e.\( \hat{\mu}_{21} \) = \((2/3)(\sigma_i^2 + (1/2)\sigma_i^2)^{1/2} \), and is estimated by \((2/3)(0.25 + (1/2)1.917)^{1/2} = 1.009 \) in Example 1.

To test hypotheses, MJ recommend constructing an approximate t-statistic from the ratio of the estimate and its standard error. It is approximate since the variance of the estimate does not have a distribution proportional to an exact chi-square distribution. MJ estimate an approximate degrees of freedom for this t-statistic using Satterthwaite's approximation (Satterthwaite, 1941).

4. MJ'S ANALYSIS IN TERMS OF THE MINIMAL SUFFICIENT STATISTICS

The relationship between the minimal sufficient statistics given in Section 2 using Hultquist and Atzinger's procedure and parameter estimates given in Section 3 using the analysis suggested by Milliken and Johnson is investigated in this section.

The estimators for \( \hat{\mu}_{11}, \hat{\mu}_{12}, \hat{\mu}_{21} \) and \( \hat{\mu}_{22} \) in Section 3 are linear functions of the minimal sufficient statistics given in Section 2. Let \( U' = [u_{11}, u_{12}, u_{21}, u_{22}, u_{13}, u_{32}] \), then

\[
\hat{\mu}_{11} = (1/4)\sqrt{2} [1 0 1 -1 1 0] U,
\]

\[
\hat{\mu}_{12} = (1/4)\sqrt{2} [1 0 1 -1 3 0] U,
\]

\[
\hat{\mu}_{21} = (1/6) [0 2 \sqrt{2} \sqrt{2} 0 2] U, \text{ and}
\]

\[
\hat{\mu}_{22} = (1/6) [0 2 \sqrt{2} \sqrt{2} 0 -4] U.
\]

It is immediately clear that there is more than one unbiased estimator for a given function of the parameters that is a function of the minimal sufficient statistics given in Section 2. For example, using the data from Table 1 and the statistics in Section 2, one has that

\[
\sqrt{2} u_{11} = \{ \text{21 estimates } \hat{\mu}_i \} = 1/2(\hat{\mu}_{11} + \hat{\mu}_{12}).
\]

From Section 3, \( \hat{\mu}_i \) can also be estimated by

\[
\hat{\mu}_i = 1/2(\hat{\mu}_{11} + \hat{\mu}_{12}) = 20.
\]

Both \( \hat{\mu}_i \) and \( \sqrt{2} u_{11} \) are functions of the minimal sufficient statistics.
The estimator given by MJ, \( \hat{\mu}_{12} \), has smaller variance in this case since
\[
\text{Var}[\hat{\mu}_{12}] = \frac{1}{2} \sigma_1^2 + \frac{1}{4} \sigma_2^2
\]
and
\[
\text{Var}[\sqrt{2} u_{12}] = \frac{1}{2} \sigma_2^2 + \sigma_3^2.
\]

To investigate this further, consider unbiased estimators of \( \mu_{12} \) which are functions of the minimal sufficient statistics. The objective is to find \( C' = [c_1, c_2, c_3, c_4, c_5, c_6] \) such that \( E[C'U] = \mu_{12} \). This equation implies that the following 4 equations with 6 unknown variables must be true:
\[
\begin{align*}
&c_1 = \sqrt{2} + c_5, \\
&c_2 = -\sqrt{2} - c_5 - \sqrt{2}c_6, \\
&c_4 = \sqrt{2} + c_5 - \sqrt{2}c_6, \text{ and} \\
&c_6 = c_2.
\end{align*}
\]
Since \( \text{Var}[C'U] \) can be written as,
\[
C'(\text{Var}[U])C = (c_1^2 + c_2^2 + c_3^2 + c_4^2 + c_5^2 + c_6^2)\sigma_2^2 + (2c_1^2 + 2c_2^2 + c_4^2 + c_5^2)\sigma_3^2
\]
\[
= (3 + 4\sqrt{2}c_2 + 4c_3^2 + 4c_1^2)\sigma_3^2 + (5 + 6\sqrt{2}c_3 + 4c_1^2 + 6c_2^2)\sigma_2^2,
\]
one must at least take \( c_5 = 0 \) to minimize \( \text{Var}[C'U] \).

Consider there are an infinite number of unbiased estimators of \( \mu_{12} \) which are functions of the minimal sufficient statistics. The minimum variance unbiased estimator of \( \mu_{12} \) which is a function of the minimal sufficient statistics is uniquely determined when \( \sigma_2^2 \) and \( \sigma_3^2 \) are known or more specifically when the ratio \( \sigma_2^2 / \sigma_3^2 \) is known. Letting \( \rho = \sigma_2^2 / \sigma_3^2 \), the \( \text{Var}[C'U] \) written as a function of \( \rho \) is
\[
\text{Var}[C'U] = [(3 + 4\sqrt{2}c_2 + 4c_3^2 + 4c_1^2) + (5 + 6\sqrt{2}c_3 + 4c_1^2 + 6c_2^2)\rho]\sigma_2^2.
\]

When \( \rho \) is known, the minimum variance unbiased estimator of \( \mu_{12} \) can be obtained by taking
\[
\begin{align*}
&c_1 = \sqrt{2}(\rho + 2)/(4(\rho + 1)), \\
&c_5 = 0, \\
&c_3 = \sqrt{2}\rho/(4(\rho + 1)), \\
&c_4 = -\sqrt{2}\rho/(4(\rho + 1)), \\
&c_5 = -\sqrt{2}(3\rho + 2)/(4(\rho + 1)), \text{ and} \\
&c_6 = 0,
\end{align*}
\]
which results in \( C'U = \rho(Y_{12} - Y_{111})/(2(\rho + 1)) + Y_{111} \).

The unbiased estimator of \( \mu_{12} \) given by MJ, \( \mu_{12} = (Y_{112} - Y_{111})/2 + Y_{111} \), is obtained by taking \( c_5 = -(3\sqrt{2})/4 \) and is the minimum variance unbiased estimator when \( \rho/(2(\rho + 1)) = 1/2 \), i.e. as \( \rho \to \infty \). The unbiased estimator of \( \mu_{12} \) given by \( Y_{112} \), the ordinary least squares estimator, is obtained by taking \( c_5 = -1/\sqrt{2} \) and is the minimum variance unbiased estimator when \( \rho/(2(\rho + 1)) = 0 \), i.e. as \( \rho \to 0 \).

In comparing the error terms obtained in Section 3 to the minimal sufficient statistics in Section 2, note that \( \text{Var}[v_j] = \sigma_j^2 \). However, SSPATIENT(TREATMENT) \( \neq v_j \). Note that the sums of squares for Patient(Treatment), often referred to as the whole plot error sums of squares, has three degrees of freedom in Example 1 while \( v_j \) has only one degree of freedom. Also, note that there are eight minimal sufficient statistics, \( u_{11}, u_{12}, u_{13}, u_{21}, u_{22}, u_{31}, u_{32}, v_1 \) and \( v_2 \), to estimate the six parameters \( \mu_{11}, \mu_{12}, \mu_{21}, \sigma_1^2 \) and \( \sigma_2^2 \). Thus, it seems reasonable that two degrees of freedom of information about the between-patient error remains in \( U \) in the form of comparisons. If they exist, the two
comparisons, denoted by \( w_i \) and \( w_2 \), must be functions of \( U \) such that 
\[ E[w_i] = 0, \quad E[w_2] = 0, \quad \text{and} \quad \text{Cov}[w_i, w_2] = 0. \]
Since \( E[u_{i1} + u_{i2}] = E[u_{i1} - u_{i2}] = \sqrt{2} \mu_{i1} \), a \( w_i \) can be constructed by 
taking any multiple of \( (u_{i1} + u_{i2}) - (u_{i2} - u_{i2}) \). Letting \( w_i = p_i'U \) 
and taking \( p_i \) to be the normalized vector 
\[ p_i' = [1/2 \quad 0 \quad -1/2 \quad 1/2 \quad 1/2 \quad 0] \]
one has \( E[w_i] = 0 \) and \( \text{Var}[w_i] = \sigma_i^2 + \sigma_j^2 \).
Since \( E[u_{i1} + u_{i2}] = \sqrt{2} E[u_{i1} + u_{i2}] = 2 \mu_{i2} \), a \( w_2 \) can be constructed 
by taking any multiple of \( (u_{i1} + u_{i2}) - \sqrt{2}(u_{i2} - u_{i2}) \). Letting \( w_2 = p_2'U \) 
and taking \( p_2 \) to be the normalized vector 
\[ p_2' = [0 \quad 1/\sqrt{6} \quad -1/2/\sqrt{6} \quad -1/2/\sqrt{6} \quad 0 \quad 1/\sqrt{6}] \]
one has \( E[w_2] = 0 \) and \( \text{Var}[w_2] = \sigma_i^2 + \sigma_j^2 \).

Now \( (w_1)^2 \) and \( (w_2)^2 \) each provide one degree of freedom for the 
whole plot error sums of squares. The sums of squares for 
Patient(Treatment) can be then be obtained from the set of minimal 
sufficient statistics as 
\[ \text{SSPATIENT(TREATMENT)} = v_1 + (w_1)^2 + (w_2)^2. \]

It can be shown that \( (w_1)^2/(\sigma_i^2 + \sigma_j^2) - \chi_1^2 \), \( (w_2)^2/(\sigma_i^2 + \sigma_j^2) - \chi_1^2 \), and \( w_1 \), 
\( w_2 \), \( v_1 \) and \( v_2 \) are independently distributed. We already have that \( v_1/(\sigma_i^2 + 2\sigma_j^2) \sim \chi_1^2 \). Thus, \( v_1 = (v_2)\sigma_j^2 \) and \( \text{SSPATIENT(TREATMENT)} \) is independently 
distributed. However, since \( \text{SSPATIENT(TREATMENT)} \) is the sum of two 
random variables with expectation \( \sigma_i^2 + \sigma_j^2 \) and one with expectation \( \sigma_i^2 + 2\sigma_j^2 \), \( \text{SSPATIENT(TREATMENT)} \) does not have a distribution that is 
\( \chi^2 \)-proportional to an exact chi-square distribution. It should also be 
noted that although \( \text{Cov}(w_i, w_2) = 0 \), \( w_i \) and \( w_2 \) are not necessarily 
distributed independently of all fixed effects. For example, \( \text{Cov}(w_i, \mu_{i2}) = -1/\sqrt{2}\sigma_i^2 \), thus \( \text{SSPATIENT(TREATMENT)} \) and \( \mu_{i2} \) (the 
MJ estimator of \( \mu_{i2} \)) are not independently distributed.

5. SUMMARY OF OPTIONS

The comparisons in Section 4 show that the analysis of unbalanced 
split-plot designs suggested by MJ is not necessarily the best 
analysis. However, examination of the minimal sufficient statistics 
for Example 1 does not reveal a better procedure for analysis of the 
example either.

The estimator of the vector of parameters \( \mu \), \( (\mu' = [\mu_{i1}, \mu_{i2}, \mu_{i3}, \mu_{i4}]) \) or of functions of \( \mu \) suggested by MJ is only one of 
an infinite number of unbiased estimators. The MJ estimator assumes that the 
random effect of a patient within a treatment group is the same for 
both weeks which would seem desirable. Computationally, the MJ 
estimator of \( \mu \) can be obtained by treating the random effects of the 
patients, \( \delta \), as fixed.

Let \( \tau' = [\mu' \delta'] \). Then \( \hat{\tau}' = [\hat{\mu}' \delta'] = W \gamma \) where 
\( W = [X, Z] \) estimates the \( \mu_i \)'s (\( \hat{\mu} \)) and the "fixed" effects of the patients (\( \delta \)). The 
MJ estimator of \( \mu_i \) is found by taking \( \hat{\mu} = B'\hat{\tau} = [I_{44}, B_2']\hat{\tau} \), where \( I_{44} \) is 
the 4x4 identity matrix and 
\[
B_2' = \begin{bmatrix}
1/2 & 1/2 & 0 & 0 & 0 \\
1/2 & 1/2 & 0 & 0 & 0 \\
0 & 0 & 1/3 & 1/3 & 1/3 \\
0 & 0 & 1/3 & 1/3 & 1/3 
\end{bmatrix}.
\]
The matrix \( B_2' \) treats the estimated effects of the patients 
within a treatment group equally for Week 1 and Week 2. The MJ
estimator, \( \hat{\mu} \), is the same estimator one would obtain using the SAS® GLM statements:

\[
\text{PROC GLM;}
\]
\[
\text{CLASS PATIENT TRTMENT WEEK;}
\]
\[
\text{MODEL RESPONSE=TRTMENT WEEK TRTMENT*WEEK;}
\]
\[
\text{LSMEANS TRTMENT*WEEK;}
\]

If there were no missing subplot measurements in Example 1 (if all patients had returned for the second examination) the estimator suggested by MJ using the matrix \( B \), would be equivalent to both the ordinary least squares (OLS) estimator of \( \mu \) and the generalized least squares (GLS) estimator of \( \mu \). This is not the case when subplot measurements are missing.

When there is unbalancing in the subplot experimental units the OLS estimator of \( \mu \), given by \( \hat{\mu} = X'y \), does not take into account the random effect of the patients within the treatment groups. In Section 4, the OLS estimator of the parameter function \( \hat{\mu}_i = \frac{1}{2}(\mu_{ii} + \mu_{i2}) \) was \( \hat{\mu}_i = \sqrt{\hat{\mu}_{ii}} = 21 \), whereas the MJ estimator was \( \hat{\mu}_i = 20 \). Although, for this particular parameter function the MJ estimator had smaller variance than the OLS estimator, this is not always true.

The uniformly minimum variance unbiased estimator of \( \mu \) is given by the GLS estimator \( \hat{\mu} = (X'\Sigma X)^{-1}X'\Sigma y \) when \( \Sigma \) is known. Since \( \Sigma \) depends on the unknown values of \( \sigma^2 \) and \( \sigma_j^2 \), the GLS estimator \( \hat{\mu} \) must be estimated. When there are no missing subplot measurements, the estimator suggested by MJ, the OLS estimator and the GLS estimator are all equivalent and thus the UMVUE estimator of \( \mu \) can be obtained from either OLS or from the MJ estimator without knowing \( \sigma^2 \) or \( \sigma_j^2 \).

The comparisons in Section 4 not only illustrate various options for obtaining estimates of the fixed effects, but suggest options for making inferences about the fixed effects. To construct a confidence interval or test hypotheses about a function of parameters, \( h'\mu \), it is necessary to find the variance of the estimator of \( h'\mu \).

In the analysis suggested by MJ, the variance of \( h'\hat{\mu} \) is given by

\[
\text{Var}[h'\hat{\mu}] = (Bh)'W\Sigma W'Bh = k(\sigma^2 + c\sigma_j^2)
\]

where \( c = \text{Tr}[WW' [W' (I-(Bh)'Bh)] [W' (I-(Bh)'Bh)]'] \) and \( k = (Bh)' (W'W) Bh \). MJ recommend estimating the variance components \( \sigma^2 \) and \( \sigma_j^2 \) using the method of moments to estimate \( \text{Var}[h'\hat{\mu}] \). The distribution of \( \text{Var}[h'\hat{\mu}] \) is approximated using results about the distribution of linear combinations of independent random variables with distributions proportional to chi-square distributions given by Satterthwaite (1941). Comparisons made in Section 4 show that this approximation may not be appropriate for unbalanced split-plot designs since the whole plot sums of squares does not always have a distribution that is proportional to an exact chi-square distribution.

MJ recommend constructing hypothesis tests and confidence intervals about \( h'\mu \) using an approximate t-statistic obtained from the ratio of the estimate and its standard error. This approximation may not be appropriate for some fixed effects when the whole plot sum of squares is not distributed independently of the estimator \( h'\mu \).

The results of Section 4 might suggest estimating the variance of \( h'\hat{\mu} \) using the set of minimal sufficient statistics, \( \nu_j \), since these statistics are all independently distributed with distributions proportional to chi-square distributions. Also, since the MJ estimators for fixed effects are all functions of the minimal sufficient statistic vector, \( U \), and the \( \nu_j \) statistics are distributed independently of \( U \), the \( \nu_j \) are independent of the MJ estimators. For Example 1, the statistics \( \nu_i \) and \( \nu_j \) could be used in place of \( \sigma^2 \) and \( \text{SSPATIENT(TREATMENT)} \) in the method of moments to estimate \( \sigma^2 \) and \( \sigma_j^2 \).

There is the potential for an unbalanced split-plot design to have more than two \( \nu \)-statistics \( \{\nu_i: \ell = 1, 2, \ldots, s\} \). Let \( f_i = m_i - q_i \)
which is the degrees of freedom for \( v_i \). The expected value of \( v_i/f_i \) is given by \( \zeta_i = \sigma_i^2 + n_i \sigma^2 \) where \( \zeta_i, i = 1, 2, \ldots, s \), are the distinct diagonal elements of \( \mathbf{RER}' \). When more than two \( v_i \)’s exist, the method of moments will not result in unique estimates for \( \sigma_i^2 \) and \( \sigma^2 \). One option, in this case, is to apply the method of moments to two selected \( v \)-statistics (perhaps those with the largest degrees of freedom).

In almost all cases one of the \( \zeta_i \)'s will be equal to \( \sigma_i^2 \). Without loss of generality, let this one be \( \zeta_i \). Then \( n_i = 0 \) and \( \zeta_i = \sigma_i^2 \). Another possible solution is to take

\[
\begin{align*}
  v^* &= \sum_{i=1}^{s-1} v_i, \quad f^* = \sum_{i=1}^{s-1} f_i, \\
  n^* &= \frac{\sum_{i=1}^{s-1} n_i f_i}{\sum_{i=1}^{s-1} f_i},
\end{align*}
\]

where the expectation of \( v^* \) is \( \sigma_i^2 + n^* \sigma^2 \) and

\[
\begin{align*}
  n^* &= \left( \sum_{i=1}^{s-1} n_i f_i \right) / \left( \sum_{i=1}^{s-1} f_i \right).
\end{align*}
\]

The method of moments can then be applied to \( v_i/f_i \) and \( v^*/f^* \) to obtain unique solutions for \( \sigma_i^2 \) and \( \sigma^2 \).

To make inferences about the fixed effects in an unbalanced split-plot example using the GLS estimator of \( \mu \), the variance of \( \mathbf{h}' \hat{\mu} \),

\[
\text{Var}[\mathbf{h}' \hat{\mu}] = \mathbf{h}' (\mathbf{X}' \mathbf{X})^{-1} \mathbf{h},
\]

must be estimated along with the GLS estimator \( \mathbf{h}' \hat{\mu} \) since \( \sigma_i^2 \) and \( \sigma^2 \) are unknown. The method of moments estimators suggested by MJ or the method of moments estimators using the minimal sufficient statistics can be used to estimate the variance components for use in the GLS analysis. Some other ways of estimating \( \sigma_i^2 \) and \( \sigma^2 \) include the maximum likelihood, restricted maximum likelihood (Harville, 1977), and MINQUE methods (Rao, 1971). To test hypotheses or construct confidence intervals about \( \mathbf{h}' \mu \), the statistic \( \mathbf{h}' \hat{\mu} / \{ \text{Var}[\mathbf{h}' \hat{\mu}] \}^{1/2} \) is used. However, the distribution of \( \mathbf{h}' \hat{\mu} / \{ \text{Var}[\mathbf{h}' \hat{\mu}] \}^{1/2} \) is unknown and can be approximated by the standard normal distribution only when the whole plot and subplot sample sizes are sufficiently large.

A number of options for analyzing unbalanced split-plot designs have been suggested in this paper. However, it has not yet been determined how these procedures compare to each other in terms of size or power. Some of these options are compared by Remmenga (1992).

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6. REFERENCES


