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Experimental designs for multiple responses with different models

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DEDICATION

To my husband Dave.

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ABSTRACT

Central composite designs [Box and Wilson (1951)] and Box-Behnken designs [Box and Behnken (1960)] are both widely accepted and used experimental designs for fitting second order polynomial models in response surface methods. However, these designs are based only on the number of explanatory variables (factors) that are being investigated, and do not take into account any prior information about the system being investigated. In a multivariate problem where prior information is available in the form of a screening experiment or previous process knowledge, investigators often know which factors will be used in the estimation of each response. This work presents alternative designs based on central composite designs and Box-Behnken designs that result in fewer required runs, saving investigators both time and money, by taking this prior information into account.

CHAPTER 1. INTRODUCTION

When conducting an experiment, the first step is to select an appropriate experimental design. Many designs with favorable properties have been suggested for the case where there is one response variable and one or more explanatory variables. However, if there is more than one response variable, and different subsets of explanatory variables are needed to model each response, these designs often require more experimental runs than are necessary for efficient model estimation. In this thesis, we develop modifications of two standard classes of experimental designs that support estimation of multiple response models using fewer experimental runs.

The situation often arises in engineering that a system has multiple response variables and multiple explanatory variables, and some additional information is available on which explanatory variables are related to each response variable. This information can come from screening experiments, or, as is often the case in industry, the information can come from process knowledge. If a particular product has been in production for many years, the engineers or scientists who work with the system often can narrow down the number of explanatory variables for each response.

If a full second order model is being considered for each response (which is often the case when, for example, system optimization is the ultimate goal of the experimental program), this additional information can be used to reduce the total number of terms required in the response models, and to allow some pairs of terms from different response models to be confounded with each other without damaging the quality of parameter estimates. Interaction terms for two factors that are not related to the same response can be removed, and pairs of first and second order terms that do not both appear in a model for any individual response can be confounded. Designs that take advantage of those facts to provide model estimation while requiring fewer experimental runs than are required for standard designs will be presented here.

1.1 Bio Fuels Application

One system that has multiple explanatory and response variables is the production of co-fire fuel pellets. Co-fire pellets are a mixture of crushed coal and oil derived from plant matter that is formed into pellets. The pellets are then used as a fuel. In a study of co-fire pellets by Friend (2013), fifteen explanatory variables were considered including coal particle size, coal moisture content, pellet aging temperature and amount of bio-oil binder. There were also twelve different response variables including the heating value, moisture content, carbon content and strength of the pellets. In this particular example, the researcher chose to conduct the experiment varying only the four explanatory variables listed here while holding the others constant. Suppose that this experiment had been conducted only as a screening study (i.e. one focused on identifying the factors that influence each response, rather than a more detailed study to quantify those relationships), and that it resulted in the identification of active factors indicated in Table 1.1 for each response. An X in the table indicates that the response associated with that row is related to the factor associated with that column. This shows that coal particle size and coal moisture content are related to the heating value, but pellet aging temperature and the amount of bio-oil binder are not. The second line indicates that coal moisture content and the amount of bio-oil binder are related to the pellet moisture content. This is physically reasonable because these two explanatory variables quantify the moisture being added to the pellet mixture. Row three indicates that pellet aging temperature and the amount of bio-oil binder are related to pellet carbon content, and row four indicates that of the four explanatory variables being considered, only coal moisture content is related to pellet strength.

Our intent now is in designing a detailed follow-up experiment that will support efficient estimation of a full quadratic response surface model for each response, including only the appropriate factors in each case. Quadratic response surface models are popular in settings where characteristics of the system quantified by the response variables are to be optimized by selection of values for the independent variables, e.g. Myers et al. (2002). The designs we will propose for this purpose are modifications of Central Composite Designs [Box and Wilson (1951)] and Box-Behnken Designs [Box and Behnken (1960)] . These two standard classes of designs are reviewed in sections 1.3 and 1.4.

Table 1.1 Relationship between explanatory and response variables for co-fire pellets

		Explanatory Variables			
		Coal particle size	Coal moisture content	Pellet aging temp	Amt. of bio-oil binder
Response Variables	Heating value	X	X		
	Moisture content		X		X
	Carbon content			X	X
	Strength		X		

1.2 Optimal Designs For Multiple Responses

Some designs, and algorithms for constructing designs, have been proposed for multivariate response surface models that have varying degrees of flexibility. The statistical package JMP includes a custom design menu that can be used to create a D-optimal design for univariate regression. A D-optimal design is one that maximizes the determinant of the design moment matrix, which minimizes the volume of the confidence region of the regression parameters (Myers et al., 2002, p. 393). This can be used in the multivariate case where each response has a different model by combining all terms that would be included in the model for any response into a single model and using the

JMP custom design menu to create a D-optimal design for that single model (Jennifer H. Van Mullekom, personal communication, November 17, 2014). This design may not be D-optimal for any individual response model, but it does offer an improvement over designs that do not take into account any of the screening information.

Another option that has been proposed is that of a so-called MD-optimal design, a multiresponse version of a D-optimal design. Fedorov (1972) proposed one such design, but this requires that the variance-covariance matrix of the response be known, which is often not a reasonable assumption. Cooray-Wijesinha and Khuri (1987) suggest an alternative where the variance-covariance matrix is estimated with an initial design and then used to add points to the design. This makes experiments difficult to plan and execute properly. Chang (1997) suggests a design that does not share either of these shortcomings, but does not offer the flexibility to use different models for each response suggested by screening experiments or previous knowledge. The design he suggests allows for each response have either a complete first- or second-order model, but all response models contain all factors.

1.3 Central Composite Design

We turn now to a review of Central Composite Designs and Box-Behnken designs. The new designs we describe in Chapters 2 and 3 are modifications of these two standard classes of designs for the multiple-response setting. A Central Composite design (CCD) [Box and Wilson (1951)] is one of the most common experimental designs for estimating a full second order polynomial regression model. It consists of three parts: a two level full or fractional factorial, axial points, and center points. This design, as well as all subsequent designs, will be described in terms of unitless coded variables that are centered on zero and scaled to a common range.

A full factorial design consists of every combination of levels for all factors (explanatory variables) being considered. In an unreplicated two-level full factorial, there are 2^k (where k is the number of factors) runs consisting of every combination of a "high" level and "low" level (denoted $+$ and $-$) for each factor. This design alone gives full estimation of all main effects, all interactions of every order, and an intercept, 2^k terms total. A subset of a full factorial that confounds one or more main effect or interaction terms with the intercept is called a regular fractional factorial, and contains a number of runs that is a smaller power of 2 (Myers et al., 2002, p. 178). Terms that likely have no effect, or whose effect is not of interest, are typically chosen; often high order interaction terms are used. Using high order interactions is also beneficial because the choice of terms to confound with the intercept will also result in certain other sets of terms being fully confounded with each other, and we typically do not want confounding between main effects or low order interaction terms. Resolution V fractional factorials are commonly used in CCDs because they are the smallest regular fractional factorials that allow estimation of all first- and second-order effects. The resolution of a fractional factorial design [Box and Hunter (1961)] is the lowest order interaction that is confounded with the intercept, so for a resolution V fraction, only five-factor and higher-order interactions are confounded with the intercept. This also guarantees that main effects are not confounded with other main effects, or two- or three-factor interactions, and that two-factor interactions are not confounded with each other. This is necessary when estimation of a full quadratic model is desired, and provides full estimation of main effects and two-factor interactions. Because designs of greater resolution require more experimental runs, fractional factorials of resolution VI, VII, etc. are not usually used in CCDs unless models of order more than two are contemplated.

The axial points in a Central Composite design are experimental runs where all factors are held constant at (coded) zero except for one. The one factor that is varied is set to $+\alpha$ for one run and $-\alpha$ for one run where α is often called a "design parameter" and can be adjusted relative to the value of 1 used in the factorial runs. This is done for each factor. These $2k$ runs along with center points allow for estimation of model parameters in squared terms. Center points are experimental runs where all factors are set to zero. This is where replication is incorporated into the design. The number of center points is also regarded as a "design parameter", and will be denoted here as n_c.

Consider a Central Composite design in three factors shown in Table 1.2. As there are no five-factor interactions here, no resolution V fraction is possible, and a 2^3 full factorial is used. For this and other designs displayed in this paper, "+" and "−" represent "+1" and "−1" for coded experimental variables. An additional $2 \times 3 = 6$ axial points are added, as well as $n_c = 4$ center points. More generally, the minimal number of experimental runs (N) required for a CCD in $k = 2, 3, 4, \ldots, 10$ factors is given in Table 1.3.

Table 1.2 Central composite design in three factors

	factor 1	factor 2	factor 3
full factorial	+	+	+
	+	+	-
	+	-	+
	+	-	-
	-	+	+
	-	+	-
	-	-	+
	-	-	-
axial points	$+\alpha$	0	0
	$-\alpha$	0	0
	0	$+\alpha$	0
	0	$-\alpha$	0
	0	0	$+\alpha$
	0	0	$-\alpha$
center points	0	0	0
	0	0	0
	0	0	0
	0	0	0

Table 1.3 Number of runs required for a Central Composite design where resolution V fractional factorials are used for $k > 5$ independent variables

k	2	3	4	5	6	7	8	9	10
N	$8+n_c$	$14+n_c$	$24+n_c$	$26+n_c$	$44+n_c$	$78+n_c$	$80+n_c$	$146+n_c$	$148+n_c$

1.3.1 Ten Factor Example – CCD

Consider an experiment with ten factors. The CCD is composed of a 2_V^{10-3} fractional factorial, that is, a 2^{-3} fraction of resolution V in $2^{10-3} = 128$ experimental runs, $2(10) = 20$ axial runs, and n_c center points for a total of $148 + n_c$ runs. This is illustrated in Table 1.4, where $\pm$ here indicates the factor is part of the fractional factorial for these runs.

Table 1.4 Central composite design in 10 factors

	1	2	3	4	5	6	7	8	9	10
res V fraction	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$
axial points	$+\alpha$	0	0	0	0	0	0	0	0	0
	$-\alpha$	0	0	0	0	0	0	0	0	0
	0	$+\alpha$	0	0	0	0	0	0	0	0
	0	$-\alpha$	0	0	0	0	0	0	0	0
					⋮					
	0	0	0	0	0	0	0	0	0	$+\alpha$
	0	0	0	0	0	0	0	0	0	$-\alpha$
center points	0	0	0	0	0	0	0	0	0	0
					⋮					
	0	0	0	0	0	0	0	0	0	0

1.4 Box-Behnken Design

Another common design for estimating quadratic models is a Box-Behnken design [Box and Behnken (1960)]. These designs typically require more runs than CCDs in the same number of variables, but are still preferred by some scientists and have desirable design properties. To construct a Box-Behnken design in k factors, first identify an incomplete block design with k treatments divided into blocks of size b. (Balanced incomplete block designs (Morris, 2011, p. 109) are often used, in which each of the k treatments is applied to the same number of experimental units, and each of the $\binom{n}{k}$ pairs of treatments are applied to the same number of pairs of experimental units in a common block.) Each of the k treatments corresponds to one of the k factors. For each block in this treatment design, add 2^b experimental runs to the regression design that form a full two-level factorial in the experimental variables corresponding to treatments that are in that block, and zero for experimental variables corresponding to treatments not in that block. As with CCDs, add an additional n_c center points where all factors are held constant at zero. Box and Behnken (1960) recommend designs with an optimal choice of b for $k = 3, 4, 5, 6, 7, 9, 10, 11, 12,$ and 16.

For example, to construct a Box-Behnken design for $k = 4$ factors, begin by considering a balanced incomplete block design (BIBD) with $k = 4$ treatments and six blocks of size $b = 2$ shown in Table 1.5. The first block has treatments 1 and 2 so the first four runs of the Box-Behnken design are a full factorial in factors 1 and 2 and zero for factors 3 and 4. These first four runs are shown in Table 1.6. Repeating this for the remaining five blocks, Table 1.7 shows the full Box-Behnken design. Here each of the first six lines represents four runs where $\pm$ denotes that factor is part of the factorial for that set of four runs. The last line represents $n_c = 3$ center points; this is the number of center points recommended by Box and Behnken (1960) for four factors.

Table 1.5 BIBD in $k = 4$ treatments and block size $b = 2$

1	1	1	2	2	3
2	3	4	3	4	4

1.4.1 Ten Factor Example – Box-Behnken

Consider again the ten factor example described in section 1.3.1. Box and Behnken (1960) recommend that in the initial incomplete block design step of construction, blocks

Table 1.6 First four runs of Box-Behnken design for $k = 4$ factors

1	2	3	4
+	+	0	0
+	-	0	0
-	+	0	0
-	-	0	0

Table 1.7 Box-Behnken design for $k = 4$ factors

1	2	3	4
$\pm$	$\pm$	0	0
$\pm$	0	$\pm$	0
$\pm$	0	0	$\pm$
0	$\pm$	$\pm$	0
0	$\pm$	0	$\pm$
0	0	$\pm$	$\pm$
0	0	0	0

of size four are used. These blocks are shown in Table 1.8. This is a partially balanced incomplete block design (PBIBD) because within a common block, each of the k treatments is applied to the same number of experimental units, but the $\binom{n}{k}$ pairs of treatments are divided into groups (typically two groups) and the pairs of treatments within each group are applied to the same number of pairs of experimental units (Morris, 2011, p. 122). The full Box-Behnken design is shown in Table 1.9. Each of the first ten rows represent sixteen runs where $\pm$ indicates that factor is part of a 2^4 full factorial for those runs and all other factors are held constant at zero. The last row represents ten center points for a total of 170 runs.

Table 1.8 BIBD in $k = 10$ treatments (factors) and blocks size $b = 4$

2	1	2	2	1	3	1	3	1	4
6	2	3	4	8	4	4	5	3	5
7	5	7	6	9	5	7	7	6	6
10	10	8	9	10	10	8	9	9	8

Table 1.9 Box-Behnken design for 10 factor example

1	2	3	4	5	6	7	8	9	10
0	±	0	0	0	±	±	0	0	±
±	±	0	0	±	0	0	0	0	±
0	±	±	0	0	0	±	±	0	0
0	±	0	±	0	±	0	0	±	0
±	0	0	0	0	0	0	±	±	±
0	0	±	±	±	0	0	0	0	±
±	0	0	±	0	0	±	±	0	0
0	0	±	0	±	0	±	0	±	0
±	0	±	0	0	±	0	0	±	0
0	0	0	±	±	±	0	±	0	0
0	0	0	0	0	0	0	0	0	0

1.5 Room for Improvement

Experiments carried out using either the CCD or Box-Behnken designs described above can be used to estimate a full quadratic response surface model in all k independent variables. These models treat all factors symmetrically, but in the multivariate case where information from a screening experiment or previous process knowledge is available, this is not always necessary. As demonstrated by the example in the next paragraph, some two-factor interactions do not need to be estimated for any response model. We can take advantage of this fact to reduce the size of the experimental design.

Consider a multivariate problem with ten explanatory variables (factors) and four response variables, where the results of a screening experiment are shown in Table 1.10. A standard CCD or Box-Behnken design, however, is the same for any ten factors regardless of these known relationships. These two standard designs are described in section 1.3.1 and section 1.4.1. The CCD and Box-Behnken designs support estimation of all 45 two-factor interactions, but the full quadratic model for response one would have only ten two-factor interactions and responses two, three and four would each have six two-factor interactions. This adds to only 28 two-factor interactions; however, the factor 3-factor 4, factor 3-factor 5, factor 3-factor 7 and factor 4-factor 8 interactions have been counted twice so there are, in fact, only 24 two-factor interactions used to estimate any of the four responses.

Table 1.10 Results of screening for example 1 (with 10 factors)

		factor									
		1	2	3	4	5	6	7	8	9	10
response	1	X	X	X	X	X					
	2			X		X	X	X			
	3			X	X			X	X		
	4				X				X	X	X

The biggest reduction in size for the CCD, however, comes from the opportunity to confound some main effects. Since not all of the terms appear in each model, pairs of effects that do not appear in any model can be confounded, permitting further reduction in the size of the design. For instance, in this example factors 1 and 6 never appear in the same model, so they can be confounded. This means that in the factorial part of the CCD, the levels for factor 1 can be exactly repeated for factor 6 without any loss of estimability. The same can be done with factors 2 and 7, 1 and 8, 2 and 9, and 3 and 10. This means that the factorial part of the CCD can actually be the same size as it would be if there were only five factors. Designs that take advantage of these facts will be presented in this work. A CCD type design presented in chapter 2 requires only $52 + n_c$ runs for the example in Table 1.10 as opposed to the standard CCD, which requires $148 + n_c$ runs. For the same example, a Box-Behnken type design presented in section 3.1 requires only $96 + n_c$ runs as opposed to the $160 + n_c$ required in the standard Box-Behnken design.

1.6 Overview of Thesis

In chapters 2 and 3, I will introduce new designs for the situation where there are multiple response variables and multiple explanatory variables, and there is either a screening experiment or process knowledge that identifies which explanatory variables are related to each response. I will introduce Central Composite type designs in chapter 2 and Box-Behnken type designs in chapter 3.

Our emphasis is on designs that employ a relatively small number of experimental runs while satisfying the estimability requirements of the problem with reasonable statistical efficiency. In most cases, the standard (larger) CCD and Box-Behnken designs produce more precise estimates of the model parameters. Hence the standard designs may still be preferable in cases where the error variances are large and the per-run cost of experimentation is not great. The primary practical value of our new designs is where the error variances are not large and/or it is important to limit the size of the experiment.

CHAPTER 2. CENTRAL COMPOSITE TYPE DESIGNS

As discussed in section 1.3, Central Composite Designs (CCD) are commonly used when a quadratic model is desired for univariate regression. These designs consist of a full factorial or resolution V fractional factorial design in all factors, axial points and center points. Here we address modifications of the CCD for situations in which there are r response variables and k experimental factors, where screening experiments or process knowledge suggests that only a subset of the k factors is needed in modeling for each response, and where these factor subsets are generally different for each response. The primary changes we propose for the CCD are associated with selection of the fractional factorial portion of the design. Axial points are still needed to estimate squared terms, but center points do not need to be added because the axial points for factors not related to a particular response provide center points for estimating that response. As discussed in section 1.5, a full factorial or resolution V fractional factorial in all factors is often a much larger design than we need to maintain estimability for each response.

The following section will describe an algorithm for constructing a fractional factorial design in all factors such that for any given response, the factors associated with that response form a full factorial. When this factorial design is combined with axial points, this will be a modified CCD with a full factorial point set for each response, but not for all k factors together, and so will require fewer runs than the traditional CCD.

2.1 Algorithm 1 for Generating Fractional Factorial for CCD

To construct a fractional factorial design that is a full factorial in the factors related to each response, begin by ordering the responses by the number of factors related to them. This will reduce the likelihood of encountering large sets of factors related to a single response with many confounded factors later in the algorithm. (We refer to the factors associated with any response as a "group" or "set" of factors in the following discussion.) Address each group of factors one at a time beginning with the largest set and working through to the smallest set. Initialize the design with a full factorial design in the first set of factors, leaving the remaining factors undefined. For each set of factors after that, the design in modified to incorporate previously undefined factors in such a way that all factor sets are represented by (possibly replicated) full factorial arrangements.

When a new set of factors is considered, there are four possible situations for each factor in that set. These cases depend on the current state of the design. First, for the factors within the set that have already been included in the design (i.e have already been included in previous factor sets), we look for the largest subset of these factors that form a full factorial. Then the first situation to consider for an individual factor is that the factor could already be a part of this largest full factorial within this set. In this case, nothing needs to be done. Second, the factor could be part of a previous set and the overall design thus far, but not part of the largest full factorial within the current set. To update the overall design so that this factor is included in the largest full factorial in the current set, repeat the overall design assembled so far, but use the negative (i.e. switch all +'s to -'s and all -'s to +'s) of this particular factor in the second copy. As a result, the previous largest full factorial set now includes the new factor. This will be referred to as doubling the design on the factor. Once all factors that fall into the first two cases have been addressed, all of the factors from this set that are a part of the overall design thus far will form a full factorial. The third and forth cases involve factors that have not yet been included in the overall design. For as many of these as possible, simply copy the levels of a factor that is not in this set (i.e. confound the factor with another factor not used in the model for this response), being careful to choose factors to copy that are not already confounded with other factors in the current set. Finally, for each remaining factor, initialize with a column of +'s and double the design on that factor. This will guarantee that the set currently being addressed forms a full factorial without disrupting the full factorial constructed for any previous sets. This process is described more formally in the algorithm below.

2.1.1 Algorithm 1

1. Order responses by number of factors important to them (decreasing order). Label the set of factors important to group i as C_i

2. Initialize the design D_1 with a full factorial of the elements of C_1.

3. For $i = 2...r$:

   (a) Divide the factors in C_i into two groups:

   - A_i that are elements of D_{i-1}
   - B_i that are not

   (b) Find the largest set of factors in A_i that form a (possibly replicated) full factorial. (Call this set $A_{1,i}$) Double* the design for each factor of A_i that is not in this set. (Call this set $A_{2,i}$) Call this design D^b_{i-1}.

   (c) For as many factors as possible in B_i, confound with factors in D^b_{i-1} that are not in A_i so that set of factors in $A_i \cup B_{1,i}$ form a (possibly replicated) full factorial, where $B_{1,i}$ is the set of factors in B_i that can be confounded with existing factors and $B_{2,i}$ is the set of factors in B_i that cannot. Call this design D^c_{i-1}.

(d) For each factor in $B_{2,i}$, double* the design. Call the resulting design D_i.

* By "double the design", I mean repeat the entire design assembled so far, using the negative (i.e. switch all +'s to -'s and all -'s to +'s) of the factor being used to "double" for the second copy.

2.1.2 Walk Through Algorithm 1

As a small example of how the algorithm works, consider the result of a screening experiment with five factors and three response variables. The first response is related to factors 1 and 4; the second to factors 1, 2 and 3; and the third to factors 3, 4 and 5. First, order the responses by the number of factors that are important to them so that the largest set of factors will be addressed first. For this system, $C_1 = \{1, 2, 3\}$, $C_2 = \{3, 4, 5\}$ and $C_3 = \{1, 4\}$. (Note that at this point you could also label them: $C_1 = \{3, 4, 5\}$, $C_2 = \{1, 2, 3\}$ and $C_3 = \{1, 4\}$.)

Begin by considering the elements of C_1 and construct a full factorial in only the factors that are elements of C_1. Call this design D_1. For C_2, factor 3 already forms a full factorial. If we repeat factor 1 as factor 4 and factor 2 as factor 5, then factors 3, 4, and 5 form a full factorial. Finally, consider the factors in C_3. Since factors 1 and 4 are now identical, we need to double the design on factor 4 (or factor 1) so that factors 1 and 4 form a full factorial. The final design D_3 is now a full factorial in the three groups of factors $C_1 = \{1, 2, 3\}$, $C_2 = \{3, 4, 5\}$ and $C_3 = \{1, 4\}$. See Table 2.1 for the design at each step of the algorithm. In this example, the final design D_3 is a full 2^4 factorial in factors $\{1, 2, 3, 4\}$ or $\{1, 3, 4, 5\}$, or a half-fraction of resolution II in all five factors since the factor 2 - factor 5 interaction is confounded with the intercept. This example was chosen to illustrate the different situations that the algorithm addresses and not the reduced size the algorithm can provide as the algorithm was designed to benefit response surface problems with a larger number of factors. (In fact, for this problem, a regular fractional factorial of resolution V in all five factors in 16 runs could have been selected, which would also yield a full factorial design in the factors associated with each response.) Further examples in section 2.3 illustrate the reduction in design size provided by the algorithm.

Table 2.1 Designs D_1, D_2 and D_3 showing each step of the algorithm

D_1					D_2					D_3				
1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
+	+	+			+	+	+	+	+	+	+	+	+	+
+	+	-			+	+	-	+	+	+	+	-	+	+
+	-	+			+	-	+	+	-	+	-	+	+	-
+	-	-			+	-	-	+	-	+	-	-	+	-
-	+	+			-	+	+	-	+	-	+	+	-	+
-	+	-			-	+	-	-	+	-	+	-	-	+
-	-	+			-	-	+	-	-	-	-	+	-	-
-	-	-			-	-	-	-	-	-	-	-	-	-
										+	+	+	-	+
										+	+	-	-	+
										+	-	+	-	-
										+	-	-	-	-
										-	+	+	+	+
										-	+	-	+	+
										-	-	+	+	-
										-	-	-	+	-

2.1.3 Proof of Algorithm 1

The following is a formal proof that designs constructed via Algorithm 1 are full factorial arrangements, possibly replicated, in the factors associated with each response.

Proof: (By induction)

Base Step: (We want to show (WWTS) that D_1 is a (possibly replicated) full factorial for the elements of C_1.)

By definition, D_1 is a full factorial for the elements of C_1.

Inductive Step: Assume D_{i-1} is a (possibly replicated) full factorial for each set of factors $C_1, \ldots, C_{i-1}$. (WWTS that D_i is a (possibly replicated) full factorial for the elements of each of $C_1, \ldots, C_{i-1}, C_i$.)

Step 1: (WWTS D_i is a (possibly replicated) full factorial for the elements of each of $C_1, \ldots, C_{i-1}$.)

By assumption, D_{i-1} is (possibly replicated) full factorial for the elements of each of $C_1, \ldots, C_{i-1}$. Each replicate from the "doubling" step will also be a (rep) full factorial for the elements of each of $C_1, \ldots, C_{i-1}$, so D^b_{i-1} is a (rep) full factorial for the elements of each of $C_1, \ldots, C_{i-1}$.

For factors in $C_1, \ldots, C_{i-1}$, D^c_{i-1} is identical to D^b_{i-1}, so D^c_{i-1} is a (rep) full factorial for the elements of each of $C_1, \ldots, C_{i-1}$.

For factors in $C_1, \ldots, C_{i-1}$, D^c_{i-1} is repeated to produce D_i, so D_i is a (rep) full factorial for the elements of each of $C_1, \ldots, C_{i-1}$.

Step 2: (WWTS D_i is a (rep) full factorial for the elements of C_i.)

By definition, D_{i-1} is (rep) full factorial for the elements of $A_{1,i}$. By doubling the design on each factor in $A_{2,i}$, D^b_{i-1} will be a (rep) full factorial for the elements of $A_{1,i} \cup A_{2,i} = A_i$.

By definition, D^c_{i-1} is a (rep) full factorial for the elements of $A_i \cup B_{1,i}$.

By doubling the design on each factor in $B_{2,i}$, D_i will be a (rep) full factorial for the elements of $A_i \cup B_{1,i} \cup B_{2,i} = C_i$.

2.2 Algorithm 2 for Generating Fractional Factorial for CCD

Algorithm 1 guarantees that the set of factors related to each response is a full factorial, but the size of the resulting design can be affected by the order in which both the factors and response variables are considered. A second, less complex algorithm will be presented here that relies only on the order of the factors. For Algorithm 2, consider each of k factors one at a time, assigning each to be a copy of one of k^* unique factors. Factor 1 will be assigned as unique factor 1^*. For each subsequent factor, consider which response variables it is related to. Then, list all unique factors (assigned at this point) that are related to any of those response variables. Assign the lowest numbered unique factor that is not on that list to the current factor. k^* is determined as the number of unique factors used once all factors have been assigned. Finally, construct a resolution $\max_i k_i + 1$ fractional factorial, where k_i is the number of factors related to response i, in all k^* unique factors. If $k^* = \max_i k_i$, a fractional factorial of resolution $\max_i k_i + 1$ does not exist, so a full factorial in the k^* unique factors is used.

Since the results of this algorithm are dependent on the order in which the factors are considered, it is wise to repeat the algorithm with multiple orderings of factors. If the number of unique factors suggested by the algorithm is equal to the largest number of factors related to a single response ($k^* = \max_i k_i$), then that is the smallest number of unique factors possible (but it is likely not the only possible assignment of those unique factors). If a larger number of unique factors is required ($k^* > \max_i k_i$), it is possible to prove that it is the smallest number on a case-by-case basis. This will be illustrated in example 2.

As discussed in section 1.3, resolution V fractional factorials are often used in CCDs. Algorithm 2 can easily be extended to resolution V, or any stated resolution, by constructing a fractional factorial of that resolution in the k^* unique factors.

2.2.1 Algorithm 2

1. Label the set of responses related to factor l as A_l.

2. Define unique factor 1^*, initialize set B_{1^*} as $B_{1^*} = \{A_1\}$ and initialize set C_{1^*} as $C_{1^*} = \{1\}$.

3. For $l \in \{2, \ldots, k\}$

   (a) If $A_l \cap B_{m^*} = \emptyset$ for some $m^* < l$, for minimum unique factor m^* s.t. $A_l \cap B_{m^*} = \emptyset$, redefine $B_{m^*} = B_{m^*}^{\text{old}} \cup \{A_l\}$ and $C_{m^*} = C_{m^*}^{\text{old}} \cup \{l\}$.

(b) If $A_l \cap B_{m^*} \neq \emptyset$ for all $m^* < l$, define a new unique factor $(\max m^* + 1)^*$ and initialize sets $B_{(\max m^*+1)^*}$ and $C_{(\max m^*+1)^*}$ as $B_{(\max m^*+1)^*} = \{A_l\}$ and $C_{(\max m^*+1)^*} = \{l\}$.

4. Construct a resolution $(\max_i k_i + 1)$ fractional factorial in all k_i^* unique factors to construct a full factorial in each set of factors related to a single response, or construct a resolution V fractional factorial in all k_i^* unique factors to construct a resolution V fractional factorial in each set of factors related to a single response.

5. For each unique factor $m^* \in \{1, \ldots, k^*\}$ and $l \in C_{m^*}$, set $l = m^*$.

2.2.2 Walk Through Algorithm 2

Consider the results of a screening experiment provided in Table 2.2. Factor 1 is assigned to unique factor 1^*. Factor 2 cannot be unique factor 1^* because both are related to response 1, so it is assigned to be unique factor 2^* (the next lowest number). Factor 3 cannot be unique factor 1^* or 2^* because all three are related to response 1, so it is assigned to be unique factor 3^*. Factor 4 cannot be unique factor 2^* or 3^* because all three are related to response 2, nor can it be unique factor 1^* because both are related to response 4, so it is assigned to be unique factor 4^*. Factor 5 cannot be unique factor 1^* or 3^* because all three are related to response 3, so it is assigned to be unique factor 2^*. The largest number of factors associated with any response is 3, so constructing a resolution 4 fractional factorial in the $k^* = 4$ unique factors yields a design that is a full factorial in the factors associated with each response. The final design is shown in Table 2.3.

2.2.3 Proof of Algorithm 2

The following is a formal proof that designs constructed via Algorithm 2 are full factorial arrangements, possibly replicated, in the factors associated with each response

Table 2.2 Results of screening for walk through algorithm 2

		factor 1	2	3	4	5
response	1	X	X	X		
	2		X	X	X	
	3	X		X		X
	4	X			X	

Table 2.3 Design for walk through algorithm 2

factor	1	2	3	4	5
unique factor	1^*	2^*	3^*	4^*	2^*
	+	+	+	+	+
	+	+	-	-	+
	+	-	+	-	-
	+	-	-	+	-
	-	+	+	-	+
	-	+	-	+	+
	-	-	+	+	-
	-	-	-	-	-

or resolution V fractional factorial arrangements, possibly replicated, in the factors associated with each response depending on the arrangement chosen in step 4.

For response $i \in \{1, \ldots, r\}$, define the set of factors related to response i as F_i. For $l, l' \in F_i$ s.t. $l \neq l'$, by definition $i \in A_l$ and $i \in A'_l$. If $l \in C_{m^*}$, then $i \in B_{m^*}$ and $A'_l \cap B_{m^*} \neq \emptyset$ so $l' \notin C_{m^*}$. Therefore, each factor related to response i corresponds to a different unique factor. The set factors related to each response are a subset of factors that form a full factorial (or resolution V fractional factorial) so they will also form a (possibly replicated) full factorial (or resolution V or higher fractional factorial).

2.3 Full Factorial Examples

Return first to the example described in section 1.5. The results of the screening experiment have been repeated here in Table 2.4. Unlike the CCDs and Box-Behnken designs described in chapter 1, the CCD with the fractional factorial constructed from

Algorithm 2 takes into account the relationships discovered in the screening experiment. The algorithm identifies $k^* = 5$ unique factors; a full factorial design in these unique factors is a 2^{-5} fractional factorial of 32 runs in all 10 factors such that the set of factors related to each of the four response variables form a full factorial. An additional 20 runs are needed for the axial points, but no center points are needed because the axial points for factors not related to a given response act as center points for estimating that response. For example, the model used for estimating response 1 relies only on factors 1, 2, 3, 4 and 5. The 32 fractional factorial runs form a full factorial in those five factors, there are 10 axial runs for those five factors, and for the axial runs for factors 6, 7, 8, 9 and 10, these five factors are held constant at zero, giving ten center points.

For this example, Algorithm 1 and the full factorial version of Algorithm 2 produce identical designs. The general class of examples for which these designs are equivalent has not yet been proven, so it is generally recommended that both algorithms are run in each example and both designs are considered if they differ. It is also recommended that multiple orderings of factors and responses are explored for each algorithm to increase the likelihood that the smallest design produced by one of these algorithms is being used. Step 1 of Algorithm 1 orders the responses from most factors to least factors. Example 1 has one response that is related to five factors and three responses that are related to four factors, so there are six possible orderings of response variables. For each of those six response orderings, 100 random orderings of factors were checked using Algorithm 1. Of the 600 total orderings tested, 330 required 32 factorial runs, 252 required 64 factorial runs, and 18 required 128 factorial runs. 1000 random orderings of factors were checked for example 1 using Algorithm 2 (the order of the response variables does not affect the design recommended by Algorithm 2) and 926 of those resulted in a design with $k* = 5$ unique factors and the remaining 74 designs required $k* = 6$ unique factors. Because a resolution VI design would be used on the $k* = 6$ unique factors, all 1000 of these designs would require 32 factorial runs in the CCD.

Table 2.4 Results of screening for example 1

		factor									
		1	2	3	4	5	6	7	8	9	10
response	1	X	X	X	X	X					
	2			X		X	X	X			
	3			X	X			X	X		
	4				X				X	X	X

A summary of the results of screening experiments for another example is shown in Table 2.5. Example 2 has 12 factors and 7 response variables. The size of the standard CCD used for this example is determined only by the total number of factors. For the resolution V fractional factorial, 256 runs are needed. An additional 24 axial points are needed for a total of $280+n_c$ required runs. A design for 12 factors suggested by Box and Behnken (1960) would require 192 runs plus center points. (Box-Behnken designs, and our suggested modification of them for this setting are described in Chapter 3.) Using the Algorithm 2, a CCD for example 2 requires only 32 factorial runs. An additional 24 axial points brings the total number of runs required to 56.

In this case, $k^* = 6$ unique factors are identified and a resolution VI ($\max_i k_i + 1$) fraction on those 6 unique factors is constructed. The resulting design is a full factorial in the factors associated with each response. Although the number of unique factors in this case is larger than the largest set of factors related to an individual response ($k^* > \max_i k_i$), it can still be proven that this is the smallest number of unique factors possible. Factors 1, 2, 3, 4, and 5 are all related to response 1, so they must all be unique factors; call them 1*, 2*, 3*, 4*, and 5*. Factor 6 and 7 cannot be unique factors 2*, 3*, or 4* because they are all related to response 2, and they can't be unique factor 5* because they are all related to response 6. Also, factors 6 and 7 are both related to responses 2 and 6, so they cannot be the same unique factor as each other. This means that only one of them can be unique factor 1* and the other must be defined as a new unique factor, 6*. The rest of the factors can be assigned to one of these 6 unique factors.

Algorithm 1 produces a design equivalent to a full factorial on the $k^* = 6$ unique factors from Algorithm 2. It requires 64 factorial runs and 24 axial runs for a total of 88 runs.

The number of runs required for examples 1 and 2 are summarized in Table 2.6. These examples illustrate the savings this model can provide. Fewer runs can mean big savings in both time and money. In addition to requiring fewer experimental runs, the designs constructed for examples 1 and 2 using our algorithm guarantee a full factorial in the set of factors related to each response. The traditional CCD using a resolution V fractional factorial in all factors may be a resolution V fractional factorial for response 1 in example 1 and responses 1 and 2 in example 2, since they each are related to five factors.

Table 2.5 Results of screening for example 2

		factor											
		1	2	3	4	5	6	7	8	9	10	11	12
	1	X	X	X	X	X							
	2		X	X	X		X	X					
	3		X	X					X	X			
response	4			X	X		X				X		
	5						X			X	X	X	
	6					X	X	X					
	7								X				X

Table 2.6 Number of runs required for examples 1 and 2

	example 1	example 2
# of factors	10	12
Algorithm 1 CCD	52	88
Algorithm 2 CCD	52	56
Res V CCD	$148 + n_c$	$280 + n_c$
Box-Behnken	$160 + n_c$	$192 + n_c$

2.4 Resolution V Examples

Consider again example 1 described in section 1.5. In section 2.3, the algorithm required a full factorial in $k^* = 5$ unique factors for a total of 32 factorial runs; here, a resolution V fractional factorial in the $k^* = 5$ unique factors will be used instead for a total of only 16 factorial runs. The same 20 additional runs are needed for axial points, and no center points are needed, bringing the total number of runs to 36 for a resolution V CCD. Table 2.7 gives the required number of runs and the mean and maximum normalized standard deviations of the parameter estimates in the main effect, interaction, and squared terms for the three designs discussed thus far. We use s to denote the standard deviation of a model parameter estimate, not the estimate of this quantity based on the mean square error (i.e. the "standard error"). Hence, the normalized standard deviation $\frac{s}{\sigma}$ is a function only of the experimental design. The value of α used for the axial points in all CCD type examples is $\alpha = \sqrt[4]{n_f}$ where n_f is the number of factorial runs in the design. This guarantees that the designs are rotatable, which means that the prediction variance is the same for any two points that are the same distance from the center of the design [(Myers et al., 2002, p. 305)]. For example 1, $\alpha = 2.38$ is chosen for the full factorial constructed using algorithm 2, $\alpha = 2$ is chosen for the resolution V fractional factorial constructed using algorithm 2, and $\alpha = 3.36$ is chosen for the standard resolution V CCD.

As clearly shown in Table 2.7, standard deviations for all model coefficient estimates are substantially larger for the algorithm-generated designs than for the conventional CCD. However, the new designs are also much smaller; other things being equal, the smaller design size alone would lead to larger standard deviations of model coefficients. A more appropriate comparison index for designs of different sizes is the "per-observation" version of the normalized standard deviations, $\sqrt{N}\frac{s}{\sigma}$. These indices are plotted in Figure 2.1 for the same three designs. While the smaller designs still have larger normalized standard deviations, even with this correction, the differences are much smaller when sample size is taken into account. This does, however, point out that the structure of the new designs in inherently less efficient than that of a conventional CCD. Our designs are appropriate in cases where experimental runs are expensive (and so smaller designs are desirable) and the variance of random errors (σ^2) is small-to-moderate.

Table 2.7 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 1 from section 1.5

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Res V Alg CCD	36	0.213	0.250	0.204	0.204	0.250	0.250	0.162	0.164
Full Alg CCD	52	0.153	0.177	0.152	0.152	0.177	0.177	0.115	0.116
Res V CCD	$148 + n_c$	0.078	0.088	0.081	0.081	0.088	0.088	0.057	0.058

If algorithm 2 is applied to example 2 from section 2.3 to construct a fractional factorial such that the set of factors related to each response forms a resolution V fractional factorial, it will require 32 runs. This is the same number of factorial runs as was required for the full factorial because the algorithm requires $k^* = 6$ unique factors, and a resolution $\max_i k_i + 1 =$ VI design and a resolution V design in those 6 unique factors both require 32 runs. Just as before, 24 axial runs are needed for the same 56 total runs. Table 2.8 gives the required number of runs and the mean and maximum standard deviation of the parameter estimates for the three designs discussed thus far, and Figure 2.2 shows the per-observation mean and maximum standard deviation for the three designs. The values used for the axial points in this example are $\alpha = 2.38$ for both designs constructed using algorithm 2 and $\alpha = 4$ for the standard resolution V CCD. The two designs constructed using Algorithm 2 above are identical, and they have standard deviations slightly larger than the standard CCD. The design constructed using Algorithm 1 has standard deviations between the Algorithm 2 designs and the standard CCD.

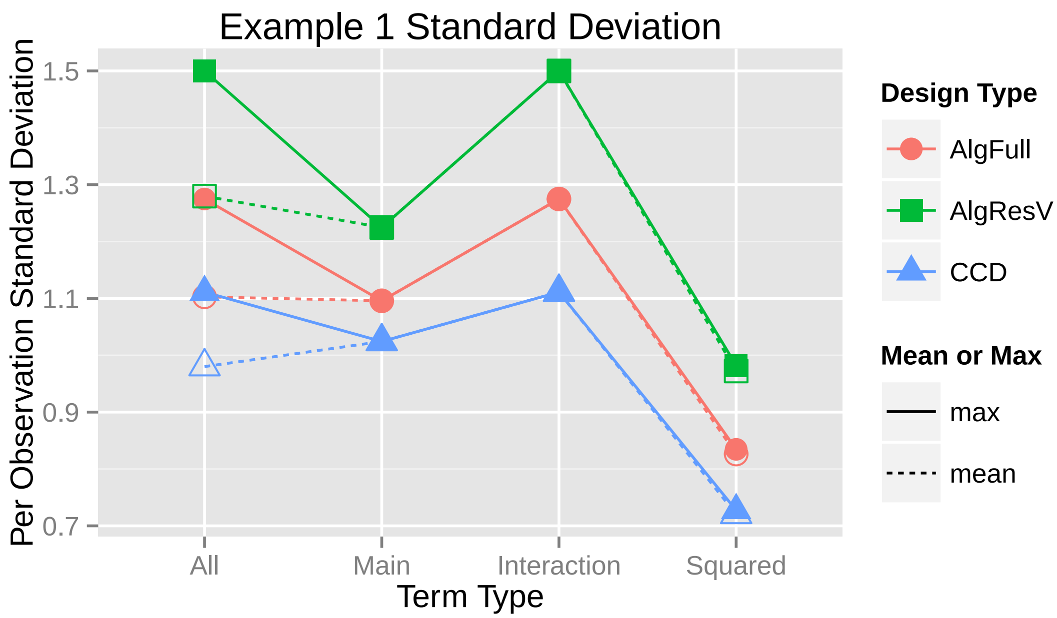

Figure 2.1 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 1 from section 1.5. AlgFull refers to the design generated from Algorithm 1 and 2 that is a full factorial in the set of factors related to each response, AlgResV refers to the design generated from Algorithm 2 that is a resolution V fractional factorial in the set of factors related to each response, and CCD refers to the standard resolution V CCD in all factors.

In example 1 above, a savings of only 16 runs, about one fourth of the total, is achieved when using a resolution V fractional factorial instead of a full factorial for each model related to an individual response, and in example 2, the two designs are the same. Notice that in both of these examples, at most five factors are related to a single response. The savings gained by using a resolution V fractional factorial as opposed to a full factorial will be larger for a larger set of factors. To illustrate this, Table 2.9 contains the results of a screening experiment with 13 factors and 5 response variables, but response 1 is related to 8 factors. Here, $k^* = 8$ unique factors are needed. A full factorial in those $k^* = 8$ unique factors would require 256 factorial runs for a total of 282 runs in the CCD. The same full factorial design is identified by Algorithm 1. If a resolution V fractional

Table 2.8 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 2 from section 2.3

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Alg 1 CCD	88	0.109	0.125	0.112	0.112	0.125	0.125	0.081	0.082
Alg 2 CCD	56	0.152	0.177	0.152	0.152	0.177	0.177	0.114	0.116
Res V CCD	$280 + n_c$	0.055	0.063	0.059	0.059	0.063	0.063	0.040	0.041

factorial is used instead for the $k^* = 8$ unique factors, 64 factorial runs are needed for a total of only 90 runs in the CCD. Here the full factorial in the $k^* = 8$ unique factors was nearly the same size as the traditional resolution V CCD (differing only by the inclusion of center points), while the resolution V fractional factorial in the $k^* = 8$ unique factors was about one third of that size. Table 2.10 and Figure 2.3 give a summary of mean and maximum standard deviation for the three designs discussed thus far. The values used for the axial points in this example are $\alpha = 4$ for the standard resolution V CCD and the full factorial CCD constructed using algorithm 2 and $\alpha = 2.83$ for the resolution V fractional factorial CCD constructed using algorithm 2. Similar to examples 1 and 2 there is a trade-off between size and standard deviation of parameter estimates within the CCD type designs; however, between the algorithm design with full factorials for each response and the conventional CCD, which are about the same size, the algorithm has slightly smaller per-observation standard deviations.

Table 2.9 Results of screening for example 3

		factor												
		1	2	3	4	5	6	7	8	9	10	11	12	13
response	1	X	X	X	X	X	X	X	X					
	2						X	X	X	X	X			
	3				X	X			X			X	X	
	4					X							X	X
	5							X					X	

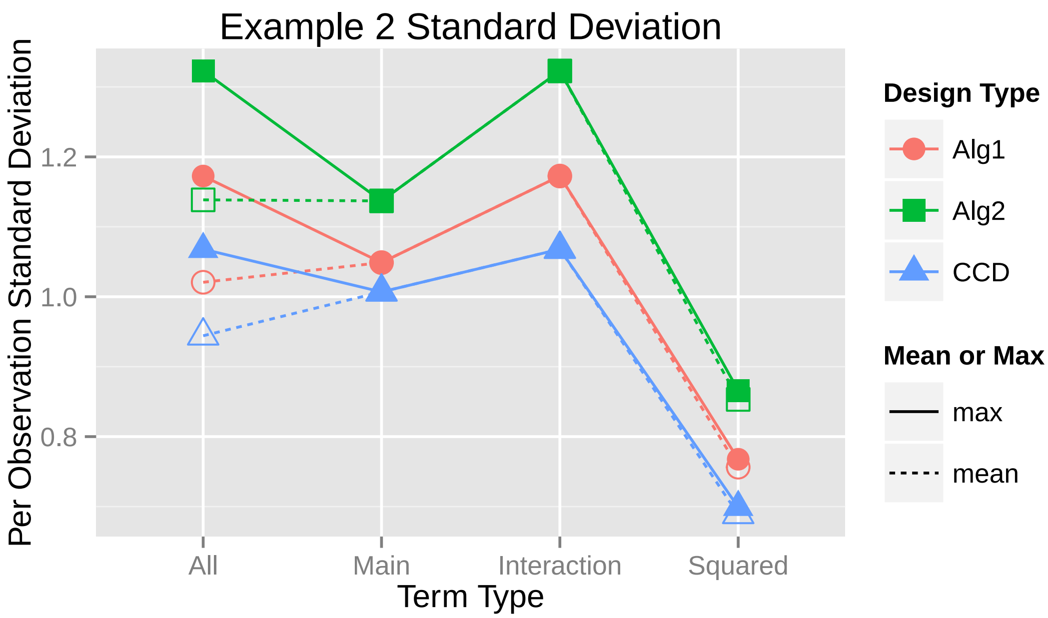

Figure 2.2 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 2 from section 2.3. Alg1 refers to the design generated from Algorithm 1, Alg2 refers to the design generated from Algorithm 2 that is a full factorial in the set of factors related to each response which is the same design generated from Algorithm 2 that is a fractional factorial with resolution at least V in the set of factors related to each response, and CCD refers to the standard resolution V CCD in all factors.

These three examples illustrate that using the algorithms presented here has the potential to dramatically decrease the number of runs required using one fifth to one third of the runs required by the conventional CCD. There is a trade-off with smaller designs having larger standard deviations of parameter estimates, so these designs are best used when standard deviations are thought to be small.

2.5 Summary

For processes with multiple response and explanatory variables where screening experiments or process knowledge indicated which subset of factors is related to each response variable, and a full second order model in that subset of factors is desired for

Table 2.10 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 3 from section 2.3

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Res V Alg CCD	90	0.111	0.125	0.112	0.112	0.125	0.125	0.082	0.084
Full Alg CCD	282	0.057	0.063	0.059	0.059	0.063	0.063	0.041	0.042
Res V CCD	$282 + n_c$	0.057	0.063	0.059	0.059	0.063	0.063	0.041	0.042

each response, a standard CCD requires more runs than is necessary for estimation. Algorithm 1 provides an alternative formulation of the factorial part of the CCD and reduces the size of the design required substantially in some situations. Algorithm 1 produces a fractional factorial that is guaranteed to be a full factorial in the subset of factors related to each response, but a standard CCD depends on only a resolution V fractional factorial. Algorithm 2 also produces fractional factorial designs that are guaranteed to be a full factorial in the subset of factors related to each response, but can also be extended to resolution V fractional factorial designs in the subset of factors related to each response. The resolution V CCDs constructed using Algorithm 2 provide the smallest designs, but also the largest per-observation variances of designs discussed in this chapter. The standard CCDs had the largest size and the smallest per-observation variance. The full factorial CCDs constructed using Algorithm 2 range in size depending on the size of the largest set of factors related to a single response, and per-observation variances also vary. In the examples discussed above, per-observation variances varied between the larger per-observation variances of the resolution V CCDs from Algorithm 2 and the smaller per-observation variances of the standard CCDs. Designs constructed using Algorithm 1 and 2 should only be used when per-observation cost is high and variances are thought to be small. In that case, a resolution V CCDs constructed using Algorithm 2 is recommended.

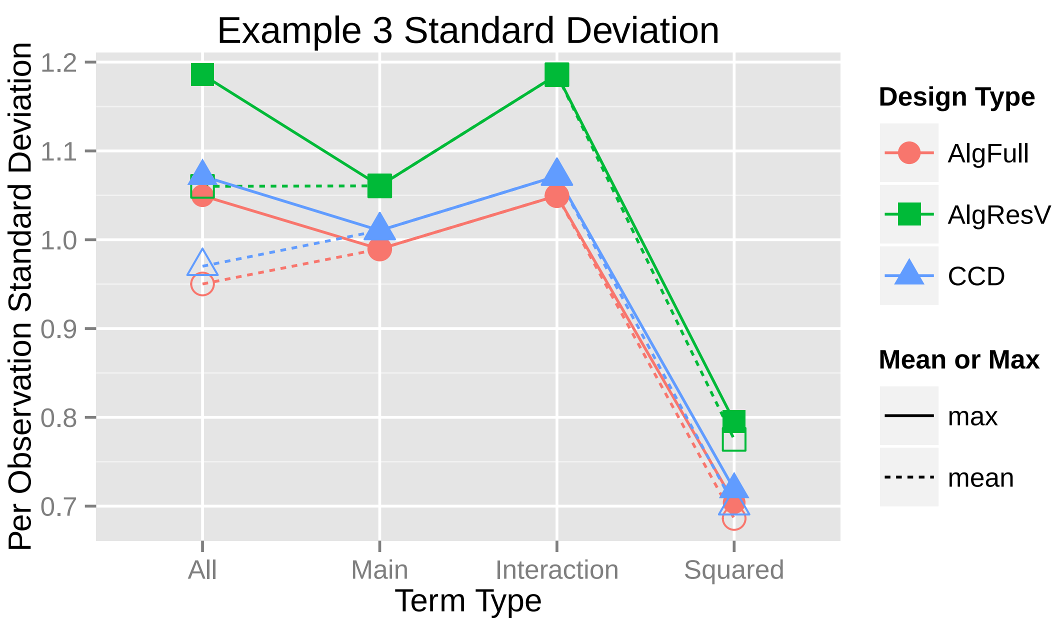

Figure 2.3 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 3 from section 2.3. AlgFull refers to the design generated from Algorithm 1 and 2 that is a full factorial in the set of factors related to each response, AlgResV refers to the design generated from Algorithm 2 that is a resolution V fractional factorial in the set of factors related to each response, and CCD refers to the standard resolution V CCD in all factors.

CHAPTER 3. BOX-BEHNKEN TYPE ALTERNATIVES

Box-Behnken designs are often used instead of Central Composite designs despite requiring more runs. Relative the Central Composite designs, Box-Behnken designs generally offer more flexible blocking options, and some investigators prefer their simple structure. As discussed in section 1.4, a typical Box-Behnken design in all factors is unnecessarily large when screening experiments or process knowledge is available. We can reduce the number of runs required in a Box-Behnken type design if we instead consider each response separately and combine the resulting designs. The original Box-Behnken designs [Box and Behnken (1960)] were constructed by first selecting a balanced incomplete block design (BIBD) or a partially balanced incomplete block design (PBIBD) with k treatments applied to units in equal size blocks of $b < k$ units each, where k is the number of factors in the final Box-Behnken design. Then each block determines a full factorial (or resolution V fractional factorial) for the factors associated with treatments in that block and all other factors are held constant at zero. Box and Behnken suggested ideal block sizes for the BIBD step that result in favorable properties in a standard one-response problem, but when considering multiple responses separately, it is helpful to choose the block sizes in a different way. The two choices of block sizes that will be discussed here are all blocks of size two and blocks for each response of size $k_i - 1$, where k_i is the number of factors related to the i^{th} response.

3.1 Box-Behnken Type Design with BIBD Block Size of Two

The first method for constructing a Box-Behnken type design is to consider each response separately and construct a Box-Behnken design for each response where the block size in the BIBD step is two for all responses regardless of the number of factors. Combine the list of blocks from all responses. For any two responses that share a pair of factors, the BIBD block associated with that pair of factors will be listed twice. We delete such duplicates because this does not affect estimability for any response.

For responses with models involving only two factors, we have a block associated with those two factors from the previous steps, but we also need to guarantee that each of these two factors appears without the other in at least one block. If this is not the case, the squared terms for these two factors will be confounded. For each factor in such a pair, add a block that has the factor in question along with a dummy factor (i.e. a factor that will not be in the final design) if needed. This will result in adding four runs to the final design where the factor in question is at the high level for two runs and the low level for two runs and all other factors are set to zero. Here four additional runs are chosen instead of two additional runs (one high and one low) to be consistent with the contribution of all other blocks.

If the model for a response has only one factor, we only need to check that the factor is present in any one of the blocks created for another response. If not, we again add a block with the factor in question and a dummy factor, so that the final design has four runs where the factor in question is at the high level for two runs and the low level for two runs and all other factors are set to zero.

Now that all blocks in the BIBD step have been constructed and duplicates have been removed, we can construct the final Box-Behnken type design. For each block remaining, we include a full factorial design (four runs) in the two factors in the block and hold all other factors constant at zero. In conventional Box-Behnken designs, it is necessary to add center points (for which all factors values are zero) to avoid confounding the intercept with the sum of all pure quadratic (x^2) coefficients. In our setting, it is not always necessary to include additional center points because the runs resulting from blocks that do not share factors with a particular response provide center points for that response. One should verify that the design for each response includes center points and add additional center points if necessary.

3.1.1 Walk Through Example

To construct a Box-Behnken type design with BIBD block size of two, we first need information from a screening experiment or process knowledge. Consider an example with three responses and six total factors where factors 1, 2 and 3 are related to response 1,factors 2, 3, 4 and 5 are related to response 2 and factors 1, 5 and 6 are related to response 3. This information is summarized in Table 3.1. For each response, treat the associated factors as if they are treatments and construct a BIBD with blocks of size two for those treatments. These blocks are listed in Table 3.2. We remove all duplicates, which in this case is only the block with treatments/factors 2 and 3, and then go about constructing the Box-Behnken type design.

Table 3.1 Summary of previous information for walk through example

		factor					
		1	2	3	4	5	6
response	1	X	X	X			
	2		X	X	X	X	
	3	X				X	X

The constructed design is shown in Table 3.3 where ± indicates that factor is part of a two factor full factorial for four runs and a zero indicates that factor is held constant at zero for those four runs. Within the set of factors associated with each response, we have a traditional Box-Behnken design with BIBD block size of two, center points due to the runs where only factors not related to that response are being varied, and in some cases,

Table 3.2 List of all BIBD blocks (including repeats) for walk through example

response 1	response 2	response 3
1 2	2 3	1 5
1 3	2 4	1 6
2 3	2 5	5 6
	3 4	
	3 5	
	4 5	

additional runs in which only some factors are being varied (from the intersection of factors associated with other responses). This design requires 44 total runs, as opposed to 54 runs in the standard Box-Behnken design with PBIBD blocks of size three. Here the total savings is not very large, but with more total factors, the potential for savings increases.

Table 3.3 Constructed Box-Behnken type design with blocks of size 2 for walk through example

1	2	3	4	5	6
$\pm$	$\pm$	0	0	0	0
$\pm$	0	$\pm$	0	0	0
0	$\pm$	$\pm$	0	0	0
0	$\pm$	0	$\pm$	0	0
0	$\pm$	0	0	$\pm$	0
0	0	$\pm$	$\pm$	0	0
0	0	$\pm$	0	$\pm$	0
0	0	0	$\pm$	$\pm$	0
$\pm$	0	0	0	$\pm$	0
$\pm$	0	0	0	0	$\pm$
0	0	0	0	$\pm$	$\pm$

3.1.2 Examples

Refer back to the example presented in section 1.5. The results of the screening experiment have been repeated here in Table 3.4. First consider response 1. We can arrange the five factors that the screening experiment indicated were related to response 1 into ten blocks of size two. The four factors related to response 2 can be arranged

Table 3.4 Results of screening for example 1

		factor									
		1	2	3	4	5	6	7	8	9	10
response	1	X	X	X	X	X					
	2			X		X	X	X			
	3			X	X			X	X		
	4				X				X	X	X

into six blocks of size two. Responses 3 and 4 also each have four factors related to them, so those two sets of four can also be arranged into six blocks of size two. None of the responses are functions of only one or two factors, so additional blocks involving a dummy factor are not needed. This makes a total of 28 blocks, but blocks with factors 3 and 4, 3 and 5, 3 and 7, and 4 and 8 all appear twice, so there are 24 unique blocks. Each of those blocks becomes a two-factor full factorial in the final design, which makes a total of 96 runs. Table 3.5 gives a summary of the number of runs required and the mean and maximum normalized standard deviation of parameter estimates for all designs discussed thus far for this example, and Figure 3.1 shows a plot of the per-observation standard deviation for all designs discussed thus far. These show that the standard deviation is smallest for the CCD type designs, and largest for the Box-Behnken type design with blocks of size two. On the other hand, the required number of runs is smallest for the CCD using the algorithm from Chapter 2, while the Box-Behnken type design with blocks of size two offers some savings in size over the standard Box-Behnken design. When choosing which design is best suited for a given situation, the number of runs required and the standard deviation of the parameter estimates should both be considered, and there will be a trade-off if a Box-Behnken type design is desired.

Consider also examples 2 and 3 described in section 2.3. The results of the screening experiments have been repeated here in Tables 3.6 and 3.8. Example 2 has seven response variables of interest that are related to 5, 5, 4, 4, 4, 3, and 2 factors respectively. Treating these factors as treatments in a BIBD with blocks of size two, each response would

Table 3.5 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 1 from section 1.5

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Res V Alg CCD	36	0.213	0.250	0.204	0.204	0.250	0.250	0.162	0.164
Full Alg CCD	52	0.153	0.177	0.152	0.152	0.177	0.177	0.115	0.116
B-B type $b = 2$	96	0.350	0.500	0.222	0.289	0.500	0.500	0.233	0.314
Res V CCD	$148 + n_c$	0.078	0.088	0.081	0.081	0.088	0.088	0.057	0.058
Box-Behnken	$160 + n_c$	0.178	0.250	0.125	0.125	0.229	0.250	0.146	0.162

require 10, 10, 6, 6, 6, 3, and 1 block respectively. There are 9 sets of duplicate blocks; after removing those, there are 33 total blocks. Each block is then used to construct a two-factor full factorial in the final Box-Behnken type design, which then requires $33 \times 2^2 = 132$ runs. Notice here that center points are not needed. Table 3.7 give a summary of the number of runs required and the mean and maximum standard deviation of parameter estimates for this example by all designs discussed thus far, and Figure 3.2 shows a plot of the per-observation standard deviation for all designs discussed thus far. The results are similar to the first example, where this design is has the largest variance, fewer runs than either the standard Box-Behnken design or the standard CCD, but more runs than the designs constructed using the algorithm described in Chapter 2.

Table 3.6 Results of screening for example 2

		factor											
		1	2	3	4	5	6	7	8	9	10	11	12
	1	X	X	X	X	X							
	2		X	X	X		X	X					
	3		X	X					X	X			
response	4			X	X		X				X		
	5						X			X	X	X	
	6					X	X	X					
	7								X				X

Example 3 has five response variables of interest that are related to 8, 5, 5, 3, and 2 factors respectively. Treating these factors as treatments in a BIBD with blocks of size

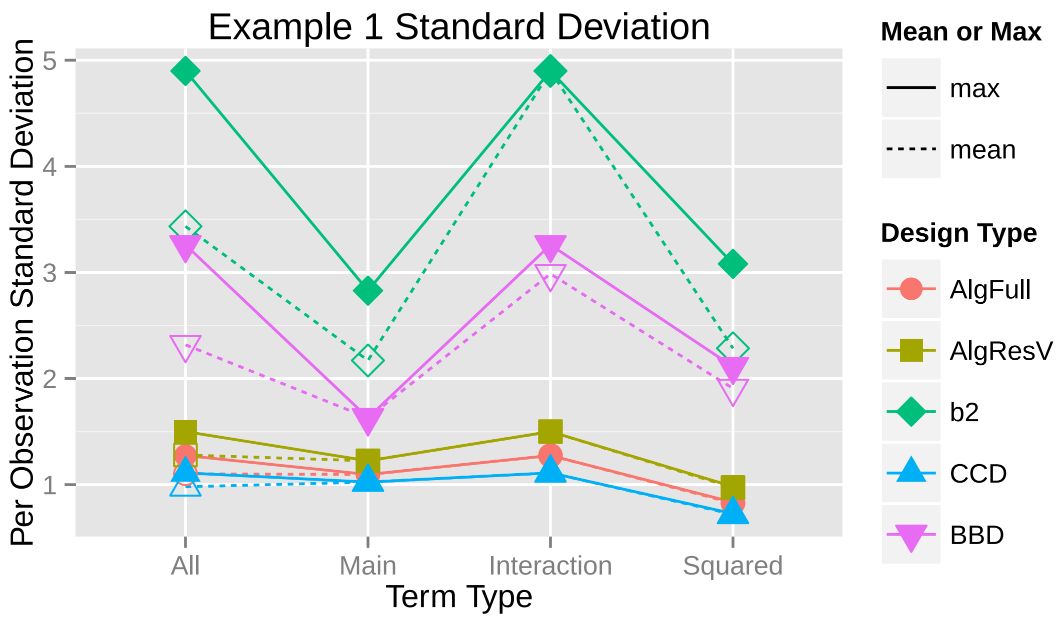

Figure 3.1 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 1 from section 1.5. AlgFull refers to the design generated from algorithm 2 that is a full factorial in the set of factors related to each response, AlgResV refers to the design generated from algorithm 2 that is a resolution V fractional factorial in the set of factors related to each response, CCD refers to the standard resolution V CCD in all factors, b2 refers to the Box-Behnken type design with blocks of size 2, and BBD refers to the standard Box-Behnken design.

two, each response would require 28, 10, 10, 3, and 1 block respectively. There are 7 sets of duplicate blocks; after removing those, there are 45 total blocks. Each block is then used to construct a two-factor full factorial in the final Box-Behnken type design, which then requires $45 \times 2^2 = 180$ runs. Notice here also that center points are not needed. Table 3.9 give a summary of the number of runs required and the mean and maximum standard deviation of parameter estimates for this example by all designs discussed thus far, and Figure 3.3 shows a plot of the per-observation standard deviation for all designs discussed thus far. Again the results are similar to the previous examples.

For all three examples discussed in this section, we see that the Box-Behnken type designs with BIBD blocks of size two require fewer runs than a traditional Box-Behnken

Table 3.7 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 2 from section 2.3

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Alg 1 CCD	88	0.109	0.125	0.112	0.112	0.125	0.125	0.081	0.082
Alg 2 CCD	56	0.152	0.177	0.152	0.152	0.177	0.177	0.114	0.116
B-B type $b = 2$	136	0.337	0.500	0.206	0.354	0.500	0.500	0.214	0.378
Res V CCD	$280 + n_c$	0.055	0.063	0.059	0.059	0.063	0.063	0.040	0.041
Box-Behnken	$192 + n_c$	0.181	0.250	0.125	0.125	0.245	0.250	0.136	0.147

Table 3.8 Results of screening for example 3

		factor												
		1	2	3	4	5	6	7	8	9	10	11	12	13
response	1	X	X	X	X	X	X	X	X					
	2						X	X	X	X	X			
	3				X	X			X			X	X	
	4					X							X	X
	5							X					X	

design, but are not as small as the traditional CCD or the CCD type designs constructed from Algorithm 2. These designs also have the largest standard deviation of any design discussed thus far, so they should only be used when variances are expected to be small and the structure of a Box-Behnken design is preferred over the structure of a CCD.

Table 3.9 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 3 from section 2.3

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Res V Alg CCD	90	0.111	0.125	0.112	0.112	0.125	0.125	0.082	0.084
Full Alg CCD	282	0.057	0.063	0.059	0.059	0.063	0.063	0.041	0.042
B-B type $b = 2$	180	0.356	0.500	0.189	0.354	0.500	0.500	0.196	0.377
Res V CCD	$282 + n_c$	0.057	0.063	0.059	0.059	0.063	0.063	0.041	0.042
Box-Behnken	$208 + n_c$	0.194	0.250	0.125	0.125	0.250	0.250	0.135	0.138

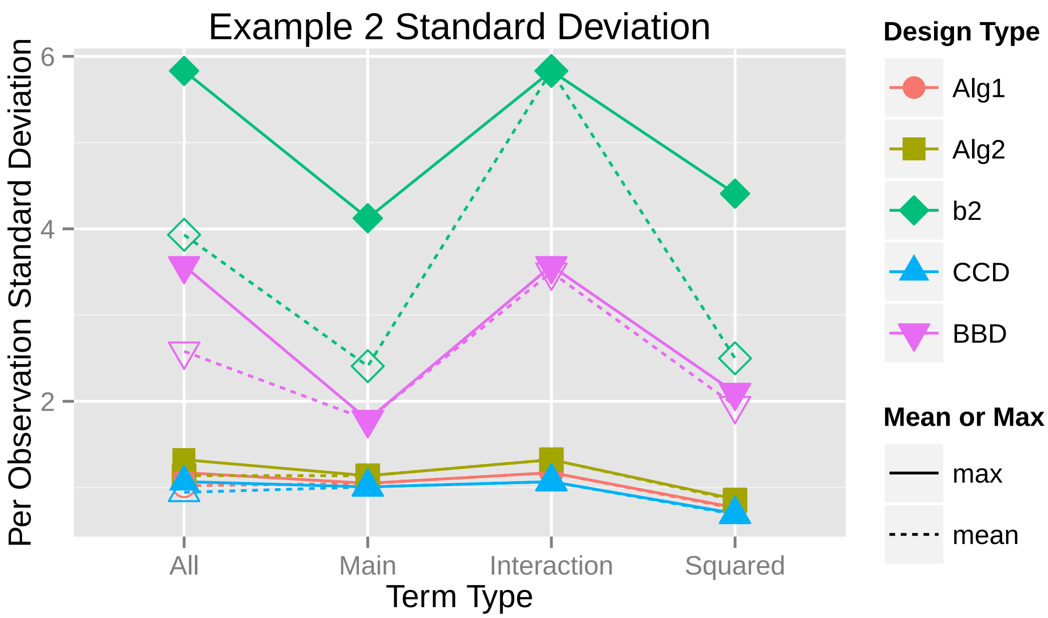

Figure 3.2 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 2 from section 2.3

3.2 Box-Behnken Type Design with BIBD Block of Varying Size

The second method for constructing a Box-Behnken type design is to start with BIBD blocks of size $k_i - 1$ for each response, where k_i is the number of factors related to response i. Before converting from the BIBDs to a combination of full factorials, we can delete duplicate blocks across responses. Any duplicate blocks (blocks containing the same treatments/factors) can be deleted, as well as any blocks that contain factors that are a subset of the factors of a larger block. These subset blocks can be deleted because the resulting factorial in the final Box-Behnken type design would be a subset of the factorial in the final design from the larger block. For example, if response 1 has a block containing treatments/factors 1, 2, 3, and 4, and response 2 has a block containing treatments/factors 1, 3, and 4, the block containing factors 1, 3, and 4 can be deleted. For response i with $k_i = 2$, a different strategy must be used to insure

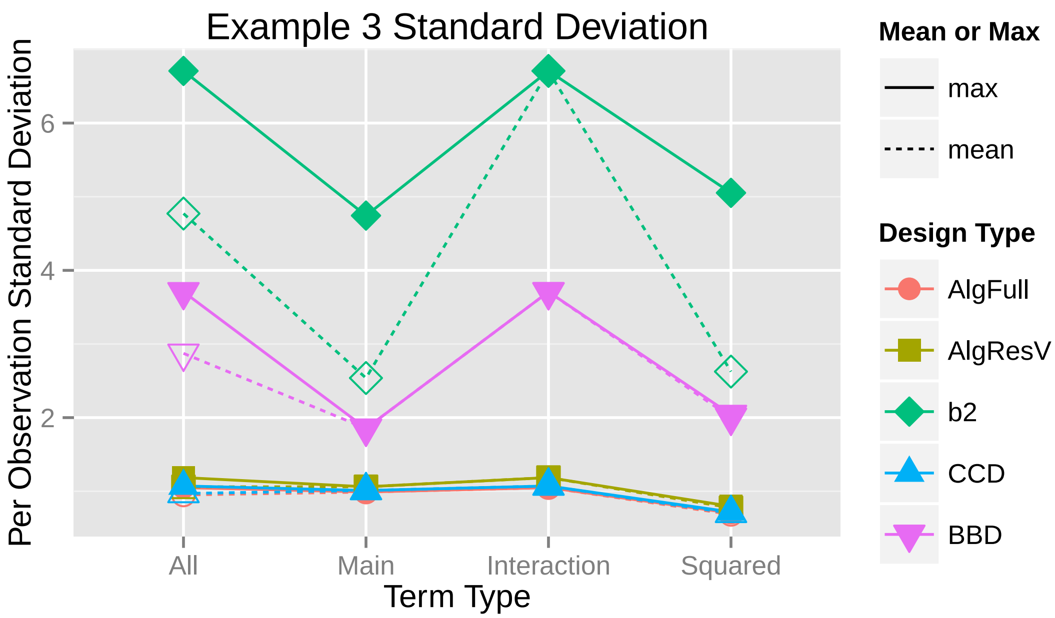

Figure 3.3 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 3 from section 2.3

estimability. Both factors appear in blocks individually, but we must insure that both factors appear in a block together; otherwise, the interaction term will not be estimable. If this is not the case, simply add such a block. This will insure a three-level full factorial in those two factors (once center points have been added, if necessary), which will allow for estimation of a full quadratic model. Finally, combine the resulting Box-Behnken type designs constructed from the reduced number of blocks in the BIBD step, holding constant at zero any factors not related to each response.

Constructing such designs may be an interesting intellectual exercise, but does not generally lead to designs that are small enough to be practical. Consider example 1 presented in section 1.5. In the BIBD step, response 1 would need 5 blocks of size 4 and responses 2, 3, and 4 would need 4 blocks of size 3. Since none of the responses overlap by three or more factors, none of these blocks can be deleted. This means that in the final design there would be $5 \times (2^4) = 80$ runs for response 1 and $4 \times (2^3) = 32$ runs for each of responses 2, 3, and 4 which gives a total size of $80+(3*32)+n_c = 176+n_c$ runs. This is even larger than the original Box-Behnken design which requires $160+n_c$ runs. Table 3.10 shows how the size for this design compares to the other designs discussed in this thesis for this example as well as examples 2 and 3 described in section 2.3. The designs constructed as described here are also larger than the standard Box-Behnken design for examples 2 and 3. For example 3, the Box-Behnken type design constructed using BIBD blocks of varying size is almost 3 times as large as the standard Box-Behnken design.

Table 3.10 Number of runs required for example 1 from section 1.5 and examples 2 and 3 from section 2.3

	example 1	example 2	example 3
# of factors	10	12	13
Res V Alg CCD	36	56	90
Full Alg CCD	52	56	282
B-B type $b=2$	96	132	180
B-B type $b=k_i-1$	$176+n_c$	$262+n_c$	$684+n_c$
Res V CCD	$148+n_c$	$280+n_c$	$282+n_c$
Box-Behnken	$160+n_c$	$192+n_c$	$208+n_c$

One reason this type of design is so large is that the number of runs required for response i is $\binom{k_i}{b} \times 2^b$ which is generally larger for larger values of b, and $b = k_i - 1$ is the largest possible value for b in an incomplete block design. The possible reduction in size for this design relies on the number of blocks that can be deleted as duplicates or subsets, but as k_i gets larger, it becomes less likely that two responses will overlap in $k_i - 1$ factors making this reduction very uncommon.

3.3 Combining Blocks for More Compact Box-Behnken Type Designs

In either of the above Box-Behnken type designs, an additional step can be taken to reduce the size of the final design. In the BIBD step, some blocks can be grouped together and the factors corresponding to treatments from those blocks can be varied over the same set of runs in the final Box-Behnken type design. For example, if a block corresponding to factors related to response 1 contained treatments 1 and 2, and a block corresponding to factors related to response 2 contained treatments 4 and 5 were combined, the two sets of factors would be varied over the same four runs as shown in Table 3.11. In order to determine if blocks i and j can be grouped together, first determine which response or responses contain all factors corresponding to treatments in block i. Call this response set i. Also determine which response or responses contain all factors corresponding to treatments in block j, and call this response set j. If no factors corresponding to treatments in block i are related to responses in set j, and no factors corresponding to treatments in block j are related to responses in set i, then blocks i and j can be grouped together.

Table 3.11 Example of combining two blocks for more compact Box-Behnken type designs

factor				
1	2	3	4	5
+	+	0	+	+
+	-	0	+	-
-	+	0	-	+
-	-	0	-	-

Suppose blocks i and j are grouped together. When constructing the final Box-Behnken type design, include a single set of runs that is a full factorial in the factors corresponding to treatments in block i and a full factorial in the factors corresponding to treatments in block j. (A replicated full factorial may be used for smaller blocks if blocks are not the same size.) Hold constant at zero all factors not corresponding to treatments in blocks i or j. This can also be extended to groups of more than two blocks as long as all pairs of blocks meet the above specifications. In that case, include a single set of runs that is a full factorial in the factors corresponding to treatments in each block in the group, with all other factors held constant at zero.

3.3.1 Algorithm for Combining Blocks

1. Let B be the set of all blocks of 2 treatments that correspond to factors that are both related to a single response.

2. For all response variables that are related to only one factor, add blocks to B with one dummy treatment and one treatment corresponding to that factor.

3. For all response variables that are related to only two factors, add blocks to B with one dummy treatment and one treatment corresponding each factor that does not appear in another block.

4. For block i, let P_i be the set of responses that are related to both factors in that block, and let E_i be the set of responses that are related to either factor in that block.

5. For $i = 1, \ldots, m$, where m is the number of blocks in B,

   (a) For $j = 1, \ldots, i - 1$

      i. Set $P_i^{\text{old}} = P_i$, $P_j^{\text{old}} = P_j$, $E_i^{\text{old}} = E_i$, and $E_j^{\text{old}} = E_j$

      ii. If $P_i \neq E_j$ and $E_i \neq P_j$, then group blocks i and j together and redefine $P_i = P_j = P_i^{\text{old}} \cup P_j^{\text{old}}$ and $E_i = E_j = E_i^{\text{old}} \cup E_j^{\text{old}}$.

3.3.2 Examples

Table 3.12 illustrates this size reduction for example 1 from section 1.5 using blocks of size two. The $\pm$ symbol indicated that a particular factor is part of a full factorial for that set of four runs. The different full factorials (coming from different blocks) are indicated by the number of *'s after the $\pm$. The first row represents four runs where factors 1 and 2 are a full factorial, factors 6 and 7 are a full factorial, and factors 8 and 9 are a full factorial. The total size of this design is 64 compared to 96 before combining blocks. Table 3.13 and Figure 3.4 compare the size and standard deviation of parameter estimates of this compact Box-Behnken type design with the standard Box-Behnken design and the Box-Behnken type design with blocks of size two discussed above. The standard Box-Behnken design has the smallest normalized standard deviation, but also the largest size. The compact Box-Behnken type design is the smallest design, and also has smaller standard deviations than the Box-Behnken type design with BIBD blocks of size 2.

Table 3.12 Compact Box-Behnken type design for example 1 from section 1.5

factor									
1	2	3	4	5	6	7	8	9	10
$\pm$	$\pm$	0	0	0	$\pm^*$	$\pm^*$	$\pm^{**}$	$\pm^{**}$	0
$\pm$	0	$\pm$	0	0	0	0	0	0	0
$\pm$	0	0	$\pm$	0	0	0	0	0	0
$\pm$	0	0	0	$\pm$	0	$\pm^*$	$\pm^*$	0	0
0	$\pm$	$\pm$	0	0	0	0	0	0	0
0	$\pm$	0	$\pm$	0	0	0	0	0	0
0	$\pm$	0	0	$\pm$	0	0	0	0	0
0	0	$\pm$	$\pm$	0	0	0	0	0	0
0	0	$\pm$	0	$\pm$	0	0	$\pm^*$	0	$\pm^*$
0	0	0	$\pm$	$\pm$	0	0	0	0	0
0	0	$\pm$	$\pm^*$	0	$\pm$	0	0	0	$\pm^*$
0	0	$\pm$	0	0	0	$\pm$	0	$\pm^*$	$\pm^*$
0	0	0	$\pm^*$	$\pm$	$\pm$	0	$\pm^*$	0	0
0	0	0	$\pm^*$	$\pm$	0	$\pm$	0	$\pm^*$	0
0	0	$\pm$	0	0	0	0	$\pm$	0	0
0	0	0	$\pm$	0	0	$\pm$	0	0	0

Table 3.13 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 1 from section 1.5

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Compact B-B	64	0.339	0.500	0.223	0.289	0.466	0.500	0.245	0.314
B-B type $b = 2$	96	0.350	0.500	0.222	0.289	0.500	0.500	0.233	0.314
Box-Behnken	$160 + n_c$	0.178	0.250	0.125	0.125	0.229	0.250	0.146	0.162

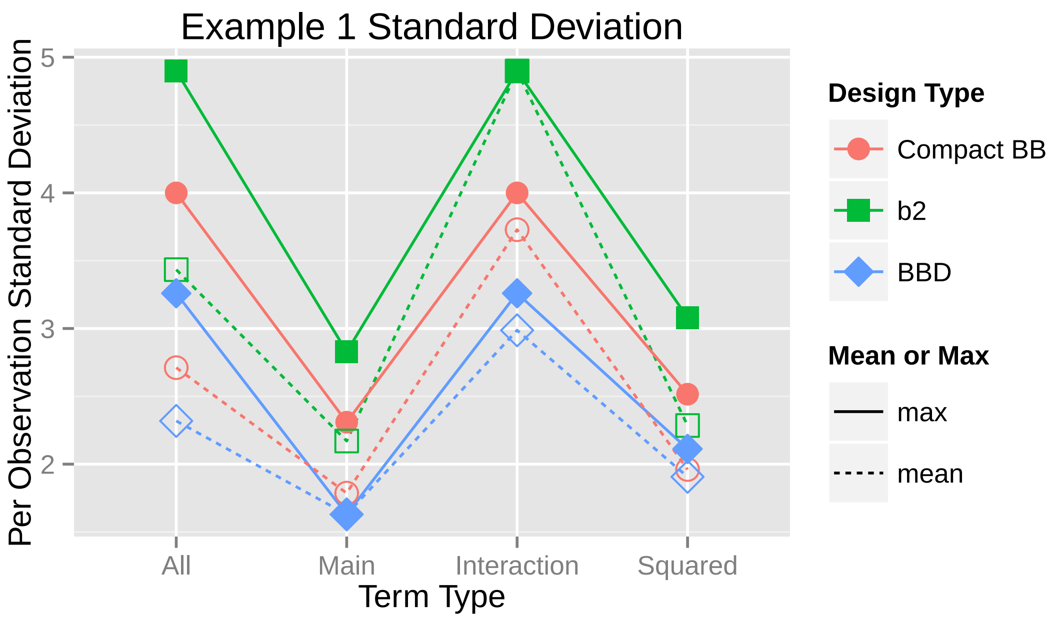

Figure 3.4 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 1 from section 1.5

Consider also examples 2 described in section 2.3. Combining blocks reduces the number of required runs from 136 to $88 + n_c$. Here the addition of center points is required because after combining blocks, there are no runs that are zero for all 5 factors related to response 2. $n_c = 6$ center points were used for the purposes of calculating the standard deviations of parameter estimates because Box and Behnken (1960) recommend $n_c = 6$ center points a design in 5 factors. Table 3.14 and Figure 3.5 compare the size and standard deviation of parameter estimates of this compact Box-Behnken type design with the standard Box-Behnken design and the Box-Behnken type design with blocks of size two discussed above. Again, the standard Box-Behnken design has the smallest normalized standard deviation and the largest size, and the compact Box-Behnken type design is the smallest design and offers competitive standard deviations.

Combining blocks in example 3 from section 2.3 only offers a small reduction in size from the Box-Behnken type design with blocks of size two. 32 fewer runs are required

Table 3.14 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 2 from section 2.3

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Compact B-B	$88 + n_c$	0.321	0.500	0.209	0.356	0.455	0.500	0.226	0.378
B-B type $b = 2$	136	0.337	0.500	0.206	0.354	0.500	0.500	0.214	0.378
Box-Behnken	$192 + n_c$	0.181	0.250	0.125	0.125	0.245	0.250	0.136	0.147

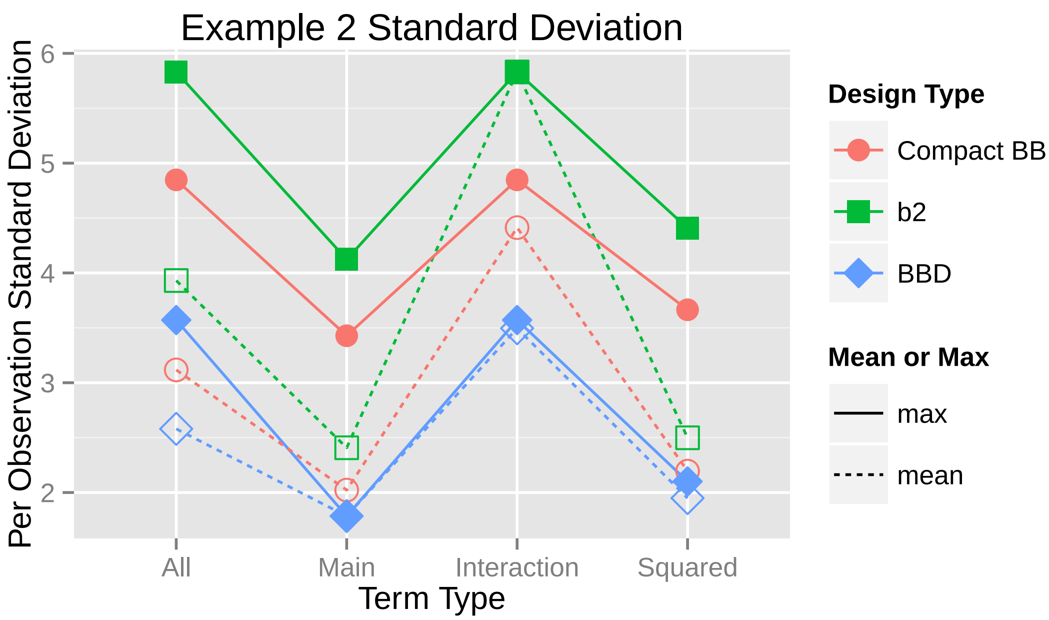

Figure 3.5 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 2 from section 2.3

from the combining of blocks, but additional center points are required because there are no runs that are zero for all 8 factors related to response 1. $n_c = 8$ center points were used for the purposes of calculating the standard deviations of parameter estimates. This number of center points was chosen because Box and Behnken (1960) do not recommend a design for 8 factors, but for 9 factors, they recommend $n_c = 8$ center points. Table 3.15 and Figure 3.6 compare the size and standard deviation of parameter estimates of this compact Box-Behnken type design with the standard Box-Behnken design and the Box-Behnken type design with blocks of size two discussed above. Here combining blocks offers more modest savings in both size and standard deviation of parameter estimates compared to the Box-Behnken type design with blocks of size two. The standard Box-Behnken design is somewhat larger, but offers much smaller standard deviations of parameter estimates.

Table 3.15 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 3 from section 2.3

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Compact B-B	$148 + n_c$	0.349	0.500	0.190	0.354	0.486	0.500	0.200	0.377
B-B type $b = 2$	180	0.356	0.500	0.189	0.354	0.500	0.500	0.196	0.377
Box-Behnken	$208 + n_c$	0.194	0.250	0.125	0.125	0.250	0.250	0.135	0.138

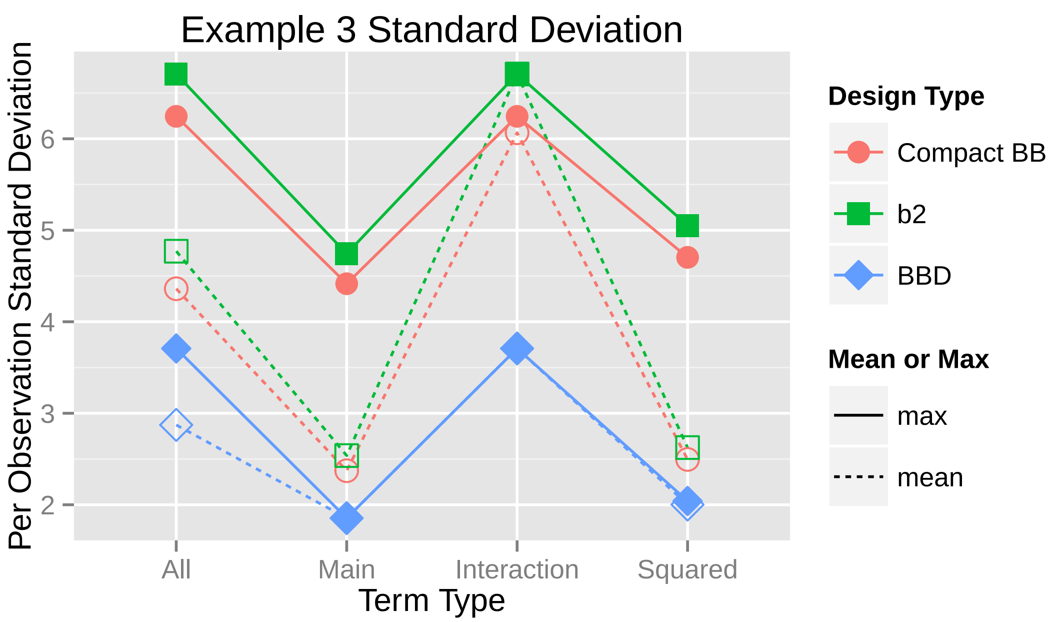

Figure 3.6 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 3 from section 2.3

3.4 Comparison to JMP Custom Designs

In section 1.2, D-optimal designs constructed using the custom design menu in JMP are suggested as an alternative to CCD and Box-Behnken Designs. Using the custom design function in JMP, the user can specify the number of factors and the model that is desired, and JMP will construct a D-optimal design for that model. For situations where screening experiments or previous process knowledge indicate which factors are related to each response, and a full quadratic model is desired for each response, some of that previous information can be taken into account when constructing a JMP Optimal design. When entering the model in JMP, include all main effect terms and squared terms, and include an interaction term for any pair of factors that appear together in the model for any response variable. In example 1 described in section 1.5, all 10 main effect terms and all 10 squared terms would be included as well as the 24 interaction term for pairs of factors that appear together in the model for any of the 4 response variables. The resulting design is D-optimal for the full model with all 10 main effects, all 10 squared terms, and these 24 interaction terms, but not necessarily for any of the 4 response models that are desired.

Table 3.16 and Figure 3.7 compare the size and standard deviation of parameter estimates for this JMP custom design, the Central Composite type design using the resolution V version of Algorithm 2 discussed in section 2.2.1, and the compact Box-Behnken type design discussed in section 3.3. The JMP design is smaller than the compact Box-Behnken design, but larger than the Algorithm 2 design. The standard deviations of parameter estimates for main effects and interaction terms in the JMP design are similar to those from the Algorithm 2 design and smaller than the compact Box-Behnken design, but for squared terms, the standard deviations of parameter estimates are largest for the JMP designs.

Table 3.16 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 1 from section 1.5

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Res V Alg CCD	36	0.213	0.250	0.204	0.204	0.250	0.250	0.162	0.164
Compact B-B	64	0.339	0.500	0.223	0.289	0.466	0.500	0.245	0.314
JMP D-optimal	52	0.224	0.479	0.152	0.159	0.162	0.178	0.397	0.479

Examples 2 described in section 2.3 has 12 factors; when using the custom design function in JMP, all 12 main effect terms and all 12 squared terms should be included in the model along with 33 interaction terms. The design JMP suggests requires 64 runs, which again is between the size of the Algorithm 2 design and the Compact Box-Behnken design. Table 3.17 and Figure 3.8 compare the size and standard deviation of parameter estimates for these three designs. Again, the JMP design has similar standard deviations of parameter estimates to the Algorithm 2 design for main effects and interaction terms, but here the per-observation standard deviations of parameter estimates for squared terms are similar to those for the compact Box-Behnken designs.

Table 3.17 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 2 from section 2.3

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Res V Alg CCD	56	0.152	0.177	0.152	0.152	0.177	0.177	0.114	0.116
Compact B-B	$88 + n_c$	0.321	0.500	0.209	0.356	0.455	0.500	0.226	0.378
JMP D-optimal	64	0.203	0.428	0.138	0.143	0.147	0.155	0.356	0.428

In example 3 from section 2.3, the model specified in constructing the JMP design includes all 13 main effect terms, all 13 squared terms, and 45 of the interaction terms. Table 3.18 and Figure 3.9 compare the size and standard deviation of parameter estimates of this design to the Algorithm 2 and compact Box-Behnken designs. Here, the JMP design is the smallest. The standard deviations of parameter estimates for main effects and interaction terms are again similar to the Algorithm 2 design and for the squared

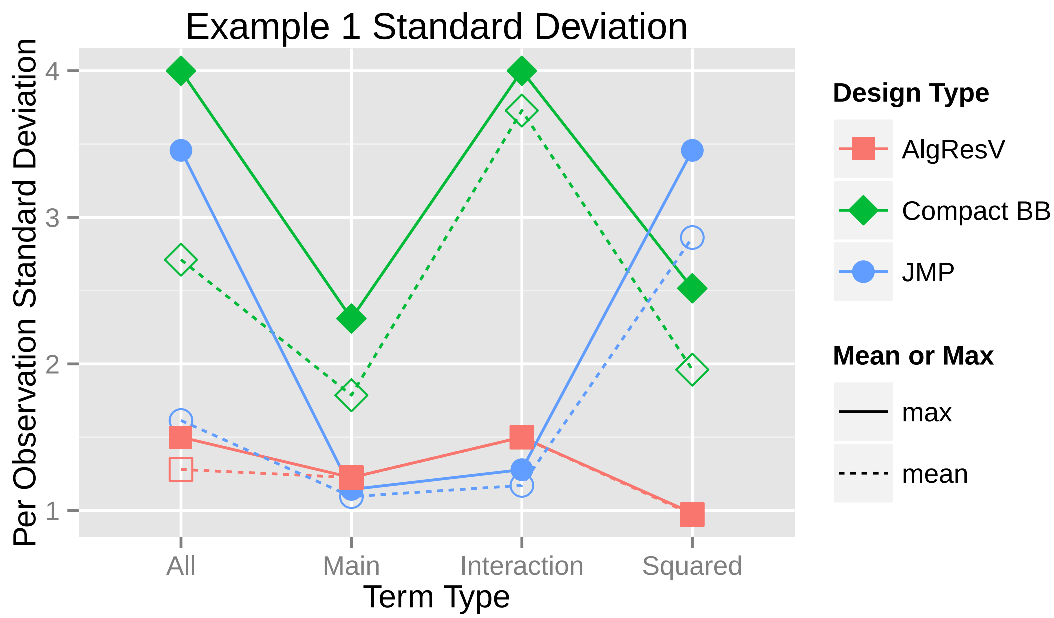

Figure 3.7 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 1 from section 1.5

terms, and the standard deviations of parameter estimates for squared terms are again similar to the compact Box-Behnken design.

Table 3.18 Number of runs and standard deviation (mean $\frac{s}{\sigma}$ and max $\frac{s}{\sigma}$) of parameter estimates for example 3 from section 2.3

		All Effects		Main Effects		Interactions		Squared	
	N	mean	max	mean	max	mean	max	mean	max
Res V Alg CCD	90	0.111	0.125	0.112	0.112	0.125	0.125	0.082	0.084
Compact B-B	$148 + n_c$	0.349	0.500	0.190	0.354	0.486	0.500	0.200	0.377
JMP D-optimal	76	0.186	0.451	0.128	0.137	0.137	0.147	0.357	0.451

3.5 Summary

The Box-Behnken type designs with BIBD blocks of size two give an intermediate size which is an improvement over the standard Box-Behnken designs, but are still larger than standard CCDs and CCD type design generated from Algorithm 2. The standard

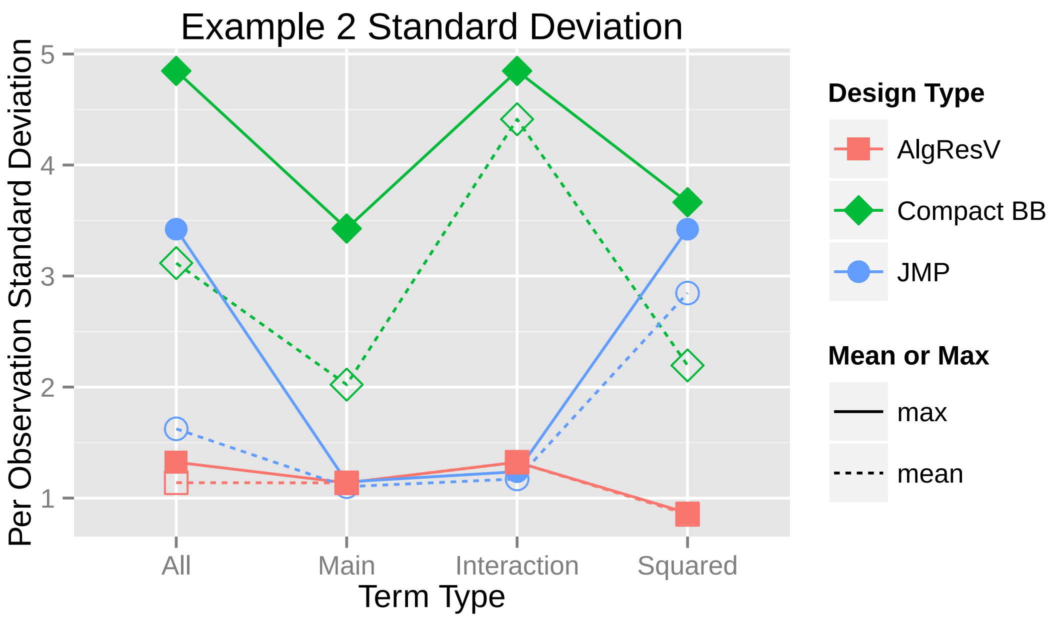

Figure 3.8 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 2 from section 2.3

deviations are larger than all of the CCD type designs and the standard Box-Behnken designs, so they should be used when variances are expected to be small and a Box-Behnken structure is preferred to a CCD structure. The Box-Behnken type designs with BIBD blocks of size $k_i - 1$ are impractically large and are not recommended. The compact Box-Behnken type designs with BIBD blocks of size two give a smaller size than even the non-compact version and they have more competitive standard deviations closer to that of the standard Box-Behnken design.

Compact Box-Behnken type designs and Central Composite type design using the resolution V version of Algorithm 2 discussed in section 2.2.1 are the smallest designs presented in this thesis. Compared to JMP custom designs, compact Box-Behnken designs are larger and have larger standard deviations of parameter estimates for main effect terms and interaction terms. Compact Box-Behnken designs have similar or smaller standard deviations of parameter estimates for squared terms. Algorithm 2 designs are

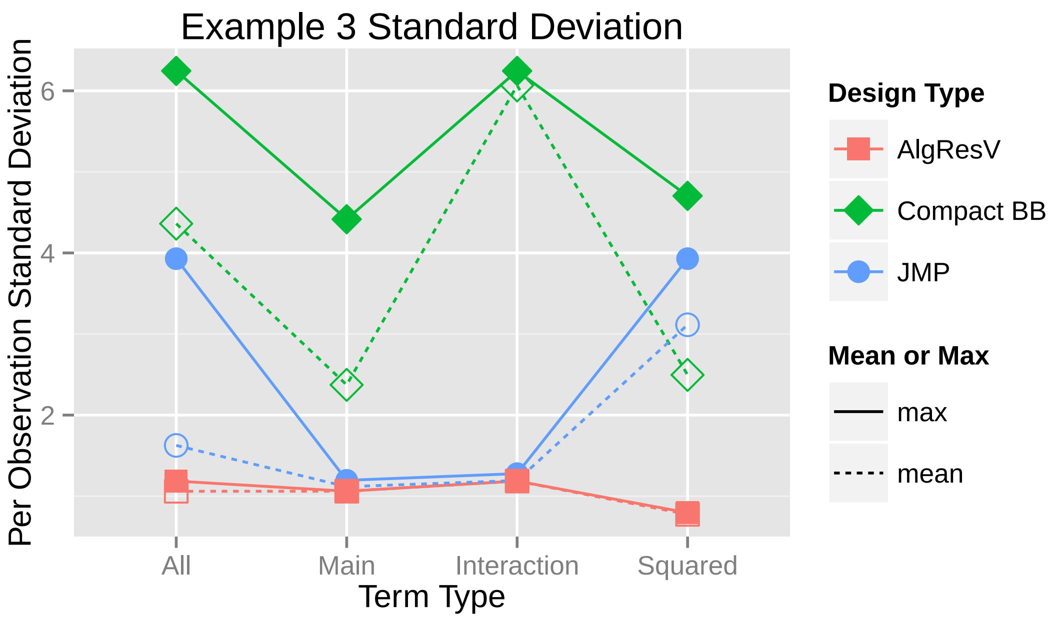

Figure 3.9 Per-observation standard deviation (mean $\sqrt{N}\frac{s}{\sigma}$ and max $\sqrt{N}\frac{s}{\sigma}$) of parameter estimates for example 3 from section 2.3

smaller than JMP designs for examples 1 and 2 and larger for example 3. Algorithm 2 designs and JMP designs have similar standard deviations of parameter estimates for main effect terms and interaction terms, but standard deviations of parameter estimates for squared terms are smaller for Algorithm 2.

CHAPTER 4. SUMMARY AND DISCUSSION

4.1 Conclusion

In the case of multiple response variables where there is previous information indicating which factors are related to each response and a full second order model is desired for each response, existing experimental designs leave room for improvement. For the MD-optimal design suggested by Fedorov (1972), Cooray-Wijesinha and Khuri (1987), and Chang (1997), additional assumptions are made that limit the usefulness of such designs. Standard Central Composite designs (CCD) and Box-Behnken designs treat all factors together, as if they are all in one model, which results in larger designs than necessary.

Two algorithms were presented in Chapter 2 for constructing a fractional factorial to use in a Central Composite type design that is a full factorial in the set of factors related to each response variable. Algorithm 2 is also extended to a fractional factorial that is a resolution V fractional factorial in the set of factors related to each response variable. These algorithms produce similar designs in many situations, and they can be much smaller than a standard CCDs, but there is a trade off between size and variability in the designs. Using the algorithms resulted in an increase in the standard deviations of parameter estimates in the models, even when expressed on a per-observation basis. CCDs using a fractional factorial from one of the algorithms should be used in situations where experimental runs are expensive and standard deviations are small.

A few variations on Box-Behnken designs were suggested in Chapter 3. The first is to use blocks of size two in the BIBD step of constructing a Box-Behnken design and including only the blocks where the set of factors corresponding to treatments in the block are both related to the same response variable. This resulted in a reduction in the size of the design, but also an increase in the standard deviations of parameter estimates. A further variation on this was suggested that involved combining blocks that were not used in the same model. This offered a further reduction in size and per-observation standard deviations of parameter estimates were closer to those in the standard Box-Behnken design. Another variation on Box-Behnken designs explored using blocks of size $k_i - 1$ for factors related to response i in the BIBD step, where k_i is the number of factors related to response i. This resulted in larger designs than the standard Box-Behnken design and is not recommended.

4.2 Future Work

There are multiple avenues for future research related to both the Central Composite type designs and the Box-Behnken type designs. First, with regard to the Central Composite type designs, further exploration into the designs produced by two algorithms presented in Chapter 2 should be done to determine general guidelines for which algorithm is preferred. If Algorithm 1 had desirable qualities that Algorithm 2 is lacking, a variation of Algorithm 1 should be explored that allows for resolution V fractional factorials in each response to be produced.

With regard to the Box-Behnken type designs discussed in Chapter 3, additional methods of combining blocks should be explored. As illustrated in example 3, when a large number of factors are related to a single response, combining blocks using the method described in Section 3.3 offers only marginal improvement in terms of both size and standard deviation of parameter estimates. Additional improvements on the Box-Behnken type designs with blocks of size two should be explored for these situations.

As the type of problem addressed by the models presented above all have multiple response variables, some questions arise about the multivariate analysis of such problems. One question that should be investigated is how much information is lost if individual univariate models are fit to each response as opposed to one multivariate model. Further research into whether model estimates will change and how much the variability of these estimates will be effected should be conducted. Investigation into what model diagnostics would be appropriate, particularly for outlier detection should also be done.

APPENDIX A. R FUNCTIONS

Included in this appendix are R functions for Algorithms 1 and 2 from Chapter 2.

R function for Algorithm 1

```
double<-function(D,d){
  #double is a function of a design (D) and a factor (d), that
  #repreats the entire design assembled so far (D), using the
  #negative of the factor being used to ''double'' (d).
  #d is the number of the column assocated with the factor.

  n<-nrow(D)
  DD<-rbind(D,D)
  DD[(n+1):(2*n),d]<- -DD[(1):(n),d]
  return(DD)
}

library(''sets'')
checkfactorial<-function(D,f){
  #A function that checks if the design D contains a full
  #factorial in the factors listed in f. It returns a list
  #where the first element is a vector of factors that are
```

```
    #a full factorial and the second is a list of factors
#that need to be used to double.
n<-length(f)
f1<-vector(''list'')
if(n>1){
  b<-vector(''list'')
  for(i in 1:n){
    a<-combn(n,i,simplify = FALSE)
    b<-c(b,a)
  }
  for(j in 1:length(b)){
    if(length(b[[j]])==1){
      f1<-c(f1,list(b[[j]]))
    }else{
      comb<-as.factor(apply(D[,f[b[[j]]]],1,paste0,
                      collapse='' ''))
      ncomb<-2^length(b[[j]])
      scomb<-summary(comb)
      if(length(scomb)==ncomb && all(scomb==mean(scomb))){
        f1<-c(f1,list(b[[j]]))
      }
    }
  }
  f2<-f1[[which.max(sapply(f1,length))]]
  return(list(f[f2],f[-f2]))
}else{
  res<-vector(''list'',2)
```

```
    res[[1]]<-f
    return(res)
  }
}

checkfactorial2<-function(D,fa,fb){
  #A function that checks if the design D contains a full
  #factorial in the factors listed in fa,fb, where all factors
  #in f1 must be included. It returns a list where the first
  #element is a vector of factors in fb that are a full
  #factorial and the second is a list of factors that need to
  #be used to double. fa must already be a full factorial.
  na<-length(fa)
  nb<-length(fb)
  f1<-list(vector())
  if((na*nb)>=1){
    b<-vector(''list'')
    for(i in 1:nb){
      a<-combn(nb,i,simplify = FALSE)
      b<-c(b,a)
    }
    for(j in 1:length(b)){
      comb<-as.factor(apply(D[,c(fa,fb[b[[j]]])],1,paste0,
                          collapse=''  ''))
      ncomb<-2^(length(b[[j]])+na)
      scomb<-summary(comb)
      if(length(scomb)==ncomb && all(scomb==mean(scomb))){
```

```
        f1<-c(f1,list(b[[j]]))
      }
    }
    f2<-f1[[which.max(sapply(f1,length))]]
    return(fb[f2])
  }
  if(na==0){
    return(checkfactorial(D,fb)[[1]])
  }
  if(nb==0){
    return(fb)
  }
}

algo1<-function(C){
  #This function returns a list of the size of the design
  # and the design itself.
  #This is a function of a matrix of treatments and responses
  #(columns are treatments, rows are responses, 1's indicate
  #that treatment matters for that response)
  #This function constructs a design based on algorithm 1 and
  #uses the functions ''double'' and ''checkfactorial'' above.
  #Currently, this function only works if the matrix is ordered
  #so that all factors are added to the design in order.
  #The matrix must also have at least 2 rows.

  #D_1
```

```
D<-list(matrix(nrow=1,ncol=dim(C)[2]))
for (i in 1:sum(C[1,])){
  D[[1]][,i]<-1
  D[[1]]<-double(D[[1]],i)
}
Dn<-list(sum(C[1,]))

#D_n, n>1
r<-dim(C)[1]
listC<-list(which(C[1,]==1))
for(i in 2:r){
  #vector of columns in Ci
  listC[[i]] <-which(C[i,]==1)
  #vector of columns in Ai (Ci and Di-1)
  A <-listC[[i]][listC[[i]]<=Dn[[(i-1)]]]
  #vector of columns in Bi (Ci not Di-1)
  B <-listC[[i]][listC[[i]]>Dn[[(i-1)]]]
  Bn <-length(B)
  if(length(A)>0){
    #vector of columns not in Ci (but in Di-1)
    E <-(1:Dn[[(i-1)]])[-A]
  }else{E<-1:Dn[[(i-1)]]}
  En <-length(E)
  #vector of columns in A_i^1 (full factorial)
  A1 <-checkfactorial(D[[(i-1)]],A)[[1]]
  #vector of columns in A_i^2 (need doubling)
  A2 <-checkfactorial(D[[(i-1)]],A)[[2]]
```

```
#get D^b_i-1
if(length(A2)>0){
  listD<-list(D[[(i-1)]])
  for(j in 1:length(A2)){
    listD[[(j+1)]]<-double(listD[[j]],A2[j])
  }
  Db<-listD[[length(A2)+1]]
}else{Db<-D[[(i-1)]]}

#Get D^c_i-1
Enew<-checkfactorial2(Db,A,E)
Enewn<-length(Enew)

Dc<-Db
if(min(Bn,Enewn)>0){
  for(j in 1:min(Bn,Enewn)){
    Dc[,B[j]]<-Dc[,Enew[j]]
  }
}

#Get D_i
listDnew<-list(Dc)
if(Bn>Enewn){
  for(j in 1:(Bn-Enewn)){
    listDnew[[j]][,B[j+Enewn]]<-1
    listDnew[[(j+1)]]<-double(listDnew[[j]],B[j+Enewn])
```

```
        }
      }
      D[[i]]<-listDnew[[length(listDnew)]]

      Dn[[i]]<-max(listC[[i]],Dn[[(i-1)]])
    }
    Design<-D[[length(D)]]
    res<-list(dim(Design)[1],Design)
    return(res)
}

#Function that will format any matrix of 0's and 1's and run
#the algorithm on it.
algo1ordercol<-function(C){
    #This function takes any matrix of 0's and 1's and reorders
    #the columns and applies ''algo1''.

    #Make C2 with no columns or rows of zeros
    if(sum(apply(C,2,sum)==0)!=0){
      C1<-C[,-which(apply(C,2,sum)==0)]}else{C1<-C}
    if(sum(apply(C1,1,sum)==0)!=0){
      C2<-C1[-which(apply(C1,1,sum)==0),]}else{C2<-C1}

    #Make C3 from C2 by ordering the columns so the algorithm
          #works.
    C3<-C2[,order(apply(C2,2,function(x)  which(x==1)[1]))]
```

```
  res<-c(algo1(C3),list(C3))
  #res<-list(algo1(C3)[[1]],C3)
  return(res)
}

#A function that will order the rows largest to smallest and
#then run algo1 on it.
algo1orderrow<-function(C){
  C1<-C[order(apply(C,1,sum),decreasing = TRUE),]
  res<-algo1ordercol(C1)
  return(res)
}
```

R function for Algorithm 2

```
algo.resolution<-function(C,resolution=(dim(C)[2]+1)){
  #A function that finds a unified design that is a full factorial
  #in each response.
  #Or if resolution is specified, it gives a fractional factorial
  #of that resolution in each response.
  #needs library("FrF2")
  k<-dim(C)[2]
  fact.columns<-rep(NA,k)
  for(i in 1:k){
    filled.in<-t(apply(C,1,function(x) x*fact.columns))
    used<-unique(c(filled.in*C[,i]))
    tf.used<-sapply(used,function(x) (1:k == x))
    fact.columns[i]<-min(which(apply(tf.used,1,
```

```
                    function(x) all(x==FALSE,na.rm=TRUE))))
  }
  nfactors<-max(fact.columns)
  res<-min(max(apply(C,1,sum))+1,resolution)
  unique.fact<-FrF2(nfactors=nfactors,resolution=res)
  design<-unique.fact[,fact.columns]
  return(design)
}
```

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