BALANCED REPEATED MEASUREMENTS DESIGNS

By Ching-Shui Cheng 1 and Chien-Fu $\mathbf{W}\mathbf{u}^2$

University of California, Berkeley and University of Wisconsin, Madison

Two types of repeated measurements designs (RMD), the strongly balanced uniform RMD, and the balanced uniform RMD, are defined and their universal optimality is proved over very broad classes of competing designs. Construction methods for strongly balanced uniform RMD are also given.

1. Introduction. In repeated measurements designs (cross over, or change over designs), experimental units are used repeatedly by exposing them to a sequence of different or identical treatments. For a discussion on the use of this kind of design, the readers may consult Hedayat and Afsarinejad (1975), which also provides an extensive bibliography containing more than 130 references on repeated measurements designs.

Using a tool due to Kiefer (1975), Hedayat and Afsarinejad (1978) proved the universal optimality of some *balanced* repeated measurements designs over the class of *uniform* designs. They considered the following model:

Let t treatments be compared via n experimental units in p periods. Altogether np observations are taken. An allocation of the t treatments into the np observations is called a *repeated measurements design* (RMD). If d is an RMD, then let d(i, j) denote the treatment assigned by d in the ith period to the jth experimental unit. Let y_{ij} be the response obtained under d(i, j). Then all the observations are assumed to be uncorrelated with common variance and

(1.1)
$$E(y_{ij}) = \alpha_i + \beta_j + \tau_{d(i,j)} + \rho_{d(i-1,j)},$$

$$i = 1, \dots, p, \qquad j = 1, \dots, n, \qquad \rho_{d(0,j)} = 0 \quad \text{for all } j,$$

where the unknown constants α_i , β_j , $\tau_{d(i,j)}$ and $\rho_{d(i-1,j)}$ are respectively called the ith period effect, the jth experimental unit effect, the direct effect of treatment d(i, j), and the first order residual effect of treatment d(i-1, j).

For convenience, a repeated measurements design with t treatments, n units and p periods is abbreviated as RMD(t, n, p). The collection of all such designs is denoted by $\Omega_{t,n,p}$.

DEFINITION 1.1. A design d is said to be uniform on the periods if, in each period, d assigns the same number of units to each treatment.

DEFINITION 1.2. A design is said to be *uniform on the units* if, on each unit, each treatment appears in the same number of periods.

DEFINITION 1.3. A design is called uniform if it is uniform on the periods and units.

Hedayat and Afsarinejad (1978) considered the setting in which t = p and $t \mid n$ (say $n = \lambda_1 t$). They also restricted the competing designs to be *uniform*. For a uniform design in $\Omega_{t,\lambda_1 t,t}$, it is clear that a treatment can not be preceded by itself. Thus, a design in $\Omega_{t,\lambda_1 t,t}$ is defined to be

1272

www.jstor.org

Received February 1979; revised August 1979.

¹ Research supported by National Science Foundation Grants No. MCS-78-01422 and MCS-79-09502.

² Research supported by Research Committee, University of Wisconsin, and National Science Foundation Grant No. MCS-79-01846.

AMS 1970 Subject Classifications. Primary 62K05; secondary 62K10, 62P10.

Key words and phrases. Repeated measurements designs, cross over designs, change over designs, strongly balanced uniform repeated measurements designs, balanced uniform repeated measurements designs, universal optimality, extra-period designs.

balanced if in the order of application, each treatment is preceded precisely λ_1 times by each other treatment, i.e., the collection of ordered pairs $(d(i,j),d(i+1,j)),\ 1 \le i \le t-1,\ 1 \le j \le \lambda_1 t$, contains each ordered pair of distinct treatments λ_1 times. In general (not necessarily t=p and $t\mid n$), an RMD is called balanced if in the order of application, each treatment is not preceded by itself and is preceded by the other treatments equally often. Using Kiefer's tool, Hedayat and Afsarinejad proved the universal optimality of a balanced uniform RMD $(t, \lambda_1 t, t)$ for the estimation of direct as well as residual effects over the uniform designs in $\Omega_{t\lambda_1 t, t}$.

There is an intrinsic difficulty in removing the restriction of uniformity which Hedayat and Afsarinejad imposed on the competing designs. From an optimality point of view, there is no reason to exclude the designs which allow a treatment to be preceded by itself. When $\lambda_1 > 1$, the t^2 ordered pairs of treatments do not appear as nearly equally often as possible in a balanced uniform RMD(t, $\lambda_1 t$, t) and hence its optimality over all possible designs is quite doubtful. This also causes difficulty in verifying the maximization of the trace of the information matrices, an important step in applying Kiefer's result. In view of this, it seems unlikely to remove entirely Hedayat and Afsarinejad's restriction. However, we are able to show that a balanced RMD(t, $\lambda_1 t$, t) is universally optimal for the estimation of residual effects over the designs in which each treatment is not preceded by itself. Thus, the restriction of uniformity is relaxed substantially. As to the estimation of direct effects, the restriction of uniformity can also be relaxed to a certain extent. The first purpose of the present paper is to extend and strengthen Hedayat and Afsarinejad's results.

If we want to dispose of the restriction entirely, then a stronger kind of balancing is needed.

DEFINITION 1.4. An RMD(t, n, p) d is called *strongly balanced* if the collection of ordered pairs (d(i, j), d(i + 1, j)), $1 \le i \le p - 1$, $1 \le j \le n$, contains each ordered pair of treatments (distinct or not) the same number of times, say λ times.

Note that in a strongly balanced RMD(t, n, p), $\lambda = t^{-2}(p-1)n$.

The second purpose of this paper is to discuss the optimality of some strongly balanced designs. We are able to prove that a strongly balanced uniform design is universally optimal for the estimation of direct as well as residual effects over all possible designs. A more interesting result says that if we repeat the observations in the last period of Hedayat and Afsarinejad's balanced uniform RMD(t, $\lambda_1 t$, t), then the resulting design is universally optimal for direct as well as residual effects over $\Omega_{t,\lambda_1 t,t+1}$. This design is strongly balanced and uniform on the periods but is *not* uniform on the units. The strongly balanced uniform designs were discussed in Berenblut (1964) and the procedure of repeating the observations in the last period was first proposed by Lucas (1957) under the name of extra-period designs. Both designs have very nice orthogonality structures which are closely related to the optimality.

The organization of this paper is the following. Section 2 contains some preliminaries. The optimality of some strongly balanced designs is proved in Section 3. Some examples and methods of construction are also presented. The results in this section can be extended in several directions including the case where there are higher-order residual effects and the model in which each unit effect has a higher-dimensional structure. These extensions are treated in Cheng and Wu (1979). Section 4 deals with the extension of Hedayat and Afsarinejad's result on balanced designs. Section 5 contains the proofs of the results in Section 4.

2. Preliminaries. We write C_d (resp., \bar{C}_d) as the C-matrix or information matrix of the direct (resp., residual) effects when design d is used. An *optimality criterion* is a function Φ : $\mathcal{B}_{t,0} \to (-\infty, \infty]$, where $\mathcal{B}_{t,0}$ is the collection of $t \times t$ nonnegative definite matrices with zero row and column sums. A design is called Φ -optimal if it minimizes $\Phi(C_d)$ or $\Phi(\tilde{C}_d)$ over the competing designs depending on which effects we are interested in. Note that C_d , $\tilde{C}_d \in \mathcal{B}_{t,0}$ in our setting.

Kiefer (1975) introduced the notion of universal optimality. A design d^* is called *universally optimal* if it is Φ -optimal for all Φ satisfying

- (i) Φ is convex,
- (ii) $\Phi(bC)$ is nonincreasing in the scalar $b \ge 0$,
- (2.1) (iii) Φ is invariant under any simultaneous permutation of rows and columns of C.

Note that if d^* is universally optimal then it is D-, A-, and E-optimal. Kiefer (1975) obtained a very simple sufficient condition for universal optimality. A simple algebraic argument shows that d^* is universally optimal as long as d^* maximizes tr C_d (or tr \tilde{C}_d) and C_{d^*} (or \tilde{C}_{d^*}) is completely symmetric in the sense that all the diagonal elements of C_{d^*} (or \tilde{C}_{d^*}) are equal and all the off-diagonals are the same.

For each design $d \in \Omega_{t,n,p}$, define

 n_{diu} = number of appearances of treatment i on unit u,

 \tilde{n}_{diu} = number of appearances of treatment *i* on unit *u* in the first p-1 periods.

 l_{dik} = number of appearances of treatment i in period k,

 m_{dij} = number of appearances of treatment *i* preceded by treatment *j* on the same unit,

where $i, j = 1, \dots, t, u = 1, \dots, n, k = 1, \dots, p$. It follows that

$$r_{di} \equiv \sum_{u=1}^{n} n_{diu} = \sum_{k=1}^{p} l_{dik} = \text{number of appearances of treatment } i$$
,

(2.2)
$$\tilde{r}_{di} \equiv \sum_{u=1}^{n} \tilde{n}_{diu} = \sum_{k=1}^{p-1} l_{dik} = \sum_{j=1}^{t} m_{dji} = \text{number of appearances of treatment } i \text{ in the first } p-1 \text{ periods.}$$

The following relations are fundamental:

$$\sum_{i=1}^{t} n_{diu} = p, \sum_{i=1}^{t} \tilde{n}_{diu} = p - 1, \sum_{i=1}^{t} l_{dik} = n,$$

(2.3)
$$s_{di} = \text{number of appearances of treatment } i \text{ in the last } p-1 \text{ periods}$$
$$= \sum_{k=2}^{p} l_{dik} = \sum_{j=1}^{l} m_{dij}, \sum_{i=1}^{l} r_{di} = np, \sum_{i=1}^{l} \tilde{r}_{di} = n(p-1).$$

From (2.2) and (2.3), uniformity on units and equal m_{dij} imply the uniformity in the first and last periods.

In vector notation, for any $d \in \Omega_{t,n,p}$,

$$(2.4) E v_d = X_d \theta.$$

where y_d is the $np \times 1$ vector of observations, X_d is the design matrix, and $\theta = (\tau_1, \tau_2, \dots, \tau_t, \rho_1, \dots, \rho_t, \alpha_1, \dots, \alpha_p, \beta_1, \dots, \beta_n)'$. Then

(2.5)
$$X'_{d}X_{d} = \begin{bmatrix} D_{d} & M_{d} & N_{dp} & N_{du} \\ M'_{d} & \bar{D}_{d} & \bar{N}_{dp} & \bar{N}_{du} \\ N'_{dp} & \bar{N}'_{dp} & nI_{p} & J_{p,n} \\ N'_{du} & \bar{N}'_{du} & J_{n,p} & pI_{n} \end{bmatrix},$$

where I_p is the identity matrix of order p, $J_{p,n}$ is the $p \times n$ matrix of ones, $D_d = \operatorname{diag}(r_{d1}, \dots, r_{dl})$, $\tilde{D}_d = \operatorname{diag}(\tilde{r}_{d1}, \dots, \tilde{r}_{dl})$, $M_d = [m_{dij}]_{1 \le i,j \le l}$, $N_{dp} = [l_{dik}]_{1 \le i \le l,1 \le k \le p}$, $\tilde{N}_{dp} = [\tilde{l}_{dik}]_{1 \le i \le l,1 \le k \le p}$ with $\tilde{l}_{dil} = 0$, $\tilde{l}_{dik} = l_{di,k-1}$ for $k \ge 2$, $N_{du} = [n_{diu}]_{1 \le i \le l,1 \le u \le n}$, and $\tilde{N}_{du} = [\tilde{n}_{diu}]_{1 \le i \le l,1 \le u \le n}$.

From (2.5), the information matrix for estimating direct and residual effects jointly is

$$\begin{bmatrix} D_d & M_d \\ M'_d & \tilde{D}_d \end{bmatrix} - \begin{bmatrix} N_{dp} & N_{du} \\ \tilde{N}_{dp} & \tilde{N}_{du} \end{bmatrix} \begin{bmatrix} nI_p & J_{p,n} \\ J_{n,p} & pI_n \end{bmatrix}^{-} \begin{bmatrix} N'_{dp} & \tilde{N}'_{dp} \\ N'_{du} & \tilde{N}'_{du} \end{bmatrix} = \begin{bmatrix} C_{d11} & C_{d12} \\ C_{d21} & C_{d22} \end{bmatrix},$$

where

$$\begin{split} C_{d11} &= D_d - n^{-1} N_{dp} N'_{dp} - p^{-1} N_{du} N'_{du} + n^{-1} p^{-1} N_{du} J_{n,n} N'_{du}, \\ C_{d12} &= C'_{d21} = M_d - n^{-1} N_{dp} \tilde{N}'_{dp} - p^{-1} N_{du} \tilde{N}'_{du} + n^{-1} p^{-1} N_{du} J_{n,n} \tilde{N}'_{du}, \\ C_{d22} &= \tilde{D}_d - n^{-1} \tilde{N}_{dp} \tilde{N}'_{dp} - p^{-1} \tilde{N}_{du} \tilde{N}'_{du} + n^{-1} p^{-1} \tilde{N}_{du} J_{n,n} \tilde{N}'_{du}. \end{split}$$

and A^- denotes a generalized inverse of A.

Then

$$(2.7) C_d = C_{d11} - C_{d12}C_{d22}^{-}C_{d21}$$

and

$$\tilde{C}_d = C_{d22} - C_{d21}C_{d11}^{-1}C_{d12}.$$

The following lemmas are useful for later developments.

LEMMA 2.1. The row sums and column sums of C_{d12} and $M_d - n^{-1}N_{dp}\tilde{N}'_{dp}$ are all equal to zero, and the column sums of $M_d - p^{-1}N_{du}\tilde{N}'_{du}$ are all equal to zero.

PROOF. From (2.2) and (2.3), it can be easily checked that the *j*th column sums of M_d , $n^{-1}N_{dp}\tilde{N}'_{dp}$, $p^{-1}N_{du}\tilde{N}'_{du}$, and $n^{-1}p^{-1}N_{du}J_{n,n}\tilde{N}'_{du}$ are all equal to \tilde{r}_{dj} . Also, the *i*th row sums of M_d and $n^{-1}N_{dp}\tilde{N}'_{dp}$ are all equal to s_{di} as defined in (2.3) and the *i*th row sums of $p^{-1}N_{du}\tilde{N}'_{du}$ and $n^{-1}p^{-1}N_{du}J_{n,n}\tilde{N}'_{du}$ are both equal to $p^{-1}(p-1)r_{di}$. The desired results follow. \square

From Lemma 2.1, it follows easily that the row and column sums of C_d and \tilde{C}_d are zero for any $d \in \Omega_{t,n,p}$.

Lemma 2.2. The following matrices are all nonnegative definite: C_{d11} , $D_d - n^{-1}N_{dp}N'_{dp}$, $D_d - p^{-1}N_{du}N'_{du}$, $N_{dp}N'_{dp} - p^{-1}N_{dp}J_{p,p}N'_{dp}$, $N_{du}N'_{du} - n^{-1}N_{du}J_{n,n}N'_{du}$, C_{d22} , $\tilde{D}_d - n^{-1}\tilde{N}_{dp}\tilde{N}'_{dp}$, $\tilde{D}_d - p^{-1}\tilde{N}_{du}\tilde{N}'_{du}$, \tilde{N}_{dv} , $\tilde{N}_{dp}\tilde{N}'_{dp} - p^{-1}\tilde{N}_{dp}J_{p,p}\tilde{N}'_{dp}$, $\tilde{N}_{du}\tilde{N}'_{du} - n^{-1}\tilde{N}_{du}J_{n,n}\tilde{N}'_{du}$.

The proof of Lemma 2.2 is straightforward. For example, $N_{du}N'_{du} - n^{-1}N_{du}J_{n,n}N'_{du} = N_{du}(I_n - n^{-1}J_{n,n})N'_{du}$, where the middle matrix is nonnegative definite; and $D_d - n^{-1}N_{dp}N'_{dp}$ is the C-matrix for the direct effects when the residual and unit effects are not present in the model.

LEMMA 2.3. For any positive integers s and t, the minimum of $\sum_{i=1}^{n} n_i^2$ subject to $\sum_{i=1}^{n} n_i = t$, where the n_i 's are nonnegative integers, is obtained when t - s[t/s] of the n_i 's are equal to [t/s] + 1 and the others are equal to [t/s], where [t/s] is the largest integer $\leq t/s$.

LEMMA 2.4. Let d^* be a uniform RMD(t, n, p). Then d^* maximizes tr C_{d11} and tr C_{d22} over $d \in \Omega_{t,n,p}$.

PROOF. We only prove that d^* maximizes tr $C_{d \cdot 22}$. The proof for the maximization of tr $C_{d \cdot 11}$ is similar and in fact is even simpler.

For any $d \in \Omega_{t,n,p}$,

$$\operatorname{tr} C_{d22} = n(p-1) - n^{-1} \sum_{i=1}^{t} \sum_{j=1}^{p-1} l_{dij}^{2} - p^{-1} \sum_{i=1}^{t} \sum_{u=1}^{n} \tilde{n}_{diu}^{2} + n^{-1} p^{-1} \sum_{i=1}^{t} \tilde{r}_{di}^{2}$$

$$= n(p-1) - p^{-1} \sum_{i=1}^{t} \sum_{u=1}^{n} \tilde{n}_{diu}^{2} - n^{-1} \left[\sum_{i=1}^{t} \sum_{j=1}^{p-1} (l_{dij} - (p-1)^{-1} \tilde{r}_{di})^{2} + \{(p-1)^{-1} - p^{-1}\} \sum_{i=1}^{t} \tilde{r}_{di}^{2} \right] \quad \text{since } \tilde{r}_{di} = \sum_{j=1}^{p-1} l_{dij}.$$

For a uniform design d^* , $\sum_{i=1}^t \sum_{j=1}^{p-1} (l_{d^*ij} - (p-1)^{-1} \tilde{r}_{d^*i})^2 = 0$, so it suffices to show that d^* minimizes $\sum_{i=1}^t \sum_{u=1}^n \tilde{n}_{diu}^2$ and $\sum_{i=1}^t \tilde{r}_{di}^2$. This follows immediately from Lemma 2.3 since $\sum_{i=1}^t \sum_{u=1}^n \tilde{n}_{diu} = n(p-1) = \sum_{i=1}^t \tilde{r}_{di}$, \tilde{r}_{d^*i} are all equal, and $|\tilde{n}_{d^*iu} - \tilde{n}_{d^*i'u'}| \le 1$, \forall $(i, u) \ne (i', u')$. \Box

Similarly, the following lemma can be established.

LEMMA 2.5. Let d^* be an RMD(t, n, p) which is uniform on the periods and is uniform on the units in the first p-1 periods, i.e., if the last period of d^* is deleted, then the resulting design is uniform on the units. Then d^* maximizes tr C_{d11} and tr C_{d22} over $d \in \Omega_{l,n,p}$.

PROOF. The proof is similar to Lemma 2.4 except that in the present case \tilde{n}_{d^*iu} are all equal, and $|n_{d^*iu} - n_{d^*i'u'}| \le 1$, $\forall (i, u) \ne (i', u')$. \Box

3. Optimality of strongly balanced repeated measurements designs.

THEOREM 3.1. Let d^* be a strongly balanced uniform design in $\Omega_{t,n,p}$. Then d^* is universally optimal for the estimation of direct as well as residual effects over $\Omega_{t,n,p}$.

PROOF. By Proposition 1 of Kiefer (1975), it suffices to show that both C_d and \tilde{C}_d are completely symmetric and d^* maximizes tr C_d and tr \tilde{C}_d over $d \in \Omega_{t,n,p}$.

The existence of a uniform design in $\Omega_{t,n,p}$ implies that $t \mid n$ and $t \mid p$. Let $n = \lambda_1 t$ and $p = \lambda_2 t$. Then it can easily be checked that $C_{d+12} = M_{d+1} - n^{-1} N_{d+p} \tilde{N}'_{d+p} - p^{-1} N_{d+u} \tilde{N}'_{d+u} + n^{-1} p^{-1} N_{d+u} J_{n,n} \tilde{N}'_{d+u} = t^{-1} \lambda_1 (p-1) J_{t,t} - n^{-1} \lambda_1^2 (p-1) J_{t,t} - p^{-1} \lambda_2 (r-\lambda_1) J_{t,t} + n^{-1} p^{-1} r (r-\lambda_1) J_{t,t} = 0$, where $r \equiv t^{-1} n p = n \lambda_2 = p \lambda_1$. Therefore $C_{d+1} = C_{d+11} = t^{-1} n p (I_t - t^{-1} J_{t,t})$ and $\tilde{C}_{d+1} = C_{d+22} = t^{-1} n (p-1) (I_t - t^{-1} J_{t,t})$ which are completely symmetric.

For any $d \in \Omega_{t,n,p}$, $C_d = C_{d11} - C_{d12}C_{d22}C_{d21} \le C_{d11}$ and $\tilde{C}_d = C_{d22} - C_{d21}C_{d11}C_{d12} \le C_{d22}$, where $A \le B$ means that B - A is nonnegative definite. Hence

tr
$$C_d \le$$
 tr $C_{d \cdot 11} \le$ tr $C_{d \cdot 11}$ (Lemma 2.4)
= tr $C_{d \cdot}$

Similarly, tr $\tilde{C}_d \leq \operatorname{tr} \tilde{C}_{d^*}$. \square

Thus, a strongly balanced uniform RMD is optimal in a very strong sense. We now show a simple construction for this kind of design. If there exists a strongly balanced uniform RMD(t, n, p) then $t^2 \mid n$ and $p = \lambda_2 t$ with $\lambda_2 \ge 2$. In case λ_2 is even, we have the following:

THEOREM 3.2. If $t^2 \mid n$ and p/t is an even integer, then there exists a strongly balanced uniform RMD(t, n, p).

PROOF. Suppose $t^2 \mid n$ and $p = \lambda_2 t$ where λ_2 is an even integer. Denote the t treatments by the nonnegative residues modulo t. Assign the treatments to the first two periods so that each treatment receives the same number of units in each period, and each ordered pair of treatments appears the same number of times. This is possible since $t^2 \mid n$. Let the rows correspond to the units and the columns correspond to the periods. Then an $n \times 2$ array is constructed.

To each symbol in this $n \times 2$ array add $i \pmod{t}$ ($i = 1, 2, \dots, t - 1$), and put the two columns obtained in this way in the (2i + 1)st and (2i + 2)nd periods. Then we get an $n \times 2t$ plan which is obviously a strongly balanced uniform RMD(t, n, 2t). A strongly balanced uniform RMD $(t, n, \lambda_2 t)$ with λ_2 even is obtained by piecing $\lambda_2/2$ copies of this design together.

For example, the following is a strongly balanced uniform RMD(3, 9, 6);

A similar method to construct a strongly balanced uniform RMD $(t, t^2, 2t)$ was reported in Berenblut (1964).

Another kind of optimal strongly balanced RMD is provided by the following:

THEOREM 3.3. Let $n = \lambda_1 t$, $p = \lambda_2 t + 1$, λ_1 , $\lambda_2 \ge 1$, and let d^* be a strongly balanced RMD(t, n, p) which is uniform on the periods and is uniform on the units in the first $p - 1 (= \lambda_2 t)$ periods. Then d^* is universally optimal for the estimation of direct as well as residual effects over $\Omega_{t,n,p}$.

PROOF. It can be easily checked that $C_{d^*12} = M_{d^*} - n^{-1}N_{d^*p}\tilde{N}'_{d^*p} - p^{-1}N_{d^*u}\tilde{N}'_{d^*u} + n^{-1}p^{-1}N_{d^*u}J_{n,n}\tilde{N}'_{d^*u} = \lambda_1\lambda_2J_{t,t} - n^{-1}(p-1)\lambda_1^2J_{t,t} - p^{-1}\lambda_2(\lambda_1 + n\lambda_2)J_{t,t} + n^{-1}p^{-1}r(r-\lambda_1)J_{t,t} \equiv 0$, where $r = t^{-1}np = p\lambda_1 = \lambda_2n + \lambda_1$. Hence $C_{d^*} = C_{d^*11}$ and $\tilde{C}_{d^*} = C_{d^*22}$ which are completely symmetric. Theorem 3.3 follows from Lemma 2.5 and the same argument as in the proof of Theorem 3.1. \square

A simple example of the design d^* in Theorem 3.3 is the one obtained by repeating the observations in the last period of a balanced uniform RMD $(t, \lambda_1 t, t)$. The resulting design is an RMD $(t, \lambda_1 t, t+1)$ which is clearly uniform on the periods and is uniform on the units in the first p-1(=t) periods. In the original design, each treatment is preceded by any other treatment λ_1 times. By repeating the observations in the last period we make each treatment also precede itself λ_1 times since $n=\lambda_1 t$. So the augmented design is strongly balanced. In summary, we have

COROLLARY 3.3.1. Let d^* be obtained by repeating the observations in the last period of a balanced uniform RMD(t, $\lambda_1 t$, t). Then d^* is universally optimal for the direct as well as residual effects over $\Omega_{t,\lambda_1 t}$, λ_{t+1} .

Therefore, from each of the Hedayat and Afsarinejad's balanced uniform designs, we can construct an optimum design satisfying the conditions in Theorem 3.3. The conditions for the existence of the designs in Theorem 3.3 are less restrictive than those for strongly balanced uniform designs. It is not necessary that $t^2 \mid n$ and $p \ge 2t$. So it is possible to construct optimal designs with fewer units and periods.

Designs satisfying the conditions in Theorem 3.3 can also be constructed from strongly balanced uniform ones. Let d^* be a strongly balanced uniform RMD(t, n, p). Then since $t^2 \mid n$, an extra period can be added so that the resulting design is still strongly balanced. This design certainly satisfies the conditions in Theorem 3.3 and hence is universally optimal over $\Omega_{t,n,p+1}$.

If we restrict the competing designs to a smaller class, then some stronger optimality results can be proved. Let $\Omega_{\ell,n,p}^* = \{d \in \Omega_{\ell,n,p} : r_{d_1} = r_{d_2} = \cdots = r_{d_\ell}\}$, i.e., $\Omega_{\ell,n,p}^*$ is the collection of all equally replicated designs in $\Omega_{\ell,n,p}$. Then we have

THEOREM 3.4. Let d^* be a strongly balanced uniform RMD(t, n, p). Then d^* minimizes the variance of the best linear unbiased estimator of any contrast among the direct effects $\{\tau_i\}_{i,n,p}^t$ over $\Omega_{t,n,p}^*$.

PROOF. By a theorem of Ehrenfeld (1955), it suffices to show that $C_{d^*} \ge C_d$ for any $d \in \Omega^*_{l,n,p}$. Since both C_d and C_{d^*} have zero row sums, it is enough to show that $x'C_{d^*}x \ge x'C_dx$ for any $t \times 1$ vector x such that $x'I_t = 0$ where I_t is the $t \times 1$ vector of ones. By the computation in the proof of Theorem 3.1, $C_{d^*} = C_{d^*11} = rI_t - aJ_{l,t}$ for some constant a, where $r = t^{-1}np$. On the other hand, for any $d \in \Omega^*_{l,n,p}$, $C_d = C_{d11} - C_{d12}C_{d22}^{-}C_{d21} \le C_{d11} = rI_t - n^{-1}N_{dp}N'_{dp} - (p^{-1}N_{du}N'_{du} - n^{-1}p^{-1}N_{du}J_{n,n}N'_{du}) \le rI_t$, since by Lemma 2.2, both $n^{-1}N_{dp}N'_{dp}$ and $p^{-1}N_{du}N'_{du} - n^{-1}p^{-1}N_{du}J_{n,n}N'_{du}$ are nonnegative definite. Thus

$$x'C_dx \le x'(rI_t)x = x'(rI_t - aJ_{t,t})x \qquad \text{(since } x'J_{t,t} = 0\text{)}$$
$$= x'C_{d} \cdot x. \qquad \Box$$

Similarly, we have

THEOREM 3.5. Let d^* be an RMD(t, n, p) satisfying the conditions in Theorem 3.3. Then d^* minimizes the variance of the best linear unbiased estimator of any contrast among the residual effects $\{\rho_i\}_1^t$ over $\Omega_{t,n,p}^{**}$, where $\Omega_{t,n,p}^{**} = \{d \in \Omega_{t,n,p} : \tilde{r}_{d1} = \cdots = \tilde{r}_{dt}\}$.

4. Optimality of balanced repeated measurements designs. In this section we will discuss the optimality of balanced uniform RMD over the class of designs d in $\Omega_{t,n,p}$ for which $m_{dii} = 0$ for $1 \le i \le t$ (i.e., no treatment is allowed to be preceded by itself in d). The collection of such designs is denoted by $\wedge_{t,n,p}$. In order to prove optimality we sometimes impose uniformity on units or periods on the class of competing designs. A related paper by Hedayat and Afsarinejad (1978) gave the same optimality result under the more restrictive assumption that the competing designs are uniform on both units and periods.

More precisely, recall that the definition of a uniform RMD(t, n, p) implies $n = \lambda_1 t$ and $p = \lambda_2 t$ for some λ_1, λ_2 . Therefore, for the rest of the section, we will only consider RMD $(t, \lambda_1 t, \lambda_2 t)$. For a balanced uniform RMD $(t, \lambda_1 t, \lambda_2 t)$ d^* ,

(4.1)
$$n_{d^*iu} = \lambda_2, \quad l_{d^*ik} = \lambda_1, \quad m_{d^*ii} = 0, \quad m_{d^*ij} = \frac{\lambda_1(p-1)}{t-1} = \lambda,$$

for all i, u, k and $i \neq j$, which, in turn, give

$$C_{d^*11} = \lambda_1 p(I_t - t^{-1}J_{t,t}), \qquad C_{d^*12} = C'_{d^*21} = -\lambda(I_t - t^{-1}J_{t,t}),$$

$$(4.2)$$

$$C_{d^*22} = \lambda_1(p - 1 - p^{-1})(I_t - t^{-1}J_{t,t}).$$

Therefore, C_{d^+} and \tilde{C}_{d^+} are both completely symmetric. To prove universal optimality, it remains to show that d^* maximizes $\operatorname{tr}(C_{d11}-C_{d12}C_{d22}C_{d21})$ and $\operatorname{tr}(C_{d22}-C_{d21}C_{d11}C_{d12})$ over the class of competing designs. However, unlike the strongly balanced RMD, the $C_{d^{+12}}$ matrix in (4.2) is not zero. It is thus necessary to compute the very intractable C_{d11}^- and C_{d22}^- for an arbitrary d, which is the major technical difficulty for the optimality proof. In the case of C_{d11}^- , the following technique circumvents this problem. Since $N_{dp}N'_{dp}$ and $N_{du}N'_{du}-n^{-1}N_{du}J_{n,n}N'_{du}$ are nonnegative definite from Lemma 2.2, $C_{d11} \leq D_d$ for any $d \in \Omega_{t,n,p}$. From Theorem 5(i) of Wu (1980), there exists a g-inverse C_{d11}^- of C_{d11}^- such that $C_{d11}^- \geq D_d^{-1}$ for any d. Furthermore, D_d^{-1} is a g-inverse of $C_{d^{+11}}$ for any balanced uniform RMD d^* . Therefore, to prove that d^* maximizes $\operatorname{tr}(C_{d22}-C_{d21}C_{d11}^-C_{d12})$ over $\wedge_{t,\lambda_1,t,\lambda_2}$, it suffices to prove that d^* maximizes the more tractable $\operatorname{tr}(C_{d22}-C_{d21}D_d^{-1}C_{d12})$ over $\wedge_{t,\lambda_1,t,\lambda_2}$. With this basic idea in mind, we will defer the technical proofs to the next section and only summarize the optimality results here.

THEOREM 4.1. Let d^* be a balanced uniform design in $\wedge_{t,\lambda_1 t,\lambda_2 t}$, $t \ge 3$. Then d^* is universally optimal for the estimation of residual effects over the class of designs d in $\wedge_{t,\lambda_1 t,\lambda_2 t}$ with $\tilde{r}_{di} = \lambda_1(p-1)$ for all i, i.e., d is equally-replicated in the first p-1 periods.

The reason for imposing the equal \tilde{r}_{di} requirement on the class of competing designs is purely technical. For $\lambda_2 = 1$, such a restriction can be removed.

THEOREM 4.2. Let d^* be a balanced uniform design in $\wedge_{t,\lambda_1 t,t}$, $t \ge 3$. Then d^* is universally optimal for the estimation of residual effects over $\wedge_{t,\lambda_1 t,t}$.

The proof of optimality for the estimation of direct effects is more difficult. Unlike the residual effect case, $C_{d+22}^{-1} - \tilde{D}_{d}^{-1} = \lambda^{-1}(p-1-p^{-1})I_t - \lambda^{-1}(p-1)^{-1}I_t$ is not zero and the minimization of $\operatorname{tr}(C_{d12}C_{d22}^{-1}C_{d21})$ over $\bigwedge_{t,\lambda_1 t,\lambda_2 t}$ can not be replaced by the minimization of the more tractable $\operatorname{tr}(C_{d12}\tilde{D}_{d}^{-1}C_{d21})$ over $\bigwedge_{t,\lambda_1 t,\lambda_2 t}$. To make the computation possible, we impose a uniformity condition on each unit and the last period.

THEOREM 4.3. Let d^* be a balanced uniform design in $\wedge_{t,\lambda_1t,\lambda_2t}$. Then d^* is universally optimal for the estimation of direct effects over the class of designs in $\wedge_{t,\lambda_1t,\lambda_2t}$ which are uniform on each unit and the last period.

When the period effect is not present in model (1.1), the optimality results are even stronger.

The C_{dii} matrices in (2.6) become

(4.3)

$$C_{d11} = D_d - p^{-1} N_{du} N'_{du}, \qquad C_{d12} = C'_{d21} = M_d - p^{-1} N_{du} \tilde{N}'_{du},$$

 $C_{d\,22} = \tilde{D}_d - p^{-1} \tilde{N}_{du} \tilde{N}'_{du},$

Let d^* be a RMD $(t, \lambda_1 t, \lambda_2 t)$ which is

- (i) uniform on each unit
- (ii) uniform in the last period
- (4.4) (iii) $m_{d \cdot ij} = \frac{\lambda_1(p-1)}{t-1} = \lambda$ for $i \neq j$ and $m_{d \cdot ii} = 0$ (i.e., in the order of application, each treatment is preceded by each other treatment the same number of times.)

From (2.2) and (2.3), one can easily verify that (i) and (iii) imply (ii) and the uniformity in the first period.

THEOREM 4.4. Assume there is no period effect in model (1.1). The design d^* defined in (4.4) is universally optimal for the estimation of residual effects over $\bigwedge_{t,\lambda_1t,\lambda_2t}$. The same design is also universally optimal for the estimation of direct effects over the class of designs in $\bigwedge_{t,\lambda_1t,\lambda_2t}$ which are uniform on each unit and the last period.

5. Proofs. The optimality proofs require some preliminary lemmas on constrained minimization. Unless otherwise stated, all the variables below are assumed to be real.

LEMMA 5.1. The minimum of $\sum_{i=1}^{t} x_i^2$, subject to $\sum_{i=1}^{t} x_i = d$, is achieved by taking $x_i = \frac{d}{t}$ for all i and is equal to $\frac{d^2}{t}$.

LEMMA 5.2. The minimum of $\sum_{i=1}^{t} \frac{x_i^2}{r_i}$, subject to $\sum_{i=1}^{t} x_i = d$, $r_i \ge 0$ and $\sum_{i=1}^{t} r_i = e > 0$, is achieved by taking $x_i = \frac{d}{e} r_i$ for all i and is equal to $\frac{d^2}{e}$.

LEMMA 5.3. Suppose two sequences $(x_i)_{i=1}^n$ and $(y_i)_{i=1}^n$ are similarly ordered in the sense that $(x_i - x_j)(y_i - y_j) \ge 0$ for all i, j, then

$$\sum_{i=1}^{n} x_i y_i \ge \frac{1}{n} \left(\sum_{i=1}^{n} x_i \right) \left(\sum_{i=1}^{n} y_i \right).$$

The first two lemmas can be easily proved by the method of Lagrange multiplier. Lemma 5.3 can be found in Hardy, Littlewood and Polya (1967), page 43.

LEMMA 5.4. Suppose $(x_i)_{i=1}^t$, λ_2 and t are all nonnegative integers. Then the minimum of $\sum_{t=1}^{t-1} x_t^2 + x_t(x_t - 1)$, subject to $x_t \ge 1$ and $\sum_{t=1}^{t} x_t = \lambda_2 t$, is achieved by taking $x_t = \lambda_2$ and is equal to $\lambda_2^2 t - \lambda_2$.

PROOF. We want to show that

(5.1)
$$\sum_{i=1}^{t} x_i^2 - x_i \ge \lambda_2^2 t - \lambda_2$$

for $\sum_{i=1}^{t} x_i = \lambda_2 t$, $x_t \ge 1$ and x_i are nonnegative integers. (5.1) is equivalent to

(5.2)
$$\sum_{i=1}^{t} x_i^2 - \lambda_2^2 t \ge x_t - \lambda_2.$$

From Lemma 5.1, the left-hand side of (5.2) is always nonnegative. Therefore, (5.2) holds if $x_t \le \lambda_2$. On the other hand, if $x_t = \lambda_2 + m$, m is a positive integer, then

$$\sum_{i=1}^{t} x_i^2 = \sum_{i=1}^{t-1} x_i^2 + x_i^2 \ge (t-1) \left(\frac{\lambda_2 t - \lambda_2 - m}{t-1} \right)^2 + (\lambda_2 + m)^2 = \lambda_2^2 t + m^2 \frac{t}{t-1}.$$

This implies that $\sum_{i=1}^{t} x_i^2 - \lambda_2^2 t \ge m^2 \frac{t}{t-1} > m = x_t - \lambda_2$, proving (5.2). \square

LEMMA 5.5. The matrix $A = [a_{ij}]$ with $a_{ii} = 1$ for $1 \le i \le n$, $a_{ij} = b$ for |i-j| = 1 and $a_{ij} = 0$ otherwise has eigenvectors $v_i = \left(\sin\frac{i\pi}{n+1}, \sin\frac{2i\pi}{n+1}, \cdots, \sin\frac{ni\pi}{n+1}\right)$ with corresponding eigenvalues $1 + 2b \cos\frac{i\pi}{n+1}$ for $1 \le i \le n$. In particular, A is nonsingular when $|b| < \left(2\cos\frac{\pi}{n+1}\right)^{-1}$

This can be verified by routine matrix multiplication and trigonometric identities. It is stated in Noble (1969), page 307.

LEMMA 5.6. For $0 \le c \le [2t(p-1)\lambda_1^2]^{-1}$, the minimum of $F(\mathbf{x}) = \sum_{i=1}^t \sum_{k=1}^{p-1} x_{ik}^2 + c(\sum_{i=1}^t \sum_{k=2}^p x_{ik} x_{i,k-1})^2$, subject to $\sum_{i=1}^t x_{ik} = \lambda_1 t$ for $1 \le k \le p$, is achieved by taking $x_{ik} = \lambda_1$ for all i, k.

PROOF. It is obvious that the minimum must be attained at some bounded x_{ik} values. Therefore, the minimum must also be a local minimum. Rewrite $F(\mathbf{x})$ as

$$\sum_{i=1}^{t-1} \sum_{k=1}^{p-1} x_{ik}^2 + \sum_{k=1}^{p-1} (\lambda_1 t - \sum_{i=1}^{t-1} x_{ik})^2 + c \{\sum_{i=1}^{t-1} \sum_{k=2}^{p} x_{ik} x_{i,k-1} + \sum_{k=2}^{p} (\lambda_1 t - \sum_{i=1}^{t-1} x_{ik})(\lambda_1 t - \sum_{i=1}^{t-1} x_{i,k-1})\}^2.$$

A necessary condition for local minimum is

$$\frac{\partial}{\partial x_{ik}} F(\mathbf{x}) = 0, \quad \text{for} \quad 1 \le i \le t - 1, \ 1 \le k \le p,$$

which gives

$$x_{i1} - x_{t1} + cA(\mathbf{x})(x_{i2} - x_{t2}) = 0,$$

$$(5.3) \quad x_{ik} - x_{tk} + cA(\mathbf{x})(x_{i,k+1} - x_{t,k+1} + x_{i,k-1} - x_{t,k-1}) = 0 \quad \text{for } 2 \le k \le p - 1$$

$$cA(\mathbf{x})(x_{i,p-1} - x_{t,p-1}) = 0,$$

where $A(\mathbf{x}) = \sum_{i=1}^{t} \sum_{k=2}^{p} x_{ik} x_{i,k-1}$.

- (i) If $A(\mathbf{x}) = 0$ at the local minimum, then (5.3) implies $x_{ik} = x_{tk}$ for $1 \le i \le t 1$, $1 \le k \le p 1$, which is equivalent to $x_{ik} = \lambda_1$ for $1 \le i \le t$, $1 \le k \le p 1$. But this, in turn, implies that $A(\mathbf{x}) > 0$. Therefore, at the local minimum $A(x) \ne 0$.
- (ii) Since $\sum_{i=1}^{t} \sum_{k=1}^{p-1} x_{ik}^2$ is minimized by $x_{ik} = \lambda_1$ for $1 \le i \le t$, $1 \le k \le p-1$ and the corresponding $A(\mathbf{x})$ value is $t(p-1)\lambda_1^2$, any $\mathbf{x} = (x_{ik})$ with $|A(\mathbf{x})| > t(p-1)\lambda_1^2$ can not give the global minimum of $F(\mathbf{x})$.
- (iii) For any \mathbf{x} with $0 < |A(\mathbf{x})| \le t(p-1)\lambda_i^2$, we want to show that the only solution of (5.3) is $x_{ik} x_{tk} = 0$ for all $1 \le i \le t 1$, $1 \le k \le p$. Since (5.3) is equivalent to $B\mathbf{y}_i = 0$ for $1 \le i \le t 1$, where $\mathbf{y}_i = (x_{i1} x_{t1}, \dots, x_{ip} x_{tp})$ and $B = [b_{ik}]$ with $b_{ii} = 1$ for i < p, $b_{pp} = 0$, $b_{ik} = cA(\mathbf{x})$ for all |i k| = 1 and $b_{ik} = 0$ otherwise, it remains to prove the nonsingularity of B. From $cA(\mathbf{x}) > 0$ and the special form of B, it can be seen that B is nonsingular if and only if its upper left $(p-2) \times (p-2)$ submatrix, called B_{11} , is nonsingular. (This can be done by showing that the p column or row vectors of B are linearly independent iff the p-2 column or row vectors of B_{11} are linearly independent.) In particular, B is always nonsingular for $P \le 3$, $cA(\mathbf{x}) > 0$. The matrix B_{11} is a special form of the matrix A in Lemma 5.5 with $b = cA(\mathbf{x})$

and n = p - 2. From Lemma 5.5, B_{11} is nonsingular since $cA(\mathbf{x}) \le (2t(p-1)\lambda_1^2)^{-1}t(p-1)\lambda_1^2 \le \frac{1}{2}$.

(iv) From (iii), a necessary condition for any \mathbf{x} with $0 < A(\mathbf{x}) \le t(p-1)\lambda_1^2$ is that $x_{ik} = z_k$ for $1 \le i \le t$, $1 \le k \le p$. From the constraint condition $\sum_{i=1}^t x_{ik} = \lambda_1 t$, we have $x_{ik} = z_k = \lambda_1$. Together with (ii), we have shown that the global minimum of $F(\mathbf{x})$ is achieved by taking $x_{ik} = \lambda_1$ for all i, k. \square

LEMMA 5.7. For $0 \le c \le [tp(p-1)\lambda_1^2]^{-1}$, the minimum of $F(x) = \sum_{i=1}^{t} \sum_{k=1}^{p-1} x_{ik}^2 - p^{-1} \sum_{i=1}^{t} (\sum_{k=1}^{p-1} x_{ik})^2 + c(\sum_{i=1}^{t} \sum_{k=2}^{p} x_{ik} x_{i,k-1})^2$, subject to $\sum_{i=1}^{t} x_{ik} = \lambda_1 t$ for $1 \le k \le p$, is achieved by taking $x_{ik} = \lambda_1$ for all i, k.

PROOF. Since the argument is very similar to that of Lemma 5.6, the proof will be sketched briefly. By rewriting $x_{tk} = \lambda_1 t - \sum_{i=1}^{t-1} x_{ik}$ in $F(\mathbf{x})$, a necessary condition for the local minimum of $F(\mathbf{x})$ is,

(5.4)
$$x_{i1} - x_{t1} - p^{-1} \sum_{k=1}^{p-1} (x_{ik} - x_{tk}) + cA(\mathbf{x})(x_{i2} - x_{t2}) = 0,$$

$$x_{ik} - x_{tk} - p^{-1} \sum_{k=1}^{p-1} (x_{ik} - x_{tk})$$

$$+ cA(\mathbf{x})(x_{i,k+1} - x_{t,k+1} + x_{i,k-1} - x_{t,k-1}) = 0,$$

$$cA(\mathbf{x})(x_{i,p-1} - x_{t,p-1}) = 0,$$

$$for 2 \le k \le p-1,$$

where $A(\mathbf{x}) = \sum_{i=1}^{t} \sum_{k=2}^{p} x_{ik} x_{i, k-1}$.

A very similar argument to (i), (ii) of the proof of Lemma 5.6 shows that $|A(\mathbf{x})|$ can not be equal to zero or greater than $t(p-1)\lambda_1^2$. For any \mathbf{x} with $0 < |A(\mathbf{x})| \le t(p-1)\lambda_1^2$, it remains to show that the only solution of (5.4) is $x_{ik} - x_{tk} = 0$ for all $1 \le i \le t-1$, $1 \le k \le p$. The linear system (5.4) is defined as $\tilde{B}\mathbf{y}_i = 0$ for $1 \le i \le t-1$, $\mathbf{y}_i = (x_{i1} - x_{t1}, \dots, x_{ip} - x_{tp})$, $\tilde{B} = B - p^{-1}J_p$, where B is given in the proof of Lemma 5.6, J_p is the $p \times p$ matrix with all entries 1. Since $cA(\mathbf{x}) > 0$, \tilde{B} is nonsingular iff its upper left $(p-2) \times (p-2)$ submatrix \tilde{B}_{11} is nonsingular. Note that $\tilde{B}_{11} = B_{11} - p^{-1}J_{p-2}$, B_{11} is defined in the proof of Lemma 5.6 and J_{p-2} is the $(p-2) \times (p-2)$ matrix with all entries 1. From Lemma 5.5, the smallest eigenvalue of B_{11} is $1 - 2c |A(\mathbf{x})| \cos \frac{\pi}{p-1}$ and the largest eigenvalue of $p^{-1}J_{p-2}$ is $\frac{p-2}{p}$. Therefore, \tilde{B}_{11}

is nonsingular since $p^{-1} - |cA(\mathbf{x})| \cos \frac{\pi}{p-1} > 0$, which is satisfied since $|A(\mathbf{x})| \le t(p-1)\lambda_1^2$ and $c \le (pt(p-1)\lambda_1^2)^{-1}$. \square

PROOF OF THEOREM 4.1. \tilde{C}_{d^*} is clearly completely symmetric. It remains to show that tr C_{d22} – tr $C_{d21}C_{d11}^-C_{d12}$ is maximized by d^* over the specified class of designs. Since $C_{d11}^- = D_d^{-1}$ for $d = d^*$ and in general there exists a generalized inverse $C_{d11}^- \ge D_d^{-1}$ (see the paragraph before Theorem 4.1), we proceed to show that tr C_{d22} – tr $C_{d21}D_d^{-1}C_{d12}$ is maximized by d^* . First, note that

tr
$$C_{d22} = \sum_{i=1}^{t} \tilde{r}_{di} - n^{-1} \sum_{i=1}^{t} \sum_{k=1}^{p-1} l_{dik}^2 - p^{-1} \sum_{i=1}^{t} \sum_{u=1}^{n} \tilde{n}_{diu}^2 + n^{-1} p^{-1} \sum_{i=1}^{t} \tilde{r}_{di}^2$$

and

tr
$$C_{d21}D_d^{-1}C_{d12} = \sum_{i=1}^t r_{di}^{-1} \sum_{j=1}^t (m_{dij} - n^{-1} \sum_{k=2}^p l_{dik} l_{dj,k-1} - p^{-1} \sum_{u=1}^n n_{diu} \tilde{n}_{dju} + n^{-1} p^{-1} r_{di} \tilde{r}_{dj})^2$$
.

Since \tilde{r}_{di} is constant over the class of competing designs and $\sum_{i=1}^{t} \sum_{u=1}^{n} \tilde{n}_{diu}^{2}$ is minimized by d^* according to Lemma 2.3, it suffices to show that d^* minimizes

(5.5)
$$n^{-1} \sum_{i=1}^{t} \sum_{k=1}^{p-1} l_{dik}^2 + \sum_{i=1}^{t} r_{di}^{-1} \sum_{j=1}^{t} (m_{dij} - q_{dij})^2,$$

where $q_{dij} = n^{-1} \sum_{k=2}^{p} l_{dik} l_{dj,k-1} + p^{-1} \sum_{u=1}^{n} n_{diu} \tilde{n}_{dju} - n^{-1} p^{-1} r_{di} \tilde{r}_{dj}$, subject to the constraints $\sum_{i=1}^{l} l_{dik} = n$, $m_{dii} = 0$, $\sum_{i=1}^{l} r_{di} = np$ and $\sum_{j=1}^{l} (m_{dij} - q_{dij}) = \sum_{i=1}^{l} (m_{dij} - q_{dij}) = 0$ (corresponding

to the fact that the row and column sums of $C_{d\,12}$ are zero). This minimization problem will be solved in several steps.

- (i) $\sum_{j=1}^{t} (m_{dij} q_{dij})^2 = \sum_{j,j\neq i} (m_{dij} q_{dij})^2 + q_{dii}^2$ and the constraint is $\sum_{j,j\neq i} (m_{dij} q_{dij}) = q_{dii}$, since $m_{dii} = 0$. From Lemma 5.1, this is minimized by taking $m_{dij} q_{dij} = \frac{1}{t-1} q_{dii}$ for $j \neq i$ and the minimum is $\frac{t}{t-1} q_{dii}^2$. It can be checked that $m_{dij} q_{dij} = \frac{1}{t-1} q_{dii}$ holds for $d = d^*$.
- (ii) From Lemma 5.2, the minimum of $\sum_{i=1}^{t} r_{di}^{-1} q_{dii}^2$, subject to $\sum_{i=1}^{t} r_{di} = np$, is achieved by taking $r_{di} = \lambda_2 n$ and $q_{dii} = t^{-1} \sum_{i=1}^{t} q_{dii}$ and is equal to $(t\lambda_2 n)^{-1} (\sum_{i=1}^{t} q_{dii})^2$. Again, for d^* , it can be checked that $r_{d^*i} = \lambda_2 n$ and $q_{d^*ii} = t^{-1} \sum_{i=1}^{t} q_{d^*ii}$ do hold.
- (iii) In $\sum_{i=1}^{l} q_{dii} = n^{-1} \sum_{i=1}^{l} \sum_{p=2}^{n} l_{dik} l_{di,k-1} + p^{-1} \sum_{i=1}^{l} \sum_{u=1}^{n} n_{diu} \tilde{n}_{diu} n^{-1} p^{-1} \sum_{i=1}^{l} r_{di} \tilde{r}_{di} = n^{-1} \sum_{i=1}^{l} \sum_{p=2}^{n} l_{dik} l_{di,k-1} + p^{-1} \sum_{i=1}^{l} \sum_{u=1}^{n} (n_{diu} n^{-1} r_{di}).$ ($\tilde{n}_{diu} n^{-1} \tilde{r}_{di}$), $\sum_{u=1}^{n} (n_{diu} n^{-1} r_{di})(\tilde{n}_{diu} n^{-1} r_{di})$) and equals zero for d^* (which gives $n_{d^*iu} = \lambda_2 = n^{-1} r_{d^*i}$). This follows from Lemma 5.3 if one can show that $(n_{diu})_{u=1}^{n}$ and $(\tilde{n}_{diu})_{u=1}^{n}$ are similarly ordered for all i. For any u and v, if $n_{diu} > n_{div}$, then $n_{diu} \ge n_{div} + 1$ which implies $\tilde{n}_{diu} \ge \tilde{n}_{div}$ and $(n_{diu} n_{div})(\tilde{n}_{diu} \tilde{n}_{div}) \ge 0$ holds. Other cases are proved similarly. Therefore $(\sum_{i=1}^{l} q_{dii})^2 \ge n^{-2} (\sum_{i=1}^{l} \sum_{k=2}^{p} l_{dik} l_{di,k-1})^2$ and equality holds for d^* .
 - (iv) From (i) (ii) (iii), it remains to show that

$$n^{-1} \sum_{i=1}^{t} \sum_{k=1}^{p-1} l_{dik}^2 + \frac{t}{t-1} \frac{1}{nt \lambda_2} \frac{1}{n^2} \left(\sum_{i=1}^{t} \sum_{k=2}^{p} l_{dik} l_{di,k-1} \right)^2,$$

subject to $\sum_{i=1}^{t} l_{dik} = n$ for all i, is minimized by d^* (which gives $l_{d^*ik} = \lambda_1$ for all i, k). This follows easily from Lemma 5.6, since $[(t-1)\lambda_2 n^2]^{-1} \le [2t(p-1)\lambda_1^2]^{-1}$ holds for $t \ge 3$. \square

PROOF OF THEOREM 4.2. The proof will be given by simply modifying that of Theorem 4.1. All the notations are the same. Only the steps involving different arguments are given below.

The complete symmetry of \tilde{C}_{d^*} is obvious. We want to show that d^* also maximizes $\operatorname{tr}(C_{d22} - C_{d21}D_d^{-1}C_{d12})$ over $\wedge_{t,\lambda_1 t,t}$. Since \tilde{r}_{di} is not assumed constant, the minimization problem (5.5) is replaced, in this case, by

$$(5.6) n^{-1} \sum_{i=1}^{t} \sum_{k=1}^{p-1} l_{dik}^2 - n^{-1} p^{-1} \sum_{i=1}^{t} \left(\sum_{k=1}^{p-1} l_{dik} \right)^2 + \sum_{i=1}^{t} r_{di}^{-1} \sum_{j=1}^{t} \left(m_{dij} - q_{dij} \right)^2,$$

subject to the same set of constraints. Here, $\tilde{r}_{di} = \sum_{k=1}^{p-1} l_{dik}$ is used. From (i) (ii) (iii) of the proof of Theorem 4.1, the third term of (5.6) is greater than or equal to $[(t-1)\lambda_2 n^3]^{-1}$ ($\sum_{i=1}^{t} \sum_{k=2}^{p} l_{dik} l_{di,k-1}$)² and equality holds for d^* . The proof will be completed by showing that

$$\sum_{i=1}^{t} \sum_{k=1}^{p-1} l_{dik}^2 - p^{-1} \sum_{i=1}^{t} \left(\sum_{k=1}^{p-1} l_{dik} \right)^2 + \left[(t-1)\lambda_2 n^2 \right]^{-1} \left(\sum_{i=1}^{t} \sum_{k=2}^{p} l_{dik} l_{di,k-1} \right)^2$$

is minimized by d^* which gives $l_{d^*ik} = \lambda_1$ for all i, k. However, this follows from Lemma 5.7, since $[(t-1)\lambda_2 n^2]^{-1} \le [tp(p-1)\lambda_1^2]^{-1}$ for $p = t \iff \lambda_2 = 1$). \square

PROOF OF THEOREM 4.3. The complete symmetry of C_d follows easily from computation (5.7). Since the class of competing designs are uniform on each unit and in the last period, one can easily verify that

$$C_{d11} = \lambda_1 p (I - t^{-1} J_{t,t}), \qquad C_{d12} = C'_{21} = M_d - t^{-1} \lambda_1 (p - 1) J_{t,t},$$

$$(5.7)$$

$$C_{d22} = \lambda_1 (p - 1 - p^{-1}) [I_t - t^{-1} J_{t,t}].$$

Since tr C_{d11} is a constant and $C_{d22}^- = \lambda_1^{-1}(p-1-p^{-1})^{-1}I_i$, $\operatorname{tr}(C_{d11} - C_{d12}C_{d22}^-C_{d21})$ is maximized iff tr $C_{d12}C_{d21}$ is minimized. However, tr $C_{d12}C_{d21} = \sum_{i,j=1}^{t} (m_{dij} - t^{-1}\lambda_1(p-1))^2$ is minimized, over the class of designs with $m_{dii} = 0$, by d^* (which gives $m_{d^*ij} = t^{-1}\lambda_1(p-1)$ for all $i \neq j$). \square

PROOF OF THEOREM 4.4. The idea of proof is essentially the same as that of Theorems 4.1 and 4.3. The only difference is for the residual effect case, where part (iii) of the proof of Theorem 4.1 is replaced by the minimization of $\sum_{u=1}^{n} \sum_{i=1}^{l} n_{diu} \tilde{n}_{diu}$, subject to $\sum_{i=1}^{l} n_{diu} = p$, which is minimized by $n_{d^*iu} = \lambda_2$ according to Lemma 5.4. Note that $n_{diu} = \tilde{n}_{diu}$ for all i not equal to some i_0 and $n_{di,u} = \tilde{n}_{di,u} + 1$. \square

Acknowledgements. We would like to thank the associate editor, the referee and Jack Kiefer for useful suggestions.

REFERENCES

- BERENBLUT, I. I. (1964). Change-over designs with complete balance for first residual effects. *Biometrics* 20 707-712.
- CHENG, C. S. and Wu, C. F. (1979). Balanced repeated measurements designs. Technical Report No. 541, Univ. of Wisconson, Madison.
- EHRENFELD, S. (1955). Complete class theorems in experimental design. *Proc. Third Berkeley Symposium* 1 57-67, Univ. of California Press.
- HARDY, G. H., LITTLEWOOD, J. E. AND POLYA, G. (1967). Inequalities. Cambridge Univ. Press.
- HEDAYAT, A. and Afsarinejad, K. (1975). Repeated measurements designs, I. In A Survey of Statistical Designs and Linear Models. (J. N. Srivastava, ed.) 229-242. North-Holland, Amsterdam.
- HEDAYAT, A. and AFSARINEJAD, K. (1978). Repeated measurements designs, II. Ann. Statist. 6 619-628. KIEFER, JACK (1975). Construction and optimality of generalized Youden designs. In A Survey of Statistical Designs and Linear Models (J. N. Srivastava, Ed.) 333-353. North Holland, Amsterdam.
- Lucas, H. L. (1957). Extra-period Latin-square change-over designs. J. Dairy Sci. 40 225-239.
- NOBLE, BEN (1969). Applied Linear Algebra. Prentice-Hall, New York.
- Wu, C. F. (1980). On some ordering properties of the generalized inverses of nonnegative definite matrices. Linear Algebra and Appl., to appear.

DEPARTMENT OF STATISTICS UNIVERSITY OF CALIFORNIA, BERKELEY BERKELEY, CALIFORNIA 94720 DEPARTMENT OF STATISTICS UNIVERSITY OF WISCONSIN 1210 W. DAYTON STREET MADISON, WISCONSIN 53706