Model-robust experimental designs for the fractional polynomial response surface models

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Abstract

Fractional polynomial response surface models are polynomial models whose powers are restricted to a small predefined set of rational numbers. Very often these models can give a good fit to the data and much more plausible behavior between design points than the polynomial models. In this paper, we propose a one-stage and two-stage design strategy for obtaining designs under model uncertainty for these nonlinear class of models.

Keywords: nonlinear, model-robust, lack of fit, nesting strategy, support points, locally optimal designs.
1 Introduction

In much of statistical practice, particularly in biological and chemical processes, nonlinear regression models are more applicable than their linear counterparts as they tend to fit the data often with few parameters and the model parameters are more scientifically meaningful. See for example Ratkowsky (1983, 1990) and Seber and Wild (1989) for general discussions on the class of nonlinear models. But before we can fit a nonlinear model to data, we actually need to carry out an experimental design. Researchers have often resorted to the theory of optimal designs to get practical designs for those models. However the complexity of these nonlinear models is such that the optimum experimental designs for these models depend on the values of the unknown parameters.

A common approach to this problem is to adopt a best guess for the parameters and then choose the design that maximizes a selected design optimality criterion evaluated at the guess value. This approach leads to what is termed locally optimal designs, introduced by Chernoff (1953). The best guess used in a locally optimal design might come from previous experiments, past experience including the analysis of related experiments or a pilot experiment conducted especially for that purpose (see Atkinson and Haines (1996) for details and extensive references on the designs for nonlinear models).

Another shortcoming of most optimal designs for nonlinear models is that these designs often have only \( p \) support points, where \( p \) is the number of parameters in the nonlinear model. This may cause no problems if the experimenter believes the postulated model is adequate. However, in practice the assumed model may be inadequate so that researchers often look for designs which are near-optimal for the assumed model but which contain “extra” design points that can be used to test for model inadequacy.
In this paper, we shall introduce and illustrate such a one-stage “robust” design procedure using the approach proposed by Atkinson (1972), Atkinson and Donev (1992) and O’Brien (1993) for the class of fractional polynomial response surface models. We shall also propose a two-stage design strategy for obtaining designs under model uncertainty for these nonlinear models.

2 Optimal design theory

The design problem for the nonlinear model

\[ y_i = \eta(x_i, \theta) + \varepsilon_i \quad i = 1, \ldots, n \]  

(typically involves choosing a \( n \)-point design, \( \xi \), to estimate some function of the \( p \)-dimensional parameter vector, \( \theta \), with high efficiency. Here \( \xi \) can be written as

\[ \xi = \left\{ \begin{array}{c} x_1, x_2, \ldots, x_n \\ \omega_1, \omega_2, \ldots, \omega_n \end{array} \right\}, \]

where the design vectors, \( x_1, x_2, \ldots, x_n \) are elements of the design space, \( \chi \) and are not necessarily distinct with the \( \omega_1, \omega_2, \ldots, \omega_n \) being the associated replicates of design points. Alternatively, \( \xi \) can be expressed in terms of its \( r \) (\( r \leq n \)) distinct design points, \( s_1, s_2, \ldots, s_r \), called its support points and their associated design weights \( \lambda_1, \lambda_2, \ldots, \lambda_r \), i.e.,

\[ \xi = \left\{ \begin{array}{c} s_1, s_2, \ldots, s_r \\ \lambda_1, \lambda_2, \ldots, \lambda_r \end{array} \right\}. \]

Whenever \( n\lambda_i \) is integral for each \( i \), \( \xi \) is said to be a discrete design, otherwise it is said to be a continuous design. The latter can be converted into practical designs by using rounding procedures given in Pukelsheim and Rieder (1992) and Pukelsheim (1993).
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Under the assumption of uncorrelated Gaussian random errors with zero mean and constant variance (taken to be one without loss of generality), the Fisher information matrix for \( \theta \) is given by \( M(\xi, \theta) = V'\Omega V \), where \( V \) is the \( n \times p \) Jacobian of \( \eta \) with \( i^{th} \) row equal to the gradient \( \partial \eta(x_i, \theta) / \partial \theta' \) and \( \Omega \) is the diagonal matrix with diagonal elements \( \{ \omega_1, \omega_2, \ldots, \omega_n \} \). Designs which maximize the determinant \( |M(\xi, \theta^0)| \) for some value \( \theta = \theta^0 \) are called locally D-optimal.

3 Model nesting as a robust design strategy

In this section, we look at the nesting strategy proposed by Atkinson and Donev (1992) and adapted by O’Brien (1993) to obtain designs with “extra” design points by embedding a given model function (called the original model function) in a larger one (called the supermodel) which reduces to the original model for certain parameter choices. Use of the nesting technique as a means of model robustness for linear models is highlighted in Atkinson (1972), Stigler (1971), Jones and Mitchell (1978), Studden (1982), DeFeo and Myers (1992). The application to nonlinear models is mentioned in Box and Lucas (1959), Cochran (1973) and Atkinson and Donev (1992). Suppose we feel that the one-parameter simple exponential model function

\[
\eta_1 = \exp(-\theta_1 x)
\]  

(2)

adequately describes a process but wish to allow for an inflection point, then we could nest (2) in the two-parameter sigmoidal supermodel

\[
\eta = \exp(-\theta_1 x^{\theta_2}).
\]  

(3)

Note that (3) reduces to (2) for \( \theta_2 = 1 \). The nesting strategy developed here is useful when the experimenter’s belief in the original model is quite high but it is desired to have
additional design points to check for possible departures. In the next section we outline the procedure of Atkinson and Donev (1992) and O’Brien (1993) to find such types of designs.

4 The first-order nesting design strategy

Consider the case where the original model function $\eta_1(\theta_1)$ is nested in the supermodel $\eta(\theta_1, \theta_2)$ which reduces to $\eta_1(\theta_1)$ for $\theta_2 = c$; here $\theta_1$ is $p \times 1$, $\theta_2$ is $q \times 1$, and $\theta = (\theta'_1, \theta'_2)'$.

One measure of information the design $\xi$ contains regarding $\theta_1$ in the model $\eta_1$ is $|M_{11}|$. Here $M_{11} = V_1'\Omega V_1$, where $V_1$ is the Jacobian of $\eta_1$ and $\Omega = \text{diag}\{\omega_1, \omega_2, \ldots, \omega_n\}$ where $\omega_1, \omega_2, \ldots, \omega_n$ are the design weights of $\xi$. Atkinson and Donev (1992) suggest that the information $\xi$ contains regarding departures from $\eta_1$ “in the direction of $\eta$” is

$$|M_{22} - M_{21} M_{11}^{-1} M_{12}| = \frac{|M|}{|M_{11}|},$$

where $M_{ij} = V_i'\Omega V_j$ for $i, j = 1, 2$ and $M = V'\Omega V$ is the information matrix for the supermodel $\eta$.

For some weight $\gamma$ ($0 \leq \gamma \leq 1$), Atkinson and Donev (1992) combine these measures into the single information measure

$$\psi(\xi, \theta, \gamma) = \frac{\gamma}{p} \log |M_{11}| + \frac{(1-\gamma)}{q} \log \left( \frac{|M|}{|M_{11}|} \right),$$

and seek designs that maximize $\psi$ for given choices of $\theta$ and $\gamma$. We shall refer to these design as the $D_\gamma$-optimal designs. When $\gamma = 1$, maximization of (4) yields the D-optimum design for $\theta_1$, $\gamma = 0$ gives the $D_s$-optimum design for $\theta_2$. In order to use this criterion a value of $\gamma$ can be specified which reflects the interest in estimating $\theta_1$ relative to checking the model (Atkinson and Donev (1992)). Approximate designs for the compound criteria of the form (4) can be readily constructed and in addition the appropriate Equivalence...
Theorem can be invoked in order to demonstrate the global optimality or otherwise of such a design. O’Brien (1993) illustrates the procedure for the class of sigmoidal models and shows with several examples, that the combined criterion (4) provides extra design points to enable a check of model adequacy for the original model. For example, if the experimenter wishes to check for an inflection point by nesting (2) into (3), then (s)/he could obtain two support points using initial estimate \( \theta_2^0 = 1 \) and the compound criterion (4). Note that this design would be preferred to the D-optimal design for (2) which will take all observations at a unique support point and consequently allow no check for model inadequacy.

We shall illustrate the above procedure for the class of fractional polynomial response surface models. Royston and Altman (1994) proposed the extended family of curves, called the fractional polynomials. These models are polynomial models whose powers are restricted to a small predefined set of rational numbers. Gilmour and Trinca (2005) have recently studied this class of models and illustrate that sometimes the fractional polynomials can give a good fit to the data and much more plausible behavior between design points than the polynomial models. To our knowledge, no work on optimal designs for these models has appeared in the literature except for a presentation by Gilmour and Trinca (2003).

We will refer to

\[
\eta = \beta_0 + \sum_{i=1}^{q} \beta_i x_i^{(\alpha_i)}
\]

as the first order fractional polynomial response surface model and to

\[
\eta = \beta_0 + \sum_{i=1}^{q} \beta_i x_i^{(\alpha_i)} + \sum_{i=1}^{q} \beta_{ii} x_i^{2(\alpha_i)} + \sum_{i=1}^{q-1} \sum_{j=i+1}^{q} \beta_{ij} x_i^{(\alpha_i)} x_j^{(\alpha_j)},
\]
where

$$x_i^{(\alpha_i)} = \begin{cases} 
    x_i^{\alpha_i}, & \alpha_i \neq 0; \\
    \log x_i, & \alpha_i = 0.
\end{cases}$$

and

$$x_i^{2(\alpha_i)} = \begin{cases} 
    x_i^{2\alpha_i}, & \alpha_i \neq 0; \\
    (\log x_i)^2, & \alpha_i = 0.
\end{cases}$$

as the second order fractional polynomial response surface model. As we can see, these models are nonlinear in some parameters and Gilmour and Trinca (2005) give an excellent description on estimation and inference for these models. In practice, the parameter $\alpha_i$ can take any real value, but there are advantages in terms of interpretation in restricting them to some interval and/or set of rational numbers. It is often sensible to restrict attention to a set such as $\{-3, -2, -1, -\frac{1}{2}, -\frac{1}{3}, 0, \frac{1}{3}, \frac{1}{2}, 1, 2, 3\}$, so that we consider only squares and cubes, square and cube roots, reciprocals, combinations of these and logarithms of the factors (Gilmour and Trinca (2005)). In linear regression the variables are usually coded between $-1$ and $+1$, but in this case the factor levels are not coded, since we require $x_i > 0$.

We now consider the nesting strategy for the class of models discussed above under the usual Gaussian random errors. We shall however, consider discrete designs in what follows. The exact designs have been found by integer approximation of the optimum continuous measure.

**Example I**

Suppose the experimenter believes that the following first order fractional polynomial model

$$\eta_1 = \beta_0 + \beta_1 x^{(\alpha)}, \quad (5)$$

adequately describes a given process, but wishes to check for a quadratic effect by nesting (5) into the following second order fractional polynomial model

$$\eta = \beta_0 + \beta_1 x^{(\alpha)} + \beta_2 x^{2(\alpha)}. \quad (6)$$
Notice in this case that the supermodel (6) reduces to the original model (5) by setting $\beta_2 = 0$. So, here $\theta_1 = (\beta_0, \beta_1, \alpha)$, $\theta = (\beta_0, \beta_1, \beta_2, \alpha)$.

The Jacobians for the original model $\eta_1$ and supermodel $\eta$ are respectively

\[
V_1 = \frac{\partial \eta_1}{\partial \theta_1} = \left[ \frac{\partial \eta_1}{\partial \beta_0}, \frac{\partial \eta_1}{\partial \beta_1}, \frac{\partial \eta_1}{\partial \alpha} \right] = \left[ 1, x^{(\alpha)}, \beta_1 x^{(\alpha)} \log(x) \right]
\]

\[
V = \frac{\partial \eta}{\partial \theta} = \left[ \frac{\partial \eta}{\partial \beta_0}, \frac{\partial \eta}{\partial \beta_1}, \frac{\partial \eta}{\partial \beta_2}, \frac{\partial \eta}{\partial \alpha} \right] = \left[ 1, x^{(\alpha)}, x^{2(\alpha)}, \beta_1 x^{(\alpha)} \log(x) + 2\beta_2 x^{2(\alpha)} \log(x) \right].
\]

Assume the range of $x \in [0.5, 5.0]$. Using the initial parameter estimates, $(\beta_0, \beta_1, \beta_2, \alpha) = (5.8, 2.2, 0, 0.5)$, $\gamma = 0.90$ and six observations, the locally $D_\gamma$ design is located at the following design points $x = 0.50(2), 1.41, 2.64, 5.0(2)$, where the numbers in brackets indicate the number of replications at the respective points. This design would be preferred to the locally D-optimal design for (5) since the latter has only three support points at $x = 0.50, 1.96, 5.0$. As an aside, it is interesting to note that the number of support points for the D-optimal designs is equal to the number of parameters in the original model and as postulated by Silvey (1980), must necessarily have weights equal to $1/p$.

**Example II**

We now consider the fractional polynomial in two explanatory variables as the original model:

\[
\eta_1 = \beta_0 + \beta_1 x_1^{(\alpha_1)} + \beta_2 x_2^{(\alpha_2)}. \tag{7}
\]

Suppose the experimenter feels that (7) reasonably describes the process but desires a design with “extra” (i.e., more than five) support points. The original model can then be
embedded in the following supermodel:

$$\eta = \beta_0 + \beta_1 x_1^{(\alpha_1)} + \beta_2 x_2^{(\alpha_2)} + \beta_{11} x_1^{2(\alpha_1)} + \beta_{22} x_2^{2(\alpha_2)}.$$

(8)

Here the original model can be recovered by setting $\beta_{11} = \beta_{22} = 0$ in the supermodel (8).

We can obtain the Jacobian matrices for (7) and (8) in a similar fashion as in Example I. Assume the ranges for $x_1$ and $x_2$ to be $[0.5, 10]$ and the initial parameter estimates, $(\beta_0, \beta_1, \beta_2, \beta_{11}, \beta_{22}, \alpha_1, \alpha_2) = (8.2, 3.2, 2.5, 0, 0, 0.5, 1.5)$ and $\gamma = 0.90$. A ten point locally $D_\gamma$-optimal design is shown in Figure 1 (The areas of the solid circles reflect the weights attached to the points).

![Design points for a locally $D_\gamma$-optimal design](image)

Figure 1: Design points for a locally $D_\gamma$-optimal design

This design with 10 points would be preferred to the locally D-optimal design for estimating the parameters of model (7) since the D-optimal design has only five support points (see Figure 2) and consequently provides no check from any possible departures from the assumed model.
So far in our discussion, we have focused on a one-stage procedure and our approach was based on the assumption that the researcher is intending to fit the original model but just required a few “extra” design points to check for model inadequacy. In the next section we shall propose a two-stage design strategy for fractional polynomial models when there is uncertainty in the specification of the original model (also referred to as the primary model).

5 A two-stage design strategy: the one variable fractional polynomial model

To explain our procedure, we use an example involving the one variable fractional polynomial model. Suppose that the experimenter postulates the following terms in the model

\[ \eta = \beta_0 + \beta_1 x^{(\alpha)}, \]  \hspace{1cm} (9)
to be necessary in modelling the response. Further, in addition to these primary terms, there are some potential terms that may be additionally important but may not have been studied thoroughly enough to justify being in the primary model. However the researcher would like to protect against these terms and, if possible, incorporate any of the important ones in the model that (s)he will eventually use to fit the data at the end of the experiment. The combined (full) model with all the primary and potential terms is as follows:

\[ \eta = \beta_0 + \beta_1 x^{(a)} + \beta_2 x^{2(a)} + \beta_3 x^{3(a)}. \] (10)

So here, the primary terms of the model are \( \{\beta_0, \beta_1 x^{(a)}\} \) and the potential terms are \( \{\beta_2 x^{2(a)}, \beta_3 x^{3(a)}\} \). Suppose past experience suggests the following local values at which “optimality” criterion will be sought, \( \{\beta_0, \beta_1, \beta_2, \beta_3, \alpha\} = \{10.0, 5.0, 1.8, 1.2, 1.5\} \) and \( x \in [0.5, 5.0] \). The researcher has resources for 10 runs in the first stage and four in the second stage.

Let that the ‘true’ model, which the experimenter is unaware of, is actually the quadratic fractional polynomial model

\[ y = 12.8 + 6.8x^{3/2} + 3.0x^{2(3/2)} + \varepsilon, \] (11)

which comprises all the primary terms and one of the potential terms. So here in the true model we have \( \{\beta_0, \beta_1, \beta_2, \alpha\} = (12.8, 6.8, 3.0, 3/2). \) The two-stage strategy we propose to obtain designs robust to model uncertainty for nonlinear models can be summarized in the following steps.

**Step I:** In the first stage experiment, the researcher would like to detect any departures from the postulated primary model specification in the direction of the potential terms and a compound design criterion of the type (4) with a moderate value of \( \gamma \), would seem
To be very desirable to get a design that enables the researcher to test for lack of fit. A moderate value of $\gamma = 0.80$, seems appropriate for that purpose (see O’Brien (1996) for his discussion on the choice of $\gamma$ and on robust design strategies for nonlinear regression models in general). Using the above local values, the $D_\gamma$-optimal design has five support points at $x = 0.5, 1.8, 3.1, 4.5, 5.0$. We can replicate each of these support points to obtain our 10 point design. Note that this design is efficient for estimation of the parameters of the primary model but also provides a check for any departures from the model in the direction of the potential terms.

**Step II**: Using this 10 point design, the experimenter performs the experiment and collects first stage data. We assume that first stage data is actually emanating from the ‘true’ model (11) where $\varepsilon$ is drawn from a $N(0,1)$ distribution. Once we obtain the simulated first stage data, we fit the full model (10) to uncover any active terms driving the system. The estimated parameters, approximate standard errors, approximate t-statistic and the corresponding p-values for the test using the Golub-Pereyra partial linear algorithm, implemented in R (see Venables and Ripley (2002) and Gilmour and Trinca (2005) for details) for one simulation are shown in Table 1.

If we use the conservative p-value of 20% used by Neff (1996) and Ruggoo (2004), the estimate of $\beta_3$ is not significant and can be dropped in the numerical construction of the second stage design. Other simulations we have examined show similar results. Hence the rearranged primary model at the end of the first stage will be the model comprising the following terms $\{\beta_0, \beta_1 x^{(\alpha)}, \beta_2 x^{2(\alpha)}\}$.

**Step III**: We can now obtain the second stage design which would be an augmented four point locally D-optimal design for the rearranged primary model using the parameter
estimates of the fitted model as updated local values in the search algorithm. Note that the nature of the information matrix for this purpose is $|M_0 + M(\xi)|$ where $M_0$ corresponds to the first stage design and $M(\xi)$ to the points of the augmented design. The four additional design points for this model are located at $x = 0.5, 1.7, 3.7, 5.0$. For the analysis, the first and second stage design can be combined, leading to a design with 14 runs. The experimenter will eventually fit the rearranged primary model to the data.

## 6 The two variable fractional polynomial model

As a second example, we consider the fractional polynomial model in two variables. Suppose the primary model is

$$
\eta = \beta_0 + \beta_1 x_1^{(\alpha_1)} + \beta_2 x_2^{(\alpha_2)}
$$

and the full model is

$$
\eta = \beta_0 + \beta_1 x_1^{(\alpha_1)} + \beta_2 x_2^{(\alpha_2)} + \beta_{11} x_1^{2(\alpha_1)} + \beta_{22} x_2^{2(\alpha_2)}.
$$
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So here the primary terms are \( \{ \beta_0, \beta_1 x_1^{(\alpha_1)}, \beta_2 x_2^{(\alpha_2)} \} \) and the potential terms are \( \{ \beta_{11} x_1^{2(\alpha_1)}, \beta_{22} x_2^{2(\alpha_2)} \} \). Suppose the best guess of the parameters from a previous experiment are

\[
\{ \beta_0, \beta_1, \beta_2, \beta_{11}, \beta_{22}, \alpha_1, \alpha_2 \} = \{ 15.0, 8.2, 5.6, 1.8, 1.2, 0.5, 1.5 \}
\]

and “optimality” is sought at these local values. Also \( x_1 \) and \( x_2 \) is in the range \([0.5, 10]\).

The researcher has 14 runs available in the first stage. The 14 runs of a D\(_\gamma\)-optimal design obtained using the compound criterion (4) and \( \gamma = 0.80 \) is displayed in Figure 3. It consists of seven support points which are each duplicated. We further assume that

\[
y = 12.8 + 7.5 x_1^{1/2} + 5.0 x_2^{3/2} + 2.7 x_1 + \varepsilon, \tag{14}
\]

where \( \varepsilon \) is simulated from a \( N(0, 1) \) distribution.

Figure 3: Design points for the D\(_\gamma\)-optimal design
Table 2: Parameter estimates and approximate p-values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Approximate standard error</th>
<th>Approximate t-statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_0$</td>
<td>16.00</td>
<td>2.0419</td>
<td>7.84</td>
<td>0.0000</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>4.97</td>
<td>1.9307</td>
<td>2.57</td>
<td>0.0329</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>6.93</td>
<td>2.5876</td>
<td>2.68</td>
<td>0.0280</td>
</tr>
<tr>
<td>$\beta_11$</td>
<td>0.14</td>
<td>0.0357</td>
<td>3.93</td>
<td>0.0043</td>
</tr>
<tr>
<td>$\beta_22$</td>
<td>1.04</td>
<td>2.3062</td>
<td>0.45</td>
<td>0.6640</td>
</tr>
<tr>
<td>$\alpha_1$</td>
<td>1.05</td>
<td>0.2618</td>
<td>4.01</td>
<td>0.0039</td>
</tr>
<tr>
<td>$\alpha_2$</td>
<td>0.98</td>
<td>0.3169</td>
<td>3.09</td>
<td>0.0147</td>
</tr>
</tbody>
</table>

Once we obtain simulated first stage data, we can fit the full model (13) to uncover any active factors driving the system. The results for the significance tests of the parameters are displayed in Table 2. Again using the conservative p-value of 20%, the parameter $\beta_{22}$ is not significant and can be dropped in the construction of the second stage design. Examination of the parameter estimates of other simulations in most cases leads to similar conclusions, so that the rearranged primary model to be used in the second stage comprises the following terms: $\{\beta_0, \beta_1 x_1^{(\alpha_1)}, \beta_2 x_2^{(\alpha_2)}, \beta_{11} x_1^{2(\alpha_1)}\}$. We can now obtain a six point augmented second stage D-optimal design for the rearranged model using the updated parameter estimates as new local values (see Figure 4). The combined first and second stage designs will thus have 20 runs in total. With this two-stage procedure, we can refine knowledge on our initial primary model entertained and include any of the prominent potential terms in the final model to be fitted by the researcher at the end of the experiment.
Figure 4: Additional design points for the D-optimal design for the rearranged model

7 Some additional remarks

The one-stage approach can be easily extended to other classes of nonlinear models. O’Brien (1993) gives several examples for the class of sigmoidal models. In case of the two-stage approach for other classes of nonlinear models, we need to find relevant and meaningful supermodels that generalize a variety of different models.

In all the development in this paper, we have adopted a best guess for the parameters and consequently obtained locally optimum designs for the fractional polynomial models. An alternative and possibly more realistic approach would be to introduce a prior distribution on the parameters and incorporate this prior into the design criteria, resulting in Bayesian optimal designs. The approach is obviously much more complicated and very often these designs are obtained using numerical methods. Gilmour and Trinca (2003) have constructed a Bayesian optimal design for the first order fractional polynomial model
in one variable by using a joint prior distribution on the unknown parameters. The procedure is very complex and an adaptive grid search algorithm is required to find the optimal design. For the second order model, as they argue, obtaining useful priors is more difficult and analytical results are not available so that sampling from the priors is needed.

8 Conclusion

The overall objective in this paper was to develop model-robust one-stage and two-stage designs for the fractional polynomial response surface models. The method outlined, provides a reasonable alternative to the conventional “optimal” designs which typically cannot be used to check the adequacy of the assumed model. The one-stage approach is useful when the experimenter will eventually fit the original model at the end of the experiment, but just requires a few “extra” design points to guard against possible model misspecification. In case the experimenter has some doubts about the primary model specification and would like to refine the model that will be used to fit the data at the end of the experiment, we recommend to use the two-stage design strategy.

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