Chapter 8

OPTIMAL DESIGNS FOR MULTIPLE REGRESSOR INTERACTION MODELS

§8.1 Introduction

While the individual effects of a toxicant are important, the researcher is often more concerned about how these substances work together or interact to produce a particular response. For example, the biologist may want to know if a certain combination of substances causes more harm to an ecosystem than the administration of each of the substances singularly. Hence, the focus of this chapter is optimal design for the multiple regressor model with interaction. Both the D- and D*-optimal designs will be detailed for the k regressor models. In addition, an interaction optimal design will be presented for the two regressor model.

While the same basic criteria are used to find these designs in the interaction model case, there is one fundamental difference from the no-interaction case. This difference is the inability to find designs in terms of IECs which results from the introduction of the interaction parameters into the model. The only alternative to finding designs in IECs is to find them in terms of natural units.
Unfortunately, this necessitates guessing at the values of the regression parameters which define the MECs. In the two regressor interaction model, three parameters must be guessed in order to determine an optimal design. First, one must consider how to obtain these guesses. After all, the researcher may not know enough about all three parameters, particularly the interaction parameter, to venture these guesses. This also means that designs must be determined on a case by case basis, meaning that a new design must be generated for each new set of parameter values. In addition, guessing three parameters creates the need for robustness studies since there are innumerable ways in which this combination of parameters can be misspecified. As the number of regressors in the model increases, so does the complexity of this design problem. For example, consider a four-regressor model. In this case, the values of the 15 parameters must be guessed. For the reasons detailed above, it is obvious that finding designs in terms of natural units for these models is an impractical solution to this design problem. An alternative solution is needed which yields a more general design that is less parameter dependent. One such solution is a conditionally optimal design. In the sections that follow, this condition is defined, conditionally optimal designs are detailed, and robustness issues under violation of the condition are explored.

§8.2 Condition for Optimality of Interaction Designs
The condition required for optimality of the designs presented later in this chapter involves the use of a convenient guess for all interaction parameters in the model. The convenient value for all of the interaction parameters in the model is zero. It is important to note that this guess does not affect the estimability of the interaction parameters. In fact, in many cases these parameters are estimated quite well. The guess is merely made for the purpose of design selection. This is not an assumption. The convenient guess of zero has many foundations for its use in this situation. First, it is precededent in the logistic case. Brunden, et. al. (1988) used this same condition to develop designs for interaction and second order logistic models in drug combination therapy studies. One could also view this condition from a Bayesian perspective in the sense that the guess of zero represents a typical point prior on each of the interaction parameters. Finally, this guess is logical because one knows neither the magnitude nor the sign of the interaction, so the value of zero represents a practical solution. Most importantly, this condition allows the formulation of designs in
terms of IECs using the same parameterization as the no-interaction model. The expected value at a point $i$ for $k$ regressor model can be expressed as

$$E(y_{ij}) = \lambda_i = q_{i1}q_{i2} \ldots q_{ik} \lambda_c$$

(8.2.1)

where $\lambda_c = e^{\beta_0}$ and $q_{ii} = e^{\beta_i x_{ii}}$. The focus now turns to the application of this technique to the two regressor model with interaction.

§8.3 D-Optimal Design for the Two Regressor Interaction Model

The two regressor exponential model is of the form

$$y_{ij} = e^{x_i^T \beta} + \varepsilon_{ij} = e^{\beta_{11}x_{i1} + \beta_{12}x_{i2} + \beta_{21}x_{i1}x_{i2} + \varepsilon_{ij}}$$

(8.3.1)

where $i=1, \ldots, 4$, $j=1, \ldots, n_i$, and $E(y_{ij}) = \lambda_i = e^{\beta_{11}x_{i1} + \beta_{12}x_{i2} + \beta_{21}x_{i1}x_{i2}}$. The development of the conditionally D-optimal design for the two regressor model follows the same patterns as that for the other designs seen in this work. It begins with the information matrix where $\lambda_i = q_{i1}q_{i2} \lambda_c$ and $x_{ii} = \frac{\ln q_{ii}}{\beta_i}$ under the condition of the guess that $\beta_{12} = 0$ as shown in (8.3.2)

$$I(X, \beta) = 
\begin{bmatrix}
\sum \lambda_i & \sum \lambda_i x_{i1} & \sum \lambda_i x_{i2} & \sum \lambda_i x_{i1}x_{i2} \\
\sum \lambda_i x_{i1} & \sum \lambda_i x_{i1}^2 & \sum \lambda_i x_{i1}x_{i2} & \sum \lambda_i x_{i1}^2x_{i2} \\
\sum \lambda_i x_{i2} & \sum \lambda_i x_{i1}x_{i2} & \sum \lambda_i x_{i2}^2 & \sum \lambda_i x_{i1}^2x_{i2} \\
\sum \lambda_i x_{i1}x_{i2} & \sum \lambda_i x_{i1}^2x_{i2} & \sum \lambda_i x_{i1}x_{i2}^2 & \sum \lambda_i x_{i1}^2x_{i2}^2
\end{bmatrix}
$$

(8.3.2)

The determinant of this matrix is
\[
|f(X, \beta)| = -abcd + abl^2 + aj^2d - 2ajkl + ack^2 + f^2dc \\
- \frac{1}{2} f^2 - 2fjdg + 2fjlh + 2fkgl - 2fchk + bdg^2 \\
- 2gblh - g^2k^2 + 2gkhj + bch^2 - h^2j^2 .
\] (8.3.3)

The design which maximizes this expression has many very attractive features. First, it is an equal allocation design. Twenty-five percent of the experimental units are placed at each of the four points. Second, the design makes use of the EC_{13.53} as do all of the other D-optimal designs for the exponential model. Finally, the design takes on the familiar form of a factorial. The design points and allocation percentages are detailed in Table 8.3.1 while the geometry of the design is shown in Figure 8.3.1.

| Table 8.3.1. D-Optimal Design for the Two Regressor Interaction Model |
|---|---|---|---|
| \( i \) | \( p_i \) | \( x_{1i} \) | \( x_{2i} \) | Contour |
| 1 | 0.25 | IEC\(_{100}\) | IEC\(_{100}\) | MEC\(_{100}\) |
| 2 | 0.25 | IEC\(_{100}\) | IEC\(_{13.53}\) | MEC\(_{13.53}\) |
| 3 | 0.25 | IEC\(_{13.53}\) | IEC\(_{100}\) | MEC\(_{13.53}\) |
| 4 | 0.25 | IEC\(_{13.53}\) | IEC\(_{13.53}\) | MEC\(_{13.83}\) |

Figure 8.3.1. Geometry of D-Optimal Design for the Two Regressor Interaction Model

Of course, the introduction of a new optimal design would not be complete without verification of its optimality through equivalence theory. As mentioned in Chapter 7 for the D-optimal case, Silvey’s theorem reduces to showing that

\[
F_\delta [M(\eta^*, \beta) \cdot J(x, \beta)] = \text{trace} [J(x, \beta)M^{-1}(\eta^*, \beta)] - p \leq 0 \text{ for all points in the design space.}
\]
from previous sections that \( J(\mathbf{x}, \beta) \) is the information matrix for a single observation, 
\[ M(\eta^*, \beta) = \frac{1}{N} I(\mathbf{X}, \beta), \]  
and \( p \) is the number of parameters. So in this case, it will be shown that 
\[ f = \text{trace}[J(\mathbf{x}, \beta)M^{-1}(\eta^*, \beta)] \leq 4 \]  
for all points in the design space. Also recall that \( f \) must take on the value \( p=4 \) at design points 1-4. The plot of the equivalence theory function, \( f \), below shows that the required relationships hold for the points in the design space. Note that \( f \) is a function of \( q_1 \) and \( q_2 \).

![Equivalence Theory Function for the D-Optimal Two Regressor Interaction Design.](image)

**§8.4 Lack of Fit Properties for the Five Point Design for the Two Regressor Model with Interaction**

Lack of fit also becomes an issue in the two regressor model with interaction. It is desirable to augment the four point D-optimal design listed in Table 8.3.1 with a fifth point in order to test LOF. As in the no interaction case, the point which maximizes the power of the test for LOF or equivalently minimizes the variance of the LOF parameter is sought. In order to determine the significance of lack of fit, one of the two quadratic coefficients, either \( \beta_{11} \) or \( \beta_{22} \), can be estimated. Since each of these parameters must be estimated with equal precision, the search for the fifth point is restricted to the line defined by \( q_1 = q_2 \). A grid search reveals again that the centroid of the square formed by the four D-optimal points, \( q=(0.565, 0.565) \), provides the most powerful test for
LOF. Of course, the power of this test increases as more points are placed at the centroid but the D-efficiency decreases. Note the similarity between the five point design for the Poisson model shown below and a factorial design with center runs for a traditional linear model.

![Figure 8.4.1. Centroid Design for LOF in the Two Regressor Interaction Model.](image)

§8.5 The D-Optimal Design for the Three Variable Interaction Model

Based on the cases presented thus far the D-optimal design for the three variable interaction model can easily be specified. The factorial-like square design seen in Figure 8.3.1 for the two variable interaction design is projected to its three-dimensional counterpart. Thus, the three variable interaction design is a cube where the vertices are comprised of the control, three pure component blends, three binary blends, and one ternary blend where all blends use the IEC\textsubscript{13.53} as the non-control level. The geometric view of this design is shown in Figure 8.5.1.

![Figure 8.5.1 Geometric View of the Three Regressor Interaction Model Design.](image)
As one might imagine, the coordinates for the design points as represented in individual ECs are the permutations of IEC\textsubscript{13.53} and IEC\textsubscript{100} as shown in Table 8.5.1.

<table>
<thead>
<tr>
<th>( i )</th>
<th>( p_i )</th>
<th>( x_{1i} )</th>
<th>( x_{2i} )</th>
<th>( x_{3i} )</th>
<th>( \text{Plane} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.125</td>
<td>IEC\textsubscript{100} _\textsubscript{13.53}</td>
<td>IEC\textsubscript{100} _\textsubscript{100}</td>
<td>IEC\textsubscript{100} _\textsubscript{13.53}</td>
<td>MEC _\textsubscript{100}</td>
</tr>
<tr>
<td>2</td>
<td>0.125</td>
<td>IEC\textsubscript{13.53} _\textsubscript{13.53}</td>
<td>IEC\textsubscript{100} _\textsubscript{100}</td>
<td>IEC\textsubscript{13.53} _\textsubscript{13.53}</td>
<td>MEC _\textsubscript{13.53}</td>
</tr>
<tr>
<td>3</td>
<td>0.125</td>
<td>IEC\textsubscript{100} _\textsubscript{13.53}</td>
<td>IEC\textsubscript{13.53} _\textsubscript{13.53}</td>
<td>IEC\textsubscript{13.53} _\textsubscript{13.53}</td>
<td>MEC _\textsubscript{0.0183}</td>
</tr>
<tr>
<td>4</td>
<td>0.125</td>
<td>IEC\textsubscript{100} _\textsubscript{13.53}</td>
<td>IEC\textsubscript{13.53} _\textsubscript{13.53}</td>
<td>IEC\textsubscript{13.53} _\textsubscript{13.53}</td>
<td>MEC _\textsubscript{0.0183}</td>
</tr>
<tr>
<td>5</td>
<td>0.125</td>
<td>IEC\textsubscript{100} _\textsubscript{13.53}</td>
<td>IEC\textsubscript{13.53} _\textsubscript{13.53}</td>
<td>IEC\textsubscript{13.53} _\textsubscript{13.53}</td>
<td>MEC _\textsubscript{0.0025}</td>
</tr>
</tbody>
</table>

While not presented here, the optimality of this design was verified using equivalence theory via a grid search on the function. A final comment on lack of fit is in order. One could easily augment this design with a centroid point to test for lack of fit. The same allocation issues apply to this augmentation as did in the previous cases.

§8.6 The I-Optimal Design for the Two Regressor Model with Interaction

As mentioned earlier, researchers are often most interested in the interaction of two substances in impaired reproduction studies. A dosage combination of drugs may be more effective in treating a certain illness or a combination of environmental toxins may react so that they have a stronger impact on an ecosystem. Hence, estimation of the interaction term is very important. Indeed, at times, interaction may be the only item of interest by the researcher. The I-optimal design for the two regressor model estimates interaction as well as possible by minimizing the variance of the interaction term, \( \text{var}(b_{12}) \).

The \( \text{var}(b_{12}) \) is taken from the inverse of the information matrix in (8.3.2) and is given by

\[
\text{var}(b_{12}) = \frac{\text{num}}{\text{det}}
\]  

(8.6.1)
where

\[
\text{num} = -abc + a^2j + f^2c - 2fgj + g^2b \quad (8.6.2)
\]

and

\[
\det = -abcd + abl^2 + aj^2d - 2ajkd + ack^2 + f^2dc
- l^2f^2 - 2fjdg + 2fjhl + 2fkgl - 2fchkl + bdg^2
- 2gblh - g^2k^2 + 2ghj + bch^2 - h^2j^2. \quad (8.6.3)
\]

The design which minimizes this expression is given in the Table 8.6.1 while a geometric view is shown in Figure 8.6.1.

Table 8.6.1. Interaction Optimal Design for the Two Regressor Model.

<table>
<thead>
<tr>
<th>(i)</th>
<th>(p_i)</th>
<th>(x_{1i})</th>
<th>(x_{2i})</th>
<th>Contour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0477</td>
<td>IEC1(_{100})</td>
<td>IEC2(_{100})</td>
<td>MEC(_{100})</td>
</tr>
<tr>
<td>2</td>
<td>0.1706</td>
<td>IEC1(_{100})</td>
<td>IEC2(_{7.8})</td>
<td>MEC(_{7.8})</td>
</tr>
<tr>
<td>3</td>
<td>0.1706</td>
<td>IEC1(_{7.8})</td>
<td>IEC2(_{100})</td>
<td>MEC(_{7.8})</td>
</tr>
<tr>
<td>4</td>
<td>0.6111</td>
<td>IEC1(_{7.8})</td>
<td>IEC2(_{7.8})</td>
<td>MEC(_{0.61})</td>
</tr>
</tbody>
</table>

Like the D-optimal design for this model, this design takes on a factorial structure. However, the effective concentration on which the factorial is based has changed as well as the percentage of
experimental units allocated to each of those points. The IEC_{13.53} has been replaced by the IEC_{7.8} in the factorial. One should note that the majority of the design points are concentrated at point 4, (IEC_{7.8}, IEC_{7.8}). This is the point that estimates the interaction parameter, \( \beta_{12} \). A point of interest is the fact that the design is based around the EC_{7.8}. One should recall that the F-optimal or slope optimal design in the single variable case which estimated the slope parameter as well as possible was based around this EC as well.

Again, equivalence theory is applied to the I-optimal design to demonstrate its optimality. The relationship that results from the application of Silvey’s theorem (Theorem 1) is shown below

\[
\text{tr} \left( a \bar{M}(\eta, \beta)^{-1} J(x, \beta) M(\eta, \beta)^{-1} a \right) - \text{tr} \left( a \bar{M}(\eta, \beta)^{-1} a \right) \leq 0
\]

(8.6.4)

where \( a = \begin{bmatrix} 0 & N^{-1} \end{bmatrix} \) and \( J(x, \beta) \) and \( M(\eta, \beta) \) are defined as in Section 7.10. Making appropriate simplifications, (8.6.4) becomes.

\[
g = \text{tr} \left( a \bar{M}(\eta, \beta)^{-1} J(x, \beta) M(\eta, \beta)^{-1} a \right) \leq \text{var}(b_{12})
\]

(8.6.5)

For the design in question \( \text{var}(b_{12}) = 10.40 \). Again \( g \) must be equal to 10.40 at the design points and less than 10.40 at all points in the design space. Figure 8.6.2 shows a plot of \( g \) to verify the relationships specified by the equivalence theory.

Figure 8.6.2. Equivalence Theory Function for the Two Regressor Interaction Optimal Design.
The Dₙ-optimal design for the two regressor model with interaction

A Dₙ-optimal design has also been found for the two variable model with interaction. In this model, an MEC is now defined by s=3 parameters as shown in (8.7.1).

\[ q_i = e^{\beta_{1,i} x_{1i} + \beta_{2,i} x_{2i} + \beta_{12,i} x_{1i} x_{2i}} \]  

(8.7.1)

The same function, \( \det(M_{22} - M_{12}' M_{11}^{-1} M_{12})^{-1} \), must be maximized to find the D-optimal design. The matrix \( M_{11} \), which is a scalar in this case, remains the same, \( M_{11} = \sum \lambda_i \) while \( M_{12} = \left[ \sum \lambda_i x_{1i} \sum \lambda_i x_{2i} \sum \lambda_i x_{1i} x_{2i} \right] \) and \( M_{22} = \left[ \sum \lambda_i x_{1i}^2 \sum \lambda_i x_{1i} x_{2i} \sum \lambda_i x_{2i}^2 \sum \lambda_i x_{1i} x_{2i} \right] \). The Dₙ-optimal design is given in Table (8.7.1).

<table>
<thead>
<tr>
<th>i</th>
<th>( p_i )</th>
<th>( x_{1i} )</th>
<th>( x_{2i} )</th>
<th>Contour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.118</td>
<td>IEC100</td>
<td>IEC200</td>
<td>MEC100</td>
</tr>
<tr>
<td>2</td>
<td>0.278</td>
<td>IEC100</td>
<td>IEC2100</td>
<td>MEC110</td>
</tr>
<tr>
<td>3</td>
<td>0.278</td>
<td>IEC110</td>
<td>IEC2100</td>
<td>MEC110</td>
</tr>
<tr>
<td>4</td>
<td>0.364</td>
<td>IEC110</td>
<td>IEC210</td>
<td>MEC0.0121</td>
</tr>
</tbody>
</table>

The optimality of this design can also be verified using equivalence theory. In this case, the equivalence theory function, \( h \), is given in (8.7.2).

\[ h = \left( x^{(s)} - M_{12}' M_{11}^{-1} M_{12} x^{(1)} \right)' \left( M_{22} - M_{12}' M_{11}^{-1} M_{12} \right) \left( x^{(s)} - M_{12}' M_{11}^{-1} M_{12} x^{(1)} \right) \leq 3. \]  

(8.7.2)

The function \( h \) is plotted Figure 8.7.1. One can see that it achieves the value s=3 at all four of the design points and is less than or equal to s=3 at all other points in the design space.

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§8.8 The $D_s$-Optimal Design for the Three Variable Interaction Model

Like the D-optimal design for the three variable interaction model, the $D_s$-optimal design also forms a cube. However, the vertices of this cube as well as the allocation percentages of the design points are altered. This is attributed to the fact that this design caters to the estimation of the seven parameters which define the EC for this model. The design points and percentage of allocation are listed in Table 8.8.1.

<table>
<thead>
<tr>
<th>$i$</th>
<th>$p_i$</th>
<th>$x_{1i}$</th>
<th>$x_{2i}$</th>
<th>$x_{3i}$</th>
<th>Plane</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.065</td>
<td>IEC1_{100}</td>
<td>IEC2_{100}</td>
<td>IEC2_{100}</td>
<td>MEC_{100}</td>
</tr>
<tr>
<td>2</td>
<td>0.124</td>
<td>IEC1_{12.40}</td>
<td>IEC2_{100}</td>
<td>IEC2_{100}</td>
<td>MEC_{12.40}</td>
</tr>
<tr>
<td>3</td>
<td>0.124</td>
<td>IEC1_{100}</td>
<td>IEC2_{12.40}</td>
<td>IEC2_{100}</td>
<td>MEC_{12.40}</td>
</tr>
<tr>
<td>4</td>
<td>0.124</td>
<td>IEC1_{100}</td>
<td>IEC2_{100}</td>
<td>IEC2_{12.40}</td>
<td>MEC_{12.40}</td>
</tr>
<tr>
<td>5</td>
<td>0.140</td>
<td>IEC1_{12.40}</td>
<td>IEC2_{12.40}</td>
<td>IEC2_{100}</td>
<td>MEC_{0.0154}</td>
</tr>
<tr>
<td>6</td>
<td>0.140</td>
<td>IEC1_{12.40}</td>
<td>IEC2_{100}</td>
<td>IEC2_{12.40}</td>
<td>MEC_{0.0154}</td>
</tr>
<tr>
<td>7</td>
<td>0.140</td>
<td>IEC1_{100}</td>
<td>IEC2_{12.40}</td>
<td>IEC2_{12.40}</td>
<td>MEC_{0.0154}</td>
</tr>
<tr>
<td>8</td>
<td>0.143</td>
<td>IEC1_{12.40}</td>
<td>IEC2_{12.40}</td>
<td>IEC2_{12.40}</td>
<td>MEC_{0.0020}</td>
</tr>
</tbody>
</table>

The allocation percentages in this design reflect the design criterion in the sense that estimation of the intercept is de-emphasized while the main effect parameters and two-way interaction
coefficients are estimated equally within their respective classes. As a final note, equivalence theory was used to confirm the optimality of this design.

§8.9 Robustness Properties of the Conditionally D-Optimal Design for the Two Regressor Interaction Model

The designs in this chapter have been developed under the convenient guess that the interaction parameters are zero. Of course, one must determine the quality of these designs in the event that the interaction parameters are not zero. The two regressor designs will be explored extensively in this situation via a robustness study. It will begin by comparing the efficiency of the conditionally D-optimal design under different magnitudes of both synergistic and antagonistic interactions to the design where $\beta_{12} = 0$. Recall that the general formula for efficiency in a D-optimal design is

$$E = \left( \frac{\det[I^*]}{\det[I]} \right)^{\frac{1}{2}} \times 100$$

where $I^*$ is the information matrix for the design in question and $I$ is the information matrix for the optimal design. Algebraic manipulation of the determinant reveals that the efficiency in this specific situation reduces to

$$E = \left( \frac{\lambda^*_4}{\lambda_4} \right)^{\frac{1}{3}} = \left( \frac{q_4}{0.0183^2} \right)^{\frac{1}{3}}$$

where $\lambda^*_4$ is the expected value at the fourth design point and $q_4$ represents the MEC for the fourth design point when $\beta_{12} \neq 0$. Hence, the efficiency is the cube root of the ratio of the “true” model effective concentration to the model effective concentration under $\beta_{12} = 0$. In addition it can be described as the cube root of the portion of the MEC for point 4 contributed by the interaction. The efficiency is graphed below with respect to the true MEC under the model where interaction is present.
Although the true classification of an interaction as synergistic or antagonistic depends on the goal of an experiment, for the purposes of this study synergism will be considered an interaction of positive sign whereas antagonism will be considered an interaction with a negative sign. For models where synergistic interaction is present (i.e. the true MEC of design point 4 is greater than 0.0183), this design performs extremely well, with efficiencies greater than much greater than 100%. However, the design does not fare as well for antagonistic interactions where the MEC is less than the conditionally optimal value of 0.0183. The enlarged view of the Figure 8.9.1 for MECs which range from 0 to 0.05 shown in Figure 8.9.2 demonstrates this.
However, there is a design that should be used if a negative interaction is suspected. That design is the I-optimal design. Efficiencies were computed for estimation of the interaction parameter and it was found that the I-optimal design estimates a negative interaction parameter very well with respect to the D-optimal design as shown in Figure 8.9.3.

![Figure 8.9.3. I-Efficiency vs. True MEC for $\beta_{12} \neq 0$.](image)

The efficiency plotted is the ratio \( \frac{\text{var}_D(b_{12})}{\text{var}_I(b_{12})} \times 100 \) for the same value of $\beta_{12} \neq 0$. One should note that the interaction design does offer an improvement over the D-optimal design with respect to a positive interaction. In conclusion, the D-optimal design should be used if positive interaction is suspected and the I-optimal design should be used if negative interaction is suspected.

Robustness issues for the three regressor design have yet to be discussed with respect to violation of the guess. In this case, there are four interaction parameters which are set equal to zero. These include $\beta_{12}, \beta_{13}, \beta_{23}$, and $\beta_{123}$. If any of these four parameters are non-zero than any of the four MECs associated with the estimation of those three parameters is affected. Namely, $\lambda_5$ through $\lambda_8$ could potentially be misspecified based on the values of $\beta_{12}, \beta_{13}, \beta_{23}$, and $\beta_{123}$. Based on the form of the determinant, the efficiency relationship with respect to positive and negative values of interaction would continue. However, it should be noted that in the k-regressor case this is viewed as whether there would be an overall increase or decrease in the determinant based on an overall positive interaction contribution or an overall negative contribution.
respectively, resulting from the presence of any of the interaction parameters \( \beta_{12}, \beta_{13}, \beta_{23}, \) and \( \beta_{123} \). So, if interactions are viewed as predominantly positive the D-optimal design will perform well but if interactions are predominantly negative it will not estimate the coefficients as well as it does under the guesses.

§8.10 Implications for \( k \)-regressor Models

Conditionally optimal designs for interaction models with two and three regressors have been presented in this chapter. Based on the form of the determinant for these models it is apparent that \( k \)-regressor designs will be equal allocation factorials using IEC_{13,53} as the non-control level. D_{s}-optimal designs must be found on an individual basis, however they will continue to take the same basic factorial form with less emphasis placed on the overall control point and equal emphasis placed on each class of design point (i.e. two-way interaction points, three-way interaction points, etc.) It should also be noted that D_{s}-optimality could be used to determine a design which estimates pre-determined interactions as precisely as possible. This would provide a design that performs the same task as the I-optimal design in the two regressor case. As a final note, designs on restricted regions for \( k \)-regressor interaction models follow the same pattern as do those in the no interaction models: IECs are pushed to the extremes of the region. Appendix F addresses this issue.