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ARTICLE

Blocking Factorial Experiment with Unequal Number of Replications for Factor Levels

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Abstract

The blocking of factorial designs become a complex task when there are many factors with multiple levels. Often, in this case, incomplete blocks are needed, as in some agronomy experiments. This paper examines a situation in which complete (orthogonal) block designs are impossible for the factorial design with no initial evident of combinatorics to design finding. One of the interesting problems we deal with is unequal number of replicates of factor levels, this is mainly due to cost restrains of practical experimentation. The presented example involves a garlic vernalization study with a factorial structure of $2^2 \times 3 \times 4$. We developed a tailor-made search algorithm to find a locally optimal (or near-optimal) design using an interchange strategy suited to the irregular factorial structure. The resulting design has interesting combinatorial properties that could not have been envisaged in advance. The methods used in this paper are not new to design theory, but are considerably underused in agronomical trials. The design itself is unprecedented in horticultural practice.

Keywords: Blocking; Incomplete block; Orthogonal; Optimal; Search algorithm; Interchange strategy.

1. Introduction

A full factorial design, in which all possible combinations of factor levels are executed, allows for the estimation of all main effects and interaction effects. This property makes it a theoretically desirable approach for experimenters. Conducting a full factorial experiment with a large number of factors is often impractical due to constraints such as cost, time, and the physical impossibility of certain combination factors, however, a fractional factorial design reduces the number of treatment effects without much loss of relevant information, Mainardi & Bidoia (2022). Furthermore,

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Rezende *et al.* (2018) optimized biomass pretreatments via fractional factorial experimental design taken its advantages of efficient cost and time, see it application in other areas of agronomy, Załuski *et al.* (2016), Sokólski *et al.* (2023) and Ribeiro *et al.* (2019). Consequently, considerable attention must be paid to blocking for local control and replication numbers of factor combinations for better precision. In an attempt to construct efficient designs prior to the randomization exercise, the most complex challenge here lies in the blocking structure. It is often necessary to note that incomplete block designs (IBDs) are inevitable in some practical situations (physical or logistical constraints) where the systems prevent all treatment combinations from being tested under the same homogeneous conditions. As such, this requires strategically grouping treatments into blocks to maximize the precision of effect estimates. A critical and often overlooked aspect of this strategy is the intentional use of unequal replication numbers for different treatment levels. This approach allows for deliberate allocation of more experimental units to specific factor levels or critical treatment combinations that are of primary interest, thus increasing the statistical power for estimating those concern, see Dutilleul (1993), Ridgman (1989) and Mead (1990).

Nevertheless, efficient designs must be constructed in such a way to address both constraints of incomplete blocking and predetermined unequal replication numbers. The main strategy is to confound block effects with less relevant interaction combinations, thereby preserving power to estimate main effects and lower order interactions. Sometimes complex factorial models can be fitted by preserving most interactions as estimable and simultaneously controlling and accounting for the complex blocking structure Trinca & Gilmour (2001), Gilmour & Trinca (2012) and Ntul *et al.* (2022). Koutra *et al.* (2023) and Koutra *et al.* (2020) strongly emphasized that the design must follow the experimental context and not just statistical optimality. As such, they further discussed the practical realities of blocking with respect to unequal sizes, non-orthogonality structures and the efficiently use of resources when balanced structure is impossible. Mead *et al.* (2012) worked on resource allocation as a direct pertinent to experimenter's goal of using unequal replication to increase power for critical treatments. Then they advocated for designs that are robust and practically align with experimenter's endeavor.

Furthermore, the search for an optimal design (OD) is also a core strategy for applying Design of Experiments (DoE) efficiently to practical problems. The central objective of OD is to identify the experimental configuration that maximizes the quantity and quality of information about a system, while adhering to constraints such as cost, time, and the number of experimental runs. This principle has been widely applied in various fields, including Agronomy and Engineering to Pharmaceutical Sciences [e.g., Chuai *et al.* (2013), Vajda *et al.* (2001)]. However, it is noted that the experimenter's task of attaining an optimal search is complex. To overcome this complexity, experimenter must have a clear and concluding understanding of the system under investigation. It is only through a thorough comprehensive analysis and evaluation of the main effects and their interactions that a viable search space for optimality could be defined. In this context, DoE serves as a tool for developing models that adequately approximate the true system response Uy & Telford (2009) and Lee (2019).

A particular challenge that arises when the search for an optimal design is when factor levels are not equally replicated. In a factorial design, having different replication numbers implies unequal variances for factor levels and might result in more complex variance-covariance structures when compared to the relative simplicity of symmetrical equireplicated designs. To address this difficulty, methods such as those proposed by Das (1960) and Sardana & Das (1965) involve mapping an asymmetrical factorial as a fraction of a larger symmetrical factorial. The optimality of the resulting design, in this case, is manifested in its elegant combinatorial properties, which maximize the efficiency of estimating the effects of interest. Those methods work at some extent when block sizes and replication numbers must be in specific combinations. The general approach does not think

of those regularities previously and hope that some of it might arise as properties of good designs. Despite being well-established in statistical theory, the methods we are implementing in this paper remain not frequent in agronomic trials, representing a significant opportunity to bring greater robustness and efficiency to horticultural practice.

In this paper, we present a design strategy in line with Tsai & Gilmour (2016), in which an efficiency based optimization criterion is used to guide our design search. Importantly, our factorial experiments are structured with combinations of both quantitative and qualitative factors simultaneously. Our approach seeks to integrate the principles to develop a design strategy that is both statistically efficient and practically feasible for experiments where large homogeneous blocks are impossible with the scientific practicalities and priorities that dictate unequal replication of treatment levels that different from approaches of Trinca & Gilmour (2001), Gilmour & Trinca (2012) and Ntul *et al.* (2022). The proposed method would produce an interchange strategy for irregular factorial structure that is efficient and cost effective in agronomic trials and bring greater robustness and efficiency to horticultural practice.

2. Methodology

In this section we present the practical agronomic problem that inspired the statistical model and the design search, describe the optimizing process, the optimality criterion, and the interchange algorithm.

2.1 Agronomic Problem and Design Factors

This is a garlic vernalization inspired study that considered four experimental factors that could interfere with plant development:

- Bacteria (B), a two level factor indicating presence or absence of a protective bacterial strain;
- Nitrogen (N), a two level factor indicating levels of this nutrient;
- Application (A), a three level factor indicating, respectivelly: 1: no vernalization (replicated 32 times), 2: first stageof vernalization (replicated 16 times) and 3: second stage of vernalization (replicated 16 times);
- Cultivars (C), a four level factor representing different garlic cultivars.
- Block (BL), four distinct blocks

$$\begin{aligned} \gamma_{ijklm} = \mu + \phi_m \\ + \tau_i + \alpha_j + \beta_k + \gamma_l \\ + (\tau\alpha)_{ij} + (\tau\beta)_{ik} + (\tau\gamma)_{il} + (\alpha\beta)_{jk} + (\alpha\gamma)_{jl} + (\beta\gamma)_{kl} \\ + (\tau\alpha\beta)_{ijk} + (\tau\alpha\gamma)_{ijl} + (\tau\beta\gamma)_{ikl} + (\alpha\beta\gamma)_{jkl} \\ + (\tau\alpha\beta\gamma)_{ijkl} \\ + \epsilon_{ijklm}. \end{aligned} \tag{1}$$

in which: μ is the constant component term; ϕ_m is the m^{th} effect of block (Blk) ($m = 1, 2, 3, 4$); τ_i is the effect of the i^{th} level of factor B ($i = 1, 2$); α_j is the effect of the j^{th} level of factor N ($j = 1, 2$); β_k is the effect of the k^{th} level of factor C ($k = 1, 2, 3, 4$); γ_l is the effect of the l^{th} level of factor A ($l = 1, 2, 3$) and ϵ_{ijklm} is a random error component.

For optimization purposes only, the variances of block effects estimates $Var(\hat{\phi}_m)$ as well as the four-level interaction ($Var(\tau\alpha\beta\hat{\gamma})_{ijkl}$) were discarded and the criterion was restricted to minimize the variance of remaining factors and lower order interactions. This is then a form of $\mathbf{A_r}$ criterion as described by Chaloner & Verdinelli (1995), evaluated as the trace of the covariance sub-matrix relative to the parameters of interest.

The protocol for constructing a starting design of this kind follows that the initial starting design is generated for a full factorial structure of $2^2 \times 3 \times 4$, which yields 48 treatment combinations. A unique constraint is applied, requiring the first level of the fourth factor (Application - A_1) to be replicated twice. This introduces an unequal replication of factor levels, effectively expanding the total number of experimental runs from 48 to 64.

The Figure 1 below presents a descriptive statistics of the criterion values for sample points in which the design space operates during the search technique. It is a simple normal kernel density summary that serves as a reference distribution to compare with good designs (that should have smaller variance).

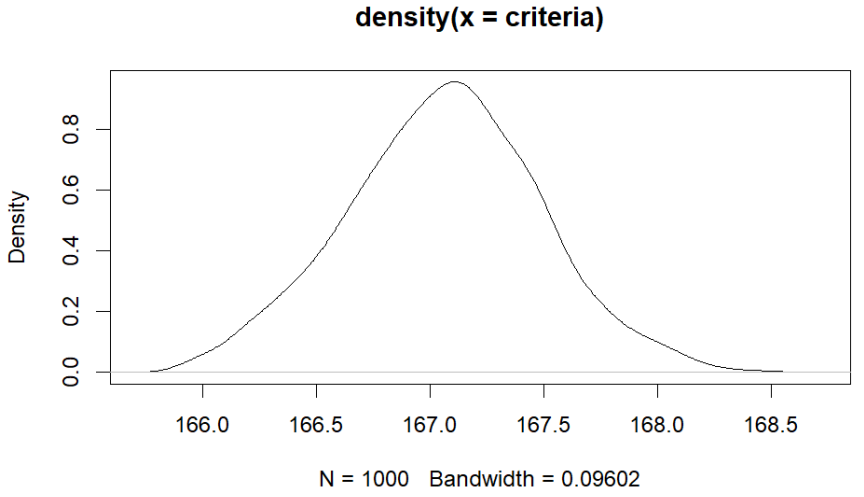


Figure 1. Normal Plot for the 1,000 Starting Designs for the Optimal Interchange Search.

2.2 Optimal Search Procedure

This section details the methodology for obtaining an optimal design for the asymmetric factorial experiment. The model we are optimizing for includes the main effects and low-order interactions. The optimality criterion is the minimization of the average variance of the estimates of these model parameters, which corresponds to an A-optimality criterion. To achieve this, we adopt an interchange search technique, applied to the starting design described previously. This algorithm is an efficient alternative to complex random sampling methods that is often associated with a required large samples, high computational cost, time consumption, and an unexplained optimal search process results to attainment of optimal designs only by chance. In contrast, the interchange algorithm allows the search process and its iterative improvements to be systematically visualized.

The specific procedure implemented follows the principles of the exchange and interchange algorithms developed by authors such as Hebble & Mitchell (1972), Steinberg, *et al.* (1984), and

Jones and Eccleston (1980). The resulting structured algorithm and its corresponding flowchart are presented in Sections 3.2 and 3.3, respectively.

2.3 Optimality Criterion Evalutation

The optimization criterion is proportional to the trace of the variance-covariance matrix:

$$\Omega_{\mathbf{D}} = \min_{\mathbf{D}} \operatorname{tr}(\mathbf{X}^T\mathbf{X})^{-1} \tag{2}$$

where $\mathbf{X}$ is the design matrix corresponding to design $\mathbf{D}$.

$$\mathbf{D} \in \mathcal{D} \quad \text{(feasible design space)} \tag{3}$$
$$\operatorname{rank}(\mathbf{X}) = p \quad \text{(full rank condition)} \tag{4}$$
$$|\mathcal{B}_i| = b \quad \forall i \in \{1, 2, 3, 4\} \quad \text{(balanced blocks)} \tag{5}$$

The complexity analysis in obtaining the optimal design:

- **Time Complexity:** $\mathcal{O}(n \cdot r^2 \cdot c^2)$ where n is the number of starting designs, r is the number of observations, and c is the number of factors
- **Space Complexity:** $\mathcal{O}(r \cdot c)$ for storing design matrices
- **Convergence Criteria:** the algorithm terminates when no improvement is found in systematic interchange.
- **Optimality Properties:** our algorithm seeks a locally optimal design with respect to the A-Optimality criterion. Meanwhile, the Global optimality is approximated through multiple random starting points to avoid local optima.

2.4 Automated Design Structures

This section provides a structured algorithm and flowchart for that shows the automated structural processes from generating starting design to interchange search strategy that eventually resulted to anticipating optimal design .

2.4.1 Algorithm

Algorithm 1: Interchange Algorithm Procedure

Input: Factors: B (Bacteria), N (Nitrogen), C (Cultivars), A (Application) and BL as (Blocks)
Output: Optimal design with minimal criterion value

```
Generate a Starting design with the all factors;
Start swaps;
for each permissible swap of treatment labels from different blocks do
    Try the swap;
    if swap is accepted (improves criterion) then
        Change the design;
    else
        Keep the current design;
    end
end
Evaluate if a full round of all possible swaps improved the design;
if improved then
    Continue new round of swaps;
else
    Report current design as a good design;
    Generate new starting design if not all starting designs are finished;
end
Report as the best (optimal) the design with the smallest criterion value;
```

2.4.2 Flowchart

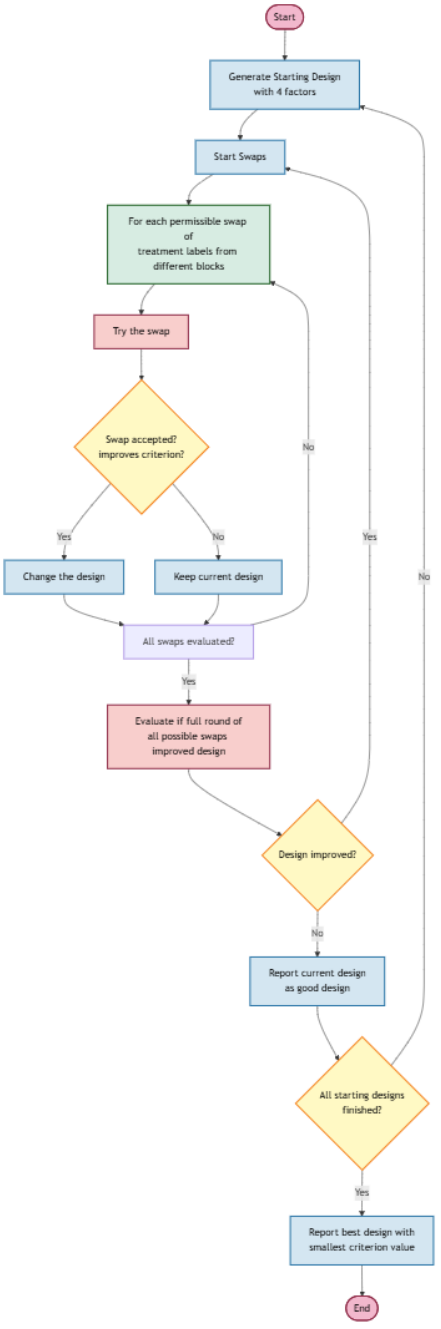


Figure 2. Flowchart of the Interchange Algorithm for A-Optimal Design.

2.5 Simulation Results

In this section the design constructed is presented in Table 1. For demonstrating feasibility of the analysis of the future experiment a mock example was simmulated and data are presented as y (yield) variable. This is a random noise with a positive average ($\mu = 20$) and fixed variance ($\sigma^2 = 1$): $y \sim N(\mu, \sigma^2)$. Analysis of variance for the fitted linear model is also presented as well as the summary of estimates coefficients to give a picture of the estimable functions from the design.

2.5.1 Best Design Found

The best design found is arranged block-wise and presented in Table 1. The variance-covariance matrix of this design for the factorial model parameters is also presented in Table 3. It is worthwhile to note that when the optimal runs are arranged in unique blocks (optimal sub-blocks) they are all structurally orthogonal with respect to the blocking treatment arrangements.

Table 1. Best Design Found by the Search, Arranged in Blocks

Block-I

B	N	C	A	y
1	1	1	2	20.8
2	2	1	2	19.9
2	1	1	1	20.4
2	2	4	1	20.0
1	1	4	1	22.6
2	2	3	1	17.6
1	2	2	1	19.8
1	1	3	1	17.2
1	1	2	2	19.6
1	2	1	1	18.6
2	1	4	2	19.7
2	1	3	2	19.8
2	1	2	1	22.8
1	2	3	2	18.6
1	2	4	2	21.1
2	2	2	2	17.3

Block-II

B	N	C	A	y
2	2	3	3	18.4
2	2	1	3	21.2
2	1	3	1	17.4
2	1	1	1	18.7
1	1	2	1	18.4
2	2	2	1	20.5
1	2	4	3	21.1
1	1	4	1	19.3
2	1	2	3	14.9
1	2	1	1	21.3
2	1	4	3	19.2
1	2	2	3	18.5
2	2	4	1	19.6
1	2	3	1	19.8
1	1	1	3	21.5
1	1	3	3	20.7

Block-III

B	N	C	A	y
2	2	1	1	21.5
1	2	1	2	20.7
2	1	4	1	20.0
1	1	4	2	20.3

Block-IV

B	N	C	A	y
1	2	3	3	21.4
1	1	1	1	21.2
1	1	2	3	18.6
1	2	1	3	23.5

1	1	2	1	20.3
2	1	2	2	25.6
2	2	3	2	19.1
1	1	1	1	17.7
2	2	4	2	20.4
1	2	3	1	19.5
2	1	3	1	21.3
1	1	3	2	16.8
2	1	1	2	19.2
2	2	2	1	17.3
1	2	2	2	19.2
1	2	4	1	18.5

2	1	1	3	21.9
1	2	2	1	23.0
1	2	4	1	23.5
1	1	3	1	18.7
2	2	4	3	20.2
2	1	3	3	20.1
2	2	2	3	22.5
1	1	4	3	22.0
2	1	2	1	20.9
2	2	3	1	19.6
2	1	4	1	19.3
2	2	1	1	22.1

The average of chosen model terms estimates from this design is proportional to the trace of the covariance sub-matrix is evaluated as $\Omega = 83.0834$.

The analysis of variance for the best design is presented in Table 2. It is interesting to note that there are still preserved 6 degrees of freedom for the four level interaction that is actually estimable in this design that was not optimized for this.

2.5.2 Efficiency Cost

The resulting matrix of $\mathbf{X}'\mathbf{X}$ from each constructed design, and their summaries, are proportional to their total information. Most design criteria use the inverse matrix $(\mathbf{X}'\mathbf{X})^{-1}$, which is proportional to the (co)variance of the model estimates. When comparing efficiency and finding the best designs, we used the A-criterion, which is a summary of the covariance matrix (i.e.,the average variance of estimates). Thus, it is the inverse of comparing the information from designs. In this paper, we propose to use a proxy for the relative cost of information from designs as an index of how efficient a design is when retrieving the parameters information, by given the same resources or monetary cost (i.e., the same number of blocks, plots, or experimental material). Thus, the relative information cost of the experiment is given by

$$\mathcal{C}(\mathbf{X}) = \frac{k}{\mathcal{I}(\mathbf{X})} \tag{6}$$

where $\mathcal{I}(\mathbf{X}) = f\left((\mathbf{X}'\mathbf{X})^{-1}\right)$ is a scalar summary of the information matrix (in our case, the A-criterion), and k is a constant that scales the cost relative to a reference design.

3. Results

3.1 Modeling, Estimation and Testing

A simple analysis of this pseudo example with the simulated y variable is given as an **R** code as follows:

```
B <- factor(B); contrasts(B) <- contr.poly
N <- factor(N); contrasts(N) <- contr.poly
A <- factor(A); contrasts(A) <- contr.poly
C <- factor(C)

# Mock example data
```

```
y <- rnorm(64)
y <- cbind(rep(1, 64), rep(1, 64))

Blocks <- factor(kronecker(1:4, rep(1, 16)))

model <- lm(y ~ Block + B*N*C*A)
anova(model)
```

Table 2. Analysis of variance Summary Table for the Full Factorial Model

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
Block	3	27.16	9.05	4.16	0.0286
B	1	0.83	0.83	0.38	0.5469
N	1	0.24	0.24	0.11	0.7463
C	3	16.89	5.63	2.59	0.0978
A	2	1.86	0.93	0.43	0.6616
B:N	1	6.06	6.06	2.79	0.1190
B:C	3	18.82	6.27	2.88	0.0764
N:C	3	5.98	1.99	0.92	0.4605
B:A	2	0.64	0.32	0.15	0.8646
N:A	2	11.90	5.95	2.73	0.1022
C:A	6	22.17	3.69	1.70	0.1992
B:N:C	3	33.70	11.23	5.16	0.0144
B:N:A	2	6.15	3.08	1.41	0.2785
B:C:A	6	14.92	2.49	1.14	0.3919
N:C:A	6	13.82	2.30	1.06	0.4340
B:N:C:A	6	9.47	1.58	0.73	0.6373
Residuals	13	28.30	2.18		

This means that resulting design has potential to estimate all main effects and interaction effects, thus, the power is concentrated on main effects. However, higher order interaction effects have larger variance and would not be easily detected.

Table 2 reveals the analysis of a mock example using the best design obtained the simulation exercise under the Null hypothesis H_0 (e.g. with no treatment or Block effects). Its should be noted that blocks were detected as significant and also with a B:N:C triple interaction.

A summary of coefficients for the estimable functions of the design model is given in Table 3. Note that for optimization purposes, only lines 5 to 45 were used to establish the criterion, but nevertheless, the resulting design is able to estimate the four factor interactions. On the other hand, Block effects and four level interactions have both relatively large standard errors and do not have the same precision. This is an interesting feature of the resulting design: only the model terms in the criterion are estimated with relatively stable precision.

Table 3. Coefficients of Estimates for the Simulated Example. Design Criterion Minimizes Variances of Estimates for Row 5 to 45 (between dashed lines)

Model Terms	Estimate	Std. Error
(Intercept)	20.49	0.70
Block2	-0.82	0.90
Block3	0.05	1.04
Block4	1.68	0.90
B.L	0.31	0.55
N.L	0.60	0.55
C2	-0.28	0.55
C3	-1.36	0.55
C4	-0.82	0.55
A.L	0.92	0.66
A.Q	0.45	0.78
B.L:N.L	0.18	0.82
B.L:C2	0.57	0.78
B.L:C3	0.31	0.78
B.L:C4	-1.47	0.78
N.L:C2	-1.30	0.78
N.L:C3	-0.16	0.78
N.L:C4	-0.29	0.78
B.L:A.L	-0.85	0.90
B.L:A.Q	1.41	1.00
N.L:A.L	0.87	0.90
N.L:A.Q	0.48	1.00
C2:A.L	-0.46	0.90
C3:A.L	0.21	0.90
C4:A.L	-2.17	0.90
C2:A.Q	-0.67	1.00
C3:A.Q	0.27	1.00
C4:A.Q	-1.28	1.00
B.L:N.L:C2	-3.18	1.15
B.L:N.L:C3	-0.63	1.15
B.L:N.L:C4	0.95	1.20
B.L:N.L:A.L	0.80	1.73
B.L:N.L:A.Q	-0.34	1.78
B.L:C2:A.L	1.88	1.28
B.L:C3:A.L	0.53	1.28
B.L:C4:A.L	0.35	1.28
B.L:C2:A.Q	-2.12	1.41
B.L:C3:A.Q	-2.18	1.41

B.L:C4:A.Q	-2.28	1.41
N.L:C2:A.L	0.47	1.28
N.L:C3:A.L	-0.13	1.28
N.L:C4:A.L	-0.30	1.28
N.L:C2:A.Q	2.44	1.41
N.L:C3:A.Q	-0.42	1.41
N.L:C4:A.Q	-0.75	1.41
B.L:N.L:C2:A.L	-1.63	2.86
B.L:N.L:C3:A.L	2.51	1.95
B.L:N.L:C4:A.L	-0.49	2.95
B.L:N.L:C2:A.Q	1.43	2.04
B.L:N.L:C3:A.Q	1.37	2.92
B.L:N.L:C4:A.Q	1.84	2.95

3.2 Optimal Cost and Time Efficiency

Comparing best design found with the distribution of criteria evaluated for a large sample of designs we can see the effectiveness of each search strategy. In Figure 3 is depicted the relative cost of the information for a sample of designs (the reference distribution presented in black) as compared to the best design found (in a vertical red line). This is a clear indication that the search strategy is cheaper to get the same information. method of sampling for optimal designs. At this juncture, it is worthwhile to emphatically emphasis that the optimal design saves cost and time and this is actually in line with the tradition and principle of industrial operations that always targeting cost and time efficiency. Indeed, the optimal design constructed for this unique garlic experiment could be extended to other agricultural experiments for cost and time minimization.

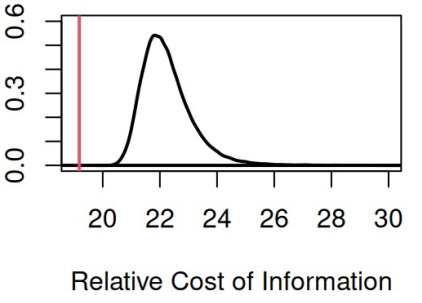


Figure 3. Comparison of Relative cost of information by Experimental Units Evaluated for the Designs: (in black) A Density Plot for a Sample of 100.000 Designs vs (in vertical red) Best Design Found by Interchange Algorithm.

Figure 3 depicts the vertical line for the best design found in comparison with the distributions of randomly chosen designs. This showcase at a glance the efficient performance of search algorithm over direct sampling methods to finding good designs.

4. Conclusions

The experimental situation considered in this paper was of a factorial design with 48 combinations of a garlic vernalization experiment out of which 1/3 of the treatment combinations are replicated twice. We implemented an interchange algorithm that produces locally optimal designs, that is a strategy suited to blocking the factorial structure of the experiment. Resulting design has smaller information cost than randomly blocked factorial structures with the same set of treatments. The resulting design has interesting combinatorial properties that could not have been envisaged in advance, hence needing the computer search. Methods used are not new in design of experiments theory, but is considerably underused in agronomical trials. The design itself is unprecedented in horticultural practice.

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Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

The authors contributed equally

Conceptualization: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Data curation**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Formal analysis**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Funding acquisition**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Investigation**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Methodology**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Project administration**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Software**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Resources**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Supervision**: SILVA, F.O.; BUENO-FILHO, J.S.S. **Validation**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Visualization**: SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S. **Writing - original draft**: SAKA, A.J. **Writing - review and editing:** SAKA, A.J.; SILVA, F.O.; BUENO-FILHO, J.S.S.

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