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# DEALING WITH NONLINEARITIES IN CATALYTIC RATE MODELLING

By  
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## Abstract

Problems arising from nonlinearities in modelling gas-solid catalytic reactions are addressed. Model/data sets taken from the literature are used to illustrate these problems and how they may be overcome.

Least Squares is one of the most widely used parameter estimation criteria in the scientific and engineering fields. Least squares regression is reviewed for models which are both linear and nonlinear in the parameters. Its simplicity and reliability with linear least squares has led to its application to nonlinear models. Unfortunately this practice often leads to misleading inferences, the severity of which depends on the extent of nonlinearity of the model/data set in question.

Often, one is not aware of the extent of nonlinearity, and thus the potential for being misled. Presently available measures of nonlinearity are reviewed and evaluated. These measures include: Beale's measure of nonlinearity, Box's bias, Ratkowsky's sampling properties, Lowry's asymmetry measure of bias and the Bates and Watts relative curvatures.

Dealing with nonlinearity is essential, as is identifying it. There are several options available when working with nonlinear model/data sets: transformations of the response, quadratic approximations and reparameterizations. Advantages and disadvantages of the methods are discussed.

The extent of nonlinearity is specific for a given model/data set. As such the extent of nonlinearity for a given model can vary for different data sets. The main objective of this work is to obtain data sets which will result in the most linear behavior. This data set will be determined in a sequential design strategy.

The aforementioned measures of nonlinearity were screened for their suitability as design criteria to meet this end. The Bates and Watts relative curvatures and Box's bias were identified as potential design criteria. These measures were tested

using simulated, sequentially designed experiments for gas-solid catalytic rate models from the literature as starting points.

The accuracy of the relative curvatures and the bias as measures of the extent of nonlinearity were evaluated before and after simulating experiments. Comparisons of linear approximate-shape and exact-shape confidence regions indicate that the relative curvatures are reliable measures of the extent of nonlinearity. Box's bias measure was found to underestimate the extent of nonlinearity. Reductions of the extent of nonlinearity as indicated by both measures was confirmed by improved coverage of the exact-shape confidence regions by the linear approximate-shape regions.

The relative curvatures and bias were formulated into two design criteria, minimum parameter effects curvature (PEC) and minimum sum of squares of biases (SSB). These two designs were also compared to the D-optimal design for precise parameter estimation. Compatibility of a minimum nonlinearity design and the D-optimal design is highly desirable. The three designs were compared based on reductions of the parameter effects curvature and the volume of the linear approximate confidence region. The designed run locations and design surface (PEC and D-optimal only) were also compared. The SSB and PEC designs were effective at improving parameter precision. The D-optimal design also lead to overall reductions of the extent of nonlinearity. However in certain cases the D-optimal design did result in minor increases of the parameter effects curvature. Based on this and comparisons of the designed run locations and design surface: the PEC and SSB design criteria were not wholly compatible with the D-optimal design.

## Acknowledgements

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Endless thanks to my parents, Bertilla and Eugenio, for their unending support and encouragement throughout my studies.





# Nomenclature

|                   |                                                                                                                      |
|-------------------|----------------------------------------------------------------------------------------------------------------------|
| $A$               | pre-exponential constant in the Arrhenius and Van't Hoff expressions                                                 |
| $A$               | the acceleration array used in calculating the relative curvatures                                                   |
| $A^N$             | intrinsic nonlinearity portion of the acceleration array                                                             |
| $A^T$             | parameter effects nonlinearity portion of the acceleration array                                                     |
| $C_O$             | concentration of oxygen (see text for units)                                                                         |
| $C_r$             | concentration of hydrocarbon (see text for units)                                                                    |
| $d$               | unit vector used to calculate the maximum relative curvatures                                                        |
| $e_i$             | random error term for the $i^{th}$ response                                                                          |
| $e$               | vector of $n$ random errors                                                                                          |
| $E_r$             | activation energy in the Arrhenius and Van't Hoff expressions                                                        |
| $F$               | equivalent to $x_i$                                                                                                  |
| $f(x, \theta)$    | representation of a nonlinear model                                                                                  |
| $f(\theta)$       | vector of $k$ models in the nonlinear multiresponse case                                                             |
| $F(\dot{\theta})$ | the $nk \times p$ matrix of first derivatives of $f(\theta)$ with respect to $\theta$                                |
| $H$               | $p \times p$ matrix of the second derivatives of a model with respect to the parameters                              |
| $g_i$             | kurtosis, measure of the peakedness of a parameter's distribution as measured in Ratkowsky's Monte Carlo simulations |
| $k_{xx}$          | equilibrium adsorption constant of gaseous component $xx$                                                            |
| $L$               | inverse of the $\tilde{R}$ matrix from the QR decomposition                                                          |

|                               |                                                                                                                    |
|-------------------------------|--------------------------------------------------------------------------------------------------------------------|
| QR                            | decomposition of $V$ , used to determine the length of the components of $\tilde{\eta}_h^T$ and $\tilde{\eta}_h^N$ |
| Q                             | orthogonal matrix from the QR decomposition<br>used to calculate the relative curvatures                           |
| $\tilde{R}$                   | upper triangular $p \times p$ matrix from the first $p$ rows of $R$ in the QR decomposition                        |
| $g_2$                         | skewness, measure of the symmetry of a parameter's distribution as measured by Ratkowsky's Monte Carlo simulations |
| $u_i$                         | first derivatives in $\phi$ space                                                                                  |
| $U$                           | matrix of first derivatives of a nonlinear model w.r.t. the $\phi$ parameters                                      |
| $u_{ij}$                      | second derivatives in $\phi$ space                                                                                 |
| $U_{..}$                      | matrix of second derivatives in $\phi$ space                                                                       |
| $y_t$                         | $t^{th}$ response                                                                                                  |
| $Y$                           | vector of $n$ responses                                                                                            |
| $\hat{y}_t$                   | predicted response for the $t^{th}$ experiment                                                                     |
| $\hat{Y}$                     | vector of $n$ predicted responses                                                                                  |
| $x_t$                         | $1 \times p$ vector of the operating variables or functions of the operating variables in a linear model           |
| $X$                           | $n \times p$ matrix of the operating variables or functions of the operating variables in a linear model           |
| $(X^T X)^{-1} \hat{\sigma}^2$ | often termed the information matrix, the variance-covariance matrix of a linear model                              |
| $V$                           | $n \times p$ matrix of first derivatives of a nonlinear model with respect to the $\theta$ parameters              |
| $V_{..}$                      | $n \times p \times p$ matrix of second derivatives of a nonlinear model with respect to the $\theta$ parameters    |
| $U$                           | $n \times p$ matrix of first derivatives of a nonlinear model with respect to the $\phi$ parameters                |
| $U_{..}$                      | $n \times p \times p$ matrix of second derivatives of a nonlinear model with respect to the $\phi$ parameters      |
| $\beta_i$                     | parameter $i$ in a linear model                                                                                    |
| $\hat{\beta}_i$               | least squares estimate of parameter $i$ in a linear model                                                          |
| $\beta$                       | a vector containing the $p$ parameters in a linear model                                                           |

|                                                            |                                                                                                                      |
|------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| $\hat{\beta}$                                              | a vector containing the $p$ least squares estimates of the parameters in a linear model                              |
| $\chi^2$                                                   | the distribution of the excess variance as determined by Ratkowsky's Monte Carlo simulations                         |
| $\frac{\partial f(\mathbf{x}, \theta)}{\partial \theta_i}$ | partial derivative of a nonlinear model with respect to model parameter $\theta_i$                                   |
| $e_i$                                                      | the residual, $y_i - \hat{y}_i$ , an estimate of $e_i$                                                               |
| $\epsilon$                                                 | a vector of $n$ residuals                                                                                            |
| $\eta_h$                                                   | a lifted line on the solution locus                                                                                  |
| $\eta(\theta)$                                             | representation of a nonlinear model with parameters $\theta$                                                         |
| $\dot{\eta}_h$                                             | tangent to the lifted line, $\eta_h$ at $b = 0$                                                                      |
| $\ddot{\eta}_h$                                            | acceleration of the lifted line, $\eta_h$ at $b = 0$                                                                 |
| $\Gamma^N$                                                 | intrinsic curvature, a measure of the intrinsic nonlinearity                                                         |
| $\Gamma^{NR}$                                              | ratio of $\Gamma^N$ to the test statistic for significant intrinsic nonlinearity (significant if $\Gamma^{NR} > 1$ ) |
| $\Gamma^T$                                                 | parameter effects curvature, a measure of the parameter effects nonlinearity                                         |
| $\Gamma^{TR}$                                              | ratio of $\Gamma^T$ to the test statistic for significant intrinsic nonlinearity (significant if $\Gamma^{TR} > 1$ ) |
| $\Gamma_S^{TR}$                                            | scaled parameter effects curvature ratio, used in simulations to account for changing variance estimates             |
| $\phi$                                                     | vector of $p$ parameters                                                                                             |
| $\Sigma$                                                   | $k \times k$ variance-covariance matrix of the responses in the multiresponse case                                   |
| $\sigma^2$                                                 | the true unknown variance of the response                                                                            |
| $\hat{\sigma}^2$                                           | an estimate of $\sigma^2$                                                                                            |
| $\theta_i$                                                 | parameter $i$ in a nonlinear model                                                                                   |
| $\theta$                                                   | vector of $p$ parameters in a nonlinear model                                                                        |
| $\frac{1}{2\sqrt{F_{p, n-p}}}$                             | test statistic for significant parameter effects or intrinsic curvatures                                             |

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# Chapter 1

## Introduction

Catalytic rate models play an important role in the sciences and engineering. They are used for investigating mechanisms of catalytic reactions as well as for designing, optimizing and controlling reactors. That they be reliable is essential.

Development of reliable models requires estimation of the model parameters and predictions as well as measures of their precision. The adequacy of the model must also be tested. Least squares regression is the most common method for parameter estimation. Under certain reasonable assumptions about the distributional nature of the error associated with the data, models which are linear in the parameters have several desirable properties. Estimates of model parameters are unique and easily obtained. The estimates of the parameters and predicted values of the response variable are accurate (unbiased), have minimum variance (precise) and are normally distributed. For linear models, statistical theories required for drawing inferences from the analysis are well developed and reliable.

Unfortunately, catalytic rate models are usually nonlinear in the model parameters (e.g. rate and adsorption constants). Unlike linear models, nonlinear models present problems in parameter estimation and the parameters and predicted responses do not have the properties of linear models. Statistical theories for nonlinear models are not well developed, making inferences difficult and unreliable. Properties of nonlinear models approach those of linear models asymptotically as the number of data approaches infinity but in most cases small data sets are encountered and all aspects of nonlinear model building are suspect. The severity of these problems depends on the degree of nonlinearity of the model/data set. Dependable inferences

are necessary as a starting point to any equipment design, process control or other goal. Consequently, a nonlinear model/data set which approaches linear behavior is desirable.

Precision estimates associated with model parameters and predicted values of the response as well as tests for model adequacy are easy to obtain and understand for linear models. This has lead to linear least squares theory being applied to nonlinear models after linearization (i.e. a first order Taylor series expansion) of the model about the least squares estimates of the parameters. The validity of this approach depends on whether the nonlinear model can be adequately described by this approximation in the vicinity of the least squares estimates; this depends on the degree of nonlinearity of the model/data set. When the model is highly nonlinear, estimates of the precisions of the predicted values of the response and parameters obtained by linearization may be very poor.

Since the reliability of the linear approximation depends on the degree of nonlinearity, an evaluation of the extent of nonlinearity of a model/data set is indispensable. Several measures of nonlinearity have been proposed, including the relative curvatures of Bates and Watts [1], Box's bias [2], Ratkowsky's sampling properties [3], Lowry's asymmetry measure of bias [3] and Beale's measures of nonlinearity [4]. However these measures have rarely been employed in catalytic rate modelling.

Having determined the extent of nonlinearity of a model/data set to be significant, the question becomes what to do about it. Transformations of the response have long been used to linearize models; this was the only way of obtaining parameter estimates before computers made optimization routines feasible. However this procedure has serious potential pitfalls which have been well documented in the literature [5,6]. An example of these problems is presented in Section 2.5.1. Reparameterizations have been shown to greatly reduce the extent of parameter-effects nonlinearity [3,5,7]. The types of nonlinearity will be discussed in detail in Section 2.4.1. Reparameterizations result in "new" parameters which are functions of the "original" parameters. Estimates of the original parameters can be obtained from the new parameters fairly easily, but estimates of their precision is not so easily recovered. This becomes increasingly difficult as the number of parameters increases. Often, the objective of a study is to obtain estimates of the parameters

and their precision; in such a case it would be preferable to use the original parameters. Also, reparameterizations do not reduce the extent of intrinsic nonlinearity. Hamilton et al. [8] suggested using a quadratic approximation to account for intrinsic nonlinearity, as opposed to the more common linear approximation. However this quadratic approximation requires non-standard software, which is not widely available. In any case, Hamilton also showed that the intrinsic nonlinearity is often not a problem.

An alternate approach to dealing with nonlinearity, which would overcome many of the disadvantages of other methods, is to *design* the experiments. Run locations would be chosen to minimize the extent of nonlinearity. Bates and Watts [1,9] noted that the ideal situation would be one where experiments were performed such that nonlinearity is minimized for the original parameters. They also noted that a design which minimizes relative curvature (their measure of nonlinearity) could be similar to a D-optimal design. Hamilton et al. [10] developed an improved D-optimal design and noted its effectiveness at reducing the extent of nonlinearity. The possibility of simultaneously improving parameter precision and reducing nonlinearity is of considerable interest in model building. However, no investigations of experimental designs aimed directly at reducing the extent of nonlinearity have been found in the literature.

As a result, the overall goal of this work was to study the use of designed experiments to reduce the extent of nonlinearity in nonlinear model/data sets for catalytic reaction kinetics.

To meet this goal, the investigation was divided into several stages, each with specific objectives. The objectives of each stage were:

- To identify problems in building catalytic rate models which arise from the nonlinearity of model/data sets.
- To review existing measures of nonlinearity while considering their suitability as design criteria.
- To evaluate present methods of dealing with nonlinearity.
- To use simulations in order to evaluate the suitability of various design criteria for reducing the extent of nonlinearity.

## Chapter 2

# Background and Literature Review

This chapter begins by presenting a basic background for both linear and nonlinear least squares, focussing on the problems caused by nonlinearities. Measures of nonlinearity which have been reported in the literature are then reviewed and evaluated. Finally, the various methods which have been reported to deal with nonlinearities are identified and evaluated, particularly as they relate to catalytic rate models. In this thesis matrix notation is used to represent quantities in a compact form; matrices being denoted by bold face letters and symbols.

### 2.1 Linear Least Squares

Models may be classified by several methods, one possible classification is based on whether a model is linear or nonlinear in the parameters. A model is linear if the response is a linear function of the parameters to be estimated (as opposed to the operating or independent variables). The linear model is represented by

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{e} \quad (2.1)$$

or equivalently

$$y_i = \beta_1 x_{i1} + \beta_2 x_{i2} + \dots + \beta_p x_{ip} + e_i \quad i = 1, 2, \dots, n \quad (2.2)$$

where  $\mathbf{Y} = [y_1, y_2, \dots, y_n]^T$  is an  $n \times 1$  vector of observed values of the response variable,  $\boldsymbol{\beta} = [\beta_1, \beta_2, \dots, \beta_p]^T$  is a  $p \times 1$  vector of parameters to be estimated,  $\mathbf{X}$  is an  $n \times p$  matrix containing values of the operating variables or functions of the operating variables

$$\mathbf{X} = \begin{bmatrix} x_{11} & \dots & x_{1p} \\ \vdots & \ddots & \vdots \\ x_{n1} & \dots & x_{np} \end{bmatrix} \quad (2.3)$$

and  $\mathbf{e}$  is a vector of random errors associated with the measured values of the response.

$$\mathbf{e} = \begin{bmatrix} e_1 \\ e_2 \\ \vdots \\ e_n \end{bmatrix} \quad (2.4)$$

The least squares estimates of the parameters,  $\hat{\boldsymbol{\beta}}$ , are those which minimize the sum of squares of the residuals

$$\text{SSR} = \sum_{i=1}^n (y_i - \hat{y}_i)^2 = \sum_{i=1}^n (y_i - \mathbf{x}_i \hat{\boldsymbol{\beta}})^2 = \boldsymbol{\epsilon}^T \boldsymbol{\epsilon} \quad (2.5)$$

where the  $n$  residuals are given by

$$\boldsymbol{\epsilon} = \begin{bmatrix} \epsilon_1 \\ \epsilon_2 \\ \vdots \\ \epsilon_n \end{bmatrix} = \mathbf{Y} - \mathbf{X} \hat{\boldsymbol{\beta}} \quad (2.6)$$

The term  $e_i$  has a probability density given by  $p(e_i)$  and represents the random error associated with the observed value of the response. The residual,  $\epsilon_i$ , is not equivalent to  $e_i$ . The residual accounts for the random error plus any discrepancies arising from model inadequacies and use of estimates of the true but unknown values of the parameters. Consequently, the residuals are used to test the model for lack of fit and, for an adequate model, provide estimates of the random errors.

The least squares estimates for a linear model can be found directly as

$$\hat{\boldsymbol{\beta}} = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{Y} \quad (2.7)$$



The least squares predicted values of the response are given by

$$\hat{Y} = X\hat{\beta} \quad (2.8)$$

Implicit in the use of least squares are several assumptions:

1.  $Var(x_{ti}) = 0$ ,  $t = 1, 2, \dots, n$ ;  $i = 1, 2, \dots, p$ . The values of the operating variables or the independent variables are known exactly. In practical terms this means that the effect of the uncertainty of any operating variable is negligible compared to the uncertainty of the measured response.
2.  $E(e) = 0$ ,  $t=1, 2, \dots, n$ ; i.e. the model is adequate.
3.  $Cor(e_u, e_v) = 0$ ,  $u, v = 1, 2, \dots, n$ ,  $u \neq v$ . The random error for any given observation is not correlated with the random error for any other observation.
4.  $Var(e_t) = \sigma^2$ ,  $t=1, 2, \dots, n$ ; The variance of the random error term is constant over the operating region. This assumption can be relaxed if the behavior of the variance is known, in which case, weighted least squares is appropriate.

Under these assumptions least squares estimates of the parameters and the predicted responses are unbiased and of all unbiased estimators have minimum variance. A fifth assumption which is usually made is that the random error is normally distributed, in which case the parameter estimates are also normally distributed.

## 2.2 Nonlinear Least Squares

A model is said to be nonlinear if it is nonlinear in the parameters and can be written as

$$\eta(\theta) = E(Y | \theta) = f(x, \theta) \quad (2.9)$$

where  $\eta(\theta)$  is the expected value of the response. The functional relationship between the operating variables,  $x$ , and the expected value of the response is  $f(x, \theta)$ , where  $\theta$  is a vector of parameters.

In a nonlinear model at least one of the partial derivatives of  $\eta(\theta)$  with respect to the parameters will be a function of one of the parameters. Most theoretical or

mechanistic models in chemical engineering, or any other field, are nonlinear with respect to the parameters.

The first problem encountered is obtaining the least squares parameter estimates. The normal equations used to solve for the least squares parameter estimates

$$\frac{\partial S(\theta)}{\partial \theta} = -2 \left[ \frac{\partial f(\mathbf{x}, \theta)}{\partial \theta} \right]^T [Y - f(\mathbf{x}, \theta)] = 0 \quad (2.10)$$

are nonlinear in  $\theta$ . As such, the solution of these equations for  $\hat{\theta}$  requires an iterative numerical procedure. Descriptions of the numerous algorithms available for obtaining  $\hat{\theta}$  are given by Himmelblau [11], Draper and Smith [12], and Bard [13]. Many use linear approximations of the model involving expansion of the response function around some value,  $\theta_0$ :

$$f(\mathbf{x}, \theta) \approx f(\mathbf{x}, \theta_0) + \sum_{i=1}^p (\theta_i - \theta_{i0}) v_i(\mathbf{x}) \quad (2.11)$$

where

$$v_i(\mathbf{x}) = \left. \frac{\partial f(\mathbf{x}, \theta)}{\partial \theta_i} \right|_{\theta_0} \quad (2.12)$$

These equations also form the basis of much of the statistical analysis of nonlinear models. One of the problems with nonlinear estimation is the possibility of multiple solutions for Eq. 2.10, or equivalently, multiple minima of the sum of squares of the residuals.

The efficiency of nonlinear regression routines depends on the accuracy of the initial estimates and on the degree of nonlinearity of the model/data set. Techniques for obtaining good initial estimates of parameters have been described in Himmelblau [11], Draper and Smith [12], and Bard [13]. The degree of nonlinearity differs for each model/data set and for different parameterizations of the same model.

However, a potentially more serious problem than parameter estimation arises when making inferences about the precision of estimates of the parameters and predicted response. Inferences are usually based on linear least squares theory applied to the linearized form of the model. The validity of this approach also depends on the degree of nonlinearity of the model/data set. If the model is highly nonlinear then the linear approximation will be a poor one and, as a result, inferences based on linear least squares theory may be misleading. This problem is accentuated in

practice if the analyst is not aware that the problem exists. In this situation a *measure* of nonlinearity is indispensable. There are several measures of nonlinearity available and these will be presented in Section 2.4.

In a linear model, the parameter estimates are a linear combination of the normally distributed observed values of the response variable. In the nonlinear case the parameters will not be a linear combination of the observations of the response, as such, the parameters will not be normally distributed and will have an unknown distribution. They will also be biased and will not have minimum variance. As a result of these undesirable properties of  $\hat{\theta}$ , the predicted response will also have an unknown distribution, be biased and not have minimum variance. Since the distribution of  $\hat{\theta}$  and  $\hat{Y}$  are not known, estimates of their precision, which is based on a normal distribution, may be misleading.

The degree to which one can be misled with respect to parameter precision is demonstrated in Figure 2.1. This figure shows the linear approximate shape and exact shape confidence regions for the parameters  $A_1$  and  $E_1$ , the pre-exponential and activation energies of the Arrhenius expression, respectively, for an oxygen adsorption rate constant. These were obtained from a nonisothermal form of the model proposed by Juusola [14] for the catalytic oxidation of benzene, incorporating Arrhenius and Van't Hoff expressions. The model consisted of four parameters which were the pre-exponential constants and activation energies for the Arrhenius type relationships. The confidence regions shown in Figure 2.1 are conditional confidence regions, the condition being that all other parameters are fixed, usually, as in this case, at their least squares estimates. A more detailed discussion of confidence regions is given in Section 2.3.

If the model proposed by Juusola were linear then the two regions would match. In fact the two regions match very poorly indicating that the linear approximation is extremely poor, i.e. the model is highly nonlinear. Inferences based on linear approximations would be misleading in several respects. The upper and lower limits of possible values of  $E_1$  agree fairly well, but those of  $A_1$  differ greatly. The linear approximation greatly overestimates the precision of  $A_1$ . As a result of the poor estimation of parameter precision, the predicted response precision based on linearizations of the model will also be misleading.

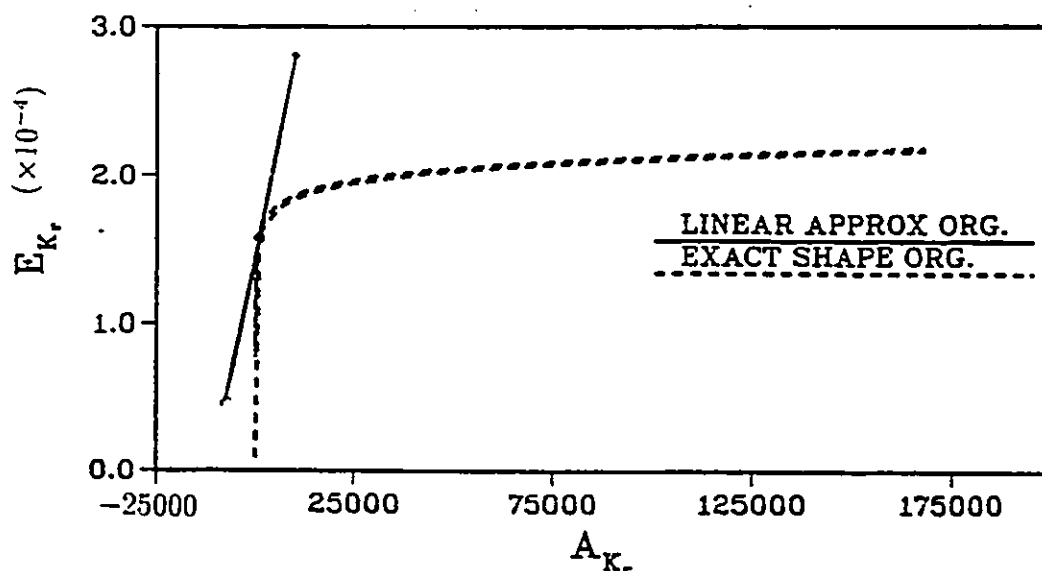


Figure 2.1: Confidence regions for a nonlinear model

The linear confidence region also includes negative values for  $A_k$ . This would suggest that oxygen adsorption is not significant or that the wrong model is being used. However, looking at the exact shape confidence region only positive values are included.

From the previous discussion it is clear that working with linear models is highly desirable from a practical point of view. After working with nonlinear models this becomes much more apparent. The ideal situation would be one where nonlinear models approach linear behavior. There are ways to achieve this end; the response may be transformed such that the parameters appear linearly, the model can be reparameterized or more experiments can be performed. The merits and shortcomings of the various methods will be discussed in Sections 2.5.1, 2.5.2 and 2.5.3 respectively.

## 2.3 Estimates of Precision

### 2.3.1 Linear Models

There may be several reasons for modelling a process and one of these is to obtain information regarding the parameters. This information usually consists of the parameter estimates themselves and their joint precision.

Individual marginal confidence intervals are by far the most common and simplest means of describing a parameter's precision. For a linear model the interval described by

$$\beta_i \pm t_{\alpha/2} \sqrt{\text{Var}(\beta_i)} \quad (2.13)$$

can be regarded as having a  $100(1 - \alpha)\%$  probability of containing the true unknown value of  $\beta_i$ , where  $\alpha$  is the level of significance. The variance of  $\beta_i$  is given by the  $i$ 'th diagonal element of the variance-covariance matrix  $(X^T X)^{-1} \sigma^2$ ,  $\nu$  is the number of degrees of freedom associated with  $\sigma^2$  and  $t_{\alpha/2}$  is the statistic taken from the  $t$  distribution. The pure error variance,  $\sigma^2$ , is generally unknown, but, for an adequate model, can be estimated by

$$\sigma^2 = \frac{\text{SSR}}{n - p} \quad (2.14)$$

The precision of a predicted value of the response can be described by the  $100(1 - \alpha)\%$  confidence interval

$$\hat{y}_i \pm t_{\alpha/2} \sqrt{\text{Var}(\hat{y}_i)} \quad (2.15)$$

where the variance of  $\hat{y}_i$  is given by:

$$\text{Var}(\hat{y}_i) = \mathbf{x}_i^T (X^T X)^{-1} \mathbf{x}_i \sigma^2 \quad (2.16)$$

While marginal confidence intervals are simple and useful, alone they cannot give a clear understanding of parameter precision. The correlation between parameters estimates must also be taken into account. If parameters are highly correlated then the value of one parameter estimate depends on that of another, which makes interpretation difficult. The correlation among the  $p$  parameters can be obtained from the variance-covariance matrix. The correlation between  $\hat{\beta}_i$  and  $\hat{\beta}_j$  is

$$\text{Corr}(\hat{\beta}_i, \hat{\beta}_j) = \frac{\text{Cov}(\hat{\beta}_i, \hat{\beta}_j)}{(\text{Var}(\hat{\beta}_i) \text{Var}(\hat{\beta}_j))^{1/2}} \quad (2.17)$$

where  $\text{Cov}(\hat{\beta}_i, \hat{\beta}_j)$  is the  $ij$ 'th element of  $(X^T X)^{-1} \sigma^2$ . In an ideal situation the parameters will not be correlated, i.e.  $\text{Corr}(\hat{\beta}_i, \hat{\beta}_j) = 0$ . In the worst case the parameters will have a correlation of  $\pm 1$ .

The precision of the parameters can be described completely by a joint confidence region. A joint confidence region is one that has a  $100(1 - \alpha)\%$  probability

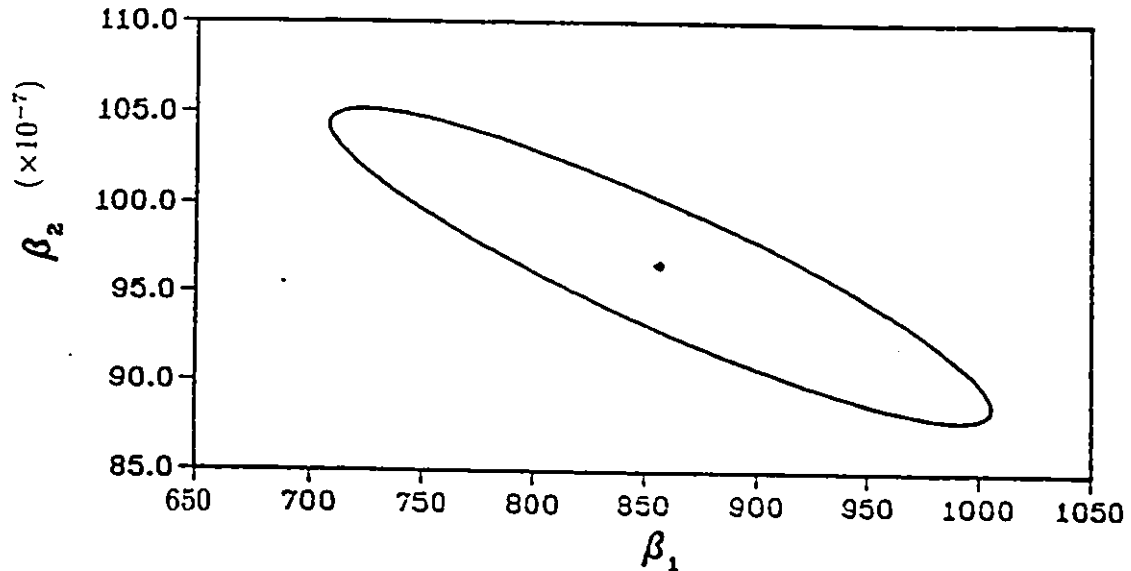


Figure 2.2: Confidence regions for a 2 parameter linear model

of containing the true but unknown values of the parameters. This region contains the values of  $\beta$  which satisfy the inequality:

$$(\beta - \hat{\beta})^T (X^T X)^{-1} (\beta - \hat{\beta}) \leq p \hat{\sigma}^2 F_{p, \nu, \alpha} \quad (2.18)$$

where  $F_{p, \nu, \alpha}$  is the appropriate F statistic with  $p$  and  $\nu$  degrees of freedom. The region described by Eq. 2.18 is ellipsoidal. Figure 2.2 is a confidence region for a two parameter model. As can be seen, the possible values of  $\beta_1$  depend on the value of  $\beta_2$ , i.e., they are correlated. One cannot simply quote the precision of a parameter estimate without knowledge of the other parameter(s). This illustrates the need to consider correlation when evaluating parameter precision.

When there are three or more parameters the region becomes a  $p$  dimensional ellipsoid. As the number of parameters increases, interpretation of parameter precision becomes increasingly difficult. Practically speaking multiparameter cases are treated with a pair of parameters at a time, fixing the other parameters, usually at their least squares estimates. These are conditional confidence regions and they represent slices of the actual volume.

### 2.3.2 Nonlinear Models

As noted earlier, inferences for nonlinear models are not as straightforward and reliable as for linear models. Precisions of parameter estimates and the predicted

response are usually determined in a manner analogous to that of linear models. However, in the nonlinear case, these estimates of precision are only approximate, their validity depending on the degree of nonlinearity.

Individual marginal confidence intervals are determined as for linear models but using an approximate variance-covariance matrix,  $(X^T X)^{-1} \sigma^2$ .  $X$  is obtained from

$$X = \begin{bmatrix} \frac{\partial f(x_1, \theta)}{\partial \theta_1} & \dots & \frac{\partial f(x_1, \theta)}{\partial \theta_p} \\ \vdots & \ddots & \vdots \\ \frac{\partial f(x_n, \theta)}{\partial \theta_1} & \dots & \frac{\partial f(x_n, \theta)}{\partial \theta_p} \end{bmatrix} \quad (2.19)$$

When dealing with a linear model, Eq. 2.19 is independent of the parameters and will give Eq. 2.3. The precision of the predicted response can be approximated by Eq. 2.15 where  $x_i$  is analogous to a row of Eq. 2.19. The correlation matrix is constructed from Eq. 2.17 and Eq. 2.19 and it too is an approximation.

The confidence region described by Eq. 2.18 will also be approximate for a nonlinear model and will be called the linear approximate shape confidence region. One can also obtain exact-shape confidence regions for a nonlinear model. These regions are based on the contours of the sum of squares of residuals. The region is defined by values of  $\theta$  satisfying the inequality

$$S(\theta) \leq S(\theta) [1 + \frac{p}{n-p} F_{p, n-p, \alpha}] \quad (2.20)$$

However, since the form of distribution for  $\theta$  is not known, the probability level is approximate. The shape of the region defined by Eq. 2.20 depends on the model, data set and must be found by some type of search. Finding these regions is demanding in terms of computational effort and the analyst's time. As with linear models, when more than two parameters are involved, slices of the confidence volume are considered. For a linear model the slices will always be ellipses as the volume itself is ellipsoidal. For a nonlinear model the exact shape confidence region may have a completely unpredictable shape. The conditional exact shape confidence regions for  $\theta_i$  and  $\theta_j$  may change shape for different values of the other parameters, as was shown by Emig and Hooten [15].

As a nonlinear model, data set approaches linear behavior, then the exact shape confidence region will match the approximate shape region. Comparing the two

types of confidence regions will give the analyst a qualitative evaluation of the degree of nonlinearity of the model/data set. A quantitative measure of nonlinearity which is simple to evaluate and accurate would be very useful. Several methods have been proposed to do this and are discussed in the next section.

## 2.4 Measures of Nonlinearity

Measurement of the extent of nonlinearity of a model/data set has been the subject of much work. One of the earliest measures was developed by Beale [4]. An important aspect of Beale's work was that it recognized that nonlinearity has two forms, a form intrinsic to the model and a form which depends on the parameterization used. Box [2] developed a quantitative measure of the model parameters' bias. Ratkowsky [3] developed a procedure using simulations to obtain a measure of the parameters' bias as well as other information about the distributional nature of the parameters. Bates and Watts [1] developed the relative curvature measures of nonlinearity. Like Beale's measures, the relative curvatures measure two types of nonlinearity, intrinsic and parameter effects. The relative curvatures are based on geometric interpretations of the solution locus and parameter co-ordinate system. Before describing the measures an example is used to illustrate what the solution locus and parameter co-ordinate system are.

### 2.4.1 Geometric Representation of Nonlinearity

An example from Ratkowsky [3] is used to describe the solution locus and coordinate system and how they are related to nonlinearity. The model is

$$y = x^\theta \quad (2.21)$$

There are two observations,  $y_1 = 2.05$  and  $y_2 = 10.0$  which were made with the operating variable at  $x_1 = 2$  and  $x_2 = 3$ . The observed responses can be represented graphically in the  $n$  dimensional response space by the vector  $\mathbf{Y}$ . As shown in Figure 2.3, the endpoint is given by  $y_1$  and  $y_2$  or  $(2.05, 10.0)$ . The solid line is the locus of the predicted value vectors for all values of  $\theta$ . For example, for  $x_1 = 2$  and  $x_2 = 3$  and  $\theta = 2$  the predicted value vector is  $(4.0, 9.0)$ . If  $\theta = 1$  then  $\hat{\mathbf{Y}} = (2.0, 3.0)$ ,



which is another point on the solution locus. The value of  $\theta$  on the solution locus is that which minimizes the distance between the vector of observed responses  $Y$  and the solution locus. Since that point on the solution locus is  $\hat{Y}$ , the length of the distance between the two vectors is

$$\|Y - \hat{Y}\| = \sum_{i=1}^n (y_i - \hat{y}_i)^2 = SSR \quad (2.22)$$

which is the sum of squares of the residuals. If there were three observations there would be a third axis,  $Y_3$  and so on for larger sample sizes.

The markings on the solution locus represent equal increments of  $\theta$  in steps of 0.5 and they represent the coordinate system for this model. For a two parameter model the coordinate system would be a grid on a surface.

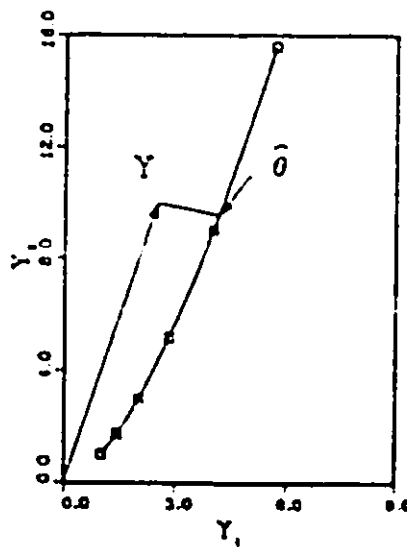


Figure 2.3: Geometric representation of nonlinearity

Nonlinearity is present in two forms in this example. The shape of the solution locus reflects the degree of intrinsic nonlinearity. The spacing of the coordinate system relates to the degree of parameter effects nonlinearity. In the case of a linear model the solution locus would be an infinite straight line and equal increments of  $\theta$  would be equally spaced. In the multiparameter case the solution locus would be an infinite hyper plane and the coordinates of the parameters would be equally spaced, straight and parallel.

Intrinsic nonlinearity is, as the name suggests, fixed for that particular model, data set and can only be changed by increasing the sample size. The operating conditions

under which the data were collected also determines the degree of nonlinearity. If the data were collected such that  $Y = (1.0, 1.0)$  then the intrinsic curvature would be greater because the solution locus is more curved in that vicinity. The parameter effects nonlinearity would also be different in this case.

The parameter effects nonlinearity can also be changed by reparameterizing the model. If the previous model is reparameterized as:

$$y = x^{\log \phi} \quad (2.23)$$

then the analogous figure for this new parameterization is that shown in Figure 2.4. Note that the solution locus has not changed, hence the intrinsic nonlinearity is also unchanged. The coordinate system has changed considerably and equal increments of  $\phi$  are more equally spaced than with the  $\theta$  parameterization.

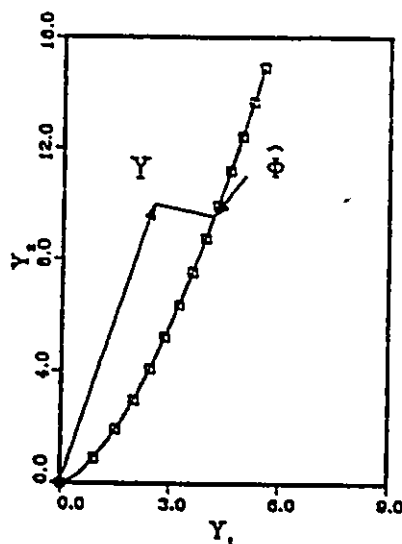


Figure 2.4: Geometric representation of a reparameterization

A reparameterization expresses the same *model* with new parameters which are a function of the original parameters alone. For this example,

$$\theta = f(\phi) = \log \phi \quad (2.24)$$

so that:

$$\phi = f^{-1}(\theta) = 10^\theta \quad (2.25)$$

$\phi$  is a function of  $\theta$  alone. Equations 2.21 and 2.23 are different parameterizations, or *forms*, of the same model. Reparameterizations do not change the relationship between operating variables. This is further illustrated by reparameterizing an analytic rate model of the Hougen-Watson type

$$r = \frac{kK_H K_S P_H P_S}{(1 + K_H P_H + K_S P_S)} \quad (2.26)$$

where the rate and adsorption equilibrium constants  $k$ ,  $K_H$  and  $K_S$  are the parameters to be estimated and the partial pressures  $P_H$  and  $P_S$  are the operating variables. The model can be reparameterized in several ways. Ratkowsky [7] suggested a general reparameterization for models of this type in which all the parameters appear in the denominator,

$$r = \frac{P_H P_S}{(\phi_1 + \phi_2 P_H + \phi_3 P_S)} \quad (2.27)$$

where

$$\begin{aligned} \phi_1 &= \frac{1}{kK_H K_S} \\ \phi_2 &= \frac{1}{kK_S} \\ \phi_3 &= \frac{1}{kK_H} \end{aligned}$$

He showed that this parameterization was particularly effective in reducing parameter effects nonlinearity. This will be discussed in more detail in Section 2.5.3

## 2.4.2 Bates and Watts Relative Curvature Measures of Nonlinearity

Bates and Watts [1] developed measures of nonlinearity with geometric interpretations called relative curvatures. They provide indications of the extent of both

intrinsic and parameter-effects nonlinearity and are calculated by

$$\Gamma^N = \| d^T A_{..}^N d \| \quad (2.28)$$

$$\Gamma^T = \| d^T A_{..}^T d \| \quad (2.29)$$

where  $d$  is a  $p$  dimensional unit vector,  $A_{..}^N$  and  $A_{..}^T$  are the intrinsic and parameter effects portions of the 3 dimensional acceleration array respectively. They also developed a test statistic,  $\frac{1}{2\sqrt{F_{p,v,\alpha}}}$ , to test for significant nonlinear behavior in the vicinity of  $\hat{\theta}$ . The intrinsic curvature is a measure of the non-flatness of the solution locus. The parameter effects curvature is a measure of the non-uniformity of the coordinate system caused by the parameterization of the model. The intrinsic curvature can be interpreted as the inverse radius of the circle which most closely approximates the solution locus. The smaller the curvature the larger the radius of the circle i.e. the flatter the solution locus. Bates and Watts have also shown that individual elements of the acceleration array,  $A_{..}$ , are related to different types of non-uniformity of the coordinate system. A detailed discussion of the curvature calculations is given in Appendix A.

### 2.4.3 Box's Bias

As described earlier, linear models have unbiased parameter estimates. The bias of parameter estimates in nonlinear models is related to the degree of nonlinearity of the model/data set. A quantitative measure of a parameter's bias was developed by Box [2] for the multiresponse, heteroscedastic (nonconstant variance) case. The measure is very easy to calculate for the single response, homoscedastic case and the expected discrepancy, or bias, is

$$E(\phi) = E(\hat{\theta} - tv) = -\frac{\sigma^2}{2} \left( \sum_{w=1}^n F_w^T F_w \right)^{-1} \sum_{u=1}^n (F_u^T \text{tr} \left( \left( \sum_{v=1}^n F_v^T F_v \right)^{-1} H_u \right)) \quad (2.30)$$

where  $E(\phi)$  is a  $p \times 1$  vector of the biases for the parameters,  $F$  is equivalent to  $x$ , and  $H$  is the  $n \times p \times p$  matrix of second derivatives of the model with respect to the parameters.

Bates and Watts [1] have shown that this expression for the bias is in fact an element of the parameter effects portion of the acceleration array; as such Box's

bias does not indicate the degree of intrinsic nonlinearity. No test statistic for determining the significance for the bias has been proposed although a value of 1% has been suggested by Ratkowsky [3,7]. Even if a test statistic were available, inferences about the degree of nonlinearity could still be misleading since the bias represents only one type of parameter effects nonlinearity. Details of the derivations and calculations are given in Appendix B.

#### 2.4.4 Ratkowsky's Sampling Properties of the Parameters

Ratkowsky [3] suggested the use of Monte Carlo simulations to study the sampling properties of each parameter. A large number of parameter estimates are obtained by generating a large number of data sets from the original data set (Ratkowsky suggests using at least 1000 such simulated data sets). The first four moments of each parameter are then calculated, the moments being the mean, variance etc. Using these four moments, estimates of the bias, variance, skewness and kurtosis of the parameter estimates are obtained. These are then compared to the known sampling properties of a normal distribution. If the estimated sampling properties are not significantly different from those of a normal distribution, this suggests that the parameters are normally distributed and that they are linear combinations of the response, i.e. the model/data set approaches linear behavior. Details of the method are given in Appendix C.

#### 2.4.5 Lowry's Assymetry Measure of Bias

Lowry [16] developed an assymetry measure of bias,  $\lambda$ , for each parameter. The measure varies between 0 and 1 for linear and highly nonlinear models respectively. While there is no test statistic available, it has been suggested that as a rule of thumb,  $\lambda < 0.01$  indicates near linear behavior. If  $\lambda > 0.05$  then the model/data set exhibits significant nonlinear behavior.

#### 2.4.6 Beale's Measures of Nonlinearity

Beale [4] proposed four measures of nonlinearity. The first,  $N_1$ , is obtained by comparing the distance between  $\eta(\theta)$  and its linear approximation to the distance

between  $\eta(\theta)$  and  $\eta(\hat{\theta})$  for a number of points  $\theta$  near  $\hat{\theta}$ . The value of  $\hat{N}_\theta$  depends on the number of points used and the parameterization and as such was called an empirical measure of nonlinearity for  $\hat{\theta}$ . As the number of points  $\theta$  goes to infinity,  $\hat{N}_\theta$  approaches a theoretical limit,  $N_\theta$ . The minimum value of  $\hat{N}_\theta$  for any parameterization is  $\hat{N}_\phi$  and represents the empirical intrinsic nonlinearity of the model. As the number of points approaches infinity,  $\hat{N}_\phi$  approaches  $N_\phi$ .

Beale's measures are useful since they provide separate measures of nonlinearity which are intrinsic to the model/data set and also dependent on the parameterization used. Calculating the measures involves simulations, making computational effort heavy. Moreover, the measure depends on the number of points and their location. The measure has also been shown to be inaccurate with highly nonlinear model/data sets by Guttman and Meeter [17].

## 2.5 Dealing with Nonlinearity

One or more of the measures described in Section 2.4 can be used to identify the extent of nonlinearity of a model/data set. If the nonlinearity is significant it is desirable to reduce it to an acceptable level in order to improve the reliability and ease of making inferences. There are several ways to do this:

- transformations of the response
- quadratic approximations of the solution locus
- reparameterizations
- performing designed experiments
- a combination of designed experiments and reparameterizations

### 2.5.1 Transformations of the Response

Transformations of the response have long been in use in data analysis, and involve transforming the response (the "y") so that the model is linear in the parameters. This method was employed for nearly every nonlinear model before computers

made nonlinear regression feasible. Transformations range from inverting the response, using logarithms or rewriting the model so that the response or dependent variable is a function of the parameters and/or the operating variables.

The main advantage is that the transformed model becomes linear in the parameters. Least squares estimates of the parameters can therefore be calculated directly. Values of the original parameters can be obtained from those estimated, as can values of the predicted response. However the original parameters obtained by this method are often quite different from those obtained from a nonlinear regression for the original model. The same applies to the predicted response and estimates of parameter precision. Furthermore different transformations can result in different values for the parameters and predicted response. Which transformation should be used?

These differences arise because each transformation leads to a minimization of a different sum of squares function. To determine which transformation should be used it is necessary to verify the assumptions implicit in least squares analysis. For the following general model, recall that the random error term is assumed to be additive and normally distributed

$$y = f(\mathbf{x}, \theta) + \epsilon \quad (2.31)$$

After transforming the response, say, by inverting it, one obtains

$$\frac{1}{y} = \frac{1}{f(\mathbf{x}, \theta) + \epsilon} \quad (2.32)$$

and not

$$\frac{1}{y} = \frac{1}{f(\mathbf{x}, \theta)} + \epsilon \quad (2.33)$$

Applying least squares to Eq. 2.32 forces the assumption of an additive random error, as given by Eq. 2.33. However, if the actual case is that given by Eq. 2.31 then the estimates of the parameters obtained in this manner will not, generally, be unbiased nor have minimum variance. Also, if the response was normally distributed for the original model, it will no longer be so for the transformed model.

An example is used to illustrate the use of such transformations. Consider the model/data set taken from Ayen and Peters [18] who proposed a model for the rate

of catalytic reduction of NO to NH<sub>3</sub>

$$r_{NO} = \frac{kK_{H_2}P_{H_2}}{(1 + K_{H_2}P_{H_2} + K_{NO}P_{NO})} \quad (2.34)$$

The model can be easily linearized by inverting the response, i.e. the rate of reaction,

$$\frac{1}{r_{NO}} = \frac{1}{k} + \frac{1}{kK_{H_2}P_{H_2}} + \frac{K_{NO}P_{NO}}{K_{H_2}P_{H_2}} \quad (2.35)$$

or

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 \quad (2.36)$$

where the new operating variables  $x_1$  and  $x_2$  are

$$x_1 = \frac{1}{P_{H_2}} \quad x_2 = \frac{P_{NO}}{P_{H_2}} \quad (2.37)$$

the new response is

$$y = \frac{1}{r_{NO}} \quad (2.38)$$

and the new parameters are

$$\beta_0 = \frac{1}{k} \quad \beta_1 = \frac{1}{kK_{H_2}} \quad \beta_2 = \frac{K_{NO}}{K_{H_2}} \quad (2.39)$$

After a linear regression on the model given by Eq. 2.36 the original parameters  $k$ ,  $K_{H_2}$  and  $K_{NO}$  can be determined from the new  $\beta$  parameters. Table 2.1 compares values for the original parameters obtained from both models in terms of the  $\theta$  parameters.

The confidence intervals for the nonlinear model are taken from the limits of 95% exact shape confidence regions for the worst case, i.e. the largest and smallest values of each parameter from all possible pairs of parameters. The confidence intervals for the linear case are obtained for the  $\beta$  parameters from the variance-covariance matrix of the transformed model. These intervals are then transformed back to the  $\theta$  parameters by using Eq. 2.39. The values obtained for all three parameters are significantly different, i.e. the intervals for the estimates do not overlap. Thus the use of this linearization transformation would lead to incorrect conclusions about the rate parameters.

Transformations are thus generally restricted to obtaining initial parameter estimates for use in nonlinear regressions, in some cases even these initial estimates are



Table 2.1: Comparison of 95% confidence intervals before and after transformation

Confidence intervals are compared for the original model parameters. Confidence intervals for the nonlinear model were taken from the limits of the exact shape confidence regions while those for the linear model are based on the limits for the parameters of the transformed model.

| Parameter | Nonlinear Model                                                | Linear Model                                                    |
|-----------|----------------------------------------------------------------|-----------------------------------------------------------------|
| $k$       | $2.5 \times 10^{-4} < 4.46 \times 10^{-4} < 20 \times 10^{-4}$ | $1.3 \times 10^{-4} < 1.62 \times 10^{-4} < 2.1 \times 10^{-4}$ |
| $K_{NO}$  | $7.5 < 10.7 < 11$                                              | $12 < 31.6 < 88$                                                |
| $K_{H_2}$ | $1.0 < 5.18 < 14$                                              | $17 < 29.86 < 54$                                               |

very poor. Transformations are valid when the error structure can be made to more closely follow the assumed behavior. Problems involved with such transformations are well documented in the literature, e.g., Bacon [5] and Kittrell et al. [6].

### 2.5.2 Quadratic Approximations

As mentioned earlier, the linear approximation replaces the solution locus by a plane and imposes a uniform co-ordinate system for the parameters. The reliability of inferences depends on the validity of this approximation. Quadratic approximations have been used in order to improve the more commonly used linear approximation.

Hamilton et al.[8] suggested using a quadratic approximation of the solution locus. They showed that intrinsic nonlinearity can influence confidence regions and that by using quadratic approximations these regions could be made more accurate. However in many cases the planar assumption of the solution locus is a good one. The intrinsic curvature was acceptable in 22 of 24 cases examined by Bates and Watts [1] and by Hamilton [8]. These observations have also been noted by Donaldson and Schnabel [10] and Ratkowsky [3,7] as well as in this work. The ability to improve inferences with nonlinear models is always welcome. However,

the quadratic approximations appear to be rarely needed. Also the method uses non-standard software (although it is available from Hamilton). The improved approximation would be useful if the intrinsic nonlinearity was determined to be significant, as it offers the only alternative to performing more experiments.

Hamilton et al. [10] also used quadratic approximations in order to improve on D-optimal designs. D-optimal designs (designs used for improving parameter precision) are based on minimizing the volume of the approximate confidence region for the parameters, as measured by the determinant of  $(\mathbf{X}^T \mathbf{X})^{-1} \hat{\sigma}^2$ . This volume is only an approximation for nonlinear model/data sets and the efficiency of the design depends on the degree of nonlinearity.

They noted that the quadratic design was consistently more efficient at improving parameter precision. This efficiency depended on the noise level, the greater the noise level, the better the quadratic design. D-optimal designs are insensitive to noise level, parameterization and residuals from previous experiments because they do not take into account nonlinearity effects. D-optimal designs are also not as robust with respect to initial parameter estimates and in cases with high noise levels the criterion can lead to inference regions of infinite size. There is no indication of what noise level is "too high" with D-optimal designs, but there is some warning with the quadratic design.

Not only did this new design provide a significant improvement for precise parameter estimation but it also proved successful in reducing the extent of nonlinearity. The design is fully explained in the original paper and examples are presented. The quadratic designs are not studied in this work but the traditional D-optimal designs will be.

### 2.5.3 Reparameterizations

The definition and effect of reparameterizations have already been introduced in Section 2.4. There is nothing to prevent the use of any parameterization, although there is usually a preferred one, being that which occurs naturally in building a mechanistic model. For catalytic rate models these parameters are usually rate and adsorption constants for the isothermal case and pre-exponential constants and activation energies for the non-isothermal case. Having estimates of these parameters

is very desirable for comparing different systems, i.e. comparing temperature sensitivity of the equilibrium adsorption constants, development of better catalysts etc. Essential to making these comparisons are estimates of the parameters's precision. Generally speaking there are no guidelines for choosing the best parameterization for reducing parameter effects nonlinearity. The analyst must simply try various options.

Ratkowsky [7] suggested a general parameterization for catalytic rate models of the Hougen-Watson type, an example of which was seen in Section 2.4. Models of the Hougen-Watson type can be represented as

$$-r = \frac{f_0(\theta)g(P)}{(h_1(P) + \theta_2 h_2(P) + \dots + \theta_m h_m(P))^2} \quad (2.40)$$

The new parameterization has all the parameters appearing in the denominator as

$$-r = \frac{g(P)}{(h_1(P) + \phi_2 h_2(P) + \dots + \phi_m h_m(P))^2} \quad (2.41)$$

where  $g$ ,  $f$  and  $h$  are some function of the parameters  $\theta$  or the operating variables. Ratkowsky studied 26 data sets dealing with catalytic rate studies for which  $\Gamma^T$  was reduced in each case by using the reparameterization described above. In 17 of 26 cases  $\Gamma^T$  was reduced to an acceptable level.

One of the cases studied was a model proposed by Hougen and Watson [20] for the hydrogenation of iso-octenes at 200 °C,

$$-r = \frac{kK_{H_2}K_U P_{H_2} P_U}{(1 + \sqrt{K_{H_2} P_{H_2}} + K_U P_U + K_S P_S)^2} \quad (2.42)$$

After the reparameterization the new model form is

$$-r = \frac{P_{H_2} P_U}{(\phi_1 + \phi_2 \sqrt{P_{H_2}} + \phi_3 P_U + \phi_4 P_S)^2} \quad (2.43)$$

Both curvatures were unacceptable for both parameterizations, however  $\Gamma^T$  for the new model form was reduced to less than 10% of its original value. The reduction in  $\Gamma^T$  is shown in Figures 2.5 and 2.6 which compare linear and exact shape confidence regions for the parameter pair exhibiting the greatest degree of nonlinearity for each parameterization. For the original model form the approximate shape poorly depicts the exact shape confidence region. The match between the

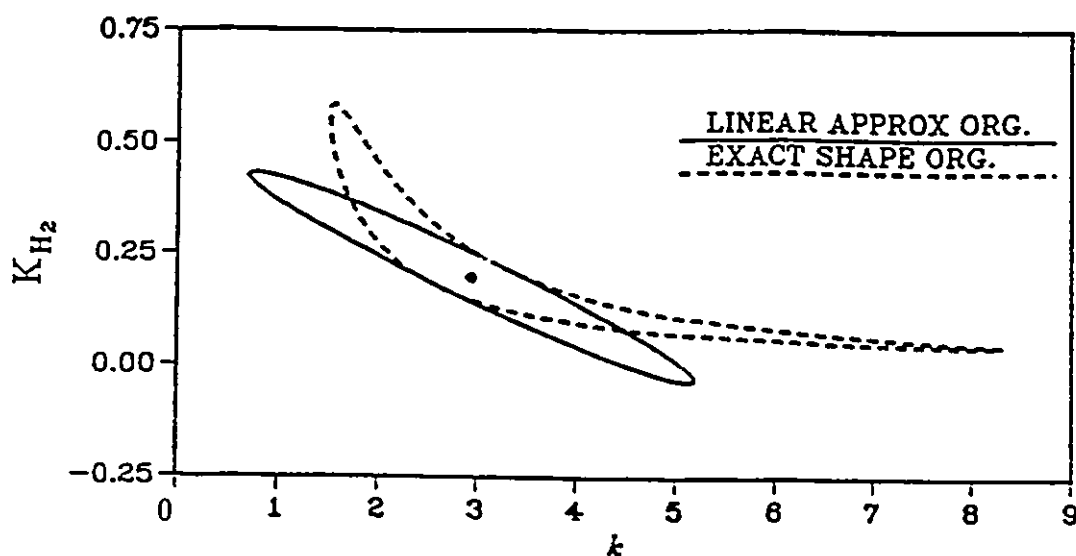


Figure 2.5: Confidence regions hydrogenation of iso-octenes, Eq. 2.42

Pair-wise conditional confidence regions showing the poorest coverage by the linear approximation for all possible pairs of parameters.

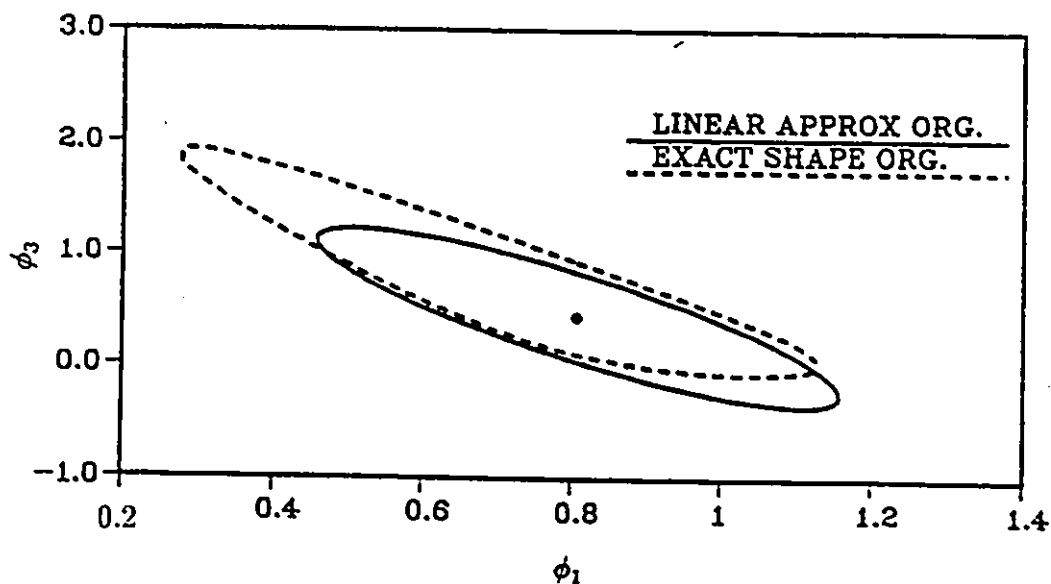


Figure 2.6: Confidence regions after Ratkowsky's reparameterization, Eq. 2.43

Pair-wise conditional confidence regions showing the poorest coverage by the linear approximation for all possible pairs of parameters.

two regions for the new model form, while still not ideal, is much better. The exact shape region is much more elliptical, as it would be for a linear model.

This general reparameterization is very effective, but it is not always sufficient to reduce the parameter effects nonlinearity to an acceptable level and intrinsic nonlinearity is not changed.

Another difficulty with this approach is that the confidence regions and estimates of parameter precision no longer apply to the original parameters but to  $\phi$ . The new parameters are nonlinear functions of the original parameters. In the previous example

$$\begin{aligned}\phi_1 &= \frac{1}{(kK_{H_2}K_U)^{1/2}} \\ \phi_2 &= \frac{\sqrt{K_{H_2}}}{(kK_{H_2}K_U)^{1/2}} \\ \phi_3 &= \frac{K_U}{(kK_{H_2}K_U)^{1/2}} \\ \phi_4 &= \frac{K_S}{(kK_{H_2}K_U)^{1/2}}\end{aligned}\tag{2.44}$$

To obtain the original parameters one must solve, in general,  $p$  simultaneous nonlinear equations. Information regarding the original parameters' precision is even more difficult to recover. Assuming that the limits of the confidence intervals for  $\phi$  are available and reliable, then the upper and lower bounds of  $\phi$  can be used to obtain the analogous values in the  $\theta$  parameters. In this case there would be  $2p$  simultaneous nonlinear equations to solve.

Reparameterizations which reduce the extent of nonlinearity also improve the precision of the predicted response and its reliability. This is because the variance of the predicted response approaches the minimum variance of a linear model. Reparameterizations do not change the predicted response,  $y_i$ , itself, but do change estimates of its precision. If reliable and precise estimates of  $y_i$  are required then reparameterizations will certainly help. On the other hand if the ultimate goal of a study is to obtain information about the original parameters it may be preferable to work with the original parameters. Bates and Watts [9] noted that, while studies

of reparameterizations are important, the ideal case would be one where the *experimental design* is selected so that the *original parameters* themselves have small parameter effects nonlinearity. The present work is an attempt to accomplish just this.

Predicting rates at temperatures other than those used to obtain the data require that the constants or parameters be expressed as Arrhenius type expressions. These expressions may be fitted individually for each constant by linearizing the expression by using a logarithmic transformations. A better approach is to incorporate the expressions into the isothermal model and estimate all the parameters simultaneously as discussed by Pritchard [21]. These models are highly nonlinear and a reparameterization is often used to overcome this. The Arrhenius expression,

$$k = A_k \exp \left( \frac{-E_k}{RT} \right) \quad (2.45)$$

can be reparameterized as

$$k = A_k^* \exp \left( \frac{-E_k}{R} \left( \frac{T_0 - T}{TT_0} \right) \right) \quad (2.46)$$

where

$$A_k^* = A_k \exp \left( \frac{-E_k}{RT_0} \right) \quad (2.47)$$

and  $T_0$  is the average or midpoint temperature of the range studied. This parameterization greatly improves the convergence of nonlinear routines and is also less demanding in terms of good initial estimates. The example used in Section 2.2 showed the confidence regions for the Arrhenius parameters as given in Eq. 2.45, the curvatures for this model are  $\Gamma^N = 0.21$  and  $\Gamma^T = 1650(!)$  and the test statistic is 0.31. After reparameterizing all the Arrhenius expressions as in Eq. 2.46,  $\Gamma^T$  was reduced to 0.90. This dramatic decrease is reflected in the shape of the exact shape confidence region, shown in Figure 2.7. The exact shape is now elliptical and the match with the linear-approximate region is quite good. The value for  $A_k$  can be easily obtained for this parameterization and  $E_k$  is estimated directly. Again the problem of using reparameterizations appears, the estimates of precision do not apply to  $A_k$  but to  $A_k^*$ . Fortunately the reparameterization is a simple one and an estimate of the precision of  $A_k$  can be obtained by taking the endpoints of the

regions for Figure 2.7 and calculating

$$A_k = \frac{A_k^*}{\exp\left(\frac{E_k}{RT_0}\right)} \quad (2.48)$$

giving

$$4.5 < A_k = 855 < 1.8 \times 10^5 \quad (2.49)$$

This confidence interval agrees poorly with that obtained from Figure 2.1, which ranged from 1.2 to at least  $5.0 \times 10^5$ . In fact the exact-shape confidence region extends beyond this, the full confidence region was not found because presenting both regions together would result in the linear approximate-shape region being compressed into a vertical line. This example shows that even with a simple reparameterization, recovering estimates of precision for the original parameters can be misleading.

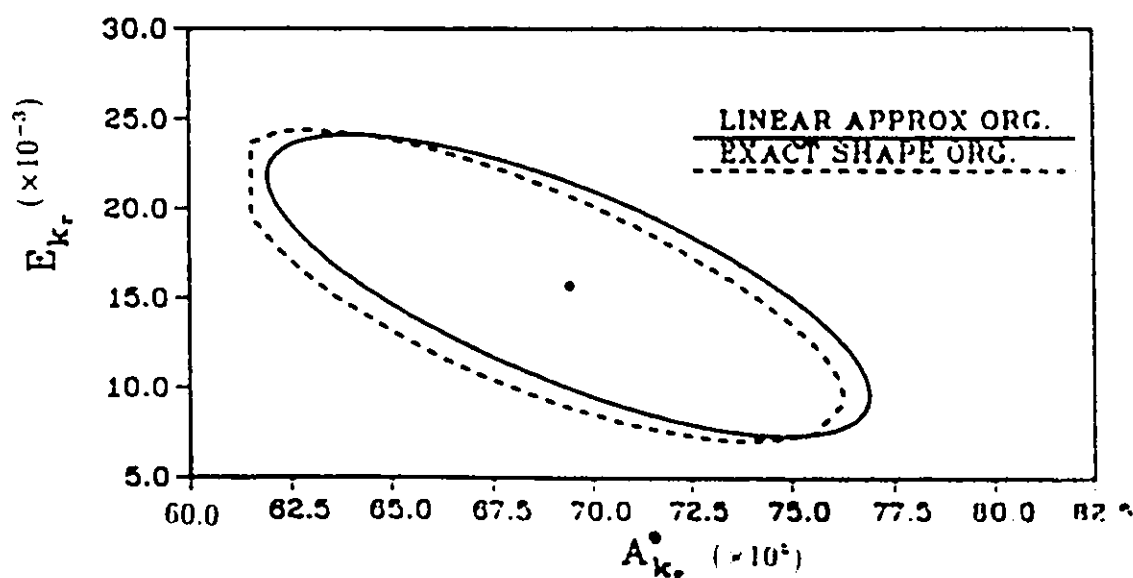


Figure 2.7: Confidence regions for reparameterized Arrhenius expression

Confidence regions from Juusola, oxidation of O-xylene, non-isothermal data set.

### 2.5.4 Previous Experimental Designs

Designed experiments have long been in use, Chernoff [22] having first proposed a D-optimal design in 1953, being later refined in 1959 to its present form by Box and Lucas [23]. Hamilton et al. [10] took D-optimal designs one step further by using a quadratic approximation of the solution locus. They noted that their quadratic design was effective at reducing the extent of nonlinearity as measured by the relative curvatures. D-optimal designs have also been shown to effectively reduce the extent of nonlinearity. Juusola [14] and Tan [24] showed that the exact-shape confidence regions were not only reduced in size by using a D-optimal design but the shape of the regions also became more elliptical. Despite such indications that D-optimal designs may be effective in reducing nonlinearity, no studies of its application as a minimum nonlinearity design have been found.

Another common experimental design is used for model discrimination. The design selects run locations such that differences between predicted values for the candidate models are maximized. Probabilities of a specific model being the "true" model are calculated based on how well a model predicts the response. As the design proceeds one model's probability will approach 1 while that of the others approaches zero. More detailed discussions are given in Bacon [5], Hunter and Reiner [25] and Box and Hill [26]. D-optimal and model discrimination designs are often combined to form a joint design criterion. At the start of the design priority is given to model discrimination. As one model's probability dominates more weight is given to the precise parameter estimation design. This design is described in detail in Bacon [5] and Hill et al [27]. The use of a model discrimination or joint design criterion may lead to designed runs which may or may not reduce nonlinearity. In the Tan [24] data set, runs for model discrimination differed from D-optimal runs, which were shown to reduce nonlinearity. Hence the model discrimination runs may be detrimental from a minimum nonlinearity view.

### 2.5.5 Summary

There are several options available to deal with nonlinearity. There are transformations of the response, quadratic approximations or reparameterizations. Transformations of the response can completely eliminate the problems associated with



nonlinear models by obtaining a linear form of the original model. Quadratic approximations allow more reliable inferences to be made and reparameterizations can greatly reduce the extent of nonlinearity.

Unfortunately each method has its shortcomings. Transformations of the response have been shown to be misleading in terms of estimates of the response and parameters as well as their precision. Quadratic approximations are only useful in the rare cases when intrinsic nonlinearity is significant. Reparameterizations result in a loss of information regarding the precision of the original parameters which may be difficult to recover.

Experimental designs currently available concentrate on discriminating among potential models, obtaining precise parameter estimates or a combination of both. As important and useful as these designs are, they do not address the problem of nonlinearity directly, although D-optimal designs and the quadratic design of Hamilton et al [10] do improve the situation.

This work is aimed at developing an experimental design for reducing the extent of nonlinearity. The criterion will also be tested for compatibility with precise parameter estimation.

## Chapter 3

# Designed Experiments

### 3.1 Introduction

Problems encountered when working with nonlinear model/data sets have been discussed in the previous sections. These problems have been dealt with by transforming the response, reparameterizing the model or using quadratic approximations. The pros and cons of these solutions have also been discussed.

An alternative is the use of experimental designs specifically aimed at reducing the extent of nonlinearity. This has been suggested in Bates and Watts [1] and Bates et al. [9] but there appears to be an absence of any published work which studies the use of designed experiments with this objective in mind.

Designed experiments for reducing the extent of nonlinearity would be useful when:

- intrinsic nonlinearity is significant.
- information about the original parameters is required.
- reparameterizations are not sufficient to reduce parameter effects nonlinearity to an acceptable level.

There could be cases when either reparameterizations or designed experiments alone will not be able to reduce the extent of nonlinearity to an acceptable level. This situation could arise when both types of nonlinearity are significant or when parameter effects nonlinearity is significant after all possible reparameterizations

have been tried. Simulations may reveal that an unacceptable number of experiments must be performed before the degree of nonlinearity is acceptable for a given parameterization. In this situation designed experiments and reparameterizations can be used in tandem.

It is known that nonlinear models approach linear behavior asymptotically as the sample size increases but there is no way of determining what sample size is required for near linear behavior (other than simulations). Bates and Watts [1] have shown that their curvatures can be reduced, by a factor of  $\frac{1}{r}$ , by replicating the experimental design  $r$  times, all other things being equal. A sequential design strategy with a suitable design criterion would undoubtedly be more efficient.

An experimental design requires a criterion which is to be optimized. A suitable measure of nonlinearity would make an ideal design criterion. The ideal measure should have several desirable traits and these can be used to screen potential candidates. The measure should:

- accurately measure the degree of nonlinearity
- be easy to calculate
- lead to a criterion compatible with other modelling objectives
- have a test statistic by which adequate reductions in nonlinearity can be judged

The measures of nonlinearity previously discussed will now be evaluated with respect to these traits.

Beale's measures are computationally demanding and there is no test statistic. Moreover, Guttman and Meeter [17], have shown that the measures can be inaccurate, especially in cases of high nonlinearity.

Ratkowsky's Monte Carlo simulations [3] are much too demanding computationally. While the simulations do provide useful information and can be tested for significant non-normal behavior, there is, in a sense, too much information. There is no apparent way to assimilate the measures into a single value, i.e. is the bias more important than the excess variance or the skewness?

Box's bias [2], on the other hand, is straightforward with respect to computational effort and would be suitable for use with micro-computers. The measure is

particularly easy to calculate when constant variance is assumed and there is only one response. There are  $p$  measures of bias and these are easily amalgamated into a single measure. Possibilities include: the worst absolute bias, the sum of absolute biases or the sum of the squares of the biases. The final measure is attractive as it takes into account the sign of the biases and gives more weight to the worst bias (es). There are several factors against using the bias as a design criterion. There is no test statistic; the suggested cut-off of 1% can be misleading. A reliable test statistic is useful for determining when to stop performing experiments or simulations without resorting to comparing confidence regions. The bias has also been found to be scale dependent for parameters appearing linearly in the model (Ratkowsky [3] and this work). The biases do not measure all types of parameter effects nonlinearity and do not measure intrinsic nonlinearity at all. Despite these shortcomings the bias (i.e. the sum of squares of the biases) was tested because of its ease of computation.

Lowry's asymmetry measure of bias was not considered because it too involved simulations in its calculation, making it computationally demanding. The measure also lacks a test statistic. The need for these simulations was later eliminated when Lowry and Morton [16] developed an analytical expression for the measure. Further investigation of the measure was restricted due to time constraints.

This leaves only the Bates and Watts curvatures. While the calculations can be demanding computationally, compared to Box's bias, they are acceptable, especially compared to Ratkowsky's simulations. They provide scale independent measures of both intrinsic and parameter effects nonlinearity and a test statistic is also available.

The compatibility of the curvatures in a design criterion with other modelling objectives can not be evaluated at this stage. Simulations will be used in order to compare minimum curvature designs to D-optimal designs. Ideally the two designs would not lead to designed runs which are detrimental to either modelling objective, i.e. D-optimal designed runs will not result in increased nonlinearity and curvature designed runs will not result in poor parameter precision.

### 3.2 Evaluation of the Relative Curvatures

The use of the Bates and Watts curvatures as a measure of the degree of nonlinearity has been reported in the literature. The accuracy of the curvatures and the test

statistic used in conjunction with them, has been evaluated by comparing them to other measures of nonlinearity and by comparing exact-shape and approximate shape confidence regions.

Ratkowsky [3,7] used the measure extensively and found it to agree well with his own simulations, Box's bias and Lowry's bias.

Cook and Witmer [28] looked at two cases where they felt the curvatures did not agree well with comparisons of exact and approximate-shape confidence regions. The first case involved a three parameter model for which the value of  $\Gamma^T$  was significant.

There is no argument that the linear approximate-shape confidence regions are adequate for two of the three parameter pairs. However, for the pair of parameters  $\theta_2$  and  $\theta_3$ , the linear approximation cannot be considered acceptable. The Bates and Watts curvatures are *maximum* relative curvatures, they reflect the extent of nonlinearity for the worst case. Cook and Witmer argue that  $\Gamma^T$  should be acceptable. However for the degree of nonlinearity to be acceptable, coverage by the linear approximate-shape confidence regions should be acceptable for all parameter pairs. In this work, models with three or more parameters and significant parameter effects nonlinearity often resulted in acceptable linear approximate-shape confidence regions for some parameter pairs while the linear approximation was very poor for others. As such, the relative curvature measures should be considered accurate in this case.

In the second case Cook and Witmer examined a model for which conflicting conclusions arose regarding the accuracy of the curvatures. For a given set of parameters the linear approximate-shape confidence regions provided very poor coverage of the exact-shape region when  $\Gamma^T$  was acceptable. For another set of parameter estimates the opposite situation was observed. However, it is not clear if Cook and Witmer were working from a single data set or many data sets (from which they obtained the widely differing model parameters). Moreover, in one case one of the parameters was fixed at zero, a situation which could suggest an inadequate model. Cook and Witmer presented four further cases (with  $\Gamma^{TH}$  above and below 1) with different model parameters where they felt that the linear approximation was acceptable for values of  $\Gamma^T$  greater than the cutoff. Whether the curvatures are

accurate or not becomes a judgment call on what can be considered acceptable coverage of the exact-shape confidence region by the linear approximate-shape region. It can also be interpreted as the test statistic being too strict. If any conclusion were to be drawn from the four later cases, it would be that the curvatures are extremely sensitive measures of nonlinearity. The curvatures correctly reflected the worsening coverage of the linear approximate-shape confidence region in the four cases.

Donaldson and Schnabel [19] compared confidence regions and intervals for the exact and approximate cases for 20 model/data sets. All the models had insignificant  $\Gamma^N$  and they found  $\Gamma^T$  to be an accurate indicator of when linearizations of the model would produce reliable approximate-shape confidence regions or intervals. They did note that in nine cases, when the  $\Gamma^T$  was between 1 and 10 times the test statistic, the linear approximate confidence region covered 83% to 92% of the exact-shape region. They interpreted this as an indication that the test statistic may be too strict. The same conclusion could be drawn in the last case presented by Cook and Witmer and, as will be seen later, this work also led to the same conclusion.

### 3.3 Experimental Design Strategy

As noted by Bates and Watts [1], the solution locus must be planar before a uniform coordinate system can be achieved. Thus, a suitable design strategy based on minimizing curvature would be to first reduce the intrinsic curvature,  $\Gamma^{NR}$ , to an acceptable level and then, if necessary reduce the parameter effects curvature (INC criterion). The inability of reparameterizations to reduce the intrinsic nonlinearity also supports this strategy. When  $\Gamma^N$  is acceptable, as is usually the case, the design strategy would be simply to minimize  $\Gamma^T$  (PEC criterion).

Incorporation of Box's bias into a design criterion was also studied because of its ease of calculation. There are several ways in which the biases could be assimilated into a design criterion, e.g., to minimize the worst absolute value of the bias, the sum of absolute values of the biases or the sum of squares of the biases. These can

be expressed, respectively, as

$$WAB = | \text{Bias}_i |_{\max} \quad i = 1, 2, \dots, p \quad (3.1)$$

$$SAB = \sum_{i=1}^p | \text{Bias}_i | \quad (3.2)$$

$$SSB = \sum_{i=1}^p \text{Bias}_i^2 \quad (3.3)$$

Since the bias of a parameter may be either positive or negative it is desirable to minimize the magnitude of the bias. The SAB design criterion would be useful when all parameters are significantly biased. The SSB design criterion would be similar to the SAB design but would give more weight to the worst bias.

### 3.3.1 Testing Procedure for Evaluating Design Criteria

The proposed design criteria were tested for their effectiveness in reducing the extent of nonlinearity with simulated experiments. Experimental model/data sets were taken from the literature and used as starting points. Experiments were designed sequentially as described below.

Experiments were designed by optimizing the design criterion in a pre-selected operating region. A grid covering the range of the original operating variables was generated, taking into account the limits of the original data and operating restrictions when such information was available. The design criterion was evaluated at the nodes of this grid and the optimal location found.

To begin the sequential design the model parameters and response variance,  $\theta$  and  $\sigma^2$  were estimated from the original data. The degree of nonlinearity was evaluated and the appropriate design criterion chosen if designed runs were required. An "experiment" was simulated at the optimal condition, as indicated by evaluation of the design criterion. The "result" of the experiment was determined by the sum of the predicted value of the response and an additive random error term. The random error term was generated using the IMSL subroutine GGNML, which generates a random number distributed as  $N(0, 1)$ . This random number was multiplied by  $\sigma$  to obtain a  $N(0, \sigma^2)$  distribution for the random errors. The simulated experiment was added to the original data set and the parameters, variance and extent of

nonlinearity re-evaluated. The simulation was repeated until the nonlinearity was reduced to an acceptable level or the reductions in nonlinearity were too small. Such a design strategy should provide the greatest reduction in nonlinearity for the fewest number of experiments.

Progress of the design was monitored by reductions in the curvatures and biases. The reductions in nonlinearity and the accuracy of the curvatures was verified by comparing approximate-shape and exact-shape confidence regions. Although the simulations were employed here to test the behavior of various design criteria, their use suggested other potential benefits for an experimenter. Using simulations may reveal that an impractical number of experiments would be required to achieve linear behavior for a particular model form. As a result, the analyst would have to try other parameterizations. Simulations could be very useful prior to or during experimental studies in that they would allow the investigator to compare various designs and obtain an idea of the progress that can be expected. They would also allow study of the potential benefits of expanded regions of operation.

### 3.3.2 Initial Model/Data Sets

The model/data sets used in developing and testing design criteria for reducing the extent of nonlinearity were taken from the literature and are summarized in Table 3.1. The data is included in Appendix D.

All the data sets involved observations collected at three temperatures. The extent of nonlinearity was evaluated for both the isothermal and non-isothermal models and the results are summarized in Table 3.2. Details are given in Appendix D.

In using these model/data sets some surprising features were encountered.  $\Gamma^T$  was significant, in every isothermal case but one. On the other hand,  $\Gamma^N$  was insignificant in every case, including the non-isothermal forms. The parameter effects curvature was found to be particularly large for the Ayen & Peters model/data set. Convergence with the non-isothermal model for Ayen & Peters (reduction to  $\text{NH}_3$ ), could not be achieved without obtaining a negative activation energy for the rate constant. As well, the Arrhenius plot using estimates of the rate constants did not



Table 3.1: Models and systems studied

The gas-solid catalytic rate models studied. M0 represents the original model form and M1 represents a reparameterized model form. See text.

| Authors and system                                                           | ISOTHERMAL MODEL                                                                                                    |                                                                                                                   |
|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|
|                                                                              | (M0)                                                                                                                | (M1)                                                                                                              |
| Ayen and Peters [18]<br>$\text{NO} \rightarrow \text{NH}_3$                  | $r_{\text{NH}_3} = \frac{k_1 P_{\text{NO}}}{(1 + K_{\text{H}_2} P_{\text{H}_2} + K_{\text{NO}} P_{\text{NO}})}$     | $r_{\text{NH}_3} = \frac{P_{\text{NO}}}{(\phi_1 + \phi_2 P_{\text{H}_2} + \phi_3 P_{\text{NO}})}$                 |
| Jaswal [29]<br>oxidation of benzene<br>Juusola [14]<br>oxidation of o-xylene | $r = \frac{k_1 k_2 C_{\text{O}} C_{\text{B}}}{(k_3 C_{\text{O}} + n k_4 C_{\text{B}})}$                             | $r = \frac{C_{\text{O}} C_{\text{B}}}{(\phi_1 C_{\text{O}} + n \phi_2 C_{\text{B}})}$                             |
| Tan [24]<br>oxidation of propylene                                           | $r = \frac{k_1 k_2 C_{\text{O}}^{\frac{1}{2}} C_{\text{P}}}{(k_3 C_{\text{O}}^{\frac{1}{2}} + n k_4 C_{\text{P}})}$ | $r = \frac{C_{\text{O}}^{\frac{1}{2}} C_{\text{P}}}{(\phi_1 C_{\text{O}}^{\frac{1}{2}} + n \phi_2 C_{\text{P}})}$ |

Table 3.2: Relative curvatures for the model/data sets studied.

Curvatures and the test statistic for iso-thermal and non-isothermal data.  
Original model form MO and reparameterized model form M1. See text.

| Authors and system                                | Temp<br>°C | IN<br>$\Gamma^N$ | PE<br>$\Gamma^T$<br>(MO) | PE<br>$\Gamma^T$<br>(M1) | Test<br>$\frac{1}{2\sqrt{F_{2,\nu,\alpha}}}$ |
|---------------------------------------------------|------------|------------------|--------------------------|--------------------------|----------------------------------------------|
| Ayen and Peters [18]<br><chem>NO -&gt; NH3</chem> | 375        | 0.14             | 31.9                     | 0.27                     | 0.25                                         |
|                                                   | 400        | 0.06             | 108.6                    | 0.11                     | 0.25                                         |
|                                                   | 425        | 0.05             | 13.0                     | 0.08                     | 0.22                                         |
| Jaswal [29]<br>oxidation of benzene               | 350        | 0.08             | 0.73                     | 0.16                     | 0.25                                         |
|                                                   | 375        | 0.06             | 0.32                     | 0.12                     | 0.27                                         |
|                                                   | 400        | 0.11             | 0.84                     | 0.20                     | 0.26                                         |
|                                                   | noniso     | 0.11             | 697.                     | 0.60                     | 0.31                                         |
| Juusola [14]<br>oxidation of o-xylene             | 270        | 0.004            | 0.25                     | 0.10                     | 0.24                                         |
|                                                   | 290        | 0.05             | 0.77                     | 0.08                     | 0.27                                         |
|                                                   | 300        | 0.04             | 0.87                     | 0.06                     | 0.27                                         |
|                                                   | noniso     | 0.21             | 1650.                    | 0.90                     | 0.31                                         |
| Tan [24]<br>oxidation of propylene                | 350        | 0.02             | 0.31                     | 0.04                     | 0.27                                         |
|                                                   | 375        | 0.03             | 0.38                     | 0.05                     | 0.27                                         |
|                                                   | 390        | 0.02             | 0.20                     | 0.03                     | 0.27                                         |
|                                                   | noniso     | 0.10             | 249.                     | 0.31                     | 0.32                                         |

follow the expected trend with increasing temperature, casting doubt on the validity of the model. Despite this, the isothermal form was used in the simulations to allow comparison to Ratkowsky's reparameterization. Whether the high degree of nonlinearity was due to the inadequacy of the model is not clear. In this case, the experimental design used by Ayen & Peters covered a very limited region. Both the inadequacy of the model and the poor experimental design contributed to the high degree of nonlinearity associated with these model/data sets, however, the relative importance of these two factors was not clear.

In the following sections, for ease of discussion, the curvatures will be given as ratios,  $\Gamma^{TR}$  and  $\Gamma^{NR}$ , of the curvature to the test statistic. As such,  $\Gamma^{TR}$  or  $\Gamma^{NR}$  greater than one indicates that the degree of nonlinearity is unacceptable. This eliminates the need to quote a test statistic with each curvature.

## Chapter 4

# Results and Discussion

The results of the minimum parameter effects curvature (PEC) and sum of squares of biases (SSB) designs are discussed in Section 4.1. The two designs are compared for each of the isothermal data sets for each model. The accuracy of the curvatures as indicators of nonlinearity is evaluated in Section 4.2 by comparing the inferences based on curvatures with observations made by comparing linear-approximate and exact-shape confidence regions. The curvatures are evaluated for the original data sets and after application of the PEC design. All the isothermal data sets were used to compare the PEC, SSB and D-optimal designs and are used to evaluate the compatibility of the different designs in Section 4.3.

### 4.1 PEC and SSB Designed Experiments

Numerous measures of nonlinearity were discussed in Section 3.1; of these measures Box's bias and the Bates and Watts relative curvatures were identified as potential design criteria. The PEC design was studied because the relative curvatures had been previously shown to be the most reliable measures of nonlinearity. The availability of a test statistic also makes this design criterion suitable for application in a sequential design strategy. The biases were assimilated into a single measure, the minimum sum of squares of biases (SSB). The SSB design was studied as an alternative to the PEC design, the SSB criterion being much simpler to compute and thus more suited for use with personal computers.

In the previous chapter, the relative curvatures were proposed for use in a design

strategy in which reduction of the intrinsic nonlinearity would be given priority. Once this was achieved the strategy would be to minimize the parameter effects curvature. Given that the intrinsic curvature was found to be acceptable in all the model/data sets studied in this work, the design strategy was to minimize the parameter effects curvature. The PEC and SSB design criteria are compared in this section for their ability to reduce the extent of nonlinearity as measured by  $\Gamma^{TR}$ .

The first model/data set studied was that proposed by Ayen and Peters [18] for the reduction of nitric oxide to ammonia. Experimental designs based on minimizing the parameter effects curvature (PEC) and the sum of squares of the biases (SSB), as outlined in Section 3.3.1, were tested at all three temperature levels of the original data. After the first PEC simulation, at 425 °C, it was noted that in some cases the parameter effects curvature,  $\Gamma^{TR}$ , increased, even though a reduction of  $\Gamma^{TR}$  from the previous value was predicted in every case. Recalling the simulation procedure described in Section 3.3.1, the optimum operating conditions are determined based on the most recent estimates of  $\theta$  and  $\sigma^2$ . The minimum parameter effects curvature predicted for the  $n$ 'th experiment is based on information available from the previous  $n - 1$  experiments. When estimates of the parameters and variance were redetermined for the  $n$ 'th experiment and the curvatures re-evaluated, the curvature usually differed from the "predicted" curvature as a result of changes in the parameter and variance estimates. The new value of  $\Gamma^{TR}$  was found to be particularly sensitive to the magnitude of the random error encountered in performing the most recent designed run. When the random error was greater than about 1.5 standard deviations the variance usually increased (relative to the previous value). If the increase in the variance estimate was large enough, the reduction of  $\Gamma^{TR}$  predicted by performing the experiment could be overridden. As shown in Appendix A, the curvatures are scaled using the variance and number of parameters such that

$$\Gamma = \gamma p = \gamma \sigma \sqrt{p}. \quad (4.1)$$

The curvatures are proportional to the square root of the variance, all else being equal. A total of four simulations were performed using the PEC criterion with different sets of random errors.

A "control" simulation was also performed in which the parameter and variance estimates were held constant at their original values.

While the use of a control simulation may not represent a realistic situation, it does allow comparison of the different design criteria without having to deal with the confounding effect of the changing values of the parameters and variances. In other words, the effects of random errors and run locations can be separated. An alternate approach would involve comparison of the mean performances of large numbers of simulations having different sets of residuals. Unfortunately this would require something of the order of 500 simulations, each consisting of 30 designed runs. Only one such comparison represents nearly two orders of magnitude more computing time than for all the simulations done in this work. It was felt that the control simulations would provide the same conclusions with a far lesser amount of computation. A control design will henceforth be designated by the suffix C, i.e. PEC-C, and a non-control simulation by the suffix S, i.e. PEC-S. A second suffix, SIMi, designates simulations for the same model/data set with different sets of random errors. The progress of the simulations is shown in Figure 4.1. Note that  $\Gamma^{TR}$  is plotted on a logarithmic scale in Figure 4.1, making reductions of  $\Gamma^{TR}$  for the 20th to 30th runs appear larger than they are. Because of the large values of  $\Gamma^{TR}$  for the original data,  $\Gamma_0^{TR}$  is not shown on the figures to avoid vertical compression of the curves.

SIM1 through SIM4 all exhibit situations where  $\Gamma^{TR}$  increased. As expected the control simulation resulted in a much "smoother" curve. As can be seen, the set of random errors can greatly affect the efficiency of the experimental design. After 30 designed runs,  $\Gamma^{TR}$  was 2.1 times as great with SIM3 as with SIM4.

The PEC design criterion was very effective in reducing  $\Gamma^{TR}$  particularly with the initial designed experiments.  $\Gamma^{TR}$  was reduced, on average, to 20% of its original value with the first experiment. In SIM4,  $\Gamma^{TR}$  was reduced by more than 95% after 10 designed experiments. In all cases reductions of  $\Gamma^{TR}$  slowed considerably after 10 designed runs. This clearly demonstrates the asymptotic nature of the relationship between the sample size and the degree of nonlinearity.

Two of the simulations were successful in reducing the parameter effects curvature to an acceptable level,  $\Gamma^{TR} \leq 1$ . SIM1 and SIM4 required 29 and 27 designed runs respectively. In most real situations performing 30 designed runs, as well as some initial experiments, would not be feasible. However the sequential use of the criterion in these situations can indicate when little progress is being made and

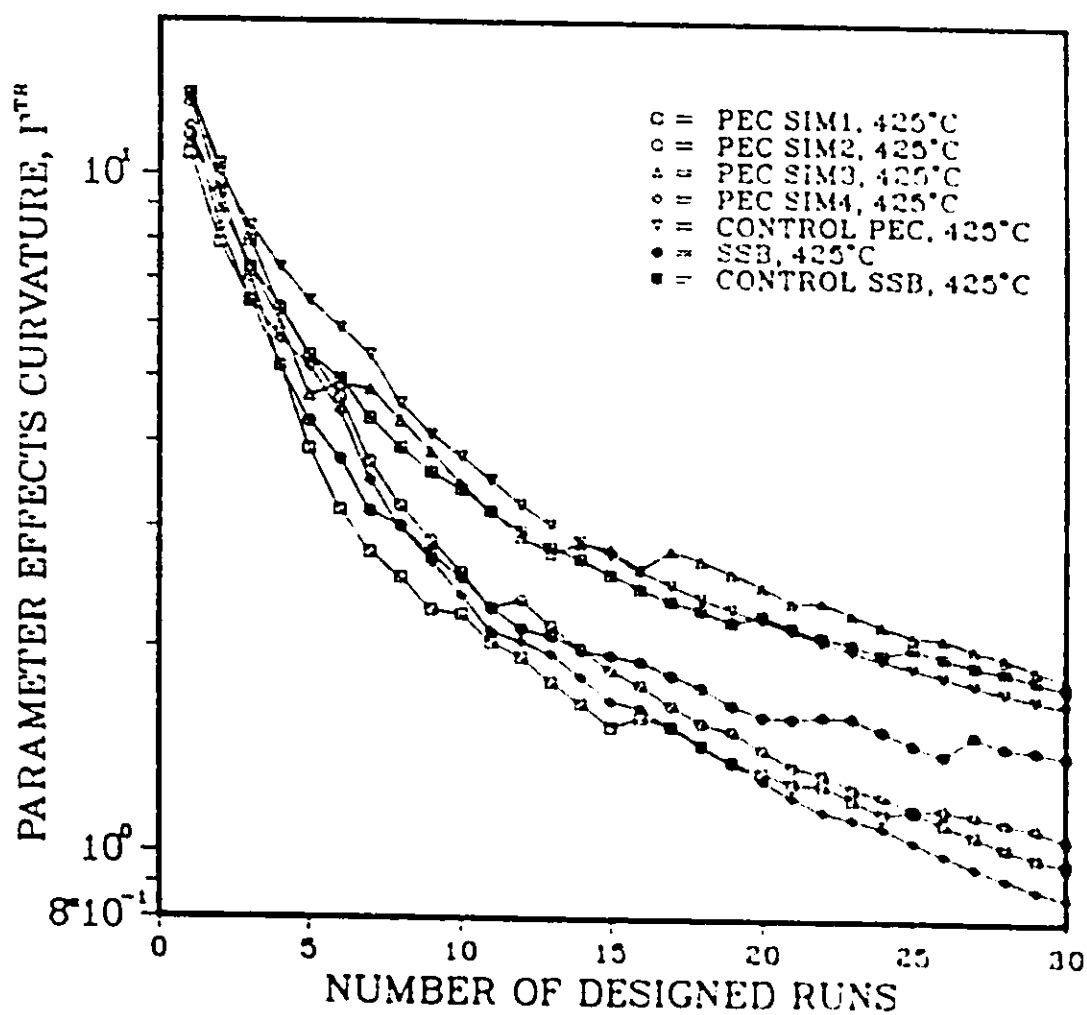


Figure 4.1: Progress of PEC and SSB designs with Ayen and Peters model/data set. NO reduction to  $NH_3$ , 425°C

$\Gamma^{TR}$  for the original data: 61

thus when design of further runs can be terminated. With the PEC criterion the worst bias was reduced to  $< 1\%$  with only one designed run in all four simulations. At this stage  $\Gamma^{TR}$  was, on average, 10.9. Hence, there is a large discrepancy as to the extent of nonlinearity as measured by the relative curvatures and the bias. This is not unexpected considering the lack of a rigorous test statistic for the bias estimates.

Figure 4.1 also shows the progress of a control and non-control SSB design. Unexpectedly, the SSB-S design was more efficient than one of the PEC designs (SIM3). This was the result of changing parameter and variance estimates and demonstrates the large effect residuals may have on the efficiency of the designs. After comparing the two control designs, PEC-C and SSB-C, the PEC design was found to be the more effective, as expected, but only marginally so.

Designed runs were also simulated at  $400^{\circ}\text{C}$  and  $375^{\circ}\text{C}$  using the PEC criterion. The progress in reducing  $\Gamma^{TR}$  is shown in Figure 4.2. As with the simulations at  $425^{\circ}\text{C}$ ,  $\Gamma^{TR}$  was greatly reduced with the initial experiments.  $\Gamma^{TR}$  was not reduced to an acceptable level at either of the lower temperatures with any of the design criteria. Again, the simulations were stopped when reductions in  $\Gamma^{TR}$  were very small. The initial parameter effects curvature,  $\Gamma^{TR}$ , was extremely high for the two lower temperatures (427 and 128 respectively) compared to the  $425^{\circ}\text{C}$  data set (61). At  $375^{\circ}\text{C}$  the SSB-S design was more efficient than the PEC-S design, however, after comparing the control simulations, the PEC design was marginally more effective. According to the bias measure and the 1% cutoff, the PEC design should have been stopped after 10 designed runs at both temperatures. However,  $\Gamma^{TR}$  was 24.1 and 6.1 at  $400^{\circ}\text{C}$  and  $375^{\circ}\text{C}$  respectively, indicating that the model/data sets were still significantly nonlinear.

Simulations with the Ayen and Peters model/data set were characterized by large reductions of  $\Gamma^{TR}$  ( $\sim 80\%$ ) after the first designed run, with any of the designs. The Ayen and Peters model/data set was also characterized by very large parameter effects curvatures and unstable parameter estimates during simulations. The two latter traits may be attributed to the initial data sets. The experimental design originally used by Ayen and Peters was of the "changing one variable at a time" type. This resulted in poor coverage of the operating region and consequently in poorly determined parameter estimates. The data sets were also small, consisting



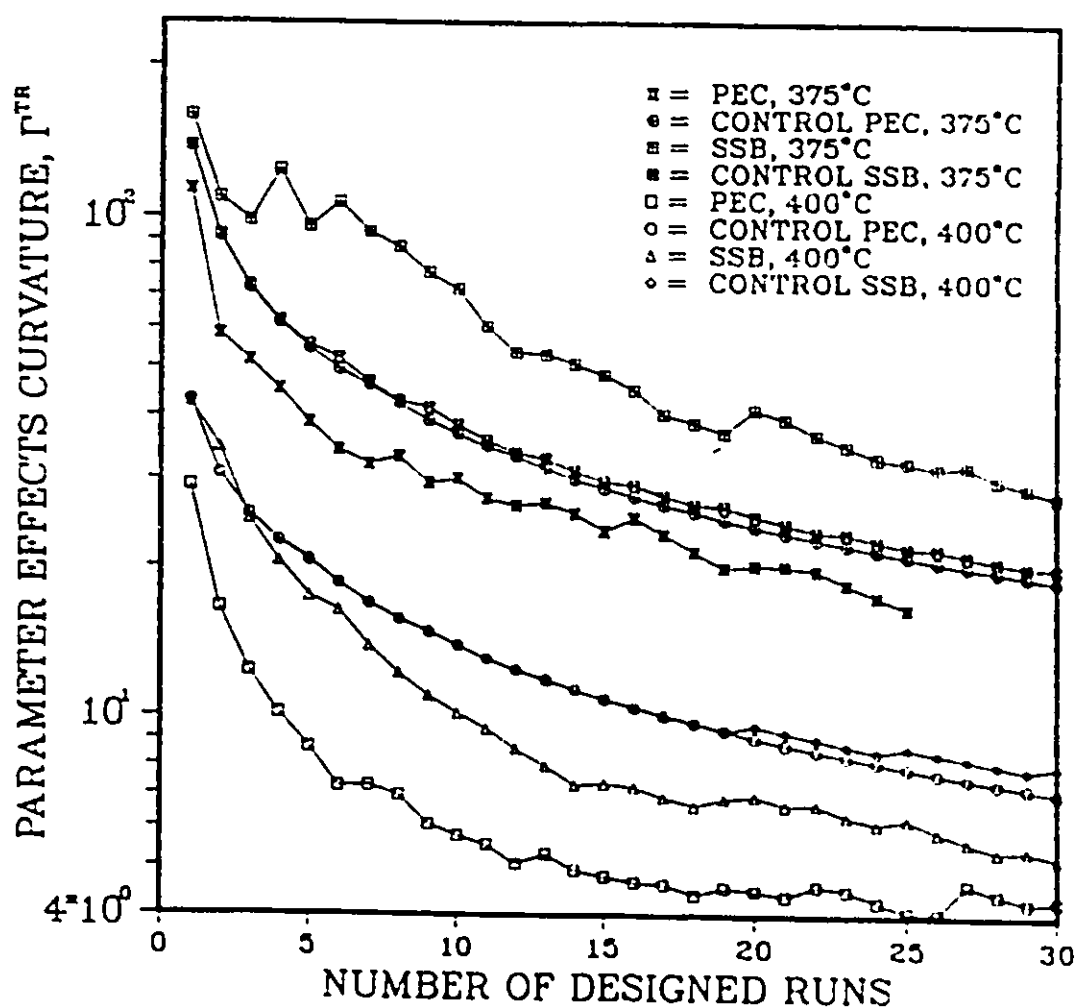


Figure 4.2: Progress of PEC and SSB designs with Ayen and Peters model data set. NO reduction to  $\text{NH}_3$ , 400°C and 375°C.

$\Gamma^{TR}$  for the original data: 427 and 128 at 400°C and 375°C respectively

of 8, 12 and 12 observations at 425°C, 400°C and 375°C respectively.

Similar simulations were performed with the other model/data sets of Jaswal, Juusola and Tan at all temperature levels. With these model/data sets only one PEC-S simulation was performed at each temperature level. SSB-S designs were not performed, only SSB-C to allow comparison to the PEC-C design.

Progress of simulations performed with the Juusola model/data sets are shown in Figure 4.3. All three designs, PEC-C, PEC-S and SSB-C reduced  $\Gamma^{TR}$  to an acceptable level with the data obtained at 270°C with only one designed run. Using the bias as an indicator of the extent of nonlinearity would require that no runs be designed. The worst bias was <1% for all the original data sets, which all had significant parameter effects nonlinearity according to  $\Gamma^{TR}$  and as will be shown in Section 4.2.

The three designs were very similar in their effectiveness at reducing  $\Gamma^{TR}$ . The differences in the four PEC-S designs with the Ayen and Peters data set at 425°C were attributed to changing parameter and variance estimates. With the Juusola model/data sets these estimates were much more stable. This resulted in the PEC-C and PEC-S designs having more similar performance. The SSB-C design performed nearly as well as the PEC-C design at all three temperatures. This was the result of the two criteria leading to similar designed run locations, and will be discussed in detail in Section 4.4.

At 290°C and 300°C none of the designs reduced  $\Gamma^{TR}$  to an acceptable level with 10 designed runs, although it was reduced to approximately half its initial value in both cases. At 290°C all three designs were similarly effective with similar designed run locations.

The inability of the PEC design to reduce  $\Gamma^{TR}$  to an acceptable level was surprising, considering the low initial parameter effects curvature. This may be the result of several factors; the sample size was relatively large at 290°C and 300°C, the original data set contained designed experiments and/or the operating region was constrained. Sample sizes for Juusola's work were 11, 23 and 22 observations at 270°C, 290°C and 300°C respectively. The extent of nonlinearity is known to decrease asymptotically as the sample size increases, as the sample size increases the potential for reductions of nonlinearity also decrease. Juusola also made use of the D-optimal design criterion to improve parameter precision. As will be demonstrated

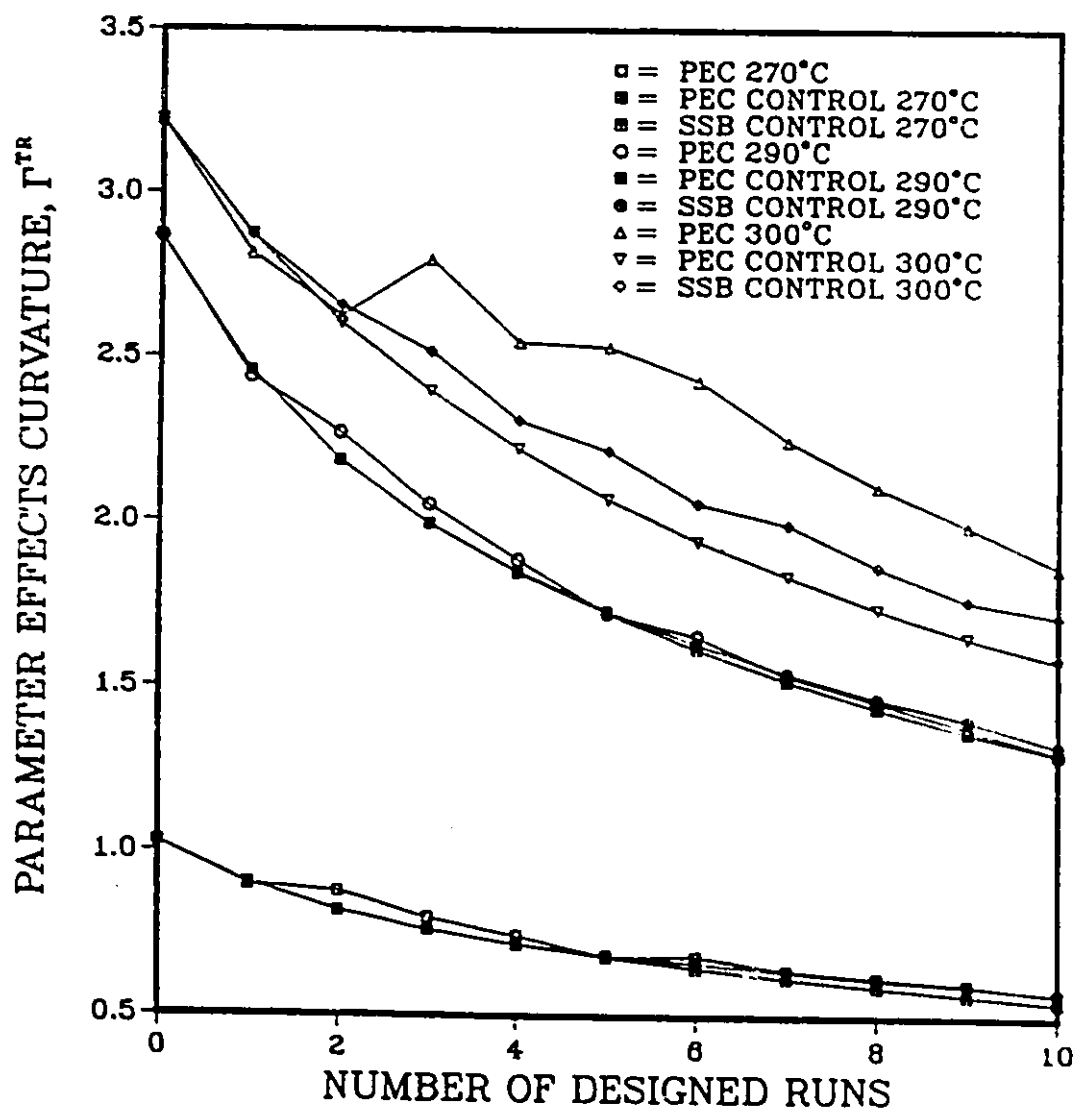


Figure 4.3: Progress of PEC and SSB designs with Juusola model/data set, oxidation of o-xylene.

in Section 4.3, the D-optimal design is also extremely effective in reducing the extent of nonlinearity. With the larger sample sizes and D-optimal designed experiments one would expect there to be less potential for large reductions of  $\Gamma^{TR}$  with the initial experiments. The operating region used by Juusola was also constrained. Section 4.4 shows that this restriction greatly hindered the potential effectiveness of the PEC design. Nonetheless, the PEC and SSB designs significantly reduced the extent of nonlinearity as measured by  $\Gamma^{TR}$  with two of the three data sets.

Simulations with the Jaswal model/data sets reduced  $\Gamma^{TR}$  to an acceptable level at all three temperatures, as shown in Figure 4.4. Again the three designs were similar in their ability to reduce  $\Gamma^{TR}$ . At all three temperatures, parameter estimates were stable for the PEC-S design. The PEC-S and SSB-C designs both required 5, 2 and 5 runs to make  $\Gamma^{TR} \leq 1$  at 350°C, 375°C and 400°C respectively. As with the previous model/data sets the bias underestimated the extent of nonlinearity, or the suggested cutoff is too lax. The worst bias was <1% after 2, 0 and 2 designed runs respectively, at which point  $\Gamma^{TR}$  was 1.47, 1.18 and 1.48.

The effectiveness of the three designs with the Tan model/data set is shown in Figure 4.5. The initial parameter effects curvature for the 390°C data set was acceptable. The data set was still used to test the two design criteria and to allow later comparison with the D-optimal design. At all three temperature levels, parameter estimates were stable, resulting in nearly identical progress for the control and stochastic simulations. In the two cases where  $\Gamma^{TR}$  was significant, both the PEC and SSB designs successfully reduced  $\Gamma^{TR}$  to an acceptable level. The worst bias at each temperature was <1% for the initial data, suggesting, again, that the bias underestimates the extent of nonlinearity.

In many of the cases studied, the SSB and PEC designs were very similar in their ability to reduce  $\Gamma^{TR}$ . As will be seen in Section 4.4 this resulted from designed run locations being common to the two design criteria. The similarity of the run locations suggests that the SSB and PEC designs are minimizing the same criteria. Bates and Watts [1] showed that Box's bias [2] was a scaled version of the diagonal elements of each "face" of the parameter effects portion of the acceleration array,  $A_{..}^T$ , used to calculate the parameter effects curvature. Examination of the parameter effects portion of the acceleration arrays of the data sets studied (see Appendix D) reveals a common characteristic. In each case the largest element in

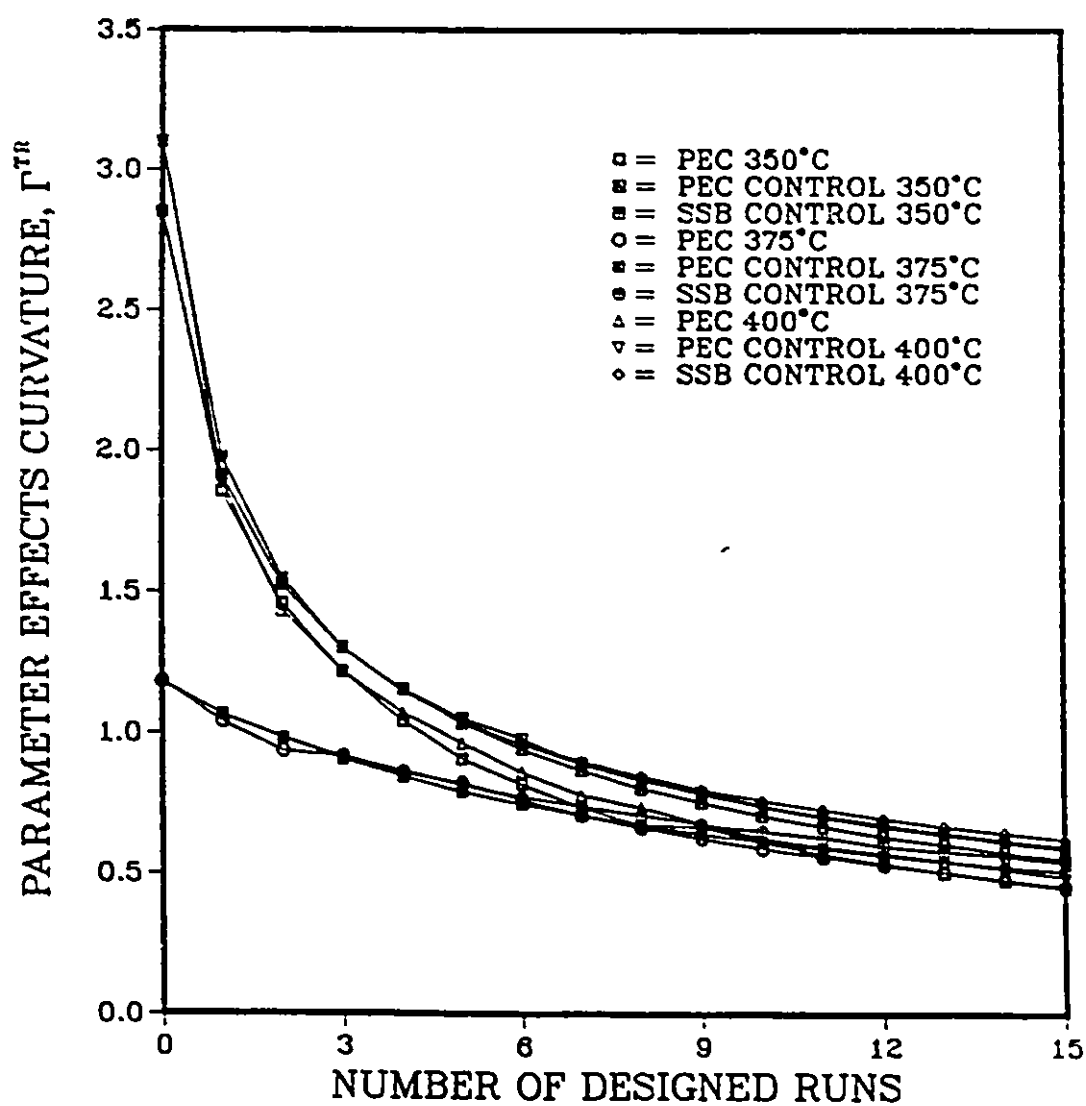


Figure 4.4: Progress of PEC and SSB designs with Jaswal model/data set, oxidation of benzene.

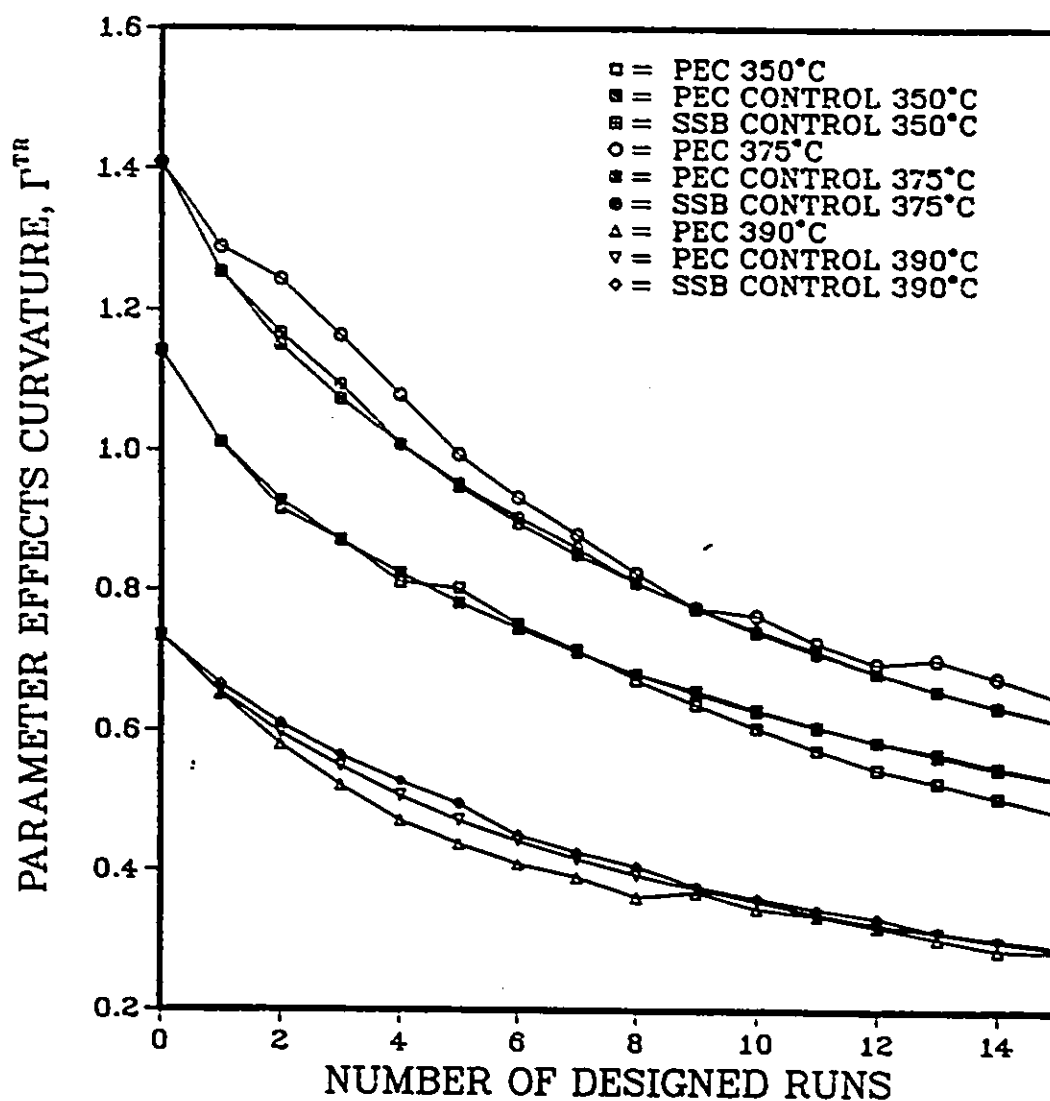


Figure 4.5: Progress of PEC and SSB designs with Tan model/data set, oxidation of propylene.

$A_{..}^T$  was a diagonal element of one of the faces. These elements of the acceleration array are used to calculate Box's bias. The off-diagonal elements are generally much smaller. Hence the similarity observed between the PEC and SSB designs would be expected in such cases. Given a model/data set for which the non-diagonal elements of  $A_{..}^T$  are of the same magnitude or larger than the diagonal elements, the SSB and PEC designs would not be expected to be similar. Examining  $A_{..}^T$  would be beneficial in the experimental design stage. If a situation similar to that observed in this work arises then the simpler SSB criterion could be used to determine the optimal run locations. When the off-diagonal elements become important, the PEC criterion should be used.

#### 4.1.1 Summary

The results of the PEC and SSB simulations are summarized in Table 4.1. In seven of eleven PEC simulations where designed experiments were required, the parameter effects curvature was reduced to an acceptable level. When  $\Gamma^{TR}$  was not reduced to an acceptable level, it was greatly reduced from its initial value. The SSB simulations also greatly reduced  $\Gamma^{TR}$  in some cases bettering the PEC design. However the SSB simulations were all control simulations while stochastic PEC simulations were used.

In cases where  $\Gamma^{TR}$  was significant Box's bias consistently predicted an acceptable degree of nonlinearity with fewer runs than required when using  $\Gamma^{TR}$  as a measure of nonlinearity. This may be due to a shortcoming of the bias measure itself, as it only measures one type of parameter effects nonlinearity, and/or an inadequate test for significance. The 1% cutoff has been suggested by Ratkowsky [3] as a rule of thumb rather than an absolute cutoff.

The SSB and PEC design criteria were both effective for reducing  $\Gamma^{TR}$ . In all cases the PEC design criterion was more effective, however the differences between the two designs were often very small. The similarities may have been due to the parameter effects portion of the acceleration array being dominated by the diagonal elements, used in calculating Box's bias. In light of this and the much greater computational effort required for the PEC design, the SSB design appears to be a suitable design criterion for reduction of the extent of nonlinearity when the intrinsic

nonlinearity is acceptable. The relative curvatures would only need to be evaluated after the optimum run location is determined and after the experiment is performed or simulated. This would allow an accurate evaluation of the predicted and obtained reduction of nonlinearity during the experimental design. However, in a case where the intrinsic nonlinearity is not acceptable the SSB design criterion would not be suitable, nor would it be expected to be suitable when the off-diagonal elements of  $A_{..}^T$  are of the same order of magnitude or larger than the diagonal elements.

Neither the PEC nor the SSB criteria can be said to have failed, failure being defined as not having reduced  $\Gamma^{TR}$  to an acceptable level. Rather the designs were terminated because reductions of  $\Gamma^{TR}$  were deemed too small to warrant continuing. It is known that replicating the experimental design  $r$  times will always reduce the curvature by  $\frac{1}{\sqrt{r}}$ . Reducing  $\Gamma^{TR}$  to acceptable levels in this manner would result in extremely large data sets. The Ayen and Peters model/data set at 425°C would require replicating the design more than 1800 times to reduce  $\Gamma^{TR}$  to 1. The PEC design required only 27 designed runs, equivalent to only 3.5 replications of the design (in terms of the number of experiments performed). The Jaswal model/data set would require 7.5 replications of the original design while the PEC and SSB designs required less than 0.5 replications. The PEC and SSB designs are undoubtedly more efficient but may still require an unduly large number of experiments. Attention should be focused on why such large numbers of experiments would be required. Expanded regions of operation may allow larger reductions of nonlinearity, although this may not be permitted from an experimental point of view, as will be seen in Section 4.4. The initial data set is also important. If any of the original data were obtained under conditions which would actually increase the nonlinearity then a larger number of experiments would be required to achieve a given reduction of nonlinearity.



Table 4.1: Summary of Results Using the PEC-S Criterion.

| Authors and System                                         | Temp<br>°C | PEC Design                  |                        | % reduction<br>of FTIR | SSB Design                  |                        | % reduction<br>of FTIR |
|------------------------------------------------------------|------------|-----------------------------|------------------------|------------------------|-----------------------------|------------------------|------------------------|
|                                                            |            | number of runs<br>performed | FTIR reduced<br>to ≤ 1 |                        | number of runs<br>performed | FTIR reduced<br>to ≤ 1 |                        |
| Ayen and Peters [18]<br>reduction of NO to NH <sub>3</sub> | 375        | 30                          | no                     | 95.6                   | 30                          | no                     | 95.1                   |
|                                                            | 400        | 30                          | no                     | 95.5                   | 30                          | no                     | 94.3                   |
|                                                            | 425        | 27                          | yes                    | 98.0                   | 30                          | no                     | 96.8                   |
| Juusola [14]<br>oxidation of o-xylene                      | 270        | 1                           | yes                    | 11.4                   | 1                           | yes                    | 10.9                   |
|                                                            | 290        | 10                          | no                     | 53.1                   | 10                          | no                     | 52.6                   |
|                                                            | 300        | 10                          | no                     | 40.7                   | 10                          | no                     | 45.3                   |
| Jaswal [29]<br>oxidation of benzene                        | 350        | 6                           | yes                    | 67.2                   | 6                           | yes                    | 70.4                   |
|                                                            | 375        | 3                           | yes                    | 15.4                   | 2                           | yes                    | 16.4                   |
|                                                            | 400        | 7                           | yes                    | 68.0                   | 6                           | yes                    | 68.6                   |
| Tan [24]<br>oxidation of propylene                         | 350        | 2                           | yes                    | 13.0                   | 2                           | yes                    | 18.1                   |
|                                                            | 375        | 6                           | yes                    | 26.8                   | 5                           | yes                    | 31.3                   |
|                                                            | 390        | none                        | —                      | —                      | none                        | —                      | —                      |

## 4.2 Evaluation of the Curvatures as Measures of Nonlinearity

The Bates and Watts [1] relative curvature measures of nonlinearity have been discussed in the literature and reviewed here in Section 3.1. Previous evaluations of the accuracy of the relative curvatures as measures of the extent of nonlinearity have involved comparisons to other measures of nonlinearity [3,7], comparisons of exact-shape and linear approximate-shape confidence intervals [19] and regions [19,28]. In this work the latter method will be used as it is perhaps the most stringent. Comparisons based on any other measures of nonlinearity do not ensure reliable evaluation of the curvatures, as the other measures may not be reliable themselves.

Consequently, confidence regions were compared for all the original isothermal data sets. This provided an initial evaluation of the accuracy of the relative curvatures. Confidence regions were also compared at the end of each sequential design, i.e. when the curvatures were reduced to an acceptable level or when reductions of  $\Gamma^{TR}$  were too small to warrant continuing the design. Confidence regions, before and after simulating experiments with the PEC-S design, are shown on the same figure to facilitate evaluating any improvements obtained with the experimental design, with respect to both reducing the extent of nonlinearity and improving parameter precision. For the sake of brevity, when a bias estimate is quoted it will be for the worst case. As previously discussed, for the linear approximation to be valid, all the model parameters should exhibit linear behavior. When the model involves three or more parameters, comparison of the confidence regions is difficult because one is comparing  $p$  dimensional volumes. In this work, pairwise confidence regions were used to compare the confidence regions. These regions were conditional on the other parameter estimates being fixed at their least squares estimates.

The model proposed by Ayen and Peters for the catalytic reduction of NO to  $\text{NH}_3$  is a three parameter model. As such, 3 confidence regions were examined when comparing conditional confidence regions. These "slices" of the confidence volume only represent the coverage at the least squares estimates and do not guarantee overall equality of coverage throughout the confidence volume. These problems have been discussed by Emig and Hosten [15]. However, the comparisons used in

this work could be expected to reveal any gross discrepancies. For convenience and space requirements only the worst case is shown here, i.e. the conditional pairwise confidence regions for which the linear approximation provided the worst coverage.

The linear approximation provided the poorest coverage for the pair of parameters  $k$  and  $K_{H_2}$ , the rate constant and the equilibrium adsorption constant of  $H_2$ . Figures 4.6 and 4.7 show the approximate-shape and exact-shape 95% confidence regions for this pair for the original data, after 10 and 27 PEC designed runs (SIM4) at which point  $\Gamma^{TR} \leq 1.0$ . The two regions clearly do not match for the original data. The exact-shape region is crescent shaped rather than being elliptical. The upper and lower limits for  $k$  are clearly asymmetrical about  $\bar{k}$ . After 10 designed runs the most apparent change is the much smaller size of the confidence region, indicating a large improvement in parameter precision. Figure 4.7 shows the confidence regions after 10 and 27 PEC designed runs on an expanded scale. The exact-shape region after 10 PEC designed runs is now nearly elliptical and the linear approximation provides very good coverage. At this point  $\Gamma^{TR} = 2.4$ , suggesting that the linear approximation should not be acceptable. However, while the regions do not match exactly, they would certainly be deemed acceptable. At this stage of the design the confidence regions for the other conditional pairwise confidence regions were virtually identical in shape and their sizes were greatly decreased. After 27 designed runs the match between the confidence regions for all pairs of parameters improved very little, but further significant reductions in the size of the regions were achieved.

At 400°C the worst approximation was, again, for the parameter pair  $k$  and  $K_{H_2}$ . As seen in Figure 4.8 the crescent shape with an elongated tip reflects the very high parameter effects curvature,  $\Gamma^{TR} = 427$ . The regions for the other stages of the design are not shown on the same figure as they are much smaller would be indistinguishable. Figure 4.9 shows the confidence regions after 25 PEC designed runs. At this point  $\Gamma^{TR} = 16.6$  and the design was stopped because reductions of  $\Gamma^{TR}$  were too small. The reduction of  $\Gamma^{TR}$  from 427 to 16.6 is clearly reflected by the change of the exact region's shape (i.e. becoming elliptical). The curvature correctly indicates that the linear approximation is not acceptable, even though the conditional confidence regions for the other parameter pairs match very well. The worst bias was acceptable after only 15 PEC designed runs at which point  $\Gamma^{TR} > 24$ , clearly underestimating the degree of nonlinearity.

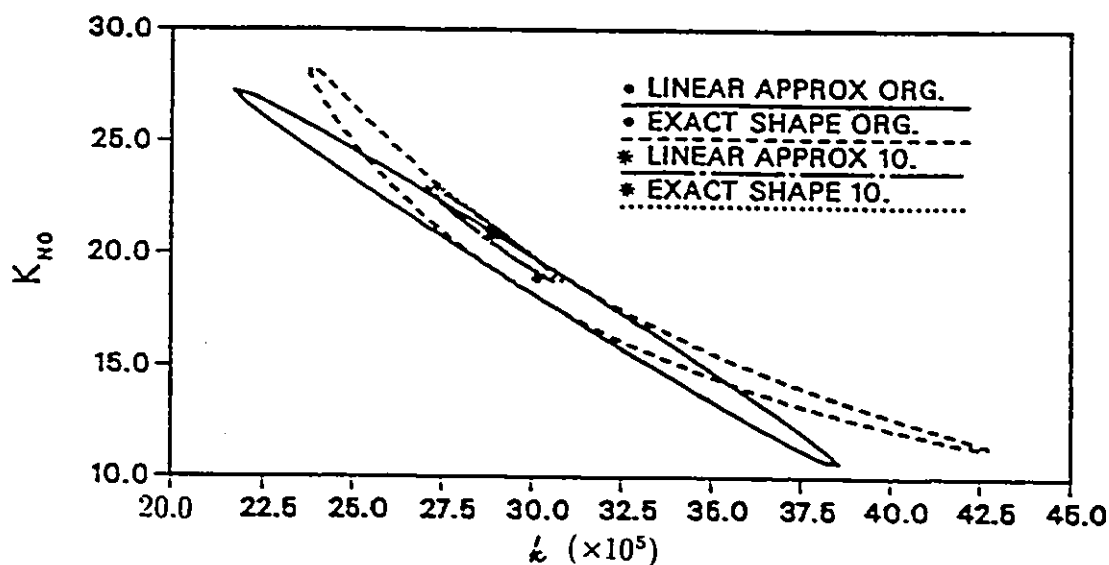


Figure 4.6: Conditional 95% confidence regions for Ayen and Peters, NO reduction to  $\text{NH}_3$ ,  $425^\circ\text{C}$ .

|               | Original Data | After 10 PEC Designed Runs |
|---------------|---------------|----------------------------|
| $\Gamma^{NR}$ | 0.23          | 0.051                      |
| $\Gamma^{TR}$ | 60.7          | 2.38                       |

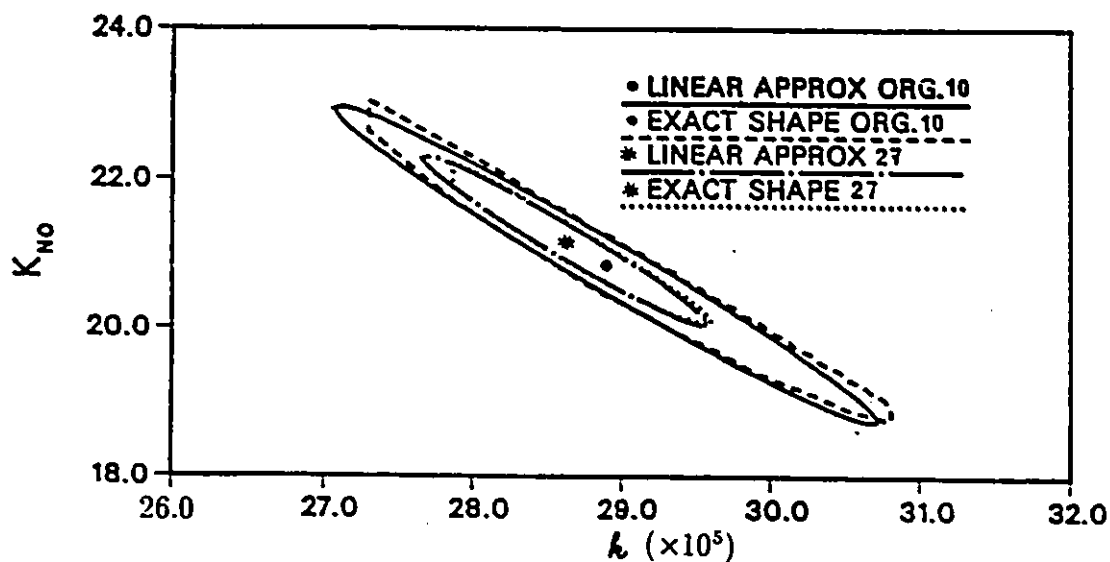


Figure 4.7: Conditional 95% confidence regions for Ayen and Peters, NO reduction to  $\text{NH}_3$ ,  $425^\circ\text{C}$ .

|               | After 10 PEC Designed Runs | After 27 PEC Designed Runs |
|---------------|----------------------------|----------------------------|
| $\Gamma^{NR}$ | 0.051                      | 0.029                      |
| $\Gamma^{TR}$ | 2.38                       | 0.96                       |

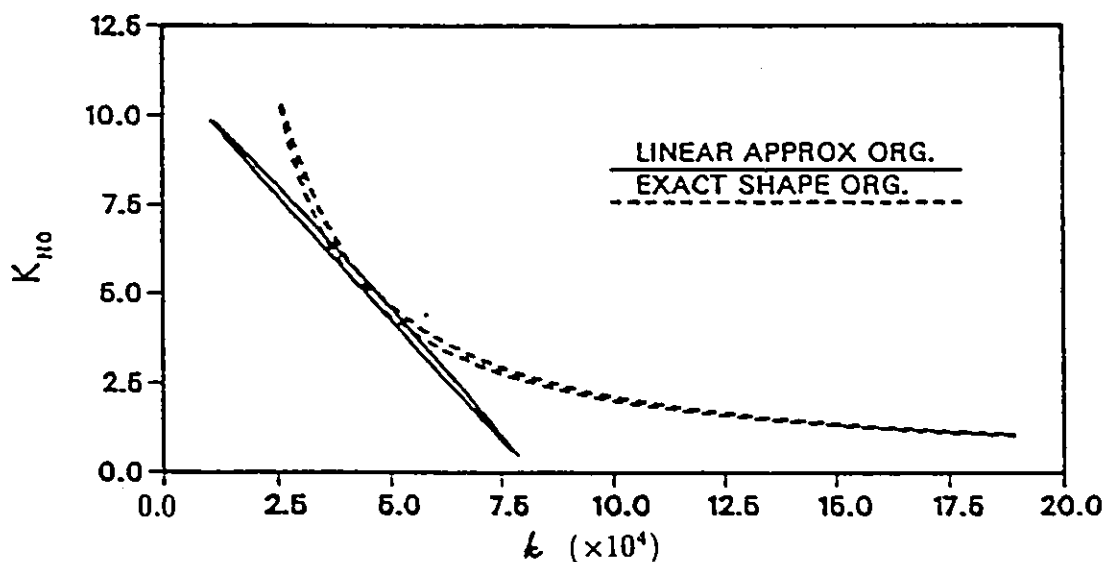


Figure 4.8: Conditional 95% confidence regions for Ayen and Peters, NO reduction to  $\text{NH}_3$ ,  $400^\circ\text{C}$ .

|               |               |
|---------------|---------------|
|               | Original Data |
| $\Gamma^{NR}$ | 0.23          |
| $\Gamma^{TR}$ | 426.8         |

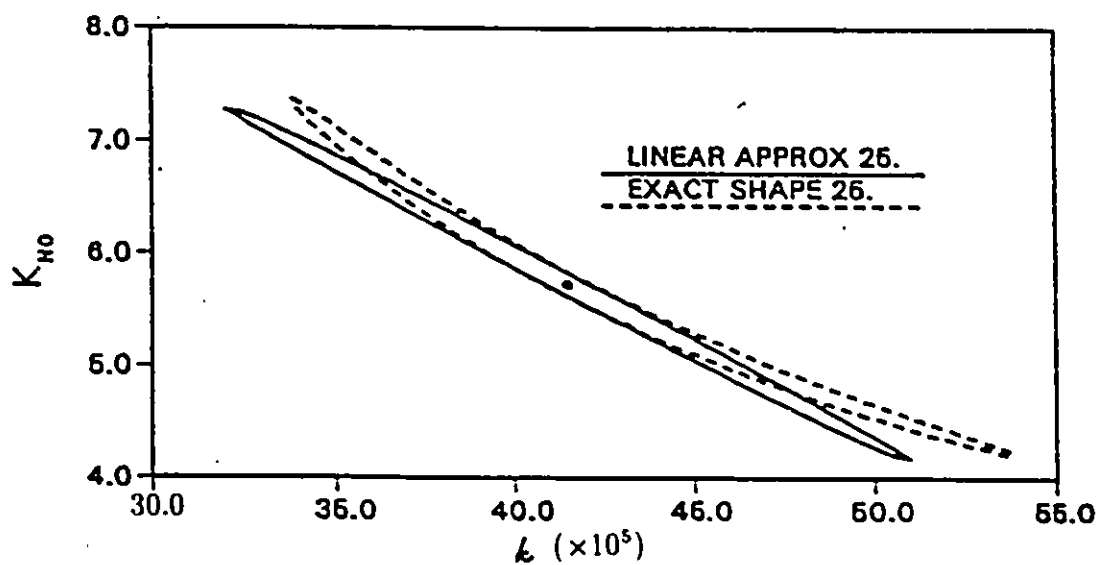


Figure 4.9: Conditional 95% confidence regions for Ayen and Peters, NO reduction to  $\text{NH}_3$ ,  $400^\circ\text{C}$ .

|               |                            |
|---------------|----------------------------|
|               | After 25 PEC Designed Runs |
| $\Gamma^{NR}$ | 0.060                      |
| $\Gamma^{TR}$ | 16.6                       |

Results obtained with the 375°C data set were similar to those at 400°C. The parameter effects curvature correctly predicted a very poor linear approximation for the original data. The measure of nonlinearity also correctly predicted a much improved but still unacceptable linear approximation after 25 PEC designed runs.

All the remaining model/data sets, Jaswal, Juusola and Tan, are two parameter models. As such, a single confidence region completely describes parameter precision. Figure 4.10 shows the confidence region for the Jaswal model with the data set obtained at 400°C. The parameter effects curvature,  $\Gamma^{TR} = 3.24$ , clearly reflects the significant degree of nonlinearity indicated by the poor coverage of the linear approximate-shape confidence region. After 7 PEC designed runs  $\Gamma^{TR} \leq 1.0$ , the linear approximation provides very good coverage and both regions are much smaller. At 375°C, Figure 4.11,  $\Gamma^{TR} = 1.18$  for the original data. The exact shape region is slightly bowed, but still well covered by the linear approximation, agreeing with the low parameter effects curvature. Only two PEC designed runs were required to reduce  $\Gamma^{TR}$  below 1. Parameter precision improved slightly, as did the linear approximation. However, these improvements were minor.

At this stage a question must be asked regarding the meaning of "an acceptable degree of nonlinearity". If the degree of nonlinearity is acceptable, then what coverage of the exact region is the linear confidence region expected to give? Perfect coverage would be expected if the degree of nonlinearity is zero, or with both curvatures,  $\Gamma^T = 0$  and  $\Gamma^N = 0$ . As such, any degree of nonlinearity would be expected to result in coverage  $< 100\%$ . This being the case, with both curvatures having a nonzero value, as in the last example, some discrepancy should be expected. In the example for Ayen and Peters at 425°C, a virtually perfect match between the linear and exact-shape regions was obtained. This certainly influenced the results expected with the Jaswal example (making the curvatures appear to underestimate the degree of nonlinearity) when the curvatures were reduced to an acceptable level. In light of this, perfect coverage by the linear approximation should not have been expected with the Jaswal data set at 375°C, nor should any great improvement be expected after reducing  $\Gamma^{TR}$  by only 0.18. Rather, the test statistic may be interpreted as being overly strict, requiring that both  $\Gamma^{TR}$  and  $\Gamma^{NR} < 1$  when in fact higher values may be acceptable. This agrees with conclusions drawn by Donaldson and Schnabel [19].

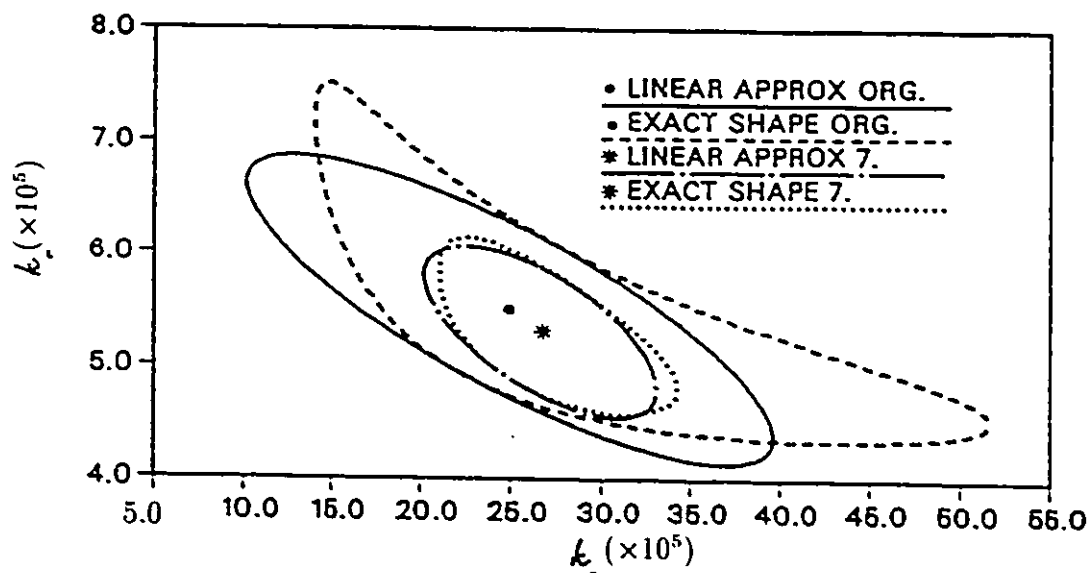


Figure 4.10: 95% Confidence regions for Jaswal, oxidation of benzene at 400°C.

|               | Original Data | After 7 PEC Designed Runs |
|---------------|---------------|---------------------------|
| $\Gamma^{NR}$ | 0.43          | 0.14                      |
| $\Gamma^{TR}$ | 3.24          | 1.00                      |

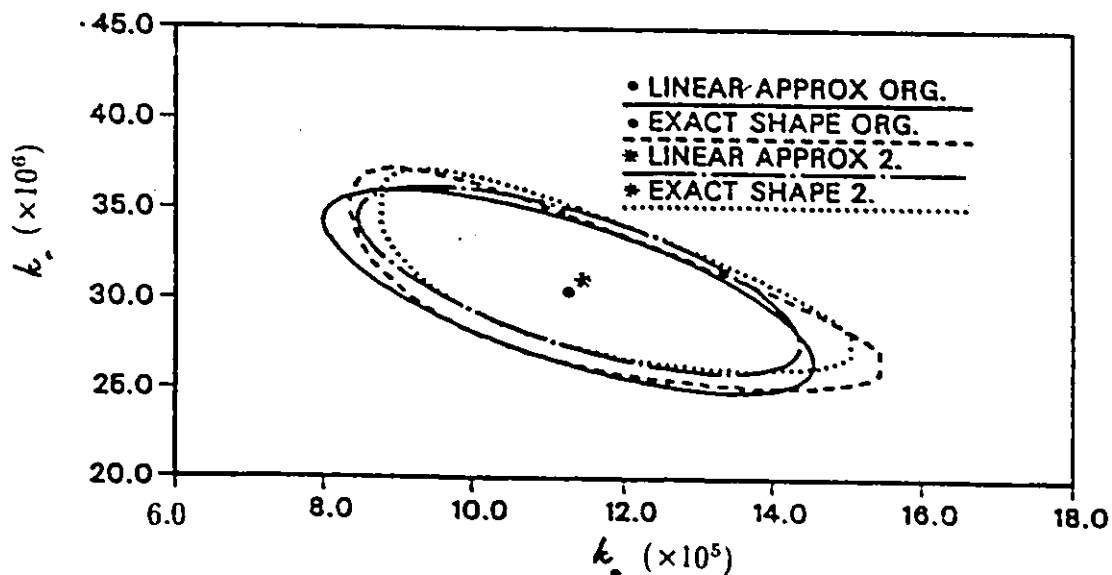


Figure 4.11: 95% Confidence regions for Jaswal, oxidation of benzene at 375°C.

|               | Original Data | After 2 PEC Designed Runs |
|---------------|---------------|---------------------------|
| $\Gamma^{NR}$ | 0.23          | 0.19                      |
| $\Gamma^{TR}$ | 1.18          | 1.00                      |

Results obtained at 350°C were similar to those obtained with the 400°C data set. The parameter effects curvature for the original data,  $\Gamma^{TR} = 2.88$ , predicted significant nonlinearity. This was supported by the poor coverage of the linear approximation. After 6 PEC designed runs,  $\Gamma^{TR} < 1$  and the linear approximation closely matched the exact-shape; parameter precision also improved.

With the Juusola model/data set the PEC design criterion did not reduce the parameter effects curvature to an acceptable level after 10 designed runs at 300°C and 290°C. At this point simulations were stopped as reductions of  $\Gamma^{TR}$  were minimal. At 300°C,  $\Gamma^{TR} = 3.23$  for the original data set and correctly predicted the poor coverage of the linear approximation shown in Figure 4.12. After 10 PEC designed runs  $\Gamma^{TR} = 1.56$ , the linear approximation provided improved coverage and parameter precision improved. Similar results were obtained at 290°C, when  $\Gamma^{TR}$  was reduced from 2.3 to 1.31. At 270°C only one PEC designed run was required. Figure 4.13 shows the confidence regions for the initial data and after 10 PEC designed runs (the extra runs were designed to allow comparison to D-optimal designs). Once again the PEC design improved parameter precision and the linear approximation.

The original model/data set obtained at 390°C by Tan had acceptable intrinsic and parameter effects curvatures. The linear approximation is very good, as seen in Figure 4.14 and predicted by  $\Gamma^{TR} = 0.74$ . At 375°C,  $\Gamma^{TR}$  was reduced from 1.41 to 0.96 after 4 PEC designed runs. The confidence regions match well for the original data set, Figure 4.15. Any nonlinearity effects appear to be minimal, as would be expected from the low parameter effects curvature. After 4 designed runs the regions have shrunk and improvement of the linear approximate confidence region's coverage was minimal. At 350°C only one PEC designed run was required. The linear approximation was very good (not shown), as was suggested by the low parameter effects curvature. As expected, improvements in parameter precision and coverage were minimal.

In evaluating the accuracy of the relative curvatures as measures of nonlinearity some discrepancies appeared as  $\Gamma^{TR}$  approached 1. The linear approximation provided extremely good coverage of the exact-shape confidence regions with the Ayen and Peters data set at 425°C when  $\Gamma^{TR}$  was still 2.54. But, the same degree of coverage was not obtained with the Jaswal data set at 375°C when  $\Gamma^{TR}$  was reduced



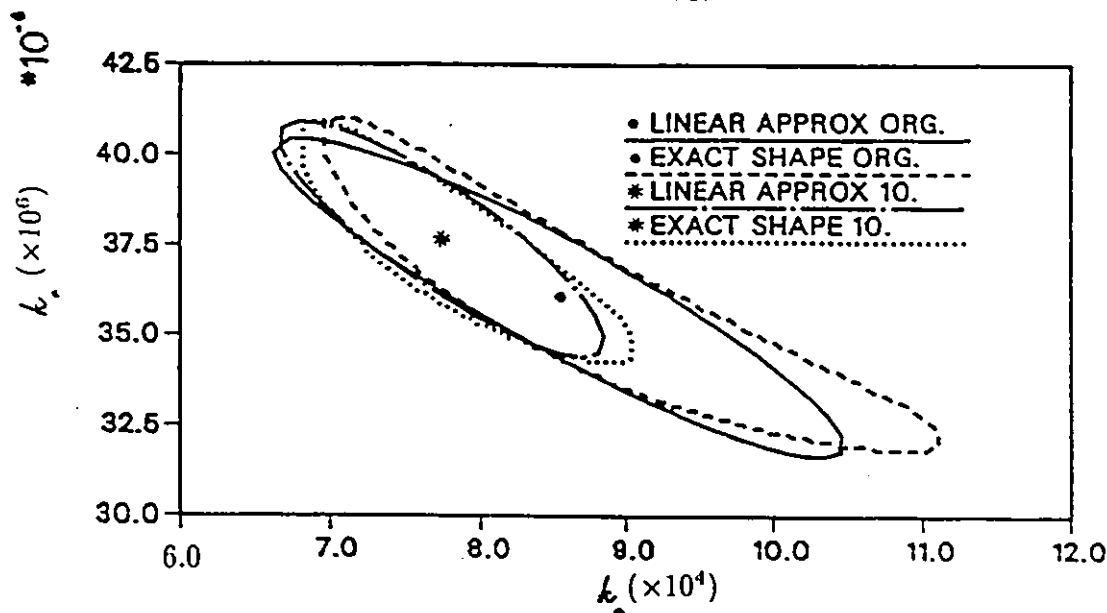


Figure 4.12: 95% Confidence regions for Juusola, oxidation of o-xylene at 300°C.

|               | Original Data | After 10 PEC Designed Runs |
|---------------|---------------|----------------------------|
| $\Gamma^{NR}$ | 0.13          | 0.089                      |
| $\Gamma^{TR}$ | 3.23          | 1.56                       |

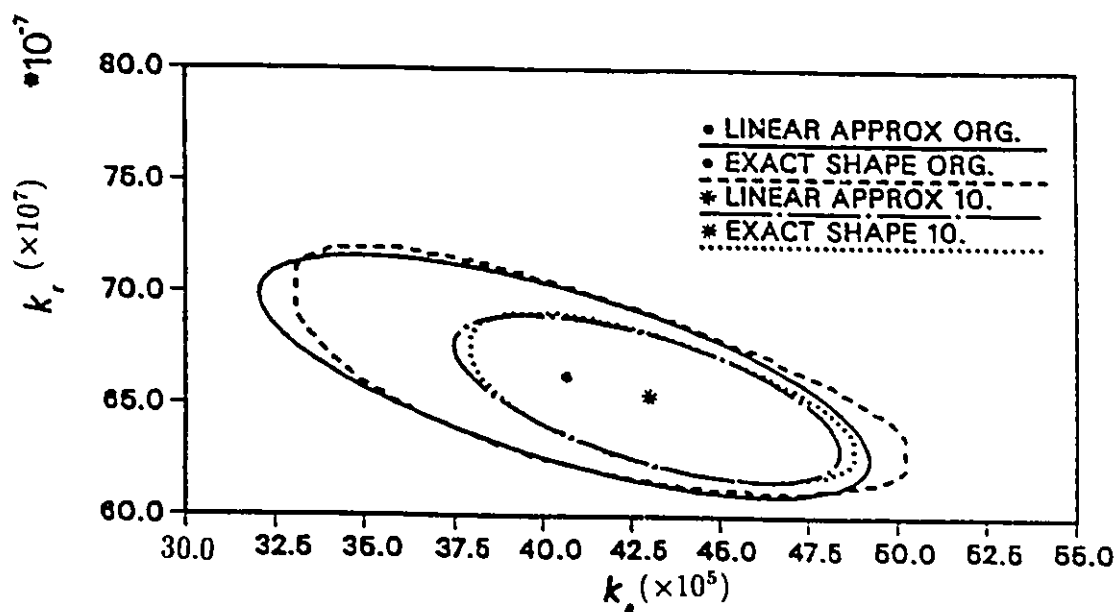


Figure 4.13: 95% Confidence Regions for Juusola, oxidation of o-xylene at 270°C.

|               | Original Data | After 10 PEC Designed Runs |
|---------------|---------------|----------------------------|
| $\Gamma^{NR}$ | 0.017         | 0.030                      |
| $\Gamma^{TR}$ | 1.05          | 0.57                       |

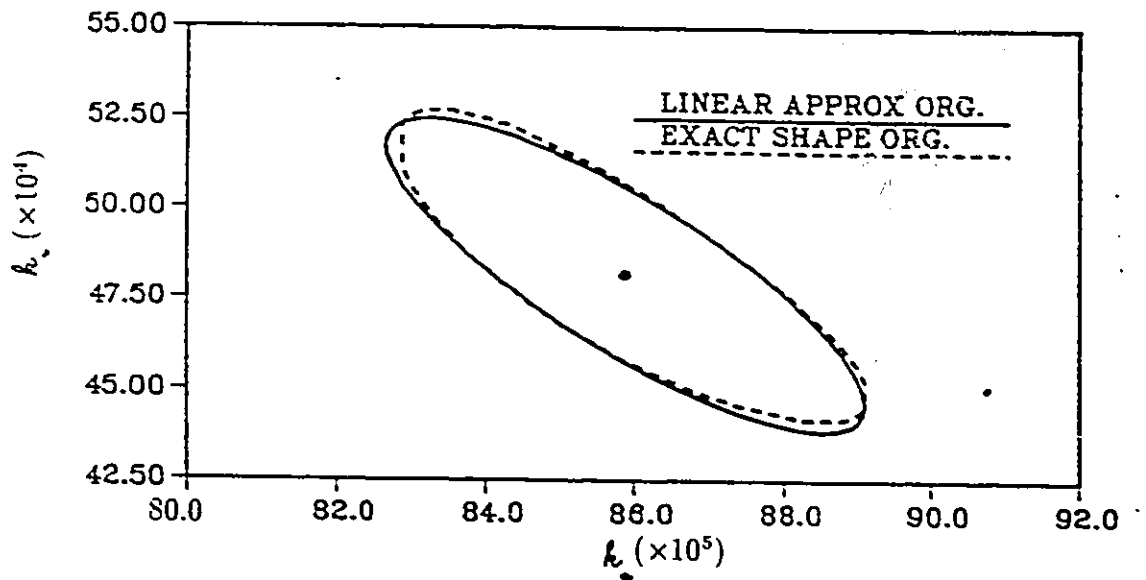


Figure 4.14: 95% Confidence regions for Tan, oxidation of propylene at 390°C.

|               | Original Data |
|---------------|---------------|
| $\Gamma^{NR}$ | 0.077         |
| $\Gamma^{TR}$ | 0.74          |

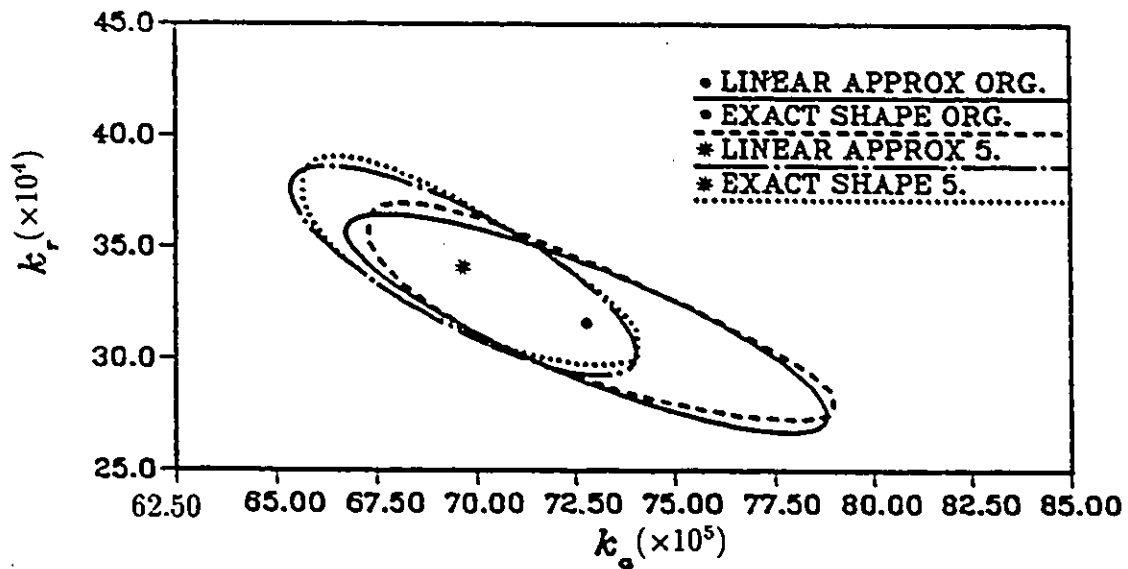


Figure 4.15: 95% Confidence regions for Tan, oxidation of propylene at 375°C.

|               | Original Data | After 5 PEC Designed Runs |
|---------------|---------------|---------------------------|
| $\Gamma^{NR}$ | 0.12          | 0.11                      |
| $\Gamma^{TR}$ | 1.41          | 0.96                      |

to an acceptable level. However, according to the previous discussion, near perfect coverage should not be expected when  $\Gamma^{NR}$  or  $\Gamma^{TR}$  are acceptable, but only when both curvatures approach zero. Differences in coverage observed for data sets with acceptable parameter effects curvature may also be accounted for by different levels of intrinsic nonlinearity, as measured by  $\Gamma^{NR}$ . The Ayen and Peters example had the best coverage with  $\Gamma^{TR} = 1$ , but it also had the lowest  $\Gamma^{NR}$  (0.03). With the Jaswal data sets at 400°C and 375°C with  $\Gamma^{TR} < 1$ ,  $\Gamma^{NR}$  was higher, 0.14 and 0.19 respectively. Hence the poorer coverage observed with the Jaswal data sets.

Small differences of  $\Gamma^{NR}$  may or may not have accounted for the differences in coverage. Such small reductions of  $\Gamma^{TR}$  produced little or no improvement in coverage for the linear approximation. However it is not known if equal differences in intrinsic and parameter-effects curvatures indicate equal differences in nonlinearity as indicated by the coverage. Given that both curvature ratios are equal, would decreasing  $\Gamma^{TR}$  by 0.5 improve the coverage of the linear approximation by more or less than an equal reduction of  $\Gamma^{NR}$ ?

#### 4.2.1 Summary

The relative curvatures of Bates and Watts have been shown to accurately reflect the extent of nonlinearity, based on comparisons of linear approximate and exact shape confidence regions. The parameter effects curvature correctly indicated when the degree of nonlinearity was acceptable for the original data for all the model/data sets studied. After application of the PEC design,  $\Gamma^{TR}$  also reflected the reduction of the extent of nonlinearity, this being confirmed by the improved coverage provided by the linear approximate confidence regions.

Differences in the coverage provided by the linear approximation as  $\Gamma^{TR}$  approached 1 may be accounted for by the intrinsic nonlinearity of the model/data set. When the linear approximate confidence region provided near perfect coverage of the exact shape confidence region,  $\Gamma^{NR}$  was extremely low. Coverage by the linear approximation worsened as  $\Gamma^{NR}$  increased and  $\Gamma^{TR} = 1$ .

In several cases the linear approximation appeared to be acceptable while  $\Gamma^{TR}$  was still significant. This was interpreted as the test statistic possibly being overly strict, requiring lower levels of curvatures than might be considered acceptable.

This agrees with the work of Donaldson and Schnabel [19] who found that the linear approximation provided between 83% and 92% for values of  $\Gamma^{TR}$  between 10 and 1 ( $\Gamma^{NR} < 1$  in all cases).

Box's measures of bias did not accurately reflect the extent of nonlinearity. The biases of all model parameters were consistently  $< 1\%$  (the suggested cutoff) while  $\Gamma^{TR}$  was still significant and the coverage of the linear approximation was poor. Whether this is due to the inaccuracy of the measure, the cutoff or both is not clear.

### 4.3 D-Optimal Designed Runs

D-optimal designs have been used extensively to improve parameter precision. Two of the four authors whose work was used in this study used D-optimal designs. One of the two, Tan, used a joint design criterion to first discriminate between two candidate models and then improve parameter precision for the most probable model. One of the desired features of a design criterion for reducing the extent of nonlinearity was compatibility with other modelling objectives. One such "other" objective of major concern is precise parameter estimation. The improvements in parameter precision noted throughout the PEC simulations, in Section 4.2, suggested that the two designs might be compatible.

Comparisons of the two designs were made with respect to each criterion's ability to reduce the parameter-effects curvature and improve parameter precision. The curvatures presented are the ratio of the curvature to the test statistic,  $\Gamma^{TR}$ . This ratio was scaled to eliminate the effect of the different variances obtained with different simulations using the variance estimate for the original data set as

$$\Gamma_S^{TR} = \Gamma^{TR} \frac{\hat{\sigma}_0}{\hat{\sigma}_i} \quad (4.2)$$

where  $\hat{\sigma}_0$  and  $\hat{\sigma}_i$  are the standard deviation of the response for the original data and after the  $i^{th}$  simulated experiment respectively. This measure was called the scaled parameter effects curvature,  $\Gamma_S^{TR}$ . The control simulations for all the design criteria are also presented. Parameter precision is presented as a fraction of the volume of the confidence region for the  $n^{th}$  experiment relative to that of the original data. The determinant of  $(X^T X)^{-1} \hat{\sigma}^2$  itself was not used, again to avoid the effect of

different variances. In the case of volume measurements,  $\hat{\sigma}^2$  has a much greater effect than with the curvatures. The volume is proportional to  $(\hat{\sigma}^2)^p$ , while the curvatures are only proportional to  $\hat{\sigma}$ .

The D-optimal, PEC and SSB criteria were first compared for the Ayen and Peters model/data set. Figure 4.16 shows the variance independent volume of the confidence region (as a fraction of the original volume) as a function of the number of designed runs for the D-optimal-S and PEC-S (SIM4) designs as well as the control PEC, SSB and D-optimal designs. As expected, the D-optimal design was the most efficient. The two PEC designs were similar but not as efficient as the SSB-C design. The D-optimal designs resulted in steady improvements of parameter precision as evidenced by the "smooth" line representing the design's performance. The SSB and PEC designs, however, resulted in two stages of improving parameter precision. In one stage the volume decreased at a given rate for 4 to 5 runs and in the next stage improved at a much higher rate for one run. As shall be seen in Section 4.4, the different rates of improving parameter precision depend on the designed run location. While the parameter precision continued to improve, it was not improving as quickly as with the D-optimal design. This suggests that the two design objectives, minimum nonlinearity and parameter precision, may not always be compatible.

The efficiency of all the designs diminished as the number of designed runs increased (note that because of the large improvements of parameter precision, the volume is plotted on a logarithmic scale and reductions of the volume are expressed as orders of magnitude). With the first D-OPT-C designed run, the volume was reduced by 1.12 orders of magnitude, then by 2.8 and 3.8 orders of magnitude after 10 and 30 designed runs respectively. The SSB-C design was almost as effective as the D-optimal design, reducing the volume by 3.6 orders of magnitude after 30 designed runs while a reduction of 3.3 was obtained with the PEC-C design.

The efficiency of the designs with respect to reducing the extent of nonlinearity is compared in Figure 4.17. As expected, the D-optimal design was not as efficient as the PEC or the SSB designs. The reductions of  $\Gamma_S^{TR}$  were generally smooth for the PEC and SSB designs but reductions obtained with the D-optimal design exhibited a stepped behavior. The pattern exhibited by the D-optimal designs was a reduction of  $\Gamma_S^{TR}$  followed by one or two designed runs in which  $\Gamma_S^{TR}$  increased a

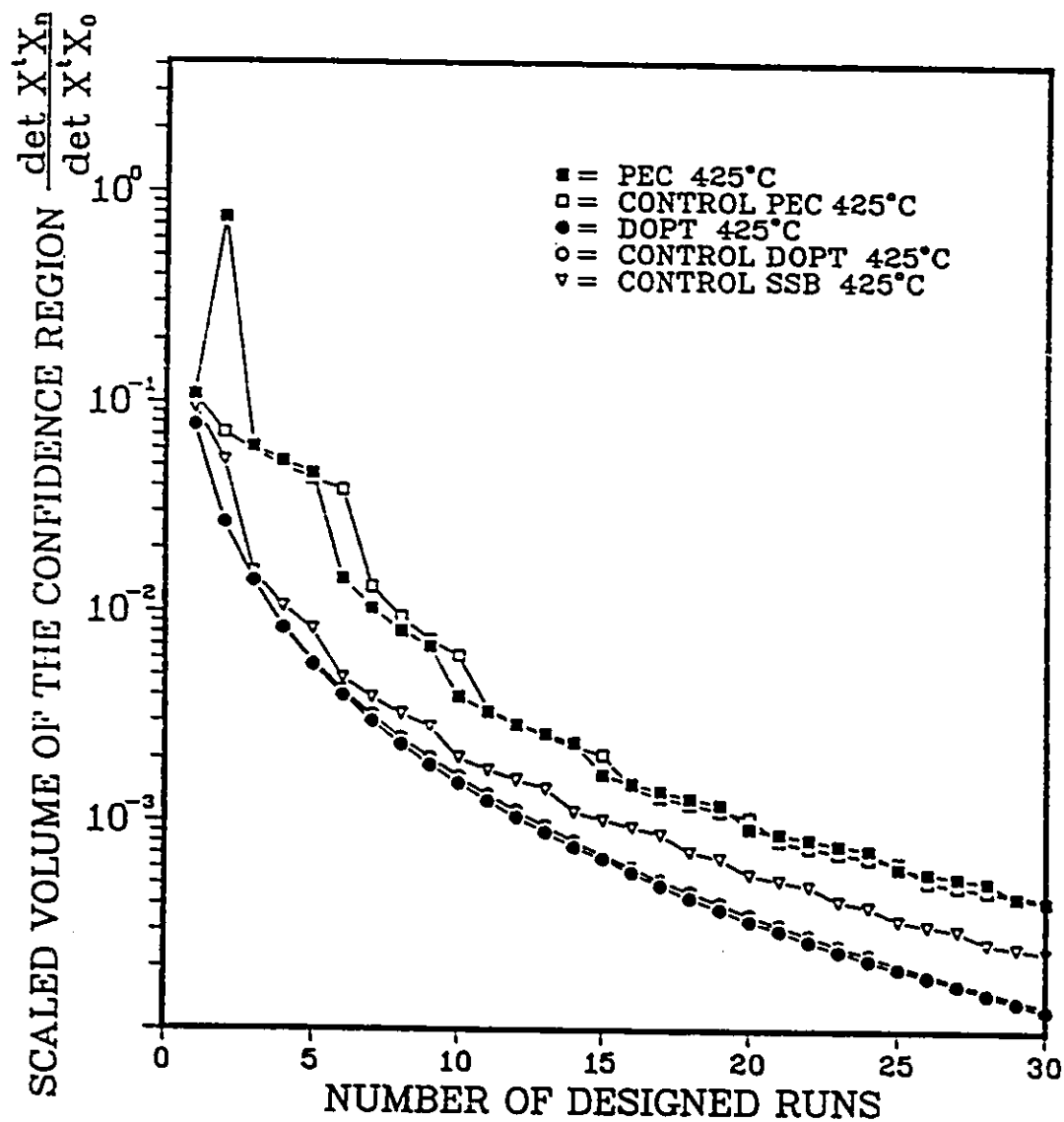


Figure 4.16: Improvements in parameter precision with the Ayen and Peters model/data set, reduction of NO to  $\text{NH}_3$ , 425°C.

The improvement of parameter precision obtained with various experimental designs is shown as a function of the number of designed runs. Parameter precision is presented as the variance independent volume of the confidence region for the  $n^{\text{th}}$  designed run as a fraction of the initial volume.

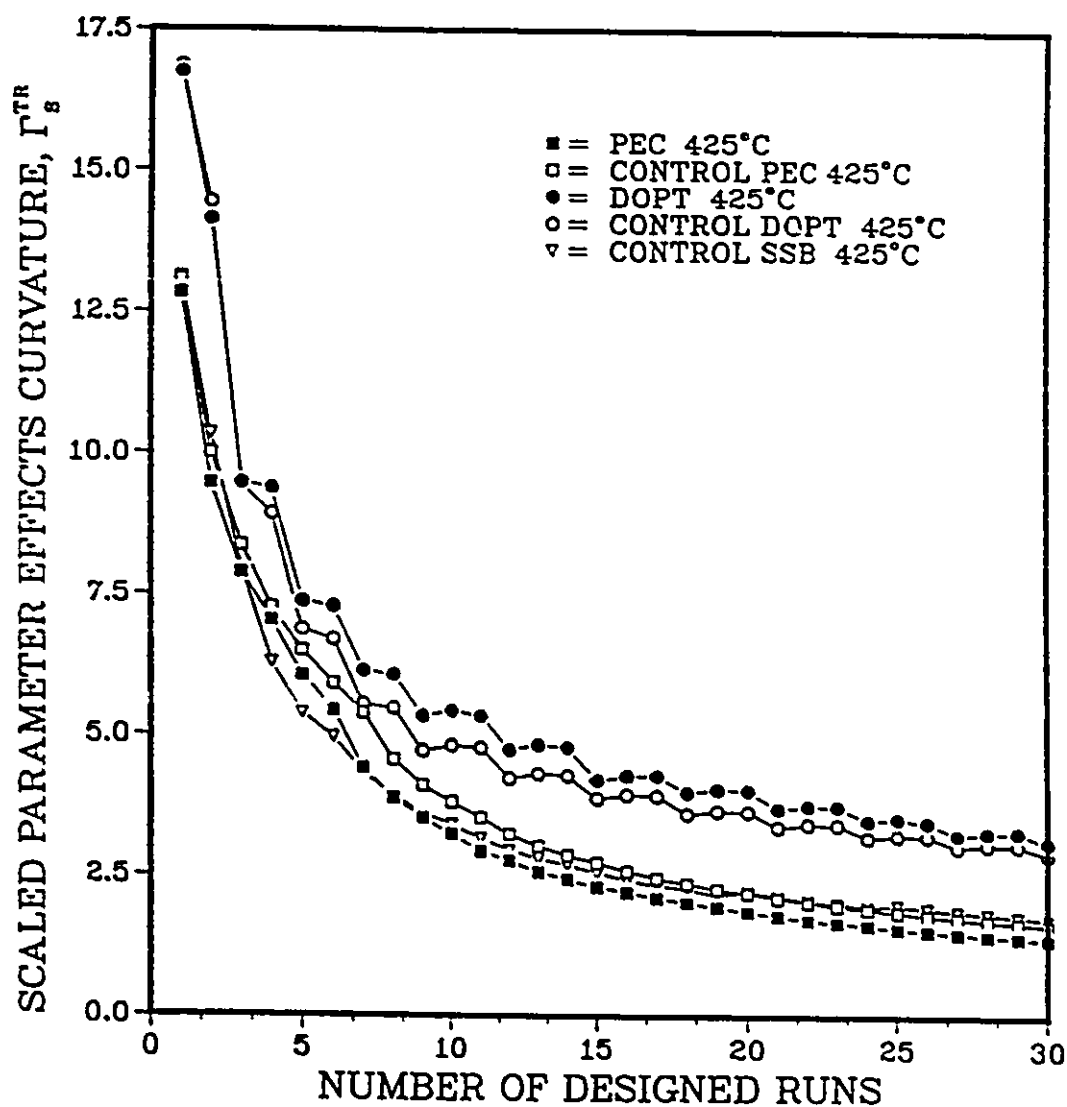


Figure 4.17: Reductions of  $\Gamma_s^{TR}$  with the Ayen and Peters model/data set, reduction of NO to  $\text{NH}_3$ , 425°C.

The reduction of the scaled parameter effects curvature obtained with various experimental designs is shown as a function of the number of designed runs. In order to avoid the effect of changing parameter estimates the control simulations have constant parameter and variance estimates

relatively small amount. As with comparisons regarding improving parameter precision with the PEC and SSB designs, this behavior was the result of the location of designed runs and will be discussed in Section 4.4.

At 400°C and 375°C the D-optimal design was, again, the most efficient at improving parameter precision, followed by the SSB and PEC designs. The D-optimal design progressed regularly while both minimum nonlinearity designs resulted in irregular improvements of parameter precision. In both cases the irregularity was linked to designed run locations. Observations similar to those at 425°C were made with respect to minimizing the degree of nonlinearity.

Results obtained with the Juusola model/data set at 300°C are shown in Figures 4.18 and 4.19 for parameter precision and parameter effects curvature respectively. The expected results were obtained; the PEC designs were more effective at reducing  $\Gamma_S^{TR}$  and the D-optimal design was more effective at improving parameter precision. The D-OPT-C design's performance was matched by that of the SSB-C design at improving parameter precision. The PEC-C design did not match the D-optimal design's performance with respect to parameter precision but was very effective nonetheless. With respect to reducing the extent of nonlinearity, all three designs were effective, but the SSB-C design exhibited a stepped behavior, similar to the D-optimal design.

Results obtained with the 290°C and 270°C data sets were similar to those at 300°C. The SSB-C design was similar to the PEC-C design with respect to reducing  $\Gamma_S^{TR}$ , the two designs were indistinguishable for the first four designed runs. The D-optimal designs at 290°C were the same as the PEC and SSB designs for the first 3 runs. Subsequent runs alternated between reductions and increases of  $\Gamma_S^{TR}$ , although the overall result was a reduction of  $\Gamma_S^{TR}$ . This was also observed at 270°C. The control and stochastic PEC and D-optimal designs were also nearly identical. This was expected as the parameter estimates were stable for these simulations, unlike simulations with the Ayen and Peters model/data set.

The improvements in parameter precision and reductions of  $\Gamma_S^{TR}$  obtained with the Jaswal model/data set at 350°C are shown in Figures 4.20 and 4.21 respectively. The performance of the PEC designs and SSB-C design were virtually the same with respect to improving parameter precision and reducing the extent of nonlinearity at all three temperatures. At all three temperatures the D-optimal designs exhibited



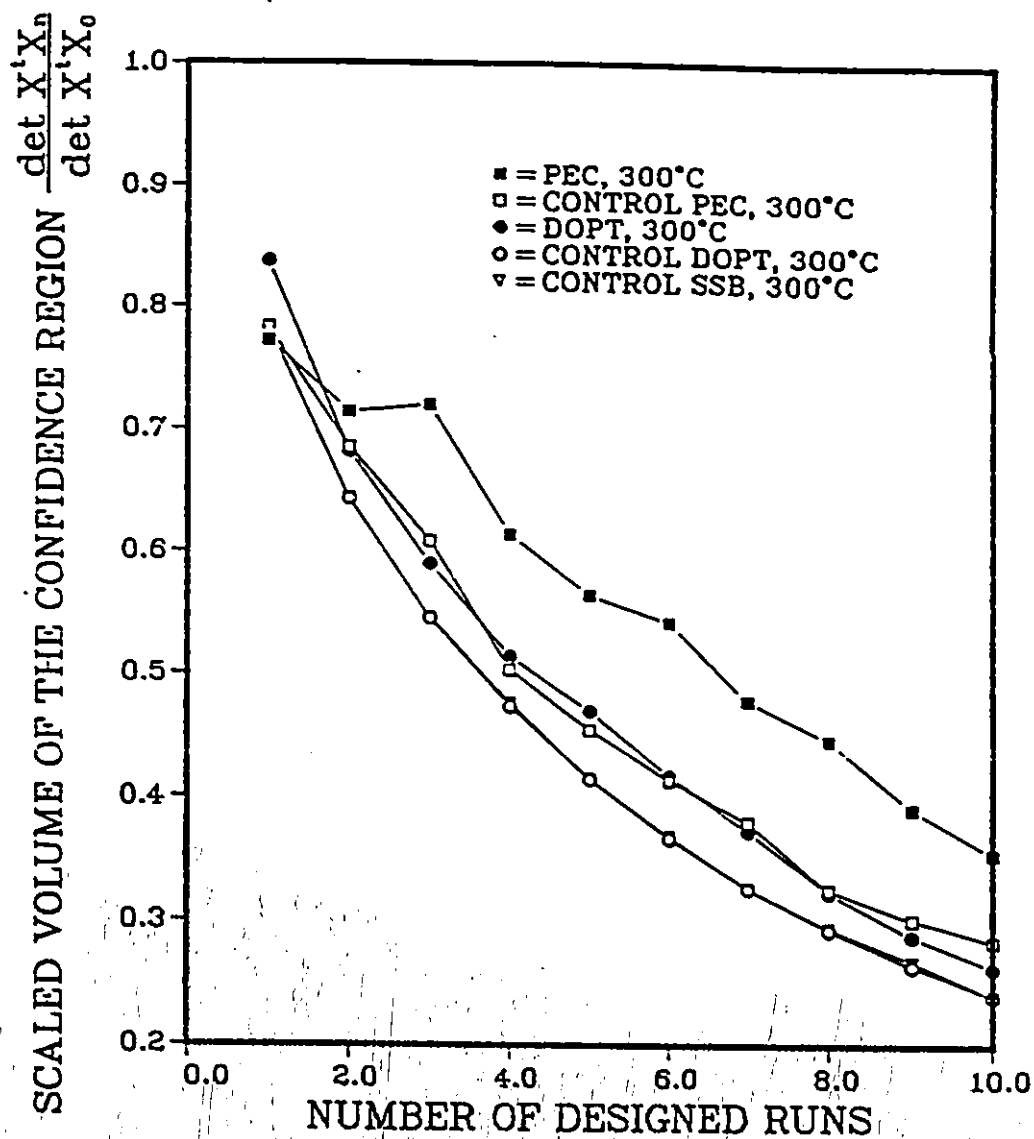


Figure 4.18: Improvements in parameter precision with the Juusola model/data set, oxidation of o-xylene, 300°C.

The improvement of parameter precision obtained with various experimental designs is shown as a function of the number of designed runs. Parameter precision is presented as the variance independent volume of the confidence region for the  $n^{\text{th}}$  designed run as a fraction of the initial volume.

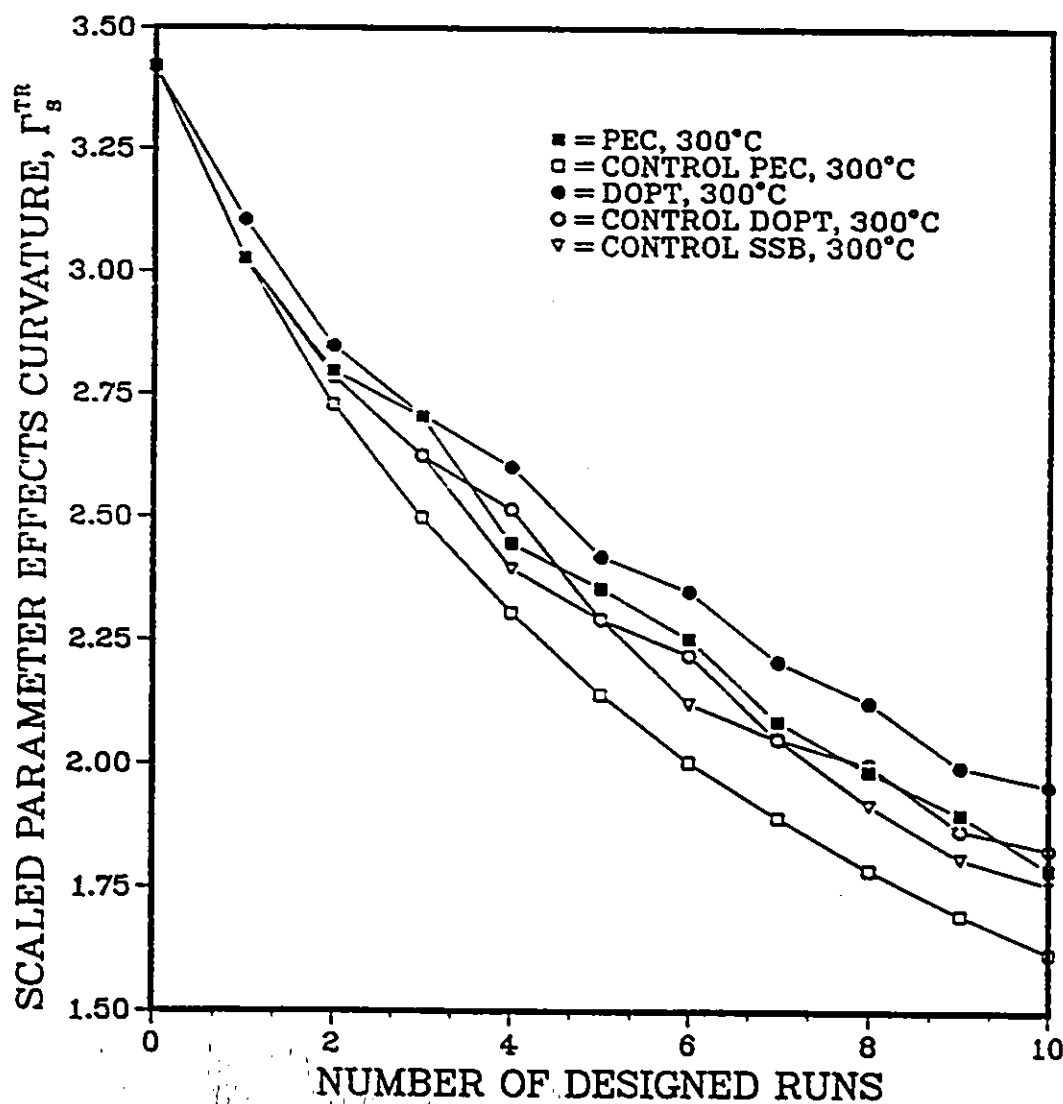


Figure 4.19: Reductions of  $\Gamma_s^{TR}$  with the Juusola model/data set, oxidation of o-xylene, 300°C.

The reduction of the scaled parameter effects curvature obtained with various experimental designs is shown as a function of the number of designed runs. In order to avoid the effect of changing parameter estimates the control simulations have constant parameter and variance estimates

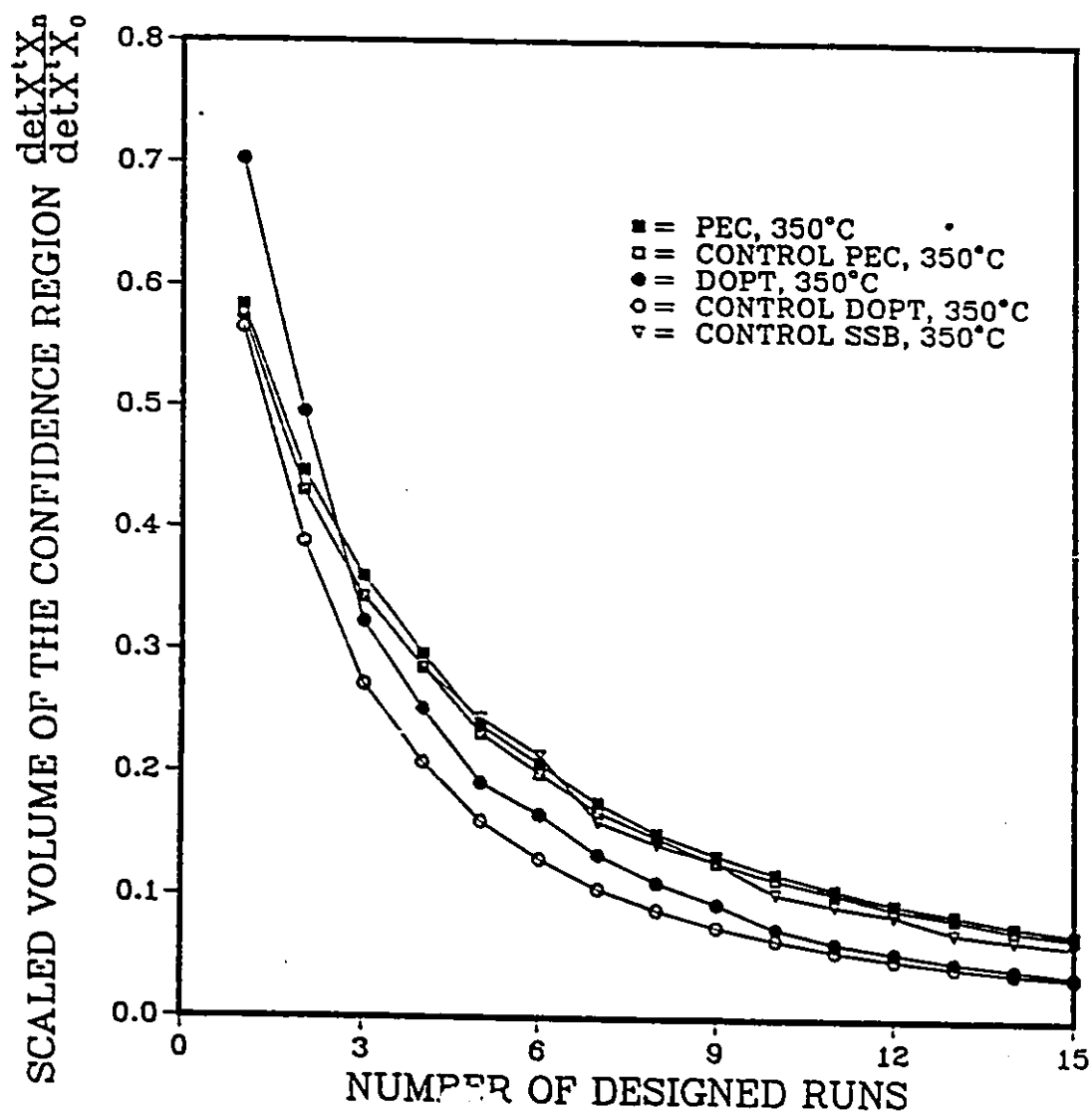


Figure 4.20: Improvements in parameter precision with the Jaswal model/data set, oxidation of benzene, 350°C.

The improvement of parameter precision obtained with various experimental designs is shown as a function of the number of designed runs. Parameter precision is presented as the variance independent volume of the confidence region for the  $n^{\text{th}}$  designed run as a fraction of the initial volume.

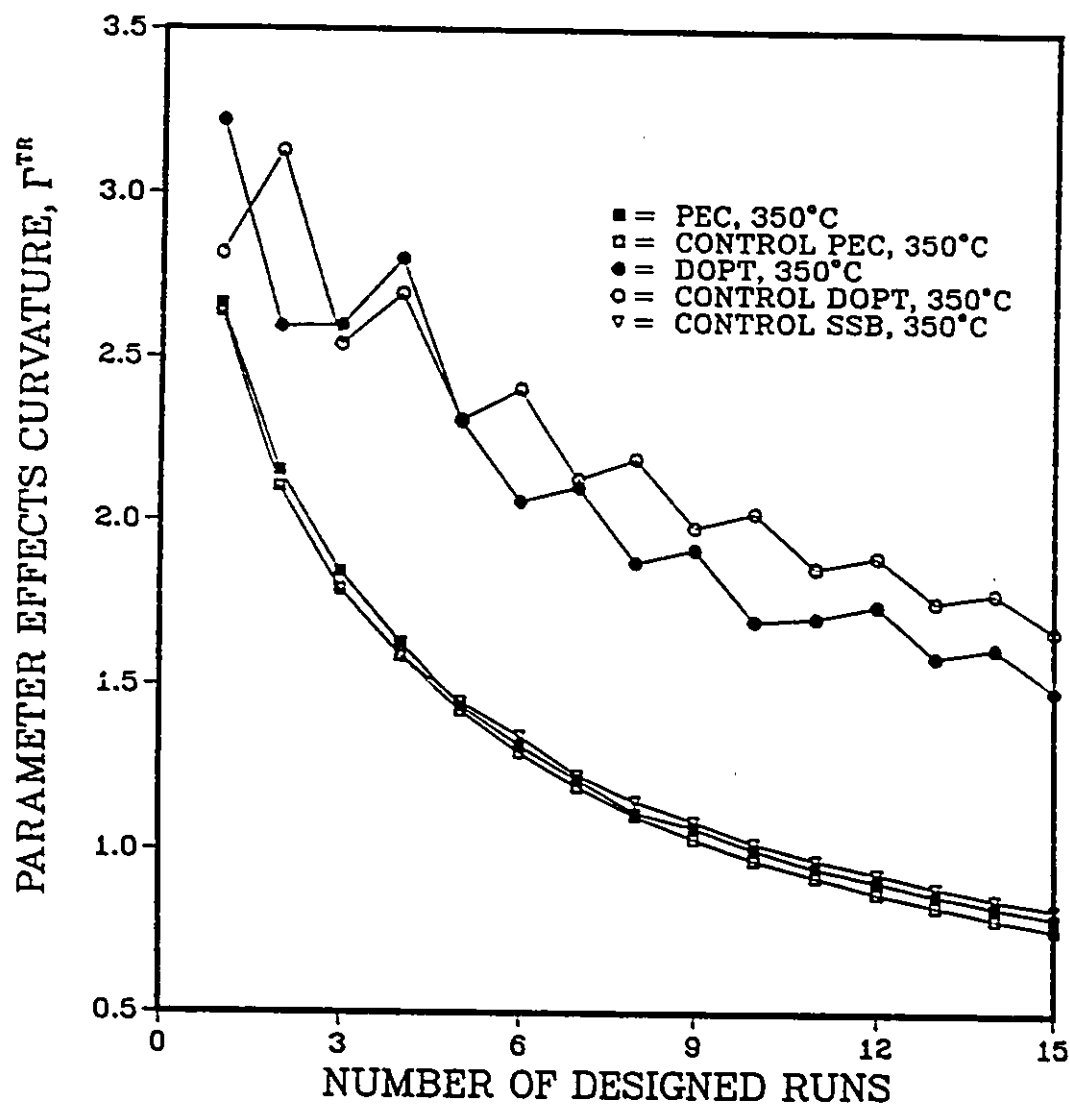


Figure 4.21: Reductions of  $\Gamma_S^{TR}$  with the Jaswal model/data set, oxidation of benzene, 350°C.

The reduction of the scaled parameter effects curvature obtained with various experimental designs is shown as a function of the number of designed runs. In order to avoid the effect of changing parameter estimates the control simulations have constant parameter and variance estimates

behavior similar to that observed with the Juusola data sets. As with the Ayen and Peters model/data set this behavior is related to the designed run locations. The similarity between the control and stochastic simulations was the result of stable parameter estimates.

Results obtained with the Tan model/data set differed from those with the Juusola and Jaswal model/data sets. The D-optimal design, Figure 4.22, resulted in varying degrees of  $\Gamma^{TR}$  reduction, although  $\Gamma_5^{TR}$  never increased, whereas  $\Gamma^{TR}$  did increase with the Juusola and Jaswal data sets. The precise parameter and minimum nonlinearity designs appear to be compatible for this model/data set. An unexpected result was that the PEC designs at 375°C and 390°C, were more effective than the SSB-C design at improving parameter precision, Table 4.2. In every other case the SSB-C design was more efficient than the PEC-C design, though in some cases they were nearly identical.

The different efficiencies of the three design criteria become more evident when comparing the number of experiments required to achieve a given level of parameter precision or degree of nonlinearity. According to Figure 4.16, the PEC-C design required 30 designed runs to obtain the same level of parameter precision that the D-optimal design attained in only 17 experiments. Likewise, when comparing the degree of nonlinearity after 30 runs, the D-OPT-C reduced  $\Gamma_5^{TR}$  to the same level as the PEC-C design with only 14 designed runs. The same discussion applies to the other model/data sets, although differences between the designs were not always so pronounced. The differences between the designs (in terms of the number of experiments required) also depended on the level of parameter precision or degree of nonlinearity obtained. In Figure 4.16, if a reduction of the volume of the confidence region to 1% of its original value was the objective of a D-optimal-C design, then only 4 designed runs would have been required. If the PEC-C design was used then 8 designed runs would have been required. The "difference" between the two designs is now only 4 experiments as opposed to the 13 experiments in the previous example.

The design criteria chosen for the experimental design will also depend on whether priority is given to precise parameter estimates or a model/data set with a minimum degree of nonlinearity. If the model/data set is significantly nonlinear, then priority

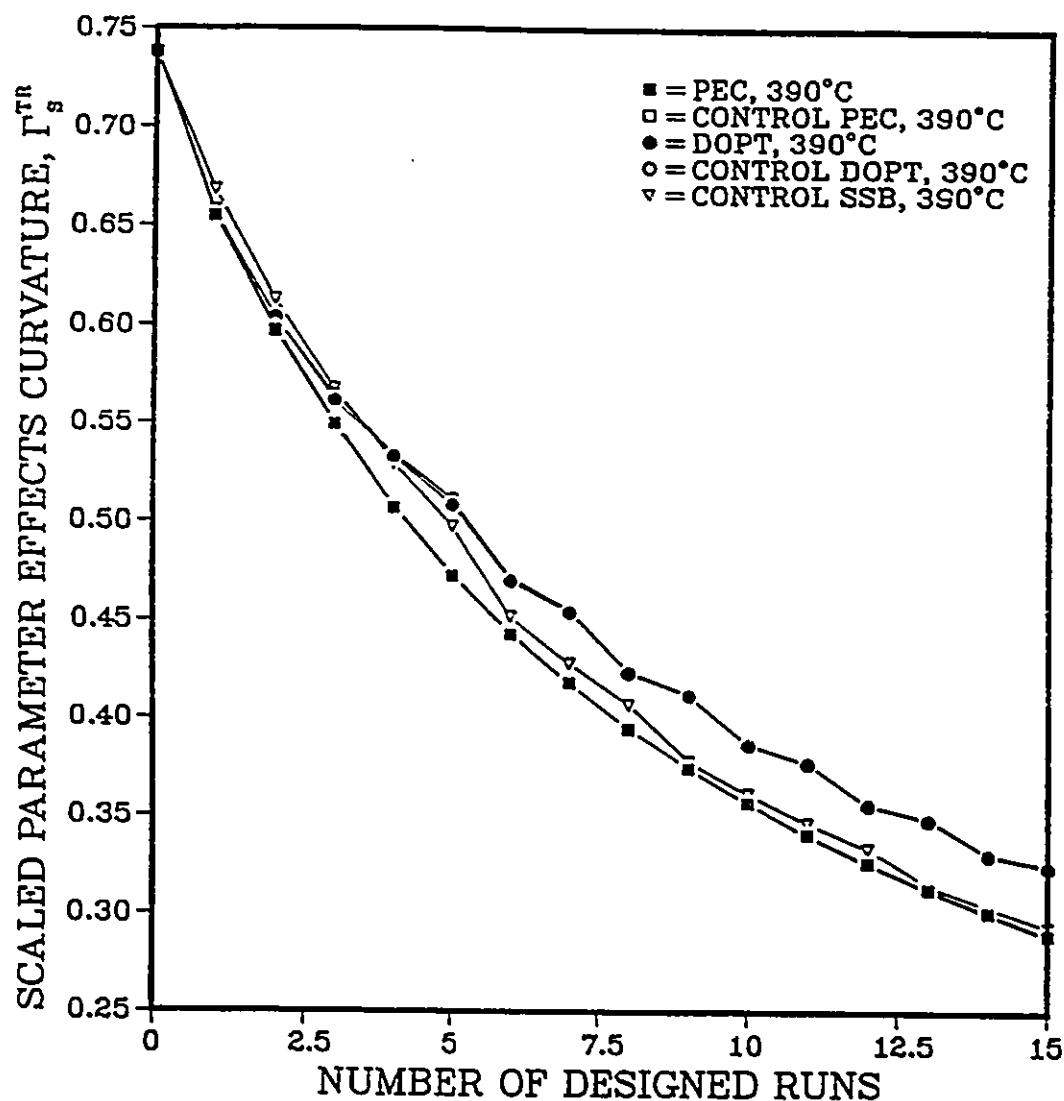


Figure 4.22: Reductions of  $\Gamma_s^{TR}$  with the Tan model/data set, oxidation of propylene, 390°C.

The reduction of the scaled parameter effects curvature obtained with various experimental designs is shown as a function of the number of designed runs. In order to avoid the effect of changing parameter estimates the control simulations have constant parameter and variance estimates

should be given to a minimum nonlinearity design. Since parameter precision usually plays an important role in making inferences then estimates of precision must be reliable. As parameter precision is usually estimated based on the assumption of a locally linear model, obtaining a model/data set with a minimum degree of nonlinearity is essential. Hence a precise parameter estimation design should only be applied to a model/data set with an acceptable degree of nonlinearity, justifying priority for a minimum nonlinearity design. Having reduced the nonlinearity to an acceptable degree the D-optimal design may be implemented should it still be necessary. During the D-optimal design the degree of nonlinearity should also be monitored to ensure that it does not increase.

#### 4.3.1 Summary

Comparisons of the control simulations for all three design criteria are summarized in Table 4.2. In all cases  $\Gamma^{TR}$  was reduced by at least 40% with the PEC-C design criterion. Particularly large reductions were obtained with the Ayen and Peters model/data set ( $> 90\%$ ). Of the three design criteria, the D-optimal design was the least effective in reducing  $\Gamma^{TR}$  but its performance was good nonetheless. The one notable exception was the Jaswal data set at  $375^{\circ}\text{C}$ , where  $\Gamma^{TR}$  was reduced by only 9 % with 15 designed runs. While the D-optimal design was effective at reducing  $\Gamma^{TR}$ , it must be considered incompatible with a minimum nonlinearity design. With each of the Ayen and Peters, Jaswal and Juusola (except at  $300^{\circ}\text{C}$ ) data sets, the D-optimal design lead to increases of the parameter effects curvature. With the remaining data sets, reductions of  $\Gamma^{TR}$  were irregular. This incompatibility was also noted by irregular improvements of parameter precision with the PEC and SSB designs. The parameter precision always improved with the minimum nonlinearity designs, however any experiment, designed or not, will result in some improvement. In Section 4.4 it will be shown that the incompatibility of the D-optimal design with the SSB or PEC design was the result of different designed run locations.

A useful indicator of the efficiency of a design criteria is one based on the number of runs required to achieve a given goal (level of parameter precision or degree of nonlinearity). This is of particular interest to the experimenter, who may be

restricted by either time and/or cost considerations.

The minimum nonlinearity design should be given preference over the D-optimal design. A major short coming of the D-optimal design is that it is based on a linear approximation of the model, which is not valid if either  $\Gamma^T$  or  $\Gamma^N$  are significant.



Table 4.2: Summary of results using the control designs.

The effectiveness of the PEC, SSB and D-optimal control designs are compared for a given number of designed runs. The parameter effects curvature and volume of the confidence region are presented as fractions of their initial values.

| Authors and system                                         | Temp<br>°C | Number<br>of runs | Reduction of $\Gamma^{TR}$ |      |       | Reduction of Volume |                   |                   |
|------------------------------------------------------------|------------|-------------------|----------------------------|------|-------|---------------------|-------------------|-------------------|
|                                                            |            |                   | PEC                        | SSB  | D-opt | PEC                 | SSB               | D-opt             |
| Ayen and Peters [18]<br>reduction of NO to NH <sub>3</sub> | 375        | 30                | 93.4                       | 92.6 | 88.6  | 2.46 <sup>†</sup>   | 2.60 <sup>†</sup> | 2.79 <sup>†</sup> |
|                                                            | 400        | 30                | 94.8                       | 94.5 | 90.7  | 2.33 <sup>†</sup>   | 2.48 <sup>†</sup> | 2.75 <sup>†</sup> |
|                                                            | 425        | 30                | 96.3                       | 96.0 | 93.4  | 3.36 <sup>†</sup>   | 3.62 <sup>†</sup> | 3.88 <sup>†</sup> |
| Juusola [14]<br>oxidation of o-xylene                      | 270        | 10                | 42.2                       | 39.3 | 31.4  | 73.2                | 76.9              | 79.3              |
|                                                            | 290        | 10                | 53.5                       | 52.6 | 38.5  | 68.4                | 68.8              | 74.5              |
|                                                            | 300        | 10                | 49.7                       | 45.3 | 43.2  | 71.6                | 75.9              | 76.0              |
| Jaswal [29]<br>oxidation of benzene                        | 350        | 15                | 79.3                       | 77.6 | 54.4  | 93.2                | 93.9              | 96.6              |
|                                                            | 375        | 15                | 55.7                       | 52.9 | 9.1   | 80.0                | 81.7              | 89.4              |
|                                                            | 400        | 15                | 80.5                       | 79.3 | 57.6  | 92.8                | 93.7              | 96.1              |
| Tan [24]<br>oxidation of propylene                         | 350        | 15                | 52.1                       | 52.1 | 41.1  | 74.1                | 76.1              | 80.1              |
|                                                            | 375        | 15                | 55.1                       | 55.1 | 48.1  | 74.1                | 72.1              | 79.1              |
|                                                            | 390        | 15                | 59.1                       | 59.1 | 54.1  | 77.1                | 74.1              | 79.1              |

<sup>†</sup> Reduction of volume represented by orders of magnitude, see text.

## 4.4 Designed Run Locations and the Design Surface

Designed run locations may be the most important criterion for comparing different experimental designs. Comparing the designs using the volume of the confidence region or  $\Gamma^{TR}$  is important but can be complicated by changing variance or parameter estimates. Using the control simulations of Sections 4.1 and 4.3 helped to solve this problem. The information the experimenter obtains with any sequential experimental design is the operating conditions under which the next experiment is to be performed. One of the desired features of a minimum nonlinearity design criteria mentioned in Section 3.1, was the compatibility of the design with other modelling objectives. Precise parameter estimation, through use of the D-optimal design, has already been identified as another modelling objective of concern in this work. In Section 4.3 the D-optimal design was shown to be not fully compatible with the two minimum nonlinearity designs. However in some cases the designs were virtually identical in their ability to improve parameter precision. Whether the designs were actually identical can only be determined by comparing the designed run locations.

D-optimal designs lead to a characteristic pattern of designed run locations, [5,23]. Designed runs are usually

- found at  $p$  locations
- approximately equally distributed at each location
- located at the limits of the experimental operating region.

Box [23] has shown that D-optimal designs will always result in  $p$  designed run locations. D-optimal designs, or any additional experiment, will always lead to an improvement in parameter precision, given that the parameter and variance estimates remain constant. In Section 4.3, the D-optimal design reduced the extent of nonlinearity in several cases. In the discussion of the original paper on relative curvatures, Bates and Watts [1] noted that there could be some similarity between minimum curvature and D-optimal designs. Hence, a minimum curvature design might be expected to exhibit some of the traits of a D-optimal design.

Contour plots of the design surface complete the comparison of the designs. It

is conceivable that similar run locations can be chosen from two surfaces having a different topology. Similarly, different run locations can be chosen from surfaces having similar topologies. Multiple minima or maxima are easier to visualize, as is the sensitivity of the design criterion to the operating conditions. If multiple minima exist, it may be preferable to perform the experiment under conditions where the design criterion is less sensitive to the operating conditions. This would avoid obtaining an undesirable result (increased nonlinearity) in the event that stringent control of the operating variables cannot be achieved. Changes in the design surface for different stages of the design can also be studied more readily. Fortunately, the isothermal forms of all the models studied are functions of only two operating variables; this will allow the design surface to be presented as a single contour plot. The design surface was generated by evaluating the design criterion over the nodes of a grid covering the operating region. The grid used for generating the contours of the design surface was generally finer than that used in Section 4.3 for the actual simulations.

Figures 4.23, 4.24 and 4.25 show the conditions under which the original data was obtained and the designed run locations of the PEC-C, D-OPT-C and SSB-C designs for the Ayen and Peters results at 425°C. After the 6 initial runs, all the PEC designed runs were at two locations. The locations  $(pNO, pH_2) = (0.002, 0.010)$  and  $(0.002, 0.012)$  may be considered the same as they are adjacent locations in the grid search. The PEC designed runs followed a pattern, one run designed near  $(0.002, 0.010)$  and 4 to 6 runs at  $(0.002, 0.050)$ . The SSB-C design was very similar to the PEC design in both run location and sequence with two exceptions. Runs 20 and 25 were located near the upper limit of both operating variables, which is also a D-optimal design location (but at which no PEC runs were designed). The SSB-C design did not result in experiments near  $(0.030, 0.014)$  which was a PEC design location. The D-OPT-C design resulted in a different set of run locations and pattern. The 2<sup>nd</sup> through 9<sup>th</sup> runs alternated between  $(0.002, 0.018)$  and  $(0.002, 0.050)$ , after which runs were also located at a third location,  $(0.050, 0.050)$ .

The characteristics of D-optimal designs were all observed, experiments were designed at three locations, with roughly equal occurrences and at the limits of the

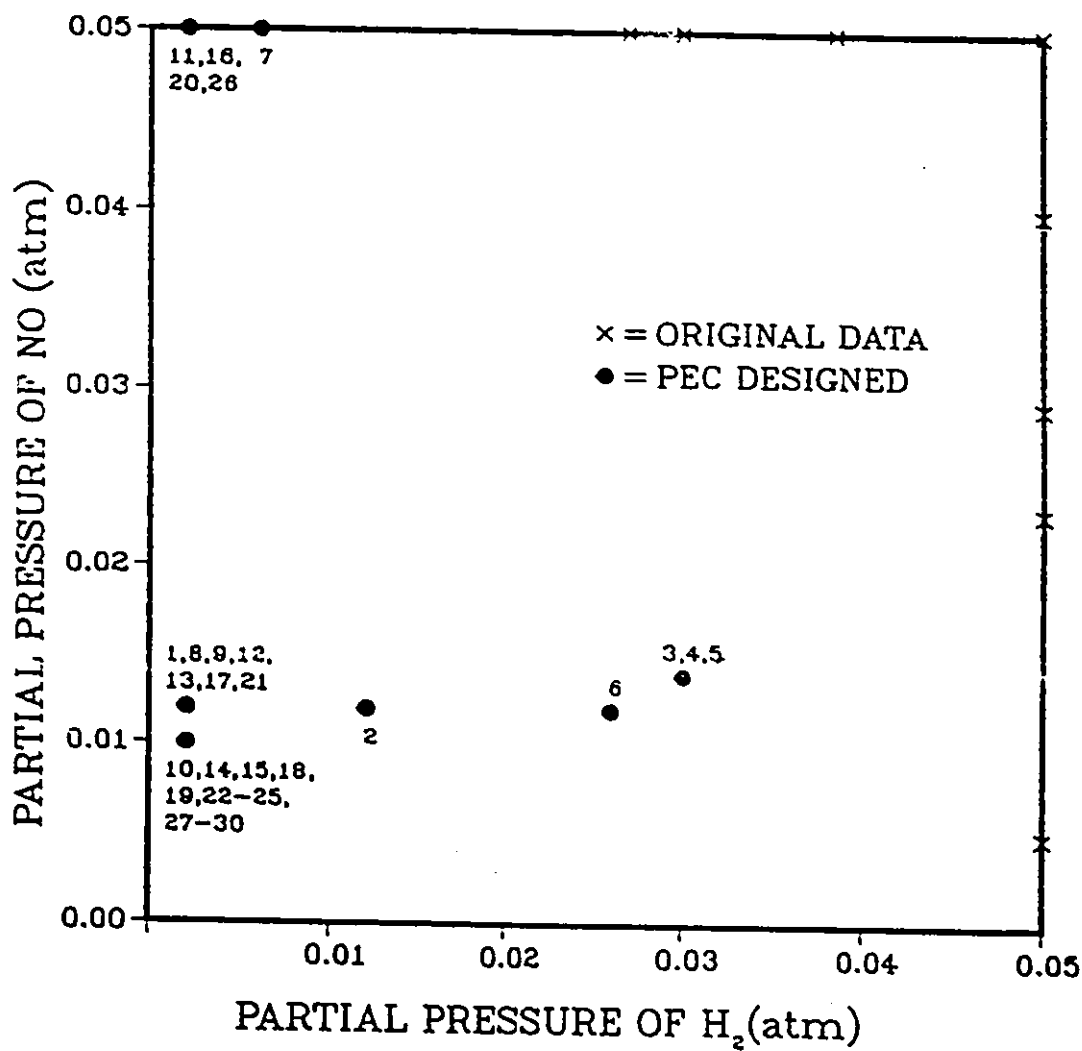


Figure 4.23: PEC designed runs for Ayen and Peters,  $425^\circ\text{C}$ .

Shown are the conditions under which the original data was obtained and the location and sequence of the designed run locations for the PEC-C design criterion.

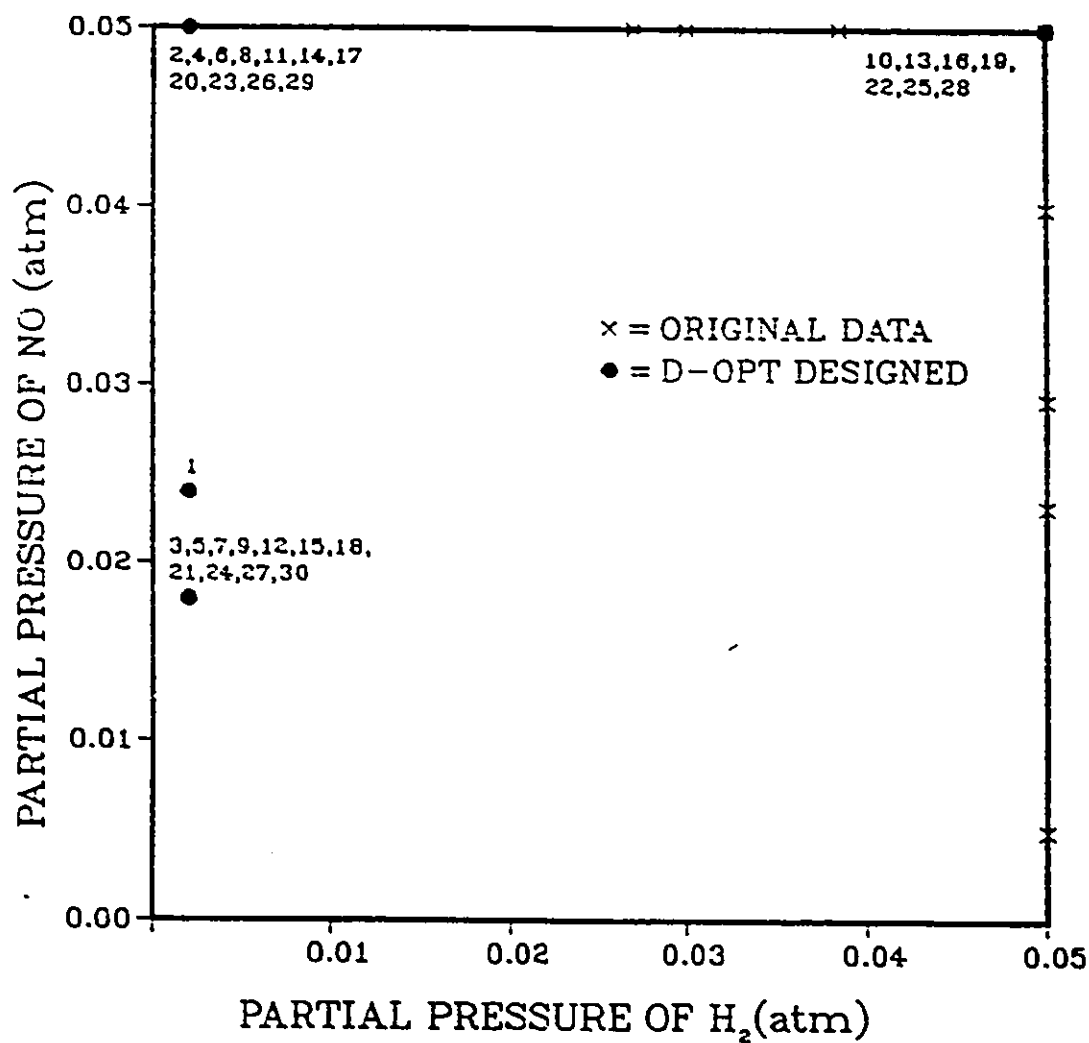


Figure 4.24: D-optimal designed runs for Ayen and Peters, 425°C.

Shown are the conditions under which the original data was obtained and the location and sequence of the designed run locations for the D-optimal design.

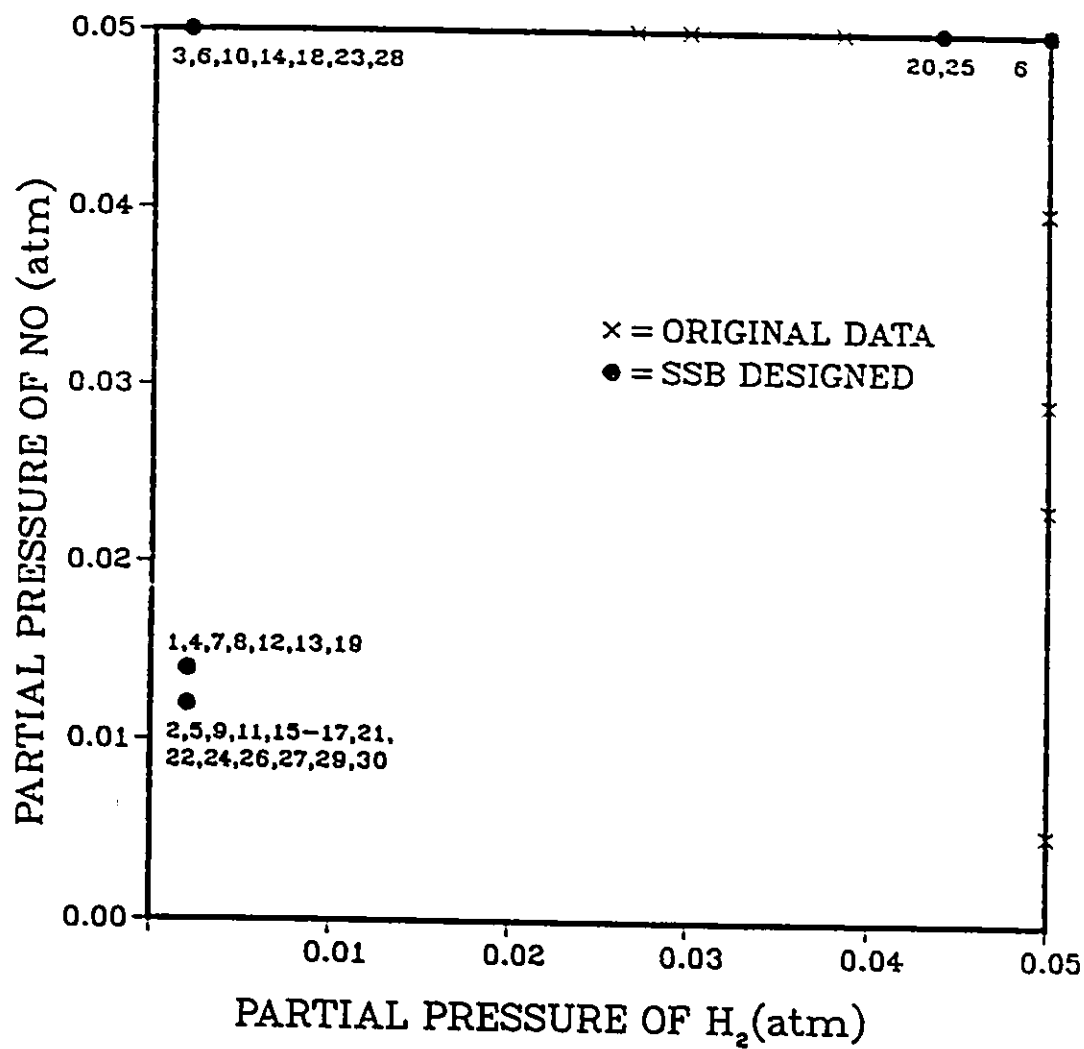


Figure 4.25: SSB designed runs for Ayen and Peters, 425°C.

Shown are the conditions under which the original data was obtained and the location and sequence of the designed run locations for the SSB-C design criterion.

operating region. The three designs were similar in that they resulted in experiments in two common areas, whereas the SSB and D-optimal designs had three common locations. The PEC and SSB designs differed from the D-optimal design by having a concentration of experiments designed near (0.002,0.010). The D-optimal design resulted in a more even occurrence of experiments at the three locations. The PEC design was unique in being the only design to result in experiments near (0.030,0.014). Initial observations suggested that the designs might have been similar, while not wholly compatible. The differences in designed run locations and the design surfaces confirm this.

The designed run locations with the PEC-S simulations were very similar to those obtained with the PEC-C criterion. The four PEC-S simulations differed only in the number of experiments designed near (0.030,0.012), the PEC-S simulations resulting in fewer runs at this location. Stochastic simulations with the D-OPT and SSB designs were also similar to their analogous control simulations. This suggested that the random errors had little effect on the actual run locations (i.e. the designs are robust) although they had a large effect on the actual degree of nonlinearity or parameter precision.

Figure 4.26 shows the parameter effects curvature design surface for the first run as a function of the two operating variables, the partial pressures of NO and H<sub>2</sub>. The surface is scaled to show the parameter effects curvature as a fraction of the original parameter effects curvature, 13.05. The design surface shows several interesting features; there are multiple minima, the global minimum at (0.002,0.012) and a local minimum at (0.050,0.050). There are also multiple maxima, the global maximum at (0.034,0.050) and a local maximum at (0.050,0.002). The minimum predicts a possible reduction of  $\Gamma^T$  to at least 25% of its initial value while the maximum predicts a possible increase of at least 5%.

The possibility of increasing the degree of nonlinearity was unexpected. Unlike the PEC design, the D-optimal designs will *always* predict an improvement of parameter precision, regardless of the operating conditions. Figure 4.27 shows the D-optimal design surface for the first run. The surface has been scaled, as with the PEC surface, to represent the volume as a fraction of the initial volume. At first glance the two surfaces appear to be very different, however they have several similarities. The global minima are in the same general area and both surfaces have a local

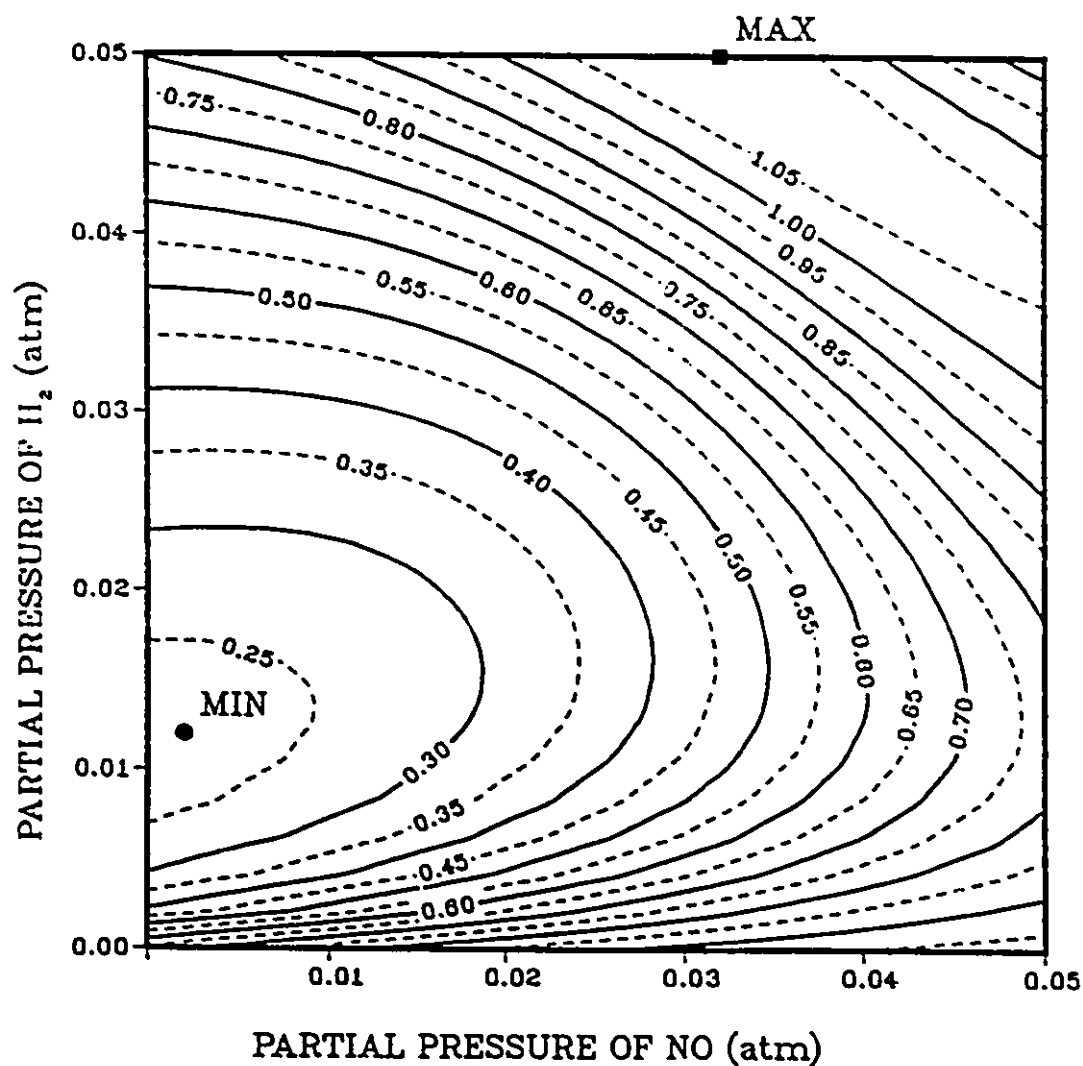


Figure 4.26: PEC design surface, Ayen and Peters, 425°C, Run 1.

The PEC design surface with contours of constant predicted parameter effects curvature as a function of the operating variables. The surface is scaled to show the predicted parameter effects curvature as a fraction of the initial curvature.



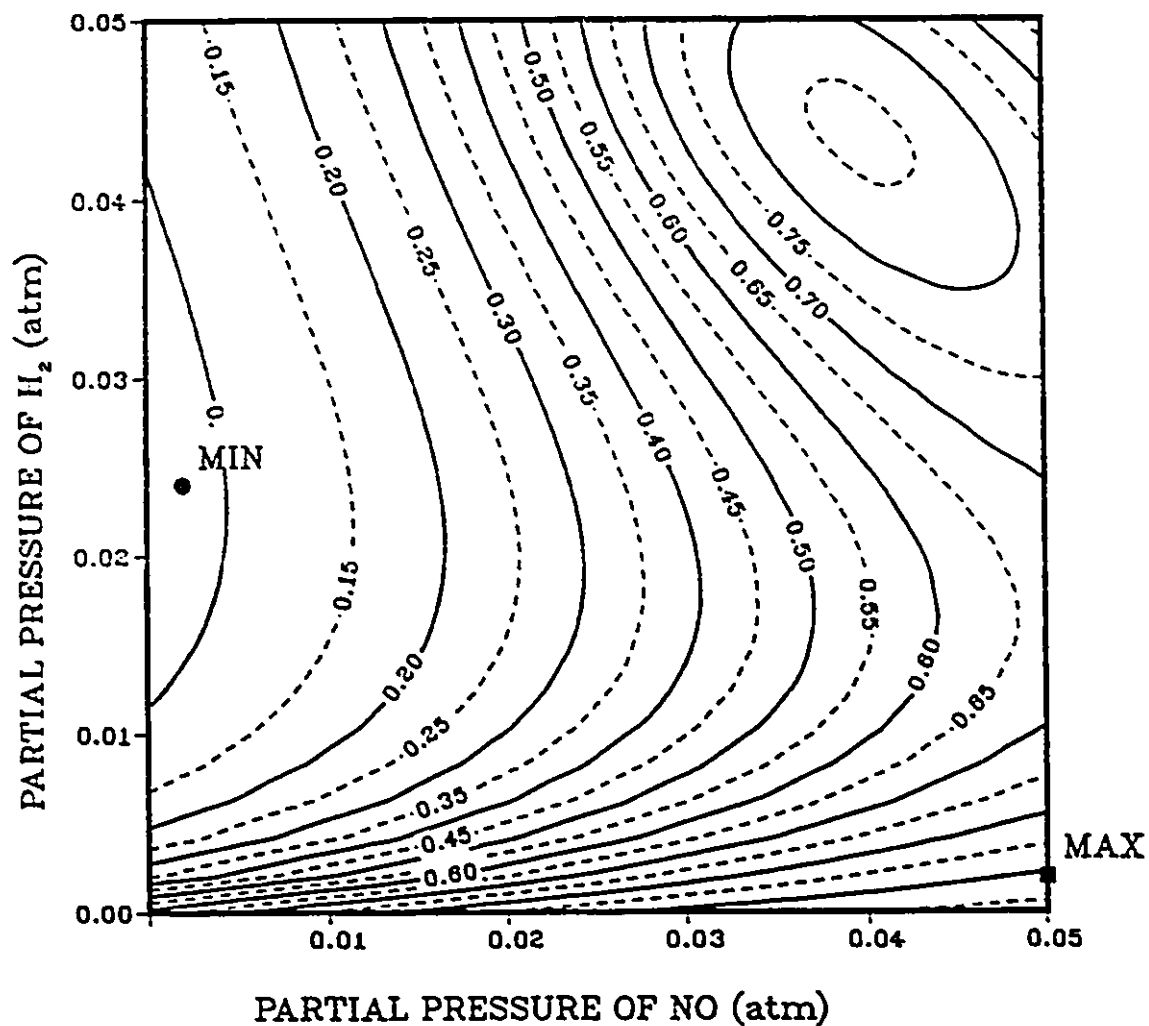


Figure 4.27: D-OPT design surface, Ayen and Peters, 425°C, Run 1.

The D-OPT design surface with contours of constant predicted volume of the confidence region as a function of the operating variables. The surface is scaled to show the predicted volume as a fraction of the initial volume.

minimum at (0.050,0.050). The local maximum of the PEC surface is the global maximum of the D-optimal surface while the global maximum of the PEC surface is near the local maximum of the D-optimal surface. Despite the common locations of maxima and minima, the two surfaces had different topologies. This was more evident after comparing the design surfaces for later runs.

The PEC design surface for the 11<sup>th</sup> run is shown in Figure 4.28 and scaled to represent the surface as a fraction of the previous value, i.e. as fractions of  $\Gamma^T$  for the 10<sup>th</sup> run. The design surface has changed considerably, but there is still a local minimum near the global minimum of the first designed run. The most striking feature is that under a large set of conditions an increase of  $\Gamma^T$  is predicted, up to 5%. At this stage of the design reductions of  $\Gamma^T$  were very small, Figure 4.3. This is also reflected by the surface for the 11<sup>th</sup> run. The greatest predicted reduction of  $\Gamma^T$  is only 8%, much lower than the possible 75% seen for the first run and almost as large as the greatest possible increase from an undesigned run. The surface is in fact much flatter than suggested by Figure 4.28, because it is scaled with  $\Gamma^T$  for the 10<sup>th</sup> run rather than the original data. Had the original curvature been used to scale the surface, the contours would only have ranged from 5.4% to 6.6% and possible increases of  $\Gamma^{TR}$  relative to the previous run would not be evident.

The D-optimal surface for the 11<sup>th</sup> PEC designed run is shown in Figure 4.29. The surface bears little resemblance to Figure 4.27 or 4.28. However there is still a local minimum at (0.050,0.050) as in Figure 4.27, which is one of the three D-optimal run locations. The surface is considerably flatter than for the first run. The greatest reduction of the volume is only 25% compared to the 90% possible with the first run. While the PEC and D-OPT designs shared a common designed run location, the dissimilarity of the design surfaces show that the designs are not the same.

Simulations with the 400°C and 375°C data sets gave results similar to those obtained at 425°C. The PEC criterion led to runs designed at the same or very similar conditions as at 425°C. At 400°C the SSB criterion resulted in only two run locations, the same as the PEC criterion, while at 375°C 5 of the runs were designed at the D-optimal conditions not common to any of the PEC designs, (0.050,0.050). At both of the lower temperatures the D-optimal design led to run conditions similar to the 425°C data set.

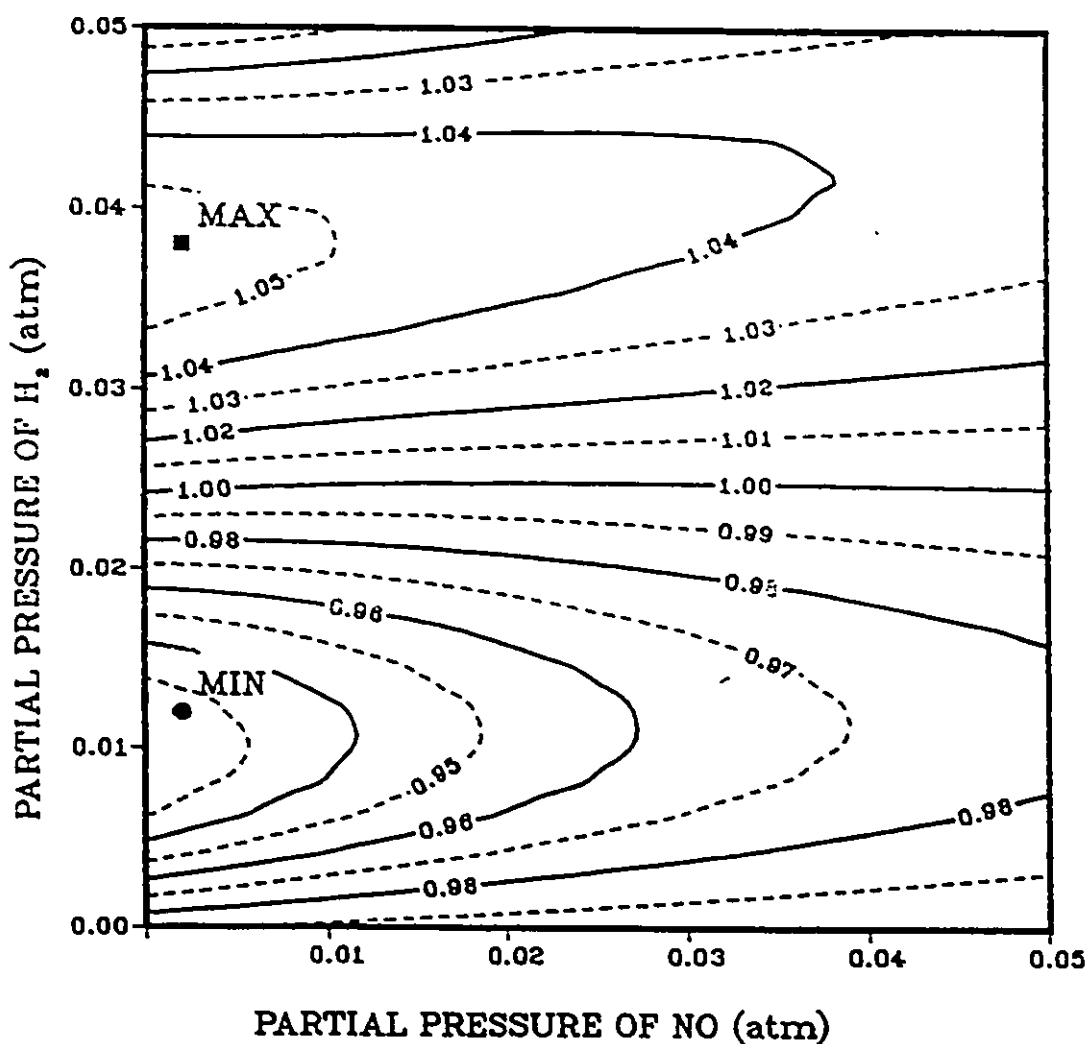


Figure 4.28: PEC design surface, Ayen and Peters, 425°C, Run 11.

The PEC design surface for the 11<sup>th</sup> run, with contours of constant predicted parameter effects curvature as a function of the operating variables. The surface is scaled to show the predicted parameter effects curvature as a fraction of the initial curvature.

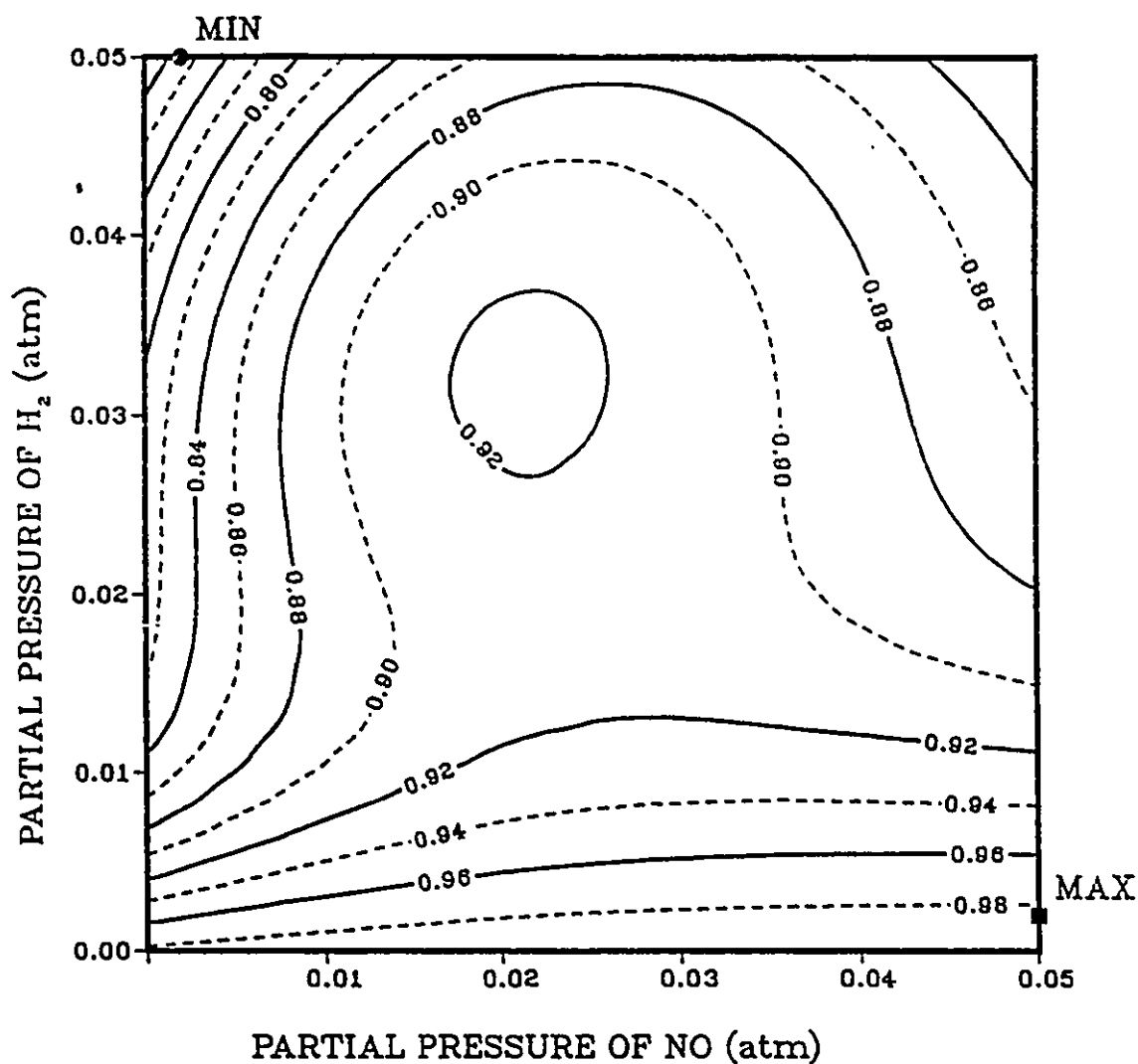


Figure 4.29: D-OPT design surface, Ayen and Peters, 425°C, Run 11.

The D-OPT design surface with contours of constant predicted volume of the confidence region as a function of the operating variables. The surface is scaled to show the predicted volume as a fraction of the initial volume.

At all three temperatures the D-optimal design initially led to runs designed at only 2 locations (rather than the expected  $p = 3$ ). The third location, (0.050,0.050), was chosen only after the 10<sup>th</sup> or 9<sup>th</sup> runs. The initial runs were designed at conditions similar or identical to the PEC and SSB designs.

In Section 4.3 it was observed that the D-optimal designs often resulted in increasing  $\Gamma_S^{TR}$ . With the Ayen and Peters model/data set at 425°C, Figure 4.17,  $\Gamma_S^{TR}$  increased with runs 10, 13, 16, 19, 22, 25, and 28. These were all experiments designed at (0.050,0.050), the D-optimal run location not common to the PEC design. Likewise, the PEC-C design did not result in steady improvements of parameter precision, Figure 4.16. Parameter precision improved at a higher rate for runs 7, 11, 16 and 20 with the PEC-C design. All these runs were performed at (0.002,0.050), a run location common to the D-optimal design. This relationship between improving parameter precision and reduction of the parameter effects curvature with designed run locations was also observed at the lower temperatures.

Simulations using the PEC criterion with the Jaswal model/data set were successful in reducing  $\Gamma^T$  to an acceptable level at all three temperatures. At 350°C, 375°C and 400°C only 6, 2 and 7 designed runs, respectively, were required. To allow comparison of the designs, 15 runs for each of the three control criteria were simulated at each of the temperatures. Figure 4.30 shows the original data and the sequence and location of the designed runs for the three control simulations at 400°C. The D-optimal design behaved as expected, alternating between 2 ( $= p$ ) run locations at the extremes of the operating region. The PEC design showed similar characteristics with one of its two design points very close to a D-optimal location. A characteristic of the PEC design, similar to that observed with the Ayen and Peters model/data set, is the preference for one of the run locations. In this case more runs were designed at the location common to the D-optimal design. The SSB-C run locations were also primarily designed at  $(pO_2, pC_6H_6) = (0.0030, 0.0045)$ , common to both the PEC and D-OPT designs. Three runs were also designed at (0.0160, 0.0030), between the second PEC and D-OPT run locations.

The PEC and D-OPT design surfaces are shown in Figure 4.31 and 4.32 respectively. The surfaces have a common global minimum. However, a local minimum on the D-optimal surface (actually the second D-OPT run location) located at (0.0160, 0.0045) is near the global maximum on the PEC surface. This explains

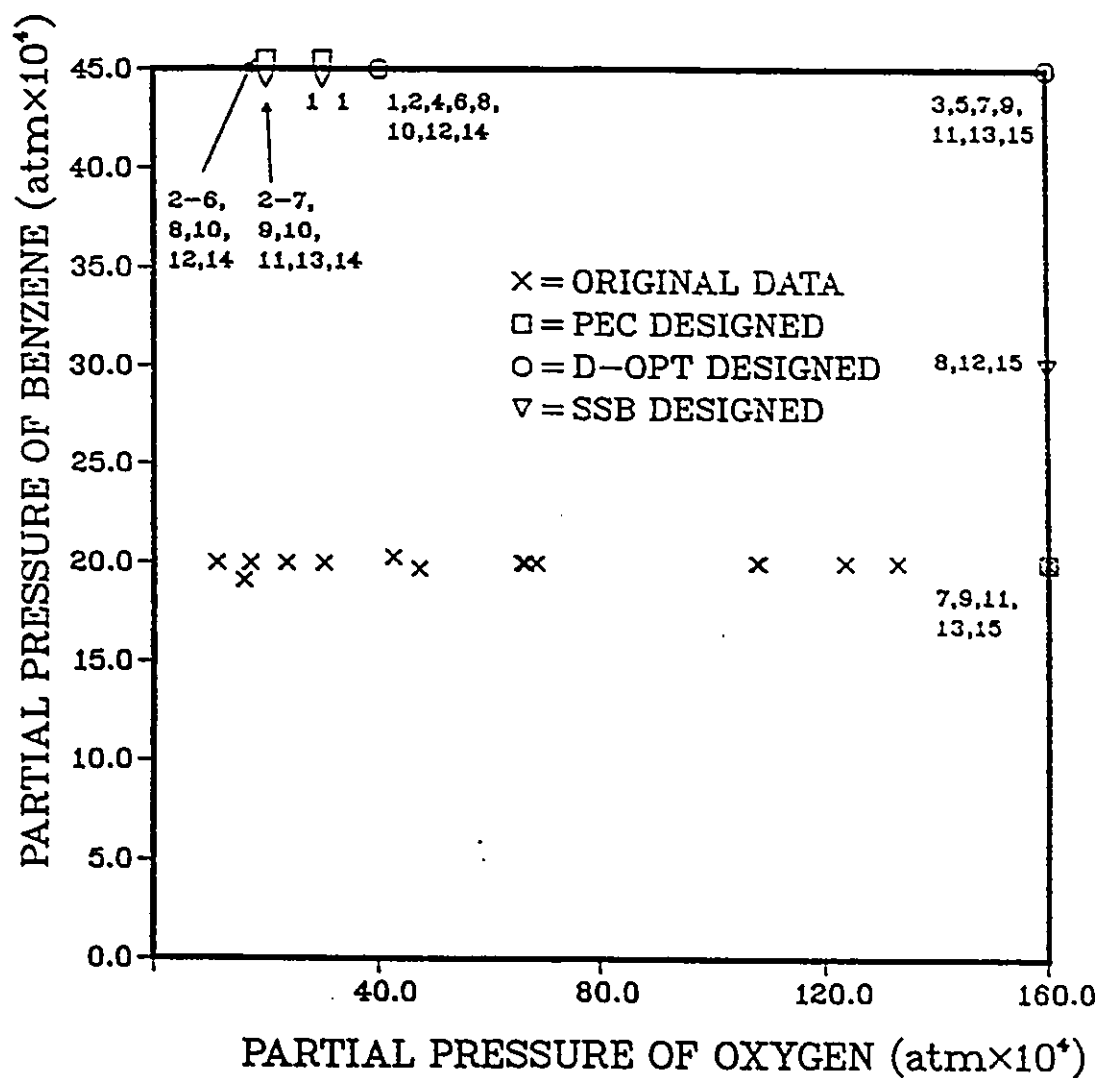


Figure 4.30: Designed runs for Jaswal, 400°C.

Shown are the conditions under which the original data was obtained and the location and sequence of the designed run locations for the PEC-C, D-OPT-C and SSB-C design criteria.

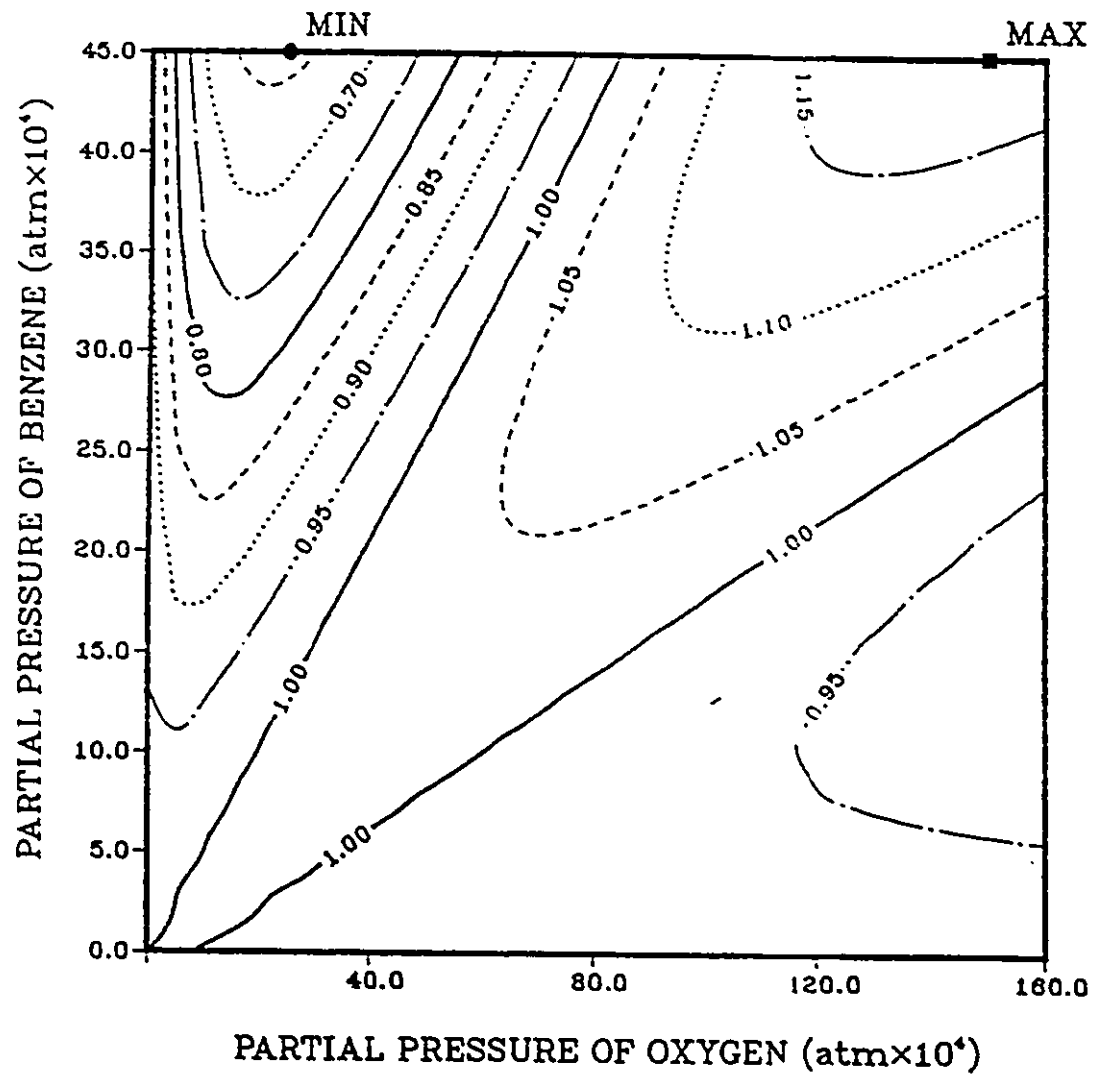


Figure 4.31: PEC design surface, Jaswal, 400°C, Run 1.

The PEC design surface with contours of constant predicted parameter effects curvature as a function of the operating variables. The surface is scaled to show the predicted parameter effects curvature as a fraction of the initial curvature.

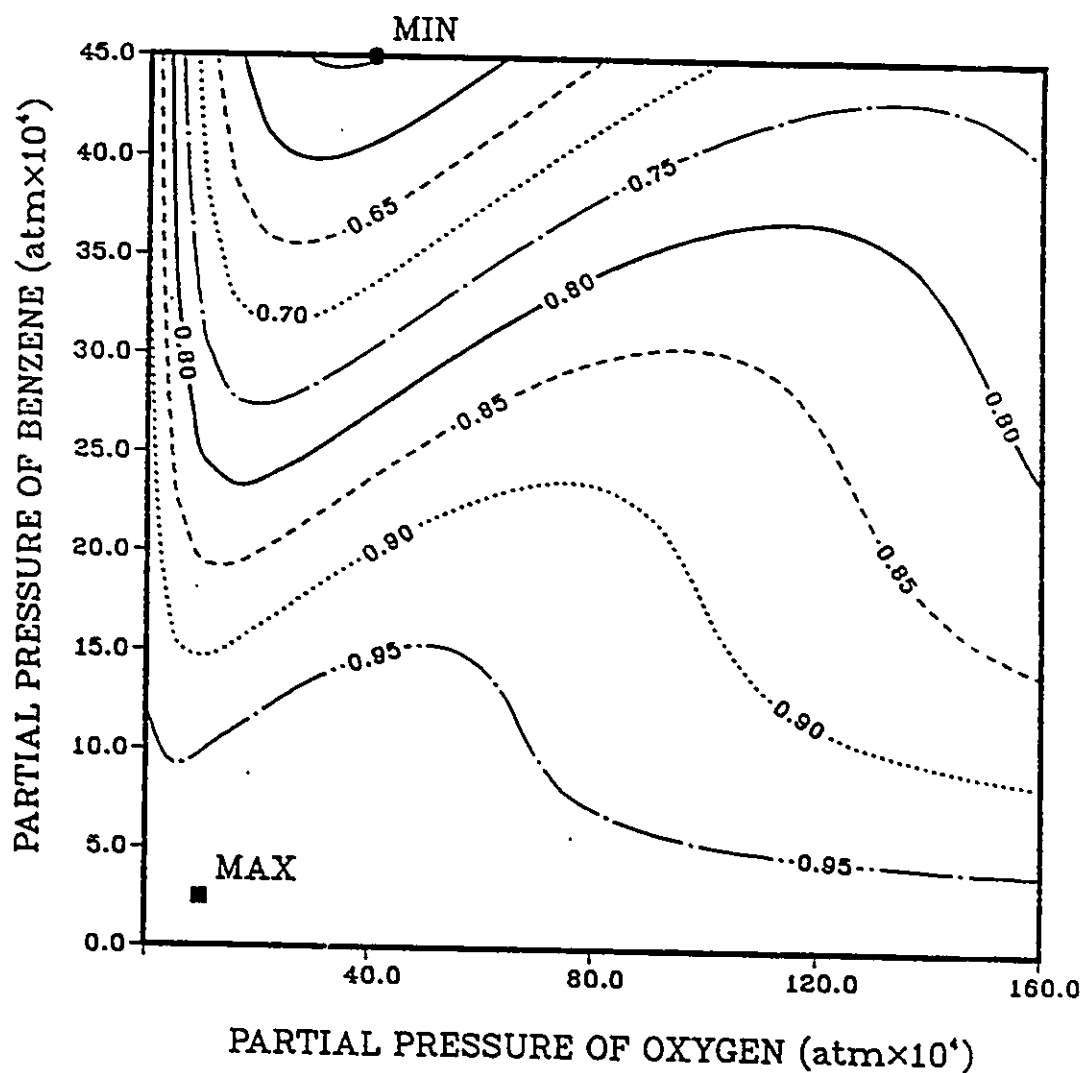


Figure 4.32: D-OPT design surface, Jaswal, 400°C, Run 1.

The D-OPT design surface with contours of constant predicted volume of the confidence region as a function of the operating variables. The surface is scaled to show the predicted volume as a fraction of the initial volume.



the alternating increase/decrease of  $\Gamma_S^{TR}$  with the D-optimal design seen in Section 4.3, Figure 4.21. The increased parameter effects curvature occurred with runs 3, 5, 7, 9, 11, 13 and 15, which corresponded to D-optimal runs at (0.0160,0.0045). The similarity in the performance of the PEC-C and SSB-C designs in Figure 4.21 is expected given the similarity in designed run locations.

The designed run locations were essentially the same for both the stochastic and control simulations. The similarity in designed run locations was also expected because parameter estimates were stable during the simulations. With the D-OPT-S simulation,  $k_a$  varied from  $0.25 \times 10^{-3}$  to  $0.31 \times 10^{-3}$ . One of the designed run locations shifted to an adjacent node on the grid covering the operating region, from (0.0040,0.0045) to (0.0030,0.0045).

The designed run locations at 375°C and 350°C for all three control designs were similar to those at 400°C, including the preference for one location with the PEC and SSB designs.

The model/data set of Juusola [14] is different from that of Ayen and Peters and Jaswal in that Juusola used a D-optimal design in his original work. Figure 4.33 shows the run locations of the original data (with differentiation of D-optimal and non-D-optimal runs in the original work) and the run locations for the control PEC, SSB and D-OPT (for this work) designs. The D-optimal designed runs obtained in this work agree with those of Juusola. The SSB-C design is very similar to the D-optimal design. This similarity was suggested in Figure 4.18 in Section 4.3 where the progress of the two designs is essentially the same with respect to improving parameter precision.

A striking feature of the PEC and D-OPT surfaces in Figure 4.34 and 4.35, is their similarity to those for the Jaswal model/data set. This similarity is actually expected when one recalls that both workers used the same model to describe the catalytic oxidation of a hydrocarbon. The lower right hand corner of each figure is cut by an operating constraint (the straight solid line) representing too high a conversion for the assumption of a differential reactor. The PEC and D-optimal surfaces are similar in that they share a common global minimum, ignoring the operating constraint, and similar local minima, which are the second designed run locations for either design. The surfaces are different with respect to the maxima, as was the case with the Jaswal model/data set.

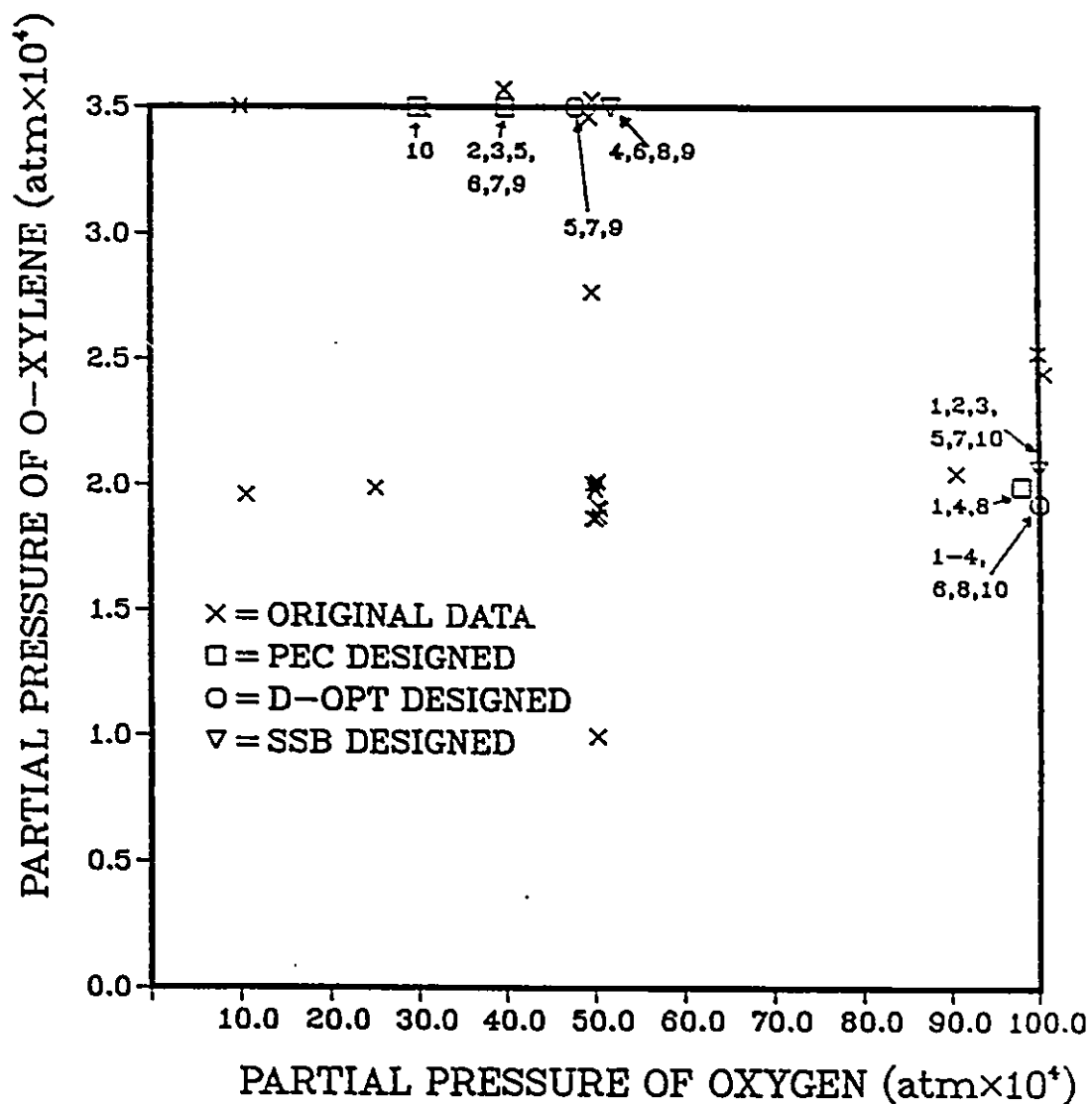


Figure 4.33: Designed runs for Juusola, 300°C.

Shown are the conditions under which the original data was obtained and the location and sequence of the designed run locations for the PEC-C, D-OPT-C and SSB-C design criteria.

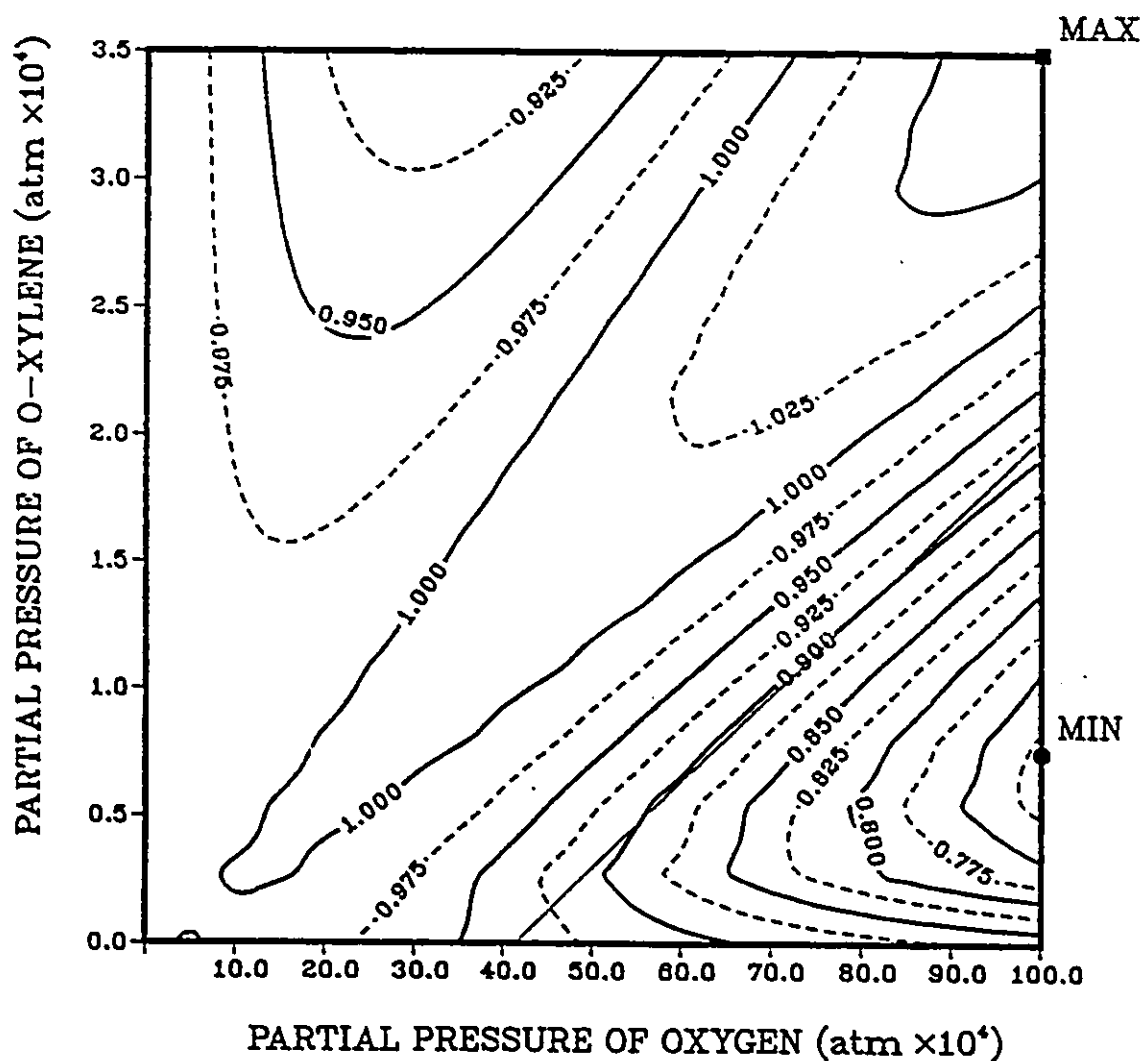


Figure 4.34: PEC design surface, Juusola, 300°C, Run 1.

The PEC design surface with contours of constant predicted parameter effects curvature as a function of the operating variables. The surface is scaled to show the predicted parameter effects curvature as a fraction of the initial curvature.

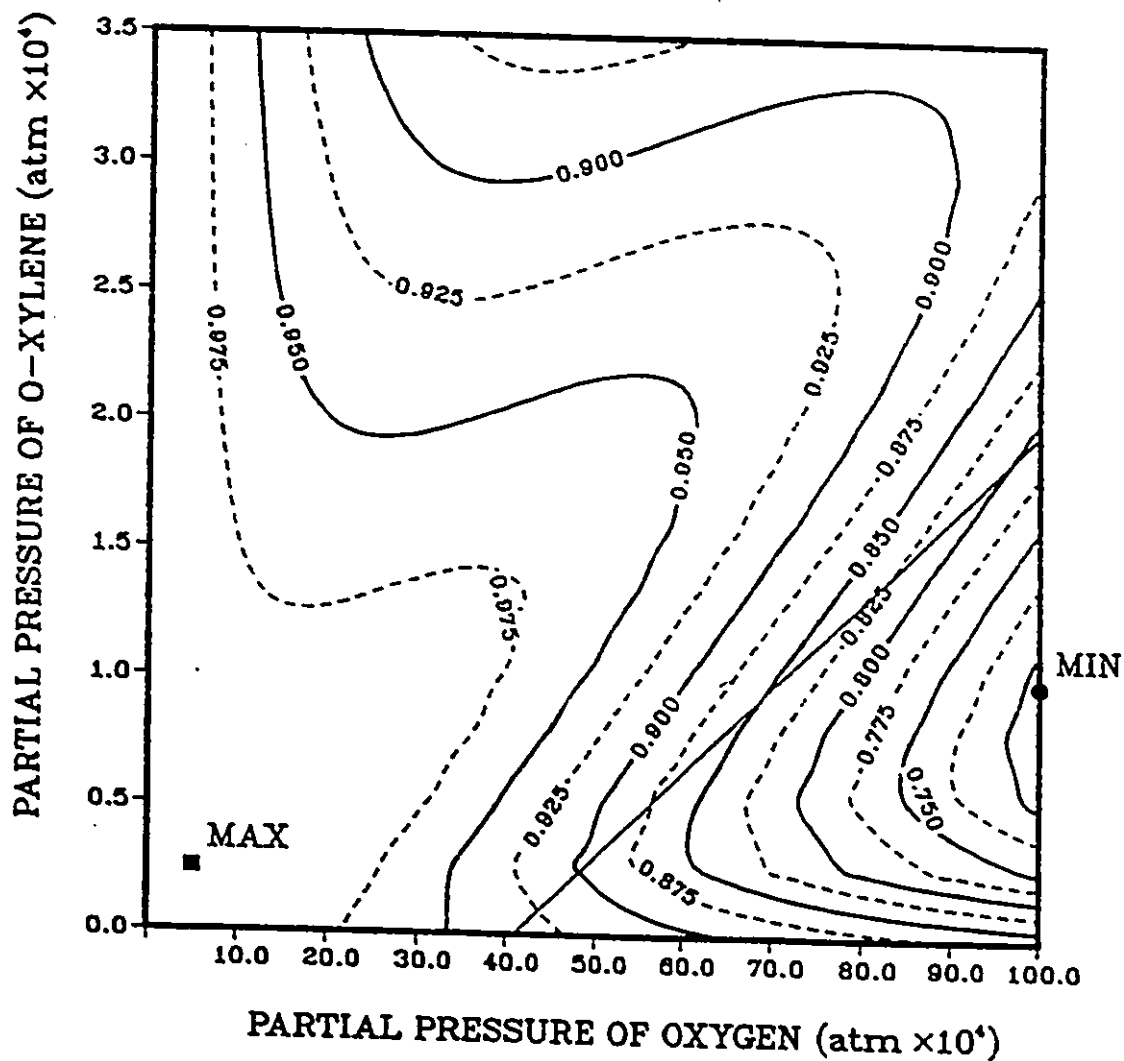


Figure 4.35: D-OPT design surface, Juusola, 300°C, Run1.

The D-OPT design surface with contours of constant predicted volume of the confidence region as a function of the operating variables. The surface is scaled to show the predicted volume as a fraction of the initial volume.

The minimum appears to be near  $(pO_2, pO\text{-xylene}) = (0.0070, 0.0001)$  in Figure 4.34 rather than that indicated in Figure 4.33. This run location was not chosen due to the coarseness of the search grid used to cover the restricted operating region (a much finer grid was used to generate Figure 4.34). The PEC surface is extremely flat, a maximum reduction of only 8% of  $\Gamma^{TR}$  is predicted over the feasible operating region while the unrestricted surface predicts a reduction of 25%. The D-OPT surface is also extremely flat, with a predicted reduction of 20% of the volume of the linear approximate confidence region when the operating constraint is observed. The Jaswal and Juusola model/data sets had similar initial degrees of parameter effects nonlinearity and the same model was used by both workers. Simulations with the Jaswal model were successful at reducing the extent of nonlinearity with all three designs at all three temperature levels while simulations with the Juusola model were successful at only one temperature. However no information regarding operating constraints was available for the Jaswal data set. If there were any constraints, reductions of  $\Gamma^{TR}$  and improvements of parameter precision may not have been so large.

The topologies of the PEC design surface suggests an alternative run location rather than the global minimum. The greatest reduction of  $\Gamma^T$  was approximately 8% for the first designed run. The local minimum at (30,3.5) predicts a similar reduction but  $\Gamma^T$  is less sensitive to the operating conditions at this point. If stringent control of the operating variables were not expected at the global minimum the predicted reduction of  $\Gamma^T$  would not be obtained.

At 300°C the D-optimal designed runs from this work agree with those chosen by Juusola. However only one PEC designed run location was common to the D-optimal design. The unique D-optimal location (also chosen by the SSB-C design) was located at (0.0010,0.00035), which was a maximum on the PEC surface at 300°C. The D-OPT and SSB runs designed at this location resulted in increasing  $\Gamma_S^{TR}$ .

Tan made extensive use of the D-optimal design in his work. Figure 4.36 shows the location of the original data and the designed run locations obtained with the three control design criteria in this work at 350°C. The designed runs in the original work were all located near  $(pO_2, p\text{Propylene}) = (8.0, 1.0)$ . The two runs near (7.0,6.5) were also designed at the former location but the local minimum was used as an

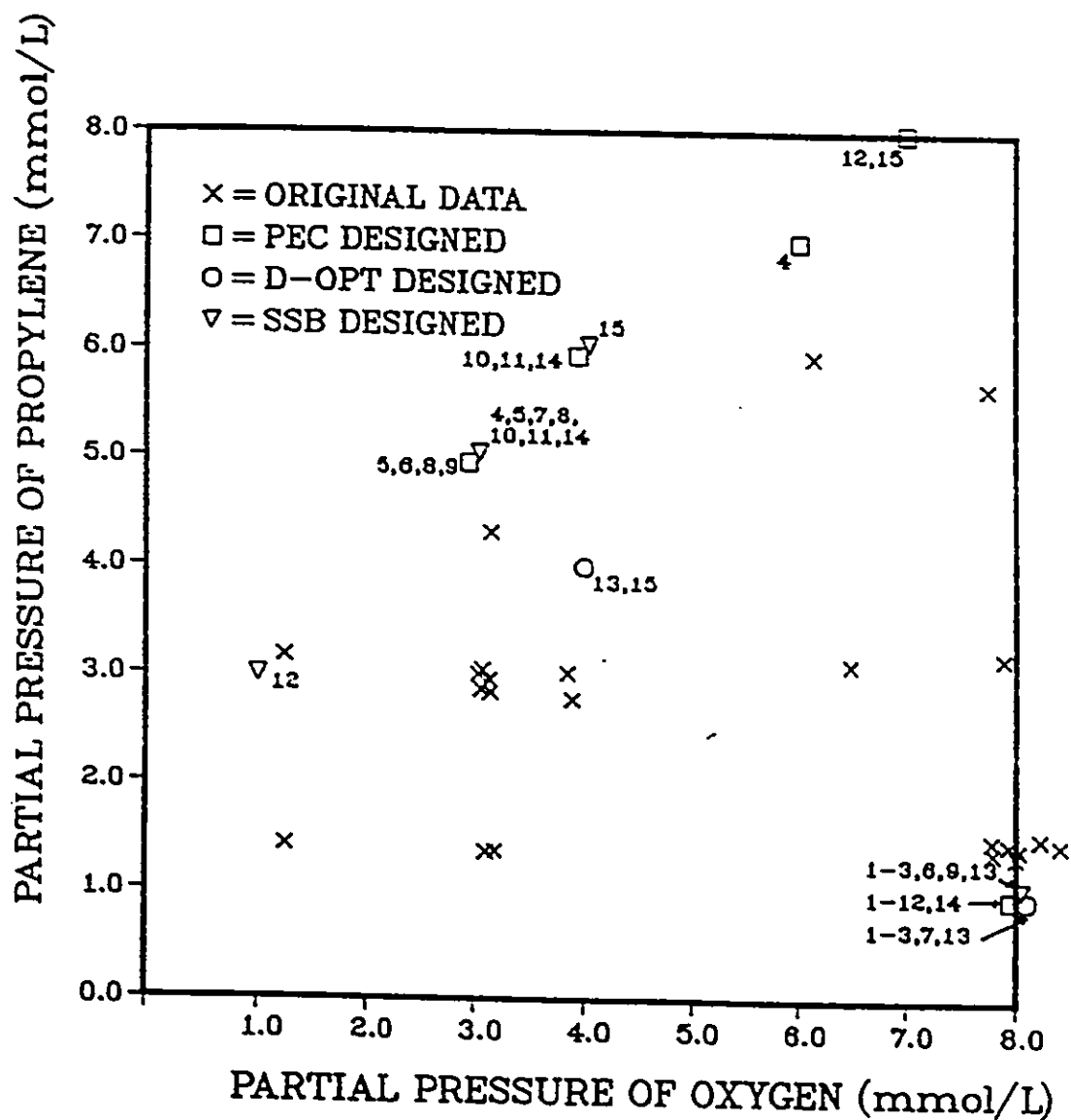


Figure 4.36: Designed runs for Tan, 350°C.

Shown are the conditions under which the original data was obtained and the location and sequence of the designed run locations for the PEC-C, D-OPT-C and SSB-C design criteria.

alternative to provide better coverage of the operating region. In this work all but two of the D-optimal runs were designed at (8.0,1.0), the exceptions being at (4.0,4.0). PEC-C and SSB-C runs were also predominantly designed at (8.0,1.0) and others at (1.0,3.0), (3.0,5.0), (4.0,6.0) and (7.0,8.0).

The PEC design surface, Figure 4.37, offers an explanation of the numerous PEC and SSB run locations. There are two maxima and minima, the global minima occurring at (8.0,0.33). However one of the operating constraints was a minimum concentration of 1 mmol/L for either reactant, hence the minimum chosen was (8.0,1.0). A local minimum was found in an elongated valley, running parallel to an operating constraint. This valley also contained the numerous run locations for the PEC and SSB designs.

The D-optimal, Figure 4.38, and PEC surfaces are very similar. They have local maxima at (1.0,8.0) and a ridge running roughly parallel to a propylene concentration of 1-2 mmol/L. The global minima are both located at (0.0,0.33) (which is in the constrained region) as well as a broad valley running parallel to the  $p_{\text{Prop}}=p_{\text{O}_2}$  line. The D-optimal and PEC designs appear to be compatible for this model/data set. In Section 4.3 the D-optimal simulated designs never resulted in increasing  $\Gamma^{TR}$ .

#### 4.4.1 Summary

The previous Section comparing the performance of the D-optimal, PEC and SSB designs suggested that the designs would be incompatible in some cases, while in others they would be. This was confirmed after comparing designed run locations and the design surfaces for the PEC and D-optimal criteria. The PEC, SSB and D-OPT designs often resulted in similar run locations. These run locations were minima on contour plots of the design surfaces. These plots also revealed obvious incompatibilities of the PEC and D-OPT designs; minima for one design coinciding with maxima for the other.

By using contour plots of the design surface, alternative run locations at local minima may be preferred to global minima. This situation would arise when the design criterion is sensitive to the operating conditions at the global minimum but relatively insensitive at a local minimum. A small sacrifice in terms of efficiency

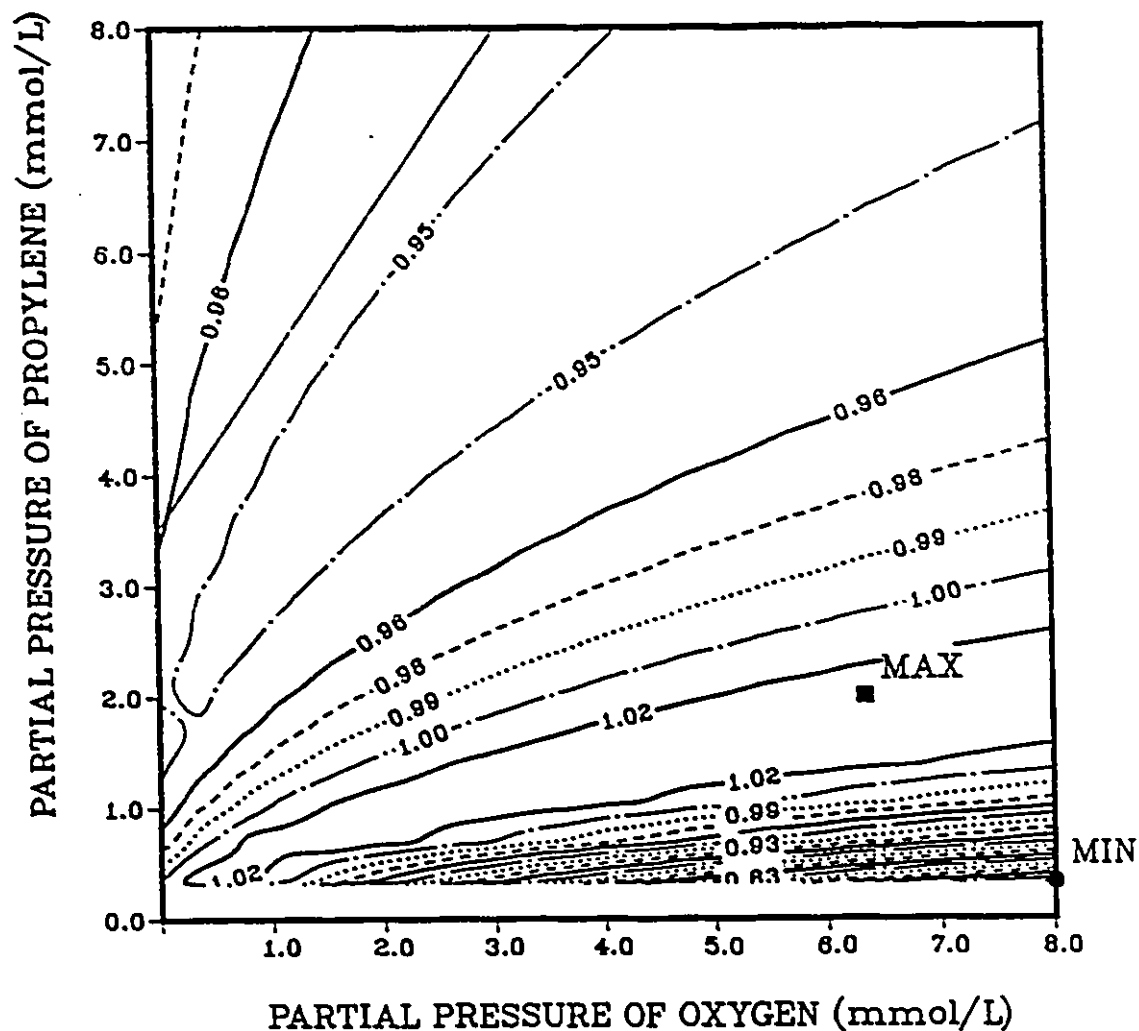


Figure 4.37: PEC design surface, Tan, 350°C, Run1.

The PEC design surface with contours of constant predicted parameter effects curvature as a function of the operating variables. The surface is scaled to show the predicted parameter effects curvature as a fraction of the initial curvature.



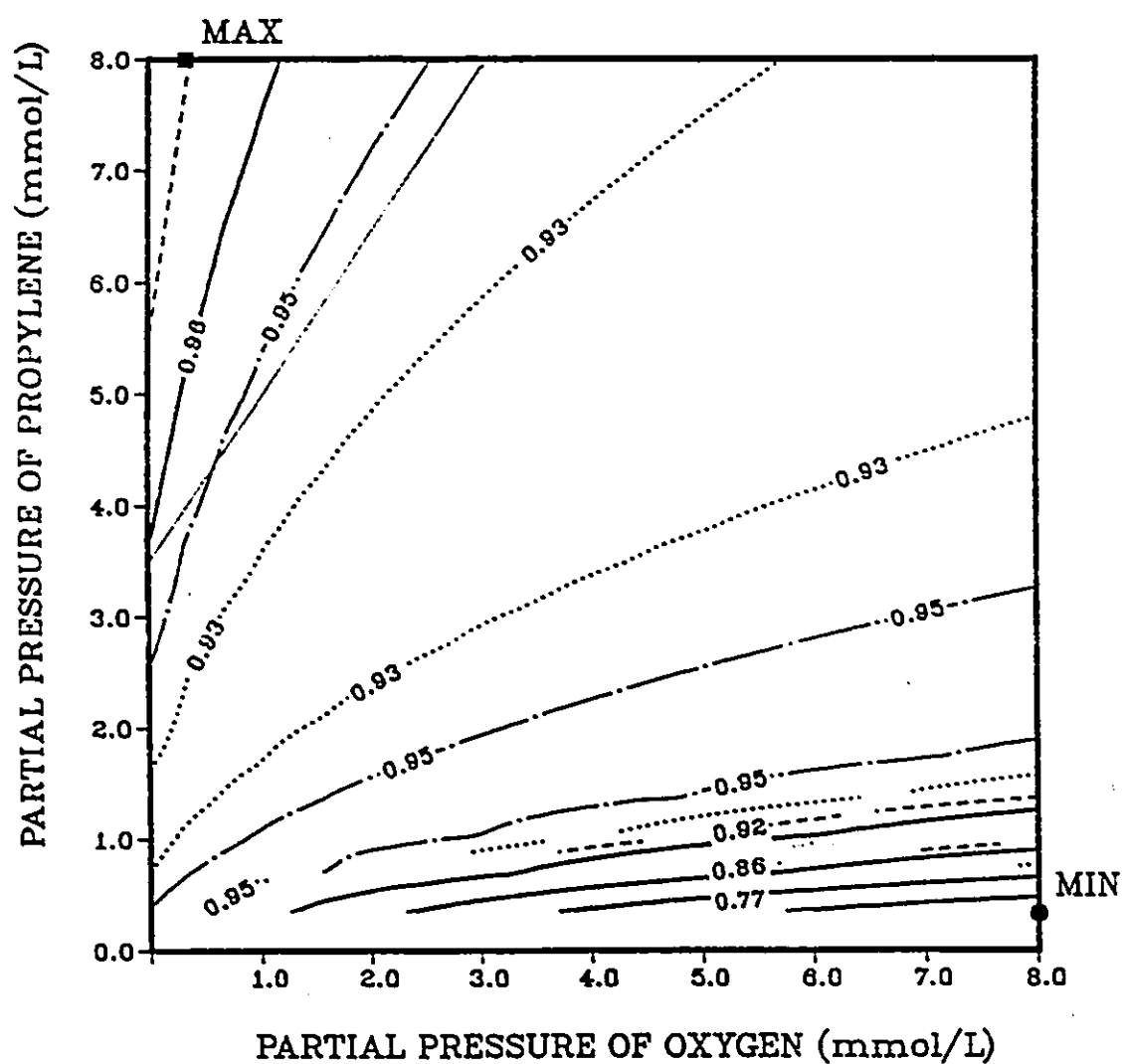


Figure 4.38: D-OPT design surface, Tan, 350°C, Run1.

The D-OPT design surface with contours of constant predicted volume of the confidence region as a function of the operating variables. The surface is scaled to show the predicted volume as a fraction of the initial volume.

could be made for a reliable improvement. An alternate run location would also be warranted if the local minima for both the D-optimal and PEC (or minimum nonlinearity) designs coincided.

The PEC design surface revealed that the extent of nonlinearity can also increase over a considerable portion of the operating region. Performing an undesigned run, for checking model adequacy or checking catalyst activity, may negate the progress obtained with earlier experiments. Simulations and contour plots obtained before entering the experimental stage would allow the experimenter to select a PEC or D-OPT run location as a standard run location for checking catalyst activity.

The use of both stochastic and deterministic simulations showed that the three design criteria are robust with respect to the effect of the random errors and changing parameter estimates on the designed run locations. This was particularly evident with the Ayen and Peters model/data set for which parameter estimates were most unstable.

## Chapter 5

# Conclusions and Recommendations

### 5.1 Conclusions

Two designs were developed for the reduction of the extent of nonlinearity of a non-linear model/data set. The parameter-effects curvature (PEC) and sum of squares of biases (SSB) design criteria, based on the Bates and Watts [1] relative curvatures and Box's bias [2] respectively, successfully reduced the nonlinearity in simulated sequentially designed experiments. Measures of nonlinearity were considered as potential design criteria. Of these:

- Beale's [4] measures of nonlinearity were not considered because of excessive computational demands, inaccuracies with highly nonlinear model/data sets and the lack of a test for significant nonlinearity.
- Ratkowsky's [3] sampling properties were also too demanding computationally. While test's for significant nonlinearity were available for the four measures, there was no apparent suitable method for assimilating the measures into a design criterion.
- Lowry's [3] measure of bias lacked a test statistic and was excessively demanding computationally. Techniques which may reduce the computational effort recently reported [16] but were not studied in this work.

- Box's bias lacked a test statistic but was extremely simple to calculate. The measure was also known to be related to the Bates and Watts relative curvatures, and, as such, the measure was studied as a potential design criterion.
- The Bates and Watts relative curvatures were shown to be reliable, if overly strict, indicators of nonlinearity in the literature and a test statistic was available. Computational effort was acceptable. The two measures of curvature were easily incorporated into a design strategy. Priority was given to reduction of the intrinsic curvature, followed by reduction of the parameter-effects curvature.

Evaluation of the measures of nonlinearity for use as design criteria required that they accurately indicate the extent of nonlinearity. Lowry's and Beale's measures were not studied in this work and Ratkowsky's sampling properties were limited to evaluation of the initial data sets. The curvatures and Box's bias were evaluated for the initial data sets and after each simulated experiment. Comparisons of linear approximate-shape and exact-shape confidence regions revealed that:

- Box's bias and the test for significant nonlinearity ( $< 1\%$ ) are not accurate. The bias itself may be accurate when the diagonal elements of  $A_{..}^T$ , which are used to calculate the bias, dominate. The test statistic however is inadequate as it does not account for the size of the data set, number of parameters nor a level of significance. The bias consistently underestimated the extent of nonlinearity.
- The curvatures and the test statistic were conservative, reliable measures of nonlinearity. The curvatures correctly predicted when the linear approximate-shape confidence regions provided poor coverage of the exact-shape confidence regions. In some cases the curvatures and/or test statistic were considered overly conservative. Similar observations were made by Donaldson and Schnabel [19] and Cook and Witmer [28].
- Reductions of nonlinearity with simulated experiments, as indicated by reductions of  $\Gamma^T$  and the bias, were confirmed by the improved coverage provided by the linear approximate-shape confidence regions.

Simulated, sequentially designed experiments were used to evaluate and compare the effectiveness of the PEC, SSB and D-optimal design criteria in reducing the extent of nonlinearity. The following observations were made during these simulations:

- The PEC design was the most effective at reducing  $\Gamma^T$ , as would be expected.
- The SSB design was also effective at reducing  $\Gamma^T$ , often nearly matching the performance of the PEC design.
- The SSB design usually resulted in designed run locations similar to the PEC design. Such similarities in the designs occurred when the parameter-effects portion of the acceleration array ( $A_{..}^T$ ) was dominated by the diagonal elements. These elements are known to be scaled versions of Box's bias, on which the SSB design is based.
- The D-optimal design was also usually effective in reducing nonlinearity. The design shared run locations with the PEC and SSB designs. However, some run locations were unique to the D-optimal design, resulting in very small reductions, or even increases, of  $\Gamma^T$ . This incompatibility of the designs is of importance to the experimenter, indicating that priority should be given to a minimum nonlinearity design. The D-optimal design is flawed because it is based on invalid linear approximations of a nonlinear model/data set.
- With highly nonlinear model/data sets, extremely high reductions of  $\Gamma^T$  were obtained with the initial designed runs with all the design criteria. Reductions of  $\Gamma^T$  decreased asymptotically as the number of designed runs increased. Simulations would prove valuable in an experimental modelling study before actually undertaking an experimental design. Information would be obtained regarding the expected degree of nonlinearity that could be achieved with a given number of experiments. In this work, simulations revealed that an unacceptable number of designed experiments would be required to reduce the nonlinearity to an acceptable level, but that large reductions could still be achieved. Expanded regions of operation could also be evaluated for potential gains in reduction of nonlinearity.

- Parameter and variance estimates were unstable in the stochastic simulations with some model/data sets when large simulated random errors were encountered. This made comparisons of the design criteria difficult. The parameter-effects curvature, which is scaled using the estimated variance, was particularly sensitive to these large errors. Scaling  $\Gamma^{TR}$  to  $\Gamma_S^{TR}$  to eliminate the effect of changing variance estimates was not entirely successful due to changing parameter estimates. This led to use of "control" simulations in which the parameter and variance estimates obtained with the initial data sets were used throughout the experimental design.

Improving parameter precision is always a primary concern in modelling. As such, the effect of the three design criteria on parameter precision was also studied. The following observations were made:

- The D-optimal design was the most effective at improving parameter precision, as measured by the volume of the linear approximate confidence region.
- The SSB design was usually more effective than the PEC design at improving parameter precision, although they were always nearly identical. Both designs compared well with the D-optimal design.
- Due to the nature of the measure of parameter precision, improvements will always be obtained, regardless of the operating conditions. In a situation where the improvement of parameter precision was given priority, if a D-optimal run would increase the nonlinearity, a minimum nonlinearity design should be given serious consideration instead. This would still provide an improvement in parameter precision and not increase the nonlinearity. Comparisons of the design surfaces would be useful in selecting alternate run locations in such situations.
- Contour plots of the design surface reveal the sensitivity of the design criteria to the operating conditions. Alternate run locations, other than the global optimum, could be chosen if the design is very sensitive to the operating conditions and tight operating control cannot be accomplished.

## 5.2 Recommendations

Gas-solid catalytic rate model/data sets from four studies were used in this work. One model was of the Hougen-Watson type while the remaining three were steady state adsorption models, one model being used in two of the studies. While the conclusions stated earlier are expected to apply to any model/data set, it would be desirable to apply the PEC and SSB design criteria to other catalytic rate models as well as nonlinear models in general. This would allow

- further comparisons of the PEC, SSB and D-optimal designs and their ability to reduce the extent of nonlinearity and improve parameter precision.
- evaluation of the relative curvatures as measures of nonlinearity based on comparisons of linear approximate-shape and exact-shape confidence regions.

Numerous questions were raised during this work but could not be fully covered. Further work should address the following points:

- Comparisons of the design surface were made for the PEC and D-optimal criteria. Comparisons should also be made with the SSB design surface. This would allow comparing the PEC and SSB surfaces when  $A_{..}^T$  is dominated by the diagonal elements, suggesting that the surfaces should be similar. The intrinsic curvature surface should also be compared to the other designs.
- The D-optimal design has been shown to be misleading in certain cases, Hamilton [10], because it does not account for nonlinearity effects. The quadratic D-optimal design does account for nonlinearity effects, comparisons of the design surface for this design should be made with the PEC, SSB, INC and normal D-optimal design.
- Box's bias has been shown to be an element of  $A_{..}^T$ , Bates and Watts [1]; it can be regarded as a simple but incomplete measure of parameter effects curvature. As such a more reliable test statistic for significant parameter bias could be developed from Bates' and Watts' own test statistic for the relative curvatures. This bias measure and test statistic would be reliable when  $A_{..}^T$  is dominated by the diagonal elements.

- In comparing linear approximate-shape confidence regions, a question was raised regarding which type of nonlinearity, intrinsic or parameter effects, had the greater effect on inferences. The design surface could be searched for a run location which would reduce one type of nonlinearity while not appreciably changing the other. Comparisons of the confidence regions would be used to evaluate which curvature had a greater effect on inferences. This would be facilitated by using a digitizer to obtain the coverage of the exact-shape region.

The intrinsic nonlinearity was acceptable for all the model/data sets used in this work and has rarely been found to be significant in the literature. As such there is no way of evaluating the effectiveness of the INC design criteria or its compatibility with any of the other designs.

Different intrinsic curvatures were obtained for a given model/data set with different parameterizations. Given the definition of a parameterization this should not have been the case. Using different starting vectors to pre and post multiply the intrinsic curvature portion of the acceleration array led to different converged values for  $\Gamma^N$ . Convergence to the true maximum curvature was tested in this work by using  $p$  unit vectors. Simulations with the non-isothermal form of several of the models lead to cases where convergence to a maximum curvature could not be obtained with any of the starting vectors with 1000 iterations. Further work should be directed to studying the multiple maxima of the relative curvatures and the failure to converge at all.

This work involved only simulated experiments using existing model/data sets as starting points. While simulations are indispensable for initial studies of the design criteria it is most desirable to apply the PEC or the SSB design criteria to an experimental modelling study in progress.



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## Appendix A

### Bates and Watts Relative Curvatures

The following discussion on the relative curvatures of Bates and Watts is taken from Bates' Ph.D thesis [30] and Bates and Watts [1] as those author's expressed the derivations clearly as concisely. Their notation was kept as closely as possible.

A nonlinear model can be approximated with a linear approximation at a fixed set of parameters,  $\theta_0$ , and is given by

$$\eta(\theta) \approx \eta(\theta_0) + \sum_{i=1}^p (\theta_i - \theta_{i,0}) v_i \quad (\text{A.1})$$

where

$$v_i = \begin{bmatrix} \frac{\partial f(x_1, \theta)}{\partial \theta_i} \\ \vdots \\ \frac{\partial f(x_n, \theta)}{\partial \theta_i} \end{bmatrix} \quad (\text{A.2})$$

The effect of the linearization is to replace the solution locus by a tangent plane at  $\eta(\theta_0)$  and the coordinate system with a uniform coordinate system. The model maps the parameter vector  $\theta$  onto a  $p$  dimensional surface (the solution locus) in the  $n$  dimensional space. If a point  $\theta_0$  in parameter space maps to a point  $\eta(\theta_0)$  on the solution locus, then a line in parameter space through  $\theta_0$  will map onto a curve on the solution locus through  $\eta(\theta_0)$ . An arbitrary line through parameter space is given by

$$\theta(b) = \theta_0 + b h \quad (\text{A.3})$$

where  $b$  is a geometric parameter and  $h$  is any  $p \times 1$  non-zero vector. This maps onto a curve, or "lifted line",  $\eta_h(b)$  on the solution locus where

$$\eta_h(b) = \eta(\theta_0 + bh) \quad (\text{A.4})$$

The tangent to the curve  $\eta_h$  at  $b = 0$  is

$$\dot{\eta}_h = \frac{\partial \eta_h}{\partial b} \big|_0 = \sum_{i=1}^p \frac{\partial \eta}{\partial \theta_i} \big|_{\theta_{i,0}} \frac{\partial \theta_i}{\partial b} \big|_0 = \sum_{i=1}^p v_i h_i = V \cdot h \quad (\text{A.5})$$

where

$$v_i^T = \left( \frac{\partial \eta}{\partial \theta_i} \right)^T = \left[ \frac{\partial \eta_1}{\partial \theta_i}, \frac{\partial \eta_2}{\partial \theta_i}, \dots, \frac{\partial \eta_n}{\partial \theta_i} \right] \quad (\text{A.6})$$

and

$$V = [v_1, v_2, \dots, v_p] \quad (\text{A.7})$$

The tangent vector to  $\eta$  is therefore a linear combination of the vectors  $v_i$  and the set of all possible combinations is the tangent plane at  $\eta(\theta_0)$ .

The acceleration of the lifted line  $\eta_h$  is also a linear combination of vectors determined by the model parameters. The second partial derivatives are given by

$$v_{ij} = \frac{\partial^2 \eta}{\partial \theta_i \partial \theta_j} \big|_{\theta_0} \quad (\text{A.8})$$

which are  $n \times 1$  vectors which can be collected in the  $n \times p \times p$  matrix  $V_{..}$ . The second derivative of  $\eta_h(b)$  at  $b = 0$  can be written

$$\ddot{\eta}_h = \frac{\partial^2 \eta_h}{\partial b^2} \big|_0 = \sum_{i=1}^p \sum_{j=1}^p v_{ij} h_i h_j = h^T V_{..} h \quad (\text{A.9})$$

If a point is moving in sample space, Fig. A.1, and is at  $\eta_h(b)$  at "time"  $b$  then the vectors  $\dot{\eta}_h$  and  $\ddot{\eta}_h$  can be interpreted as the instantaneous velocity and acceleration of the point at  $b = 0$ . The acceleration vector  $\ddot{\eta}_h$  is composed of three components

$$\ddot{\eta}_h = \ddot{\eta}_h^N + \ddot{\eta}_h^P + \ddot{\eta}_h^G. \quad (\text{A.10})$$

The normal acceleration  $\ddot{\eta}_h^N$  determines the change in direction of the vector  $\dot{\eta}_h$  normal to the tangent plane. The geodesic acceleration  $\ddot{\eta}_h^G$  determines the change in direction of the vector  $\dot{\eta}_h$  parallel to the tangent plane. The parallel component  $\ddot{\eta}_h^P$  determines the change in speed of the moving point and therefore determines whether the point moves uniformly across the solution locus.

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Figure A.1: Solution Locus and Acceleration Components

A "point" on the solution locus at  $\eta(\theta)$  has an instantaneous velocity and acceleration of magnitude and direction given by  $\dot{\eta}_h$  and  $\ddot{\eta}_h$  respectively. The acceleration has three normal components. The component normal to the solution locus,  $\ddot{\eta}_h^N$ , determines the curvature of the solution locus and the intrinsic nonlinearity. The two remaining acceleration components are on the same plane as  $\dot{\eta}_h$ , tangent to  $\eta(\theta)$ . The geodesic acceleration,  $\ddot{\eta}_h^G$ , determines the change in direction of  $\dot{\eta}_h$  parallel to the tangent plane while  $\ddot{\eta}_h^P$  determines the change in speed.

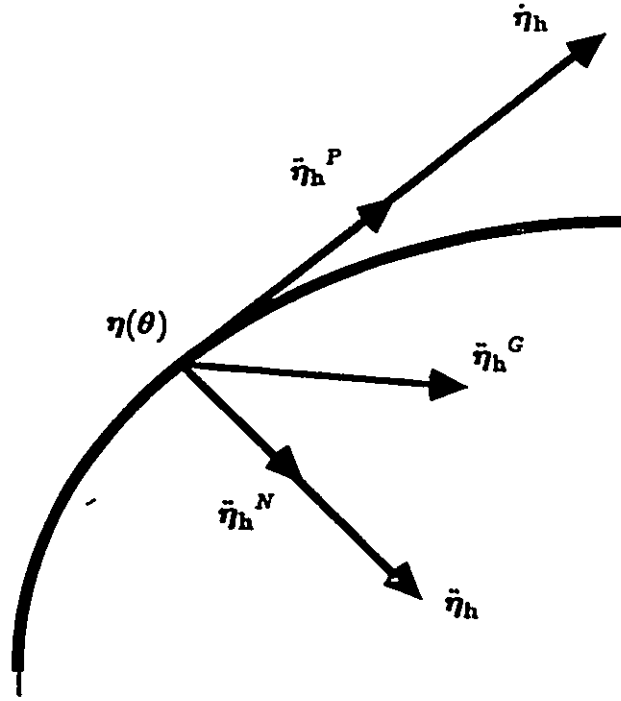


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The acceleration components can be converted to curvatures as

$$K_{\beta}^N = \frac{\|\ddot{\eta}_h^N\|}{\|\dot{\eta}_h\|^2} \quad (\text{A.11})$$

which gives the normal curvature in the direction  $h$ . The normal curvature can be interpreted as the inverse of the radius of a circle which best approximates the solution locus in the direction  $\dot{\eta}_h$  at  $\theta_0$ . The tangential acceleration components are combined in a total tangential acceleration and converted to a curvature as

$$K_h^T = \frac{\|\ddot{\eta}_h^T + \ddot{\eta}_h^G\|}{\|\dot{\eta}_h\|^2} \quad (\text{A.12})$$

The curvatures are converted to standardized relative curvatures (using the standard radius  $\rho$ ) which are invariant under changes of scale of the response. The standard radius

$$\rho = \sigma\sqrt{p} \quad (\text{A.13})$$

is a convenient scaling factor because in the linear case the confidence region is given by  $\theta$  such that

$$\|\eta(\theta) - \eta(\hat{\theta})\|^{\frac{1}{2}} \leq \rho\sqrt{F_{p,\nu,\alpha}} \quad (\text{A.14})$$

which is equivalent to the region described by Eq. 2.18 in Section 2.3. The intrinsic and parameter effects curvatures respectively are then defined by

$$\gamma_h^N = K_h^N \rho \quad (\text{A.15})$$

$$\gamma_h^T = K_h^T \rho \quad (\text{A.16})$$

For the intrinsic effects the relative curvature can be regarded as a ratio of the radii of the standard radius and the radius of curvature of the solution locus. So, when the relative curvature is large then the radius of the solution locus is small compared to the standard radius, i.e. the solution locus is highly curved. The value  $\frac{1}{\sqrt{F}}$  can be regarded as the radius of curvature of the 100(1 -  $\alpha$ )% confidence region. If, for all directions  $h$ ,  $\gamma_h^N$  is small then the solution locus is fairly flat over the confidence region disc. The same argument applies to  $\gamma_h^T$  and the validity of assuming a uniform coordinate system for  $\theta$ .

In practice the curvatures are calculated using scaled data;  $Y$ ,  $\eta$ ,  $V$ , and  $V_{..}$  are divided by the standard radius. In the following derivations this is assumed



to have been done. Calculating the curvatures is greatly simplified by rotating the coordinates of sample space so the first  $p$  co-ordinate vectors are parallel to the tangent plane and the remaining  $n - p$  vectors are orthogonal to it. This is useful because in calculating the curvatures one has to determine the length of the components  $\bar{\eta}_h^T$  and  $\bar{\eta}_h^N$ . This is done by premultiplying all the vectors in sample space by the orthogonal matrix  $Q^T$  which is part of the QR decomposition of  $V_{..}$  (Businger and Golub [31]).

$$V_{..} = QR = Q \begin{matrix} \bar{R} \\ 0 \end{matrix} \quad (A.17)$$

where  $\bar{R}$  is  $p \times p$  and is upper triangular. The co-ordinates in the parameter space are transformed from  $\theta$  to

$$\phi = \bar{R}(\theta - \hat{\theta}) \quad (A.18)$$

so that the derivatives  $u_i$

$$u_i = \frac{\partial \eta}{\partial \phi} \Big|_{\phi=0} \quad (A.19)$$

are orthogonal unit vectors which are in fact the first  $p$  columns of  $Q$ . The second derivative vectors,  $u_{ij}$ , are given by

$$u_{ij} = \frac{\partial^2 \eta}{\partial \phi_i \partial \phi_j} \Big|_0 \quad (A.20)$$

where

$$L = \bar{R}^{-1} \quad (A.21)$$

so that

$$\theta = \hat{\theta} + L\phi. \quad (A.22)$$

The matrix of second derivatives in the  $\phi$  co-ordinates is

$$U_{..} = L^T V_{..} L \quad (A.23)$$

The coefficients, in terms of the rotated sample space co-ordinates, are determined in the acceleration array  $A_{..}$  by

$$A_{..} = [Q^T][U_{..}] = A_{..}^T \mid A_{..}^N \quad (A.24)$$

which is partitioned into  $A_{..}^T$  which is  $p \times p \times p$  and  $A_{..}^N$  which is  $p \times p \times n - p$ . In the  $\phi$  parameters, the lifted line  $\hat{\eta}_{Ld}$  has a length of 1 if  $d$  is a  $p \times 1$  unit vector.

Therefore the curvatures can be calculated directly as

$$\gamma_{Ld}^T = \| (d^T U_{..} d)^T \| = \| d^T A_{..}^T d \| \quad (A.25)$$

and

$$\gamma_{Ld}^N = \| (d^T U_{..} d)^N \| = \| d^T A_{..}^N d \| \quad (A.26)$$

The relative curvatures determined by Eq. A.15 and A.16 correspond to a particular parameter space direction  $h$ . The severity of the nonlinearity can be measured by the maximum relative curvatures, i.e. the curvatures obtained with  $d$  such that Eq. A.15 and A.16 are maximized. The initial direction  $d_i$  is updated by the gradient

$$g_i = \nabla(\gamma_d^N)^2 \mid d_i = 4[d_i^T A_{..}^N d_i][A_{..}^N d_i] \quad (A.27)$$

if

$$\bar{g}_i^T d_i < 1 - \epsilon \quad (A.28)$$

then  $d_{i+1}$  is updated to the gradient, otherwise the maximum relative curvature is determined by Eq. A.15. The initial starting direction for  $d$  suggested by Bates and Watts is  $d_0 = (0, 0, \dots, 1)^T$ . However convergence to false maximum curvatures has been observed in this work. To avoid this problem the  $p$  starting vectors pointing along each axis have been used in calculating each curvature.

The FORTRAN VS program used to calculate the maximum relative curvatures in this thesis is given in Appendix E. The bulk of the program was taken from Ratkowsky [3] and includes Box's bias and Ratkowsky's Monte Carlo simulations. The program was modified for this work to facilitate the sequential experimental design simulations and to help avoid convergence to false maximum curvatures.

## Appendix B

### Box's Bias

Box developed a quantitative measure of a parameter's bias in a nonlinear model. The measure was developed for the multiresponse case for  $n$  observations of all  $k$  responses having a known variance-covariance matrix for the responses given by

$$\sum_u = \{\sigma_{ij}^u\} \quad i, j = 1, 2, \dots, k \quad u = 1, 2, \dots, n \quad (\text{B.1})$$

$$= \begin{bmatrix} \sigma_{1,1} & \sigma_{1,2} & \dots & \sigma_{1,k} \\ \sigma_{2,1} & \sigma_{2,2} & \dots & \sigma_{2,k} \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{n,1} & \sigma_{n,2} & \dots & \sigma_{n,k} \end{bmatrix}^u \quad (\text{B.2})$$

This variance-covariance matrix is not that discussed in section 1.3 for the parameter estimates but describes the covariance structure of the observations and allows for different covariance structures for each run location. For this general case, the derivation of the biases is simplified by using the following  $nk \times 1$  vectors for the  $nk$  residuals, observations and predictions for a given  $\theta$

$$\begin{aligned} \epsilon &= \{\epsilon_1^T, \dots, \epsilon_n^T\}^T \\ &= \{\epsilon_{1,1}, \epsilon_{1,2}, \dots, \epsilon_{1,k}, \epsilon_{2,1}, \epsilon_{2,2}, \dots, \epsilon_{2,k}, \dots, \epsilon_{n,1}, \dots, \epsilon_{n,k}\} \\ Y &= \{Y_1^T, \dots, Y_n^T\}^T \\ f(\theta) &= \{f_1(x_1, \theta), \dots, f_k(x_1, \theta), \dots, f_1(x_n, \theta), \dots, f_k(x_n, \theta)\}^T \end{aligned} \quad (\text{B.3})$$

In this case the sum of squares of the residuals to be minimized

$$(Y - f(\theta))^T \Sigma^{-1} (Y - f(\theta)) \quad (\text{B.4})$$

or

$$\epsilon^T \Sigma^{-1} \epsilon \quad (\text{B.5})$$

where

$$\Sigma = \begin{bmatrix} \Sigma_1 & 0 & \dots & 0 \\ 0 & \Sigma_2 & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & \Sigma_n \end{bmatrix} \quad (\text{B.6})$$

The minimum SSR corresponds to the parameters  $\theta$  which satisfy

$$F(\hat{\theta})^T \Sigma^{-1} (Y - f(\hat{\theta})) = 0 \quad (\text{B.7})$$

where  $F(\hat{\theta})$  is the  $nk \times p$  matrix of first derivatives of  $f(\theta)$ . If  $\phi = \hat{\theta} - \theta$  denotes the discrepancy in the parameter estimates  $\hat{\theta}$ , then the vector of residuals can be written

$$Y - f(\hat{\theta}) = \epsilon - F(\hat{\theta})\phi - \frac{1}{2}G\phi \quad (\text{B.8})$$

The models are assumed to be adequately represented by their Taylor series expansion in powers of  $\phi$ , truncated after two terms with

$$G = (H_{1,1}\phi, \dots, H_{1,k}\phi, H_{2,1}\phi, \dots, H_{2,k}\phi, H_{n,1}\phi, \dots, H_{n,k}\phi)^T \quad (\text{B.9})$$

and  $H_{ui}$  is a  $p \times p$  matrix of second derivatives with respect to the parameters. Also

$$F(\hat{\theta}) = F(\theta) + G \quad (\text{B.10})$$

Suppose that the discrepancy in the parameter estimate is of the form

$$\phi = A\epsilon + q \quad (\text{B.11})$$

where  $q$  ( $p \times 1$ ) is a quadratic function of the random errors

$$q = (\epsilon^T B_1 \epsilon, \dots, \epsilon^T B_p \epsilon) \quad (\text{B.12})$$

and the matrix  $A$  is  $p \times nk$  and  $B$  is  $nk \times nk$ , which are all to be determined. With this assumed form the expectation of the discrepancy, the bias, is zero when the random errors have zero variance. Taking the expectation of Eq. B.11

$$E(\phi) = E(q) \quad (\text{B.13})$$

Using Eq.B.8 and B.7 in B.10, the following is obtained

$$(F + G)^T \Sigma^{-1} (\epsilon - F\phi - \frac{1}{2}G\phi) = 0 \quad (B.14)$$

where  $F(\theta)$  is now written as  $F$ . Eq.B.11 is substituted into Eq. B.14, the coefficients are equated to zero so that the expression is identically zero to the second order in the random errors  $\epsilon$ . From the linear term in  $\epsilon$

$$F^T \Sigma^{-1} (\epsilon - FA\epsilon) = 0 \quad (B.15)$$

from which

$$A = VF^T \Sigma^{-1} \quad (B.16)$$

where

$$V = (F^T \Sigma^{-1} F)^{-1} \quad (B.17)$$

The second order term in  $\epsilon$  is

$$F^T \Sigma^{-1} (Fq - \frac{1}{2}JA\epsilon) + J^T \Sigma^{-1} (\epsilon - FA\epsilon) = 0 \quad (B.18)$$

where  $J$  is the  $nk \times p$  matrix

$$J = (H_{1,1}A\epsilon, \dots, H_{1,k}A\epsilon, H_{2,1}A\epsilon, \dots, H_{2,k}A\epsilon, H_{n,1}A\epsilon, \dots, H_{n,k}A\epsilon) \quad (B.19)$$

Taking expectations of Eq. B.18 gives

$$F^T \Sigma^{-1} (-FE(q) - \frac{1}{2}m) = 0 \quad (B.20)$$

Where  $m$  is an  $nk \times 1$  vector

$$m = [tr(H_{11}V), \dots, tr(H_{1k}V), \dots, tr(H_{n1}V), \dots, tr(H_{nk}V)] \quad (B.21)$$

where  $tr(argument)$  denotes the trace of a matrix, the trace being the sum of the diagonal elements. In taking the expectation of Eq. B.18, the second term,  $J^T \Sigma^{-1} (\epsilon - FA\epsilon)$  is zero. Therefore, with Eq. B.13 and Eq. B.20 the bias is

$$E(\phi) = E(q) = -\frac{1}{2}VF^T \Sigma^{-1} m \quad (B.22)$$

which, when expanded with  $F$  as  $k \times p$  matrices of first derivatives for the  $v = 1, 2, \dots, n$  observations, becomes

$$E(\phi) = -\frac{1}{2} \left( \sum_{w=1}^n F_w^T \Sigma_w^{-1} F_w \right)^{-1} \sum_{u=1}^n F_u^T \Sigma_u^{-1} \begin{bmatrix} \text{tr}\{(\sum_{v=1}^n F_v^T \Sigma_v^{-1} F_v)^{-1} H_{u1}\} \\ \vdots \\ \text{tr}\{(\sum_{v=1}^n F_v^T \Sigma_v^{-1} F_v)^{-1} H_{uk}\} \end{bmatrix} \quad (\text{B.23})$$

The general expression for bias simplifies greatly for the single response case and further still for the single response constant variance case. The former reduces to

$$E(\phi) = -\frac{1}{2} \left( \sum_{w=1}^n \frac{F_w^T F_w}{\sigma_u^2} \right)^{-1} \sum_{u=1}^n \left( \frac{F_u^T}{\sigma_u^2} \text{tr} \left( \left( \sum_{v=1}^n \frac{F_v^T F_v}{\sigma_v^2} \right)^{-1} H_u \right) \right) \quad (\text{B.24})$$

where now each  $F_w$  is  $1 \times p$  and the  $p \times p$  matrices  $H_u$  no longer require a second suffix to indicate which response is being considered. The single response, homoscedastic case

$$E(\phi) = -\frac{\sigma^2}{2} \left( \sum_{w=1}^n F_w^T F_w \right)^{-1} \sum_{u=1}^n (F_u^T \text{tr} \left( \left( \sum_{v=1}^n F_v^T F_v \right)^{-1} H_u \right)) \quad (\text{B.25})$$

Again the reader is referred to the original paper by Box [2] for a more detailed discussion of the derivation (from which the above was taken) and examples. As mentioned earlier, Bates and Watts have shown that for the last and simplest case above, the bias for  $\theta_j$  is in fact a scaled average of the diagonal elements of the  $j^{\text{th}}$  face of their parameter effects portion of the acceleration array  $A_{..}^T$ . As such the bias is never actually calculated directly in the program presented in Appendix 3, but is determined from

$$E(\hat{\theta} - \theta) = \frac{-\sigma^2}{2s^2p} L \left( \sum_{i=1}^p a_{ii}^T \right) \quad (\text{B.26})$$

## Appendix C

# Ratkowsky's Monte Carlo Simulations

Ratkowsky [3] suggested a novel method for studying the nonlinearity of a model/data set. He used Monte Carlo simulations to obtain a large number of estimates of the parameters from which he obtained their sampling properties and compared them to the known sampling properties of the normal distribution. Recall that the parameters in a linear model are linear combinations of the normally distributed values of the response and so the parameters are normally distributed themselves. Then the degree of non-normal behavior of the parameters in a nonlinear model reflects the extent to which the parameters are nonlinear combinations of the response.

A large number of parameter estimates are obtained by performing nonlinear regressions on a large number of pseudo-random data sets. These data sets are generated from the model using the parameter and variance estimates,  $\hat{\theta}$  and  $\hat{\sigma}^2$ , obtained from the original data. These are the best available estimates of their true unknown values. The pseudo-random data sets are generated by adding a simulated random error,  $\epsilon_t$ , to the *predicted response*

$$y_t = f(\mathbf{x}, \theta) + \epsilon_t \quad (\text{C.1})$$

with  $\epsilon_t$  assumed to be normally distributed with mean zero and variance  $\sigma^2$ . Library routines which produce the required random numbers with normal distributions are widely available.

A random error is generated and added to each predicted response and then

the parameters re-estimated and stored. This procedure is repeated NSIM times. Ratkowsky suggests using NSIM= 1000, stating that misleading inferences can be made with fewer simulations. The idea of performing 1000 simulations may at first seem to be very demanding computationally. While the simulations do require a fair amount of computing (they are not at all suitable for microcomputers) the situation is not as bad as it may seem. The original parameter estimates used to generate the data are used as excellent initial estimates and so convergence may be obtained very quickly.

From the 1000 estimates of each parameter, the first four sample moments are calculated. The first moment is simply the average or mean and the second moment is the sample variance. The third and fourth moments are used to determine the skewness and kurtosis. The skewness is a measure of the distribution's symmetry and the kurtosis is a measure of the distribution's peakedness.

The  $k$ 'th moment is given by:

$$m^k = \sum_{i=1}^{NSIM} (\theta_i - \bar{\theta}_i)^k \times \frac{1}{NSIM} \quad (C.2)$$

where  $\bar{\theta}_i$  is the average value (first moment) for that parameter. The skewness  $g_2$  is given by

$$g_2 = \frac{m_3}{m_2^{3/2}} \quad (C.3)$$

and the kurtosis

$$g_1 = \frac{m_4}{m_2^2} \quad (C.4)$$

An estimate of the parameter's bias can be obtained from the first moment. It is simply the difference between the assumed true parameter's value and the mean obtained from the simulations. The bias

$$Bias(\theta_i) = \theta_i - m_1 \quad (C.5)$$

can also be expressed conveniently as a percent bias. This measure can be tested for significance using the true asymptotic variance of the parameter, given by the  $i$ 'th element of the variance-covariance matrix of Section 2.3. The bias corresponds to an approximate standard normal deviate of

$$stdnormdev = \frac{bias(\theta_i)}{\sqrt{\frac{var(\theta_i)}{1000}}} \quad (C.6)$$



This value can be compared to a  $t$  distribution for significant bias at the  $\alpha/2$  level. For significant bias:

$$\text{Probability} < 0.05 \text{ for } | \text{stdnormdev} | \text{ of } > 1.960 \quad (\text{C.7})$$

$$\text{Probability} < 0.01 \text{ for } | \text{stdnormdev} | \text{ of } > 2.576 \quad (\text{C.8})$$

The asymptotic variance is also used to test whether the sample variance is significantly in excess of the minimum variance of a linear model. If the model under study is nearly linear then the parameter variance estimates from the simulation study should be similar. If the model is nonlinear then the parameter sample variance will be greater than that obtained from the variance-covariance matrix. The sample variance can also be expressed as a percent excess variance. The statistic

$$\chi^2 = \frac{(999)(m_2)}{\text{Var}(\theta_i)} \quad (\text{C.9})$$

is distributed as chi-square with 999 degrees of freedom and can be transformed so as to be closely approximated by the standard normal distribution by

$$Z = \sqrt{2\chi^2} - \sqrt{2(999) - 1} \quad (\text{C.10})$$

which is compared to the normal distribution for significant excess variance:

$$\text{Probability} < 0.05 \text{ for } Z > 1.960 \quad (\text{C.11})$$

$$\text{Probability} < 0.01 \text{ for } Z > 2.576 \quad (\text{C.12})$$

The skewness for a normal distribution is zero and the sample skewness can be tested for non-normal behavior. For a large sample size the skewness is approximately normally distributed as  $N(0, \frac{6}{NSIM})$ . For  $NSIM = 1000$  the skewness is tested for significance as

$$\text{Probability} < 0.05 \text{ for } | g_1 | > 0.152 \quad (\text{C.13})$$

$$\text{Probability} < 0.01 \text{ for } | g_1 | > 0.200 \quad (\text{C.14})$$

The kurtosis is three for a normal distribution, hence the excess kurtosis is defined as:

$$g_2 = \frac{m_4}{m_2^2} - 3 \quad (\text{C.15})$$

which can be tested for significance as:

$$\text{Probability} < 0.05 \text{ for } |g_2| > 0.304 \quad (\text{C.16})$$

$$\text{Probability} < 0.01 \text{ for } |g_2| > 0.399 \quad (\text{C.17})$$

Ratkowsky also used histograms to depict the frequency of occurrence of the parameters obtained in the simulation study. While the histograms are a good visual aid, the statistics described are much more reliable and accurate. A difficulty arises in using the sampling properties. The analyst is presented with four statistics. The question is: what if all the statistics are not significant? Is a case of significant bias more serious than one of significant excess variance or skewness? Presumably if even one statistic is significant then the parameter must be assumed to behave non-normally. The FORTRAN VS routines needed for the simulation studies are included in Appendix E and have been taken from Ratkowsky [3].

# Appendix D

## Models and Data Sets

### D.1 Ayen and Peters, Reduction of NO to NH<sub>3</sub>

$$r_{NH_3} = \frac{kK_{H_2}P_{H_2}}{(1 + K_{H_2}P_{H_2} + K_{NO}P_{NO})}$$

| Temp | $k$                    | % Bias | $K_{NO}$ | % Bias | $K_{H_2}$ | % Bias | $r^{NR}$ | $r^{TR}$ |
|------|------------------------|--------|----------|--------|-----------|--------|----------|----------|
| 425. | $3.014 \times 10^{-4}$ | 1.28   | 11.87    | 4.01   | 18.9      | 3.21   | 0.22     | 59.3     |
| 400. | $4.456 \times 10^{-4}$ | 21.34  | 10.66    | 1.84   | 5.18      | 5.59   | 0.24     | 434.4    |
| 375. | $7.178 \times 10^{-5}$ | 13.02  | 11.65    | 27.19  | 20.5      | 26.67  | 0.54     | 128.2    |

Table D.1: Summary of parameter estimates, Box's bias and the Bates and Watts relative curvatures.

| TEMP | $k$    | $K_{NO}$ | $K_{H_2}$ |
|------|--------|----------|-----------|
| 425  | 0.000  | -0.046   | -0.176    |
|      | -0.046 | -0.024   | 1.672     |
|      | -0.176 | 1.672    | 12.822    |
|      | 0.000  | -0.012   | -0.012    |
|      | -0.012 | -0.103   | -0.072    |
|      | 0.000  | -0.072   | 0.472     |
|      | 0.000  | 0.000    | -0.012    |
|      | 0.000  | -0.021   | -0.077    |
|      | -0.012 | -0.072   | 0.472     |
|      | 0.000  | -0.026   | -0.778    |
|      | -0.026 | -0.028   | 1.826     |
|      | -0.778 | 1.826    | 108.6     |
| 400  | 0.000  | -0.014   | -0.000    |
|      | -0.014 | -0.055   | 0.202     |
|      | 0.000  | 0.202    | -0.037    |
|      | 0.000  | 0.000    | -0.014    |
|      | 0.000  | -0.011   | -0.064    |
|      | -0.014 | -0.064   | 0.349     |
|      | 0.000  | -0.102   | -0.573    |
|      | -0.102 | -0.093   | 2.815     |
|      | -0.573 | 2.815    | 31.66     |
|      | 0.000  | -0.046   | 0.000     |
|      | -0.046 | -0.188   | 0.640     |
|      | 0.000  | 0.640    | -0.087    |
| 375  | 0.000  | 0.006    | -0.046    |
|      | 0.000  | -0.073   | -0.189    |
|      | 0.000  | -0.189   | 1.321     |

Table D.2: Parameter effects portion of the acceleration array,  $A_{..}^T$ .

| Parameter                  | Temp<br>°C | % Bias              | % Excess<br>Variance | Skewness | Excess<br>Kurtosis |
|----------------------------|------------|---------------------|----------------------|----------|--------------------|
| k                          | 425.       | 1.06**              | 16.1**               | 0.99**   | 1.93**             |
| K <sub>NO</sub>            | 425.       | 3.21**              | 8.8**                | 0.80**   | 1.11**             |
| K <sub>H<sub>2</sub></sub> | 425.       | 13.49**             | 11.8**               | 0.75**   | 0.94**             |
| k                          | 400.       | 27.3**              | 597.**               | 6.92**   | 81.0**             |
| K <sub>NO</sub>            | 400.       | -0.43 <sup>ns</sup> | 71.**                | -1.44**  | 6.29**             |
| K <sub>H<sub>2</sub></sub> | 400.       | 3.78**              | -2.88 <sup>ns</sup>  | 0.58**   | 0.90**             |
| k                          | 375.       | 36.3**              | 18675.**             | 26.7**   | 762.**             |
| K <sub>NO</sub>            | 375.       | 59.4**              | 1076.**              | 8.78**   | 116.2**            |
| K <sub>H<sub>2</sub></sub> | 375.       | 57.6**              | 1430.**              | 10.6**   | 176.1**            |

Table D.3: Summary of results of Ratkowsky's Monte Carlo simulations, *ns* not significant, \*  $P < 0.05$ , \*\*  $P < 0.01$ .

| DATA # | RATE OF REACTION<br>(gmole NO/g.cat.min) | pNO<br>atm | pH <sub>2</sub><br>atm | TEMP<br>°C |
|--------|------------------------------------------|------------|------------------------|------------|
| 1      | 0.0000176                                | 0.0500     | 0.00474                | 425.       |
| 2      | 0.0000414                                | 0.0500     | 0.01360                | 425.       |
| 3      | 0.0000766                                | 0.0500     | 0.02900                | 425.       |
| 4      | 0.0000971                                | 0.0500     | 0.04000                | 425.       |
| 5      | 0.0001140                                | 0.0500     | 0.05000                | 425.       |
| 6      | 0.0001267                                | 0.0269     | 0.05000                | 425.       |
| 7      | 0.0001241                                | 0.0302     | 0.05000                | 425.       |
| 8      | 0.0001153                                | 0.0387     | 0.05000                | 425.       |
| 1      | 0.0000116                                | 0.05000    | 0.00659                | 400.       |
| 2      | 0.0000186                                | 0.05000    | 0.01130                | 400.       |
| 3      | 0.0000310                                | 0.05000    | 0.02280                | 400.       |
| 4      | 0.0000414                                | 0.05000    | 0.03110                | 400.       |
| 5      | 0.0000516                                | 0.05000    | 0.04020                | 400.       |
| 6      | 0.0000658                                | 0.05000    | 0.05000                | 400.       |
| 7      | 0.0000872                                | 0.00696    | 0.05000                | 400.       |
| 8      | 0.0000822                                | 0.01000    | 0.05000                | 400.       |
| 9      | 0.0000835                                | 0.01530    | 0.05000                | 400.       |
| 10     | 0.0000740                                | 0.02700    | 0.05000                | 400.       |
| 11     | 0.0000693                                | 0.03610    | 0.05000                | 400.       |
| 12     | 0.0000679                                | 0.04320    | 0.05000                | 400.       |
| 1      | 0.0000135                                | 0.05000    | 0.00922                | 375.       |
| 2      | 0.0000105                                | 0.05000    | 0.01360                | 375.       |
| 3      | 0.0000136                                | 0.05000    | 0.01970                | 375.       |
| 4      | 0.0000169                                | 0.05000    | 0.02800                | 375.       |
| 5      | 0.0000189                                | 0.05000    | 0.02910                | 375.       |
| 6      | 0.0000223                                | 0.05000    | 0.03890                | 375.       |
| 7      | 0.0000278                                | 0.05000    | 0.04850                | 375.       |
| 8      | 0.0000338                                | 0.00918    | 0.05000                | 375.       |
| 9      | 0.0000333                                | 0.01840    | 0.05000                | 375.       |
| 10     | 0.0000318                                | 0.02980    | 0.05000                | 375.       |
| 11     | 0.0000299                                | 0.03780    | 0.05000                | 375.       |
| 12     | 0.0000300                                | 0.04910    | 0.05000                | 375.       |

Table D.4: Original experimental data of Ayen and Peters for the reduction of NO to NH<sub>3</sub>.

## D.2 Juusola, Oxidation of O-Xylene

$$r = \frac{k_a k_r C_O C_r}{(k_a C_O + n k_r C_r)}$$

| Temp | $k_a$                  | % Bias | $k_r$                  | % Bias | $\Gamma^{NR}$ | $\Gamma^{TR}$ |
|------|------------------------|--------|------------------------|--------|---------------|---------------|
| 300  | $8.546 \times 10^{-3}$ | 0.76   | $3.604 \times 10^{-4}$ | 0.15   | 0.13          | 3.21          |
| 290  | $6.937 \times 10^{-3}$ | 0.90   | $2.027 \times 10^{-4}$ | 0.22   | 0.18          | 2.86          |
| 270  | $4.062 \times 10^{-3}$ | 0.31   | $6.627 \times 10^{-5}$ | 0.08   | 0.0018        | 1.05          |

Table D.5: Summary of parameter estimates, Box's bias and the Bates and Watts relative curvatures.

| TEMP | $k_a$  | $k_r$  |
|------|--------|--------|
| 300  | 0.016  | -0.116 |
|      | -0.116 | 0.814  |
|      | 0.005  | -0.035 |
|      | -0.035 | 0.246  |
| 290  | 0.017  | 0.109  |
|      | 0.109  | 0.721  |
|      | -0.005 | -0.034 |
|      | -0.034 | -0.226 |
| 270  | 0.011  | 0.047  |
|      | 0.047  | 0.213  |
|      | -0.006 | -0.026 |
|      | -0.026 | -0.115 |

Table D.6: Parameter effects portion of the acceleration array,  $A_{..}^T$ .



| Parameter | Temp<br>°C | % Bias             | % Excess<br>Variance | Skewness           | Excess<br>Kurtosis |
|-----------|------------|--------------------|----------------------|--------------------|--------------------|
| $k_a$     | 300.       | 1.19**             | 2.89 <sup>ns</sup>   | 0.67**             | 0.88**             |
| $k_r$     | 300.       | 0.09 <sup>ns</sup> | -4.8 <sup>ns</sup>   | 0.15 <sup>ns</sup> | 0.05 <sup>ns</sup> |
| $k_a$     | 290.       | 0.53 <sup>ns</sup> | 7.36 <sup>ns</sup>   | 0.68**             | 0.93**             |
| $k_r$     | 290.       | 0.53**             | 1.29 <sup>ns</sup>   | 0.25**             | 0.01**             |
| $k_a$     | 270.       | 0.16 <sup>ns</sup> | -0.67 <sup>ns</sup>  | 0.26**             | 0.20 <sup>ns</sup> |
| $k_r$     | 270.       | 0.24 <sup>ns</sup> | 1.75 <sup>ns</sup>   | 0.07 <sup>ns</sup> | 0.07 <sup>ns</sup> |

Table D.7: Summary of results of Ratkowsky's Monte Carlo simulations, *ns* not significant, \*  $P < 0.05$ , \*\*  $P < 0.01$ .

| DATA | RATE OF OXIDATION<br>(gmole/g.cat.sec) $\times 10^3$ | O-XYLENE<br>mmol/L | O <sub>2</sub><br>mmol/L | NBAR<br>$\bar{n}$ | TEMP<br>°C |
|------|------------------------------------------------------|--------------------|--------------------------|-------------------|------------|
| 1    | 5.43                                                 | 1.91               | 50.7                     | 2.23              | 300.0      |
| 2    | 5.61                                                 | 1.87               | 50.2                     | 2.23              | 300.0      |
| 3    | 5.60                                                 | 1.92               | 50.5                     | 2.23              | 300.0      |
| 4    | 5.78                                                 | 1.88               | 50.6                     | 2.23              | 300.0      |
| 5    | 5.42                                                 | 2.01               | 50.0                     | 2.23              | 300.0      |
| 6    | 1.97                                                 | 3.50               | 10.0                     | 2.23              | 300.0      |
| 7    | 5.59                                                 | 2.02               | 50.5                     | 2.23              | 300.0      |
| 8    | 4.14                                                 | 3.49               | 30.6                     | 2.23              | 300.0      |
| 9    | 4.67                                                 | 1.98               | 50.2                     | 2.23              | 300.0      |
| 10   | 4.68                                                 | 2.01               | 50.4                     | 2.23              | 300.0      |
| 11   | 9.33                                                 | 2.45               | 100.7                    | 2.23              | 300.0      |
| 12   | 5.09                                                 | 1.87               | 49.9                     | 2.23              | 300.0      |
| 13   | 9.55                                                 | 2.53               | 100.0                    | 2.23              | 300.0      |
| 14   | 6.50                                                 | 3.46               | 49.6                     | 2.23              | 300.0      |
| 15   | 9.02                                                 | 2.53               | 100.0                    | 2.23              | 300.0      |
| 16   | 5.32                                                 | 1.99               | 50.2                     | 2.23              | 300.0      |
| 17   | 5.52                                                 | 3.57               | 39.9                     | 2.23              | 300.0      |
| 18   | 1.84                                                 | 1.96               | 10.7                     | 2.23              | 300.0      |
| 19   | 6.63                                                 | 3.53               | 49.9                     | 2.23              | 300.0      |
| 20   | 4.09                                                 | 1.00               | 50.3                     | 2.23              | 300.0      |
| 21   | 8.31                                                 | 2.05               | 90.6                     | 2.23              | 300.0      |
| 22   | 3.26                                                 | 1.99               | 25.1                     | 2.23              | 300.0      |
| 23   | 5.80                                                 | 2.77               | 49.9                     | 2.23              | 300.0      |
| 1    | 4.08                                                 | 2.01               | 57.0                     | 2.23              | 290.0      |
| 2    | 3.80                                                 | 2.01               | 55.2                     | 2.23              | 290.0      |
| 3    | 3.20                                                 | 2.02               | 55.1                     | 2.23              | 290.0      |
| 4    | 3.99                                                 | 1.86               | 55.1                     | 2.23              | 290.0      |
| 5    | 3.71                                                 | 2.02               | 55.4                     | 2.23              | 290.0      |
| 6    | 3.68                                                 | 1.99               | 55.3                     | 2.23              | 290.0      |
| 7    | 0.630                                                | 0.51               | 10.8                     | 2.23              | 290.0      |
| 8    | 3.33                                                 | 0.99               | 70.7                     | 2.23              | 290.0      |
| 9    | 3.22                                                 | 1.97               | 55.4                     | 2.23              | 290.0      |
| 10   | 4.13                                                 | 3.51               | 60.5                     | 2.23              | 290.0      |
| 11   | 3.44                                                 | 2.02               | 55.2                     | 2.23              | 290.0      |
| 12   | 5.43                                                 | 1.89               | 100.6                    | 2.23              | 290.0      |
| 13   | 3.72                                                 | 2.00               | 55.2                     | 2.23              | 290.0      |
| 14   | 2.29                                                 | 0.49               | 60.3                     | 2.23              | 290.0      |
| 15   | 5.63                                                 | 2.01               | 100.0                    | 2.23              | 290.0      |
| 16   | 4.90                                                 | 1.51               | 101.0                    | 2.23              | 290.0      |
| 17   | 5.95                                                 | 3.54               | 80.5                     | 2.23              | 290.0      |
| 18   | 3.52                                                 | 1.99               | 55.2                     | 2.23              | 290.0      |
| 19   | 2.24                                                 | 1.98               | 24.9                     | 2.23              | 290.0      |
| 20   | 1.98                                                 | 0.49               | 57.1                     | 2.23              | 290.0      |
| 21   | 4.63                                                 | 3.47               | 55.5                     | 2.23              | 290.0      |
| 22   | 3.70                                                 | 2.74               | 54.9                     | 2.23              | 290.0      |
| 23   | 2.58                                                 | 0.95               | 55.4                     | 2.23              | 290.0      |

| DATA | RATE OF OXIDATION<br>(gmole/g.cat.sec) $\times 10^8$ | O-XYLENE<br>mmol/L | O <sub>2</sub><br>mmol/L | NBAR<br>$\bar{n}$ | TEMP<br>°C |
|------|------------------------------------------------------|--------------------|--------------------------|-------------------|------------|
| 1    | 1.14                                                 | 2.00               | 50.4                     | 2.41              | 270.0      |
| 2    | 1.17                                                 | 2.00               | 50.5                     | 2.41              | 270.0      |
| 3    | 2.30                                                 | 3.51               | 101.0                    | 2.41              | 270.0      |
| 4    | 1.21                                                 | 0.49               | 101.0                    | 2.41              | 270.0      |
| 5    | 1.16                                                 | 2.00               | 50.2                     | 2.41              | 270.0      |
| 6    | 1.06                                                 | 0.50               | 103.0                    | 2.41              | 270.0      |
| 7    | 2.30                                                 | 3.61               | 104.0                    | 2.41              | 270.0      |
| 8    | 1.20                                                 | 1.90               | 49.9                     | 2.41              | 270.0      |
| 9    | 1.27                                                 | 0.50               | 101.0                    | 2.41              | 270.0      |
| 10   | 1.15                                                 | 0.50               | 101.0                    | 2.41              | 270.0      |
| 11   | 2.45                                                 | 3.51               | 100.0                    | 2.41              | 270.0      |

Table D.8: Original experimental data by Juusola for the oxidation of O-xylene.

## D.3 Jaswal, Oxidation of Benzene

$$r = \frac{k_a k_r C_O C_r}{(k_a C_O + n k_r C_r)} \quad (D.1)$$

| Temp | $k_a$                  | % Bias | $k_r$                  | % Bias | $\Gamma^{NR}$ | $\Gamma^{TR}$ |
|------|------------------------|--------|------------------------|--------|---------------|---------------|
| 400  | $2.487 \times 10^{-3}$ | 2.53   | $5.503 \times 10^{-4}$ | 0.26   | 0.42          | 3.22          |
| 375  | $1.127 \times 10^{-3}$ | 0.69   | $3.043 \times 10^{-4}$ | 0.07   | 0.24          | 1.18          |
| 350  | $5.570 \times 10^{-4}$ | 2.27   | $1.423 \times 10^{-4}$ | 0.13   | 0.34          | 2.92          |

Table D.9: Summary of the parameter estimates, Box's bias and the Bates and Watts relative curvatures.

| TEMP | $k_a$  | $k_r$  |
|------|--------|--------|
| 400  | 0.029  | -0.096 |
|      | -0.096 | 0.721  |
|      | 0.011  | -0.077 |
|      | -0.077 | 0.390  |
| 375  | 0.032  | -0.050 |
|      | -0.050 | 0.220  |
|      | 0.016  | -0.070 |
|      | -0.070 | 0.195  |
| 350  | 0.032  | 0.091  |
|      | 0.091  | 0.593  |
|      | -0.014 | -0.087 |
|      | -0.087 | -0.388 |

Table D.10: Parameter effects portion of the acceleration array,  $A_{..}^T$ .

Parameter effects portion of the acceleration array,  $A_{..}^T$ .

| Parameter | Temp<br>°C | % Bias             | % Excess<br>Variance | Skewness | Excess<br>Kurtosis |
|-----------|------------|--------------------|----------------------|----------|--------------------|
| $k_a$     | 400.       | 2.47**             | 13.47**              | 0.95**   | 2.62**             |
| $k_r$     | 400.       | 0.80**             | 9.38**               | 0.55**   | 0.55**             |
| $k_a$     | 375.       | 0.49 <sup>ns</sup> | -1.43 <sup>ns</sup>  | 0.18*    | 0.06 <sup>ns</sup> |
| $k_r$     | 375.       | 0.65**             | 1.68 <sup>ns</sup>   | 0.23**   | 0.07 <sup>ns</sup> |
| $k_a$     | 350.       | 1.94**             | 7.99 <sup>ns</sup>   | 0.70**   | 1.21**             |
| $k_r$     | 350.       | 0.87 <sup>ns</sup> | 5.43 <sup>ns</sup>   | 0.36**   | 0.46**             |

Table D.11: Summary of results of Ratkowsky's Monte Carlo simulations, *ns* not significant, \*  $P < 0.05$ , \*\*  $P < 0.01$ .

| DATA # | RATE OF REACTION<br>(gmole/g.cat.min) $\times 10^8$ | BENZ<br>(gmol/L) $\times 10^4$ | O <sub>2</sub><br>(gmol/L) $\times 10^4$ | NBAR<br>$\bar{n}$ | TEMP<br>°C |
|--------|-----------------------------------------------------|--------------------------------|------------------------------------------|-------------------|------------|
| 1      | 429.0                                               | 16.0                           | 19.1                                     | 6.1               | 400.0      |
| 2      | 475.0                                               | 23.5                           | 20.0                                     | 6.1               | 400.0      |
| 3      | 1129.0                                              | 132.8                          | 20.0                                     | 6.1               | 400.0      |
| 4      | 957.0                                               | 107.7                          | 20.0                                     | 6.1               | 400.0      |
| 5      | 745.0                                               | 68.5                           | 20.0                                     | 6.1               | 400.0      |
| 6      | 649.0                                               | 47.2                           | 19.7                                     | 6.1               | 400.0      |
| 7      | 742.0                                               | 42.5                           | 20.3                                     | 6.1               | 400.0      |
| 8      | 662.0                                               | 30.1                           | 20.0                                     | 6.1               | 400.0      |
| 9      | 373.0                                               | 11.2                           | 20.0                                     | 6.1               | 400.0      |
| 10     | 440.0                                               | 17.1                           | 20.0                                     | 6.1               | 400.0      |
| 11     | 662.0                                               | 65.8                           | 20.0                                     | 6.1               | 400.0      |
| 12     | 724.0                                               | 108.2                          | 20.0                                     | 6.1               | 400.0      |
| 13     | 915.0                                               | 123.5                          | 20.0                                     | 6.1               | 400.0      |
| 14     | 944.0                                               | 160.0                          | 20.0                                     | 6.1               | 400.0      |
| 15     | 713.0                                               | 66.4                           | 20.0                                     | 6.1               | 400.0      |
| 16     | 736.0                                               | 66.5                           | 20.0                                     | 6.1               | 400.0      |
| 1      | 229.0                                               | 23.3                           | 20.0                                     | 5.7               | 375.0      |
| 2      | 296.0                                               | 40.8                           | 20.0                                     | 5.7               | 375.0      |
| 3      | 547.0                                               | 140.3                          | 20.0                                     | 5.7               | 375.0      |
| 4      | 582.0                                               | 140.8                          | 19.9                                     | 5.7               | 375.0      |
| 5      | 480.0                                               | 141.2                          | 20.0                                     | 5.7               | 375.0      |
| 6      | 493.0                                               | 140.0                          | 19.7                                     | 5.7               | 375.0      |
| 7      | 513.0                                               | 121.2                          | 20.0                                     | 5.7               | 375.0      |
| 8      | 411.0                                               | 104.7                          | 19.7                                     | 5.7               | 375.0      |
| 9      | 349.0                                               | 40.8                           | 20.0                                     | 5.7               | 375.0      |
| 10     | 226.0                                               | 22.6                           | 20.0                                     | 5.7               | 375.0      |
| 11     | 338.0                                               | 55.2                           | 20.0                                     | 5.7               | 375.0      |
| 12     | 351.0                                               | 55.4                           | 20.0                                     | 5.7               | 375.0      |
| 13     | 295.0                                               | 29.5                           | 20.0                                     | 5.7               | 375.0      |
| 14     | 294.0                                               | 30.0                           | 20.0                                     | 5.7               | 375.0      |
| 15     | 233.0                                               | 16.3                           | 20.0                                     | 5.7               | 375.0      |
| 16     | 222.0                                               | 16.5                           | 20.0                                     | 5.7               | 375.0      |
| 17     | 188.0                                               | 20.4                           | 12.5                                     | 5.7               | 375.0      |
| 18     | 231.0                                               | 20.5                           | 16.6                                     | 5.7               | 375.0      |
| 19     | 239.0                                               | 20.8                           | 20.0                                     | 5.7               | 375.0      |
| 20     | 301.0                                               | 21.3                           | 30.0                                     | 5.7               | 375.0      |
| 21     | 252.0                                               | 19.6                           | 43.3                                     | 5.7               | 375.0      |
| 22     | 217.0                                               | 20.6                           | 20.0                                     | 5.7               | 375.0      |
| 23     | 276.0                                               | 20.5                           | 30.0                                     | 5.7               | 375.0      |
| 24     | 467.0                                               | 20.3                           | 42.7                                     | 5.7               | 375.0      |

| DATA # | RATE OF REACTION<br>(gmole/g.cat.min) $\times 10^3$ | BENZ<br>(gmol/L) $\times 10^4$ | O2<br>(gmol/L) $\times 10^4$ | NBAR<br>$\bar{n}$ | TEMP<br>$^{\circ}\text{C}$ |
|--------|-----------------------------------------------------|--------------------------------|------------------------------|-------------------|----------------------------|
| 1      | 218.0                                               | 134.5                          | 19.1                         | 5.5               | 350.0                      |
| 2      | 189.0                                               | 108.0                          | 20.0                         | 5.5               | 350.0                      |
| 3      | 192.0                                               | 68.6                           | 19.9                         | 5.5               | 350.0                      |
| 4      | 192.0                                               | 49.5                           | 20.0                         | 5.5               | 350.0                      |
| 5      | 152.0                                               | 41.7                           | 20.0                         | 5.5               | 350.0                      |
| 6      | 139.0                                               | 29.4                           | 19.9                         | 5.5               | 350.0                      |
| 7      | 118.0                                               | 22.5                           | 20.0                         | 5.5               | 350.0                      |
| 8      | 120.0                                               | 17.2                           | 19.9                         | 5.5               | 350.0                      |
| 9      | 122.0                                               | 17.0                           | 19.7                         | 5.5               | 350.0                      |
| 10     | 132.0                                               | 22.8                           | 20.0                         | 5.5               | 350.0                      |
| 11     | 167.0                                               | 41.3                           | 20.0                         | 5.5               | 350.0                      |
| 12     | 208.0                                               | 59.6                           | 20.0                         | 5.5               | 350.0                      |
| 13     | 216.0                                               | 119.7                          | 20.0                         | 5.5               | 350.0                      |
| 14     | 294.0                                               | 158.2                          | 20.0                         | 5.5               | 350.0                      |

Table D.12: Summary of original experimental data Jaswal for the oxidation of benzene.



## D.4 Tan, Oxidation of Propylene

$$r = \frac{k_a k_r C_O^{\frac{1}{2}} C_r}{(k_a C_O^{\frac{1}{2}} + n k_r C_r)} \quad (D.2)$$

| Temp | $k_a$                  | % Bias | $k_r$                  | % Bias | $\Gamma^{NR}$ | $\Gamma^{TR}$ |
|------|------------------------|--------|------------------------|--------|---------------|---------------|
| 390  | $8.588 \times 10^{-4}$ | 0.020  | $4.817 \times 10^{-3}$ | 0.090  | 0.08          | 0.73          |
| 375  | $7.277 \times 10^{-4}$ | 0.091  | $3.159 \times 10^{-3}$ | 0.27   | 0.12          | 1.40          |
| 350  | $5.180 \times 10^{-4}$ | 0.075  | $1.645 \times 10^{-3}$ | 0.11   | 0.06          | 1.14          |

Table D.13: Summary of parameter estimates, Box's bias and the Bates and Watts relative curvatures.

| TEMP | $k_a$  | $k_r$  |
|------|--------|--------|
| 390  | 0.005  | -0.031 |
|      | -0.031 | 0.176  |
|      | 0.002  | -0.013 |
|      | -0.013 | 0.073  |
| 375  | 0.014  | 0.069  |
|      | 0.069  | 0.340  |
|      | -0.005 | -0.026 |
|      | -0.026 | -0.128 |
| 350  | 0.014  | 0.063  |
|      | 0.063  | 0.283  |
|      | -0.004 | -0.017 |
|      | -0.017 | -0.077 |

Table D.14: Parameter effects portion of the acceleration array,  $A_{..}^T$ .

| Parameter | Temp<br>°C | % Bias              | % Excess<br>Variance | Skewness            | Excess<br>Kurtosis  |
|-----------|------------|---------------------|----------------------|---------------------|---------------------|
| $k_a$     | 390.       | 0.09*               | -2.58 <sup>ns</sup>  | -0.00 <sup>ns</sup> | -0.21 <sup>ns</sup> |
| $k_r$     | 390.       | -0.04 <sup>ns</sup> | -6.64 <sup>ns</sup>  | 0.25**              | -0.11 <sup>ns</sup> |
| $k_a$     | 375.       | 0.14 <sup>ns</sup>  | 5.89 <sup>ns</sup>   | 0.20**              | 0.09 <sup>ns</sup>  |
| $k_r$     | 375.       | 0.50**              | 5.28 <sup>ns</sup>   | 0.26**              | -0.17 <sup>ns</sup> |
| $k_a$     | 350.       | 0.14 <sup>ns</sup>  | 2.84 <sup>ns</sup>   | 0.17*               | 0.23 <sup>ns</sup>  |
| $k_r$     | 350.       | 0.18 <sup>ns</sup>  | 4.70 <sup>ns</sup>   | 0.21 <sup>ns</sup>  | 0.13 <sup>ns</sup>  |

Table D.15: Summary of results of Ratkowsky's Monte Carlo simulations, <sup>ns</sup> not significant, \*  $P < 0.05$ , \*\*  $P < 0.01$ .

## APPENDIX D. MODELS AND DATA SETS

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| DATA # | % CONV | PROP<br>mmol/L | O2<br>mmol/L | FLOW<br>cc/min | NBAR<br>$\bar{n}$ | TEMP<br>C |
|--------|--------|----------------|--------------|----------------|-------------------|-----------|
| 1      | 3.53   | 2.62           | 3.66         | 580.9          | 2.07              | 390.0     |
| 2      | 3.40   | 2.79           | 2.96         | 577.2          | 2.07              | 390.0     |
| 3      | 3.82   | 3.02           | 6.12         | 566.4          | 2.07              | 390.0     |
| 4      | 3.96   | 3.07           | 7.32         | 566.7          | 2.07              | 390.0     |
| 5      | 4.69   | 1.36           | 7.52         | 566.2          | 2.07              | 390.0     |
| 6      | 3.88   | 1.31           | 1.12         | 575.1          | 2.07              | 390.0     |
| 7      | 4.47   | 1.42           | 7.47         | 565.7          | 2.07              | 390.0     |
| 8      | 3.48   | 2.72           | 3.48         | 585.1          | 2.07              | 390.0     |
| 9      | 2.06   | 6.86           | 2.86         | 567.1          | 2.07              | 390.0     |
| 10     | 2.09   | 7.13           | 2.89         | 561.3          | 2.07              | 390.0     |
| 11     | 4.57   | 1.32           | 7.48         | 563.0          | 2.07              | 390.0     |
| 12     | 2.21   | 7.09           | 3.27         | 561.5          | 2.07              | 390.0     |
| 13     | 3.59   | 2.88           | 3.76         | 576.1          | 2.07              | 390.0     |
| 14     | 4.72   | 1.33           | 7.84         | 565.4          | 2.07              | 390.0     |
| 15     | 2.02   | 7.14           | 3.22         | 578.5          | 2.07              | 390.0     |
| 16     | 4.50   | 1.37           | 7.89         | 586.7          | 2.07              | 390.0     |
| 17     | 3.32   | 5.39           | 7.25         | 559.6          | 2.07              | 390.0     |
| 18     | 4.21   | 1.31           | 2.90         | 570.5          | 2.07              | 390.0     |
| 19     | 3.56   | 2.74           | 3.54         | 570.6          | 2.07              | 390.0     |
| 20     | 3.94   | 2.89           | 7.48         | 569.6          | 2.07              | 390.0     |
| 21     | 3.36   | 5.29           | 7.23         | 562.5          | 2.07              | 390.0     |
| 1      | 2.59   | 2.94           | 2.96         | 552.4          | 2.35              | 375.0     |
| 2      | 3.22   | 1.35           | 3.06         | 568.9          | 2.35              | 375.0     |
| 3      | 1.57   | 3.04           | 1.19         | 563.4          | 2.35              | 375.0     |
| 4      | 2.60   | 2.90           | 3.70         | 562.7          | 2.35              | 375.0     |
| 5      | 2.19   | 4.14           | 3.03         | 554.5          | 2.35              | 375.0     |
| 6      | 2.83   | 2.69           | 3.76         | 565.3          | 2.35              | 375.0     |
| 7      | 2.77   | 2.99           | 6.23         | 562.2          | 2.35              | 375.0     |
| 8      | 2.54   | 2.85           | 3.03         | 564.1          | 2.35              | 375.0     |
| 9      | 2.47   | 5.46           | 7.46         | 546.5          | 2.35              | 375.0     |
| 10     | 3.79   | 1.39           | 7.67         | 554.9          | 2.35              | 375.0     |
| 11     | 3.03   | 1.34           | 1.15         | 562.1          | 2.35              | 375.0     |
| 12     | 2.52   | 2.73           | 3.02         | 567.7          | 2.35              | 375.0     |
| 13     | 3.90   | 1.46           | 7.65         | 552.2          | 2.35              | 375.0     |
| 14     | 3.60   | 1.39           | 7.56         | 559.9          | 2.35              | 375.0     |
| 15     | 3.83   | 1.33           | 7.49         | 553.8          | 2.35              | 375.0     |
| 16     | 3.63   | 1.37           | 7.75         | 545.2          | 2.35              | 375.0     |
| 17     | 1.22   | 7.02           | 2.93         | 554.3          | 2.35              | 375.0     |
| 18     | 2.52   | 2.89           | 2.91         | 580.6          | 2.35              | 375.0     |
| 19     | 1.24   | 7.30           | 2.96         | 547.8          | 2.35              | 375.0     |
| 20     | 3.62   | 1.35           | 7.66         | 549.5          | 2.35              | 375.0     |
| 21     | 3.01   | 3.15           | 7.52         | 551.3          | 2.35              | 375.0     |
| 22     | 2.44   | 2.75           | 2.93         | 567.1          | 2.35              | 375.0     |

| DATA # | % CONV | PROP<br>mmol/L | O2<br>mmol/L | FLOW<br>cc/min | NBAR<br>$\bar{n}$ | TEMP<br>C |
|--------|--------|----------------|--------------|----------------|-------------------|-----------|
| 1      | 1.47   | 3.05           | 3.07         | 533.4          | 2.76              | 350.0     |
| 2      | 2.13   | 1.37           | 3.18         | 548.1          | 2.76              | 350.0     |
| 3      | 0.960  | 3.17           | 1.24         | 540.8          | 2.76              | 350.0     |
| 4      | 1.55   | 3.02           | 3.85         | 540.9          | 2.76              | 350.0     |
| 5      | 1.00   | 4.31           | 3.15         | 532.9          | 2.76              | 350.0     |
| 6      | 1.60   | 2.78           | 3.89         | 546.6          | 2.76              | 350.0     |
| 7      | 1.64   | 3.11           | 6.48         | 540.5          | 2.76              | 350.0     |
| 8      | 1.45   | 2.96           | 3.13         | 544.6          | 2.76              | 350.0     |
| 9      | 1.56   | 2.84           | 3.14         | 546.2          | 2.76              | 350.0     |
| 10     | 2.45   | 1.46           | 7.93         | 534.1          | 2.76              | 350.0     |
| 11     | 2.38   | 1.38           | 7.79         | 533.0          | 2.76              | 350.0     |
| 12     | 2.55   | 1.42           | 8.03         | 525.9          | 2.76              | 350.0     |
| 13     | 2.44   | 1.49           | 7.78         | 528.7          | 2.76              | 350.0     |
| 14     | 1.37   | 3.01           | 3.03         | 557.4          | 2.76              | 350.0     |
| 15     | 2.45   | 1.35           | 8.00         | 527.7          | 2.76              | 350.0     |
| 16     | 2.39   | 1.52           | 8.22         | 541.5          | 2.76              | 350.0     |
| 17     | 1.00   | 5.95           | 6.13         | 543.2          | 2.76              | 350.0     |
| 18     | 2.34   | 1.46           | 8.41         | 551.0          | 2.76              | 350.0     |
| 19     | 1.17   | 5.68           | 7.75         | 525.8          | 2.76              | 350.0     |
| 20     | 2.07   | 1.36           | 3.10         | 535.0          | 2.76              | 350.0     |
| 21     | 1.72   | 1.42           | 1.25         | 546.2          | 2.76              | 350.0     |
| 22     | 1.78   | 3.18           | 7.89         | 536.7          | 2.76              | 350.0     |
| 23     | 1.42   | 2.87           | 3.06         | 543.9          | 2.76              | 350.0     |

Table D.16: Summary of original experimental data by Tan for the oxidation of propylene.

## Appendix E

# Fortran Code for Nonlinear Regression

The following is an example of an exec file which compiles, defines input and output files, runs and then displays the result file for the program which performs a nonlinear regression on the model defined in SUBROUTINE EVAL. The program is run by typing EX1 *filename*. EX1 is the name of the exec, *filename* is the name of the program. *Filename* is the argument &1 in the exec. As such the input data for the program is found in a data file called *filename* DATA. Results are written to a file called *filename* RESULT. This program should be run by this method only to perform a nonlinear regression and obtain measures on nonlinearity for that model/data set. If experimental designs are to be simulated then the program should be run in batch mode. This will allow the user to work on other tasks, run the program faster and make use of the lower computing costs usually available when running programs in batch mode. Computing costs can run high when a large number of experiments and/or a large operating region are used. Actual CPU run times vary greatly, from ~50 sec (for a set of simulations with the Juusola data set) to ~600 sec (for a set of simulations with the Ayen and Peters data set).

```
VMFCLEAR
GLOBAL TITLIB VLKMLIB VFORTLIB CMLIB INSLDLIB LINPACK PLOTLIB TSOLIB
FORTVS &1
FILE 5 DISK XY DATA * (LRECL 80 BLKSIZE 80 RECFM F PERM
FILE 7 DISK GD DATA *
FILE 8 DISK &1 DATA *
FILE 9 DISK PE DATA * (LRECL 80 BLKSIZE 80 RECFM F PERM
```

```
FILE 10 DISK DOPT DATA * (LRECL 80 BLKSIZE 80 RECFM F PERM  
FILE 11 DISK SSB DATA * (LRECL 80 BLKSIZE 80 RECFM F PERM  
FILE 6 DISK #1 RESULT A (PERM RECFM F LRECL 132  
LOAD #1 (CLEAR START  
XEDIT #1 RESULT A
```

The following is a example of a data file that is to be read by the FORTRAN program of the same name which performs the nonlinear regression and simulates an experimental design. Explanations of the entrys are self explanatory. The descriptions preceded by an (I) are integer arguments, DSEED is the only double precision entry, the remainder being real. The first two lines are read as titles and used to identify the model/data set used, and the type of simulation performed, if any. In the next line the single quotes represent the limits of the columns of the original data and that of the designed runs. Descriptions of the output should be centered within the quotes. The next two lines are headers for the original data in the output file, the response being the second column. The sixth line is the header for the designed run locations, the simulated response is not included in this output, only the operating variables.

TAN, PROPYLENE OXIDATION, ISOTHERMAL,  
MODEL FORM MO, 350 C, PEC-S

| DATA #   | RATE OF REACT<br>(gmole/g.cat.min)E10                           | BENZ<br>(gmol/L)E4 | O2<br>(gmol/L)E4 | NBAR | TEMP<br>C |
|----------|-----------------------------------------------------------------|--------------------|------------------|------|-----------|
| RUN #    | x1                                                              | x2                 | x3               | x4   | x5        |
| 1        | (I) 1 WILL GIVE A STOCHASTIC SIMULATION, 0 A CONTROL SIMULATION |                    |                  |      |           |
| 12       | (I) IS THE NUMBER OF DATA POINTS                                |                    |                  |      |           |
| 3        | (I) IS THE NUMBER OF PARAMETERS IN THE MODEL                    |                    |                  |      |           |
| 0.0004   | IS THE INITIAL ESTIMATE FOR PARAMETER 1                         |                    |                  |      |           |
| 10.00    | IS THE INITIAL ESTIMATE FOR PARAMETER 2                         |                    |                  |      |           |
| 10.00    | IS THE INITIAL ESTIMATE FOR PARAMETER 3                         |                    |                  |      |           |
| 1.0000   | IS THE SCALING FACTOR FOR THE RESPONSE                          |                    |                  |      |           |
| 5        | (I) IS THE NUMBER OF VARIABLES                                  |                    |                  |      |           |
| 1.000    | IS A SCALING FACTOR FOR X1 IE $X1=X1 \cdot X1FACTOR$            |                    |                  |      |           |
| 1.000    | IS A SCALING FACTOR FOR X2 IE $X2=X2 \cdot X2FACTOR$            |                    |                  |      |           |
| 1.000    | IS A SCALING FACTOR FOR X3 IE $X3=X3 \cdot X3FACTOR$            |                    |                  |      |           |
| 1.000    | IS A SCALING FACTOR FOR X4 IE $X4=X4 \cdot X4FACTOR$            |                    |                  |      |           |
| 1.000    | IS A SCALING FACTOR FOR X5 IE $X5=X5 \cdot X5FACTOR$            |                    |                  |      |           |
| 1.0E-4   | IS THE TOLERANCE FOR CONVERGENCE (CHANGES IN PARAMETERS)        |                    |                  |      |           |
| 1.64421D | IS A DSEED NUMBER OF THE FORM 1.23456D8 TO GENERATE RANDOM #'S  |                    |                  |      |           |
| 10       | (I) IS THE NUMBER OF RUNS TO BE DESIGNED (ZERO IS VALID)        |                    |                  |      |           |
| 144      | (I) IS THE NUMBER OF POINTS TO BE SEARCHED FOR DESIGNED RUNS    |                    |                  |      |           |
| 0        | (I) IF RATKOWSKY'S SIMULATION DESIRED ENTER 1 ELSE ENTER 0      |                    |                  |      |           |
| 0.95     | IS THE LEVEL OF SIGNIFICANCE FOR THE F STATISTIC                |                    |                  |      |           |
| 999      | (I) MAX NUMBER OF ITERATIONS FOR SOLVE                          |                    |                  |      |           |
| 11111    | (I) IF THE JOB CARD CONTROLLING OUTPUT FROM SOLVE               |                    |                  |      |           |
| 75       | (I) MAX NUMBER OF ITERATIONS FOR BATES                          |                    |                  |      |           |
| 00111    | (I) JOB CARD CONTROLLING OUTPUT FROM BATES                      |                    |                  |      |           |
| 1        | (I) DESIGN CRITERION                                            |                    |                  |      |           |
|          | 0 FOR AUTO CURVATURE CHOICE                                     |                    |                  |      |           |
|          | 1 FOR FORCED PE CURVATURE CRITERION                             |                    |                  |      |           |
|          | 2 FOR FORCED IN CURVATURE CRITERION                             |                    |                  |      |           |
|          | 3 FOR FORCED PI CURVATURE CRITERION                             |                    |                  |      |           |
|          | 4 FOR FORCED D-OPT CRITERION                                    |                    |                  |      |           |
|          | 5 FOR FORCED SUM OF SQUARES OF BIASES                           |                    |                  |      |           |

The following program is largely as found in Ratkowsky [3] and was originally entered by Mr. Rafael Diaz, to whom I am grateful for supplying a copy of the program. I have modified the original program in several ways :

- The main program now reads parameter estimates, number of points and such from a data file of the same name as the fortran file.
- The major modification was to allow simulation of designed experiments. The design criterion for determining the optimum operating variables is specified in the file &1 DATA.
- The intrinsic and parameter effects curvature are the maximum converged curvatures obtained after using the  $p$  unit vectors as starting values for the vector DIR in the subroutine BATES.



```

CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C      FILE 8 MUST HAVE LRECL = 132 (LOGICAL RECORD LENGTH)
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C      NP      NUMBER OF MODEL PARAMETERS
C      NPTS    NUMBER OF OBSERVATIONS IN THE ORIGINAL DATA SET
C      LUNOUT   NUMBER DEFINING WRITE FILE
C      DIRET   JOB CONTROLLING OUTPUT OF DIREC FROM ROUTINE BATES
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C      Y      ARRAY USED TO STORE THE RESPONSE VARIABLE
C      PARAM   ARRAY USED TO STORE THE PARAMETER ESTIMATES
C      PAR     ARRAY USED TO STORE TEMPORARY PARAMETER ESTIMATES
C      VARC    ARRAY USED TO STORE THE VARIANCE-COVARIANCE MATRIX
C      DERIVS  ARRAY USED TO STORE THE FIRST DERIVATIVES
C      DRIVS   ARRAY USED TO STORE THE FIRST DERIVATIVES
C      DRIVT   ARRAY USED TO STORE THE FIRST DERIVATIVES
C      A      ARRAY USED TO STORE THE SECOND DERIVATIVES AND THE
C             ACCELERATION ARRAY
C      QRAUX   ARRAY USED TO STORE THE VARIANCE-COVARIANCE MATRIX
C      DIREC   STORAGE FOR CONVERGED VECTOR DIR FOR THE INC AND PEC
C      WK1     TEMPORARY WORK ARRAY
C      WK2     TEMPORARY WORK ARRAY
C      T       TEMPORARY WORK ARRAY
C      WK      TEMPORARY WORK ARRAY
C      STMATE  STORAGE OF PARAMETER ESTIMATES FROM RATKOWSKY'S SIM
C      STORE   STORAGE OF THE IN AND PE CURVATURES FOR EACH STARTING
C             VECTOR DIR AND THE MAXIMUM CURVATURE
C      X1,X2,X3,X4,X5,X6,X7
C             STORAGE OF THE OPERATING VARIABLES FOR THE ORIGINAL
C             DATA AND DESIGNED RUNS
C      X1M,X2M,X3M,X4M,X5M,X6M,X7M
C             STORAGE OF THE DESIGNED RUN LOCATIONS
C      F      ARRAY CONTAINING F STATISTIC
C      S      ARRAY CONTAINING TEST STATIC FOR SIGNIFICANT CURVATURE
C      PECOB  STORAGE OF OBTAINED PEC AFTER EACH RUN
C      INCOB  STORAGE OF OBTAINED INC AFTER EACH RUN
C      PECM   STORAGE OF PREDICTED PEC AT THE DESIGNED RUN LOCATION
C      INCM   STORAGE OF PREDICTED INC AT THE DESIGNED RUN LOCATION
C      DOPTH  PREDICTED VOLUME OF THE CONFIDENCE REGION
C      DETM   OBTAINED VOLUME OF THE CONFIDENCE REGION
C      BIAS   TEMPORARY STORAGE OF BOY'S BIAS
C      BIS    PREDICTED BIAS AT EACH NODE OF GRID SEARCH
C      BISM   OBTAINED BIAS FOR EACH PARAMETER FOR EACH RUN
C      SS     STORAGE OF SUM OF SQUARES OF BIASES FOR DESIGNED RUNS
C      SA     STORAGE OF SUM OF ABSOLUTE OF BIASES FOR DESIGNED RUNS
C      SSP    STORAGE OF PREDICTED SSB FOR EACH RUN
C      SAP    STORAGE OF PREDICTED SAB FOR EACH RUN
C      SSO    STORAGE OF OBTAINED SSB FOR EACH RUN
C      SAO    STORAGE OF OBTAINED SAB FOR EACH RUN
C      YHT    PREDICTED RESPONSE (DETERMINISTIC COMPONENT)
C      RNN    RANDOM N(0,1) NUMBER USED TO GENERATE RER
C      RER    STOCHASTIC COMPONENT OF THE PREDICTED RESPONSE

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C      YHTE      PREDICTED RESPONSE (STOCHASTIC I.E. YHT + RER)
C      PARM      STORAGE OF THE PARAMETER ESTIMATES AFTER EACH DESIGNED
C                RUN
C      VARM      VARIANCE ESTIMATE FOR EACH DESIGNED RUN
C      DOPTM     PREDICTED VOLUME OF THE CONFIDENCE REGION
C      DETM      OBTAINED VOLUME OF THE CONFIDENCE REGION
C      STDER     STANDARD ERROR, APPROXIMATE MEASURE OF PARAMETER PRECI
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      DOUBLE PRECISION DSEED
      INTEGER JPVT(6),LUNOUT,NPTS,NP,NITS,ND1,I,J,JOB,NSIM,NS,
+ IPAIL,Z,W,NSERC,SMM,P,JOB3,OUT,D,NPT,
+ MINPE,MINPI,MININ,MINVOL,LOC,DES(30),DIRET,KK,II,NOCON
      REAL Y(99),PARAM(6),PAR(6),VARC(6,6),DERIVS(999),A(9999),QRAUX(6),
+ WK1(21),WK2(9999),DIFF(999),BIAS(6),STMATE(1000,4),
+ ITX(3,3),ITXI(3,3),T(6,6),WK(6,6),DRIVS(999,6),DRIVT(6,999),
+ X1M(99),X2M(99),X3M(99),X4M(99),X5M(99),X6M(99),X7M(99),XF(7),
+ YHT(99),YHTE(99),RER(99),RNN(99),PARM(99,6),G(1),
+ PECOB(99),INCOB(99),INCH(99),PECM(99),VARM(99),DETM(99),DOPTM(99),
+ SS(999),SA(999),BIS(999,4),BISM(999,4),SSP(99),SAP(99),
+ SSO(99),SAO(99),
+ COFAC(6),STDER(30,2),DIREC(6),F(99),S(99),STORE(999,2,7),
+ IH,IL,NBAR,LOW
      CHARACTER*130 TITLE1,TITLE2,TITLE3
      COMMON X1(99),X2(99),X3(99),X4(99),X5(99),X6(99),X7(99)
      DATA LUNOUT/6/
      READ(8,9001) TITLE1
      WRITE(6,9001) TITLE1
      READ(8,9001) TITLE1
      WRITE(6,9001) TITLE1
      READ(8,9001) TITLE1
      READ(8,9001) TITLE1
      READ(8,9001) TITLE2
      READ(8,9001) TITLE3
9001 FORMAT(A130)
      WRITE(6,*) ' '
      READ(8,*) ISTOCH
      WRITE(6,*) '1 WILL GIVE A STOCHASTIC SIMULATION, 0 WILL GIVE A
+CONTROL SIMULATION'
      WRITE(6,*) 'WITH CONSTANT PARAMETER AND VARIANCE ESTIMATES',ISTOCH
      READ(8,*) NPTS
      WRITE(6,9002) NPTS
9002 FORMAT(1H , '          NUMBER OF POINTS = ',I3)
      READ(8,*) NP
      WRITE(6,9003) NP
9003 FORMAT(1H , '          NUMBER OF PARAMETERS = ',I3,/)
      ND1=NP
      DO 1000 I=1,NP
          READ(8,*) PARAM(I)
1000      WRITE(6,9004) I,PARAM(I)
9004 FORMAT(1H , '          INITIAL GUESS FOR THETA',I1,' = ',G12.6)
      READ(8,*) YF
      WRITE(6,*) 'SCALING FACTOR FOR THE RESPONSE:',YF
      READ(8,*) NUMXF
      WRITE(6,9005) NUMXF

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```

9005 FORMAT(1H ,/,1H ,'          NUMBER OF VARIABLES = ',I2)
      DO 1010 I=1,NUMXF
        READ(8,*) XF(I)
1010   WRITE(6,9006) I,XF(I)
9006 FORMAT(1H ,'          SCALING FACTOR FOR X',I1,' = ',G12.6)
      READ(8,*) ALPHA
      WRITE(6,9009) ALPHA
9009 FORMAT(1H ,'          TOLERANCE FOR CONVERGENCE = ',G12.6)
      READ(8,*) DSEED
      WRITE(6,9010) DSEED
9010 FORMAT(1H ,'          DSEED FOR RANDOM ERRORS = ',D16.8,/)
      READ(8,*) NSERC
      WRITE(6,9011) NSERC
9011 FORMAT(1H ,' NUMBER OF RUNS TO BE DESIGNED = ',I5)
      READ(8,*) P
      WRITE(6,9012) P
9012 FORMAT(1H ,'          SIZE OF DESIGN SURFACE = ',I5,/)
      READ(8,*) SMM
      WRITE(6,9013) SMM
9013 FORMAT(1H ,'          RATKOWSKYS SIMULATIONS? = ',I5)
      READ(8,*) PR
      WRITE(6,9014) PR
9014 FORMAT(1H ,'          1-ALPHA FOR SIGNIFICANCE = ',F5.2)
      READ(8,*) ITS
      WRITE(6,9015) ITS
9015 FORMAT(1H ,'          MAX ITERATIONS FOR SOLVE = ',I5)
      READ(8,*) JOB1
      WRITE(6,9016) JOB1
9016 FORMAT(1H ,'          JOB CARD FOR SOLVE OUTPUT = ',I5)
      READ(8,*) NITS
      WRITE(6,9017) NITS
9017 FORMAT(1H ,'          MAX ITERATIONS FOR BATES = ',I5)
      READ(8,*) JOB2
      WRITE(6,9018) JOB2
9018 FORMAT(1H ,'          JOB CARD FOR BATES OUTPUT = ',I5,/)
      READ(8,*) IDESGH
      WRITE(6,9020) IDESGH
9020 FORMAT(1H ,'          CHOICE OF DESIGN CRITERION = ',I5,/)
      NSERCS=NSERC
      NPT=NPTS
      D1=NP
      D2=1
      DO 1100 I=1,99
        CALL MDFI(PR,D1,D2,FSTAT,IER)
        F(I)=FSTAT
C      WRITE(6,*) F(I)
        D2=D2+1
1100 CONTINUE
      WRITE(6,533) TITLE1
      WRITE(6,533) TITLE2
533  FORMAT(A80)
      FBAR=0.0
      DO 1200 I=1,NPTS
        READ(6,*) X1(I),X2(I),X4(I),X3(I),X5(I),Y(I)
        WRITE(6,534) I,Y(I),X1(I),X2(I),X3(I),X5(I)

```

```

534      FORMAT(1H ,3I,13,5I,8(2I,G12.5))
        Y1(I)=Y1(I)*YF(1)
        Y2(I)=Y2(I)*YF(2)
        Y3(I)=Y3(I)*YF(3)
        Y4(I)=Y4(I)*YF(4)
        Y5(I)=Y5(I)*YF(5)
        Y6(I)=Y6(I)*YF(6)
        Y7(I)=Y7(I)*YF(7)
        Y(I)=Y(I)*YF
1200 CONTINUE
        FBAR=FBAR/FLOAT(NPTS)
100 CONTINUE
        WRITE(6,*) 'FBAR=',FBAR
        Z=NPTS-NPT
        WRITE(6,*) 'REGRESSION FOR RUN',Z,'AFTER SEARCH'
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C  LEAST SQUARES NONLINEAR REGRESSION
C
C  JOB 1 PARAMETER ESTIMATES AT EACH ITERATION
C  JOB 2 PARAMETER ESTIMATES AT CONVERGENCE, STANDARD ERROR AND
C      T-VALUE
C  JOB 3 PARAMETER VARIANCE-COVARIANCE MATRIX
C  JOB 4 PARAMETER CORRELATIONS
C  JOB 5 RUN #, ACTUAL RESPONSE, PREDICTED RESPONSE AND RESIDUAL
C
C  ITS IS THE NUMBER OF ITERATIONS USED FOR THE CALL TO SOLVE
C  IN THE SIMULATED RUNS ONLY, IE NOT IN THE MONTE CARLO SIMULATIONS
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
        IF(ISTOCH.EQ.1.OR.Z.EQ.0) THEN
            CALL SOLVE(Y,PARAM,ALPHA,ITS,NPTS,NP,ND1,LUNOUT,JOB1,
+              VARC,RSS,IFAIL,DERIVS,QRAUX,JPVT,DIFF,WK1)
            VAR=RSS/FLOAT(NPTS-NP)
        END IF
        RVAR=VAR
        IF(Z.EQ.0) VARORG=VAR
        IF(IFAIL.NE.0) THEN
            WRITE(6,*) '*****'
            WRITE(6,*) 'SUBROUTINE SOLVE HAS CRASHED'
            WRITE(6,*) 'GOING TO WRITE STATEMENTS TO OUTPUT'
            WRITE(6,*) 'RESULTS OBTAINED UP TO THIS POINT .'
            WRITE(6,*) '*****'
            GO TO 999
        END IF
        CALL DOD(NP,NPTS,RVAR,PARAM,IFAIL,WK1,DET,XTI,XTII,DRIVS,
+DRIVT,T,WK,COFAC,IFLAG)
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C  CALCULATION OF BOX'S BIAS AND BATES & WATTS CURVATURES
C
C  JOB 1 FIRST DERIVATIVES
C  JOB 2 SECOND DERIVATIVES (FIRST NP FACES ONLY)
C  JOB 3 FIRST P FACES OF THE ACCELERATION ARRAY (PE PORTION)
C  JOB 4 BOX'S BIASES

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```

C      JOB 5 BATES & WATTS CURVATURES
C
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C      IF ISTOCH = 0 THEN THE VARIANCE IS RESET TO THAT OBTAINED WITH
C      THE INITIAL DATA. THIS IS ONLY DONE WITH CONTROL SIMULATIONS IN
C      ORDER TO STUDY THE EFFECTS OF DESIGNED RUN LOCATIONS WITHOUT
C      WORRYING ABOUT DIFFERENT PARAMETER AND VARIANCE ESTIMATES FOR THE
C      DIFFERENT DESIGNS.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      IF(ISTOCH.EQ.0) THEN
        VAR=VARORG
        RVAR=VARORG
      END IF
      DIRET=1
      CALL BATES(PARAM,VAR,NITS,NPTS,NP,LUNOUT,JOB2,BIAS,IFAIL,
+          A,DERIVS,VARC,QRAUX,WK1,WK2,JPVT,C1,C2,DIREC,DIRET,
+          STORE,K,NOCON)
      IF(IFAIL.NE.0) THEN
        WRITE(6,*) IFAIL,'FAILURE IN EXPT SIM'
        IF(IFAIL.EQ.6) THEN
          WRITE(6,*) 'ENDING SIMULATION'
          GO TO 999
        END IF
      END IF
      IFAIL=0
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C      THIS IS RATKOWSKY'S MONTECARLO SIMULATION CHECKING FOR NON-NORMAL
C      BEHAVIOUR OF THE PARAMETERS WITH SOME EXTRA OUTPUT FOR COMPARISON
C      TO MEASURES FROM THE MODEL ITSELF.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      IF(SHM.EQ.0) GO TO 200
      NSIM=1000
      JOB=1111
      IF(NSIM.GT.10) JOB=0
      SD=SQRT(VAR)
      II=0
      DO 1300 I=1,NSIM
        DO 1400 J=1,NP
          PAR(J)=PARAM(J)
1400    CONTINUE
          CALL GNRATE(PAR,SD,NPTS,LUNOUT,Y,WFAIL,DSEED)
          CALL SOLVE(Y,PAR,ALPHA,ITS,NPTS,NP,ND1,LUNOUT,JOB,VARC,
+          RSS,IFAIL,DERIVS,QRAUX,JPVT,DIFF,WK1)
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C      WHEN USING RATKOWSKY'S MONTE CARLO SIMULATIONS, A GIVEN SET OF
C      RESIDUALS MAY RESULT IN A FAILURE OF CONVERGENCE. THIS WILL
C      USUALLY RESULT IN UNREALISTIC PARAMETER ESTIMATES. THE FOLLOWING
C      LINES OF PROGRAMMING ARE USED TO CHECK FOR SUCH OCCURRENCES.
C      THE LIMITS OF ACCEPTABLE PARAMETER ESTIMATES SHOULD BE QUITE

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C      GENEROUS (TWO OR THREE ORDERS OF MAGNITUDE). WHEN A FAILURE TO
C      CONVERGENCE OCCURS THE SIMULATIONS CONTINUE BUT THE NUMBER OF
C      SIMULATIONS IS REDUCED.
C      THE PROBLEM GENERALLY OCCURS WITH HIGHLY NONLINEAR DATA SETS.
C      THIS CHECK CAN BE BYPASSED FOR MOST CASES.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C      IF(PAR(1).GE.1.E6.OR.PAR(1).LE.-1.E6) THEN
C          II=II+1
C          GO TO 1500
C      END IF
C      IF(PAR(2).GE.1.E6.OR.PAR(2).LE.-1.E6) THEN
C          II=II+1
C          GO TO 1500
C      END IF
C      IF(PAR(3).GE.1.E6.OR.PAR(3).LE.-1.E6) THEN
C          II=II+1
C          GO TO 1500
C      END IF
C      IF(IFAIL.NE.0) THEN
C          WRITE(6,*) 'SOLVE FAILED IN RAT SIM',I
C          II=II+1
C          GO TO 1500
C      END IF
C      IF(IFAIL.NE.0) STOP
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      DO 1500 J=1,NP
          STMATE(I,J)=PAR(J)
1500      CONTINUE
1300 CONTINUE
      JOB=11
      JOB3=1
      NSIM=NSIM-II
      WRITE(6,*) NSIM, 'IS THE ACTUAL NUMBER OF SIMULATIONS PERFORMED'
      DO 1600 I=1,NP
          WRITE(LUNOUT,40) I
          W=I
          CALL SUMRY(STMATE(1,I),NSIM,LUNOUT,JOB,IFAIL,PARAM,W,BIAS,
+              XTII,RVAR,JOB3,NP)
1600      CONTINUE
200  CONTINUE
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C      RECORDING RESULTS AFTER DESIGNED EXPERIMENT IS PERFORMED
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
909  CONTINUE
      D=Z
      IF(D.EQ.0) VARO=RVAR
      VARM(D)=RVAR
      DETH(D)=DET
      INCOB(D)=C1
      PECOB(D)=C2
      IPSIGN=0
      SAO(D)=0.0

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SSO(D)=0.0
IPSIGN=0
DO 1701 W=1,NP
  PARM(D,W)=PARAM(W)
  IF(PARM(W).LE.0.0) IPSIGN=1
  STDER(D,W)=SQRT(IXXI(W,W)*RVAR)*2.0
  SSO(D)=(BIAS(W)/PARAM(W)*100)**2+SSO(D)
  SAO(D)=ABS(BIAS(W)/PARAM(W))*100+SAO(D)
  BISM(D,W)=BIAS(W)/PARAM(W)*100.0
1701 CONTINUE
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   PARAMETERS ARE ASSUMED TO BE > ZERO. IF A PARAMETER ESTIMATE GOES
C   NEGATIVE THEN THE SIMULATIONS ARE TERMINATED AND RESULTS UP TO
C   THAT POINT ARE PRINTED.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
IF(IPSIGN.NE.0) THEN
  WRITE(6,*) '*****'
  WRITE(6,*) 'ONE OF THE PARAMETERS HAS GONE NEGATIVE'
  WRITE(6,*) 'GOING TO WRITE STATEMENTS TO OUTPUT'
  WRITE(6,*) 'RESULTS OBTAINED UP TO THIS POINT .'
  WRITE(6,*) '*****'
  GO TO 999
END IF
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   DECIDING IF SHOULD CONTINUE: IF THE NUMBER OF DESIGNED RUNS
C   EXCEEDS A PRESPECIFIED LIMIT THEN THE SIMULATIONS ARE STOPPED.
C   SIMULATIONS ARE ALSO STOPPED WHEN BOTH THE INTRINSIC AND PARAMETER
C   EFFECTS CURVATURES HAVE REACHED ACCEPTABLE LEVELS.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
TEST=0.5/SQRT(F(NPTS-NP))
IF(FLOAT(NSERC).LT.0.5) GO TO 999
IF(C1.LT.TEST.AND.C2.LT.TEST) GO TO 999
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   BEGINNING SEARCH FOR NEXT EXPERIMENT
C   IF BATES DOES NOT CONVERGE THEN THAT RUN IS SKIPPED
C   THE RUN IS NOW ONLY SKIPPED IF CONVERGENCE FAILED NP
C   TIMES. IE FOR EVERY UNIT NORMAL VECTOR USED AS A STARTING
C   VECTOR IN DIR. IF NOCON = NP THEN THE RUN IS SKIPPED.
C
C   THE TEMP** VARIABLES ARE USED TO CHECK FOR MINIMUM DESIGN
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
TEMPPE=9.E60
TEMPIN=9.E60
TEMPRI=9.E60
TEMPSS=9.E60
MININ=0
MINPI=0
MINPE=0
MINVOL=0

```

[illegible]



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      IF(C1.EQ.0.0.OR.C2.EQ.0.0) THEN
        WRITE(6,*) '*****'
        WRITE(6,*) ' ONE OF THE CURVATURES IS ZERO AND SO '
        WRITE(6,*) ' QUIT SIMULATIONS, PRINT OUT RESULTS '
        WRITE(6,*) ' OBTAINED TO THIS POINT '
        WRITE(6,*) '*****'
        GO TO 999
      END IF
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   IF THE INTRINSIC CURVATURE FOR THE PREVIOUS SIMULATED EXPERIMENT
C   IS ACCEPTABLE THEN THE DESIGN CRITERIA BECOMES TO MINIMIZE THE
C   PARAMETER EFFECTS CURVATURE. IF THE INTRINSIC CURVATURE WAS NOT
C   ACCEPTABLE FOR THE PREVIOUS RUN THEN THE DESIGN CRITERIA IS TO
C   MINIMIZE THE INTRINSIC CURVATURE. IF THE PREDICTED INTRINSIC
C   CURVATURE WOULD BE MADE ACCEPTABLE WITH THE CURRENT RUN THEN
C   THE NEXT RUN IS CHOSEN SUCH THAT INC IS ACCEPTABLE AND THE
C   PARAMETER EFFECTS CURVATURE IS MADE ACCEPTABLE.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      IF(INCOB(D).LE.TEST) GO TO 400
      IF(C1.LE.TEMPI) THEN
        TEMPI=C1
        MINPI=K
      END IF
      IF(C1.LE.TEST.AND.C2.LE.TEMPPI) THEN
        TEMPI=C2
        MINPI=K
      END IF
400    CONTINUE
      IF(C2.LE.TEMPPE) THEN
        TEMPPE=C2
        MINPE=K
      END IF
      IF(C1.LE.IL) THEN
        IL=C1
        INMM=K
      END IF
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   CHECKING FOR THE MINIMUM VOLUME AND SSB RUN LOCATION FOR THE
C   D-OPTIMAL AND SSB DESIGN CRITERIA.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
4567    CONTINUE
      IF(DET.LE.DL) THEN
        DL=DET
        MINVOL=K
      END IF
      IF(SS(K).LE.TEMPSS) THEN
        TEMPSS=SS(K)
        MSS=K
      END IF
      WRITE(6,*) K,'IN=',C1,'PE=',C2,'VOL=',DET,'SSB=',SS(K)

```

# APPENDIX E. FORTRAN CODE FOR NONLINEAR REGRESSION

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CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   IF CONTOUR PLOTS ARE NOT REQUIRED OR MORE THAN ONE RUN IS
C   BEING SIMULATED COMMENT OUT THE NEXT THREE WRITE STATEMENTS
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      WRITE(9,*) C2
      WRITE(10,*) DET
      WRITE(11,*) SS(K)
1900 CONTINUE
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   SEARCH IS OVER AND DESIGNED LOCATION AND SIMULATED
C   EXPERIMENT ADDED TO ORIGINAL DATA
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      WRITE(6,*) ' '
      WRITE(6,*) 'MINPE=',MINPE
      WRITE(6,*) 'MININ=',INMM
      WRITE(6,*) 'MINPI=',MINPI
      WRITE(6,*) 'MINVOL=',MINVOL
      WRITE(6,*) 'MINSSB=',MSS
      WRITE(6,*) ' '
      IF(IDESGN.EQ.1) THEN
        LOC=MINPE
        DES(Z)=1
        GO TO 500
      END IF
      IF(IDESGN.EQ.2) THEN
        LOC=MININ
        DES(Z)=2
        GO TO 500
      END IF
      IF(IDESGN.EQ.3) THEN
        IF(MINPI.EQ.0) THEN
          LOC=MINPE
          DES(Z)=1
          WRITE(6,*) 'CRITERION CHOICE OF MINPI INVALID'
          GO TO 500
        END IF
        LOC=MINPI
        DES(Z)=3
        GO TO 500
      END IF
      IF(IDESGN.EQ.4) THEN
        LOC=MINVOL
        DES(Z)=4
        GO TO 500
      END IF
      IF(IDESGN.EQ.5) THEN
        LOC=MSS
        DES(Z)=5
        GO TO 500
      END IF

```

```

      IF(IDESGX.EQ.0) THEN
        LOC=MINPE
        DES(Z )=1
        IF(INCOB(D).GT.TEST) THEN
          LOC=MININ
          DES(Z )=2
        END IF
        IF(MINPI.NE.0) THEN
          LOC=MINPI
          DES(Z )=3
        END IF
500    END IF
        WRITE(6,*) '1001 HAVE FOUND LOC REWINDING 7'
        WRITE(6,*) '***** LOC=',LOC
        THE OPTIMUM RUN LOCATION HAS BEEN CHOSEN, THE FILE CONTAINING THE
        GRID IS REWOUND AND THE OPTIMUM RUN LOCATION ADDED TO THE ORIGINAL
        DATA FILE AND STORED FOR LATER OUTPUT. THE READ STATEMENT FOR FILE
        7 MUST MATCH THAT IN THE LOOP 1900. THE OPERATING VARIABLES ARE
        ALSO SCALED AFTER BEING STORED.
        REWIND 7
        DO 2001 I=1,LOC
          READ(7,*) X1(NPTS),X2(NPTS)
2001    CONTINUE
          X1M(Z)=X1(NPTS)
          X2M(Z)=X2(NPTS)
          X3M(Z)=X3(NPTS)
          X4M(Z)=X4(NPTS)
          X5M(Z)=X5(NPTS)
          X6M(Z)=X6(NPTS)
          X7M(Z)=X7(NPTS)
          X1(NPTS)=X1(NPTS)*XF(1)
          X2(NPTS)=X2(NPTS)*XF(1)
          X3(NPTS)=X3(NPTS)*XF(1)
          X4(NPTS)=X4(NPTS)*XF(1)
          X5(NPTS)=X5(NPTS)*XF(1)
          X6(NPTS)=X6(NPTS)*XF(1)
          X7(NPTS)=X7(NPTS)*XF(1)
          JOB=00000
          WRITE(6,*) 'ABOUT TO CALL BATES TO GET PEPR'
          CALL BATES(PARAM,VAR,NITS,NPTS,NP,LUNOUT,JOB,BIAS,IFAIL,
+             A,DERIVS,VARC,QRAUX,WK1,WK2,JPVT,C1,C2,DIREC,DIRET,
+             STORE,K,NOCON)
          CALL DOD(NP,NPTS,RVAR,PARAM,IFAIL,WK1,DET,ITX,ITXI,DRIVS,
+DRIVT,T,WK,COFAC,IFLAG)
          SS(K)=0.0
          SA(K)=0.0
          DO 2100 J=1,NP
            SS(K)=(BIAS(J)/PARAM(J)*100)**2+SS(K)
            SA(K)=ABS(BIAS(J)/PARAM(J))*100+SA(K)
            BIS(K,J)=BIAS(J)/PARAM(J)*100.0
2100    CONTINUE
          WRITE(6,*) 'PEPR VOLPR CALCULATED',C1,C2,DET
          SSP(Z )=SS(K)
          SAP(Z )=SA(K)
          DOPTH(Z)=DET

```

## APPENDIX E. FORTRAN CODE FOR NONLINEAR REGRESSION

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      INCH(Z)=C1
      PECH(Z)=C2
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   THE SUBROUTINE GGNML IS USED TO GENERATE A N(0,1) NUMBER WHICH
C   IS USED TO GENERATE THE STOCHASTIC TERM OF THE SIMULATED EXPERIMEN
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      CALL GGNML(DSEED,1,RR)
      CALL GGNML(DSEED,1,RR)
      RNN(Z)=RR
      RER(Z)=SQRT(RVAR)*RR
      ITASK=0
      IFAIL=0
      CALL EVAL(PARAM,NPTS,ITASK,G,IFAIL,NPTS)
      YHT(Z)=G(1)
      IF(IDESGN.EQ.6) THEN
        YHTE(Z)=YHT(Z)
      ELSE
        YHTE(Z)=YHT(Z)+RER(Z)
      END IF
      Y(NPTS)=YHTE(Z)
      NSERC=NSERC-1
      IF(FLOAT(NSERC).GT.-0.5) THEN
        WRITE(6,*) 'GOING TO 100'
        GO TO 100
      ELSE
        WRITE(6,*) 'ENDING'
      END IF
2000 CONTINUE
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   PRINTING OUT SUMMARY OF SEARCH AND SIM
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      WRITE(6,1) TITLES
      DO 2200 I=1,Z
2200  WRITE(6,2) I,X1M(I),X2M(I),X3M(I),X4M(I),X5M(I),X6M(I),X7M(I)
      WRITE(6,11)
      DO 2201 I=1,Z
2201  WRITE(6,2) I,YHT(I),RNN(I),RER(I),YHTE(I),VARM(I)
      WRITE(6,33)
      WRITE(6,3) (I,I=1,NP)
      DO 2300 J=0,Z
2300  WRITE(6,4) J,(PARM(J,II),STDER(J,II),II=1,NP),VARM(J)
      WRITE(6,5)
      DO 2500 J=0,Z
        K=NPT -NP+J
        S(J)=0.5/SQRT(P(K))
        WRITE(LUNOUT,6) J,DES(J),PECH(J),PECOB(J),
+       PECOB(J)*SQRT(VARO/VARM(J)),INCH(J),INCOB(J),
+       INCOB(J)*SQRT(VARO/VARM(J)),S(J),
+       DOPTH(J),DETM(J),DETM(J)*(VARO/VARM(J))*NP,VARM(J)
2500 CONTINUE
      WRITE(6,70)

```

```

      WRITE(6,72) (I,I=1,NP)
      WRITE(6,*) '
      DO 2600 J=0,Z
        I=J-1
2600    WRITE(6,71) J,SSO(J),SSP(J),(BISM(J,K),K=1,NP)
      STOP
1      FORMAT(//1H ,2X,A80)
11     FORMAT(//1H ,2X,'RUN#',11X,'YPR',9X,'RNR',13X,'BER',9X,'YSIM',11X,
+ 'VAR',/)

2      FORMAT(1H ,3X,I3,5X,7(2X,G12.5))
33     FORMAT(//1H , 'RUN#')
3      FORMAT(1H+,3X,4(6X,'PAR',I1,6X,'2SIGMA'))
4      FORMAT(1H ,1X,I2,2X,9(1X,G10.4))
88     FORMAT(//1H , 'RUN#',4X,'PAR4',6X,'2SIGMA',6X,'PAR5',6X,'2SIGMA',
+ 6X,'PAR6',6X,'2SIGMA',8X,'VAR',/)
89     FORMAT(1H ,1X,I2,2X,6(1X,G10.4),1X,G12.6)
5      FORMAT(//1H , 'RUN#',1X,'DC',4X,'PEPR',6X,'PEOB',6X,'PESCL',6X,
+ 'INPR',8X,'INOB',7X,'INSCL',4X,'TEST',8X,
+ 'VOLPR',6X,'VOLOB',6X,'VOLSCL',6X,'VAR',/)
6      FORMAT(1H ,1X,I2,2X,I1,11(1X,G10.4))
7C     FORMAT(//1H ,1X,'RUE',5X,'SSO',9X,'SSP',3X)
71     FORMAT(1H ,1X,I2,8(1X,G11.4))
72     FORMAT('+',31X,4('BIAS',I1,7X))
62     FORMAT(F6.2)
9      FORMAT(//1H , 'THIS IS SIM FOR O-XYLENE OXIDATION RUN #',I2)
10     FORMAT(//1H ,6X,'O-XYLENE OXIDATION , MODEL FORM NO',//1H ,3X,
+ 'POINT #',3X,'O-XYLENE',4X,'OXYGEN',4X,'RATE',7X,'N',5X,'TEMP',/,
+ 16X,'*E4',10X,'*E4',5X,'*E8',15X,'C',/)
20     FORMAT(F7.5,F7.5,F9.7)
25     FORMAT(//1H , 'THE VARIANCE IS :',E16.6,/)
30     FORMAT(1H ,4X,I2,8X,F4.2,8X,F5.1,3X,F5.2,5X,F4.2,4X,F5.1)
31     FORMAT(//1H , 'DIR ',6(2X,E13.6))
40     FORMAT(//1H ,10X,'PARAMETER NO. ',I4)
15     FORMAT(D8.6)
      END

C
      SUBROUTINE ACCEL(A,DERIVS,RINV,ALPHA,TEMPV,JPVT,NPTS,NP)
C
      INTEGER JPVT(1),NPTS,NP,I,J,K,L,IMIN1,JJ,JPLUS1
      REAL A(NPTS,NP,1),DERIVS(NPTS,1),RINV(NP,1),ALPHA(1),
+ TEMPV(1),ACCUM,GAMMA,ZERO,ONE
      DATA ZERO/0.0EO/,ONE/1.0EO/
      DO 100 I=1,NP
      DO 200 J=1,I
      DO 300 K=1,NP
      ACCUM=ZERO
      DO 400 L=K,NPTS
      ACCUM=ACCUM+DERIVS(L,K)*A(L,I,J)
400    CONTINUE
      GAMMA=ACCUM/(ALPHA(K)*DERIVS(K,K))
      DO 500 L=K,NPTS
      A(L,I,J)=A(L,I,J)+GAMMA*DERIVS(L,K)
500    CONTINUE
300    CONTINUE

```

# APPENDIX E. FORTRAN CODE FOR NONLINEAR REGRESSION

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```

      DO 600 K=1,NPTS
        A(K,J,I)=A(K,I,J)
600  CONTINUE
200  CONTINUE
100  CONTINUE
C
C
      DO 700 I=1,NP
        DO 800 J=1,NP
          TEMPV(J)=ZERO
800  CONTINUE
          TEMPV(I)=ONE/ALPHA(I)
          IMIN1=I-1
          IF(IMIN1.LT.1) GO TO 1111
          DO 900 JJ=1,IMIN1
            J=IMIN1-JJ+1
            JPLUS1=J+1
            ACCUM=ZERO
            DO 1000 K=JPLUS1,NP
              ACCUM=ACCUM+DERIVS(J,K)*TEMPV(K)
1000  CONTINUE
              TEMPV(J)=-ACCUM/ALPHA(J)
900  CONTINUE
1111  CONTINUE
          DO 1100 J=1,NP
            K=JPVT(J)
            RINV(K,I)=TEMPV(J)
1100  CONTINUE
700  CONTINUE
C
C
      DO 1200 I=1,NPTS
        DO 1300 J=1,NP
          DO 1400 K=1,NP
            ACCUM=ZERO
            DO 1500 L=1,NP
              ACCUM=ACCUM+A(I,J,L)*RINV(L,K)
1500  CONTINUE
              DERIVS(J,K)=ACCUM
1400  CONTINUE
1300  CONTINUE
          DO 1600 J=1,NP
            DO 1700 K=1,J
              ACCUM=ZERO
              DO 1800 L=1,NP
                ACCUM=ACCUM+RINV(L,J)*DERIVS(L,K)
1800  CONTINUE
              A(I,J,K)=ACCUM
              A(I,K,J)=ACCUM
1700  CONTINUE
1600  CONTINUE
1200  CONTINUE
      RETURN
      END

```

```

      SUBROUTINE ARRAYS(A,DERIVS,STRAD,NPTS,NP,LUNOUT,JOB)
C
      INTEGER NPTS,NP,JOB,LUNOUT,I,J,K,MOD
      REAL A(NPTS,NP,1),DERIVS(NPTS,1),STRAD
      LOGICAL PRND1,PRND2
      PRND1=JOB/10000.NE.0
      PRND2=MOD(JOB,10000)/1000.NE.0
      IF((.NOT.PRND1).AND.(.NOT.PRND2)) GO TO 1111
      WRITE(LUNOUT,10) STRAD
1111 CONTINUE
      IF(.NOT.PRND1) GO TO 2222
      WRITE(LUNOUT,20)
      DO 100 I=1,NPTS
      WRITE(LUNOUT,30) I,(DERIVS(I,J),J=1,NP)
100 CONTINUE
2222 CONTINUE
      IF(.NOT.PRND2) GO TO 3333
      WRITE(LUNOUT,40)
      DO 200 I=1,NP
      WRITE(LUNOUT,50) I
      DO 300 J=1,NP
      WRITE(LUNOUT,60) (A(I,J,K),K=1,NP)
300 CONTINUE
200 CONTINUE
3333 CONTINUE
      RETURN
10  FORMAT(////,1H ,10X,'STANDARD RADIUS =',E13.6)
20  FORMAT(////,1H ,10X,'FIRST ORDER PARTIAL DERIVATIVES,
+ (STANDARDIZED)',//1H , 'DATA POINT')
30  FORMAT(1H ,I10,8E12.5/(1H ,20X,8E12.5))
40  FORMAT(////1H ,10X,'SECOND ORDER PARTIAL DERIVATIVES,
+ (STANDARDIZED)',//1H , 'DATA POINT')
50  FORMAT(1H ,I6)
60  FORMAT(1H ,10X,8E12.5/(1H ,10X,8E12.5))
      END
C
      SUBROUTINE BATES(PARAM,VAR,NITS,NPTS,NP,LUNOUT,JOB,BIAS,
+ IFAIL,A,DERIVS,RINV,QRAUX,WK1,WK2,JPVT,C1,C2,DIREC,DIRET,
+ STORE,KK,NOCON)
C
      INTEGER JPVT(1),NITS,NPTS,NP,LUNOUT,JOB,IFAIL,I,J,K,NW,M,ITASK,
+ DIRET,DIRO,II,KK,NOCON,NOIN,NOPE
      REAL PARAM(1),A(NPTS,NP,1),DERIVS(NPTS,1),RINV(NP,1),QRAUX(1),
+ BIAS(1),WK1(1),WK2(1),VAR,STRAD,TEMP,C1,C2,W,ZERO,SQRT,FLOAT,
+ DIREC(NP),STORE(1000,2,NP+1),MMAX1,MMAX2
      DATA ZERO/0.0E0/
      IFAIL=0
      IF(VAR.LE.ZERO.OR.NP.LE.0) GO TO 2222
      STRAD=SQRT(VAR*FLOAT(NP))
      DO 100 I=1,NPTS
      ITASK=1
      CALL EVAL(PARAM,I,ITASK,WK1,IFAIL,NPTS)
      IF(IFAIL.NE.0) GO TO 4444

```

```

      DO 200 J=1,NP
      DERIVS(I,J)=WK1(J)/STRAD
200  CONTINUE
      ITASK=2
      CALL EVAL(PARAM,I,ITASK,WK1,IFAIL,NPTS)
      IF(IFAIL.NE.0) GO TO 4444
      NW=0
      DO 300 J=1,NP
      DO 400 K=1,J
      NW=NW+1
      W=WK1(NW)/STRAD
      A(I,J,K)=W
      IF(J.NE.K) A(I,K,J)=W
400  CONTINUE
300  CONTINUE
100  CONTINUE
      CALL ARRAYS(A,DERIVS,STRAD,NPTS,NP,LOGOUT,JOB)
      DO 700 I=1,NP
      JPVT(I)=0
700  CONTINUE
      CALL SQRDC(DERIVS,NPTS,NPTS,NP,QRAUX,JPVT,WK1,1)
      DO 500 I=1,NP
      IF(QRAUX(I).EQ.ZERO.OR.DERIVS(I,I).EQ.ZERO) GO TO 3333
      TEMP=QRAUX(I)
      QRAUX(I)=DERIVS(I,I)
      DERIVS(I,I)=TEMP
      DO 600 J=I,NPTS
      DERIVS(J,I)=-DERIVS(J,I)*QRAUX(I)
600  CONTINUE
500  CONTINUE
      CALL ACCEL(A,DERIVS,RINV,QRAUX,WK1,JPVT,NPTS,NP)
      CALL BOX(A,RINV,BIAS,WK1,NPTS,NP)
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C  THE LOOP 1112 IS USED TO EVALUATE THE CURVATURES WITH THE NP NORMAL
C  VECTORS AS STARTING VALUES FOR DIR, THE CONVERGED VALUES ARE STORED
C  IN STORE(#POINTS,IN OR PE,NP VALUES WITH NP AS THE MAX
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      M=NP+1
      MMAX1=0.0
      MMAX2=0.0
      NOIN=0
      NOPE=0
      NOCON=0
      IF(DIRET.EQ.1) WRITE(6,32)
      DO 1112 II=1,NP
      CALL CURVE(A,DERIVS,WK1,QRAUX,WK2,C1,M,NPTS,NITS,NPTS,NP,IFAIL,
+DIREC,II)
      IF(DIRET.EQ.1) WRITE(6,33) II,C1,(DIREC(I),I=1,NP)
      IF(IFAIL.EQ.0) GO TO 1111
      IFAIL=5
      NOIN=NOIN+1
      C1=0.0
1111 CONTINUE

```



```

      CALL CURVE(A,DERIVS,WK1,QRAUX,WK2,C2,1,NP,NITS,NPTS,NP,IFAIL,
+DIREC,II)
      IF(DIRET.EQ.1) WRITE(6,33) II,C2,(DIREC(I),I=1,NP)
      IF(IFAIL.EQ.6) THEN
        NOPE=NOPE+1
        WRITE(LUNOUT,30) NITS
        WRITE(6,12) DIRET,IFAIL,II,KK
        C2=0.0
      END IF
      STORE(KK,1,II)=C1
      STORE(KK,2,II)=C2
      IF(C1.GE.MMAX1) THEN
        MMAX1=C1
        STORE(KK,1,NP+1)=C1
      END IF
      IF(C2.GE.MMAX2) THEN
        MMAX2=C2
        STORE(KK,2,NP+1)=C2
      END IF
1112 CONTINUE
      IF(NOPE.EQ.NP.OR.NOIN.EQ.NP) NOCON=NP
      C1=STORE(KK,1,NP+1)
      C2=STORE(KK,2,NP+1)
      CALL WATTS(A,BIAS,PARAM,C1,C2,NPTS,NP,LUNOUT,JOB)
      RETURN
2222 CONTINUE
      IFAIL=3
      WRITE(LUNOUT,10)
      RETURN
3333 CONTINUE
      IFAIL=4
      WRITE(LUNOUT,20)
      RETURN
4444 CONTINUE
      IFAIL=8
      WRITE(LUNOUT,40)
      RETURN
10  FORMAT(//1H , '*** SUBROUTINE BATES INCORRECT STANDARD RADIUS',//)
12  FORMAT(/1H , 'DIRET',1X,I1,2X,'IFAIL',1X,I2,2X,'DIR',1X,I1,2X,'LOC'
+      ,1X,I3)
20  FORMAT(//1H , '*** SUBROUTINE BATES SINGULAR MATRIX',//)
30  FORMAT( /1H , '*** SUBROUTINE BATES CONVERGENCE NOT ACHIEVED ',
+'AFTER ', I4,2X,'ITERATIONS',/ )
31  FORMAT(/1H , 'DIR ',7(2X,E13.6))
32  FORMAT(/1H , 'ALL THE CONVERGED DIR VECTORS AND THE IN AN PE CURVAT
+URES',/)
33  FORMAT(1H , 'DIR',I1,1X,E13.6,1X,6(F9.7,1X))
40  FORMAT(//1H , '*** SUBROUTINE BATES USER-FLAGGED ERROR',
+'IN SOUBROUTINE EVAL',//)
      END

```

```

      SUBROUTINE BOX(A,RINV,BIAS,TEMPV,NPTS,NP)
C
      INTEGER NPTS,NP,I,J
      REAL A(NPTS,NP,1),RINV(NP,1),BIAS(1),TEMPV(1),ZERO,FLOAT
      DATA ZERO/0.0EO/
      DO 100 I=1,NP
      TEMPV(I)=ZERO
      DO 200 J=1,NP
      TEMPV(I)=TEMPV(I)+A(I,J,J)
200  CONTINUE
      TEMPV(I)=-TEMPV(I)/FLOAT(2*NP)
100  CONTINUE
      DO 300 I=1,NP
      BIAS(I)=ZERO
      DO 400 J=1,NP
      BIAS(I)=BIAS(I)+RINV(I,J)*TEMPV(J)
400  CONTINUE
300  CONTINUE
      RETURN
      END
C
      SUBROUTINE CNTEST(DIR,GRAD,COSA,SINA,THQA,NP,CNVGED)
C
      INTEGER NP,I
      REAL DIR(1),GRAD(1),COSA,SINA,THQA,EPS,PI,TEST,ABS,SIGN,ATAN2,
+      SGN,ZERO,ONE,TWO,PSF,SQRT
      LOGICAL CNVGED
      DATA EPS/1.0E-4/,PI/3.14159EO/,ZERO/0.0EO/,ONE/1.0EO/,
+      TWO/2.0EO/,PSF/7.5E-1/
      CNVGED=.FALSE.
      TEST=ONE-EPS
      IF(ABS(COSA).LE.TEST) GO TO 1111
      SGN=SIGN(ONE,COSA)
      DO 100 I=1,NP
      DIR(I)=SGN*GRAD(I)
100  CONTINUE
      CNVGED=.TRUE.
      RETURN
1111 CONTINUE
      SINA=SQRT(ONE-COSA**2)
      IF(SINA.NE.ONE) GO TO 2222
      THQA=PSF*PI/TWO
      RETURN
2222 CONTINUE
      IF(COSA.GE.ZERO) GO TO 3333
      THQA=PSF*(ATAN2(SINA,COSA)+PI)
      RETURN
3333 CONTINUE
      THQA=PSF*(ATAN2(SINA,COSA))
      RETURN
      END

```

```

      SUBROUTINE CURVE(A,TEMPML,DIR,GRAD,TEMPL,CMAX,IM,IN,NITS,NPTS,
      +               NP,IFAIL,DIREC,II)
C
      INTEGER IM,IN,NITS,NPTS,NP,IFAIL,I,J,K,ITER,NPMIN1,DIRO,II
      REAL A(NPTS,NP,1),TEMPML(NPTS,1),DIR(1),GRAD(1),TEMPL(1),FLOAT,
      +     CMAX,ACCUM,ALENG,SINA,COSA,SIN,COS,SQRT,THQA,C1,C2,ZERO,ONE,
      +DIREC(NP)
      LOGICAL CHVGED
      DATA ZERO/0.0EO/,ONE/1.0EO/
      NPMIN1=NP-1
      IF(NPMIN1.LT.1) GO TO 1111
      DO 400 I=1,NP
         DIR(I)=ZERO
400    CONTINUE
1111   CONTINUE
      DIR(II)=ONE
      ITER=1
2222   CONTINUE
      DO 500 I=IM,IN
         DO 600 J=1,NP
            ACCUM=ZERO
            DO 700 K=1,NP
               ACCUM=ACCUM+A(I,J,K)*DIR(K)
700    CONTINUE
            TEMPML(I,J)=ACCUM
600    CONTINUE
500    CONTINUE
      DO 800 I=IM,IN
         ACCUM=ZERO
         DO 900 J=1,NP
            ACCUM=ACCUM+TEMPML(I,J)*DIR(J)
800    CONTINUE
            TEMPL(I)=ACCUM
800    CONTINUE
      DO 1000 I=1,NP
         ACCUM=ZERO
         DO 1100 J=IM,IN
            ACCUM=ACCUM+TEMPML(J,I)*TEMPL(J)
1100   CONTINUE
            GRAD(I)=ACCUM
1000   CONTINUE
            ACCUM=ZERO
            DO 1200 I=1,NP
               ACCUM=ACCUM+GRAD(I)*GRAD(I)
1200   CONTINUE
            ALENG=SQRT(ACCUM)
            IF(ALENG.EQ.ZERO) GO TO 4444
            DO 1300 I=1,NP
               GRAD(I)=GRAD(I)/ALENG
1300   CONTINUE
            COSA=ZERO
            DO 1400 I=1,NP
               COSA=COSA+DIR(I)*GRAD(I)
1400   CONTINUE

```

```

      CALL CNTEST(DIR,GRAD,COSA,SINA,THQA,NP,CNVGED)
      IF(CNVGED) GO TO 4444
      ITER=ITER+1
      IF(ITER.LE.NITS) GO TO 3333
      IFAIL=6
      GO TO 4444
3333  CONTINUE
      C2=SIN(THQA)/SINA
      C1=COS(THQA)-C2*COSA
      DO 1500 I=1,NP
      DIR(I)=C1*DIR(I)+C2*GRAD(I)
1500  CONTINUE
      GO TO 2222
4444  CONTINUE
      DO 1234 Z=1,NP
      DIREC(Z)=DIR(Z)
1234  CONTINUE
      DO 1600 I=IM,IN
      DO 1700 J=1,NP
      ACCUM=ZERO
      DO 1800 K=1,NP
      ACCUM=ACCUM+A(I,J,K)*DIR(K)
1800  CONTINUE
      TEMPML(I,J)=ACCUM
1700  CONTINUE
1600  CONTINUE
      DO 1900 I=IM,IN
      ACCUM=ZERO
      DO 2000 J=1,NP
      ACCUM=ACCUM+TEMPML(I,J)*DIR(J)
2000  CONTINUE
      TEMPL(I)=ACCUM
1900  CONTINUE
      ACCUM=ZERO
      DO 2100 I=IM,IN
      ACCUM=ACCUM+TEMPL(I)*TEMPL(I)
2100  CONTINUE
      CMAX=SQRT(ACCUM)
      RETURN
      END

C
C   THIS SUBROUTINE CALLED DOD WILL CALL EVAL NPTS TIMES AND CONSTRUCT
C   NPTS*NP MATRIX OF FIRST DERIVATIVES CALLED DRIVS. THE TRANSPOSE
C   DRIVS IS STORED IN DRIVT(NP*NPTS). THEN ITX=DRIVT*DRIVS IS
C   CALCULATED. THE INVERSE OF ITX (SYMMETRIC) IS DETERMINED BY A
C   CHOLESKY DECOMPOSITION IN TWO STAGES, THE INTERMEDIATE BEING STORED
C   IN T(NP*NP). THE FINAL INVERSE IS IN ITXI. THE DETERMINANT OF ITXI
C   IS THEN DETERMINED.
C
      SUBROUTINE DOD(NP,NPTS,RVAR,PARAM,IFAIL,WK1,DET,ITX,ITXI,DRIVS,
+DRIVT,T,WK,COFAC,IFLAG)
      INTEGER I,K,J,ITASK,IFAIL,NP,NPTS,M
      REAL SN1,SN2,SM2,SM1,WK1(1),DRIVS(NPTS,NP),
+ITX(NP,NP),ITXI(NP,NP),T(NP,NP),DET,Q,S,U,PARAM(NP),RVAR,
+COFAC(NP-2),WK(NP,NP),ITXII(9,9),DRIVT(NP,NPTS),ITXN(6,6).

```

```

      *XTXIM(6,6),WKAREA(132),PROD(6,6),I(999,6),C(6,6),B(1)
      IFAIL=0
      DO 501 I=1,NPTS
        ITASK=1
        CALL EVAL(PARAM,I,ITASK,WK1,IFAIL,NPTS)
        DO 502 J=1,NP
          DRIVS(I,J)=0.0
          DRIVS(I,J)=WK1(J)
          I(I,J)=WK1(J)/(SQRT(RVAR*NP))
502      CONTINUE
501      CONTINUE
        DO 503 I=1,NPTS
          DO 504 J=1,NP
            DRIVT(J,I)=0.0
            DRIVT(J,I)=DRIVS(I,J)
504      CONTINUE
503      CONTINUE
        DO 1 I=1,NP
          DO 2 J=1,NP
            XTX(I,J)=0.0
            XTXI(I,J)=0.0
            T(I,J)=0.0
2          CONTINUE
1          CONTINUE
        DO 505 I=1,NP
          DO 506 J=1,NP
            DO 507 K=1,NPTS
              XTX(I,J)=XTX(I,J)+DRIVT(I,K)*DRIVS(K,J)
507      CONTINUE
506      CONTINUE
505      CONTINUE
        SM1=0.0
        SM2=0.0
        SM1=0.0
        SM2=0.0
        DO 111 I=1,NP
          DO 222 J=I,NP
            IF(I.NE.J) GO TO 370
            M=I-1
            DO 333 K=1,M
              SM1=SM1+T(K,I)**2
333      CONTINUE
            IF((XTX(I,J)-SM1).LT.0.000) THEN
              WRITE(6,*) 'ROOT OF NEG IN DOD A'
              IFLAG=1
              GO TO 233
            END IF
            T(I,J)=SQRT(XTX(I,J)-SM1)
            SM1=0.0
            GO TO 430
370      CONTINUE
            M=I-1
            DO 444 K=1,M
              SM2=SM2+T(K,I)*T(K,J)
444      CONTINUE

```

```

      IF(T(I,I).LE.1.0E-66.AND.T(I,I).GE.-1.0E-66) THEN
        IFLAG=1
        WRITE(6,*) 'DIVIDING BY ZERO'
        GO TO 233
      END IF
      T(I,J)=(XTX(I,J)-SM2)/T(I,I)
      T(J,I)=T(I,J)
      SM2=0.0
430    CONTINUE
222    CONTINUE
111    CONTINUE
      DO 555 J=NP,1,-1
        DO 666 I=J,1,-1
          IF(I.NE.J) GO TO 570
          M=1+I
          DO 777 K=M,NP
            SN1=SN1+T(I,K)*XTXI(I,K)
777    CONTINUE
            IF(T(I,I).LE.1.0E-66.AND.T(I,I).GE.-1.0E-66) THEN
              IFLAG=1
              WRITE(6,*) 'DIVIDING BY ZERO'
              GO TO 233
            END IF
            XTXI(I,I)=1.0/T(I,I)**2-SN1/T(I,I)
            SN1=0.0
            GO TO 640
570    CONTINUE
            M=1+I
            DO 888 K=M,NP
              SN2=SN2-T(I,K)*XTXI(K,J)
888    CONTINUE
              IF(T(I,I).LE.1.0E-66.AND.T(I,I).GE.-1.0E-66) THEN
                IFLAG=1
                WRITE(6,*) 'DIVIDING BY ZERO'
                GO TO 233
              END IF
              XTXI(I,J)=SN2/T(I,I)
              XTXI(J,I)=SN2/T(I,I)
              SN2=0.0
640    CONTINUE
666    CONTINUE
555    CONTINUE
      IF(DET.LT.0.000) THEN
        DET=9.855
        IFLAG=1
        WRITE(6,*) 'DET IS NEGATIVE'
        GO TO 233
      END IF
      CALL DTRMNT(NP,XTXI,DET,WK,COFAC,RVAR)
233    CONTINUE
      IF(IFLAG.EQ.1) THEN
        DO 234 I=1,NP
          WRITE(6,*) 'XTX AFTER DTRMNT',(XTX(I,J),J=1,NP)
234        DO 235 I=1,NP
          WRITE(6,*) 'XTXI AFTER DTRMNT',(XTXI(I,J),J=1,NP)
235

```

```

      END IF
      RETURN
      END
C
      SUBROUTINE DSPLAY(Y,VARC,PARAM,WK1,VAR,NPTS,NP,ND1,
+          LUNOUT,JOB,IFAIL)
C
      INTEGER JOB,MOD,LUNOUT,ND1,NP,I,J,NPTS,IFAIL,ITASK
      REAL Y(1),VARC(ND1,1),PARAM(1),WK1(1),VAR,SQRT,T,SE,YHAT,RES
      LOGICAL PRNTAB,PRNVCV,PRNCOR,PRNFIT
      PRNTAB=MOD(JOB,10000)/1000.NE.0
      PRNVCV=MOD(JOB,1000)/100.NE.0
      PRNCOR=MOD(JOB,100)/10.NE.0
      PRNFIT=MOD(JOB,10).NE.0
      IF(.NOT.PRNTAB) GO TO 1111
      WRITE(LUNOUT,10)
      DO 100 I=1,NP
      SE=SQRT(VARC(I,I))
      T=PARAM(I)/SE
      WRITE(LUNOUT,20) I,PARAM(I),SE,T
100  CONTINUE
1111 CONTINUE
      IF(.NOT.PRNVCV) GO TO 2222
      WRITE(LUNOUT,30)
      DO 200 I=1,NP
      WRITE(LUNOUT,40) I,(VARC(I,J),J=1,I)
200  CONTINUE
2222 CONTINUE
      IF(.NOT.PRNCOR) GO TO 3333
      WRITE(LUNOUT,50)
      DO 300 I=1,NP
      DO 400 J=1,I
      WK1(J)=VARC(I,J)/SQRT(VARC(I,I)*VARC(J,J))
400  CONTINUE
      WRITE(LUNOUT,60) I,(WK1(J),J=1,I)
300  CONTINUE
3333 CONTINUE
      IF(.NOT.PRNFIT) GO TO 4444
      WRITE(LUNOUT,70)
      DO 500 I=1,NPTS
      ITASK=0
      CALL EVAL(PARAM,I,ITASK,WK1,IFAIL,NPTS)
      IF(IFAIL.NE.0) RETURN
      YHAT=WK1(1)
      RES=Y(I)-YHAT
      WRITE(LUNOUT,80) I,Y(I),YHAT,RES
500  CONTINUE
4444 CONTINUE
      RETURN
10  FORMAT(/1H ,10X,'PARAMETER ESTIMATES AT CONVERGENCE',/1H ,
+ ' PARAMETER',4X,'ESTIMATE',11X,'SE',11X,'T')
20  FORMAT(1H ,15,4X,E12.6,1X,E12.6,2X,F10.2)
30  FORMAT(/1H ,10X,'PARAMETER VARIANCE-COVARIANCE MATRIX',/)
40  FORMAT(1H ,15,8(2X,E12.6)/(1H ,5X,8(2X,E12.6)))
50  FORMAT(/1H ,10X,'PARAMETER CORRELATIONS',/)

```

```

60  FORMAT(1H ,I5,8(2X,F12.6))/((1H ,5X,8(2X,F12.6)))
70  FORMAT(/1H ,11X,'UNIT',14X,'Y',9X,'FITTED',7X,'RESIDUAL')
80  FORMAT(1H ,I15,3E15.6)
    END
C
    SUBROUTINE DTRMNT(NP,XTXI,DET,WK,COFAC,RVAR)
C
    INTEGER NP,NPS,I,J,K,Z,M,P
    REAL XTXI(NP,NP),WK(NP,NP),COFAC(NP-2),DET,RVAR
    NPS=NP
    DO 11 I=1,NP
        DO 22 J=1,NP
            WK(I,J)=XTXI(I,J)*RVAR
22    CONTINUE
11    CONTINUE
        Z=1
33    CONTINUE
        IF(NPS.EQ.2) GO TO 44
        DO 1 K=NPS,2,-1
            DO 21 P=1,1
                FAC=WK(K,1)/WK(1,1)
                DO 2 J=1,NPS
                    WK(K,J)=WK(K,J)-FAC*WK(1,J)
2    CONTINUE
21    CONTINUE
1    CONTINUE
        COFAC(Z)=WK(1,1)
        Z=Z+1
        DO 3 J=2,NPS
            DO 4 K=2,NPS
                WK((J-1),(K-1))=WK(J,K)
4    CONTINUE
3    CONTINUE
        NPS=NPS-1
        GO TO 33
44    CONTINUE
        DET=WK(1,1)*WK(2,2)-WK(2,1)*WK(1,2)
        DO 5 J=1,NP-2
            DET=DET*COFAC(J)
5    CONTINUE
        RETURN
    END
C
C
    SUBROUTINE FREQNC(X,N,MEAN,VAR,LUNOUT)
C
    INTEGER N,LUNOUT,KOUNT,I
    REAL X(1),MEAN,VAR,SD,CATING,XX,CAT,AINT,SQRT
    DATA CATING/2.5E-1/
    SD=SQRT(VAR)
    KOUNT=0
    XX=(X(1)-MEAN)/SD
    CAT=AINT(XX/CATING)*CATING
    WRITE(LUNOUT,10)
    DO 100 I=1,N
        XX=(X(I)-MEAN)/SD

```



```

1111 CONTINUE
      IF(IX.LE.CAT) GO TO 2222
      IF(KOUNT.EQ.0) GO TO 3333
      WRITE(LUNOUT,20) CAT,KOUNT
      KOUNT=0
3333 CONTINUE
      CAT=CAT+CATING
      GO TO 1111
2222 CONTINUE
      KOUNT=KOUNT+1
100 CONTINUE
      WRITE(LUNOUT,20) CAT,KOUNT
      RETURN
10  FORMAT(///1H ,10X,'FREQUENCY TABLE',/)
20  FORMAT(1H ,10X,F10.2,I10)
      END

C
C   THIS IS AN EXAMPLE OF THE SUBROUTINE EVAL.
C   THIS IS FOR THE OXIDATION OF BENZENE WITH THE PARAMETERS IN THE
C   NUMERATOR DETERMINED INDIVIDUALLY
C
      SUBROUTINE EVAL(PARAM,I,ITASK,WK1,IFAIL,K)
C
      INTEGER I,ITASK,IFAIL,K,ON
      REAL PARAM(3),WK1(6),YVAL,B,X1,X2,X3,X4,X5,X6,X7
      COMMON X1(99),X2(99),X3(99),X4(99),X5(99),X6(99),X7(99)
      DATA ZERO/0.0E0/
      IFAIL=0
      IF(ITASK.NE.0) GO TO 1111
      WK1(1)=PARAM(1)*PARAM(2)*X1(I)*X2(I)/
      +(PARAM(1)*X1(I)+PARAM(2)*X2(I)*X3(I))
      RETURN
1111 CONTINUE
      IF(ITASK.NE.1) GO TO 2222
      YVAL=PARAM(1)*PARAM(2)*X1(I)*X2(I)/
      +(PARAM(1)*X1(I)+PARAM(2)*X2(I)*X3(I))
      B=PARAM(1)*X1(I)+PARAM(2)*X2(I)*X3(I)
      WK1(1)=YVAL/PARAM(1)-YVAL*X1(I)/B
      WK1(2)=YVAL/PARAM(2)-YVAL*X2(I)*X3(I)/B
      RETURN
2222 CONTINUE
      IF(ITASK.NE.2) GO TO 3333
      YVAL=PARAM(1)*PARAM(2)*X1(I)*X2(I)/
      +(PARAM(1)*X1(I)+PARAM(2)*X2(I)*X3(I))
      B=PARAM(1)*X1(I)+PARAM(2)*X2(I)*X3(I)
      WK1(1)=-2.0*X1(I)*YVAL/PARAM(1)/B+2.0*X1(I)**2*YVAL/B**2
      WK1(2)=YVAL/PARAM(1)/PARAM(2)-X3(I)*X1(I)*YVAL/PARAM(1)/B
      +-X2(I)*YVAL/PARAM(2)/B+2.0*X1(I)*X3(I)*X2(I)*YVAL/
      +B**2
      WK1(3)=-2.0*X2(I)*X3(I)*YVAL/PARAM(2)/B+2.0*(X3(I)-X2(I))**2*
      +YVAL/B**2
      RETURN
3333 CONTINUE
      IFAIL=1
      RETURN
      END

```

```

      SUBROUTINE GNRATE(PARAM,SD,NPTS,LUNOUT,Y,IFAIL,DSEED)
C
      DOUBLE PRECISION DSEED
      INTEGER NPTS,N,I,LUNOUT,ITASK,IFAIL
      REAL Y(1),PARAM(1),ERR(2),SD,W
      IFAIL=0
      N=0
1111  CONTINUE
      CALL NORMAL(ERR,DSEED)
      DO 100 I=1,2
      N=N+1
      IF(N.GT.NPTS) GO TO 2222
      ITASK=0
      CALL EVAL(PARAM,N,ITASK,W,IFAIL,NPTS)
      IF(IFAIL.NE.0) GO TO 3333
      Y(N)=W+ERR(I)*SD
100   CONTINUE
      GO TO 1111
2222  CONTINUE
      RETURN
3333  CONTINUE
      IFAIL=8
      WRITE(LUNOUT,10)
      RETURN
10   FORMAT(/1H , '*** SUBROUTINE GNRATE USER-FLAGGED ERROR ',
+ 'IN SUBROUTINE EVAL',/)
      END
C
      SUBROUTINE MOMENT(X,N,M1,VAR,G1,G2)
C
      INTEGER N,I
      REAL X(1),XX,XN,M1,M2,VAR,M3,M4,G1,G2,ZERO,ONE,THREE,FLOAT,
+   SQRT
      DATA ZERO/0.0E0/,ONE/1.0E0/,THREE/3.0E0/
      XN=FLOAT(N)
      M1=ZERO
      DO 100 I=1,N
      M1=M1+X(I)
100   CONTINUE
      M1=M1/XN
      M2=ZERO
      M3=ZERO
      M4=ZERO
      DO 200 I=1,N
      XX=X(I)-M1
      M2=M2+XX**2
      M3=M3+XX**3
      M4=M4+XX**4
200   CONTINUE
      M2=M2/XN
      M3=M3/XN
      M4=M4/XN
      VAR=M2*XN/(XN-ONE)
      G1=M3/(M2*SQRT(M2))
      G2=M4/(M2**2)-THREE

```

```

      RETURN
      END
C
      SUBROUTINE NORMAL(ERR,DSEED)
C
      REAL ERR(2),E1,E2
      DOUBLE PRECISION DSEED
      CALL GGNML(DSEED,1,E1)
      CALL GGNML(DSEED,1,E2)
      ERR(1)=E1
      ERR(2)=E2
      RETURN
      END
C
      SUBROUTINE SOLVE(Y,PARAM,ALPHA,NITS,NPTS,NP,ND1,LUNOUT,JOB,
+   VARC,RSS,IFAIL,DERIVS,QRAUX,JPVT,DIFF,WK1)
C
      INTEGER JPVT(1),IFAIL,NPTS,NP,NITS,ND1,LUNOUT,JOB,
+   I,J,K,L,ITER,ITASK
      REAL DERIVS(NPTS,1),VARC(ND1,1),Y(1),PARAM(1),DIFF(1),
+   WK1(1),QRAUX(1),DUM(1),COR(6),
+   ALPHA,RSS,RES,TEST,RESVAR,ACCUM,DENOM,ABS,FLOAT,ZERO,ONE
      LOGICAL CNVRGD,PRNPAR
      DATA ZERO/0.0EO/,ONE/1.0EO/
      IFAIL=0
      PRNPAR=JOB/10000.NE.0
      IF(.NOT.PRNPAR) GO TO 1111
      WRITE(LUNOUT,10) (I,I=1,NP)
      RSS=ZERO
      DO 100 I=1,NPTS
      ITASK=0
888  FORMAT (E12.6,3I8)
      CALL EVAL(PARAM,I,ITASK,WK1,IFAIL,NPTS)
      IF(IFAIL.NE.0) GO TO 6666
      RES=Y(I)-WK1(1)
      RSS=RSS+RES*RES
100  CONTINUE
      WRITE(LUNOUT,20) RSS,(PARAM(I),I=1,NP)
1111 CONTINUE
      ITER=1
2222 CONTINUE
      DO 200 I=1,NPTS
      ITASK=0
      CALL EVAL(PARAM,I,ITASK,WK1,IFAIL,NPTS)
      IF(IFAIL.NE.0) GO TO 6666
      DIFF(I)=Y(I)-WK1(1)
      ITASK=1
      CALL EVAL(PARAM,I,ITASK,WK1,IFAIL,NPTS)
      IF(IFAIL.NE.0) GO TO 6666
      DO 300 J=1,NP
      DERIVS(I,J)=WK1(J)
300  CONTINUE
200  CONTINUE
      DO 400 I=1,NP
      JPVT(I)=0

```

```

400  CONTINUE
      CALL SQDC(DERIVS,NPTS,NPTS,NP,QRAUX,JPVT,WK1,1)
      CALL SQSL(DERIVS,NPTS,NPTS,NP,QRAUX,DIFF,DUM,DIFF,WK1,DUM,DUM,
+ 100,IFAIL)
      IF(IFAIL.NE.0) GO TO 5555
      CNVRGD=.TRUE.
      DO 500 I=1,NP
        J=JPVT(I)
        PARAM(J)=PARAM(J)+WK1(I)
        IF(PARAM(J).GT.1.0E9.OR.PARAM(J).LT.-1.0E9) THEN
          IFAIL= 9
          RETURN
        END IF
        DENOM=PARAM(J)
        IF(DENOM.EQ.ZERO) DENOM=ONE
        TEST=WK1(I)/DENOM
        IF(ABS(TEST).GT.ALPHA) CNVRGD=.FALSE.
500  CONTINUE
      RSS=ZERO
      DO 600 I=1,NPTS
        ITASK=0
        CALL EVAL(PARAM,I,ITASK,WK1,IFAIL,NPTS)
        IF(IFAIL.NE.0) GO TO 6666
        RES=Y(I)-WK1(I)
        RSS=RSS+RES*RES
600  CONTINUE
      IF(.NOT.PRNPARG) GO TO 3333
      WRITE(LUNOUT,20) RSS,(PARAM(I),I=1,NP)
3333 CONTINUE
      ITER=ITER+1
      IF(ITER.GT.NITS) GO TO 4444
      IF(.NOT.CNVRGD) GO TO 2222
      IF(NPTS.EQ.NP) GO TO 7777
      CALL STRDI(DERIVS,NPTS,NP,DUM,011,IFAIL)
      IF(IFAIL.NE.0) GO TO 5555
      RESVAR=RSS/FLOAT(NPTS-NP)
      DO 700 I=1,NP
        DO 800 J=I,NP
          ACCUM=ZERO
          DO 900 K=J,NP
            ACCUM=ACCUM+DERIVS(I,K)*DERIVS(J,K)
900  CONTINUE
          ACCUM=ACCUM*RESVAR
          K=JPVT(I)
          L=JPVT(J)
          VARC(K,L)=ACCUM
          VARC(L,K)=ACCUM
800  CONTINUE
700  CONTINUE
      CALL DSPLAY(Y,VARC,PARAM,WK1,RESVAR,NPTS,NP,ND1,
+ LUNOUT,JOB,IFAIL)
      IF(IFAIL.NE.0) GO TO 6666
      RETURN
4444 CONTINUE
      WRITE(LUNOUT,30) NITS

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```

      IFAIL=1
      RETURN
5555 CONTINUE
      WRITE(LUNOUT,40)
      IFAIL=2
      RETURN
6666 CONTINUE
      WRITE(LUNOUT,50)
      IFAIL=8
      RETURN
7777 CONTINUE
      WRITE(LUNOUT,60)
      IFAIL=9
      RETURN
10  FORMAT(//1H ,13X,'PARAMETERS ESTIMATES',
+ /1H ,15X,'RSS',9(I13)/(1H ,13X,9(I13)))
20  FORMAT(1H ,5X,10(E13.6)/(1H ,13X,9(E13.6)))
22  FORMAT(1H ,5X,10(E13.6)/(1H ,13X,9(E13.6)))
22  FORMAT(1H ,5X,10(E13.6)/(1H ,13X,9(E13.6)))
30  FORMAT(//1H ,13X,'*** SUBROUTINE SOLVE CONVERGENCE NOT ',
+ 'ACHIEVED AFTER',2X,I10,2X,'ITERATIONS',//)
40  FORMAT(//1H ,13X,'*** SUBROUTINE SOLVE SINGULAR MATRIX',//)
50  FORMAT(//1H ,13X,'*** SUBROUTINE SOLVE USER FLAGGED ERROR',
+ ' IN SUBROUTINE EVAL',//)
60  FORMAT(//1H ,13X,'*** SUBROUTINE SOLVE RESIDUAL VARIANCE ZERO',//)
      END
C
      SUBROUTINE SORT(A,II,JJ)
C
      INTEGER IU(16),IL(16),I,II,J,JJ,IJ,K,M,L
      REAL A(1),T,TT
      M=1
      I=II
      J=JJ
5  IF(I.GE.J) GO TO 70
10  K=I
      IJ=(J+I)/2
      T=A(IJ)
      IF(A(I).LE.T) GO TO 20
      A(IJ)=A(I)
      A(I)=T
      T=A(IJ)
20  L=J
      IF(A(J).GE.T) GO TO 40
      A(IJ)=A(J)
      A(J)=T
      T=A(IJ)
      IF(A(I).LE.T) GO TO 40
      A(IJ)=A(I)
      A(I)=T
      T=A(IJ)
      GO TO 40
30  A(L)=A(K)
      A(K)=TT
40  L=L-1
      IF(A(L).GT.T) GO TO 40

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```

      TT=A(L)
50    K=K+1
      IF(A(K).LT.T) GO TO 50
      IF(K.LE.L) GO TO 30
      IF(L-I.LE.J-K) GO TO 60
      IL(M)=I
      IU(M)=L
      I=K
      M=M+1
      GO TO 80
60    IL(M)=K
      IU(M)=J
      J=L
      M=M+1
      GO TO 80
70    M=M-1
      IF(M.EQ.0) RETURN
      I=IL(M)
      J=IU(M)
80    IF(J-I.GE.11) GO TO 10
      IF(I.EQ.II) GO TO 5
      I=I-1
90    I=I+1
      IF(I.EQ.J) GO TO 70
      T=A(I+1)
      IF(A(I).LE.T) GO TO 90
      K=I
100   A(K+1)=A(K)
      K=K-1
      IF(T.LT.A(K)) GO TO 100
      A(K+1)=T
      GO TO 90
      END
C
      SUBROUTINE SUMRY(STMATE,NSIM,LUNOUT,JOB,IFAIL,PARAM,W,BIAS,
+XTXI,RVAR,JOB2,NP)
C
      INTEGER NSIM,LUNOUT,JOB,MOD,I,IFAIL,W,K,JOB2,NP
      REAL STMATE(1),MEAN,VAR,G1,G2,PARAM(1),BIAS(1),BIASS,PBIAS,BIASR,
+XTXI(NP,NP), TAVAR,STDER,ZZ,STDND,CHI2,PEVAR
      LOGICAL PRNVAL,PRNMOM,PRNFRQ
      PRNVAL=JOB/100.NE.0
      PRNMOM=MOD(JOB,100)/10.NE.0
      PRNFRQ=MOD(JOB,10).NE.0
      CALL SORT(STMATE,1,NSIM)
      IF(.NOT.PRNVAL) GO TO 1111
      WRITE(LUNOUT,10) (STMATE(I),I=1,NSIM)
1111 CONTINUE
      IF(NSIM.LE.1) GO TO 4444
      CALL MOMENT(STMATE,NSIM,MEAN,VAR,G1,G2)
      IF(.NOT.PRNMOM) GO TO 2222
      BIASS=MEAN-PARAM(W)
      PBIAS=BIASS/PARAM(W)*100.0
      BIASR=BIAS(W)/PARAM(W)*100.0
      TAVAR=XTXI(W,W)*RVAR

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        STDER=SQRT(TAVAR/LOAT(NSIM))
        STDND=BIASS/STDER
        CHI2=LOAT(NSIM-1)*VAR/TAVAR
        ZZ=SQRT(2.0*CHI2)-44.688
        PEVAR=(VAR-TAVAR)/TAVAR*100.0
        IF(JOB2.NE.1) GO TO 56
        WRITE(LUNOUT,31) PARAM(W)
        WRITE(LUNOUT,32) MEAN
        WRITE(LUNOUT,33) BIAS(W)
        WRITE(LUNOUT,34) BIASS
        WRITE(LUNOUT,35) BIASR
        WRITE(LUNOUT,36) PBIAS
        WRITE(LUNOUT,37) STDND
        WRITE(LUNOUT,38) TAVAR
        WRITE(LUNOUT,39) VAR
        WRITE(LUNOUT,41) PEVAR
        WRITE(LUNOUT,42)
        WRITE(LUNOUT,43)
        WRITE(LUNOUT,44) ZZ
        WRITE(LUNOUT,40) G1,G2
56      CONTINUE
2222    CONTINUE
        IF(.NOT.PRNFRQ) GO TO 3333
        CALL FREQNC(STMATE,NSIM,MEAN,VAR,LUNOUT)
3333    CONTINUE
        RETURN
C
4444    CONTINUE
        IFAIL=7
        WRITE(LUNOUT,50)
        RETURN
10      FORMAT(///1H ,10X,'ORDERED VALUES',/(1H ,10F12.6))
20      FORMAT(///1H ,10X,'MOMENTS OF DISTRIBUTION')
31      FORMAT(1H , 'THE PARAMETER ESTIMATE FROM REGRESSION IS:',E16.6)
32      FORMAT(1H , 'THE PARAMETER ESTIMATE FROM SIMULATION IS :',E16.6)
33      FORMAT(1H , 'THE ACTUAL BIAS AS DETRMINED BY BOX:',E16.6)
34      FORMAT(1H , 'THE BIAS FROM SIM IS GIVEN BY SIM-REG:',E16.6)
35      FORMAT(1H , '% BIAS AS DETERMINED BY BOX:',E16.6)
36      FORMAT(1H , '% BIAS AS DETERMINED BY SIM:',E16.6)
37      FORMAT(1H , 'THE SIM BIAS CORRESPONDS TOA STD.NORM.DEV OF:',E16.6)
38      FORMAT(1H , 'THE TRUE ASYMPTOTIC VARIANCE OF PARAMETER IS:',E16.6)
39      FORMAT(1H , 'THE PARAMETER VARIANCE FROM SIMULATION IS      ',E16.6)
41      FORMAT(1H , 'THE % EXCESS VARIANCE IS SIM-REGRESSION VAR :',F10.3)
42      FORMAT(1H , 'THE FOLLOWING STATISTIC IS COMPARED TO A STANDARD ')
43      FORMAT(1H , 'NORMAL DISTRIBUTION FOR SIM VAR SIGNIFICANTLY ')
44      FORMAT(1H , 'DIFFERENT FROM TRUE ASYMP VARIANCE :',F16.6)
40      FORMAT(//1H ,10X,'SKEWNESS COEFFICIENT',1X,F20.9,//1H ,
+10X,'EXCESS KURTOSIS',6X,F20.9)
50      FORMAT(//1H , '*** SUBROUTINE SUMRY TOO FEW DEGREES OF ',
+ 'FREEDOM',//)
        END

```

```

SUBROUTINE WATTS(A,BIAS,PARAM,C1,C2,NPTS,NP,LUNOUT,JOB)
C
  PRNC=MOD(JOB,10).NE.0
  INTEGER NPTS,NP,LUNOUT,JOB,MOD,I,J,K
  REAL A(NPTS,NP,1),BIAS(1),PARAM(1),C1,C2,PERCEN,ZERO,HUNDRD
  LOGICAL PRNC,PRNB,PRNA
  DATA ZERO/0.0E0/,HUNDRD/1.0E2/
  PRNC=MOD(JOB,10).NE.0
  PRNB=MOD(JOB,100)/10.NE.0
  PRNA=MOD(JOB,1000)/100.NE.0
  IF(.NOT.PRNA) GO TO 1111
  WRITE(LUNOUT,10)
  DO 200 I=1,NP
  WRITE(LUNOUT,20)
  DO 300 J=1,NP
  WRITE(LUNOUT,30) (A(I,J,K),K=1,NP)
300 CONTINUE
200 CONTINUE
1111 CONTINUE
  IF(.NOT.PRNB) GO TO 3333
  WRITE(LUNOUT,40)
  DO 400 I=1,NP
  IF(PARAM(I).EQ.ZERO) GO TO 2222
  PERCEN=BIAS(I)/PARAM(I)*HUNDRD
  WRITE(LUNOUT,50) I,PARAM(I),BIAS(I),PERCEN
  GO TO 400
2222 CONTINUE
  WRITE(LUNOUT,50) I,PARAM(I),BIAS(I)
400 CONTINUE
3333 CONTINUE
  IF(.NOT.PRNC) GO TO 4444
  WRITE(LUNOUT,60) C1,C2
4444 CONTINUE
  RETURN
10  FORMAT(/1H ,10X,'ACCELERATION ARRAY',
+ ' (PARAMETER EFFECTS PORTION)')
20  FORMAT(/1H )
30  FORMAT(1H ,10X,10F12.4)
40  FORMAT( /1H ,10X,'BOX S BIAS', //1H ,8X,'PARAMETER',2X,
+ 'LS ESTIMATE',08X,'BIAS',12X,'PERCENT BIAS',/)
50  FORMAT(1H ,8X,'PARAMETER',I2,2E16.8,F16.4)
60  FORMAT(/1H ,10X,'MAXIMUM CURVATURE MEASURES',//1H ,
+ 'INTRINSIC (IN)',11X,F12.4/1H , 'PARAMETER-EFFECTS (PE)',
+ 3X,F12.4)
  END

```



## Appendix F

# Fortran Code for Confidence Regions

The following exec is used to compile, define input and output files, and run the program TREG as a batch program. TREG is used to obtain points defining the boundary of the exact-shape confidence regions with significance at the  $\alpha \approx 0.05$  level and the linear approximate-shape confidence regions with significance at the  $\alpha = 0.05$  level. As with simulating experiments, it is suggested that TREG is run in batch mode. If only linear approximate confidence regions are required then interactive mode is acceptable as computations are demanding only for the exact-shape confidence regions. MDCPC is the user's identifier on the computing system (one using CMS); replace this with your own identifier.

```
&TRACE OFF
GLOBAL TYTLIB VLKMLIB VFORTLIB CMSLIB INSLDLIB LINPACK PLOTLIB
FORTVS TREG
FILE 5 DISK TY DATA(LRECL 80 BLKSIZE 80 RECFM F PERM
FILE 6 DISK TREG DATA(LRECL 80 BLKSIZE 80 RECFM F PERM
FILE 6 DISK TREG RESULT A (PERM RECFM F LRECL 132
FILE 12 DISK AREG1 DATAA A (PERM RECFM F LRECL 132
FILE 13 DISK AREG2 DATAA A (PERM RECFM F LRECL 132
FILE 14 DISK AREG3 DATAA A (PERM RECFM F LRECL 132
FILE 15 DISK AREG4 DATAA A (PERM RECFM F LRECL 132
FILE 16 DISK AREG5 DATAA A (PERM RECFM F LRECL 132
FILE 17 DISK AREG6 DATAA A (PERM RECFM F LRECL 132
FILE 27 DISK EREG1 DATAA A (PERM RECFM F LRECL 132
FILE 28 DISK EREG2 DATAA A (PERM RECFM F LRECL 132
FILE 29 DISK EREG3 DATAA A (PERM RECFM F LRECL 132
FILE 30 DISK EREG4 DATAA A (PERM RECFM F LRECL 132
FILE 31 DISK EREG5 DATAA A (PERM RECFM F LRECL 132
```

```
FILE 32 DISK EREG6  DATAA A (PERM RECFM F LRECL 132
LOAD REGJUU (CLEAR START
EXEC SENDFILE AREG1 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE AREG2 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE AREG3 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE AREG4 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE AREG5 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE AREG6 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE EREG1 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE EREG2 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE EREG3 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE EREG4 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE EREG5 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE EREG6 DATAA TO MDCPC AT UOTTAWA
EXEC SENDFILE TREG RESULT TO MDCPC AT UOTTAWA
&EXIT
```

The following file is read by TREG and supplies the number of observations, number of parameters etc.

```
INPUT DATA FOR PROGRAM FINDING CONFIDENCE REGIONS
TAN, PROPYLENE OXIDATION, MODEL FORM NO, 350 C
12      (I) NUMBER OF OBSERVATIONS
2       (I) NUMBER OF PARAMETERS
0.0004  LEAST SQUARES ESTIMATE FOR PARAMETER 1
10.000  LEAST SQUARES ESTIMATE FOR PARAMETER 2
5       (I) NUMBER OF VARIABLES
1.000   SCALING FACTOR FOR VARIABLE 1
1.000   SCALING FACTOR FOR VARIABLE 2
1.000   SCALING FACTOR FOR VARIABLE 3
1.000   SCALING FACTOR FOR VARIABLE 4
1.000   SCALING FACTOR FOR VARIABLE 5
1.000   SCALING FACTOR FOR THE RESPONSE
```

The following is the program TREG used to obtain the exact shape and linear approximate shape confidence regions presented in Section 4.2. The linear approximate confidence regions are determined in the subroutine MIKE, written by Michael Margerum (1987). The points on the ellipse are found by solving Eq. 2.18. When a model has more than two parameters, conditional linear approximate confidence regions are found by fixing all but two of the parameters. Eq. 2.18 can be solved by fixing one of the two parameters, this results in a quadratic equation which can be solved for the other parameter. Some user interaction is required to determine the step size used, typically 100 to 300 points usually produce an acceptable plot of the confidence regions, however this should always be verified.

The exact shape confidence regions are determined in the subroutine XXACTN. Again some user interaction is required to determine a suitable step size so that a reasonable number of points defining the region are obtained. The number of points required for an acceptable plot may vary greatly. When the degree of nonlinearity is low (both reduced curvatures  $< 4$ ) 100 to 300 points may be sufficient. When higher degrees of nonlinearity are encountered the exact shape confidence region may be elongated, necessitating a larger number of points, again plots should be used to verify that the region is well determined. Problems may be encountered when determining the exact shape confidence regions for the pre-exponential constant and activation energies in the original form of the Arrhenius equation. These confidence regions often result in extremely elongated crescents (see Section 2.5). Unless the search for points along this elongated portion are stopped at some pre-determined

value ( say 100 times the value of the parameter itself) run time errors are usually obtained or a ridiculously high number of points are generated. This problem has been addressed by putting such an upper limit on the parameters place and also by increasing the step size used after predetermined numbers of points on the contour have been found (see comments in the program itself).

Finding an acceptable step size is further complicated when there are more than 2 model parameters, a suitable step size for one parameter may be too coarse for another parameter. A strategy to minimize wasted effort and computing time would be to use a coarse step size for all parameter pairs. Then based on the number of points obtained for each pair, reset the step size for each pair of parameters individually. Again, the user is forewarned, you will run into problems using this program, particularly with models involving exponentials!

```

CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC

```

```

C
C      WRITTEN BY MAURO DAL-CIN, 1987
C

```

```

C      THIS PROGRAM IS USED TO GENERATE THE LINEAR APPROXIMATE CONFIDENCE
C      REGIONS AND THE EXACT SHAPE CONFIDENCE REGIONS FOR A NONLINEAR
C      MODEL. OUTPUT IS IN THE FORM OF SEPERATE FILES FOR EACH TYPE OF
C      REGION FOR EACH PAIR OF PARAMETERS. APPROXIMATE AND EXACT REGIONS
C      ARE WRITTEN TO FILES CALLED, RESPECTIVELY:

```

```

C
C      AREG1  DATAA  A      EREG1  DATAA  A
C      AREG2  DATAA  A      EREG2  DATAA  A
C      AREG3  DATAA  A      EREG3  DATAA  A
C      AREG4  DATAA  A      EREG4  DATAA  A

```

```

C
C      ETC.

```

```

C      SOME POINTS TO NOTE WHEN RUNNING THIS PROGRAM:

```

```

C      WHEN THE EXACT SHAPE REGION IS CALCULATED RUNNING TIME
C      MAY BE EXCESSIVE, PARTICULARLY IF THE STEP SIZE IN
C      SUBROUTINE XYACTN IS SMALL, THE REGION IS LARGE OR SEVERAL
C      REGIONS ARE BEING FOUND. AS SUCH RUNNING THIS PROGRAM
C      VIA BATCH IS ADVISED.

```

```

C      WHEN DEALING WITH A MODEL WITH 3 OR MORE PARAMETERS, A
C      GIVEN STEP SIZE MAY NOT BE APPROPRIATE FOR ALL THE PAIRS
C      OF PARAMETERS. IN SUCH CASES IN IS ADVISABLE THAT A SMALLER
C      STEP SIZE BE USED FOR ALL THE REGIONS, THOSE WITH TOO FEW
C      POINTS CAN BE REDETERMINED INDIVIDUALLY WITH AN APPROPRIATE
C      STEP SIZE.

```

```

C      A SUITABLE NUMBER OF POINTS FOR EACH REGION CAN RUN ANYWHERE
C      FROM 100 TO 300. IF MORE POINTS ARE KEPT PROBLEMS CAN BE
C      ENCOUNTERED DUE TO EXCESSIVE SPACE UTILIZATION ON ONE'S DISC

```

```

C      THE MODEL FORM AND ITS 1ST DERIVATIVES ARE REQUIRED AND ARE FOUND
C      IN THE SUBROUTINE EVAL, WHICH IS THE SAME AS THAT USED IN THE
C      NONLINEAR REGRESSION PROGRAM.

```

```

C      THE INPUT REQUIRED IS:

```

```

C      THE NUMBER OF DATA POINTS
C      THE NUMBER OF PARAMETERS
C      THE LEAST SQUARES ESTIMATES
C      THE NUMBER OF VARIABLES
C      SCALING FACTORS FOR THE VARIABLES
C      SCALING FACTORS FOR THE RESPONSE
C      THE DATA ITSELF (OPERATING VARIABLES AND
C      RESPONSE)

```

```

C      THE SUBROUTINE ELIPS CALLS THE SUBROUTINE MIKE (WRITTEN BY MICHEAL
C      MARGERUM 1987) AND CALCULATES THE LINEAR APPROXIMATE CONFIDENCE
C      REGIONS FOR EACH PAIR OF PARAMETER ESTIMATES. IN CASES WHERE THE

```

```

C      MODEL HAS MORE THAN 2 PARAMETERS THE CONFIDENCE REGIONS ARE
C      CONDITIONAL ON THE OTHER PARAMETERS BEING FIXED AT THEIR LEAST
C      SQUARES ESTIMATES.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      INTEGER NPTS,NP,I,J,NS,Z,W,P,JOBS,OUT,D,
+         OUT2,SET
      REAL Y(99),PARAM(3),PAR(3),DP(3),WK1(6),XF(7),
+         RSS,VAR,FLOAT,SQRT,DET,XTX(3,3),STP,CONV(9999,2),
+         ITXI(3,3),DRIVS(999,3),DRIVT(3,999),RVAR,F(199),G,T(3,3)
      CHARACTER*132 TITLE1
      COMMON X1(99),X2(99),X3(99),X4(99),X5(99),X6(99),X7(99)
      READ(8,1) TITLE1
      READ(8,1) TITLE1
      READ(8,*) NPTS
      WRITE(6,*) '          THE NUMBER OF OBSERVATIONS',NPTS
      READ(8,*) NP
      WRITE(6,*) '          THE NUMBER OF PARAMETERS ',NP
      DO 100 I=1,NP
        READ(8,*) PARAM(I)
        WRITE(6,*) 'LEAST SQUARES ESTIMATE OF PARAMETER',I,'=',NPTS
100    CONTINUE
      READ(8,*) NVAR
      WRITE(6,*) '          NUMBER OF VARIABLES = ',NVAR
      DO 200 I=1,NVAR
        READ(8,*) XF(I)
        WRITE(6,*) '          SCALING FACTOR FOR VARIABLE',I,'=',XF(I)
200    CONTINUE
      READ(8,*) YF
      WRITE(6,*) '          SCALING FACTOR FOR THE RESPONSE = ',YF
      PR=0.95
      D1=NP
      D2=1
      DO 300 I=1,99
        CALL MDFI(PR,D1,D2,FSTAT,IER)
        F(I)=FSTAT
        D2=D2+1
300    CONTINUE
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C      THE READ STATE MUST BE MODIFIED TO MATCH THE PARTICULAR DATA FILE
C      BEING USED, BY ADDING OR DELETING OR CHANGING THE ORDER OF
C      OCCURENCE OF THE ARRAYS.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      WRITE(8,1) TITLE1
1      FORMAT(A132)
      DO 400 I=1,NPTS
        READ(6,*) X1(I),X2(I),X3(I),X4(I),X5(I),X6(I),X7(I),Y(I)
        WRITE(6,*) X1(I),X2(I),X3(I),X4(I),X5(I),X6(I),X7(I),Y(I)
        Y(I)=Y(I)*YF
        X1(I)=XF(1)*X1(I)
        X2(I)=XF(2)*X2(I)
        X3(I)=XF(3)*X3(I)
        X4(I)=XF(4)*X3(I)

```

[illegible]

C THIS SUBROUTINE CALLED DOD WILL CALL EVAL NPTS TIMES AND CONSTRUCT  
 C AN NPTS\*NP MATRIX OF FIRST DERIVATIVES CALLED DRIVS. THE TRANSPOSE  
 C OF DRIVS IS STORED IN DRIVT(NP\*NPTS). THEN ITX=DRIVT\*DRIVS IS  
 C CALCULATED. THE INVERSE OF ITX (SYMMETRIC) IS DETERMINED BY A  
 C CHOLESKY DECOMPOSITION IN TWO STAGES, THE INTERMEDIATE BEING STORED  
 C IN T(NP\*NP). THE FINAL INVERSE IS IN ITXI.

```

C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
SUBROUTINE DOD(NP,NPTS,PARAM,IFAIL,WK1,DET,ITX,ITXI,DRIVS,DRIVT,T)
  INTEGER I,K,J,ITASK,IFAIL,NP,NPTS,M
  REAL SN1,SN2,SM2,SM1,WK1(1),DRIVS(999,NP),DRIVT(NP,999),
+ITXI(NP,NP),ITX(NP,NP),T(NP,NP),DET,S,Q,U,PARAM(NP)
  IFAIL=0
  DO 501 I=1,NPTS
    ITASK=1
    CALL EVAL(PARAM,I,ITASK,WK1,IFAIL)
    DO 502 J=1,NP
      DRIVS(I,J)=0.0
      DRIVS(I,J)=WK1(J)
502    CONTINUE
501  CONTINUE
    DO 503 I=1,NPTS
      DO 504 J=1,NP
        DRIVT(J,I)=0.0
        DRIVT(J,I)=DRIVS(I,J)
504    CONTINUE
503  CONTINUE
    DO 1 I=1,NP
      DO 2 J=1,NP
        ITX(I,J)=0.0
        ITXI(I,J)=0.0
        T(I,J)=0.0
2      CONTINUE
1    CONTINUE
    DO 505 I=1,NP
      DO 506 J=1,NP
        DO 507 K=1,NPTS
          ITX(I,J)=ITX(I,J)+DRIVT(I,K)*DRIVS(K,J)
507    CONTINUE
506  CONTINUE
505  CONTINUE
    SN1=0.0
    SN2=0.0
    SM1=0.0
    SM2=0.0
    DO 111 I=1,NP
      DO 222 J=I,NP
        IF(I.NE.J) GO TO 370
        M=I-1
        DO 333 K=1,M
          SM1=SM1+T(K,I)**2
333    CONTINUE
        T(I,J)=SQRT(ITX(I,J)-SM1)
        SM1=0.0
        GO TO 430

```



```

370      CONTINUE  

       M=I-1  

        DO 444 K=1,M  

          SM2=SM2+T(K,I)*T(K,J)  

444     CONTINUE  

         T(I,J)=(XTX(I,J)-SM2)/T(I,I)  

         T(J,I)=T(I,J)  

         SM2=0.0  

430     CONTINUE  

222    CONTINUE  

111   CONTINUE  

DO 555 J=NP,1,-1  

  DO 666 I=J,1,-1  

    IF(I.NE.J) GO TO 570  

    M=1+I  

    DO 777 K=M,NP  

      SN1=SN1+T(I,K)*XTXI(I,K)  

777   CONTINUE  

      XTXI(I,I)=1.0/T(I,I)**2-SN1/T(I,I)  

      SN1=0.0  

      GO TO 840  

570   CONTINUE  

      M=1+I  

      DO 888 K=M,NP  

        SN2=SN2-T(I,K)*XTXI(K,J)  

888   CONTINUE  

        XTXI(I,J)=SN2/T(I,I)  

        XTJI(J,I)=SN2/T(I,I)  

        SN2=0.0  

640   CONTINUE  

666   CONTINUE  

555   CONTINUE  

      RETURN  

      END  

CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC  

C      IN SUBROUTINE MIKE THE POINTS ON THE ELIPSE ARE FOUND BY CHOOSING  

C      A VALUE FOR THE 'U' PARAMETER. THE 'W' PARAMETER CAN BE FOUND BY  

C      SOLVING A QUADRATIC EXPRESSION. THE U PARAMETER IS INCREMENTED  

C      UNTIL THE RADICAL IN THE QUADRATIC EXPRESSION IS ZERO OR NEGATIVE.  

C      THIS CORRESPONDS TO THE UPPER LIMIT OF THE U PARAMTER.  

C      AT THIS STAGE THE W PARAMETER IS INCREMENTED BY REGULAR INTERVALS  

C      AND THE QUADRATIC EXPRESSION SOLVED FOR THE U PARAMETER UNTIL THE  

C      RADICAL AGAIN BECOMES ZERO OR NEGATIVE. THIS CORRESPONDS TO THE  

C      LOWER LIMIT OF THE W PARAMETER. THE U PARAMETER IS THEN  

C      INCREMENTED BY REGULAR INTERVALS, SOLVING FOR THE W PARAMETER  

C      UNTIL THE LEAST SQUARES ESTIMATE OF PARAMETER U IS REACHED.  

C  

CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC  

SUBROUTINE MIKE(K,PARAM,NP,I,J,XTX,OUT)  

IMPLICIT REAL (A-Z)  

INTEGER NDATA,IER,IND,NPTS,OUT,NP,I,J,III  

DIMENSION UC(999),WC(999),PARAM(NP),XTX(NP,NP)  

U=PARAM(I)  

W=PARAM(J)
```

```

      X11=XTX(I,I)
      X22=XTX(J,J)
      X12=XTX(I,J)
      AW=X22
      AU=X11
      DELTAU=PARAM(I)/499.
      DELTAW=PARAM(J)/499.
      UC(1)=U
      WRITE(6,*) '
      WRITE(6,*) 'IN SUBROUTINE MIKE'
      WRITE(6,*) 'U=',U,'W=',W
      WRITE(6,*) 'AW=',AW,'AU=',AU
      WRITE(6,*) 'X11=',X11,'X22=',X22,'X12=',X12
      WRITE(6,*) 'K=',K
      WRITE(6,*) '
      DO 56 III=1,NP
         WRITE(6,1239) (XTX(III,JJ),JJ=1,NP)
56      CONTINUE
      WRITE(6,*) '
      NPTS=1
1239  FORMAT(1X,6(2X,E11.4))
      IND=0
      SGN=1.
1005  BW=2.*((UC(NPTS)-U)*X12-W*X22)
      CW=W**2*X22-2.*W*(UC(NPTS)-U)*X12+(UC(NPTS)-U)**2*X11-K
      IF (BW**2-4.*AW*CW.GE.0.) GO TO 1006
1004  WC(NPTS)=WC(NPTS-1)-SGN*DELTAW
      BU=2.*((WC(NPTS)-W)*X12-U*X11)
      CU=U**2*X11-2.*U*(WC(NPTS)-W)*X12+(WC(NPTS)-W)**2*X22-K
      IF (BU**2-4.*AU*CU.LT.0.) GO TO 1003
      UC(NPTS)=(-BU+SGN*SQRT(BU**2-4.*AU*CU))/2./AU
      IF (IND.GE.2.AND.UC(NPTS).GE.U) GO TO 1008
      NPTS=NPTS+1
      IF(NPTS.GT.999) GO TO 1008
      GO TO 1004
1003  IND=IND+1
      SGN=-1.*SGN
      GO TO 1007
1006  WC(NPTS)=(-BW+SGN*SQRT(BW**2-4.*AW*CW))/2./AW
C      WRITE(6,*) 'CALC WC 1006',WC(NPTS),NPTS
      IF (IND.GE.2.AND.UC(NPTS).GE.U) GO TO 1008
      NPTS=NPTS+1
      IF(NPTS.GT.999) GO TO 1008
1007  UC(NPTS)=UC(NPTS-1)+SGN*DELTAW
      GO TO 1005
1008  CONTINUE
      IF(N.GT.999) WRITE(OUT,*) ' N GT 999'
         WRITE(OUT,10) I
         WRITE(OUT,10) J
      WRITE(OUT,*) NPTS,'THE NUMBER OF POINTS FOUND IN SUB MIKE'
      WRITE(6,*) NPTS,'THE NUMBER OF POINTS FOUND IN SUB MIKE'
      DO 101 II=1,NPTS
         WRITE (OUT, '(2G15.6,I4)') UC(II),WC(II),NPTS
101  CONTINUE
10  FORMAT(1H , 'THETA ',I1)

```

```

RETURN
END
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
C   IN SUBROUTINE XIACTN THE EXACT CONFIDENCE REGION IS DETERMINED
C   BY CHOOSING A VALUE FOR THE 'U' PARAMETER AND SOLVING FOR THE
C   'W' PARAMETER. THE U PARAMETER IS INCREMENTED BY STPI. THE
C   CORRESPONDING Y PARAMETER IS THEN FOUND BY SIMPLY INCREASING W BY
C   STPJ UNTIL THE EDGE OF THE CONFIDENCE REGION IS FOUND. THE U
C   PARAMETER IS INCREMENTED AND THE W PARAMETER IS FOUND BY
C   INCREMENTING PARAMETER W STARTING AT THE LAST RECORDED VALUE.
C   THIS WILL USUALLY RESULT IN A SOLUTION WITHIN 5 ITERATIONS.
C   IF THE SOLUTION DIVERGES AFTER 2 ITERATIONS THE INCREMENTATION OF
C   U PROCEEDS IN THE OPPOSITE DIRECTION UNTIL A SOLUTION IS OBTAINED.
C   IF CONVERGENCE IS NOT OBTAINED THEN THE ENDPOINT OF THE CONFIDENCE
C   REGION HAS BEEN REACHED AND PARAMETER U INCREMENTED IN THE OPPOSITE
C   DIRECTION.
C
C   NOTE THAT THE PARAMETER I ULTIMATELY CONTROLS THE NUMBER OF POINTS
C   GENERATED. PARAMETER J HOWEVER DETERMINES THE RESOLUTION OF THE
C   CONTOUR ALONG WITH PARAMETER I. AS SUCH STPJ IS USUALLY SET SMALLER
C   THAN STPI.
C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
SUBROUTINE XIACTN(NP,NPTS,PARAM,F,Y,OUT2,RSS,PAR,SET)
INTEGER I,J,K,N,NP,NPTS,OUT2,C1,C2,SET
REAL PARAM(NP),PAR(NP),EXREG(9999,2),F(150),RHS,RES,RSS,SSR,
+   FLOAT,STPI,STPJ,WK1(1),Y(NPTS),WKAREA(200)
C
C   CALCULATE THE SUM OF SQUARES OF THE RESIDUALS
C
      IFAIL=0
      WRITE(6,434)
434  FORMAT(1H ,/,9X,'I',7X,'Y REAL',7X,'THAT',7X,'RES',7X,'SSR',/)
      RSS=0.0
      DO 4 I=1,NPTS
        ITASK=0
        CALL EVAL(PARAM,I,ITASK,WK1,IFAIL)
        RES=Y(I)-WK1(1)
        RSS=RSS+RES*RES
        WRITE(6,*) I,Y(I),WK1(1),RES,RSS
4      CONTINUE
      WRITE(6,*) 'SET IN XIACTN',SET
      IF(SET.EQ.1) RETURN
C
C   CALC THE RHS OF THE GOVERNING EQUATION THE LHS IS SSR
C
      K=NPTS-NP
      RHS=RSS*(1.0+FLOAT(NP)/FLOAT(K)*F(K))
      WRITE(6,*) ' THE RHS OF GOVERNING EQUATION',RHS
      OUT2=27
      DO 1 I=1,NP-1
        IT=1+I
        DO 2 J=IT,NP
          ID=99

```

```

      TOL=1.0005
C
      K=NPTS-NP
      RHS=RSS*(1.0+FLOAT(NP)/FLOAT(K)*F(K))
      WRITE(6,*) ' THE RHS OF GOVERNING EQUATION',RHS
      OUT2=27
      DO 1 I=1,1
        IT=1+I
        DO 2 J=3,3
          ID=99
          TOL=1.0005
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
      C      EXTRAI IS USED TO RESET STPI. STPI MAY HAVE BEEN CHANGED IF
      C      AN EXCESSIVELY LARGE NUMBER OF POINTS HAVE BEEN FOUND ON THE CONTOU
      C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
          STPI=PARAM(I)/399.
          EXTRAI=499.
          STPJ=PARAM(J)/599.
          N=1
          DO 121 K=1,NP
            PAR(K)=PARAM(K)
121      CONTINUE
          PAR(I)=PARAM(I)
          PAR(J)=PARAM(J)
          SIGNJ=1.
          IEND=0
          IT=0
          IDCHK=0
          GO TO 101
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C
      C      THE FOLLOWING IF STATEMENTS ARE USED TO STOP THE SEARCH WHEN AN
      C      EXCESSIVE NUMBER OF POINTS ARE GENERATED. PRIOR TO THIS, THE STPI
      C      IS INCREASED WHEN PRESET NUMBERS OF POINTS ARE FOUND. THIS IS USED
      C      TO REDUCE THE TIME REQUIRED TO FIND THE ENDPOINTS OF THE EXACT
      C      SHAPE CONFIDENCE REGION.
      C
      C      THESE LIMITS/STEP CHANGES SHOULD BE CHANGED TO SUIT THE CURRENT
      C      CASE
      C
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
      99  PAR(I)=PAR(I)+STPI
          IF(N.GT.500.OR.PAR(I).GT.99*PARAM(I)) GOTO 200
          IF(N.GT.99) STPI=PARAM(I)*2.
          IF(N.GT.149) STPI=PARAM(I)*5.
          IF(N.GT.199) STPI=PARAM(I)*10.
          IF(N.GT.249) STPI=PARAM(I)*100.
          PAR(J)=XIREG(N-1,2)
          SIGNJ=0.
100  PAR(J)=PAR(J)+STPJ*SIGNJ
101  CONTINUE
C      CALC SSR
          SSR=0.0

```

```

      DO 5 K=1,NPTS
        ITASK=0
        IFAIL=0
        CALL EVAL(PAR,K,ITASK,WK1,IFAIL)
        RES=Y(K)-WK1(1)
        SSR=SSR+RES*RES
5      CONTINUE
      WRITE(6,*) 'JUST CALC D   SSR',PAR(I),PAR(J),SSR,SIGNJ
      IF(SSR.LE.RHS*TOL) THEN
        ICHECK=1
        TPI=PAR(I)
        TPJ=PAR(J)
        IF(SIGNJ.LT.-0.5) THEN
          EXREG(N,1)=PAR(I)
          EXREG(N,2)=PAR(J)+STPJ
          N=N+1
          IEND=0
          ICHECK=0
          IT=0
          GO TO 99
        END IF
        SIGNJ=1.
        GO TO 100
      ELSE
        IF(SSR.GT.RHS.AND.ICHECK.EQ.1) THEN
          EXREG(N,1)=PAR(I)
          EXREG(N,2)=PAR(J)
          N=N+1
          IEND=0
          ICHECK=0
          IT=0
          GO TO 99
        END IF
        IF(SSR.GT.RHS.AND.ICHECK.EQ.0) THEN
          IEND=IEND+1
          IF(IEND.EQ.1) TTJ=PAR(J)
          WKAREA(IEND)=SSR
          IF(IT.EQ.1) GO TO 150
          IF(IEND.GE.2) THEN
            GRAD=WKAREA(IEND)-WKAREA(IEND-1)
            IF(GRAD.GT.0.0) THEN
              IT=1
              IEND=1
              PAR(J)=TTJ
              GO TO 100
            ELSE
              SIGNJ=1.
              GO TO 100
            END IF
          ELSE
            SIGNJ=-1.
            GO TO 100
          END IF
        ELSE
          SIGNJ=1.
          GO TO 100
        END IF
      CONTINUE
      SIGNJ=-1.
150

```

```

        IF(IEND.GE.3) THEN
            GRAD=WKAREA(IEND)-WKAREA(IEND-1)
            IF(GRAD.GT.0.0.OR.IEND.GT.ID) THEN
                IEND=0
                GO TO 200
            ELSE
                GO TO 100
            END IF
        ELSE
            GO TO 100
        END IF
    END IF
END IF
200 CONTINUE
NN=1
SIGNJ=0.
IEND=0
IT=0
GO TO 202
201 IF(NN.GT.99) STPI=PARAM(I)*2.
    IF(NN.GT.149) STPI=PARAM(I)*5.
    IF(NN.GT.199) STPI=PARAM(I)*10.
    IF(NN.GT.249) STPI=PARAM(I)*100.
    IF(PAR(I).LE.2.*PARAM(I)) STPI=PARAM(I)/EXTRAI
    PAR(I)=PAR(I)-STPI
    IT=0
    PAR(J)=EXREG(N-1,2)
    SIGNJ=0.
202 PAR(J)=PAR(J)+STPJ*SIGNJ
C    CALC SSR
        SSR=0.0
        DO 555 K=1,NPTS
            ITASK=0
            IFAIL=0
            CALL EVAL(PAR,K,ITASK,WK1,IFAIL)
            RES=Y(K)-WK1(1)
            SSR=SSR+RES*RES
555    CONTINUE
        IF(SSR.LE.RHS*TOL) THEN
            ICHECK=1
            TPI=PAR(I)
            TPJ=PAR(J)
            IF(SIGNJ.GT.0.5) THEN
                EXREG(N,1)=PAR(I)
                EXREG(N,2)=PAR(J)-STPJ
                N=N+1
                NN=NN+1
                IEND=0
                IT=0
                ICHECK=0
                GO TO 201
            END IF
            SIGNJ=-1.
            GO TO 202
        ELSE

```

```

      IF(SSR.GT.RHS.AND.ICHECK.EQ.1) THEN
        EXREG(N,1)=PAR(I)
        EXREG(N,2)=PAR(J)
        N=N+1
        NN=NN+1
        IEND=0
        IT=0
        ICHECK=0
        GO TO 201
      END IF
      IF(SSR.GT.RHS.AND.ICHECK.EQ.0) THEN
        IEND=IEND+1
        IF(IEND.EQ.1) TTJ=PAR(J)
        WKAREA(IEND)=SSR
        IF(IT.EQ.1) GO TO 250
        IF(IEND.GE.2) THEN
          GRAD=WKAREA(IEND)-WKAREA(IEND-1)
          IF(GRAD.GT.0.0) THEN
            TGRAD=GRAD/WKAREA(IEND)
            IF(TGRAD.LT.1.E-6) THEN
              IF(PAR(I).GT.PARAM(I)) GO TO 201
              WRITE(6,*) 'TGRAD TO 300'
              WRITE(OUT2,*) 'TGRAD TO 300'
              GO TO 300
            END IF
            IT=1
            IEND=1
            PAR(J)=TTJ
            GO TO 202
          ELSE
            SIGNJ=1.
            GO TO 202
          END IF
        ELSE
          SIGNJ=1.
          GO TO 202
        END IF
      ELSE
        SIGNJ=-1.
        IF(IEND.GE.3) THEN
          GRAD=WKAREA(IEND)-WKAREA(IEND-1)
          IF(GRAD.GT.0.0.OR.IEND.GT.ID) THEN
            IEND=0
            IF(PAR(I).GT.PARAM(I)) GO TO 201
            GO TO 300
          ELSE
            GO TO 202
          END IF
        ELSE
          GO TO 202
        END IF
      END IF
      GO TO 202
    END IF
  END IF
  CONTINUE
  IT=0

```

```

      IEND=0
      NN=1
      PAR(I)=TPI
      PAR(J)=TPJ
      SIGNJ=0.
      STPI=PARAM(I)/EXTRA1
      GO TO 302
301  PAR(I)=PAR(I)+STPI
      IT=0
      IF(PAR(I).GT.PARAM(I)) GO TO 400
      PAR(J)=EXREG(N-1,2)
302  PAR(J)=PAR(J)-STPJ*SIGNJ
C    CALC SSR
      SSR=0.0
      DO 55 K=1,NPTS
        ITASK=0
        IFAIL=0
        CALL EVAL(PAR,K,ITASK,WK1,IFAIL)
        RES=Y(K)-WK1(1)
        SSR=SSR+RES*RES
55   CONTINUE
      WRITE(6,*) 'JUST CALC D   SSR',PAR(I),PAR(J),SSR,SIGNJ
      IF(SSR.LE.RHS*TOL) THEN
        ICHECK=1
        TPI=PAR(I)
        TPJ=PAR(J)
        IF(SIGNJ.GT.0.5) THEN
          EXREG(N,1)=PAR(I)
          EXREG(N,2)=PAR(J)+STPJ
          N=N+1
          IEND=0
          NN=NN+1
          IT=0
          ICHECK=0
          SIGNJ=0.
          GO TO 301
        END IF
        SIGNJ=-1.
        GO TO 302
      ELSE
        IF(SSR.GT.RHS.AND.ICHECK.EQ.1) THEN
          EXREG(N,1)=PAR(I)
          EXREG(N,2)=PAR(J)
          N=N+1
          NN=NN+1
          IEND=0
          IT=0
          ICHECK=0
          GO TO 301
        END IF
        IF(SSR.GT.RHS.AND.ICHECK.EQ.0) THEN
          IEND=IEND+1
          IF(IEND.EQ.1) TTJ=PAR(J)
          WKARRA(IEND)=SSR
          IF(IT.EQ.1) GO TO 350

```



```

      IF(IEND.GE.2) THEN
        GRAD=WKAREA(IEND)-WKAREA(IEND-1)
        IF(GRAD.GT.0.0) THEN
          IT=1
          IEND=1
          PAR(J)=TTJ
          GO TO 302
        ELSE
          SIGNJ=-1.
          GO TO 302
        END IF
      ELSE
        SIGNJ=-1.
        GO TO 302
      END IF
    END IF
    CONTINUE
350    SIGNJ=1.
        IF(IEND.GE.3) THEN
          GRAD=WKAREA(IEND)-WKAREA(IEND-1)
          IF(GRAD.GT.0.0.OR.IEND.GT.ID) THEN
            IEND=0
            GO TO 400
          ELSE
            GO TO 302
          END IF
        ELSE
          GO TO 302
        END IF
      END IF
    END IF
400  CONTINUE
      N=N-1
      WRITE(OUT2,*) N,'IS THE NUMBER OF POINTS'
      WRITE(6,*) N,'IS THE NUMBER OF POINTS'
      WRITE(OUT2,*) PARAM(I),PARAM(J),'THETA I AND J RESPECTIVELY'
      + ,I,J
      DO 11 K=1,N
        WRITE(OUT2,*) EXREG(K,1),EXREG(K,2)
11    CONTINUE
      OUT2=OUT2+1
1212 CONTINUE
2    CONTINUE
1    CONTINUE
      RETURN
      END

C
C THIS IS EVAL FOR PROPYLENE OXIDATION, MODEL FORM M0, HOCK SENG TAM
C WITH % CONVERSION AS THE DEPENDENT VARIABLE.
      SUBROUTINE EVAL(PARAM,I,ITASK,WK1,IFAIL,K)
      INTEGER I,ITASK,IFAIL,K,ON
      REAL PARAM(2),WK1(3),YVAL,B,X1,X2,TRE,X3,SQRT,X4,X5,X6,X7
      COMMON X1(99),X2(99),X3(99),X4(99),X5(99),X6(99),X7(99)
      IFAIL=0
      IF(ITASK.NE.0) GO TO 1111
      WK1(1)=60.5/X4(I)*PARAM(1)*PARAM(2)*SQRT(X2(I))/

```

```
      +(X3(I)*X1(I)*PARAM(1)+PARAM(2)*SQRT(X2(I)))
      RETURN
1111 CONTINUE
      IF(ITASK.NE.1) GO TO 2222
      YVAL=60.5/Y4(I)*PARAM(1)*PARAM(2)*SQRT(X2(I))/
      +(X3(I)*X1(I)*PARAM(1)+PARAM(2)*SQRT(X2(I)))
      B=(X3(I)*X1(I)*PARAM(1)+PARAM(2)*SQRT(X2(I)))
      WK1(1)=YVAL/PARAM(1)-X3(I)*X1(I)*YVAL/B
      WK1(2)=YVAL/PARAM(2)-SQRT(X2(I))*YVAL/B
      RETURN
2222 CONTINUE
      IF(ITASK.NE.2) GO TO 3333
      YVAL=60.5/Y4(I)*PARAM(1)*PARAM(2)*SQRT(X2(I))/
      +(X3(I)*X1(I)*PARAM(1)+PARAM(2)*SQRT(X2(I)))
      B=(X3(I)*X1(I)*PARAM(1)+PARAM(2)*SQRT(X2(I)))
      WK1(1)=-2.0*X3(I)*X1(I)*YVAL/PARAM(1)/B+2.0*(X3(I)*X1(I))**2*
      +YVAL/B**2
      WK1(2)=YVAL/PARAM(1)/PARAM(2)-X3(I)*X1(I)*YVAL/PARAM(2)/B
      +-SQRT(X2(I))*YVAL/PARAM(1)/B+2.0*X1(I)*X3(I)*SQRT(X2(I))*YVAL/
      +B**2
      WK1(3)=-2.0*SQRT(X2(I))*YVAL/PARAM(2)/B+2.0*X2(I)*YVAL/B**2
      RETURN
3333 CONTINUE
      IFAIL=1
      RETURN
      END
```