COMPARISON OF CLASSES OF CHANGEOVER DESIGNS

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BU-1257-MA April 1995

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SUMMARY

Several classes of repeated measure experiment designs of the changeover type have appeared in the literature. It was decided to compare members of five classes of these designs for three and four treatments in several sequences (3, 6, and 9 and 4, 8, and 12) over several periods (2 to 15 or 16). These designs are also compared on their ability to estimate various interactions. In many trials in medicine, nutrition, exercise, education, agriculture, marketing, etc., the number of different sequences is often much less than the number of sampling units (individuals, field plots, etc.). Frequently, many periods are required to assess long-term effects such as kth period carryover effects and continuing effects of treatments. Likewise for sequential experimentation, properties of designs over many sequences and many periods are required. The measures of efficiency used for comparison were the determinant of a multiple of the variance-covariance matrix (D-optimality) and the determinant of a variance-covariance matrix for a set of linear and independent contrasts (Kershner efficiency). Using these measures, it was found that none of the classes was invariant for number of sequences, treatments, or periods, for type of effects [direct, residual, and cumulative (direct plus residual)], or for measures of efficiency. However, if consideration were limited to direct and first-order residual effects, a new class of designs denoted as foldover-tied-changeover designs, was superior or equal to all others except in one instance. Designs where treatments follow themselves for one or two periods are generally superior for estimating cumulative effects. Since no class was found to be universally optimal, the investigator needs to specify the number of treatments, periods, and sequences, the type of effects, and the measure of efficiency in order to select the particular design which is best for the situation contemplated.

Some key words: D-optimality; Kershner measure of efficiency; direct, residual, and cumulative effects; tied-changeover designs; foldover-tied-changeover designs; crossover design; interaction effects.

1. INTRODUCTION

The topic of the changeover, crossover, residual effects, or repeated measures experiment designs has received attention for many years and is a current topic of research interest. Several types of these designs have been constructed with corresponding statistical analyses. One purpose of this paper is to compare several classes of these designs over many periods using a measure of efficiency developed by Kershner (1980). Since a variety of treatment effects occur in repeated measure experiments, the measure of efficiency needs to be applied to the various treatment effects. There are several measures of efficiency that could be used as well (see, e.g., Raktoe *et al.*, 1981). We shall compare several classes of experiment designs on the basis of first period residual effects, direct effects, and cumulative (residual plus direct) effects of the treatments using the Kershner (1980) measure of efficiency and the D-optimality measure for some special cases.

In several types of investigation, the experiment needs to be conducted over many periods in order to assess second period, third period, etc. carryover effects and/or to assess continuing effects of treatments. For example, in a nutritional study at Cornell University, 24 subjects and 11 periods were used. The experiment was stopped only because some of the subjects would be dropping out of the study to leave on Spring break. The long-term effects of some of the diets were revealing. Since trials often have many sampling units (individuals, plots, etc.), several sequences may be used efficiently. Also, for sequential experimentation, it is useful to know which designs have good properties as sequences and periods are added through time. Hence designs with several sequences and periods need to be studied. The various experiment designs, abridged for our purpose, that we compare are listed below.

LL designs: Lucas (1957) and Linnerud, Gates, and Donker (1962) suggested that one or more (2 or 3) extra periods be added to a $t \times t$ Latin square design where the rows are the periods and the columns represent the sequence of treatments in a column. The treatments in the last period of the $t \times t$ Latin square are repeated in the $t+1$st, $t+2$nd, and/or $t+3$rd periods. The particular experiment designs we consider for $t = 3$ and 4 treatments are

t = 3: Period	Sequence 1 2 3 4 5 6 7 8 9	t = 4: Period	Sequence 1 2 3 4 and 1 2 3 4
1	A B C A B C A B C	1	A B C D A B C D
2	C A B C A B C A B	2	D A B C D A B C
3	B C A B C A B C A	3	C D A B B C D A
4	B C A B C A B C A	4	B C D A C D A B
5	B C A B C A B C A	5	B C D A C D A B
⋮		⋮	
15	B C A B C A B C A	16	B C D A C D A B

For t = 4 treatments, sequences 5 to 8 and 9 to 12 are a repeat of sequences 1 to 4. A cyclic Latin square is used for the first design for t = 4 treatments and a Latin square balanced for first order residual effects is used for the second design. Also, for s = 12 sequences, the three pairwise orthogonal Latin squares of order four could be used for sequences 1 to 4, 5 to 8, and 9 to 12 with the treatments in the fifth, sixth, etc. periods being the same as those in period four. Note that we use 12 extra periods of repeated treatments for t = 3 and for t = 4 treatments. This is many more than suggested by the authors. Designs of this type are useful to study long-term effects of treatments.

FA designs: Federer (1955) and Federer and Atkinson (1964) put forth a class of designs which was called tied-double-changeover designs. For t = 3 treatments, the two pairwise orthogonal Latin squares are

$$\text{L3(1)} = \begin{bmatrix} A & B & C \\ C & A & B \\ B & C & A \end{bmatrix} \quad \text{and} \quad \text{L3(2)} = \begin{bmatrix} A & B & C \\ B & C & A \\ C & A & B \end{bmatrix}.$$

For sequences 1 to 3, L3(1) [or L3(2)] is used for periods 1 to 3, L3(2) for periods 4 to 6, L3(1) for periods 7 to 9, L3(2) for periods 10 to 12, and so forth. For sequences 4 to 6, L3(2) is used for periods 1 to 3, L3(1) for periods 4 to 6, L3(2) for periods 9 to 12, and so forth. For sequences 7 to 9 the ordering of Latin squares used for sequences 1 to 3 is repeated.

For t = 4 treatments, consider the Latin squares

$$\underset{\text{L4(B)}}{\begin{bmatrix} A & B & C & D \\ D & A & B & C \\ B & C & D & A \\ C & D & A & B \end{bmatrix}} \quad \underset{\text{L4(1)}}{\begin{bmatrix} A & B & C & D \\ D & C & B & A \\ B & A & D & C \\ C & D & A & B \end{bmatrix}} \quad \underset{\text{L4(2)}}{\begin{bmatrix} A & B & C & D \\ C & D & A & B \\ D & C & B & A \\ B & A & D & C \end{bmatrix}} \quad \underset{\text{L4(3)}}{\begin{bmatrix} A & B & C & D \\ B & A & D & C \\ C & D & A & B \\ D & C & B & A \end{bmatrix}}.$$

L4(B) is balanced for first order residual effects, i.e., every treatment is preceded by each of the other treatments but not itself. For four sequences, L4(B) is repeated four times for the 16 periods. For 12 sequences and 16 periods, the order of squares for sequences 1 to 4 was L4(1), L4(2), L4(3), and L4(1), for sequences 5 to 8 the ordering was L4(2), L4(3), L4(1), and L4(2), and for sequences 9 to 12, the ordering was L4(3), L4(1), L4(2), and L4(3). For eight sequences, the first two sets of the previous ordering was used. Alternatively, for eight sequences L4(B) could have been used for both sequences 1 to 4 and for 5 to 8. For our comparisons, we used LB(4) for sequences 1 to 4 and used the first eight sequences of the 12-sequence design as given above.

A2 designs: Atkinson (1964) constructed a class of designs which is more efficient for estimating residual and cumulative effects, by repeating each row of the FA design two times. For $t = 3$ treatments and $s = 9$ sequences, the plan is

	Sequence								
Period	1	2	3	4	5	6	7	8	9
1	A	B	C	A	B	C	A	B	C
2	A	B	C	A	B	C	A	B	C
3	C	A	B	B	C	A	C	A	B
4	C	A	B	B	C	A	C	A	B
5	B	C	A	C	A	B	B	C	A
6	B	C	A	C	A	B	B	C	A
7	A	B	C	A	B	C	A	B	C
etc.									

For $t = 4$ treatments, the FA designs above are used with each row being repeated.

Ak designs: Atkinson (1964) also presented another class of designs using FA designs and having each row repeated k times. For A3 designs, $k = 3$, and these are the designs we consider herein.

QBP designs: Quenouille (1953), Berenblut (1964), and Patterson (1970, 1973) constructed a class of experiment designs which requires 2t periods and t^2 sequences and is balanced for first-order residual effects in *each* periods, i.e., direct and first-order residual effects are orthogonal. For $t = 3$ treatments in $2(3) = 6$ periods and $3^2 = 9$ sequences, the design is:

Period	Sequence 1	2	3	4	5	6	7	8	9
1	A	B	C	A	B	C	A	B	C
2	C	A	B	B	C	A	A	B	C
3	B	C	A	B	C	A	B	C	A .
4	B	C	A	A	B	C	C	A	B
5	C	A	B	C	A	B	C	A	B
6	A	B	C	C	A	B	B	C	A

For periods 7 to 12, the above plan is repeated and likewise for periods 13 to 18. The design for $t = 4$ treatments in 16 sequences and 16 periods is given in Appendix QBP of Federer and Kershner(1993).

The Kershner (1980) measure of efficiency is presented and discussed in Section 2. The results of comparing LL, FA, A2, and A3 designs for residual, direct, and cumulative treatment effects are given in Section 3 and also in Appendices LL, FA, A2, A3, QBP, and FO of Federer and Kershner (1993).

A new class of changeover designs denoted as foldover tied-double-changeover (FO designs) experiment designs is presented in Section 4. These designs are more efficient for direct and residual but not for cumulative effects. The direct and first-order residual effects are more nearly orthogonal than for LL, FA, A2, and A3 designs. Also, designs are available for t or more sequences and p periods, which is not the case for QBP designs requiring 2t periods and t^2 sequences.

In Section 5, direct by first-order residual treatment interaction effects are discussed for LL, FA, and A2 designs. The interaction of cumulative treatment effects by period effects is also discussed to some extent.

2. KERSHNER MEASURE OF EFFICIENCY

For two treatments, the criterion for choosing efficient designs is based on minimizing the variance of a difference of effects. When the number of treatments is $t \geq 3$, there will be $t-1$ linearly independent (LIN) contrasts among direct, residual, and cumulative effects which are considered in assessing variance optimality. The Kershner (1980) measure of efficiency used herein is the determinant of the variance-covariance matrix of a set of LIN estimators of contrasts.

A changeover design has two-way blocking of s distinct sequences and p periods. For the nsp observations, where n is the number of times a set of sequences is repeated, any linear model based on (3.1) of Kershner and Federer (1981) may be put in matrix form as:

$$\mathbf{y} = \mathbf{Xb} + \mathbf{e} \tag{2.1}$$

where $\mathbf{y} = \left\{y_{ijk}\right\}$ is the lexicon-ordered $nsp \times 1$ vector of observations, $\mathbf{X}$ is a design matrix consisting of 0's and 1's of order $nsp \times q$, $\mathbf{b}$ is the $q \times 1$ vector of population parameters, and the covariance structure is such that

$$\text{var}(\mathbf{e}) = \mathbf{V} = \mathbf{\Omega}_p * \mathbf{I}_{ns} = \sigma^2\left[(1-\rho)\mathbf{I}_p + \rho\mathbf{J}_p\right] * \mathbf{I}_{ns}\,, \tag{2.2}$$

where $*$ denotes a right Kronecker product. Note that $\mathbf{V}$ will be positive definite when $-1/(p-1) < \rho < 1$.

A set of generalized Aitken estimators of $\mathbf{b}$ in (2.1) is given by

$$\mathbf{b}^0 = (\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^-\mathbf{X}'\mathbf{V}^{-1}\mathbf{y}\,, \tag{2.3}$$

where $(\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^-$ is a symmetric reflexive generalized inverse of $\mathbf{X}'\mathbf{V}^{-1}\mathbf{X}$ satisfying certain conditions (see Kershner, 1980). The covariance matrix of $\mathbf{b}^0$ in (2.3) is then

$$\text{var}(\mathbf{b}^0) = (\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^-\,. \tag{2.4}$$

One set of $t-1$ linearly independent (LIN) contrasts among, say, the direct effects is

$$\mathbf{K}'\mathbf{b} = \begin{bmatrix} \tau_1 - \tau_t \\ \tau_2 - \tau_t \\ \vdots \\ \tau_{t-1} - \tau_t \end{bmatrix}. \tag{2.5}$$

Equivalently, one could consider a set of $t-1$ LIN contrasts among the residual effects such as

$$\mathbf{L}'\mathbf{b} = \begin{bmatrix} \rho_1 - \rho_t \\ \rho_2 - \rho_t \\ \vdots \\ \rho_{t-1} - \rho_t \end{bmatrix}. \tag{2.6}$$

In (2.5) $\mathbf{K}'$ is a $t-1 \times t$ matrix of contrast coefficients having full row rank $t-1$. The BLUE of (2.5) is:

$$\hat{\mathbf{K}'\mathbf{b}} = \mathbf{K}'\mathbf{b}^0 = \mathbf{K}'(\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^-\mathbf{X}'\mathbf{V}^{-1}\mathbf{y}\,, \tag{2.7}$$

which has a variance-covariance matrix of order $t-1$ given by

$$\text{var}(\mathbf{K}'\mathbf{b}^0) = \mathbf{K}'(\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^-\mathbf{K}\,. \tag{2.8}$$

Berenblut and Webb (1974) use the criteria of D-optimality (e.g., Kiefer, 1958; Raktoe *et al.*, 1981) to compare the variance optimality of certain designs. This procedure ranks designs on their

ability to maximize $|\mathbf{X}'\mathbf{V}^{-1}\mathbf{X}|$ or equivalently to minimize $|(\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^{-1}|$. Although this procedure demands that $\mathbf{X}$ in (2.1) be of full column rank, Berenblut and Webb (1974) note that ranking designs on the basis of this criteria is independent of the manner in which the model in (2.1) is reparameterized to yield a design matrix of full column rank.

3. VARIANCE OPTIMALITY WITH RESPECT TO CONTRASTS AMONG TREATMENT EFFECTS

Using the notation in the above section, several classes of crossover designs for three and four treatments are compared on the basis of the variance optimality of estimators of contrasts among direct, first-order residual, and cumulative treatment effects, i.e. using (2.8), these are:

$$\min \mathrm{D} = \min \left|\mathbf{K}'\mathrm{var}(\mathbf{b}^0)\mathbf{K}\right| = \left|\mathrm{var}\begin{bmatrix} \tau_1 - \tau_t \\ \vdots \\ \tau_{t-1} - \tau_t \end{bmatrix}\right|, \tag{3.1}$$

$$\min \mathrm{R} = \min \left|\mathbf{L}'\mathrm{var}(\mathbf{b}^0)\mathbf{L}\right| = \left|\mathrm{var}\begin{bmatrix} \rho_1 - \rho_t \\ \vdots \\ \rho_{t-1} - \rho_t \end{bmatrix}\right|, \tag{3.2}$$

$$\begin{aligned} \min \mathrm{C} = \min \left|(\mathbf{K}+\mathbf{L})'\mathrm{var}(\mathbf{b}^0)(\mathbf{K}+\mathbf{L})\right| &= \left|\mathrm{var}\begin{bmatrix} \tau_1 + \rho_1 - \tau_t - \rho_t \\ \vdots \\ \tau_{t-1} + \rho_{t-1} - \tau_t - \rho_t \end{bmatrix}\right|, \\ &= \left|\mathrm{var}\begin{bmatrix} \mathrm{T}_1 - \mathrm{T}_t \\ \vdots \\ \mathrm{T}_{t-1} - \mathrm{T}_t \end{bmatrix}\right|, \end{aligned} \tag{3.3}$$

respectively. Expression (3.3) utilizes the standard definition (e.g., Yates, 1949) of cumulative treatment effects as $\mathrm{T}_i = \tau_i + \rho_i$ for $i = 1, \cdots, t$.

The values of (3.1), (3.2), and (3.3) are computed for each of the LL, FA, Ak and QBP designs. The values of the determinants are unique to within a multiple of $|\mathbf{Q}|^2[\sigma^2(1-\rho)]^2$ where $\mathbf{Q}$ is an arbitrary nonsingular matrix of order $(t-1)$ as considered in $\mathbf{QK}'\mathbf{b} = \mathbf{C}'\mathbf{b}$. Note that since $\sigma^2(1-\rho)$ is a common factor, the relative ranking of the designs is invariant with respect to ρ. For all computations,

a single observation in (2.1) is defined to have the expected value:

$$E(y_{ghij}) = \mu + \pi_g + \delta_h + \tau_i + \rho_j \,, \tag{3.4}$$

where μ is a general mean effects, π_g is the effect of period g, g = 1, 2, $\cdots$, p, δ_h is the effect of the h^{th} sequence, h = 1, 2, $\cdots$, s, τ_i is the direct effect of treatment i in the period in which it is applied, i = 1, 2, $\cdots$, t, and ρ_j is the carryover or residual effect of treatment j in the first period after it was applied, j = 1, 2, $\cdots$, t. Note that for these designs, the δ_h, τ_i, and ρ_j are orthogonal to the π_g and μ. Therefore, to obtain solutions for the δ_h, τ_i, and ρ_j, we need only consider these set of reduced normal equations:

$$\begin{bmatrix} \mathrm{pI}_s & \mathbf{A}_{s\times t} & \mathbf{B}_{s\times t} \\ \mathbf{A}'_{t\times s} & \mathrm{npI}_t & \mathbf{C}_{t\times t} \\ \mathbf{B}'_{t\times s} & \mathbf{C}'_{t\times t} & \mathrm{n(p\text{-}1)I}_t \end{bmatrix} \begin{bmatrix} \hat{\delta} \\ \hat{\tau} \\ \hat{\rho} \end{bmatrix} = \mathbf{Y}^* \,. \tag{3.5}$$

The restraints $\Sigma\hat{\delta} = \Sigma\hat{\tau}_i = \Sigma\hat{\rho}_j = 0$ were used in evaluating (3.5). The form of $\mathbf{Y}^*$ involves the use of $Y_{.h..} - p\bar{y}....$, $Y_{..i.} - np\bar{y}....$, and $Y_{...j} - n(p-2)\bar{y}.... - n\bar{y}_1...$ rather than just the $Y_{.h..}$, $Y_{..i.}$, and $Y_{...j}$ totals. Values of determinants of (2.4), D-optimality, and of (2.8), Kershner efficiency, are given in the Appendices of Federer and Kershner (1993).

Note that a QBP design for t = 3 treatments is defined only for 9 sequences and hence it was not compared with other designs for s = 6 sequences. From Table 1 using D-optimality, no design is best for all effects, periods, and sequences for t = 3 treatments. The superiority of A2 designs is noted for cumulative effects which have a high correlation between the direct and residual effect of treatment i. This correlation needs to be balanced off against correlation with other treatment direct and residual effects. Otherwise, the LL designs would have been superior. The QBP designs have zero correlation between direct and residual effects in each period and are superior for estimating direct and residual effects for s = 9 sequences; the A2 and A3 designs are superior for estimating cumulative effects.

Values obtained for the determinant of equation (2.8), Kershner (1980) efficiency, were used to obtain Tables 2 and 3 giving the design which has the minimum value of the determinant of (2.8) for each value of t, s, and p. Here again there is no one design that is consistently better for t = 3 treatments, for s sequences, and p periods. A2 and A3 designs are superior for cumulative effects and QBP designs for residual and direct effects for 9 sequences. There is some inconsistency in ranking the

designs using determinants of (2.4) and (2.8) but in general they agree (Tables 1 and 2).

For t = 4 and s = 4, 8, and 12, FA designs showed superiority in many cases for direct and residual effects but not for cumulative effects (Table 3). The A2 and A3 designs exhibit superiority for cumulative effects. The patterns in Tables 1 and 2 for three treatments differs from that in Table 3 for four treatments. The relative merits of classes of designs are illustrated later in Figures 1 to 6.

4. FOLDOVER-TIED-CHANGEOVER DESIGN

Since none of the published experiment designs were optimal under all conditions, is there such a class of designs which is? If only direct and residual, and not cumulative, effects are considered, the answer is in the affirmative, at least for most cases. This class of designs is as named above, or simply foldover (FO) designs for short. To illustrate, the construction of these designs let t = 3 and s = 6 and t = 4 and s = 4:

	Sequence								Sequence			
Period	1	2	3	4	5	6	Period	1	2	3	4
1	A	B	C	A	B	C	1	A	B	C	D
2	C	A	B	B	C	A	2	D	A	B	C
3	B	C	A	C	A	B	3	B	C	D	A
4	B	C	A	C	A	B	4	C	D	A	B
5	C	A	B	B	C	A	5	C	D	A	B
6	A	B	C	A	B	C	6	B	C	D	A
7 etc.	repeat periods 1–6						7	D	A	B	C
							8	A	B	C	D
							9 etc.	repeat periods 1–8			

Note that for t = 3 treatments, periods 4, 5, and 6 are a mirror image, i.e. a foldover, of the first three periods. For s = 9 sequences and t = 3 treatments, simply repeat sequences 1 to 3 (or 4 to 6), but a QBP design would be better. For t = 4 and s = 8 or 12 sequences, repeat sequences 1 to 4; for 16 sequences it would appear that a QBP design would be more efficient than an FO design since direct and residual effects are orthogonal for every period.

To demonstrate the superiority of FO designs over LL, FA, A2, and A3 designs, Figures 1 to 6 have been prepared. Ratios of determinants for equation (2.8) have been used to compare the designs. In Figure 1, the ratio of the determinants of equation (2.8), i.e., $|\mathbf{K'ZK}|$, for t = 3 treatments and s = 3 sequences for p = 4 to 15 periods, has been used for residual effects. The FO design is superior to all

other designs, i.e., the ratios are greater than one. As the number of periods increases, A2 designs approach FO designs in efficiency. LL designs become increasingly worse as p increases. As was noted in Table 1 for the four classes, we see that LL designs are best for $p = 4$ and 5, FA and A2 designs are tied for $p = 6$, and A3 designs are better than LL, FA, and A2 designs for $p = 7$ to 15. The results for direct effects are similar to those for residual effects. With respect to cumulative effects for $t = 3$ treatments in $s = 3$ sequences in Figure 2, we note that A2 and/or A3 designs are superior to LL, FA, and FO designs, that A2 and A3 designs alternate for $p = 4$, 5, 6, and that A3 is superior from period 7 on as indicated in Table 1.

The ratios of determinants of (2.8) for $t = 3$ treatments and $s = 6$ sequences for residual effects are given in Figure 3. Since LL and FO are the same design for $p = 2$, 3, and 4 and FA, LL, and FO are the same for $p = 2$ and 3, the ratios are one. For $p = 5$ to 15 periods, FO designs are superior although not much better than A2. With respect to the other four classes, LL and FA are best for periods 2 and 3 and LL is best for period 4. From periods 5 to 15, A2 designs are superior. Again the picture for direct effects is similar. With respect to cumulative effects in Figure 4 for $t = 3$ treatments and $s = 6$ sequences, FA, LL, and FO designs are the same for $p = 2$ and 3 as are LL and FO designs for $p = 4$. When $p = 5$, 6, and 7, A2 designs are best. When $p = 8$ to 15, A3 designs are superior to all others including FO designs.

For $t = 4$ treatments and $s = 4$ sequences and for residual effects, FO designs are superior to all other designs except for LL in $p = 6$ periods. With respect to the other four classes, LL and FA are the best for $p = 4$, LL is best for $p = 5$, 6, and 7, and FA and A2 alternate for $p = 8$ to 16. For cumulative effects (Figure 6), A2 is the best design for $p = 4$, 6, 7, and 8, LL for $p = 5$, and A3 for $p = 9$ to 16.

In the above, ratios of determinants of $\mathbf{K'ZK}$, i.e. Kershner (1980) efficiency, were used. If D-optimality, i.e. $|\mathbf{Z}|$, was used as a measure of efficiency, the ratios would be similar to those for ratios of $|\mathbf{K'ZK}|$. For $t = 4$ and $s = 4$ these ratios are given in Table FO-4.2 of Appendix FO in Federer and Kershner (1993).

5. DIRECT-BY-FIRST ORDER RESIDUAL AND CUMULATIVE TREATMENT-BY-PERIOD INTERACTIONS

A linear model having direct, residual and direct-by-residual treatment interaction is given by:

$$E(y_{ghij}) = \mu + \pi_g + \delta_h + \tau_i + \rho_j + \tau\rho_{ij} , \tag{5.1}$$

where $\tau\rho_{ij}$ is an interaction effect of i^{th} direct and j^{th} one-period residual effect and the other effects are as defined for (3.4). Kershner (1980) presents a linearly independent set of contrasts for estimating a direct-by-residual interaction. Treatments need to precede themselves in order to estimate this interaction. Hence, this interaction is not estimable in FA designs.

Treatment-by-period interaction effects for linear models having both direct and residual treatment effects are parameterized in terms of cumulative treatment by period interactions (CTPI) effects. This parameterization arises from considering models having both direct and residual effects and their corresponding interactions with periods. Designs which permit estimation of CTPI are characterized by the application of the same treatment to individual s.u.'s for k successive periods. The number of successive applications that are required for estimability is a function of the number of residual effects present in the model. Consider a model with m^{th} order residual effects. In order to estimate at least one contrast among CTPI within a minimum number of periods, the s.u.'s must receive $m+2$ successive applications of the same treatment as it takes $m+1$ periods for the cumulative effects to manifest themselves on the individual e.u.'s and at least one more treatment application is needed in order that the cumulative treatment (CT) effects appear in at least two periods, thus defining a within-s.u. contrast among the CTPI. The successive applications of treatments causes part of the sequences to define a completely randomized (CR) design. By using factorial theory, contrasts among CTPI can be constructed as in CR designs.

The model that is considered in this section is:

$$E(y_{ghij}) = \mu + \pi_g + \delta_h + \tau_i + \rho_j + \eta_{gij}\alpha\pi_{gi} , \tag{5.2}$$

where $\alpha\pi_{gi}$ defines the interaction between the i^{th} cumulative treatment effect and the g^{th} period effect and

$$\eta_{gij} = \begin{cases} = 1 & \text{if } g = i = j \\ = 0, & \text{otherwise} \end{cases} .$$

The remaining effects in (5.2) are defined according to (3.4). Define a contrast among CTPI as:

$$\theta_{gi,g'i'} = \alpha\pi_{gi} - \alpha\pi_{gi'} - \alpha\pi_{g'i} + \alpha\pi_{g'i'} \tag{5.3}$$

for $i, i' = 1, \cdots, t$, $i \neq i'$ and $g, g' = 1, \cdots, p$, $g \neq g'$. Contrasts among the interaction effects in (5.2) can be defined in terms of LIN θ's in (5.3) or LIN sets of linear combinations of the θ's.

The designs that provide estimators of contrasts among cumulative treatment-by-period interaction (CTPI) effects are LL for $p = 5$, A3 for $p \geq 6$ and QBP for $p \geq 2t$. Note that for FA designs $\eta_{gij} = 0$ every i and j so that contrasts among CTPI are not estimable under (5.2). For A2, the contrasts among CTPI are completely confounded with sequences. The LL design for three treatments has CTPI effects appearing only in periods four and five.

For QBP, contrasts among CTPI are estimable under (5.2) only when $p > 2t + 1$. Consider the QBP design for $t = 3$. To form a design with $p > 2t$ the additional periods can be obtained by repeating the basic design in such a way that periods $1, \cdots, 2t$ are QBP as are periods $2t + 1, \cdots, 4t$, etc. Certain contrasts among the CTPI will be estimable for the QBP design when $t = 3$ and $p > 2t + 1$.

The A3 design not only minimizes the variances of estimators of contrasts among CT, but it also minimizes the variances to estimators of contrasts among CTPI. In general, the efficiency of an Ak design for estimating contrasts among CT and CTPI will improve with increasing k, but the disadvantage of doing so is that the number of treatment periods may become large. A more detailed discussion of these interactions may be found in Kershner (1980).

6. SUMMARY

From the results presented herein, no one class of designs is superior for all situations. The superiority of an experiment design is not invariant with respect to:

1. number of periods,
2. number of sequences,
3. number of treatments,
4. residual, direct, or cumulative effect, or
5. measure of efficiency (Bishop and Jones, 1986).

The proposed class denoted as foldover designs are generally superior to all other designs except QBP

designs for direct and residual effects. QBP designs are defined only for $p = 2t$ and $s = t^2$, or multiples thereof. Partial sets of sequences of QBP designs were not investigated, but in several cases they would be inferior to FO designs. For cumulative effects the A2 and A3 designs generally exhibit the lowest values for determinants of $\mathbf{K'ZK}$ in (2.8) or of $\mathbf{Z}$ in (2.4).

If the investigator planning a repeated measures experiment specifies the number of treatments t, the number of periods p, the number of sequences s, the effect of interest, and the measure of efficiency, the best design may be selected using the above results and method. For a sequential selection of periods and/or sequences, FO designs for direct and residual effects and A2 or A3 designs for cumulative effects would be an appropriate choice of a design. If direct-by-residual treatment interaction or if a cumulative effect-by-period interaction is of interest, the experimenter needs to carefully select a design that allows estimation of these interactions.

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Table 1. Best design for t = 3 treatments, s = 6 and 9 sequences for p periods by D-optimality

	s = 6 sequences			s = 9 sequences		
Periods	residual	direct	cumulative	residual	direct	cumulative
3	FA	FA	FA	QBP	QBP	A2
4	FA	FA	FA	QBP	QBP	A2
5	A2	A2	A3	QBP	QBP	A3
6	A2	A2	A2	QBP	QBP	A2
7	A2	A2	A2	QBP	QBP	A2
8	A2	A2	A3	QBP	QBP	A3
9	A2	A2	A3	QBP	QBP	A3
10	A2	A2	A3	QBP	QBP	A3
11	A2	A2	A3	QBP	QBP	A3
12	A2	A2	A3	QBP	QBP	A3
13	A2	A2	A3	QBP	QBP	A3
14	A2	A2	A3	QBP	QBP	A3
15	A2	A2	A3	QBP	QBP	A3

Table 2. Best design for t = 3 treatments, s = 3, 6 and 9 sequences for p periods using equation (2.8).

Periods	3 sequences			6 sequences			9 sequences		
	residual	direct	cumulative	residual	direct	cumulative	residual	direct	cumulative
2	–	–	–	–	–	–	QBP	QBP	QBP
3	A2	A2	A2	FA^{+}	FA^{+}	FA^{+}	FA	FA	FA
4	LL	LL	A2	FA	FA	A2	QBP	QBP	A2
5	LL	A2	A3	A2	A2	A2	QBP	QBP	A2
6	FA*	FA*	A2	A2	A2	A2	QBP	QBP	A2
7	FA*	FA*	A3	A2	A2	A2	QBP	QBP	A2
8	A2	FA	A3	A2	A2	A3	QBP	QBP	A3
9	A2	A2	A3	A2	A2	A3	QBP	QBP	A3
10	A2	A2	A3	A2	A2	A3	QBP	QBP	A3
11	A2	A2	A3	A2	A2	A3	QBP	QBP	A3
12	A2	A2	A3	A2	A2	A3	QBP	QBP	A3
13	A2	A2	A3	A2	A2	A3	QBP	QBP	A3
14	A2	A2	A3	A2	A2	A3	QBP	QBP	A3
15	A2	A2	A3	A2	A2	A3	QBP	QBP	A3

* Tied with A2.

$^{+}$ Tied with LL.

Table 3. Best design for t = 4 treatments, s = 4, 8 and 12 sequences for p periods using equation (2.8).

Periods	4 sequences			8 sequences			12 sequences		
	residual	direct	cumulative	residual	direct	cumulative	residual	direct	cumulative
2	–	–	–	–	–	–	FA	FA	FA
3	A2	A2	A2	FA	FA	FA	FA	FA	FA
4	FA^{+}	FA^{+}	A2	LL	LL	A2	FA^{+}	FA^{+}	A2
5	LL	LL	LL	LL	LL	LL	LL	LL	LL
6	LL	LL	A2	LL	LL	A2	LL	LL	A2
7	LL	A2	A2	LL	FA	A2	FA^{+}	A2	A2
8	FA	FA	A2	FA	FA	A2	FA	FA	A2
9	A2	A2	A3	FA*	FA*	A3	FA*	FA*	A3
10	FA	FA	A3	FA	FA	A3	FA	FA	A3
11	A2	A2	A3	FA	FA	A3	FA*	FA*	A3
12	FA	FA	A3	FA	FA	A3	FA	FA	A3
13	A2	A2	A3	FA	FA	A3	FA	FA*	A3
14	FA	FA	A3	FA	FA	A3	FA	FA	A3
15	A2	A2	A3	FA	FA	A3	FA*	FA*	A3
16	FA*	A2	A3	FA	FA	A3	FA	FA	A3

* Tied with A2.

$^{+}$ Tied with LL.

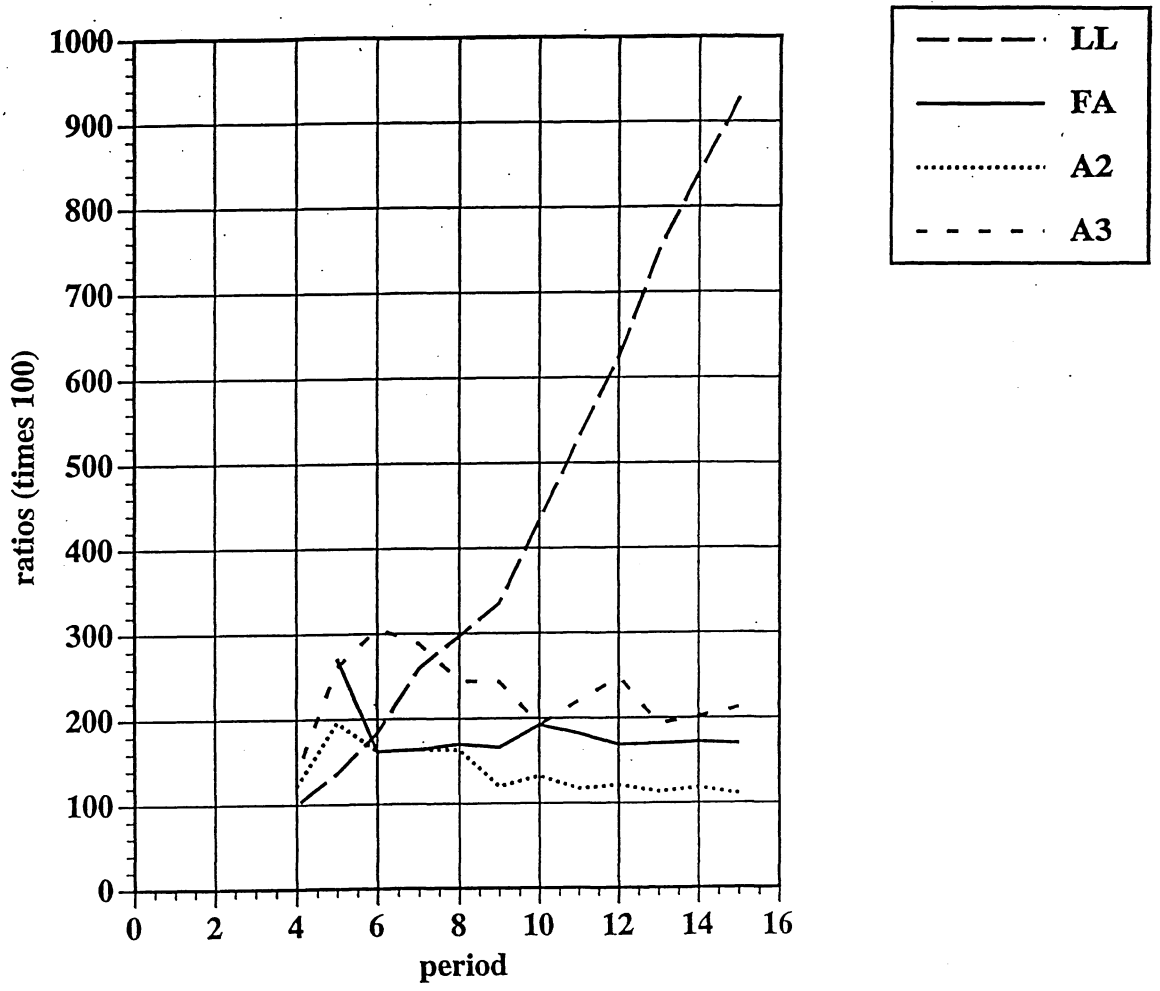

Figure 1. Ratios (times 100) of determinants of (2.8) for residual effects when t = 3 and s= 3.

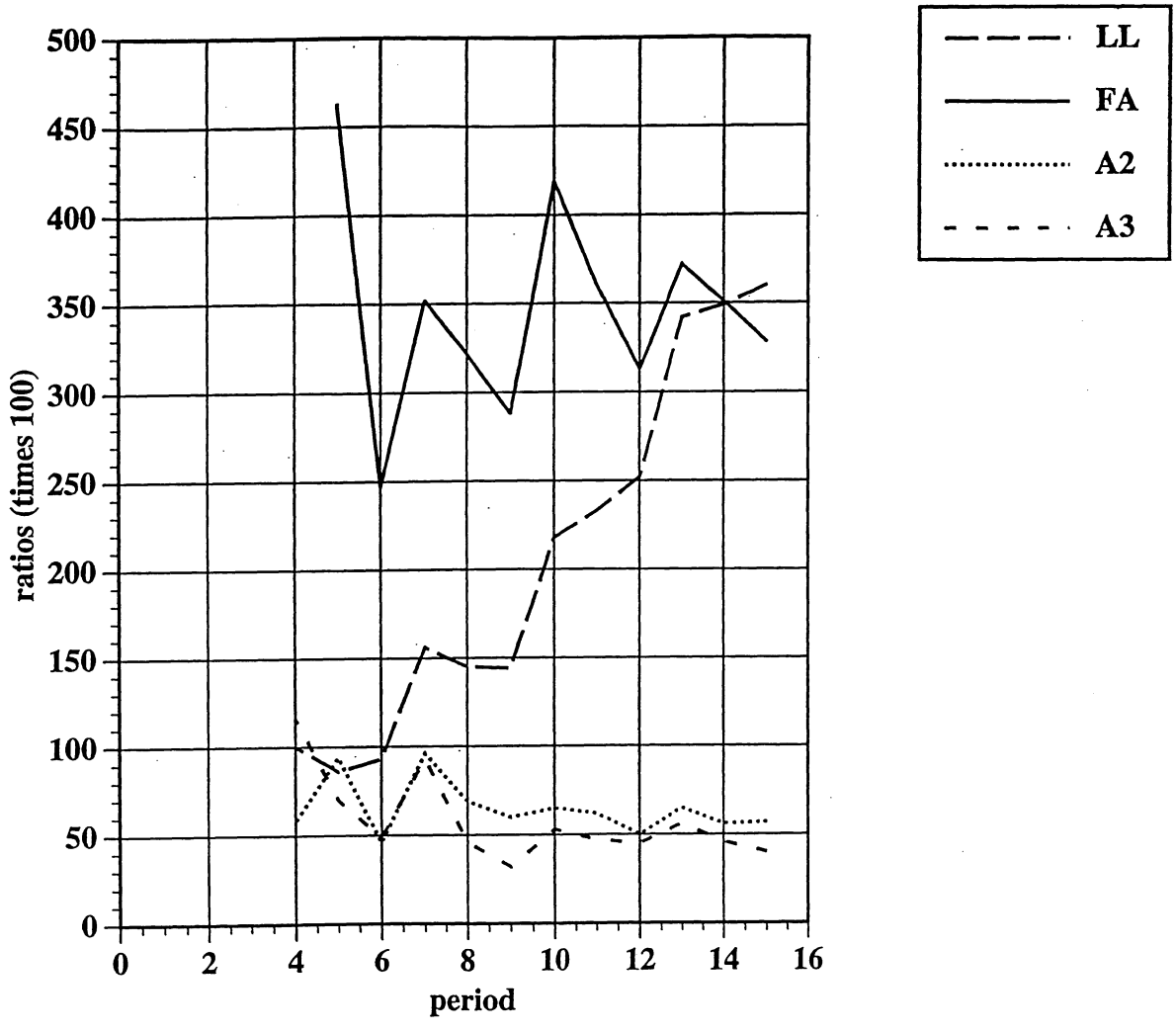

Figure 2. Ratios (times 100) of determinants of (2.8) for cumulative effects when t = 3 and s =3.

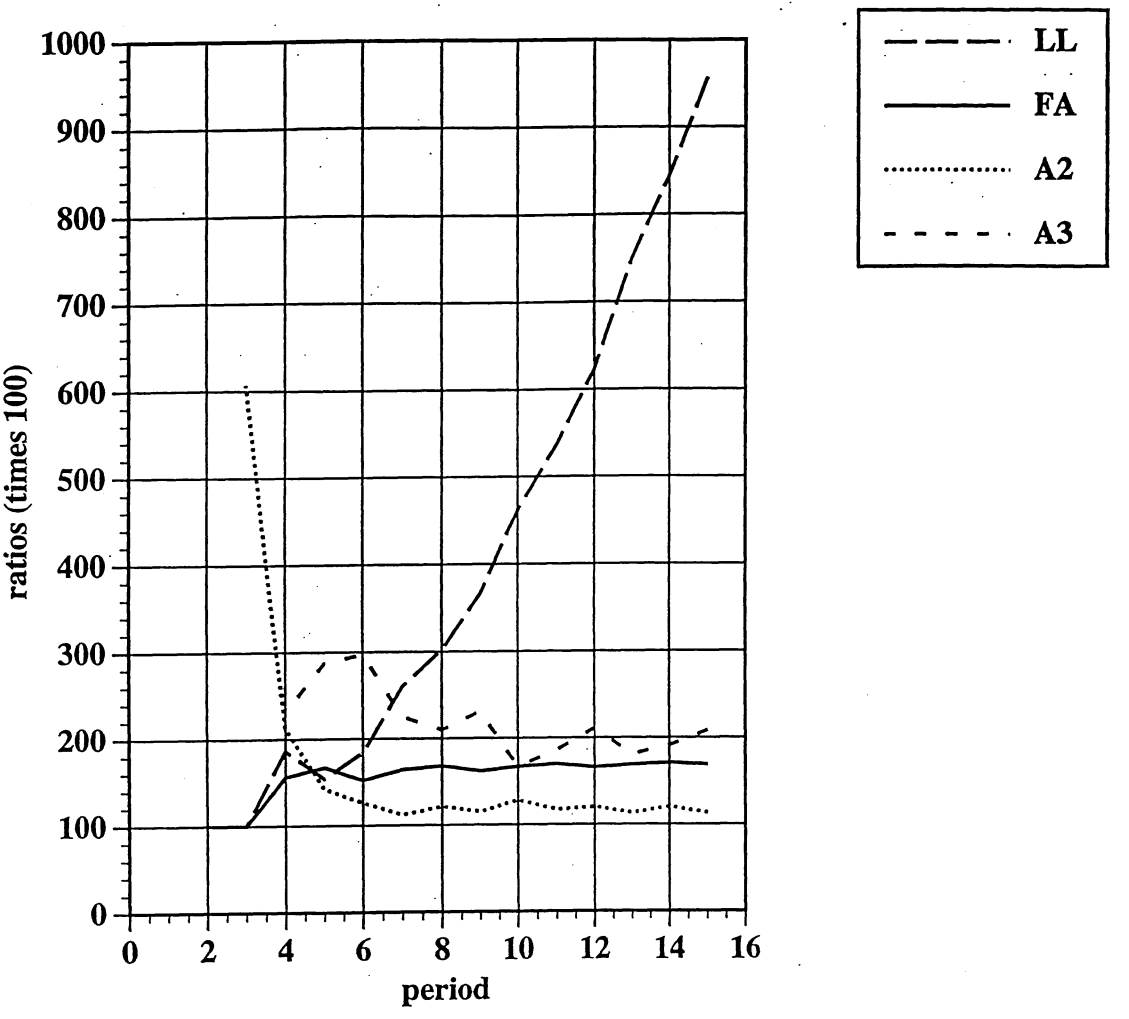

Figure 3. Ratios (times 100) of determinants of (2.8) for residual effects when t = 3 and s = 6.

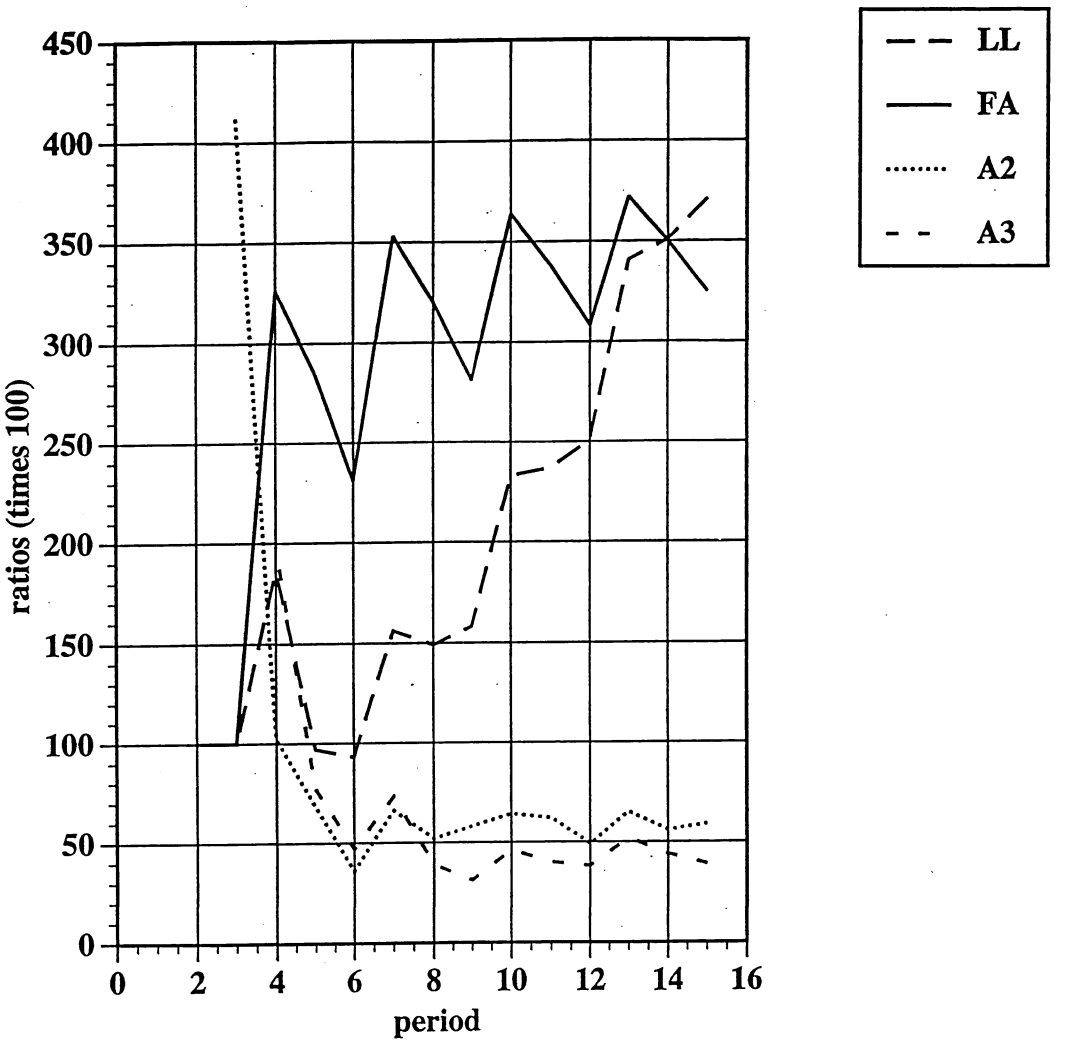

Figure 4. Ratios (times 100) of determinants of (2.8) for cumulative effects when t = 3 and s = 6.

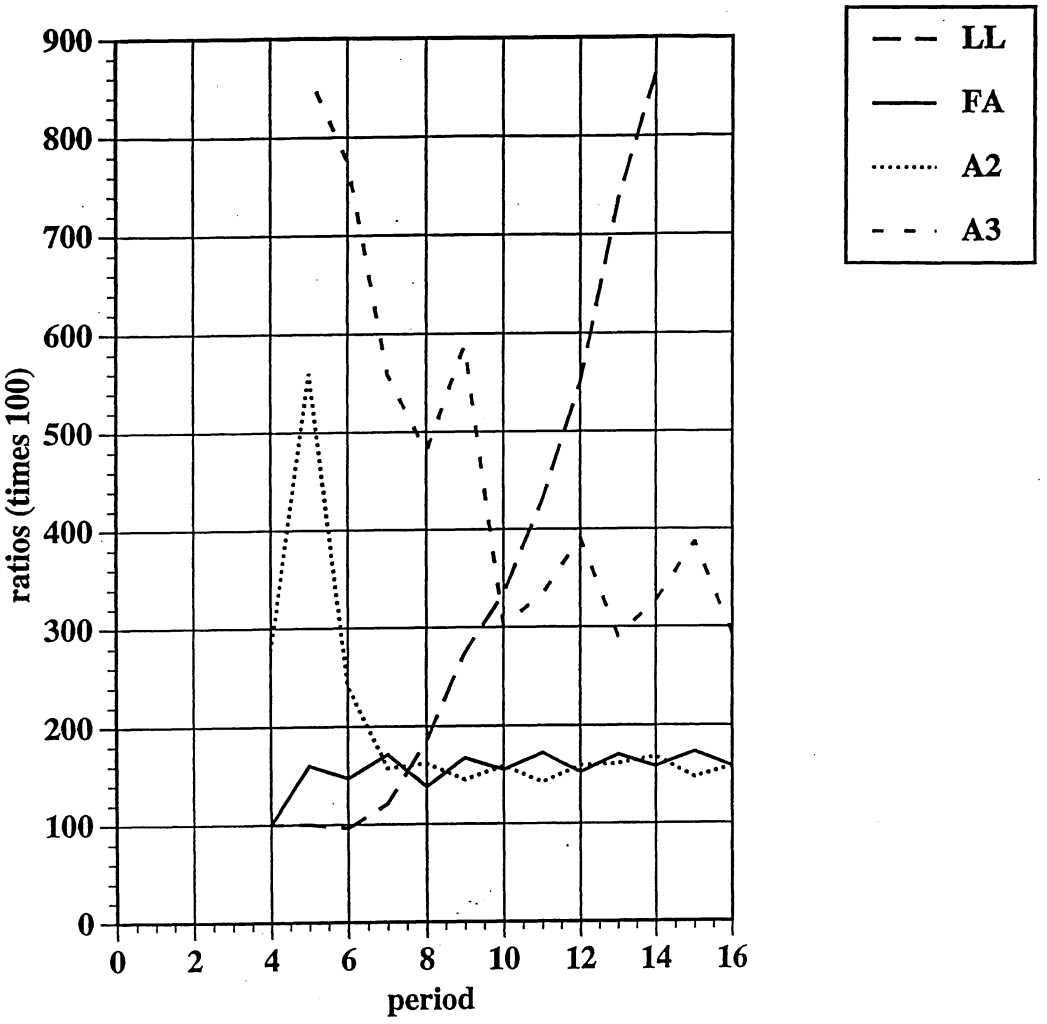

Figure 5. Ratios (times 100) of determinants of (2.8) for residual effects when t = 4 and s = 4.

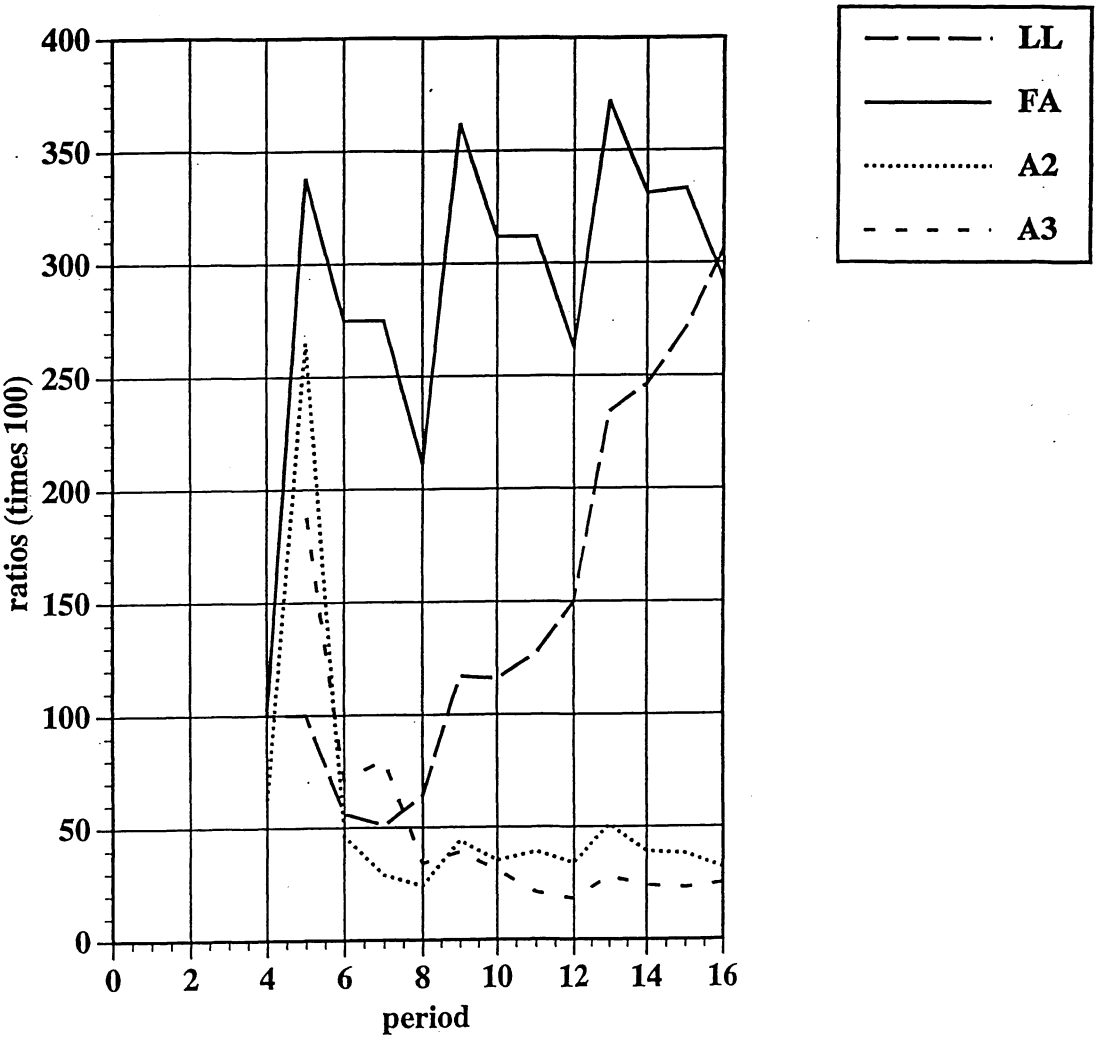

Figure 6. Ratios (times 100) of determinants of (2.8) for cumulative effects when t = 4 and s = 4.