**D- and A-Optimal Screening Designs**

Jonathan Stallrich\(^a\), Katherine Allen-Moyer\(^a\), and Bradley Jones\(^b\)

\(^a\)Department of Statistics, North Carolina State University, Raleigh, NC; \(^b\)JMP Statistical Discovery Software LLC, Cary, NC

**ABSTRACT**

In practice, optimal screening designs for arbitrary run sizes are traditionally generated using the D-criterion with factor settings fixed at ±1, even when considering continuous factors with levels in \([-1, 1]\). This article identifies cases of undesirable estimation variance properties for such D-optimal designs and argues that generally A-optimal designs tend to push variances closer to their minimum possible value. New insights about the behavior of the criteria are gained through a study of their respective coordinate-exchange formulas. The study confirms the existence of D-optimal designs comprised only of settings ±1 for both main effect and interaction models for blocked and unblocked experiments. Scenarios are also identified for which arbitrary manipulation of a coordinate between \([-1, 1]\) leads to infinitely many D-optimal designs having different variance properties. For the same conditions, the A-criterion is shown to have a unique optimal coordinate value for improvement. We also compare how Bayesian versions of the A- and D-criteria balance minimization of estimation variance and bias. Multiple examples of screening designs are considered for various models under Bayesian and non-Bayesian versions of the A- and D-criteria.

**1. Introduction**

A screening experiment is an initial step in a sequential experimental procedure to understand and/or optimize a process dependent upon many controllable factors. Such experiments are common in pharmaceuticals, agriculture, genetics, defense, and textiles (see Dean and Lewis (2006) for a comprehensive overview of screening design methodology and applications). The screening analysis aims to identify the few factors that drive most of the process variation, often according to a linear model comprised of main effects, interaction effects, and, in the case of numeric factors, quadratic effects (Jones and Nachtsheim 2011a). Each effect corresponds to one or more factors, and a factor is said to be active if at least one of its corresponding effects is large relative to the process noise; otherwise the factor is said to be inert. Analyses under this class of models often follow effect principles of sparsity, hierarchy, and heredity (see chap. 9 of Wu and Hamada 2009), with the primary goal of correctly classifying each factor as active or inert.

A screening design is represented by an \(n \times k\) matrix, \(X_d\), with rows \(x_i^d = (x_{i1}, \ldots, x_{ik})\) where \(x_{ij}\) represents the \(j\)th factor’s setting for run \(i\). To standardize screening designs across applications, continuous factor settings are scaled so \(x_{ij} \in \{-1, 1\}\) while categorical factor settings are often restricted to two levels, making \(x_{ij} = \pm 1\). We compare \(X_d\)’s based on the statistical properties of the effects’ least-squares estimators because their properties are tractable, particularly their variances and potential biases. The goal then is to identify an \(X_d\) that minimizes the individual variances and biases of these effect estimators.

Suppose the model is correctly specified and there are designs having unique least-squares estimators for all effects. Then these estimators are unbiased and designs may be compared based on their estimation variances. A design having variances that are as small as possible will improve one’s ability to correctly classify factors as active/inert. For models comprised solely of main effects and interactions, orthogonal designs have estimation variances simultaneously equal to their minimum possible value across all designs. Such designs exist only when \(n\) is a multiple of 4; for other \(n\) it is unclear which design will have the best variance properties. Still, designs should be compared based on how close their variances are to their respective minimum possible values. This approach requires knowledge of the minimum values as well as some measure of closeness.

One approach for identifying minimum variances is to approximate them using the theoretical value assuming an orthogonal design exists, but such values may be unattainable. The \(c\)-criterion (Atkinson, Donev, and Tobias 2007) may be used to identify the minimum variance for a given effect, but without any guarantee of the estimability of the other effects of interest. To remedy this estimability issue, Allen-Moyer and Stallrich (2022) proposed the \(c_E\)-criterion to calculate these minimum variances exactly. It is less clear how to measure the proximity of a design’s variances to their \(c_E\) values. One solution is to evaluate and rank designs according to a single criterion that involves a scalar measure of all the variances. Such a criterion should be straightforward to evaluate and optimize, and the resulting optimal designs should have variances close to their \(c_E\) values.
Different forms of the $D$- and $A$-criterion (see Section 2.1) are popular variance-based criteria employed in the screening design literature and will be the focus of this article.

Designs that optimize $D$- and $A$-criteria can coincide for some $n$, but this does not mean the criteria equivalently summarize variances. Consider a screening problem with $n = 7$ runs and $k = 5$ factors that assumes a main effect model. It is well-known that there always exists a $D$-optimal design comprised of $x_{ij} = \pm 1$, even when $x_{ij} \in \{-1, 1\}$ (Box and Draper 1971). While other $D$-optimal designs having $x_{ij} \in \{-1, 1\}$ may exist, the screening literature predominantly fixes $x_{ij} = \pm 1$ with no assumed degradation to the resulting variances. For example, Jones, Allen-Moyer, and Goos (2020) found an $A$-optimal design with $x_{ij}$ values of $\pm 1$ and 0 having smaller variances compared to $D$-optimal designs comprised of $x_{ij} = \pm 1$ only. Figure 1 shows this $A$-optimal design, which has $x_{14} = x_{15} = 0$. Figure 1 also shows the corresponding main effect variances (in ascending order) of the $A$-optimal design and two $D$-optimal designs comprised of $x_{ij} = \pm 1$. The minimum possible variances assuming an orthogonal design exists are $1/7 = 0.1429$ and the minimum variances under the $cz$-criterion are 0.1459. Each of the $A$-optimal design’s variances are equal to or smaller than the two competing $D$-optimal designs comprised of $\pm 1$.

Coincidentally, the $A$-optimal design in Figure 1 is also $D$-optimal despite having some $x_{ij} = 0$. In fact, changing either $x_{14}$ or $x_{15}$ to any value in $\{-1, 1\}$ produces yet another $D$-optimal design but with equal or larger variances than the $A$-optimal design. The $A$-optimal design in this case is unique. The existence of infinitely many $D$-optimal designs, each with equal or larger variances relative to the $A$-optimal design, is cause for concern about the $D$-criterion’s ranking of screening designs. The $A$-criterion was better able to differentiate designs in terms of their ability to minimize the main effect variances simultaneously.

This is not to say $D$-optimal designs are less practical than $A$-optimal designs. The relative differences of the variances in Figure 1 are not large. Whether these differences impact the analysis depends on the ratio of the true main effect, denoted $\beta_j$, and the process variance, $\sigma^2$. For a two-sided $t$-test of the null hypothesis $\beta_j = 0$, the noncentrality parameter will be $\beta_j / \sigma$ divided by the square root of the Figure 1 variances. When $\beta_j / \sigma$ is large, the noncentrality parameter will remain large under slight differences in the variances, and so will not affect power of the tests. The differences in variances will have a greater impact for small $\beta_j / \sigma$. Suppose $\beta_j / \sigma = 1$ and we perform a $t$-test for $\beta_j = 0$ with significance level $\alpha = 0.05$. The power for this test under the $D$-optimal design with $x_{14} = x_{15} = 1$ is 0.6355 while for the $A$-optimal design it is 0.7135. Without any prior knowledge of the $\beta_j / \sigma$, it is important then to find a design that decreases the individual variances as much as possible.

Based on the effect principles, it is common to fit a main effect model even though interactions and/or quadratic effects may be active. The least-squares estimators for the main effect model may then become biased. Rather than try to estimate all potentially important effects, one can quantify the bias of the estimators and identify a design that simultaneously reduces estimation variance and bias. Let $\mathbf{b}$ be the vector of the largest collection of effects that may be important and hence captures the true model. Partition $\mathbf{b}$ into $\mathbf{b}_1$ and $\mathbf{b}_2$ where $\mathbf{b}_1$ are effects we believe are most likely to be important and correspond to the effects in the fitted model, and $\mathbf{b}_2$ are the remaining effects that are potentially important but ignored in the fitted model. The possible bias from estimating $\hat{\mathbf{b}}_1$ under the fitted model when the true model includes all $\mathbf{b}$ is $A \mathbf{b}_2$ where $A$ is the design’s so-called alias matrix. DuMouchel and Jones (1994) construct designs under model uncertainty by assigning a prior distribution to $\mathbf{b}_1$ and $\mathbf{b}_2$, and ranking designs according to the $D$-criterion applied to $\mathbf{b}$’s posterior covariance matrix. These Bayesian $D$-optimal designs balance minimizing bias and variance (see eq. (7) of Jones and Nachtsheim 2011b), but the possible flaws of the $D$-criterion pointed out earlier are still concerning. Better designs may then be found with a Bayesian $A$-criterion, which has not received much attention in the screening literature.

This article makes two important contributions that build a case for constructing screening designs under different forms of the $A$-criterion. The first contribution is a comparison of the behavior of $D$- and $A$-criteria in response to manipulating a single coordinate of a given design. Our investigation provides insights into the criteria’s coordinate exchange algorithms, and establishes the existence of $D$-optimal designs with $x_{ij} = \pm 1$ for models including main effects and/or interactions, as well as nuisance effects, such as block effects. We are only aware of such a result for main effect models with an intercept. Cases are identified for which the $D$-criterion is invariant to any coordinate exchange, leading to infinitely many $D$-optimal designs having different variances. For such cases, we show that the $A$-criterion has a unique optimal coordinate exchange.

Our second contribution is the promotion of a weighted Bayesian

![Figure 1](image-url)
A-criterion for constructing designs that balance bias and variance minimization in the presence of nuisance effects. We compare new screening designs generated under coordinate-exchange algorithms for common factorial models and show Bayesian A-optimal designs have more appealing variance and bias properties than Bayesian D-optimal designs.

The article is organized as follows. Section 2 reviews traditional and current screening models and criteria. Section 3 investigates the behavior of D- and A-criteria following coordinate exchanges to an existing design for models including nuisance effects. It also introduces the Bayesian A-criterion and how nuisance effects may be addressed under this criterion through a weight matrix. Examples of A-optimal and Bayesian A-optimal designs constructed for main effect models, a two-factor interaction model, and a quadratic model are provided in Section 4. Section 5 constructs a blocked screening design for a pharmaceutical application under our new criteria. We conclude the article with a discussion of current and future work in Section 6.

### 2. Background

The fitted model for the ith continuous response, $y_i$, has the form

$$y_i = f^T(x_i)\beta + z_i^T\theta + \epsilon_i,$$

where $\epsilon_i \sim N(0, \sigma^2)$ and $i = 1, \ldots, n$. Henceforth and without loss of generality, we set $\sigma^2 = 1$, since $\sigma^2$ is constant across all designs. Every element of $f(x_i)$, a $p \times 1$ vector, is a function of one or more elements of $x_i$, while $z_i$ is a $b \times 1$ vector that does not depend on $x_i$ and corresponds to nuisance effects, $\theta$.

The simplest screening model is the main effect model where $f^T(x_i) = x_i^T$, $z_i = 1$, corresponding to an intercept effect, while a blocked main effect model with block $b$ has $z_i$ comprised of all zeroes except for a 1 in the bth position when $y_i$ comes from block $b$. Full quadratic models append the terms $x_{ij}^T \otimes x_{ij}^T = (x_{ij}x_{ij})^T$ to the main effect model's $f^T(x_i)$, where $\otimes$ denotes the Kronecker product. Two-factor interaction models remove all $x_{ij}^T$ terms from the full quadratic model's $f(x_i)$. For a given $X_d$, let $F$ and $Z$ denote matrices with rows $f(x_i)$ and $z_i$, respectively, and define $L = (F|Z)$.

#### 2.1. Variance Criteria

When model (1) is believed to contain the true model and $n \geq p + b$, we assume there exists at least one $X_d$ with a unique least-squares estimator $\hat{\beta} = (L^TL)^{-1}L^Ty$. The estimator is unbiased and has variance $L^TL^{-1}$. Then $\text{var}(\hat{\beta}) = E(\hat{\beta} - \beta_Z)^2 (L^TL)^{-1}$ where $P_Z = Z(Z^T Z)^{-1}Z^T$ and screening inferences for the elements of $\hat{\beta}$ perform best under an $X_d$ whose $\text{var}(\hat{\beta})$ has small diagonal elements. Designs may then be ranked based on a scalar function of $(L^TL)^{-1}$ that measures variance in some overall sense.

The D-criterion ranks designs according to $|L^TL|^{-1}$ while the D1-criterion is $|\text{var}(\hat{\beta})|$. In both cases, smaller values are desirable. This article uses the equivalent criterion of $|L^TL|$ and $|E(\hat{\beta} - \beta_Z)^2|$, with larger values being desirable. Under a normality assumption of $\epsilon$, the D-optimal and D1-optimal designs minimize the volume of the confidence ellipsoids for $(\beta^T, \theta^T)^T$ and $\beta$, respectively. Hence, these criteria are well-suited for an overall test of the significance of all effects, but not necessarily for individual testing of the parameters. The A-criterion ranks designs with respect to $\text{tr}((L^TL)^{-1})$ and the $A_v$-criterion is $\text{tr}(|\text{var}(\hat{\beta})|)$, being the sum of the individual variances of the parameters of interest. In both cases we want to minimize the chosen criterion.

For main effect and interaction models, a design is said to be orthogonal when $L^TL = nI$, meaning $F$ is comprised of orthogonal columns of elements $\pm 1$ (Mukerjee and Wu 2006; Wu and Hamada 2009; Schoen, Vo-Thanh, and Goos 2017). Such designs estimate all main and interaction effects with the minimum possible variance, $1/n$. By minimizing the individual variances, such designs will be both $D$- and $A_v$-optimal. However, orthogonal designs can only exist when $n$ is a multiple of 4, otherwise the $D$- and $A_v$-optimal designs may differ from each other. Existing literature for constructing $A_v$- and $D$-optimal screening designs under arbitrary $n$ predominantly focuses on main effect models. These designs are more commonly referred to as chemical balance and spring balance designs (Cheng 1980; Masaro 1983; Jacroux, Wong, and Masaro 1983; Wong and Masaro 1984; Cheng 2014a). To our knowledge, there are no theoretical results concerning $A_v$-optimal chemical balance designs with $x_{ij} \in \{-1, 0\}$ for main effect models with an intercept nuisance effect.

Jones, Allen-Moyer, and Goos (2020) algorithmically constructed and compared $A$- and $D$-optimal designs under different screening models and arbitrary $n$. They found that for $n = 3 \pmod 4$ and $n$ small relative to $k$, $A$-optimal designs often had $x_{ij} \in \{-1, 0\}$. In fact, they algorithmically constructed $A$-optimal designs allowing $x_{ij} \in \{-1, 1\}$, yet still found the $A$-optimal designs only took on these three integer settings. Similar to the $D$-optimal designs tendency to only have values $x_{ij} = \pm 1$, Sections 3.2 and 4.1 explore the conjecture that an $A$-optimal design exists where $x_{ij} \in \{-1, 0\}$.

#### 2.2. Variance and Bias Criteria

Though fitting the largest possible model incurs little to no bias, this requires a screening design with a large run size ($n \geq p + b$). Partitioning $\hat{\beta}$ as in Section 1, a submodel may be thought of as fitting model (1) assuming $\beta_2 = 0$. Similarly partitioning $F = (F_1|F_2)$ and defining $L_1 = (F_1|Z)$, the least-squares estimator $(\hat{\beta}_{1|Z}^T \theta_{1|Z}^T)^T = (L_1^T L_1)^{-1} L_1^T y$.

Fitting submodels introduces potential bias, namely the bias of $(\hat{\beta}_{1|Z}^T \theta_{1|Z}^T)^T$ is $A_{\beta_2}$ where

$$A = (L_1^T L_1)^{-1}L_1^TF_2$$

is referred to as the alias matrix. While variances for $\hat{\beta}$ can be ignored when comparing designs, we should consider its bias with respect to $\beta_2$ because we anticipate that some of these potential terms will be eventually considered in the analysis. The experimenter should identify a design that minimizes both the diagonals of $\text{var}(\hat{\beta}_{1|Z})$ and the absolute value of elements of $A$.

For $n = 0 \pmod 4$, one strategy is to rank all strength 2 or 3 orthogonal arrays based on an aliasing-based criterion such as minimum aberration or one of its generalizations (Mukerjee...
and Wu 2006; Cheng 2014b; Vazquez, Schoen, and Goos 2022). Doing so guarantees minimum variances after fitting the main effect model with minimal bias due to model misspecification. For arbitrary \( n \), Jones and Nachtsheim (2011b) algorithmically optimizes criteria that are some combination of the \( D \)-criterion and \( \text{tr}[A^2 A] \) under a given partition of \( \beta \). Bias may also be reduced through one’s ability to fit many possible submodels, which is the goal of estimation capacity and model robust designs (Li and Nachtsheim 2000; Chen and Cheng 2004; Tsai and Gilmour 2010; Smucker et al. 2012), but such criteria are computationally intensive to calculate.

DuMouchel and Jones (1994) proposed a flexible Bayesian \( D \)-criterion to balance main effect variance and bias minimization. A uniform, improper prior is assigned to \( \beta_1 \) and \( \theta \), and a \( N(0, \tau^2I_q) \) prior to \( \beta_2 \). For \( y | \beta, \theta \sim N(F\beta + Z\theta, I) \), the posterior covariance matrix for \( (\beta^T, \theta^T)^T \) is then \( (L^TL + \tau^{-2}K)^{-1} \) where \( K \) is a diagonal matrix with 0’s for the corresponding \( p \) primary terms and 1 for the corresponding \( q \) potential terms. The Bayesian \( D \)-criterion is \( L^TL + \tau^{-2}K \), where \( \tau^{-2} \) tunes the importance of minimizing bias and/or estimation of the potential terms. As \( \tau^{-2} \to \infty \), the criterion will be less influenced by changes in aliasing between the primary and potential terms since \( \tau^{-2}I_q \) will have large diagonal elements. As \( \tau^{-2} \to 0 \), the potential terms become primary terms. DuMouchel and Jones (1994) recommended \( \tau^{-2} = 1 \) and constructed optimal designs via a coordinate exchange algorithm. Other Bayesian approaches have been considered (Toman 1994; Joseph 2006; Bingham and Chipman 2007; Tsai, Gilmour, and Mead 2007) but with only two or three level factors. This article also explores the Bayesian A-criterion, \( \text{tr}(L^TL + \tau^{-2}K)^{-1} \), and Bayesian A \( \tau \)-criterion, being the trace of the submatrix of \( (L^TL + \tau^{-2}K)^{-1} \) corresponding to \( \beta \).

### 3. Properties of the \( D \)- and \( A \)-Criterion

It is challenging to analytically derive optimal designs for a given criterion under an arbitrary \( n \) and \( k \). In practice, these criteria are optimized via some computer search algorithm, such as the coordinate exchange algorithm (Meyer and Nachtsheim 1995), branch-and-bound algorithms (Ahipaşaoğlu 2021), and nonlinear programming (Esteban-Bravo, Leszkiewicz, and Vidal-Sanz 2017; Duarte, Granjo, and Wong 2020). While the two latter algorithms offer some guarantees of identifying the true optimum, the coordinate exchange algorithm is straightforward to implement and is employed in popular statistical software. We focus on the Coordinate Exchange Algorithm (CEA) in this section not only because of its wide adoption, but because it provides an analytical tool to study the behavior of these different forms of the \( D \)- and \( A \)-criterion defined in Section 2.

Let \( X_i \) denote the set of permissible coordinates for \( x_{ij} \), making the set of permissible rows for \( X_d \) equal to \( X = X_1 \times \ldots \times X_k \), where \( X \) denotes the Cartesian product. Then \( X_i = \{1\} \) for categorical factors and \( X_i = \{-1, 1\} \) for numeric factors. A row exchange of an initial design, \( X_{i0} \), exchanges one of its existing rows, \( x_{ij} \), with a candidate row \( \tilde{x} \in X \). This leads to a row exchange of \( f(x_i) \), the \( i \)th row of the initial design’s model matrix, \( F_0 \), with the candidate model matrix row, \( f(\tilde{x}) \). Hence an exchange gives a new design and model matrix, denoted \( \tilde{X} \) and \( \tilde{L} \), respectively.

A CEA is a specific Row Exchange Algorithm (REA) that only manipulates \( x_{ij} \). Then we may partition \( x_i^T = (x_{ij}|x_{i,-j}) \) and represent the \( i \)th row of \( L \) as

\[
l_i(x_i) = \begin{pmatrix} f_1(x_{ij}) \\ f_2(x_{i-}) \end{pmatrix} = \begin{pmatrix} l_1(x_{ij}) \\ l_2(x_{i-}) \end{pmatrix},
\]

where \( f_1(x_{ij}) = l_1(x_{ij}) \) is the subvector of \( f(x_i) \) that only involves \( x_{ij} \) and \( f_2(x_{i-}) \) are the remaining elements. For example, exchanging \( x_{ij} \) for a two-factor interaction model with an intercept nuisance parameter has \( l_1^T(x_i) = (x_{ij}, x_{i1}, x_{i2}, \ldots, x_{i,k}) \) and \( l_2^T(x_i) = (x_{i2}, \ldots, x_{ik}, x_{i2}x_{i3}, \ldots, x_{i(k-1)}x_{ik}, 1) \). Meyer and Nachtsheim (1995) proposed the CEA that proceeds in the same fashion as a REA, but for a given \( x_i \), each coordinate \( x_{ij} \) is updated sequentially. As the number of candidate coordinates \( X_i \) is smaller than \( X \), a CEA involves fewer computations and does not require the user to specify all possible candidate points in \( X \). Moreover, there exist fast update formulas for the forms of the \( D \)- and \( A \)-criterion considered in this article that do not require repeated matrix inversion. We now investigate the behavior of the CEA for different forms of the \( D \)- and \( A \)-criterion.

### 3.1. Properties of \( D \)-Criterion

The \( D \)-criterion’s REA involves a quadratic form of \( V = [1 - \nu(x_i)]D + Dl(x_i)l^T(x_i)D^{-1} \) with \( D = (L_0^T L_0)^{-1} \) and \( \nu(x_i) = l(x_i)^T D l(x_i) \). The matrix \( V \) is symmetric and it is positive definite if and only if \( \nu(x_i) < 1 \). If \( \nu(x_i) = 1 \) then \( V \) is positive semidefinite. For a coordinate exchange of \( x_{ij} \) for \( \tilde{x} \), we can permute the rows and columns of \( V \) following (3) giving a function with respect to \( \tilde{x} \):

\[
\Delta_D^{ij}(\tilde{x}) = l_1^T(\tilde{x})V_{11}l_1(\tilde{x}) + a^T l_1(\tilde{x}) + c
\]

where \( a = 2V_{12}l_2(x_{i-}) \) and \( c = l_2^T(x_{i-})V_{22}l_2(x_{i-}) + [1 - \nu(x_i)] \) are fixed.

The CEA for the \( D \)-criterion can be done equivalently through the CEA for the \( D \)-criterion because \( |L^TL| = |Z^T Z| = |F^T (I - P_Z) F| \). That is, \( \Delta_D^{ij} \) evaluates the ratio \( (F^T (I - P_Z) F)/|F_0^T (I - P_Z) F_0| \), corresponding to the \( D \)-criterion. The CEA for the Bayesian \( D \)-criterion has a similar update formula to (4) but with matrix \( D = (L_0^T L_0 + \tau^{-2}K)^{-1} \) (DuMouchel and Jones 1994). The CEA for the Bayesian \( D \)-criterion is easily shown to be equivalent to the Bayesian \( D \)-criterion, similar to the equivalence of the CEAs for the \( D \)- and \( D \)-criterion. We refer to the collection of these four criteria (i.e., \( D, D_\tau, \text{Bayesian } D, \) and Bayesian \( D_\tau \)) as the \( D \)-criterion.

We now provide a general result about optimal designs for the \( D \)-criterion under what we call an \( m \)-factor interaction model. Let \( J_m = \{j_1, \ldots, j_m\} \) be a subset of \( m \) of the \( k \) factor indices. An \( m \)-factor interaction model has elements of \( f(x) \) comprised only of

- all \( k \) main effect coordinates \( (x_{ij}); \)
- at least one coordinate of the form \( \prod_{j \in J_m} x_{ij} \) for some \( J_m; \)
- any remaining coordinates are of the form \( \prod_{j \notin J_m} x_{ij} \) where \( |J| = 2, \ldots, m. \)
The main effect model is then the one-factor interaction model. Equation (4) provides a proof technique for the following theorem:

**Theorem 1.** For any \( m \)-factor interaction model where \( X'_j = \pm 1 \) or \( \theta_j' \in [−1, 1] \), there exists an optimal design comprised of \( x_{ij} = \pm 1 \) for each of the \( D \)-criteria.

This proof and all subsequent proofs are provided in the supplementary materials. To our knowledge this result has been proven only for main effect models (Box and Draper 1971; Mitchell 1974; Galil and Kiefer 1980) and non-Bayesian criteria. Not only does our result extend to \( m \)-factor interaction models, it also applies to any nuisance effect structure that is design independent.

A practical consequence of Theorem 1 is that to algorithmically construct an optimal design for such models under one of the \( D \)-criteria, we can restrict \( X'_j = \pm 1 \). An unfortunate consequence of Theorem 1 that highlights a potential deficiency is the following corollary:

**Corollary 1.** For any \( m \)-factor interaction model, suppose there exists an optimal design with respect to one of the \( D \)-criteria where at least one \( x_{ij} \neq \pm 1 \) where \( X'_j \in [−1, 1] \). Then that criterion's coordinate update formula at such an \( x_{ij} \) is constant across \( X'_j \), and so any exchange of \( x_{ij} \) with an \( \tilde{x} \in X'_j \) produces another optimal design.

The phenomenon described in Corollary 1 occurred in Figure 1 for both coordinates \( x_{14} \) and \( x_{15} \) under the \( D \)- and \( D_2 \)-criterion. Indeed, the designs with \((x_{14}, x_{15}) = (+1, +1)\) produced the worst individual main effect variances. This example raises doubts about the \( D \)-criterion's suitability to evaluate a design's screening abilities.

### 3.2. Properties of \( A \)-Criterion

The \( A \)-criterion's REA involves a quadratic form of \( U = VD + DV - \{T - v(x_i)\} D + \phi(x_i)\} D\) and \( \phi(x_i) = I^T(X_i)DD(X_i)\). Unlike \( V \), \( I^T(x)U(x) \) can take on positive and negative values. As with \( V \), \( U \) is partitioned to define the coordinate objective function:

\[
\Delta_A^U(\tilde{x}) = \frac{I^T_1(\tilde{x})U_{11}l_1(\tilde{x}) + b^Tl_1(\tilde{x}) + d}{\Delta^U_{ij}(\tilde{x})}, \quad (5)
\]

where \( b = 2U_{12}l_2(x_{i,j}) \) and \( d = I^T_2(x_{i,j})U_{22}l_2(x_{i,j}) - \phi(x_i) \) are constant.

The equivalence between the \( D \)- and \( D_2 \)-criterion does not hold for the \( A \)- and \( A_2 \)-criterion. Other than special cases (Cook and Nachtsheim 1989) there is no closed-form coordinate exchange formula for \( A_2 \). Computing the update after a row/coordinate exchange may be accomplished by first updating \( (L_1^T)D^{-1} \) via the Sherman-Morrison-Woodbury formula (Sherman and Morrison 1950) and directly calculating the change, denoted \( \Delta_A^U \). This will not be as computationally efficient as evaluating (5).

Following Stallings and Morgan (2015), let \( W \) be a diagonal matrix of \( p + b \) elements where the first \( p \) diagonal entries corresponding to \( \beta \) equal 1 and the last \( b \) elements corresponding to \( \theta \) equal an arbitrarily small value, \( w > 0 \). The weighted \( A \)-criterion, or \( A_W \)-criterion, is then

\[
tr[WL^{-1}L^T] = \sum_j \text{var}(\hat{\beta}_j) + w \sum h \text{var}(\hat{\theta}_h). \quad (6)
\]

The coordinate exchange update for the \( A_W \)-criterion, denoted \( \Delta_A^W \), is similar to (5) and is derived in the supplementary materials. Note the \( A \)-criterion is a special case of the \( A_W \)-criterion with \( W = I \). From (6), we see \( \lim_{w \to 0} tr[WL^{-1}L^T] = tr[(F^T(I - P_2)F)^{-1}] \), the \( A \)-criterion. Therefore, \( \lim_{w \to 0} \Delta_A^{W} = \Delta_A^{I} \). This result provides an efficient way to perform a CEA for the \( A \)-criterion using the \( A_W \)-criterion and setting \( w \) to an arbitrarily small value. We have found \( w = 10^{-6} \) to perform well for most applications. This limiting result also allows us to study the behavior of \( \Delta_A^{W} \) through the more tractable \( \Delta_A^{I} \).

The update formula for a coordinate exchange under the Bayesian \( A \)-criterion takes the same form as (5) but with \( D = (L_1^T L_1 + \tau^{-2}K)^{-1} \). For the Bayesian \( A \)-criterion, we can apply the weighted approach to the posterior covariance matrix,

\[
tr[WL^{-1}L^T + \tau^{-2}K]. \quad (7)
\]

We refer to this as the Bayesian \( A_W \)-criterion. We collectively refer to the different criteria discussed here as the \( A \)-criterion. To our knowledge, this is one of the earliest attempts at combining techniques from the weighted and Bayesian optimality literature.

The Bayesian \( A_W \)- and Bayesian \( A \)-criterion's ability to balance minimization of the primary variances and their aliasing with the potential terms is investigated with examples in Section 4.

We initially sought to prove the conjecture that for any of the \( A \)-criterion there always exists an optimal design such that all \( x_{ij} \in \{\pm 1\} \) for \( m \)-factor interaction models. For such models and criteria, the coordinate update formula is a ratio of two quadratic polynomials with respect to \( \tilde{x} \) and the optimum coordinate exchange can be found using fractional programming methods (Dinkelbach 1967). In the supplementary materials, we identify situations where the optimum is unique and occurs at a non-integer value. This result by itself does not disprove the conjecture, but it does provide evidence to the contrary. Section 4.1 further explores this conjecture algorithmically for certain \( n \) and \( k \) under the main effect model.

We next considered the unfortunate scenario in Corollary 1 with respect to the \( A \)-criterion. As demonstrated in (5), the coordinate update formula for each \( A \)-criterion involves a coordinate update for some \( D \)-criterion.

**Corollary 2.** For an \( m \)-factor interaction model and design, \( X_{00} \), consider one of the weighted criteria among the \( A \)-criterion for \( w > 0 \). If the update formula for the corresponding criterion among the \( D \)-criterion is constant, then \( \Delta_A^{W} \) is uniquely maximized. Moreover, \( \Delta_A^{W} \) is uniquely maximized when \( x_i^T (Z^T Z)^{-1} z_i < 1 \).

The corollary's condition \( x_i^T (Z^T Z)^{-1} z_i < 1 \) holds for practical cases of an intercept-only nuisance effect and block effects from \( b \) blocks each of size 2 or more. It provides further support for the \( A \)-criterion's ability to better differentiate designs than the \( D \)-criterion.
4. Examples

This section compares properties of algorithmically-generated optimal designs for three common screening models: (i) main effect models, (ii) two-factor interaction models, and (iii) quadratic models. All models have an intercept-only nuisance effect. For main effect models, we use the $A_*$- and $D_*$-criterion. For the other models, we also consider their Bayesian versions. The best designs generated are compared in terms of their main effect variances after fitting the main effect submodel and, when applicable, their aliasing with potential terms (two-factor interactions and/or quadratic effects).

4.1. Optimal Main Effect Plans

We constructed $A_*$- and $D_*$-optimal designs under the main effect model for $k = 3, \ldots, 20$ factors and $n = k + 1, \ldots, 24$ runs assuming either only discrete settings ($X_j = \{\pm 1, 0\}$) or only continuous settings ($X_j = [-1, 1]$). For continuous settings, we optimized (5) with box-constrained L-BFGS over $[-1, 1]$ (Byrd et al. 1995). Due to the demanding computations involved as $n$ and $k$ increase, each CEA was first performed with 100 random starts for both the continuous and discrete CEAs. We then recorded the best criterion value for the algorithms separately and the overall best value. If the two values were equal, we declared the value as optimal. Otherwise, the CEA with the inferior value was performed again with another 100 random starts. If the best value among this new batch did not improve the previous overall best value, the search was stopped. If the value did improve the overall best value, the other CEA was run for another 100 starts and the iterative process continued. Our back-and-forth search took no more than 1000 overall total starting designs. The $D_*$- or $A_*$-optimal designs were the designs with the best $D_*$- or $A_*$-value found across all iterations of both the discrete and continuous CEAs.

Figure 2(a) shows how many of the initial 100 constructed designs under the continuous CEA were $A_*$-optimal. A 0 value means the continuous CEA never found an $A_*$-optimal design among the initial batch of 100 random starting designs. Figure 2(b) shows the difference between the counts in Figure 2(a) with the same counts under the discrete CEA. Generally, when $n = k + 1$ or $k + 2$, the continuous CEA identified an $A_*$-optimal design more frequently than the discrete CEA. The discrete CEA found the $A_*$-optimal design more frequently in only 24% of the scenarios considered and struggled particularly in the cases of $(n, k) = (11, 10)$ and $(19, 18)$. For these cases, even increasing the number of starting designs to 10,000, the discrete CEA was unable to find an $A_*$-optimal design. The continuous CEA was able to find an $A_*$-optimal design for all cases when we increased the number of starting designs to 1000. We therefore recommend the continuous CEA for constructing $A_*$-optimal designs.

Contrary to our conjecture in Section 3.2, the $A_*$-optimal designs found by the continuous CEA for scenarios (11, 10) and (19, 18) contained non-integer values and are displayed in the supplementary materials. These designs do not significantly decrease the $A_*$-criterion compared to the best constructed designs requiring $X_j = \{\pm 1, 0\}$ as given in Jones, Allen-Moyer, and Goos (2020). The criterion value for the $(11, 10)$ $A_*$-optimal design we constructed was only 0.28% and 0.35% more $A_*$-efficient than the three- and two-level designs, respectively. The efficiency for the $(19, 18)$ $A_*$-optimal design with non-integer factor settings was 0.08% more efficient than the best discrete-level $A_*$-optimal design we generated.

Similar to Jones, Allen-Moyer, and Goos (2020), the main effect variances the $A_*$- and $D_*$-optimal designs we generated were the same except when $n$ was close to $k$ or when $n = 3 \pmod{4}$. For the designs where $n = 3 \pmod{4}$, we calculated the paired differences between the ordered main effect variances of the two designs. Across all such scenarios and pairs, 78% of the main effect variances from the $A_*$-optimal designs were smaller than those from $D_*$-optimal designs, 6% of them were equal, and 16% of them had larger variances for the $A_*$-optimal design. The largest individual decrease an $A_*$-optimal design's variance had compared to the $D_*$-optimal design was 0.05. There was one scenario where the $D_*$-optimal design decreased a variance over the $A_*$-optimal design by 0.06.
4.2. Two-Factor Interaction Model with $n = 15$, $k = 6$

Under the main effect model for scenario $n = 15$, $k = 6$, the $A_6$- and $D_6$-optimal designs were different, with the $A_6$-optimal design having zero coordinates for factors 5 and 6. We now consider this scenario under a two-factor interaction model including all interaction effects, which cannot be fully estimated. Thus, we constructed Bayesian $A_6$- and Bayesian $D_6$-optimal designs where the intercept is a nuisance effect, main effects are primary terms, and two-factor interaction effects are potential terms. We set $\tau^{-2} = 1, 5, 10, \ldots, 100$ and for each value we performed a CEA with 1000 starting designs.

Figure 3 depicts variances (in ascending order) under the main effect model for four designs with $n = 15$ and $k = 6$, (Left) Heatmap of alias matrices in absolute value form for main effects. (Right) Heatmap of alias matrices in absolute value form for interaction effects.

Figure 3 depicts variances (in ascending order) under the main effect model for scenario $n = 15$, $k = 6$, and was found for all 20 designs where the intercet is a nuisance effect, main effects are primary terms, and two-factor interaction effects are potential terms. We set $\tau^{-2} = 1, 5, 10, \ldots, 100$ and for each value we performed a CEA with 1000 starting designs.

As the main effect model and alias matrices for the Bayesian $A_6$- and Bayesian $D_6$-optimal designs generated in Section 4.1. The Bayesian $A_6$-optimal design was found for all $15 \leq \tau^{-2} \leq 100$ and had settings $x_{ij} \in \{\pm 1, 0\}$. The Bayesian $A_6$-optimal design for $\tau^{-2} = 10$ had a smaller $\text{tr}(A^T A)$ and had non-integer settings. The design is provided in the supplementary materials. The Bayesian $D_6$-optimal design shown in Figure 3 is comprised of $x_{ij} = \pm 1$ and was found for all $20 \leq \tau^{-2} \leq 100$. It was chosen due to its minimizing $\text{tr}(A^T A)$ among all constructed Bayesian $D_6$-optimal designs.

The $D_6$-optimal design estimates all main effects with equal variance, while the $A_6$-optimal design has smaller variances except for $\beta_6$. The Bayesian $A_6$-optimal design has both the smallest and largest individual variances. The Bayesian $A_6$- and $D_6$-optimal designs have superior aliasing properties over their non-Bayesian counterparts. The Bayesian $A_6$-optimal design minimized $\text{tr}(A^T A)$ compared to the other three designs. This reduced aliasing can in part be attributed to the 0 coordinates. When $x_{ij} = \pm 1$, a design with an odd number of runs will necessarily have some degree of column correlation. A design having some $x_{ij} = 0$ can achieve orthogonality between columns for such $n$ and hence zero elements in the alias matrix. Orthogonality through including $x_{ij} = 0$ will lead to larger variances for the associated main effects.

4.3. Screening Quadratic Models

Effect principles applied to a quadratic model leads to the partitioning of main effects as primary terms and potential terms of all two-factor interaction and quadratic effects. We assigned different prior precisions for the two-factor interaction and quadratic effects, denoted $\tau_{i}^{-2}$ and $\tau_{Q}^{-2}$, respectively. We constructed Bayesian $A_6$- and $D_6$-optimal designs under $\tau_{i}^{-2} \in \{1, 16\}$ and $\tau_{Q}^{-2} \in \{0, 1, 16\}$ using 10,000 starting designs. For $\tau_{Q}^{-2} = 0$, the quadratic effects become primary terms. We considered $k = 6, 8, 10$ and $n = (2k + 1), \ldots, (1 + k + k^2)$. The minimum $n$ value considered is that for a definitive screening design (Jones and Nachtsheim 2011a) and the last is a run size that allows estimation of the full model. A definitive screening design (DSD) has $k$ foldover pairs of $x_i$, each comprised of a single zero coordinate and $k - 1$ coordinates of $\pm 1$. DSDs have no aliasing of the main effects with the interaction and quadratic terms.

For a given design, let $F_M$, $F_I$, and $F_Q$ be the model matrices corresponding to the main effects, interactions, and quadratic effects, respectively. Each design is summarized using three metrics: (i) $\log(A_M)$ where $A_M$ is the sum of the main effect variances for a fitted main effect model; (ii) $\log(SS_Q)$ where $SS_Q$ is the sum of squared off-diagonals of $F_I^T F_I$ and (iii) $\log(SS_M + 1)$ where $SS_M$ is the sum of squared values of $F_M^T F_I$. The metrics $\log(SS_Q)$ and $\log(SS_M + 1)$ are surrogates for the information dedicated to quadratic effects and aliasing between main effects and interactions, respectively.

Figure 4 shows the numerical results for $k = 6$ factors; similar conclusions were reached for the $k = 8$ and $k = 10$ scenarios (see supplementary materials). Generally, the Bayesian $A_6$-optimal design’s variances under the main effect model were worse than those under the Bayesian $D_6$-optimal design. However, for fixed values $\tau_{Q}^{-2}$ and $\tau_{I}^{-2}$, the Bayesian $A_6$-optimal design had comparable or smaller values for $\log(SS_Q)$ and $\log(SS_M + 1)$, implying better estimation capacity and aliasing properties for the potential effects. The Bayesian $A_6$-optimal designs for $\tau_{Q}^{-2} = \tau_{I}^{-2} = 16$ closely resemble the structure of DSDs for $n = 13, \ldots, 20$ with no aliasing between main effects and interactions. The Bayesian $A_6$-optimal designs for $n = 13$ and 17 were a DSD and augmented DSD (Jones and Nachtsheim 2017), respectively. For $n = 14$ and $n = 18, 19, 20$, the Bayesian $A_6$-optimal designs added center runs (i.e., $x_i = 0$) to the DSD and augmented DSD, respectively. The Bayesian $A_6$-optimal design for $n = 15$ had one center run and seven pairs of foldover runs, mimicking the DSD structure. The Bayesian

Figure 3. (Left) Variance under main effect model for four designs with $n = 15$ and $k = 6$. (Right) Heatmap of alias matrices in absolute value for main effects.
$D_s$-optimal designs were less likely to identify designs with structures similar to DSDs for the $\tau_Q^{-2}$ and $\tau_I^{-2}$ we considered.

The behavior of the Bayesian $A_s$-optimal designs was influenced by the criterion’s implicit emphasis on quadratic effects due to their estimators having larger minimum variances than main effects and interactions. This phenomenon was mentioned for the $A_s$-criterion by Gilmour and Trinca (2012) and discussed thoroughly by Allen-Moyer and Stallrich (2022). To equally emphasize minimizing variances among all effects, both articles recommend an $A_W$-criterion that incorporates the minimum variances. Allen-Moyer and Stallrich (2022) refer to this $A_W$-criterion as the standardized $A_W$-criterion. Note, this modification is unnecessary for main effect and interaction models because these effects have the same minimum variance. Extending the weighted approach by Allen-Moyer and Stallrich (2022) to the Bayesian $A_s$-criterion requires the introduction of a weight matrix based on the minimum posterior variances for given prior variances. For the quadratic model, this would lead to a diagonal weight matrix with smaller weights assigned to quadratic effects. However, $\tau_Q^{-2}$ also controls the magnitude of the quadratic effects’ posterior variances so manipulating posterior variances for potential terms via weighting can be done equivalently through manipulation of $\tau_Q^{-2}$. Indeed, in Figure 4 we see that as $\tau_Q^{-2}$ increases, $\log(A_M)$ decreases and $\log(SS_Q)$ increases implying less focus on quadratic effects. We would expect the same behavior if we were to assign smaller weights to the quadratic effects.

5. A Blocked Screening Design for Vitamin Photosensitivity

Goos and Jones (2011) discuss a blocked screening experiment performed by a pharmaceutical manufacturer that aimed to determine a combination of vitamins and certain fatty molecules to reduce the vitamins’ photosensitivity, thereby increasing the product’s shelf life. There were six factors studied corresponding to the presence/absence of riboflavin as well as five fatty molecules. The measuring device required daily recalibration, allowing only four measurements per day. The experiment was broken up across eight days that allowed four runs per day, leading to a study of $k = 6$ factors and $b = 8$ blocks each of size $u = 4$. The experimenters wanted to be able to estimate all six main effects and 15 two-factor interactions because they were concerned about possible large interactions.

Many of the techniques for constructing fractional factorial designs can be employed to create blocked screening experiments but only for certain values of $b$ and $u$. For example, if $n = bu = 2^k$ and $b = 2^u$, we can block all $2^k$ treatment combinations by confounding $2^u - 1$ factorial effects with the block effects. All remaining factorial effects are estimated with minimal variance. If $n = bu = 2^{k-m}$ and $b = 2^u$, then we may block a fractional factorial design based on certain confounding patterns (Bisgaard 1994; Chen and Cheng 1999; Cheng and Mukerjee 2001; Cheng and Wu 2002). However, Cheng, Li, and Ye (2004) demonstrate nonregular fractional factorial design may have superior estimation and variance properties. For the vitamin photosensitivity experiment, a blocked regular fractional factorial will not be able to estimate all two factor interactions, an important property for their application.

Goos and Jones (2011) constructed a $D$-optimal blocked design algorithmically that can estimate all main effects and two-factor interaction effects. The experiment had only categorical factors, but we will treat them here as if they were continuous. We constructed blocked designs with the $D_s$-criterion, $A_s$-criterion, and a Bayesian $A_s$-criterion with $\tau_I^{-2} = 16$. The block effects were assigned weight $w = 10^{-6}$ and 10,000 starting designs were used. Although three different designs were constructed corresponding to the different criteria, the best design found under the Bayesian $A_s$-criterion, shown in Figure 5, was optimal across all criteria. Even after increasing the number of starting designs to 100,000, the CEAs for the $D_s$- and $A_s$-criteria were still unable to identify this design.

The optimal design we constructed is more $D$-efficient than the design reported in Goos and Jones (2011), and consists entirely of $\pm 1$ coordinates and so can be used in their application. The design turned out to be a nonregular fractional factorial with generalized resolution 3.75 and has only six words.

**Figure 4.** Performance measures for best Bayesian-$D_s$ and $A_s$ designs when $k = 6$ found with $\tau_Q^{-2} \in \{0, 1, 16\}$ and $\tau_I^{-2} \in \{1, 16\}$. (Left) The $A_s$-criterion for the main effect model on the log scale. (Middle) The sum of squares of the off-diagonals for the quadratic terms on the log scale. (Right) The sum of squares of the cross products of the main effects and interactions on the log scale with offset 1.
of length 4.5. Cheng, Li, and Ye (2004) tabulated designs with similar structure but only for \( n = 12, 16, \) and \( 20. \) Others have looked at minimizing generalized aberration for larger run sizes (see Fang, Zhang, and Li 2007; Schoen, Vo-Thanh, and Goos 2017), but not in the context of blocking. The main effects of the design are all estimated with optimal variance (1/32) and have zero aliasing with the block and interaction effects. Five of the 15 interactions are also estimated with optimal variance. The remaining interaction effects are partially correlated with the block effects, with eight of the interactions having a variance of 0.047 and the other two having a variance of 0.063.

6. Discussion

This article compares different forms of the \( D- \) and \( A- \) criterion for constructing screening designs that simultaneously minimize variances and bias of a predetermined set of effects in a linear model. We challenge two commonly held beliefs concerning screening designs:

- For arbitrary \( n, \) algorithmic optimization of the \( D- \) criterion produces a screening design that minimize variances.
- When constructing screening designs, one needs only to consider \( x_{ij} = \pm 1 \) even if \( x_{ij} \) is numeric and can take on other values in \([-1, 1]\).

Gilmour and Trinca (2012) and Jones, Allen-Moyer, and Goos (2020) have also pointed out the failing of the \( D- \) criterion, and we have further clarified these failings. Our investigation of the \( D_s- \) criterion’s CEA shows that many \( D_s- \) optimal designs can exist for a given scenario, having different variance and bias properties. The superior performance of our continuous CEA in Section 4.1 indicates that even if an \( A_s- \) optimal design is comprised of only \( x_{ij} \in \{\pm 1, 0\}, \) the continuous CEA more frequently constructs an \( A_s- \) optimal design than a discrete CEA. We also found some combinations of \( n \) and \( k \) where the \( A_s- \) optimal design included non-integer coordinates.

Our investigation of Bayesian \( A_s- \) and Bayesian \( D_s- \) optimal designs in Sections 4.2 and 4.3 revealed that the Bayesian \( A_s- \) criterion better balances variance and bias minimization for the prior variance values considered. In Section 5, we found that the optimal design constructed under the Bayesian \( A_s- \) criterion was also optimal under the \( A_s- \) and \( D_s- \) criterion, and that it was better than the designs constructed directly under these two criteria. This is unfortunately a possibility with algorithmic construction and we recommend practitioners generate multiple designs under different design criteria and compare them by inspecting their variances and biases directly, similar to Allen-Moyer and Stallrich (2022).

There are many directions of future research we are currently investigating. First, this article is combines weighted and Bayesian criteria, but mainly to ignore the variances of nuisance effects. Section 4.3 hinted at redundancies in weighting posterior effects but there may be opportunities for more flexible weighting applied to primary effects. Next, more investigation is needed to compare the Bayesian \( A_s- \) criterion to more brute force methods that minimize variance and bias. These methods commonly employ some type of \( D- \) criterion to measure variance which could easily be modified to be an \( A- \) criterion. Following Li, Sudarsanam, and Frey (2006), more investigation is needed on the difference of the optimal designs under the \( D- \) and \( A- \) criteria when higher-order interactions are considered. Finally, following Gilmour and Trinca (2012) and Jones et al. (2020), we are currently developing an \( A_s- \) criterion that includes external variance estimation through replication or fake factors.

Supplementary Materials

A PDF file includes proofs of all results and additional details of the optimization of the continuous coordinate exchange formula for the \( A- \) criteria. Tables for the optimal designs from Sections 4.2 are also included in the PDF as well as additional results for the quadratic screening designs from Section 4.3. The optimal main effect designs for \((n,k) = (11,10)\) and \((19,18)\) that include non-integer coordinates are given as .txt files. R files and jul scripts are included to perform algorithmic optimization of the described criteria.

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References

Ahipoaşoglu, S. D. (2021), "A Branch-and-Bound Algorithm for the Exact Optimal Experimental Design Problem," *Statistics and Computing*, 31, 65. [495]

Allen-Moyer, K., and Stallrich, J. (2022), "Incorporating Minimum Variances into Weighted Optimality Criteria," *The American Statistician*, 76, 262–269. [492,499,500]

Atkinson, A. C., Donev, A. N., and Tobias, R. D. (2007), *Optimum Experimental Design*, with SAS, Oxford: Oxford University Press. [492]

Bingham, D. R., and Chipman, H. A. (2007), "Incorporating Prior Information in Optimal Design for Model Selection," *Technometrics*, 49, 155–163. [495]

Bisgaard, S. (1994), "A Note on the Definition of Resolution for Blocked 2k−p Designs," *Technometrics*, 36, 308–311. [499]

Box, M., and Draper, N. R. (1971), "Factorial Designs, the |X^T|X| Criterion, and some Related Matters," *Technometrics*, 13, 731–742. [493,496]

Byrd, R. H., Lu, P., Nocedal, J., and Zhu, C. (1995), "A Limited Memory Algorithm for Bound Constrained Optimization," *SIAM Journal on Scientific Computing*, 16, 1190–1208. [497]

Chen, H. H., and Cheng, C.-S. (2004), "Optimal Design of Factorial Designs with Generalized Minimum Aberration," *Technometrics*, 46, 269–279. [499,500]

Cheng, C.-S. (1980), "Optimality of Some Weighing and 2\textsuperscript{a−m} Designs," *Annals of Statistics*, 8, 436–446. [494]

Cheng, C.-S. (2014a), "Optimal Biased Weighing Designs and Two-Level Main-Effect Plans," *Journal of Statistical Theory and Practice*, 8, 83–99. [494]

Cheng, C.-S., and Mukerjee, R. (2001), "Blocked Regular Fractional Factorial Designs with Maximum Estimation Capacity," *Annals of Statistics*, 29, 530–548. [499]

Cheng, S.-W., Li, W., and Ye, K. Q. (2004), "Blocked Nonregular Two-Level Factorial Designs," *Technometrics*, 46, 269–279. [499,500]

Cheng, S.-W., and Wu, C. F. J. (2002), "Choice of Optimal Blocking Schemes in Two-Level and Three-Level Designs," *Technometrics*, 44, 269–277. [499]

Cook, R. D., and Nachtsheim, C. J. (1989), "Computer-Aided Blocking of Factorial and Response-Surface Designs," *Technometrics*, 31, 339–346. [496]

Dean, A., and Lewis, S. (2006), *Screening: Methods for Experimentation in Industry, Drug Discovery, and Genetics*, New York: Springer. [492]

Dinkelbach, W. (1967), "On Nonlinear Fractional Programming," *Management Science*, 13, 492–498. [496]

Duarte, B. P. M., Granjo, J. O., and Wong, W. K. (2020), "Optimal Exact Designs of Experiments via Mixed Integer Nonlinear Programming," *Statistics and Computing*, 30, 93–112. [495]

DuMouchel, W., and Jones, B. (1994), "A Simple Bayesian Modification of D-Optimal Designs to Reduce Dependence on an Assumed Model," *Technometrics*, 36, 37–47. [493,495]

Esteban-Bravo, M., Leszkiewicz, A., and Vidal-Sanz, J. M. (2017), "Exact Optimal Experimental Designs with Constraints," *Statistics and Computing*, 27, 845–863. [495]

Fang, K.-T., Zhang, A., and Li, R. (2007), "An Effective Algorithm for Generation of Factorial Designs with Generalized Minimum Aberration," *Journal of Complexity*, 23, 740–751. [500]

Galil, Z., and Kiefer, J. (1980), "D-Optimum Weighing Designs," *Annals of Statistics*, 8, 1293–1306. [496]

Gilmour, S. G., and Trincu, L. A. (2012), "Optimum Design of Experiments for Statistical Inference," *Journal of the Royal Statistical Society*, Series C, 61, 345–401. [499,500]

Goos, P., and Jones, B. (2011), *A Screening Experiment in Blocks*, chap. 8, pp. 163–185, West Sussex: Wiley. [499]

Jacroux, M., Wong, C., and Masaro, J. (1983), "On the Optimality of Chemical Balance Weighing Designs," *Journal of Statistical Planning and Inference*, 8, 231–240. [494]

Jones, B., Allen-Moyer, K., and Goos, P. (2020), "A-Optimal versus D-Optimal Design of Screening Experiments," *Journal of Quality Technology*, 53, 369–382. [493,494,500]

Jones, B., Lekivetz, R., Majumdar, D., Nachtsheim, C. J., and Stallrich, J. W. (2020), "Construction, Properties, and Analysis of Group-Orthogonal Supersaturated Designs," *Technometrics*, 62, 403–414. [500]

Jones, B., and Nachtsheim, C. J. (2011a), "A Class of Three-Level Designs for Definitive Screening in the Presence of Second-Order Effects," *Journal of Quality Technology*, 43, 1–15. [492,498]

——— (2011b), "Efficient Designs with Minimal Aliasing," *Technometrics*, 53, 62–71. [493,495]

——— (2017), "Effective Design-Based Model Selection for Definitive Screening Designs," *Technometrics*, 59, 319–329. [498]

Joseph, V. R. (2006), "A Bayesian Approach to the Design and Analysis of Fractionated Experiments," *Technometrics*, 48, 219–229. [495]

Li, W., and Nachtsheim, C. J. (2000), "Model-Robust Factorial Designs," *Technometrics*, 42, 345–352. [495]

Li, X., Sudarshanam, N., and Frey, D. D. (2006), "Regularities in Data from Factorial Experiments," *Complexity*, 11, 32–45. [500]

Masaro, J. C. (1983), "Optimality of Chemical Balance Weighing Designs," Ph.D. thesis, University of Windsor. [494]

Meyer, R. K., and Nachtsheim, C. J. (1995), "The Coordinate-Exchange Algorithm for Constructing Exact Optimal Experimental Designs," *Technometrics*, 37, 60–69. [495]

Mitchell, T. J. (1974), "An Algorithm for the Construction of D-Optimal Experimental Designs," *Technometrics*, 16, 203–210. [496]

Mukerjee, R., and Wu, C. F. J. (2006), *A Modern Theory of Factorial Designs* (1st ed.), New York: Springer. [494,495]

Schoen, E. D., Vo-Thanh, N., and Goos, P. (2017), "Two-Level Orthogonal Screening Designs With 24, 28, 32, and 36 Runs," *Journal of the American Statistical Association*, 112, 1354–1369. [494,500]

Sherman, J., and Morrison, W. J. (1950), "Adjustment of an Inverse Matrix Corresponding to a Change in One Element of a Given Matrix," *The Annals of Mathematical Statistics*, 21, 124–127. [496]

Smucker, B. J., del Castillo, E., and Rosenberger, J. L. (2012), "Model-Robust Two-Level Designs Using Coordinate Exchange Algorithms and a Maximin Criterion," *Technometrics*, 54, 367–375. [495]

Stallings, J. W., and Morgan, J. P. (2015), "General Weighted Optimality of Designed Experiments," *Biometrika*, 102, 925–935. [496]

Toman, B. (1994), "Bayes Optimal Designs for Two- and Three-Level Factorial Experiments," *Journal of the American Statistical Association*, 89, 937–946. [495]

Tsay, P.-W., and Gilmour, S. G. (2010), "A General Criterion for Factorial Designs Under Model Uncertainty," *Technometrics*, 52, 231–242. [495]

Tsay, P.-W., Gilmour, S. G., and Mead, R. (2007), "Three-Level Main-Effects Designs Exploiting Prior Information About Model Uncertainty," *Journal of Statistical Planning and Inference*, 137, 619–627. [495]

Vazquez, A. R., Schoen, E. D., and Goos, P. (2022), "Two-Level Orthogonal Screening Designs with 80, 96, and 112 Runs, and up to 29 Factors," *Journal of Quality Technology*, 54, 338–358. [495]

Wong, C. S., and Masaro, J. C. (1984), "A Optimal Design Matrices X = (x_0)_{n×m} with x_0 = [−1, 0, 1]^T," *Linear and Multilinear Algebra*, 15, 23–46. [494]

Wu, C. F. J., and Hamada, M. (2009), *Experiments: Planning, Analysis, Optimization*, Hoboken, NJ: Wiley. [492,494]