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REPEATED MEASUREMENTS DESIGNS FOR CORRELATED OBSERVATIONS

by

K. BENCHEKROUN

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REPEATED MEASUREMENTS DESIGNS FOR CORRELATED OBSERVATIONS

KAMAL BENCHEKROUN
University of North Carolina
Chapel Hill, NC 27599-3260

ABSTRACT

Based on the combinatorial concept of association scheme, some new series of repeated measurements designs in t treatments, N subjects and $p(\leq t)$ periods are constructed. Assuming an arbitrary within subject correlation structure on the error terms, these are shown to provide efficient alternatives when a universally optimal and/or a variance balanced design does not exist, or is difficult to construct.

1. INTRODUCTION

An experiment in which each of N subjects is exposed to a sequence of treatments during p periods of time, there being t treatments in all, is called a repeated measurements design. Other names are crossover and change–over design. The collection of all such designs is denoted by RMD(t,N,p). Formally, a design d in RMD(t,N,p) is an array in p rows (periods), N columns (subjects) and t symbols (treatments) whose (i,j)–th entry d(i,j) determines the treatment applied in the i–th period to the j–th subject.

Two models have been extensively used in the literature for the analysis of RMD's: (a) The first model assumes that each treatment manifests its effect only during the period of application and not afterwards, but incorporate an autoregressive within subject correlation structure on the error terms; (b) in the second model errors are uncorrelated, but each treatment manifests an additional residual effect during the period following its application.

The theory of RMD's aims at the search for "good" designs in terms of some optimality criterion and/or variance balance; that is, all elementary treatment contrasts are estimated with the same variance. In case (b): Williams (1949) was the first to provide "good" designs for both issues, but for cases p=t. Blaisdell and Raghavarao (1980) used the concept of association scheme to construct partially balanced designs for both direct and residual treatment effects with uncorrelated errors. Constantine and Hedayat (1982), constructed designs that are balanced for residual effects with p < t. In case (a): Kunert (1985) showed that Williams designs

are universally optimal, in the sense of Kiefer (1975), over a subclass of RMD(t,N,t). A comprehensive review on the theory of RMD's is given by Matthews (1988).

In many experiments, the assumption of autoregressive errors seems reasonable; however there are situations where the experimenter may not know precisely the underlying correlation. In this paper, a class of partially variance balanced RMD's with $p \leq t$ is constructed, assuming an arbitrary within subject correlation. The efficiency of these designs relative to universal optimality is assessed by two measures used by Gill and Shukla (1985) to measure the efficiency of nearest neighbor balanced block designs in the autoregressive case.

RMD's with $p < t$ find applications in many areas like animal feeding trials (Cochran et al. 1941) and drug trials in the pharmaceutical industry. The case $p = 2$ is of great importance in clinical trials (Grizzle 1965, Armitage and Hill 1982, Willan and Pater 1986).

The following notations are maintained throughout this paper. $PBIB(b,k,v,r;\lambda_1,...,\lambda_s)$, is an s–associate class partially balanced incomplete block design in v symbols and b blocks each of size k, with replication number r and index parameters $\lambda_1,\lambda_2,...,\lambda_s$; OA(b,k,v,2), SBA(b,k,v,2) and TA(b,k,v,2) are respectively, an orthogonal array, a semibalanced array and a transitive array in b columns, k rows, v symbols and strength 2; GD(m,n), is a group divisible association scheme in m groups of n elements each; T(n) is a triangular association scheme in $\binom{n}{2}$ elements. For definitions and properties of PBIBD's and association schemes, please see Bose and Mesner (1959), Raghavarao (1971), Delsarte (1973) and Bailey (1985). OA's are defined in Rao (1947), SBA's and TA's are defined in Rao (1961) as OA's of Type I and II, respectively, and later renamed semibalanced and transitive arrays in the literature.

2. STATISTICAL MODEL

For $d \in RMD(t,N,p)$, the following linear model is assumed:

$$Y_{d,ij} = \tau_{d(i,j)} + \alpha_i + \beta_j + \epsilon_{ij} \quad 1 \leq i \leq p \quad 1 \leq j \leq N \qquad (1)$$

where $Y_{d,ij}$, is the measurement at period i on subject j, $\tau_{d(i,j)}$ is the fixed effect of treatment d(i,j) assigned by d to subject j at period i($d(i,j) \in \{0,1,...,t-1\}$); α_i, the effect of period i;β_j, the effect of subject j; ϵ_{ij}'s are random errors with zero means and correlation structure given by:

$$\mathrm{Var}[(\epsilon_{1j},...,\epsilon_{pj})'] = V \quad j = 1,...,N,$$

$$\mathrm{cov}(\epsilon_{ij}, \epsilon_{i'j'}) = 0 \quad \text{if } j \neq j',$$

V is an arbitrary p × p covariance matrix.

Observations on different subjects are uncorrelated, and observations on any given subject have covariance matrix V. Write I_r, the r×r identity matrix; 1_r, the r × 1 vector of ones and ⊗, the Kronecker product symbol. In vector notation model (1) becomes:

$$Y_d = T_d\,\tau + (1_N \otimes I_p)\alpha + (I_N \otimes 1_p)\beta + \epsilon, \quad \mathrm{Var}(\epsilon) = I_N \otimes V, \qquad (2)$$

where $Y_d = (y_{d.11},...,y_{d.p1},\ y_{d.12},...,y_{d.pN})'$; $\epsilon = (\epsilon_{11},...,\epsilon_{p1},\epsilon_{12},...,\epsilon_{pN})'$; $\alpha = (\alpha_1,...,\alpha_p)'$; $\beta = (\beta_1,...,\beta_N)'$; $\tau = (\tau_0,\ \tau_1,...,\tau_{t-1})'$; $T_d = [T'_{d1} \vdots ... \vdots T'_{dN}]'$, T_{du} (u=1,...,N) being the p × t 0–1 matrix whose (k,i)th entry $t_{du.ki}$ is equal to 1 if and only if d(k,u) = i.

To avoid non estimability problems, estimation will be based on the set of contrasts $\theta = (I_t - \frac{1}{t}J_t)\tau$, $J_t = 1_t 1'_t$. It should cause no harm to do so since $c'\theta = c'\tau$ for any contrast vector c. Denote by $\hat{\tau}$ the weighted least squares estimator of θ.

A design d is said to be binary, if each treatment is tried at most once on each subject; and uniform on the periods, if each treatment occurs equally often at each period. As in Kunert (1985), the information matrix for estimating θ by weighted least squares and from a design d uniform on the periods is:

$$C_d = \sum_{u=1}^{N} T'_{du}\, W\, T_{du} \qquad W = V^{-1} - (1'_p\, V^{-1}\, 1_p)^{-1} V^{-1} J_p V^{-1} \qquad (3)$$

and $\mathrm{Var}(\hat{\tau}) = C_d^-$ a g–inverse of C_d.

Variance balance calls for a design d such that C_d^- is completely symmetric (i.e. $\mathrm{var}(\hat{\tau}_i) = $ constant for all i, and $\mathrm{cov}(\hat{\tau}_i,\hat{\tau}_j) = $ constant for all i and j, i ≠ j). Universal optimality calls for a design d* such that C_{d*} is completely symmetric and maximizes trace of C_d over a class of designs with the same size (t,N,p). In many combinations of the parameters t,N and p, such designs do not exist, even for a specified covariance matrix V. The next section introduces a class of designs that partially fulfill these properties.

3. PARTIALLY BALANCED ARRAYS AND RMD'S

Given an association scheme with s classes, a p × N array with t symbols will be called an s–associate class partially balanced array, if it satisfies the following conditions:

C1 : No symbol occurs more than once in each column,

C2 : Each symbol occurs r times in each row,

C3 : Any two symbols that are i–th associates occur λ_i times as a column of any two–rowed subarray.

Such a structure will be denoted by $PBA(N,p,t,r;\lambda_1,...,\lambda_s)$.

REMARKS: (i) The columns of a $PBA(N,p,t,r;\lambda_1,...,\lambda_s)$ form a $PBIB(N,p,t,rp;\gamma_1,...,\gamma_s)$, where $\gamma_i = \lambda_i\binom{p}{2}$, i = 1,...,s. (ii) A PBA with all λ_i's equal is simply a SBA which has been shown to be universally optimal over binary RMD's for any covariance matrix V (Cheng 1988), and also shown to be weakly universally optimal for a moving average type covariance V (Morgan and Chakravarti (1988).

Necessary conditions for the existence of a $PBA(n,p,t,r;\lambda_1,...,\lambda_s)$ are easily obtained from those of a PBIBD as:

$$N = rt, \quad 2r = \sum_{i=1}^{s} n_i\lambda_i$$

where n_i is the number of i–th associates of any given symbol. Let $w_{k\ell}$ be the (k,ℓ)–th entry of W in (3). The (i,j)–th entry of C_d is then:

$$C_{d.ij} = \sum_{k=1}^{p} \sum_{\ell=1}^{p} \sum_{u=1}^{n} t_{du.ki}\, t_{du.\ell j}\, w_{k\ell}$$

If $i \neq j$, $t_{du.ki}\, t_{du.kj} = 0$; if d is a PBA, C1 implies $t_{du.ki}\, t_{du.\ell i} = 0$ for all k and ℓ with $k \neq \ell$.

Hence
$$C_{d.ii} = \sum_{k=1}^{P} \left\{ \sum_{u=1}^{N} t_{du.ki} \right\} w_{kk}$$

and C2 implies $C_{d.ii} = r\, tr(W)$.

If $i \neq j$, $\quad C_{d.ij} = \sum_{1 \leq k < \ell \leq p} \left\{ \sum_{u=1}^{N} (t_{du.ki}\, t_{du.\ell j} + t_{du.\ell i}\, t_{du.kj}) \right\} w_{k\ell}$

since W is symmetric.

If i and j are g–th associates, the above expression and C3 give

$$C_{d.ij} = \lambda_g \sum_{k<\ell} w_{k\ell} .$$

W is a symmetric matrix such that $W1_p = 0$, which imply that $\sum_{k<\ell} w_{k\ell} = -\text{tr}(W)/2$.

If $A_0 = I$, $A_1,...,A_s$ are the association matrices of the underlying association scheme, then the above expressions can be written as

$$C_d = \text{tr}(W)\{r\, I - \tfrac{1}{2}(\lambda_1 A_1 + ... + \lambda_s A_s)\} \qquad (4)$$

The matrix C_d belongs to the association algebra $\sigma(A_0, A_1,...,A_s)$ generated by the matrices $A_0, A_1,...,A_s$, which is closed under the g–inverse operation.

Hence $\qquad C_d^- = \dfrac{1}{\text{tr}(W)} \sum_{i=0}^{s} \varphi_i A_i$ for some real numbers $\varphi_0,...,\varphi_s$ $\qquad (5)$

If i and j are g–th associates, (5) gives

$$\text{var}(\hat{\tau}_i - \hat{\tau}_j) = 2(\varphi_0 - \varphi_g)/\text{tr}(W) \qquad (6)$$

this proves the following theorem.

THEOREM 1: If the design d, in model (1) with an arbitrary covariance V, is a PBA, then $\text{var}(\hat{\tau}_i - \hat{\tau}_j)$ is constant for all pairs of treatments (i,j) in the same associate class.

Explicit expressions of the coefficients φ_i's in (6), may be obtained, using a well known property of association schemes summarized in the following lemma (see Bailey (1985) for details).

LEMMA 1: For each association matrix A_j (j = 0,1,...,s), there exist real numbers e_{ij}(i = 0,1,...,s) such that

$$A_j = \sum_{i=0}^{s} e_{ij} S_i$$

where $S_0, S_1,...,S_s$ are t×t symmetric, idempotent and mutually orthogonal matrices. The matrix $E = [e_{ij}]$ is invertible.

E is called the character table of the scheme, its inverse $F = [f_{ij}]$ is such that

$$S_i = \sum_{j=0}^{s} f_{ji} A_j \quad i = 0,1,...,s.$$

(4) implies $C_d = tr(W) \sum\limits_{i=0}^{s} \psi_i A_i$ with $\psi_0 = r$ and $\psi_i = -\dfrac{\lambda_i}{2}$ $1 \leq i \leq s$

$$= tr(W) \sum_{j=0}^{s} e_j S_j \text{ with } e_j = \sum_{i=0}^{s} \psi_i e_{ji}.$$

Hence $C_d^- = \dfrac{1}{tr(W)} \sum\limits_{\{j=e_j \neq 0\}} e_j^{-1} S_j$

$$= \frac{1}{tr(W)} \sum_{i=0}^{S} \left\{ \sum_{\{j=e_j \neq 0\}} e_j^{-1} f_{ij} \right\} A_i,$$

and $\qquad\qquad\qquad \varphi_i = \sum\limits_{\{j=e_j \neq 0\}} e_j^{-1} f_{ij}$ $i = 0,1,...,s$ $\qquad\qquad$ (7)

In particular, if a PBA has only $s = 2$ associate classes, the variances of elementary treatment contrasts take only 2 distinct values

$$\text{var}(\hat{\tau}_i - \hat{\tau}_j) = \begin{cases} v_1 = 2(\varphi_0 - \varphi_1)/tr(W) & \text{if } i \text{ and } j \text{ are first associates} \\ v_2 = 2(\varphi_0 - \varphi_2)/tr(W) & \text{if } i \text{ and } j \text{ are second associates} \end{cases}$$

4. CONSTRUCTION OF PBA'S

THEOREM 2: The existence of a PBIB$(b,k,t,r;\gamma_1,...,\gamma_s)$ and of a SBA$(\lambda\binom{k}{2},p,k,2)$, $p \leq k$, imply the existence of a PBA$(N,p,t,r; \lambda_1,...,\lambda_s)$ with $N = \lambda b\binom{k}{2}$, $r = N/t$ and $\lambda_i = \lambda\gamma_i$, $i = 1,...,s$.

Proof: Write $S = SBA(\lambda\binom{k}{2},p,k,2)$ and $P = PBIB(b,k,t,r;\gamma_1,...,\gamma_s)$. The b blocks of P provide b sets of k symbols each; using each set once in S, one gets b semibalanced arrays $S_1,S_2,...,S_b$; if these are juxtaposed to each other, the resulting array $[S_1 \vdots S_2 \vdots ... \vdots S_b]$ has $N = \lambda b\binom{k}{2}$ columns, p rows, t symbols and is indeed a PBA with index parameters $\lambda\gamma_i$, $i = 1,...,s$.

The above theorem provide several series of PBA's from known PBIBD's and SBA's.

Series 1: GD–PBA$(n^2\binom{m}{2}$, m,mn, $\frac{n(m-1)}{2}$;0,1), n is a prime power and m $\leq$ n+1 is an odd prime power:

Obtain a group divisible PBIB$(n^2$,m,mn,n;0,1) from theorem 8.5.7 (p. 133) of Raghavarao (1971) and a SBA$(\binom{m}{2}$,m,m,Z) from Rao (1961).

From the character table of GD(m,n) given in Bailey (1985) and expressions (7) and (8) above, the variances of elementary treatment contrasts for this series are

$$v_1 = \frac{4}{n(m-1)tr(W)} \qquad v_2 = \frac{t-1}{t} v_1 \qquad (9)$$

Series 2: T–PBA$((n-2)\binom{n}{2}$,n–1,$\binom{n}{2}$,n–2;1,0), n–1 is an odd prime power: Obtain a triangular PBIB$(n$,n–1,$\binom{n}{2}$,2;1,0) from theorem 8–8–1 in Raghavarao (1971) and SBA$(\binom{n-1}{2}$,n–1,n–1,2) from Rao (1961).

The character table of the triangular association scheme is given by its inverse in Ogawa and Ishii (1965), the variances v_1 and v_2 for these series turn out to be:

$$v_1 = \frac{n+1}{t\,tr(W)} \qquad v_2 = \frac{n+2}{t\,tr(W)} \qquad t = \binom{n}{2} \qquad (10)$$

(9) and (10) show that these designs are not far from exact variance balance.

Other series of PBA's based on rectangular, L_2 and cyclic association schemes can be constructed by the same technique.

THEOREM 3: A GD–PBA$(3n^2$,3,3n,n;0,1) can always be constructed for any n $\geq$ 2.

Proof: Let the three groups of GD(3,n) be $G_i = \{t_{i1},...,t_{in}\}$, i = 1,2,3.

Write
$$\bar{t}_{ij} = (\underbrace{t_{ij},t_{ij},\,...,t_{ij}}_{n\ times}) \qquad j = 1,...,n \quad i = 1,2,3$$

$t_i = (t_{i1},...,t_{in})$; $t_i^{(u)} = (t_{i,u+1},...,t_{i.n},t_{i.1},...,t_{i.u})$, u = 1,...,n–1. Simple combinatorial arguments show the required array to be:

$$\begin{bmatrix} \bar{t}_{11}\ \bar{t}_{12} \cdots \bar{t}_{1n} & \bar{t}_{21}\ \bar{t}_{22} \cdots \bar{t}_{2n} & \bar{t}_{31}\ \bar{t}_{32} \cdots \bar{t}_{3n} \\ t_2\ \ t_2\ \cdots\ t_2 & t_3\ \ t_3\ \ \ \ t_3 & t_1\ \ t_1\ \ \ \ t_1 \\ t_3\ t_3^{(1)} \cdots t_3^{(n-1)} & t_1\ \ t_1^{(1)}\ \ \ t_1^{(n-1)} & t_2\ \ t_2^{(1)}\ \ \ t_2^{(n-1)} \end{bmatrix}$$

Example 1: GD–PBA(12,3,6,2;0,1)

$$G_1 = \{0,3\} \quad G_2 = \{1,4\} \quad G_3 = \{2,5\}$$

$$\begin{array}{cccccccccccc} 0 & 0 & 3 & 3 & 1 & 1 & 4 & 4 & 2 & 2 & 5 & 5 \\ 1 & 4 & 1 & 4 & 2 & 5 & 2 & 5 & 0 & 3 & 0 & 3 \\ 2 & 5 & 5 & 2 & 0 & 3 & 3 & 0 & 1 & 4 & 4 & 1 \end{array}$$

THEOREM 4: The existence of $SBA(\gamma_i\binom{s_i}{2}, p_i,s_i,2)$ $i = 1,2$, and of $OA(\delta s_1^2,q,s_1,2)$ imply the existence of a GD–PBA$(N,p,t,r;\lambda_1,\lambda_2)$ with $t = s_1 s_2, p = \min(p_1,p_2,q)$, $N = \gamma_1 s_2\binom{s_1}{2} + \delta\gamma_2 s_1^2\binom{s_2}{2}$, $\lambda_1 = \gamma_1$, and $\lambda_2 = \delta\gamma_2$.

Proof: The $t = s_1 s_2$ symbols are identified with the ordered pairs (i,j), $i = 0,1,...,s_1-1$, $j = 0,1,...,s_2-1$; two symbols being first associates if they have the same second coordinates and second associates otherwise.

$$\text{Let } A = \begin{bmatrix} a_{11} & \cdots & a_{1c} \\ \vdots & & \vdots \\ a_{p1} & \cdots & a_{pc} \end{bmatrix} \quad c = \delta s_1^2 \quad a_{ij} \in \{0,1,...,s_1-1\}$$

represents $OA(\delta s_1^2,p,s_1,2)$ and

$$B_i = \begin{bmatrix} b_{11}^{(i)} & \cdots & b_{1d_i} \\ \vdots & & \vdots \\ b_{p1}^{(i)} & \cdots & b_{pd_i}^{(i)} \end{bmatrix}, \quad d_i = \gamma_i\binom{s_i}{2}, \quad b_{k\ell}^{(i)} \in \{0,1,...,s_i-1\}$$

represents $SBA\left[\gamma_i\binom{s_i}{2}, p,s_i,2\right]$, $i = 1,2$.

Define
$$A(j) = \begin{bmatrix} (a_{11},b_{1j}^{(2)}) & \cdots & (a_{1c},b_{1j}^{(2)}) \\ \vdots & & \vdots \\ (a_{p1},b_{pj}^{(2)}) & \cdots & (a_{pc},b_{pj}^{(2)}) \end{bmatrix}, \quad j = 1,\ldots,d_2$$

and
$$B(j) = \begin{bmatrix} (b_{11}^{(1)},j) & \cdots & (b_{1d_1}^{(1)},j) \\ \vdots & & \vdots \\ (b_{p1}^{(1)},j) & \cdots & (b_{pd_1}^{(1)},j) \end{bmatrix}, \quad j = 0,1,\ldots,s_2-1$$

Write $\mathscr{A} = [A(1) \vdots \ldots \vdots A(d_2)]$, $\mathscr{B} = [B(0) \vdots \ldots \vdots B(s_2-1)]$ and $\mathscr{C} = [\mathscr{A} \vdots \mathscr{B}]$.

The array $\mathscr{C}$ so constructed is the required PBA. Proof is similar to that given in Mukhopadhyay (1978) for the construction of SBA's and will be omitted.

Corollary 1: The existence of $SB(\gamma\binom{m}{2}$, $k,m,2)$ and of $OA(n^2,q,n,2)$ imply the existence of $GD-PBA(N,p,t,r;\lambda_1,\lambda_2)$ with $N = \gamma n^2\binom{m}{2}$, $p = \min(k,q)$, $t = mn$, $r = N/t$, $\lambda_1 = 0$ and $\lambda_2 = \gamma$.

Proof: Apply the above construction with $s_1 = n$, $s_2 = m$, $\gamma_1 = 0$, $\gamma_2 = \gamma$, $\delta = 1$, $B_2 = SBA(\gamma\binom{m}{2},p,m,2)$ and take $\mathscr{C} = \mathscr{A}$, omitting the part coming from $\mathscr{B}$.

5. EFFICIENCY OF PBA'S RELATIVE TO UNIVERSAL OPTIMALITY

All designs d considered in this section are connected. Let $\mu_{d1},\mu_{d2},\ldots,\mu_{dt-1}$ be the nonzero eigenvalues of C_d. The usual A and D optimality criteria call for the maximization of the functions

$$\phi_A(d) = (t-1)\left\{\sum_{i=1}^{t-1} \mu_{di}^{-1}\right\}^{-1}$$

and
$$\phi_D(d) = \left[\prod_{i=1}^{t-1} \mu_{di}\right]^{\frac{1}{t-1}}$$

For any binary design d in RMD(t,N,p), expression (4) implies

$$tr(C_d) = rt, \quad tr(W) = N, \quad tr(W) = \text{constant}$$

Hence, a design d is universally optimal over binary RMD's if its information matrix C_d is completely symmetric, or equivalently, if all μ_{di}'s are equal. Let d* be a hypothetical universally optimal design whose information matrix has all eigenvalues equal to $\nu = (\mu_{d1} + \dots + \mu_{d.t-1})/(t-1)$ then $\phi_A(d)$ and $\phi_D(d)$ are maximized for this design with common maximum value: $\phi_A(d^*) = \phi_D(d^*) = \nu$. The A and D efficiencies relative to the hypothetical universally optimal design, as defined by Gill and Shukla are

$$e_A(d) = \phi_A(d)/\phi_A(d^*), \quad e_D(d) = \phi_D(d)/\phi_D(d^*) \tag{11}$$

These are equal to 1 if d is a SBA.

Let d be a PBA$(N,p,t,r;\lambda_1,\dots,\lambda_s)$ and N_d its symbol − column incidence matrix (i.e. $= N_d(i,j) = 1$ if symbol i occurs in column j of d and 0 otherwise), and let $B_d = N_d N_d'$.

Then
$$B_d = rp\, I_t + \binom{P}{2}(\lambda_1 A_1 + \dots + \lambda_s A_s) \tag{12}$$

(4) and (12) gives an alternative expression of C_d as

$$C_d = tr(W)\left\{\frac{rp}{(p-1)} I_t - \frac{1}{p(p-1)} B_d\right\} \tag{13}$$

Bose and Mesner (1959) gave the eigenvalues of B_d where d is a two−associate class PBIB design. From this and remark (i) above, the eigenvalues of C_d where d is a two associate class PBA are easily computed. The tables below give e_A and e_D efficiencies of some PBA's whose constructions is described in Section 4.

TABLE 1: GD–PBA$(n^2\binom{m}{2}, p, m, \frac{n(m-1)}{2}; 0, 1)$

m	n	t	N	p	e_A	e_D	construction
2	2	4	4	2	0.9000	0.944	trivial
3	2	6	12	3	0.961	0.980	theorem 3
	3	9	27	3	0.963	0.983	theorem 3
	4	12	48	3	0.975	0.986	theorem 3
5	2	10	40	3	0.987	0.993	Corollary 1
	3	15	90	4	0.989	0.994	Corollary 1

TABLE 2: T–PBA$((n-2)\binom{n}{2}, n-1, \binom{n}{2}, n-2; 1, 0)$

n	t	N	p	e_A	e_D	construction
3	3	3	2	1.000	1.000	trivial
4	6	12	3	0.961	0.980	Series 2
6	15	60	5	0.942	0.972	Series 2

For instance, the design considered in the second row of table 1; given in Example 1 is more than 90% efficient with respect to both e_A and e_D and has balancing ratio for elementary treatment contrasts $v_2/v_1 = 5/6$. A fully efficient SB array with the same number of treatments t = 6, would require at least N = 30 subjects to be constructed.

6. DESIGNS FOR RESIDUAL EFFECT MODEL

In this section, the model assumed is

$$y_{d,ij} = \tau_{d(i,j)} + \beta_j + \rho_{d(i-1,j)} + \epsilon_{ij} \tag{14}$$

where $y_{d,ij}$, $\tau_{d(i,j)}$ and β_j are defined as before; ϵ_{ij}'s have the same correlation

structure as in model (1); $\rho_{d(i-1,j)}$ is the fixed residual effect of treatment d(i−1,j) applied to subject j in the period before. No residual effect on the first period is assumed, so that $\rho_{d(0,j)} = 0$.

Let T_d be the design matrix for direct treatment effects defined in Section 2; define R as a p×p matrix whose entries r_{ij} are 1 if i = j+1 and j < p, and 0 otherwise. If $F_{du} = R\ T_{du}$ (u=1,...,N), then the design matrix for residual effects is $F_d = [F'_{d1} \vdots F'_{d2} \cdots \vdots F'_{dN}]'$. In vector notation, model (14) becomes

$$Y_d = T_d\ \tau + (I_N \otimes 1_p)\beta + F_d\rho + \epsilon \tag{15}$$

$$Var(\epsilon) = I_N \otimes V.$$

If S is a p×p matrix such that $SVS' = I_p$, the variance stabilizing transform of model (15) is

$$(I_N \otimes S)Y_d = (I_N \otimes S)T_d\tau + (I_N \otimes S1_p)\beta + (I_N \otimes S)F_d\rho + (I_N \otimes S)\epsilon$$

or $\bar{Y}_d = \bar{T}_d\ \tau + U\beta + \bar{F}_d\rho + e$ with $Var(e) = I_{Np}$

The information matrix for direct treatment effects is derived as

$$C_d = C_{d.11} - C_{d.12}\ C_{d.22}^- \ C_{d.21} \tag{16}$$

and for residual treatment effects as

$$\bar{C}_d = C_{d.22} - C_{d.21}\ C_{d.11}^-\ C_{d.12} \tag{17}$$

where

$$C_{d.11} = \bar{T}'_d\ \omega^\perp(U)\bar{T}_d \quad C_{d.22} = \bar{F}'_d\ \omega^\perp(U)\bar{F}_d$$

$$C_{d.12} = C'_{d.21} = \bar{T}'_d\ \omega^\perp(U)\bar{F}_d \tag{18}$$

$\omega^\perp(U) = I - U(U'U)^-U'$ is the projection onto the orthogonal complement of the column space of $U = (I_N \otimes S1_p)$.

Simple but lengthy algebraic calculations show that

$$C_{d.11} = \sum_{u=1}^{N} T'_{du} W T_{du} \qquad (19)$$

$$C_{d.12} = C'_{d.21} = \sum_{u=1}^{N} T'_{du} WRT_{du} \qquad (20)$$

$$C_{d.22} = \sum_{u=1}^{N} T'_{du} R' WRT_{du}. \qquad (21)$$

Define a $p \times N$ array with t symbols to be partially transitive if it satisfies conditions C1 and C2 in the definition of PBA and the following condition:

(C4): Every ordered pair of treatments that are i–th associates occur λ_i times as a column of any two rowed subarray. The array so defined will be denoted $PTA(N,p,,t,r;\lambda_1,...,\lambda_s)$.

Clearly, a $PTA(N,p,t,r;\lambda_1,...,\lambda_s)$ is also a $PBA(N,p,t,r;2\lambda_1,...,2\lambda_s)$ and not conversely, a PTA with all λ_i's equal is simply a transitive array.

EXAMPLE 2: GD–PTA(8,2,4,2;0,1) based on the association scheme GD(2,2) with groups {0,2} and {1,3}:

$$\begin{array}{cccccccc} 0 & 1 & 2 & 3 & 1 & 2 & 3 & 0 \\ 1 & 2 & 3 & 0 & 0 & 1 & 2 & 3 \end{array}$$

a transitive array with four symbols has at least 12 columns.

THEOREM 5: If the design d in model (14) is a PTA, then it is partially variance balanced for direct effects $(\tau_i - \tau_j)$ and for residual effects $(\rho_i - \rho_j)$.

Proof: From (16) and (17), it suffices to show that the matrices $C_{d.11}$, $C_{d.12}$ and $C_{d.22}$ given by (19), (20) and (21) belong to the association algebra $\sigma(A_0, A_1,...,A_s)$. Since d is also a $PBA(n,p,t,r;2\lambda_1,...,2\lambda_s)$, (4) implies

$$C_{d.11} = tr(W)[r\, I - (\lambda_1 A_1 + ... + \lambda_s A_s)] \in \sigma(A_0, A_1,...,A_s)$$

Write $C_d(A) = \sum_{u=1}^{N} T'_{du} A\, T_{du}$ where A is any $p \times p$ matrix with entries (a_{ij}).

For a PTA d, the entries of $C_d(A)$ are easily shown to be

$$[C_d(A)]_{ii} = r \, tr(A)$$

$$[C_d(A)]_{ij} = \lambda_g \sum_{k \neq \ell} a_{k\ell} \quad \text{if i and j are g--th associates}$$

Let W be partitioned as

$$W = \begin{bmatrix} w_{11} & w_{12} \cdots w_{1p} \\ \hline \begin{matrix} w_{12} \\ \vdots \\ w_{1p} \end{matrix} & W_{22} \end{bmatrix} = [w_1 \vdots w_2 \vdots \dots \vdots w_p]$$

then

$$WR = [w_2 \vdots \dots \vdots w_p \vdots 0]$$

and

$$R'WR = \begin{bmatrix} W_{22} & 0 \\ \hline 0 & 0 \end{bmatrix} \tag{22}$$

Since all rows and columns of W sum up to 0, (20), (21) and (22) above give

$$C_{d.12} = C_d(WR) = tr(WR)[r \, I - (\lambda_1 A_1 + \dots + \lambda_s A_s)] \in \sigma(A_0, \dots, A_s)$$

$$C_{d.22} = C_d(R'WR) = (r \, tr(W) - w_{11})I - (tr(W) - 2w_{11})(\lambda_1 A_1 + \dots + \lambda_s A_s) \quad \square$$

Some series of PTA's can be constructed from known transitive arrays by methods similar to those of theorems 2 and 4. The analogy is straightforward and needs no further details.

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