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Minimum cost linear trend-free 12-run fractional factorial designs

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Time trend resistant fractional factorial experiments have often been based on regular fractionated designs where several algorithms exist for sequencing their runs in minimum number of factor-level changes (i.e. minimum cost) such that main effects and/or two-factor interactions are orthogonal to and free from aliasing with the time trend, which may be present in the sequentially generated responses. On the other hand, only one algorithm exists for sequencing runs of the more economical non-regular fractional factorial experiments, namely Angelopoulos *et al.* [1]. This research studies sequential factorial experimentation under non-regular fractionated designs and constructs a catalog of 8 minimum cost linear trend-free 12-run designs (of resolution III) in 4 up to 11 two-level factors by applying the interactions-main effects assignment technique of Cheng and Jacroux [3] on the standard 12-run Plackett–Burman design, where factor-level changes between runs are minimal and where main effects are orthogonal to the linear time trend. These eight 12-run designs are non-orthogonal but are more economical than the linear trend-free designs of Angelopoulos *et al.* [1], where they can accommodate larger number of two-level factors in smaller number of experimental runs. These non-regular designs are also more economical than many regular trend-free designs. The following will be provided for each proposed systematic design:

(1) The run order in minimum number of factor-level changes.
(2) The total number of factor-level changes between the 12 runs (i.e. the cost).
(3) The closed-form least-squares contrast estimates for all main effects as well as their closed-form variance–covariance structure.

In addition, combined designs of each of these 8 designs that can be generated by either complete or partial foldover allow for the estimation of two-factor interactions involving one of the factors (i.e. the most influential).

Keywords: sequential fractional factorial experiments; non-regular fractional factorial designs; time trend robust run orders; number of factor-level changes and the experimental cost; the interactions-main effects assignment; orthogonal and non-orthogonal designs; full and partial foldover run augmentation

1. Introduction

Factorial experiments (confirmatory or exploratory) are experiments for investigating the effect of several factors and their joint effects on a particular response. Exploratory factorial experiments

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are often carried out sequentially one run (or one block) at a time, mainly for screening purposes in order to identify the most influential factor(s). To economize on experimentation cost, many factorial experiments are fractionated under the assumption that three-factor and higher-order interactions are negligible. Fractional factorial experiments (systematic or non-systematic) are based on either regular or non-regular designs. Regular designs are orthogonal yielding uncorrelated factor effects estimates whereas many non-regular designs are non-orthogonal but are more economical requiring less number of experimental runs. Sequential factorial experimentation (full or fractionated) suffers from two main problems: (1) successive responses may drift with time and/or with any uncontrollable factor(s) aliased with it, hence biasing factor effects, (2) certain run orders of these experiments may be costly requiring large number of factor-level changes between successive runs.

To overcome these two problems, many algorithms have been proposed for constructing run orders for regular factorial experiments (full or fractionated) in minimum number of factor-level changes (i.e. minimum cost) such that main effects and/or two-factor interactions are orthogonal to the time trend. Experimental cost can further be reduced if factors with expensive or difficult-to-vary-levels are minimally varied during successive experimentation, by assigning these factors to design columns with fewer number of level changes. For complete regular 2^n factorial experiments, there are four main algorithms for sequencing their 2^n runs such that factor-level changes are minimal and/or main effects orthogonal to the time trend. These algorithms are: Cheng and Jacroux [3], Coster and Cheng [6], Cui and John [7] and Correa *et al.* [5]. Hilow [10] has conducted a comparison among these algorithms according to the three criteria: (1) which algorithm produces run orders less costly than the others, (2) which algorithm produces run orders with more linear/quadratic time trend-free main effects and (3) which run order of an algorithm can be generated by another algorithm using either the generalized foldover scheme of Coster and Cheng [6] or the interactions-main effects assignment technique of Cheng and Jacroux [3]. On the other hand and for the incomplete regular 2^{n-k} experiments, Cheng and Jacroux [3] have extensively researched these two problems and proposed the interactions-main effects assignment technique for constructing trend resistant fractionated designs and they also summarized the relevant literature. The work of Cheng *et al.* [4] represents also another major contribution for systematic regular 2^{n-k} experiments, where they have proposed an algorithm based on the interactions-main effects assignment for constructing of systematic $2^{n-(n-k)}$ designs (of resolutions at least III/IV) from the full 2^k factorial experiment such that factor-level changes between runs are extreme (i.e. minimum or maximum) but regardless of factors' trend resistance and also without regard to how the $2^{n-(n-k)}$ runs of these designs can be sequenced in minimum number of factor-level changes.

Cheng *et al.* [4] minimum/maximum cost $2^{n-(n-k)}$ designs can be constructed based on three facts about the standard order 2^k factorial experiment, the first and second proved by Cheng and Jacroux [3], the first stating that any t-factor interaction effect ($t \geq 1$) in the standard 2^k factorial experiment is orthogonal to time trend of degree $(t-1)$, the second stating that all k main effects of the standard 2^k experiment and all their $(2^k - k - 1)$ interactions can be arranged in increasing number of level changes from 1 up to $(2^k - 1)$. The third fact – proved by Cheng *et al.* [4] – states that regular $2^{n-(n-k)}$ designs (of resolutions at least III/IV) can be constructed from the standard 2^k experiment by the interactions-main effects assignment through selecting sub-tables (i.e. $2^{n-(n-k)}$ designs) in n columns from the $(2^k - 1)$ effects columns and assigning them to new factors. For resolution at least III, minimum cost $2^{n-(n-k)}$ designs $(2^{k-1} \leq n \leq 2^k - 1)$ select and assign the first n effects columns, whereas maximum cost $2^{n-(n-k)}$ designs select and assign the last n effects columns. The total number of these $2^{n-(n-k)}$ designs of resolution at least III is 2^{k-1}. On the other hand and for resolution at least IV, minimum cost $2^{n-(n-k)}$designs $(2^{k-2} + 1 \leq n \leq 2^{k-1})$ select and assign the first n effects columns from the 2^{k-1} candidate effects columns, whereas maximum cost $2^{n-(n-k)}$ designs select and assign the last n effects columns. That is, only 2^{k-1} effects of the $(2^k - 1)$ effects of the 2^k experiment are eligible for selection-assignment yielding a total of

2^{k-2} systematic $2^{n-(n-k)}$ designs of resolution at least IV. These 2^{k-1} candidate effects include interactions of all orders and some but not all of the k main effects.

For the purpose of improving on Cheng *et al.* [4], minimum cost $2^{n-(n-k)}$ designs (of resolution at least III) but non-time trend free, Hilow [9] has reported a catalog of $(2^{k-1}-1)$ minimum cost linear trend-free $2^{n-(n-k)}$ designs of resolution at least III $(2^{k-1}-(k-1) \leq n \leq 2^k - 1 - k)$ by applying the interactions-main effects assignment on the standard 2^k factorial experiment, where all k main effects are excluded from assignment due to their nonlinear time trend resistance, according to one of the facts of Cheng and Jacroux [3]. The condition $(2^{k-1}-(k-1) \leq n \leq 2^k - 1 - k)$ on the number of factors ensures design's non-singularity and runs non-replication besides ensuring main effects linear time trend resistance.

In contrast and for the more economical non-regular fractionated factorial experiments, only one algorithm exists for sequencing their runs in minimum number of factor-level changes (i.e. minimum cost) such that main effects and/or two-factor interactions are orthogonal to the time trend. This algorithm is due to Angelopoulos *et al.* [1]. The number of runs in these designs ranges between 12 and 28, while the number of factors ranges only from 4 to 6. That is, Angelopoulos *et al.* [1] designs are not economical in terms of the number of experimental runs, where they are neither saturated nor nearly so. Also their algorithm produces sometimes systematic non-regular designs with replicated runs. Therefore, it is intended in this research to economize further than Angelopoulos *et al.* [1] only for 12-run non-regular designs, where we proceed parallel to Hilow [9] procedure and produce a catalog of 8 systematic 12-run non-regular designs (in 4 up to 11 factors) by applying the interactions-main effects assignment on the standard 12-run Plackett–Burman design, where factor-level changes are minimal and where all main effects are orthogonal to the linear time trend. The construction process starts by identifying in the standard 12-run Plackett–Burman design 55 effects out of all $2047 = (2^{11} - 1)$ main effects and interactions that are time trend resistant, then it applies the interactions-main effects assignment of Cheng and Jacroux [3] on this standard 12-run design by selecting 11 of these 55 candidate effects and assigning them to new main effects. It is worth to note here that the use of interactions-main effects assignment replaces the need to investigate time trend resistance of all (12)!=479001600 run permutations of the standard 12-run design in order to locate more time trend resistant runs order than the standard order. Sections 3–5 clarify this construction process.

For larger size non-regular designs with more than 12 runs, a procedure similar to the one employed in this research can be followed for constructing catalogs of minimum cost linear trend-free non-regular designs accommodating more than 11 factors, but this requires a lot of computer work. The rest of the paper is organized as follows: Section 2 examines the time trend resistance of the standard 12-run Plackett–Burman design when conducted sequentially run after run. Sections 3–5 employ the main effects-interactions assignment technique on the standard 12-run Plackett–Burman design and construct three catalogs of minimum cost linear trend-free 12-run designs in (4 up to 6 factors), in (4 up to10 factors) and in (4 up to11 factors), respectively. Section 6 considers the statistical analysis of the saturated minimum cost linear trend-free 12-run design of Section 5 and provides closed-form least-squares contrast estimates for all main effects as well as provides their closed-form variance–covariance structure. Section 7 considers the problem of de-aliasing two-factor interactions of a single two-level factor (i.e. the most influential one) through run augmentation of each of these 8 systematic designs by either the complete or partial foldover.

2. Time trend resistance of the standard 12-run Plackett–Burman design

The standard run order for this 12-run design is generated by starting with the generating vector of plus and minus ones $(+1, +1, -1, +1, +1, +1, -1, -1, -1, +1, -1)$ then cyclically shifting this row vector one place to the right until the 11th run. The 12th run is a row vector of minus ones. The resulting design is given in Table 1 with total number of factor-level changes (i.e. cost) $66 = (7 + 5 + 6 + 7 + 7 + 5 + 6 + 6 + 6 + 5 + 6)$. The Linear Time Count Statistic at the bottom of this table will be illustrated in the sequel.

This non-regular orthogonal design is quite economical where it can accommodate up to 11 two-level factors for screening purposes under the assumption that all interaction effects are negligible. In contrast, the smallest regular fractional factorial design accommodating 11 two-level factors is a 16-run 2^{11-7} design with 4 extra runs. The least-squares estimates for all main effects $A_j (j = 1, 2, 3, \ldots, 11)$ under the main effects linear model

$$Y_i = b_0 + A_1x_1 + A_2x_2 + A_3x_3 + A_4x_4 + A_5x_5 + A_6x_6 + A_7x_7 + A_8x_8 + A_9x_9 + A_{10}x_{10} + A_{11}x_{11} + \epsilon_i \tag{1}$$

are orthogonal contrasts among its 12 responses ($Y_i : i = 1, 2, 3, \ldots, 12$), where $x_i = +1 \text{or} - 1$ and b_0 is the model intercept. The variance of each main effect estimate $A_j (j = 1, 2, 3, \ldots, 11)$ is $\sigma^2/12$ where the covariance between any two main effects estimates is zero.

For sequential implementation of this 12-run design in Table 1 run after the other, it will be assumed that its 12 runs are conducted at equally spaced time intervals, where if time trend is present among the 12 successive responses in linear form then it is represented by the run order vector $(1, 2, 3, \ldots, 12)$ of the first column of Table 1. Therefore, orthogonality/nonorthogonality of any of the 11 main effects to the linear time trend can be established by the Linear Time Count Statistic of Draper and Stoneman [8]:

$$\text{Linear Time Count for main effect } A_j = \sum t_i * x_{ij}, \tag{2}$$

where x_{ij} is the ith entry of the main effect column A_j (containing 6 1's and 6 -1's). That is, the statistic in Equation (2) is the dot product between a factor's column and the first column vector $\mathbf{t} = (1, 2, 3, \ldots, 12)$, where t_i is the ith entry of this vector ($i = 1, 2, 3, \ldots, 12$). Any Linear Time Count statistic taking the value zero indicates that its associated main effect is orthogonal to the linear time trend, while non-zero values of this Time Count indicate non-orthogonality to the linear time trend. Therefore, when the standard 12-run Plackett–Burman design is conducted sequentially run one after the other, it will only yield main effect of the first factor A_1 orthogonal to the time trend, while the other 10 main effects are not. This result can clearly be seen from the last row of Table 1.

Table 1. The standard 12-run Plackett–Burman design.

	Factors										
Standard run order	A_1	A_2	A_3	A_4	A_5	A_6	A_7	A_8	A_9	A_{10}	A_{11}
1	+1	+1	−1	+1	+1	+1	−1	−1	−1	+1	−1
2	−1	+1	+1	−1	+1	+1	+1	−1	−1	−1	+1
3	+1	−1	+1	+1	−1	+1	+1	+1	−1	−1	−1
4	−1	+1	−1	+1	+1	−1	+1	+1	+1	−1	−1
5	−1	−1	+1	−1	+1	+1	−1	+1	+1	+1	−1
6	−1	−1	−1	+1	−1	+1	+1	−1	+1	+1	+1
7	+1	−1	−1	−1	+1	−1	+1	+1	−1	+1	+1
8	+1	+1	−1	−1	−1	+1	−1	+1	+1	−1	+1
9	+1	+1	+1	−1	−1	−1	+1	−1	+1	+1	−1
10	−1	+1	+1	+1	−1	−1	−1	+1	−1	+1	+1
11	+1	−1	+1	+1	+1	−1	−1	−1	+1	−1	+1
12	−1	−1	−1	−1	−1	−1	−1	−1	−1	−1	−1
Number of level changes	7	5	6	7	7	5	6	6	6	5	6
Linear Time Count	0	−10	2	−8	−18	−28	−16	−4	8	−2	10

To establish orthogonality/nonorthogonality to the linear time trend of the $(2^{11} - 1 - 11) = 2036$ interaction effects of the standard 12-run design in Table 1, the Linear Time Count Statistic for each of these interactions can be defined similar to Equation (2) as the dot product between the interaction column (of $+1$'s and -1's) and the run order vector $\mathbf{t} = (1, 2, 3, \ldots, 12)$. These interactions Time Counts reveal that only 54 interactions have zero Linear Time Count, i.e. orthogonal to the linear time trend, while the remaining 1982 interactions are not linear trend free. These time trend resistance results for the standard 12-run design are different from that for the regular standard factorial 2^{11} design, where by one the three facts of Cheng and Jacroux [3] none of the 11 main effects is linear trend free, while each of the 2036 interaction effects is at least linear time trend free. These 54 interaction effects and the main effect (i.e. A_1) that are linear trend free in the standard 12-run design are now listed in Table 2 in increasing number of level changes (between the $+1$'s and -1's) from 2 up to 10.

That is, Table 2 reveals that in the standard 12-run Plackett–Burman design, one 10-factor, four 9-factor, one 8-factor, zero 7-factor, eighteen 6-factor, twenty-three 5-factor, two 4-factor, one 3-factor, four 2-factor interactions and main effect A_1 are orthogonal to the linear time trend. All these 55 linear trend-free effects have balanced effects columns (i.e. $6 + 1$'s and $6 - 1$'s) except the 4 interaction effects E2, E3, E4 and E17, where the 3 interaction effects E2, E4 and E17 have each ($4 + 1$'s and $8 - 1$'s) while effect E3 has ($8 + 1$'s and $4 - 1$'s). This imbalance is due to the fact that the 12-run Plackett–Burman design is a main effects design where only main effects

Table 2. The 55 linear trend-free factorial effects of the standard 12-run Plackett–Burman design in increasing number of level changes (from 2 up to 10).

Factorial effect	Effect code	Number of level changes	Factorial effect	Effect code	Number of level changes
A3A4A7A8A10	E1	2	$A_2A_3A_4A_5A_6A_7A_8A_9A_{10}A_{11}$	E30	7
A1A2A4A5A6A7A8A11	E2	3	$A_1A_2A_4A_7A_8A_9$	E31	7
A3A9A10	E3	3	$A_2A_3A_5A_6A_8A_9$	E32	7
A2A4A6A7	E4	3	$A_1A_2A_5A_8A_9$	E33	7
A1A2A3A4A5A7A8A9A11	E5	4	$A_1A_4A_7A_{10}A_{11}$	E34	7
A4A5A6A7A10A11	E6	4	$A_2A_4A_5A_8A_9$	E35	7
A1A2A3A8A9	E7	4	$A_3A_5A_6A_{10}A_{11}$	E36	7
A2A3A5A9A11	E8	4	A_1	E37	7
A2A4A6A7A10	E9	4	$A_1A_2A_3A_5A_6A_7A_8A_9A_{11}$	E38	8
A6A10	E10	4	$A_1A_3A_5A_6A_7A_8A_9A_{10}A_{11}$	E39	8
A1A4A6A7A8A10	E11	4	$A_1A_2A_3A_4A_5A_9$	E40	8
A2A4A5A7A9A11	E12	5	$A_1A_6A_7A_8A_9A_{11}$	E41	8
A1A2A5A7A9	E13	5	$A_2A_3A_4A_6A_8A_{10}$	E42	8
A1A3A6A8A10	E14	5	$A_2A_4A_5A_7A_9A_{10}$	E43	8
A2A3A4A10A11	E15	5	$A_1A_3A_6A_8A_{11}$	E44	8
A2A5A6A7A9	E16	5	$A_1A_5A_7A_9A_{11}$	E45	8
A1A2A4A8	E17	5	$A_2A_3A_4A_5A_{10}$	E46	8
A1A3A4A8A10A11	E18	5	$A_6A_7A_8A_{10}A_{11}$	E47	8
A1A5A6A7A8A9	E19	5	A_2A_4	E48	8
A1A2A3A7A9A11	E20	6	A_4A_{10}	E49	8
A1A5A6A8A10A11	E21	6	$A_2A_3A_4A_8A_9A_{10}$	E50	9
A2A5A6A8A9A10	E22	6	$A_5A_6A_7A_9A_{10}A_{11}$	E51	9
A1A3A4A7A11	E23	6	$A_1A_2A_3A_4A_8$	E52	9
A2A3A4A7A9	E24	6	$A_1A_5A_6A_7A_{11}$	E53	9
A2A4A5A6A9	E25	6	$A_1A_2A_3A_4A_7A_{10}$	E54	10
A2A5A6A10A11	E26	6	$A_5A_6A_8A_9A_{11}$	E55	10
A5A6	E27	6			
A1A3A4A8A10A11	E28	6			
A1A5A6A7A8A9	E29	6			

are orthogonal (i.e. balanced with $6 + 1$'s and $6 - 1$'s) but interaction effects are not necessarily orthogonal. This column imbalance differs also from regular two-level designs, where main effect columns and their interactions are balanced each with half of its entries $+1$'s and the other half -1's.

After having completed trend resistance assessment of main effects and interactions in the standard 12-run Plackett–Burman design and found that there is need to search for more time trend resistant 12-run designs than the standard 12-run design, we next apply the main effects-interactions assignment on these 55 linear trend-free effects in Table 2 for constructing proposed 8 systematic 12-run designs. To this end, Sections 3–5 propose three catalogs of minimum cost linear trend-free 12-run designs in (4 up to 6 factors), in (4 up to 10 factors) and in (4 up to 11 factors), respectively.

3. Minimum cost linear trend-free 12-run designs in 4 up to 6 factors

In this Section, minimum cost linear trend-free 12-run designs (in 4 up to 6 factors) will be constructed from the standard 12-run Plackett–Burman design by the main effects-interactions assignment utilizing only 11 of the 55 linear trend-free factorial effects of Table 2 into this assignment. To minimize the number of factor-level changes (i.e. cost) between the 12 runs, we select the first 11 linear trend-free effects of Table 2 (in 2, 3 and 4 level changes) and assign them to new 11 main effects as follows:

$$\begin{aligned}&\texttt{A3A4A7A8A10} \to \texttt{E1},\quad \texttt{A1A2A4A5A6A7A8A11} \to \texttt{E2},\quad \texttt{A3A9A10} \to \texttt{E3},\\&\texttt{A2A4A6A7} \to \texttt{E4},\quad \texttt{A1A2A3A4A5A7A8A9A11} \to \texttt{E5},\quad \texttt{A4A5A6A7A10A11} \to \texttt{E6},\\&\texttt{A1A2A3A8A9} \to \texttt{E7},\quad \texttt{A2A3A5A9A11} \to \texttt{E8},\quad \texttt{A2A4A6A7A10} \to \texttt{E9},\\&\texttt{A6A10} \to \texttt{E10},\quad \texttt{A1A4A6A7A8A10} \to \texttt{E11}\end{aligned}\tag{3}$$

The resulting systematic 12-run design is listed in Table 3 where its 11 main effects are orthogonal to the linear time trend but are not orthogonal to each other. That is, the first 11 linear trend-free effects of Table 2 are not linearly independent, but only 6 of them are. Therefore, this design in Table 3 is singular under the linear model (1), where its alias structure is as follows:

```
Intercept
E1
E2- E3 -E8 + E11
E4+ E8- E11
E5- E10
E6- E7- E8+ E11
E9
```
(4)

Now and based on the alias structure (4), we delete the 5 main effects columns (E3, E7, E8, E10 and E11) from Table 3 and consider only the 12-run design under the remaining 6 effects columns. This produces the non-singular minimum cost linear trend-free 12-run 6-factor design in Table 4, where the total number of factor-level changes (i.e. cost) is $20 = (2 + 3 + 3 + 4 + 4 + 4)$, which is minimal given trend resistance is preserved.

Table 3. The 12-run 11-factor design resulting from the interaction-main effects assignment in Equation (3).

Run order	Factors										
	E1	E2	E3	E4	E5	E6	E7	E8	E9	E10	E11
1	−1	−1	1	−1	−1	1	−1	−1	−1	1	1
2	−1	−1	1	−1	1	1	−1	−1	1	−1	1
3	−1	−1	1	−1	1	−1	1	1	1	−1	−1
4	1	−1	1	−1	−1	−1	1	1	1	1	−1
5	1	−1	1	−1	−1	−1	1	1	−1	1	−1
6	1	1	−1	−1	−1	−1	1	−1	−1	1	1
7	1	−1	1	−1	1	1	−1	−1	−1	−1	1
8	1	−1	1	1	1	1	−1	1	−1	−1	−1
9	1	−1	1	1	1	1	−1	1	1	−1	−1
10	−1	1	−1	1	1	−1	1	1	1	−1	−1
11	−1	1	−1	−1	−1	−1	1	−1	1	1	1
12	−1	1	−1	1	−1	1	−1	−1	−1	1	1
Number of level changes	2	3	3	3	4	4	4	4	4	4	4

Table 4. A minimum cost linear trend-free 12-run design in 6 factors.

Run order	Factors					
	E1	E2	E4	E5	E6	E9
1	−1	−1	−1	−1	1	−1
2	−1	−1	−1	1	1	1
3	−1	−1	−1	1	−1	1
4	1	−1	−1	−1	−1	1
5	1	−1	−1	−1	−1	−1
6	1	1	−1	−1	−1	−1
7	1	−1	−1	1	1	−1
8	1	−1	1	1	1	−1
9	1	−1	1	1	1	1
10	−1	1	1	1	−1	1
11	−1	1	−1	−1	−1	1
12	−1	1	1	−1	1	−1
Number of level changes	2	3	3	4	4	4

The run composition of this systematic 12-run design is: {e, def, df, af, a, ab, ade, acde, acdef, bcdf, bf, bce} and its 6 main effects are estimable under the main-effects model (1) as least-squares contrasts among the design's 12 responses (Y1, Y2, Y3, ... ,Y12). These estimates and the intercept I are:

$$\mathrm{I} = \left(\frac{1}{1184}\right)[40\mathrm{Y1} + 56\mathrm{Y2} + 40\mathrm{Y3} + 72\mathrm{Y4} + 56\mathrm{Y5} + 136\mathrm{Y6} + 72\mathrm{Y7} + 136\mathrm{Y9} + 168\mathrm{Y10} + 120\mathrm{Y11} + 168\mathrm{Y12}]$$

$$\mathrm{E1} = \left(\frac{1}{1184}\right)[-192\mathrm{Y1} - 32\mathrm{Y2} - 192\mathrm{Y3} + 128\mathrm{Y4} - 32\mathrm{Y5} + 176\mathrm{Y6} + 128\mathrm{Y7} + 16\mathrm{Y8} + 176\mathrm{Y9} - 96\mathrm{Y10} + 16\mathrm{Y11} - 96\mathrm{Y12}]$$

$$E2 = \left(\frac{1}{1184}\right)[-184Y1 + 68Y2 - 184Y3 - 124Y4 - 228Y5 + 292Y6 + 172Y7 - 108Y8 - 4Y9 + 56Y10 + 188Y11 + 56Y12]$$

$$E4 = \left(\frac{1}{1184}\right)[8Y1 - 196Y2 + 8Y3 + 44Y4 + 100Y5 - 180Y6 - 252Y7 + 172Y8 + 116Y9 + 152Y10 - 124Y11 + 152Y12]$$

$$E5 = \left(\frac{1}{1184}\right)[-148Y1 + 74Y2 + 148Y3 - 222Y4 - 74Y5 + 74Y6 + 222Y7 + 74Y8 - 74Y9 + 148Y10 - 74Y11 - 148Y12]$$

$$E6 = \left(\frac{1}{1184}\right)[52Y1 + 206Y2 - 244Y3 - 10Y4 - 238Y5 + 14Y6 + 138Y7 - 66Y8 + 162Y9 - 196Y10 + 82Y11 + 100Y12]$$

$$E9 = \left(\frac{1}{1184}\right)[-96Y1 + 132Y2 - 96Y3 + 212Y4 - 164Y5 - 60Y6 - 84Y7 - 140Y8 + 236Y9 - 48Y10 + 156Y11 - 48Y12] \quad (5)$$

Taking variances and covariances of these linear contrasts estimates in Equation (5) produces the variance–covariance structure in Equation (6).

	I	E1	E2	E4	E5	E6	E9
I	120	16	40	24	0	8	8
E1	16	160	104	-56	0	80	80
E2	40	104	260	-140	74	126	52
E4	24	-56	-140	212	-74	-102	-28
E5	0	0	74	-74	185	-37	-74
E6	8	80	126	-102	-37	225	114
E9	8	80	52	-28	-74	114	188

(6)

where each entry in Equation (6) must be multiplied by $(\sigma^2/1184)$ and where the letter I is the model intercept. This variance–covariance structure in Equation (6) shows that the systematic 12-run design in Table 4 is non-orthogonal but its 6 main effects (E1, E2, E4, E5, E6, E9) are linear trend-free and the number of factor-level changes is minimal (i.e. 20).

Non-orthogonality is due to the fact main effect columns of this design in Table 4 are originally interaction effects of the standard 12-run Plackett–Burman design which are not pair-wise orthogonal but only main effects are. This non-orthogonality can clearly be noticed from the sign imbalance in the two main effects columns E2, and E4, where each has (4 +1's and 8 −1's), while the other 4 main effect columns (E1, E5, E6 and E9) are balanced each with 6 +1's and 6 −1's. For comparison purposes, Angelopoulos *et al.* [1] has proposed the following two minimum cost linear trend-free 24-run designs in 6 two-level factors each:

Design One: (1), ac, acdf, abcdf, abdef, bde, bd, bf, bef, cef, ce, cde, abcde, abce, abcef, aef, af, ad, ade, def, cdf, bcdf,, bc, ab.

Design Two: (1), ac, acd, abcdf, abcef, bcef, be, bf, bdf, def, de, cde, abcde, abde, abdef, adf, af, ae, acef, cef, cdf, bcd, bc, ab,

where their total number of factor-level changes (i.e. cost) are $35 = (5 + 5 + 5 + 6 + 6 + 8)$ and $36 = (5 + 5 + 6 + 6 + 6 + 8)$, respectively. Clearly, the proposed non-orthogonal minimum cost linear trend-free 6-factor design in Table 4 in only 12 runs with total number of factor-level changes 20 (i.e. cost) is more economical.

To construct minimum cost linear trend-free 12-run designs in less than 6 two-level factors (i.e. 4 and 5 factors), we delete the last column from Table 4 to produce a minimum cost linear trend-free 12-run design in 5 factors, whereas we delete the last two columns to produce a minimum cost linear trend-free 12-run design in 4 factors. Of course, other effect columns could be dropped from columns of the 12-run 6-factor design in Table 4 but minimality of factor-level changes will not be preserved. So, for the minimum cost linear trend-free 12-run 5-factor design under the first 5 columns of Table 4, it is non-orthogonal and all its 5 main effects (E1, E2, E4, E5 and E6) are orthogonal to the linear time trend where the total number of factor-level changes (i.e. cost) is $16 = (2 + 3 + 3 + 4 + 4)$. The 12 runs of this design are: e, de, d, a, a, ab, ade, acde, acde, bcd, b, bce where main effects contrast estimates as well as their variance–covariance structure can be found by similar reasoning as Equations (5) and (6). For comparison purposes, Angelopoulos *et al.* [1] has proposed the following two minimum cost linear trend-free 16-run 5-factor designs:

Design Three: (1), ab, abcd, abce, acde, de, ce, cd, bd, bcde, be, ae, abde, ad, ac, bc,
Design Four: (1), ae, acde, abcd, abce, bc, bd, de, cd, bcde, be, ab, abde, ad, ac, ce,

where their total number of factor-level changes are $31 = (4 + 7 + 8 + 8 + 4)$ and $30 = (4 + 4 + 5 + 6 + 11)$, respectively. Clearly, the proposed non-orthogonal minimum cost linear rend-free 12-run 5-factor design is more economical.

Now for the minimum cost linear trend-free 12-run design in 4 factors under the first 4 columns of Table 4, it is non-orthogonal and all its 4 main effects (E1, E2, E4 and E5) are orthogonal to the linear time trend where the total number of factor-level changes (i.e. cost) is $12 = (2 + 3 + 3 + 4)$, which is minimal. The 12 runs of this design are {(1), d, d, a, a, ab, ad, acd, acd, bcd, b, bc} where main effects least-squares contrast estimates as well as their variance–covariance structure can similarly be found as in Equations (5) and (6). For comparison purposes, Angelopoulos *et al.* [1] has proposed the following two minimum cost linear trend-free 12-run 4-factor designs:

Design Five: (1), abcd, ac, ad, bcd, bd, ab, bc, c, d, ab, acd,
Design Six: (1), acd, abc, bcd, ad, ab, bd, bc, (1), cd, abd, ac,

where their total number of level changes (i.e. cost) are $25 = (5 + 6 + 7 + 7)$ and $6 = (5 + 6 + 7 + 8)$, respectively. Clearly, the proposed non-orthogonal minimum cost linear trend-free 12-run 4-factor design is more economical.

Finally, if there is interest to investigate more than 6 factors in minimum cost linear trend-free 12-run designs, we need to select and assign more than the first 11 linear trend-free effects from Table 2. Section 4 selects and assigns the first 19 effects of Table 2 and produces (after removing dependencies among them) a minimum cost linear trend-free 12-run design in 10 factors, while Section 5 selects and assigns the first 29 effects of this table and produces (after removing dependencies) a saturated minimum cost linear trend-free 12-run design.

4. Minimum cost linear trend-free 12-run designs in 4 up to 10 factors

In this section, 7 minimum cost linear trend-free 12-run designs (in 4 up to 10 factors) will be constructed from the standard 12-run Plackett–Burman design by the main effects-interactions assignment employing 19 of the 55 linear trend-free factorial effects of Table 2 into this assignment. To minimize the number of factor-level changes (i.e. cost) between the 12 runs, we select the first

19 interaction effects of Table 2 (in 2, 3, 4 and 5 level changes) and assign them to new 19 main effects as follows:

$$\begin{aligned}
&\mathtt{A3A4A7A8A10} \rightarrow \mathtt{E1}, \quad \mathtt{A1A2A4A5A6A7A8A11} \rightarrow \mathtt{E2}, \quad \mathtt{A3A9A10} \rightarrow \mathtt{E3},\\
&\mathtt{A2A4A6A7} \rightarrow \mathtt{E4}, \quad \mathtt{A1A2A3A4A5A7A8A9A11} \rightarrow \mathtt{E5}, \quad \mathtt{A4A5A6A7A10A11} \rightarrow \mathtt{E6},\\
&\mathtt{A1A2A3A8A9} \rightarrow \mathtt{E7}, \quad \mathtt{A2A3A5A9A11} \rightarrow \mathtt{E8}, \quad \mathtt{A2A4A6A7A10} \rightarrow \mathtt{E9},\\
&\mathtt{A6A10} \rightarrow \mathtt{E10}, \quad \mathtt{A1A4A6A7A8A10} \rightarrow \mathtt{E11}, \quad \mathtt{A2A4A5A7A9A11}\\
&\quad \rightarrow \mathtt{E12}, \quad \mathtt{A1A2A5A7A9} \rightarrow \mathtt{E13},\\
&\mathtt{A1A3A6A8A10} \rightarrow \mathtt{E14}, \quad \mathtt{A2A3A4A10A11} \rightarrow \mathtt{E15}, \quad \mathtt{A2A5A6A7A9}\\
&\quad \rightarrow \mathtt{E16}, \quad \mathtt{A1A2A4A8} \rightarrow \mathtt{E17},\\
&\mathtt{A1A3A4A8A10A11} \rightarrow \mathtt{E18}, \quad \mathtt{A1A5A6A7A8A9} \rightarrow \mathtt{E19}
\end{aligned} \tag{7}$$

All 8 linear trend-free effects (E12, ..., E19) selected beyond the 11 effects selected in Section 3 have the same number of level changes, namely 5.Therefore, the resulting 12-run design in 19 two-level factors under assignment (7) is singular with more factors than the number of runs, where the alias structure is:

```
Intercept
E1
E2- E3- E8 +E11- E16+E18
E4+ E8- E11+ E16- E18
E5- E10
E6- E7- E8+ E11- E16+E18
E9- E16+ E18
E12- E14
E13
E15+ E16 -E18- E19
E17
```
(8)

That is, the first 19 linear trend-free effects of Table 2 are not linearly independent but only 10 of them are. Therefore and based on alias structure (8), we delete the 9 main effects columns (E3, E7, E8, E10, E11, E14, E16, E18 and E19) then considering the 12-run design under the remaining 10 columns (E1, E2, E4, E5, E6, E9, E12, E13, E15 and E17) produces the minimum cost linear trend-free 12-run 10-factor design in Table 5, where the total number of factor-level changes is $40 = (2+3+3+4+4+4+5+5+5+5+5)$, which is minimal given time trend resistance is preserved.

This design in Table 5 is both non-regular and non-orthogonal yet it is minimum cost and all its 10 main effects are linear trend free. Main effects least-squares contrast estimates and their variance–covariance structure can be found similar to Equations (5) and (6). The first 6 columns of this 12-run 10-factor design are exactly the same as those of Table 4,where 3 minimum cost linear trend-free12-run designs (in 4, 5 and 6 factors) were constructed in Section 3.

Table 5. A minimum cost linear trend-free 12-run design in 10 factors.

	Factors									
Run order	E1	E2	E4	E5	E6	E9	E12	E13	E15	E17
1	−1	−1	−1	−1	1	−1	−1	1	1	−1
2	−1	−1	−1	1	1	1	1	1	1	−1
3	−1	−1	−1	1	−1	1	1	−1	−1	−1
4	1	−1	−1	−1	−1	1	−1	−1	−1	−1
5	1	−1	−1	−1	−1	−1	1	−1	−1	−1
6	1	1	−1	−1	−1	−1	1	−1	1	−1
7	1	−1	−1	1	1	−1	−1	1	−1	1
8	1	−1	1	1	1	−1	−1	1	−1	−1
9	1	−1	1	1	1	1	−1	−1	1	1
10	−1	1	1	1	−1	1	−1	1	1	−1
11	−1	1	−1	−1	−1	1	1	1	1	1
12	−1	1	1	−1	1	−1	1	−1	−1	1
Number of level changes	2	3	3	4	4	4	5	5	5	5

Now if there is interest to investigate less than 10 factors but more than 6 in 12-run minimum cost linear trend-free designs, one can drop columns from this 12-run 10-factor design in Table 5 similar to the columns dropping procedure used in Section 3. To preserve minimality of factor-level changes only last columns of Table 5 can be dropped, where dropping the last effect column produces the minimum cost linear trend-free 12-run 9-factor design {ehi, defghi, dfg, af, ag, abgi, adeh, acdeh, acdefi, bcdfhi, bfghi, bceg} with total number of level changes (i.e. cost) 35, while dropping the last 2 effects columns produces the minimum cost linear trend-free 12-run 8-factor design {eh, defgh, dfg, af, ag, abg, adeh, acdeh, acdef, bcdfh, bfgh, bceg} with total number of level changes 30, whereas dropping the last 3 effects columns produces the minimum cost linear trend-free 12-run 7-factor design {e, def, dfg, af, ag, abg, ade, acde, acdef, bcdf, bfg, bceg} with total number of level changes 25. All these 3 systematic 12-run designs (in 9, 8 and 7 two-level factors) are non-orthogonal but their main effects are linear trend free. Main effects contrast estimates and the variance–covariance structure can be found similar to Equations (5) and (6). No comparison between these 3 systematic 12-run designs with Angelopoulos *et al.* [1] designs is possible, since their designs incorporate at most 6 two-level factors.

Hence, a total of 7 minimum cost linear trend-free 12-run designs can be constructed from the systematic 12-run design in Table 5 (in 4 up to 10 factors) using the interactions-main effects assignment. Clearly, none of these seven 12-run designs is saturated. Section 5 produces some saturated trend resistant 12-run designs.

5. A saturated minimum cost linear trend-free 12-run design

In this section, a saturated minimum cost linear trend-free 12-run design will be constructed from the standard 12-run Plackett–Burman design by the main effects-interactions assignment utilizing 29 of the 55 linear trend-free factorial effects of Table 2 into this assignment. To minimize the number of factor-level changes (i.e. cost) between the 12 runs, we select the first 29 interaction effects of Table 2 (in 2, 3, 4, 5 and 6 level changes) and assign them to new 29 main effects. That is, we expand the first 19 linear trend-free effects with the next 10 linear trend-free effects (E20, E21, . . ., E29). All these 10 effects have the same number of level changes (i.e. 6) where all are chosen for assignment, since it is not yet known which of them is linearly independent of the 10 independent effects (E1, E2, E4, E5, E6, E9, E12, E13, E15 and E17) identified in Section 4. The resulting 12-run design in 29 two-level factors is singular with more factors than runs, where the alias structure is:

$$
\begin{aligned}
&\texttt{Intercept}\\
&\mathrm{E1} + \mathrm{E25} - \mathrm{E27}\\
&\mathrm{E2} - \mathrm{E3} - \mathrm{E8} + \mathrm{E11} - \mathrm{E16} + \mathrm{E18} - \mathrm{E20} - \mathrm{E21} + \mathrm{E24} - \mathrm{E27} + \mathrm{E28}\\
&\mathrm{E4} + \mathrm{E8} - \mathrm{E11} + \mathrm{E16} - \mathrm{E18} + \mathrm{E20} + \mathrm{E21} - \mathrm{E24} + \mathrm{E27} - \mathrm{E28}\\
&\mathrm{E5} - \mathrm{E10} - \mathrm{E20} - \mathrm{E21} + \mathrm{E24} + \mathrm{E26} - \mathrm{E27}\\
&\mathrm{E6} - \mathrm{E7} - \mathrm{E8} + \mathrm{E11} - \mathrm{E16} + \mathrm{E18} - \mathrm{E26} + \mathrm{E28}\\
&\mathrm{E9} - \mathrm{E16} + \mathrm{E18} - \mathrm{E26} + \mathrm{E28}\\
&\mathrm{E12} - \mathrm{E14} + \mathrm{E20} + \mathrm{E25}\\
&\mathrm{E13} + \mathrm{E20} + \mathrm{E25}\\
&\mathrm{E15} + \mathrm{E16} - \mathrm{E18} - \mathrm{E19} - \mathrm{E28} - \mathrm{E29}\\
&\mathrm{E17}\\
&\mathrm{E22} - \mathrm{E23} - \mathrm{E27}
\end{aligned}
\tag{9}
$$

A glance at this alias structure in (9) shows that when deleting the 18 effects columns (E3, E7, E8, E10, E11, E14, E16, E18, E19, E20, E21, E23, E24, E25, E26, E27, E28 and E29) and considering this 12-run design under the remaining 11 effects columns (E1, E2, E4, E5, E6, E9, E12, E13, E15, E17 and E22) produces the saturated minimum cost linear trend-free 12-run design in Table 6, where the total number of factor-level changes is $46 = (2 + 3 + 3 + 4 + 4 + 4 + 5 + 5 + 5 + 5 + 5 + 6)$, which is minimal given main effects time trend resistance is preserved.

This saturated design in Table 6 is non-regular and non-orthogonal but its 11 main effects are linear trend free and the number of factor-level changes (i.e. cost) is 46, while the saturated standard 12-run Plackett–Burman design in Table 1 is orthogonal but only one of its 11 main effects is linear time trend resistant, namely main effect A_1. This non-orthogonal design is also more economical as far as the number of factor-level changes (i.e. cost) is concerned. The first 6 columns of this saturated 12-run design are exactly the same as those of the systematic 12-run 6-factor design in Table 4 and its first 10 columns are exactly the same as those of the systematic 12-run 10-factor design in Table 5. Therefore, all 8 minimum cost linear trend-free 12-run designs

Table 6. A saturated minimum cost linear trend-free 12-run design.

	Factors										
Run order	E1	E2	E4	E5	E6	E9	E12	E13	E15	E17	E22
1	−1	−1	−1	−1	1	−1	−1	1	1	−1	1
2	−1	−1	−1	1	1	1	1	1	1	−1	−1
3	−1	−1	−1	1	−1	1	1	−1	−1	−1	1
4	1	−1	−1	−1	−1	1	−1	−1	−1	−1	1
5	1	−1	−1	−1	−1	−1	1	−1	−1	−1	−1
6	1	1	−1	−1	−1	−1	1	−1	1	−1	−1
7	1	−1	−1	1	1	−1	−1	1	−1	1	−1
8	1	−1	1	1	1	−1	−1	1	−1	−1	1
9	1	−1	1	1	1	1	−1	−1	1	1	−1
10	−1	1	1	1	−1	1	−1	1	1	−1	−1
11	−1	1	−1	−1	−1	1	1	1	1	1	1
12	−1	1	1	−1	1	−1	1	−1	−1		1
Number of level changes	2	3	3	4	4	4	5	5	5	5	6

(in 4 up to 11 factors) proposed in this research can be generated from this saturated 12-run design in Table 6 by column deletion, where the first non-saturated design is the systematic 12-run 10-factor design in Table 5 that can be generated by deleting the last column of Table 6 and where the second design is the minimum cost linear trend-free 12-run 9-factor design that can be generated by deleting the last two columns and so on until the deletion of the last 7 columns which generates the minimum cost linear trend-free 12-run 4-factor design of Section 3.

It is worth to note that the systematic 12-run design in Table 6 is not the only saturated linear trend-free 12-run non-orthogonal design that can be generated from 11 of the 55 linear trend-free effects in Table 2 by the interactions-main effects assignment. Two other assignments leading to two saturated but non-minimum cost linear trend-free 12-run non-orthogonal designs are:

Assignment One:

Selecting and assigning the interactions (E7, E13, E14, E17, E23, E24, E34, E44, E45, E46 and E47) leads to a systematic 12-run design with total number of level factor changes $70 = (4 + 5 + 5 + 5 + 6 + 6 + 7 + 8 + 8 + 8 + 8)$.

Assignment Two:

Selecting and assigning interactions (E3, E13, E14, E23, E24, E33, E34, E37, E44, E45 and E52) leads to a systematic 12-run design with total number of factor-level changes $71 = (3 + 5 + 5 + 6 + 6 + 7 + 7 + 78 + 8 + 9)$.

Therefore, an open question arises now as to whether if there exists an orthogonal saturated linear trend-free 12-run design with number of factor-level changes less than 46 beating the non-orthogonal saturated minimum cost linear trend-free design in Table 6. Next and in Section 6, we carry out the statistical analysis of this saturated 12-run non-orthogonal design in Table 6, where we derive closed-form contrasts estimates for all main effects and closed-form for the variance–covariance structure.

6. Statistical analysis of the saturated minimum cost linear trend-free 12-run design in Table 6

For this purpose, we employ the main effects model (1) and denote the 12 successive responses by $\{Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, Y_{10}, Y_{11}$ and $Y_{12}\}$, then the least-squares estimates for the 11 linear trend-free main effects are the closed-form linear contrasts:

$$E1 = \left(\frac{1}{468}\right)[-102Y_1 + 30Y_2 - 72Y_3 + 60Y_4 - 42Y_5 + 90Y_6 - 12Y_7 + 120Y_8 + 18Y_9 - 84Y_{10} + 48Y_{11} - 54Y_{12}]$$

$$E2 = \left(\frac{1}{468}\right)[-90Y_1 + 54Y_2 - 36Y_3 + 108Y_4 - 216Y_5 + 162Y_6 + 72Y_7 - 18Y_8 - 108Y_9 + 36Y_{10} - 54Y_{11} + 90Y_{12}]$$

$$E4 = \left(\frac{1}{468}\right)[-18Y_1 - 36Y_2 - 54Y_3 - 72Y_4 + 144Y_5 - 108Y_6 - 126Y_7 + 90Y_8 + 72Y_9 + 54Y_{10} + 36Y_{11} + 18Y_{12}]$$

$$\mathrm{E5} = \left(\frac{1}{468}\right)[-24\mathrm{Y}_1 - 48\mathrm{Y}_2 + 162\mathrm{Y}_3 - 96\mathrm{Y}_4 - 120\mathrm{Y}_5 + 90\mathrm{Y}_6 + 66\mathrm{Y}_7 + 42\mathrm{Y}_8$$
$$+ 18\mathrm{Y}_9 - 6\mathrm{Y}_{10} - 30\mathrm{Y}_{11} - 54\mathrm{Y}_{12}]$$

$$\mathrm{E6} = \left(\frac{1}{468}\right)[-30\mathrm{Y}_1 + 174\mathrm{Y}_2 - 90\mathrm{Y}_3 + 114\mathrm{Y}_4 - 150\mathrm{Y}_5 + 54\mathrm{Y}_6 + 24\mathrm{Y}_7 - 6\mathrm{Y}_8$$
$$- 36\mathrm{Y}_9 - 66\mathrm{Y}_{10} - 96\mathrm{Y}_{11} + 108\mathrm{Y}_{12}]$$

$$\mathrm{E9} = \left(\frac{1}{468}\right)[-105\mathrm{Y}_1 + 141\mathrm{Y}_2 - 81\mathrm{Y}_3 + 165\mathrm{Y}_4 - 57\mathrm{Y}_5 - 45\mathrm{Y}_6 - 33\mathrm{Y}_7 - 21\mathrm{Y}_8$$
$$- 9\mathrm{Y}_9 + 3\mathrm{Y}_{10} + 15\mathrm{Y}_{11} + 27\mathrm{Y}_{12}]$$

$$\mathrm{E12} = \left(\frac{1}{468}\right)[-78\mathrm{Y}_1 + 78\mathrm{Y}_2 + 0.\mathrm{Y}_3 - 78\mathrm{Y}_4 + 78\mathrm{Y}_5 + 0.\mathrm{Y}_6 - 78\mathrm{Y}_7 + 78\mathrm{Y}_8$$
$$+ 0.\mathrm{Y}_9 - 78\mathrm{Y}_{10} + 78\mathrm{Y}_{11} + 0.\mathrm{Y}_{12}]$$

$$\mathrm{E13} = \left(\frac{1}{468}\right)[-33\mathrm{Y}_1 + 51\mathrm{Y}_2 - 99\mathrm{Y}_3 - 15\mathrm{Y}_4 + 69\mathrm{Y}_5 - 81\mathrm{Y}_6 + 3\mathrm{Y}_7 + 87\mathrm{Y}_8$$
$$- 63\mathrm{Y}_9 + 21\mathrm{Y}_{10} + 105\mathrm{Y}_{11} - 45\mathrm{Y}_{12}]$$

$$\mathrm{E15} = \left(\frac{1}{468}\right)[90\mathrm{Y}_1 - 54\mathrm{Y}_2 + 36\mathrm{Y}_3 - 108\mathrm{Y}_4 - 18\mathrm{Y}_5 + 72\mathrm{Y}_6 - 72\mathrm{Y}_7 + 18\mathrm{Y}_8$$
$$+ 108\mathrm{Y}_9 - 36\mathrm{Y}_{10} + 54\mathrm{Y}_{11} - 90\mathrm{Y}_{12}]$$

$$\mathrm{E17} = \left(\frac{1}{468}\right)[9\mathrm{Y}_1 - 99\mathrm{Y}_2 + 27\mathrm{Y}_3 - 81\mathrm{Y}_4 + 45\mathrm{Y}_5 - 63\mathrm{Y}_6 + 63\mathrm{Y}_7 - 45\mathrm{Y}_8$$
$$+ 81\mathrm{Y}_9 - 27\mathrm{Y}_{10} + 99\mathrm{Y}_{11} - 9\mathrm{Y}_{12}]$$

$$\mathrm{E22} = \left(\frac{1}{468}\right)[27\mathrm{Y}_1 - 63\mathrm{Y}_2 + 81\mathrm{Y}_3 - 9\mathrm{Y}_4 - 99\mathrm{Y}_5 + 45\mathrm{Y}_6 - 45\mathrm{Y}_7 + 99\mathrm{Y}_8$$
$$+ 9\mathrm{Y}_9 - 81\mathrm{Y}_{10} + 63\mathrm{Y}_{11} - 27\mathrm{Y}_{12}]. \tag{10}$$

Taking variances and covariances of these linear contrast estimates in Equation (10) generates the variance–covariance structure in Table 7, where each entry must be multiplied by $(\sigma^2/468)$.

Table 7. The variance–covariance structure for the 12-run design in Table 6.

Effect	Intercept	E1	E2	E4	E5	E6	E9	E12	E13	E15	E17	E22
Intercept	50	5	6	15	−2	−7	1	4	7	−3	12	0
E1	5	122	60	−12	7	56	55	49	34	6	−33	45
E2	6	60	270	−153	48	186	93	−60	−51	−81	−99	9
E4	15	−12	−153	162	−69	−102	−24	66	66	27	36	−18
E5	−2	7	48	−69	152	−26	−76	−16	−64	57	15	72
E6	−7	56	186	−102	−26	224	130	−20	−26	−84	−105	−18
E9	1	55	93	−24	−76	130	155	8	32	−87	−66	−36
E12	4	49	−60	66	−16	−20	8	104	56	21	6	18
E13	7	34	−51	66	−64	−26	32	56	107	−24	6	−18
E15	−3	6	−81	27	57	−84	−87	21	−24	126	45	63
E17	12	−33	−99	36	15	−105	−66	6	6	45	99	9
E22	0	45	9	−18	72	−18	−36	18	−18	63	9	99

So now tests of significance on main effects can be conducted when the 12-run trend resistant design in Table 6 is implemented sequentially run after run, if an error estimate is available. However, if such estimate is not available then Normal Probability Plots can be used instead for judging effects significance.

7. Foldover augmentation of minimum cost linear trend-free 12-run designs to de-alias two-factor interactions

It is well known that implementation of each of the proposed 8 minimum cost linear time trend-free 12-run designs sequentially run after the other will identify the most influential factor (if there is any). Therefore, to estimate two-factor interactions involving this influential factor with the other factors, reference can be made to Bisgaard *et al.* [2] and Scibilia *et al.* [11] regarding design run augmentation, where it is possible to augment each of these eight 12-run designs with additional 12 runs through either complete foldover on all factors or through partial foldover on a subset of them. However, this foldover process does not preserve linear time trend resistance of main effects in the combined designs. For illustration, complete foldover leaves only the 4 factors (E1, E4, E5 and E6) of the systematic 12-run design in Table 4 linear trend-free, while it only leaves linear trend-free the 7 factors (E1, E4, E5, E6, E7, E8 and E9) of the systematic 12-run design in Table 5 and the 8 factors (E1, E4, E5, E6, E7, E8, E9 and E11) of the systematic 12-run design in Table 6. Therefore, if complete foldover is to be applied and the most influential factor is not among the linear trend-free factors (in the combined design), then one should try different modes of partial and semi-foldover augmentation.

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