Repeated Measurements Designs, I* 

by

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FSU Statistics Report M261

June, 1973
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Abstract  

Repeated measurements designs are concerned with scientific experiments in which subjects (experimental units) are repeatedly exposed to a sequence of different or identical tests (treatments). These designs have application in many branches of scientific inquiry such as: Biology, education, food science, marketing, environmental engineering, medicine and pharmacology. Our objectives in this paper are threefold: (1) To construct some families of repeated measurements designs which researchers have been seeking. These designs are useful for those cases where a subject cannot participate in all tests as in many pharmacological studies; (2) To provide an extensive list of references on repeated measurements designs which we hope will be useful to those who want to do further research in this area; (3) To state some unsolved problems which have an immediate application.


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Repeated Measurements Designs, I

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1. **Introduction.** An experiment design in which experimental units (subjects) are used repeatedly by exposing them to a sequence of different or identical treatments is called a repeated measurements design (for brevity an RM design). Such designs are known by different names in the literature: **crossover** or **changeover** designs, (multiple) time series designs, or **before-after** designs in some special cases.

It may be of interest here to note that an extreme form of an RM design is the one in which the entire experiment is planned on one experimental unit. An obvious disadvantage of such a design is that if the total time during which a given subject can be under observation is fixed, the number of treatments that can be compared may be severely limited. For more details on these types of designs, see Finney and Outhwaite (1956), Kiefer (1960), and Williams (1952).

Note that we differentiate between RM designs and multiple criteria designs; by multiple criteria design we mean a design where each experimental unit receives several scores for each test. For example, in a multiple choice reaction time task, the subject might be scored on both accuracy and speed.

The need for these designs can be justified in several ways.

(i) Due to limitation of the budget, the experimenter has to use each experimental unit for several tests.

(ii) In some experiments the treatments' effects do not have a serious
damaging effect on the experimental units and; therefore, these experimental units can be used for the second, third, etc. experiments.

(iii) In some experiments, the experimental units are human beings or animals and often the nature of the experiment is such that it calls for special training over a long period of time. Therefore, due to time limitation, one is forced to use these experimental units for several tests.

(iv) One of the objectives of the experiment is to find out the effect of different sequences as in drug, nutrition or learning experiments.

(v) Sometimes the experimental units are scarce, therefore the experimental units have to be used repeatedly.

RM designs have application in many branches of scientific inquiry such as: agriculture, animal husbandry, biology, education, food science, market research, medicine, pharmacology, psychology, and social engineering. More than a hundred papers have been written on this subject. But there are still many challenging and practically useful unsolved problems awaiting solutions. Our main purpose in this paper is to answer some of the unsolved problems by constructing some families of RM designs. These designs are useful for those cases where: (i) the first order residual effects are likely to exist, and (ii) the number of periods are strictly less than the number of treatments. In addition, we shall provide at the end of this paper an extensive list of references on RM designs which we hope will be useful for further research in this field.

2. Terminologies. The area of RM designs like any other area of statistics contains certain terms which are not found or used elsewhere. Terms like "direct effect" and "residual effect" are the two most commonly used ones.
Therefore, for the benefit of those who are not acquainted with this area of statistical designs these terms are defined below via an example. Suppose an experimental unit receives treatments A, B and C in periods 1, 2 and 3 respectively. Further, suppose that the corresponding responses can be expressed as:

response in the first period = f_1(\alpha, u) + error
response in the second period = f_2(\beta, \alpha', u) + error
response in the third period = f_3(\gamma, \beta', \alpha'', u) + error.

Then \alpha, \beta and \gamma are referred to as the direct effects of A, B and C respectively. \alpha' and \beta' are said to be the first order residual effects of A and B. \alpha'' is said to be the second order residual effect of A. One can similarly define the m-th order residual effect of a treatment. u represents those features of the experimental units which contribute to the overall response. For example, in a drug experiment on animals, age and weight might be the only features of the animals which influence the response. An experimental unit is said to be k-dimensional if its corresponding u has k components.

In this paper, we assume the response function f( ) to be linear and additive and u contains a single component.

3. Results. In the rest of this paper by an RM(t, n, p) design we mean an RM design based on t treatments, n experimental units each being used for p distinct treatments in p periods.

Definition 3.1. An RM(t, n, p) design is said to be balanced with respect to sets of direct and residual effects if (i) each treatment is tested equally frequently (\lambda_1) in each period, (ii) in the order of application each treatment is preceded by each other treatment equally frequently (\lambda_2).
Here we are interested in characterizing and constructing minimal size designs viz., those designs which are balanced and require the minimum possible number of experimental units. Clearly, in a balanced RM\( (t, n, p) \) design we have the following relations

\[
\begin{align*}
(i) \quad n &= \lambda_1 t \\
(ii) \quad n(p-1) &= \lambda_2 t(t-1).
\end{align*}
\]

Therefore for the given \( t \) and \( p \) the above conditions lead us to the following definition.

**Definition 3.2.** For the given \( t \) and \( p \), then a balanced RM\( (t, n, p) \) design is said to be minimal if its parameter \( \lambda_1 \) is the smallest integer such that \( \lambda_1(p-1) \equiv 0 \mod (t-1) \).

The class of minimal balanced RM\( (t, n, p) \) designs can be divided into two families:

**Family One.** \( p = t \). For this family \( \lambda_1 \) achieves its minimum value viz., one. Now it is interesting to find out whether or not these designs exist for all possible \( t \). Note that for this family \( n = t \) and thus each of its members can be represented by an RM\( (t, t, t) \) design. We shall now consider two cases.

**Case One.** \( t \) even. Williams (1949), Bradley (1958), Gordon (1961), Sheehe and Brass (1961), and Gilbert (1965) have all considered and constructed a minimal balanced RM\( (t, t, t) \) design for all even \( t \)'s. For the sake of completeness, we give a method of construction due to Bradley (1958).

**Construction.** Construct a \( t \times t \) table in which columns represent experimental units and rows represent periods. Number the \( t \) experimental units
successively from 1 to t. Assign integers 1 to t to the t cells in the
first column by entering successive numbers in every other cell from
top to bottom, beginning with the first and reversing the direction
once the end of the column has been reached, but making sure that the
return starts from the last t-th cell. Thus, if t = 4, the first column
will be (1, 4, 2, 3)' . Finally, complete each row in a cyclic manner,
i.e., in each row, starting with the number already entered in the first
cell, proceed to the left entering in each cell the integer immediately
following the one in the preceding cell, except that the integer t is
to be followed by the integer 1.

Example.

<table>
<thead>
<tr>
<th>Experimental units</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6</td>
</tr>
<tr>
<td>1 2 3 4 5 6</td>
</tr>
<tr>
<td>2 6 1 2 3 4 5</td>
</tr>
<tr>
<td>3 2 3 4 5 6 1</td>
</tr>
<tr>
<td>4 5 6 1 2 3 4</td>
</tr>
<tr>
<td>5 3 4 5 6 1 2</td>
</tr>
<tr>
<td>6 4 5 6 1 2 3</td>
</tr>
</tbody>
</table>

Case Two. t odd. A tedious exhaustive count shows that no minimal balanced
RM(t, t, t) design is possible for t = 3, 5 and 7. Group theoretic results
obtained by Gordon (1961) are very useful for this case. It can be shown
that if a minimal balanced RM(t, t, t) design (odd or even) can be con-
structed, then the Hamiltonian decomposition of the complete directed t-
graph is possible. Thus we may use this result and show the non-existence
of minimal balanced RM(t, t, t) designs, for some odd t's, if we can show
that the Hamiltonian decomposition of the complete directed t-graph for
the given t's are not possible. However, no one has succeeded in doing so. Therefore, there is a hope for the existence of these designs if \( t \geq 9 \). The example for \( t = 21 \) constructed by Mendelsohn (1968) supports our optimism. This example constitutes the only known minimal balanced \( RM(t, t, t) \) design for \( t \) odd. This design is exhibited below.

**Example**

<table>
<thead>
<tr>
<th>Experimental units</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21</td>
</tr>
<tr>
<td>A D G R S E L Q H P N C J B I K M U F T O</td>
</tr>
<tr>
<td>B C I N D Q J U L G T S H M P F A E O R K</td>
</tr>
<tr>
<td>C E S I L N G P U B D F M Q O H T K A J R</td>
</tr>
<tr>
<td>D U C G H R P I Q A S K B E F J N O M L T</td>
</tr>
<tr>
<td>E K F S U I B O P C L H Q N A M D R T G J</td>
</tr>
<tr>
<td>F N L O J D S B K Q E A T P R U J H C M I</td>
</tr>
<tr>
<td>G B N Q T M R L D J A I F H U S O C P K E</td>
</tr>
<tr>
<td>H I U A B L F C R N K T D O J P G M E Q S</td>
</tr>
<tr>
<td>I M T U R A N J C H B P O L E D K S G F Q</td>
</tr>
<tr>
<td>J G Q M A H K D T R O N S F L I P B U E C</td>
</tr>
<tr>
<td>K R H F P S C A O E U M N I T Q L J D B G</td>
</tr>
<tr>
<td>L P E B M J O S N T F R C K H G I A Q U D</td>
</tr>
<tr>
<td>M S P T C U H E J I R D L A G O B Q K N F</td>
</tr>
<tr>
<td>N H A L K O Q R B F G U P D C T E I J S M</td>
</tr>
<tr>
<td>O T J K I C D M F U Q B R G N E H L S A P</td>
</tr>
<tr>
<td>P A R E N B T H S L M G K J Q C F D I O U</td>
</tr>
<tr>
<td>Q F O D E P M K G S J L U T B A C N R I H</td>
</tr>
<tr>
<td>R J M H O F E T A K P Q I S D N U G L C B</td>
</tr>
<tr>
<td>S Q D P J T I G E M C O A U K L R F B H N</td>
</tr>
<tr>
<td>T L B J F K U N M O I E G C S R Q P H D A</td>
</tr>
<tr>
<td>U O K C Q G A F I D H J E R M B S T N P L</td>
</tr>
</tbody>
</table>
Remark. While the existence or non-existence of minimal balanced RM(t, t, t) designs for $9 \leq t$ odd, $t \neq 21$ is in doubt, one can trivially construct balanced RM(t, 2t, t) designs for all odd t's. Williams (1949) and Sheehe and Bross (1961) give methods for constructing these designs. An easily remembered method is given below. First, construct a design for t experimental units analogous to the method outlined for t even. Similarly, construct for the remaining t experimental units a design by letting the first column be the reverse of the first column of the design constructed for the initial t units. The following example elucidates the above method.

Example. Let $t = 5$. Then the above procedure produces the following design.

<table>
<thead>
<tr>
<th>Experimental units</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  2  3  4  5</td>
</tr>
<tr>
<td>1  2  3  4  5</td>
</tr>
<tr>
<td>2  5  1  2  3</td>
</tr>
<tr>
<td>periods</td>
</tr>
<tr>
<td>3  2  3  4  5</td>
</tr>
<tr>
<td>4  4  5  1  2</td>
</tr>
<tr>
<td>5  3  4  5  1</td>
</tr>
</tbody>
</table>

A major shortcoming with the designs in family one is that each experimental unit is used for t tests, i.e., each unit has to receive all the treatments. This may not be possible in many experiments such as drug testing or other medical experiments. Or in many other experiments this limitation is undesirable. In these situations, the experimenter has to search for his design among the designs in family two where $p < t$.

Family Two. $p < t$. For the given t and p, a minimal balanced RM(t, n, p) has at least $n = 2t$ experimental units. Therefore, it is interesting to see whether or not minimal balanced RM(t, 2t, p) designs with $p < t$ exist.
In this regard, we have the following lemma and theorem.

**Lemma 3.1.** A minimal balanced $RM(t, 2t, p)$ design with $p < t$ exists only if $p = (t + 1)/2$ and $\lambda_2 = 1$.

This follows directly from the two basic relations $n = \lambda_1 t$ and $n(p - 1) = \lambda_2 t(t - 1)$ mentioned previously.

**Theorem 3.1.** A minimal balanced $RM(t, 2t, p)$ design with $p < t$ exists whenever $t$ is a prime power.

**Proof:**

By construction. Identify the $t$ treatments with the elements of the $GF(t)$ with $x$ as a primitive element. Now consider a $(t + 1)/2 \times 2t$ rectangle $D$ with the $(i, j)$ entry equals

\begin{align*}
    x^i + \delta(j)x^j, & \quad \text{if } j = 0, 1, \ldots, t - 1 \\
    -x^i + \delta(j)x^j, & \quad \text{if } j = t, t + 1, \ldots, 2t - 1 \\
    i = 0, 1, \ldots, (t - 1)/2
\end{align*}

where $\delta(j) = 0$ for $j = 0, t$ and $1$ otherwise. Now we show that if one identifies the columns with experimental units and rows with periods then $D$ is a minimal balanced $RM(t, 2t, (t + 1)/2)$ design. Note that each element of $GF(t)$ appears twice in each row and at most once in each column of $D$. Therefore, $D$ is a minimal balanced $RM(t, 2t, (t + 1)/2)$ design if we can show that each element of $GF(t)$ in $D$ is preceded once by each other element of $GF(t)$ (see Lemma 3.1). To prove this fix an element of $GF(t)$ say $w$. Then $w$ appears in the $(i, r)$ and $(i, s)$ cells with $r$ and $s$ satisfying
\[ x^i + \delta(r)x^r = w \quad i = 0, 1, \ldots, (t - 1)/2. \]
\[ -x^i + \delta(s)x^s = w \]

First, note that the two preceding elements say \( u \) and \( u^* \) in the \((i - 1)\)th row of \( D \) right above \( w \) can be written as

\[
\begin{align*}
   u &= x^{i-1} + \delta(r)x^r \\
   u^* &= -x^{i-1} + \delta(s)x^s
\end{align*}
\]

for \( i = 1, \ldots, t/2 \).

Now because \( u - w = -(u^* - w) \) therefore \( u \neq u^* \). Second, one can argue that as \( i \) runs from 1 to \((t - 1)/2\) the collection of \( d_i, s, d_i = x^{i-1} - x^i \) are all distincts and thus the collection of \( u \)'s and \( u^* \)'s exhausts \( \text{GF}(t) - w \).

To clarify the method of Theorem 3.1, we give two examples one for \( t \) a prime and one for \( t \) a prime power.

**Example.** \( t = 5 \). Here \( \text{GF}(t) = \{0, 1, 2, 3, 4\} \) with 2 as a primitive root.

Thus we obtain

<table>
<thead>
<tr>
<th>Experimental units</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>periods 1</td>
</tr>
<tr>
<td>2</td>
</tr>
</tbody>
</table>

**Example.** \( t = 9 \). \( \text{GF}(9) = \{0, 1, 2, x, 2x, 1 + x, 2 + x, 1 + 2x, 2 + 2x\} \) with the irreducible polynomial \( x^2 + x + 2 \) and \( x \) as a primitive element.

Coding the elements of \( \text{GF}(9) \) by \( \{0, 1, 2, 3, 4, 5, 6, 7, 8\} \) the corresponding design is
Experimental units

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
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<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>5</td>
<td>8</td>
<td>4</td>
<td>0</td>
<td>7</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>7</td>
<td>1</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>6</td>
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<tr>
<td>1</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>0</td>
<td>8</td>
<td>7</td>
<td>5</td>
<td>4</td>
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<td>6</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>periods</td>
<td>2</td>
<td>7</td>
<td>1</td>
<td>6</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>0</td>
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<td>8</td>
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<td>6</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>5</td>
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<td>3</td>
<td>1</td>
<td>4</td>
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<td>7</td>
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<tr>
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<td>2</td>
<td>6</td>
<td>4</td>
<td>7</td>
<td>1</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td>4</td>
<td>0</td>
<td>7</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

Patterson (1951) and Patterson and Lucas (1962) have also given a few examples of RM(t, n, p) designs with p ≤ t.

**Definition 3.3.** A minimal balanced RM(t, 2t, p) design with p < t is said to have property Y if the design with respect to the experimental units is balanced in the sense of a BIB design.

Note that in this case the entire design forms an extended Youden design, i.e., the rows are λ1 copies of an RCB design while with respect to the experimental units the design is a BIB design.

**Theorem 3.2.** A minimal balanced RM(t, 2t, p) design, p < t, with property Y exists whenever t is a prime power of the form 4γ + 3.

**Proof:**

By construction. Identify the t treatments with the elements of the GF(t) with x as a primitive element. Now consider a \((t + 1)/2 \times 2t\) rectangle \(\bar{D}\) with the \((i, j)\) entry equals

\[
\begin{align*}
x^{2i} + \delta(j)x^j, & \text{ if } i = 0, 1, \ldots, (t - 3)/2; \quad j = 0, 1, \ldots, t-1 \\
-x^{2i} + \delta(j)x^j, & \text{ if } i = 0, 1, \ldots, (t - 3)/2; \quad j = t, t + 1, \ldots, 2t - 1 \\
\delta(j)x^j, & \text{ if } i = (t - 1)/2; \quad j = 0, 1, \ldots, 2t - 1,
\end{align*}
\]

where \(\delta(j)\) is the same function as in Theorem 3.1. By an analogous proof
to the proof of Theorem 3.1, one can show that \( \tilde{D} \) is a desired design.

**Example.** Let \( t = 7 \). Then we have

<table>
<thead>
<tr>
<th>Experimental units</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
</tbody>
</table>

Note that with respect to the experimental units the above design is a BIB(7, 14, 8, 4, 4) and with respect to the periods it is a 2-fold randomized complete block design.

Currently we are doing research on the theory and application of 2 or more dimensionals repeated measurements designs. The results will be reported in another paper.
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