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ABSTRACT

A statistical method has been developed for nested incomplete samples in a longitudinal study in which part of the sample has dropped out in such a way that the data have a nested pattern. A procedure which performed well in a Monte Carlo experiment was extended to a two-factor incomplete design with repeated measures on one factor. Methods designed for this type of analysis included two multivariate techniques--likelihood ratio and step-down procedures with between subjects and within subjects variables--and univariate methods involving use of the EM algorithm in conjunction with restricted maximum likelihood estimation of variance components. Nested data were subjected to analysis of variance and step-down tests. It was concluded that step-down statistics were simple to use and did not require restrictive assumptions--type H covariance matrix--of univariate analysis of variance. They were appropriate for a mixed model, and calculation software was available. Step-down statistics were preferable to analysis of variance when the sample was nested and assumption violations were likely. References and four data tables conclude the document. (GDC)

Analysis of Repeated Measures Designs with Nested Incomplete Samples

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Introduction

In the behavioral and health sciences, it is common to encounter research where subjects are observed across an extended period of time. Treatment of longitudinal data is often approached as a univariate problem, using a repeated measures analysis of variance. Because of assumptions required by this approach, some prefer to consider the analysis of longitudinal data as a multivariate problem. Either approach is relatively simple to deal with, using current computer software - unless data values are lost and the layout becomes incomplete. If missing values occur in a non-random manner, they may bias results to a point where the experiment is invalidated. Even if subjects "drop out" at random (Rubin, 1976), analysis of incomplete data is a difficult task.

Halperin (1984), in a Monte Carlo experiment, compared several inferential procedures developed for a single nested incomplete sample. One procedure which performed well in the Monte Carlo study has been extended to a two-factor incomplete design with repeated measures on one factor. It is my objective to illustrate the use of this inferential method which is appropriate to a class of incomplete layouts, including user-oriented explanations and computer software considerations.

Inferential Methods

Inferences from incomplete data are often simplified when values are missing in a pattern. Because of this, much of the literature is concerned with special cases, as is well summarized by Little (1976). One special pattern occurs commonly in data collected over time. When subjects "drop out" and fail to return, by reordering the observations we can form a table which displays a triangular pattern. Such a pattern is termed "nested" or "monotone" in the literature, and represents an important special case.

Two inferential methods studied by Halperin (1984) were devised for nested data. One was a likelihood ratio statistic derived by Bhargava (1962,1975). A second, closely related to the likelihood ratio test, is one based on step-down procedures (Roy and Bargmann, 1958; Roy, 1958). The latter has been extended to a design with one "Between Subjects" variable and one "Within Subjects" variable.

Both the likelihood ratio and step-down tests are multivariate analyses. When performed on full data, the likelihood ratio statistic equals the Wilk's Lambda statistic used in multivariate analysis of variance. Univariate procedures for incomplete data have also been developed and are discussed next.

Yates (1933) and Bartlett (1937) suggested procedures to analyze randomized blocks and split-plot designs when data values were missing at random. With current software, such analyses are easily performed, using general linear models programs. It should be noted, however, that these procedures were developed for fixed effects models, where randomness is provided by the random assignment of treatments to experimental units. This is contrasted with the repeated measures design, where "treatments" are really trials over time, and "blocks" are randomly selected subjects. For such data, a mixed, rather than fixed, model is required. Laird and Ware (1982) consider random and mixed designs appropriate to longitudinal data. They recommend use of the EM algorithm (Dempster, Laird, and Rubin, 1977) in conjunction with restricted maximum likelihood estimation of variance components and provide an extremely flexible model for analysis of data collected over time.

Practical Considerations

In selecting an analysis to use on incomplete data, we must consider a series of "trade-offs." Given valid procedures, we should choose among them based on several considerations. The first deals with simplicity. It is not sufficient that the consulting statistician understand the method; the person who "owns" the data and is ultimately responsible for their analysis, must understand the statistics, at least on an intuitive level. Such is possible with step-down tests, but less so with the likelihood ratio test of Bhargava, and still less so with use of the method of Laird and Ware (1982). Step-down procedures, though far from trivial, are well documented in the multivariate literature and are the most "user-friendly" of the tests considered. They may not be the most powerful, however.

A second practical consideration is availability of computer software to calculate the statistics and their probabilities. Here again, step-down procedures are relatively good, while others suffer from a lack of computer software designed to perform the analysis.

Next, various methods of analysis are illustrated, using currently popular statistical packages.

Analysis of Variance

To illustrate the various inferential procedures, an example was taken from Cochran and Cox (1957, p.300). The Between Subjects variable, Conditions, has three levels, and the Within Subjects variable, Trials, has six levels. Values were deleted at random to form a nested pattern within each condition. Table 1 contains these three nested samples, after observations are reordered to display the nested pattern.

Insert Table 1 about here

Let

$$Y(ijk) = \mu + \tau(j) + \pi(i(j)) + \tau(k) + \tau\tau(jk) + \tau\pi(ki(j))$$

be the usual split-plot factorial analysis of variance model for Subject i in Condition j at Trial k, subject to the conventional restrictions that effects sum to zero. We test the hypotheses

H(C): all $\tau(j) = 0$
H(T): all $\tau(k) = 0$
H(CT): all $\tau\tau(jk) = 0$.

For each subject with no missing values, we average to obtain

$$Y(ij.) = \mu + \tau(j) + \pi(i(j))$$

This can be recognized as a one-way completely randomized model. The analysis of variance on Y(ij.) p will provide the Between Subjects portion of the split-plot source table. Scaling by the square root of p yields results traditionally reported in a split-plot source table. These results are reported in Table 2.

Insert Table 2 about here

Hypotheses T and CT consider main effects for Trials and interactions of Conditions and Trials, respectively. These tests, reported in Table 2, result from fitting the split-plot model to all available data. I used PROC GLM on SAS (1982) to find the values in Table 2.

Step-Down Tests

There are several weaknesses inherent in the analysis of variance reported in Table 2. First, the methods used to calculate the analysis presume a fixed effects design, and that is unrealistic. Second, the analysis requires that the covariance matrices be homogeneous, and that the common covariance matrix be "Type H" (Huyhn and Feldt, 1970). If the latter condition is not true, the F-tests for T and CT become quite unstable. Although it might be anticipated that they would turn liberal, recent information (LaLonde, 1985) suggests that this may not always be the case with nested incomplete data.

Alternative means of testing Hypotheses T and CT, without requiring assumptions with yield Type H covariance matrices, are available. Step-down tests, when applied to full data, provide test statistics "which are statistically independent but depend

upon an a priori ordering of criterion measures" (Finn, 1974, p. 157). Further discussion may be found in Subbaiah and Mudholkar (1978).

As they are with full data, it has been demonstrated that step-down statistics are statistically independent when applied to nested incomplete data. This fact stems from our ability to factor likelihood functions when the data form a nested pattern. Details of this have been observed by many, including Anderson (1957), Hocking and Marx (1979), Morrison (1976), and Marini, Olson, and Rubin (1980).

Before testing hypotheses T and CT, we transform the data as is done in profile analysis (e.g., Morrison, 1976, p. 146). Differences

$$D(ijk) = Y(ijk) - Y(ij,k+1)$$
$$=(\tau(k)-\tau(k+1)) + (\tau\tau(jk)-\tau\tau(j,k+1)-) + (\tau\pi(ki(j))-\tau\pi(k+1,i(j)))$$

are formed for k=1,...,p-1, or 5 in our example, and are reported in Table 3. Treating D(ijk) as p-1 dependent variables in a multivariate analysis, we can test that the (p-1) grand means, $\tau(k)-\tau(k+1)$, are zero, and that the (p-1) main effects, $\tau\tau(jk)-\tau\tau(j,k+1)$, are zero. These are precisely H(T) and H(CT), and can also be tested with step-down statistics.

Insert Table 3 about here

With full data, step-down tests are calculated using a Cholesky factoring, but with nested incomplete data, it is convenient to use a series of analyses of covariance. Differences D(ijk) are treated as the dependent variables, with independent variables of conditions and covariates of the previous trial differences. If k=1, we use no covariate. This re-parameterization leads to the series of models:

$$D(ij1) = \delta(1) + \eta(j1) + e(ij1)$$
$$D(ij2) = \delta(2) + \eta(j2) + \beta(21)D(ij1) + e(ij2)$$
$$\cdot$$
$$\cdot$$
$$D(ij5) = \delta(5) + \eta(j5) + \beta(51.234)D(ij1) + \beta(52.134)D(ij2) + \beta(53.124)D(ij3) + \beta(54.123)D(ij4) + e(ij5).$$

The t-test for each grand mean, $\delta(j)$, forms the set of "Trial" step-down statistics, while the F-statistics for the "Condition" parameters, $\eta(jk)$, are the step-down set for the interactions. These statistics, along with df and exceedance probabilities, are reported in Table 4. All results were obtained by running a series of analyses of variance and covariance on PROC GLM of SAS. Care should be exercised not to interpret the constant in GLM as a grand mean. Each statistic is

tested at $\alpha(k)=.0102$, so that the simultaneous error rate for each set is $\alpha = 1-(1-\alpha(k))^5 = .05$. Subbaiah and Mudholdar (1978) suggest more general ways of choosing $\alpha(k)$.

Insert Table 4 about here

As can be seen, grand means for differences 2,3, and 4 differ significantly from zero, suggesting a trials effect. This was also found in the univariate analysis of Table 2. None of the CT effects were significantly different from zero, although the statistic for the fourth difference was close.

Summary

Step-down statistics are simple to use when data are missing in a nested pattern. They do not require restrictive assumptions (Type H covariance matrix) of univariate analysis of variance, and are appropriate for a mixed model. The software currently available makes their calculation quite accessible. They should always be preferred to ANOVA when the sample is nested and assumption violations are likely.

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Table 1
Split-Plot Factorial Nested Layout

	SUBJ	TRIAL_1	TRIAL_2	TRIAL_3	TRIAL_4	TRIAL_5	TRIAL_6	AVERAGE
	1	42	46	47	39	53	42	109.819
	2	47	29	35	47	57	45	106.145
C	3	32	32	37	43	45	45	95.530
o	4	26	32	35	24	39	26	74.301
n	5	28	30	31	37	41	47	87.365
d	6	24	22	22	29	35	26	64.503
i	7	26	23	25	27	33	.	.
t	8	24	33	23	32	31	.	.
i	9	24	27	28	33	.	.	.
o	10	24	33	27	31	.	.	.
n	11	33	39	33	.	.	.	.
	12	28	31	27	.	.	.	.
1	13	29	28	.	.	.	.	.
	14	24	40	.	.	.	.	.
	15	26	28	.	.	.	.	.
	16	39	46	51	49	55	42	115.126
	17	35	46	47	39	52	61	114.310
C	18	34	30	42	35	42	35	88.998
o	19	25	26	28	46	37	37	81.241
n	20	31	30	29	35	40	36	82.058
d	21	24	29	29	29	24	.	.
i	22	22	25	26	26	29	.	.
t	23	26	23	24	31	.	.	.
i	24	27	26	32	28	.	.	.
o	25	21	24	24	.	.	.	.
n	26	20	27	33	.	.	.	.
	27	23	28	.	.	.	.	.
2	28	32	35	.	.	.	.	.
	29	23	25	.	.	.	.	.
	30	21	21	.	.	.	.	.
	31	46	44	45	46	48	63	119.209
	32	43	43	43	46	47	58	114.310
C	33	33	24	40	37	41	38	86.957
o	34	38	41	38	30	36	35	88.998
n	35	21	25	31	35	33	23	68.586
d	36	24	33	30	30	37	.	.
i	37	20	21	31	24	30	.	.
t	38	24	23	21	24	21	.	.
i	39	24	18	21	26	.	.	.
o	40	26	28	27	.	.	.	.
n	41	28	25	26	.	.	.	.
	42	24	30	28	.	.	.	.
3	43	28	29	.	.	.	.	.
	44	19	22	.	.	.	.	.
	45	21	28	.	.	.	.	.

Table 2
Split-Plot Factorial ANOVA

Source	SS	df	MS	F	p
Between Subjects					
Conditions: C	153.450	2.	76.725	0.22	.8043
Subjects (C)	4503.717	13.	346.440		
Within Subjects					
Trials: T	1331.024	5.	266.205	12.81	.0001
CT	225.434	10.	22.543	1.08	.3783
TxSubjects (C)	2742.847	132.	20.779		

Table 3
Trial Differences

	SUBJ	D_1	D_2	D_3	D_4	D_5
	1	-4	-1	8	-14	11
	2	18	-6	-12	-10	12
C	3	0	-5	-6	-2	0
o	4	-6	-3	11	-15	13
n	5	-2	-1	-6	-4	-6
d	6	2	0	-7	-6	9
i	7	3	-2	-2	-6	.
t	8	-9	10	-9	1	.
i	9	-3	-1	-5	.	.
o	10	-9	6	-4	.	.
n	11	-6	6	.	.	.
	12	-3	4	.	.	.
1	13	1	.	.	.	.
	14	-16	.	.	.	.
	15	-2	.	.	.	.
	16	-7	-5	2	-6	13
	17	-11	-1	8	-13	-9
C	18	4	-12	7	-7	7
o	19	-1	-2	-18	9	0
n	20	1	1	-6	-5	4
d	21	-5	0	0	5	.
i	22	-3	-1	0	-3	.
t	23	3	-1	-7	.	.
i	24	1	-6	4	.	.
o	25	-3	0	.	.	.
n	26	-7	-6	.	.	.
	27	-5	.	.	.	.
2	28	-3	.	.	.	.
	29	-2	.	.	.	.
	30	0	.	.	.	.
	31	2	-1	-1	-2	-15
	32	0	0	-3	-1	-11
C	33	9	-16	3	-4	3
o	34	-3	3	8	-6	1
n	35	-4	-6	-4	2	10
d	36	-9	3	0	-7	.
i	37	-1	-10	7	-6	.
t	38	1	2	-3	3	.
i	39	6	-3	-5	.	.
o	40	-2	1	.	.	.
n	41	3	-1	.	.	.
	42	-6	2	.	.	.
3	43	-1	.	.	.	.
	44	-3	.	.	.	.
	45	-7	.	.	.	.

Table 4
Step-Down Tests

	Trial Effects			CT Effects		
Difference	t	df	p	F	df	p
1 vs. 2	-2.35	42	.0235	0.34	2,42	.7138
2 vs. 3	-3.02	31	.0050*	2.65	2,31	.0868
3 vs. 4	-2.92	23	.0077*	0.55	2,23	.5059
4 vs. 5	-4.96	17	.0001*	5.65	2,17	.0131
5 vs. 6	-0.18	9	.8641	0.26	2, 9	.7740

* Significant at $\alpha(k) = .0102$